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BILTEN ZA TRANSFUZIOLOGIJU
Institut za transfuziju krvi Srbije
11000 Beograd, Svetog Save 39
Tel: + 381 11 308 53 46, Fax: + 381 11 245 83 28
e-mail: biltenzatransfuziologiju@yahoo.com

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Dear coleagues, dear friends,

It is our pleasure to welcome you to the 7th Transfusion Medicine Congress of Serbia accredited as international and Second International Congress of TMAS. Although, the Covid-19 pandemic has changed a lot off in our lives in the past two years, professional meetings are still a platform for the exchange of knowledge and experiences, where we must all continue to acquire new knowledges and share our experiences.

The Congress traditionally brings together the biggest experts in the field of transfusion and regenerative medicine from Serbia, the region and the world. Congress is dedicated to contemporary topics that are important for the promotion and motivation of voluntary blood donors, treatment of the sick and injured, especially in the field of transplantation medicine and safe transfusion, as a priority of modern clinical transfusion therapy. It will be will be discussed about place and role of immunohaematology in the molecular era of blood group studies, modern apheresis procedures and the role of transfusion medicine specialists in tissue and organ transplants.

We expect a large number of technicians working in the transfusion medicine service in the country and region.

Lectures and abstracts were printed in the journal Bulletin for Transfusiology (Lectures and Abstract Book).

We invite you to contribute to the quality of the congress with your active participation and to contribute to the development and affirmation of new transfusion ideas in the time ahead through lectures, poster presentations and discussions.

We wish you welcome to the 7th Transfusion Medicine Congress of Serbia and the accredited as international and Second International Congress of TMAS.

Prim. dr sc. med. Ana Antić
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Naučni saradnik prim dr sc. med.
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Poštovane koleginice i kolege, dragi prijatelji,

Zadovoljstvo nam je da Vam poželimo dobrodošlicu na 7. Kongres transfuziologa Srbije i 2. Međunarodni Kongres u organizaciji Udruženja transfuziologa Srbije i Sekcije za transfuziologiju Srpskog lekarskog društva. Iako je Covid-19 pandemija mnogo toga promenila u našim životima u protekle dve godine, stručni sastanci predstavljaju i dalje platformu razmene znanja i iskustava, gde svi mi moramo nastaviti da stičemo nova znanja i razmenjujemo svoja iskustva.

Kongres već tradicionalno okuplja najveće stručnjake iz oblasti transfuzione i regenerativne medicine iz Srbije, regiona i sveta. Ovaj veliki skup je posvećen savremenim temama koje su od važnosti za promociju i motivaciju dobrovoljnih davalaca krvi, lečenje bolesnih i povređenih, posebno u domenu transplatacione medicine i bezbedne transfuzije, kao prioriteta savremene kliničke transfuzione terapije. Govoriće se o mestu i ulozi imunohematologije u molekularnoj eri izučavanja krvnih grupa, savremenim afereznim procedurama i ulozi specijalista transfuzione medicine u transplantacijama tkiva i organa.

I na ovom Kongresu očekujemo veliki broj tehničara koji rade u službi za transfuzionu medicinu u zemlji i regionu.

Predavanja i sažeci su štampani u časopisu Bilten za transfuziologiju (Zbornik predavanja i sažetaka).

Pozivamo Vas da svojim aktivnim učešćem doprinesete kvalitetu kongresa i da kroz predavanja, poster prezentacije i diskusije svi zajedno doprinesemo razvoju i afirmaciji novih transfuzioloških ideja u vremenu koje je pred nama.

Dobrodošli na 7. Kongres transfuziologa Srbije i 2. Međunarodni kongres transfuziologa u organizaciji UTS.

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PLENARY LECTURES

HOTEL CROWNE PLAZA
Beograd, Srbija / Belgrade, Serbia
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HEMOSTATIC ABNORMALITIES IN COVID-19: THE ROLE OF LABORATORY IN THE DIAGNOSIS, UNDERSTANDING UNDERLYING MECHANISM AND TREATMENT ADJUSTMENT

Jovan P. Antovic[1,2]
[1]Coagulation, Karolinska Institutet,
Department of Molecular Medicine and Surgery, Stockholm, Sweden
[2]Karolinska University Hospital,
Clinical Chemistry, Stockholm, Sweden

Abstract

A significant amount of published data (more than 5000 publications with keywords thrombosis and COVID-19 are available on PubMed in late August 2022), but also our own experience at Karolinska University Hospital point toward hemostatic abnormalities in a significant number of severe patients with COVID-19. The majority of those patients experienced persistent hypercoagulation with massively increased D-dimer and fibrinogen. As a consequence, clinical thrombotic events, including venous thromboembolism were common in COVID-19 patients and we postulated that increased anticoagulant prophylaxis may be beneficial for hospitalized patients. After implementation of such an approach decreased D-dimer levels, increased platelet counts, and significant risk reductions for death and thrombosis were observed in the retrospective cohort study performed at Karolinska University Hospital. It seems that the lungs are most severely injured by the virus and that the potential underlying mechanism is crosstalk between inflammation/complement and hemostasis. Despite significant research within the field, the potential mechanism of the pathological effect of SARS-Cov2 spike protein is not fully understood but it seems that its binding to both endothelial cells and platelets can induce hemostatic abnormalities. This mechanism may be one plausible explanation for the development of seldom complications of DNA-vector, but also mRNA SARS-Cov2 vaccines presented as thrombocytopenia with bleeding and/or thrombosis.

Keywords: COVID-19, hemostasis, D-dimer

Disseminated Intravascular Coagulation (DIC) or COVID-19 Associated Coagulopathy (CAC) - What Happened?

Already in February 2020, in the early days of the SARS- CoV-2, the first reports about coagulation abnormalities were available on PubMed [1]. At that time, it was reported that 71.4% of non-survivors with COVID-19 infection met the criteria for disseminated intravascular coagulation (DIC), while in one meta-analysis the conclusion that almost 3/4 of COVID-19 patients fulfilled laboratory criteria for DIC was drawn [2]. Increased D-dimer and its importance for disease prognosis have been observed in many studies [for review see 3]. Our experience at Karolinska University Hospital was the same: massive increase of D-dimer (even values > 35 mg/L in some patients, compared to normal values of <0.5 mg/L). Increased D-dimer levels in the first week in the hospital were significantly associated with death and thrombosis [4].

However, DIC is commonly associated with bleeding, after initial micro thrombosis in different organs, due to the consumption of coagulation factors, fibrinogen, and platelets. Very soon, it was observed that the COVID-19 coagulation abnormalities pattern is different. In the majority of patients, prothrombin time (PT) was normal, while fibrinogen was even increased [5]. In our laboratory, we have observed fibrinogen levels approximately 1.5-2 times above the limit of the reference range during the intra-hospital course (longer than 2 weeks in the majority of cases), in both survivors and non-survivors. Although thrombocytopenia was described in some cohorts it does not seem to be a common finding. In our cohort initially, a normal platelet count was observed. Additionally, we observed that if platelet count increased more than 35x109/L per day, the mortality and thrombotic risk decreased [4].

Therefore, it seems that the term COVID-19 associated coagulopathy (CAC) [6] which includes both intra- and extravascular coagulopathy may better reflect hemostatic abnormalities which contribute to the morbidity and mortality of patients infected with SARS- CoV-2.

Clinical Manifestations of Hemostatic Abnormalities

Clinical manifestations of coagulation abnormalities were very different. The majority of patients had acute respiratory distress (ARDS) or ARDS-like conditions, but many patients experienced deep vein thrombosis (DVT) and particularly pulmonary embolism (PE). Some patients had arterial thrombotic events. In a meta-analysis, the cumulative

incidence of venous thromboembolism (VTE) was 28.3% (38.0% in severe compared to 17.2% in patients with milder diseases) [7]. The impression of ICU doctors at Karolinska University Hospital was that this number may be even higher (up to 40%) (personal communication). However, some patients develop peripheral and acro-ischemic necrosis typical of thrombotic microangiopathies (TMA).

Anticoagulant Treatment in COVID-19

It has been shown early that anticoagulant treatment decreases mortality from COVID-19 [8] and Karolinska University Hospital was among the first to introduce clear recommendations for anticoagulant treatment in these patients. Additionally, some specific recommendations as the double dose prophylaxis in hospitalized patients with, among other risk factors,

D-dimer above 3 mg/L and/or fibrinogen over 8 g/L were given by Karolinska University Hospital coagulation experts very early (at the beginning of April 2020). This approach has not been widely accepted, and most consensus statement recommendations are based on more conventional standard dose prophylaxis and limited intermediate-full dose anticoagulant treatment to selected hospitalized patients [9]. At Karolinska University Hospital, after the implementation of updated hospital-wide recommendations (including escalated – intermediate prophylaxis for more severe patients), a significant decrease in D-dimer and increase in platelet counts, as well as risk reductions for death and thrombosis, were observed [4]. Current recommendations also include up to one month of extended prophylaxis with some direct oral anticoagulants (DOAC), e.g. Rivaroxaban, and Apixaban in selected patients after hospital discharge [9].

Potential Mechanisms of Thrombo-Inflammatory Conditions in COVID-19

It seems that the lungs were most severely injured by this virus and that the underlying mechanism is the fibrin deposition, a consequence of extravascular coagulopathy, release of pro-inflammatory cytokines, and extravasation of blood cells, primarily neutrophils. The complement system as an important part of the innate immunity to viral infections was also included, as well as microparticles (MPs), released from different cells after activation and/or apoptosis. Finally, neutrophil extracellular traps (NETs), which represent part of the host defense was involved in the signaling process and communication between inflammation/compliment and hemostasis [for review see 10]. Pathohistological and autopsy reports demonstrated the deposition of fibrin, neutrophils, and C5b-9 and C4d in the lungs and peripheral tissues [11]. We have observed increased coagulation and denser fibrin structure as well as increased concentration of total, platelet, neutrophil, and C5b-9 positive MPs in COVID-19 patients. Those MPs were identified even in the cerebrospinal fluid of COVID-19 patients with neurological symptomatology [manuscript submitted].

Hemostatic Abnormalities after COVID-19 Vaccination

Vaccination against COVID-19 started in late December 2020. Although in the clinical trials such adverse effects were not described, hemostatic abnormalities after vaccination were observed already in early 2021. Vaccine-induced immune thrombotic thrombocytopenia (VITT) was a rare but serious adverse syndrome, mimicking heparin-induced thrombocytopenia (HIT) and occurred primarily after adenoviral vector COVID-19 vaccination (in Sweden ChAdOx1 nCoV-19, Oxford-AstraZeneca) [for review see 12], but it was described even after mRNA (BNT162b2 Pfizer BioNTech) vaccine [13]. Both thrombosis and thrombocytopenia may occur after vaccination with all vaccines available in the Nordic countries (apart from those two, also mRNA-1273, Moderna) even without the presence of VITT [14]. Laboratory diagnosis of anti-PF4 VITT antibodies which is based on ELISA assays, since rapid assays used in the HIT diagnostics may be false negative, is of particular importance for distinguishing those different conditions [15].

Instead of Conclusion

Hemostatic abnormalities are common in COVID-19 and it seems that increased anticoagulant prophylaxis may be beneficial for some patients. The coagulation laboratory has an important role in the diagnosis of coagulation abnormalities, treatment monitoring, diagnosis of post-vaccinal hemostatic complications, and investigation of the pathophysiological mechanism of thrombo-inflammatory disturbances.

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STEM CELLS - EVOLVING CONCEPTS, EX VIVO MANIPULATIONS AND CLINICAL (AUTO)GRAFTING

Bela Balint[1,2], Mirjana Pavlovic[3], Milena Todorovic Balint[4,5]
[1]Department of Medical Sciences, Serbian Academy of Sciences and Arts, Belgrade, Serbia;
[2]Institute of Cardiovascular Diseases "Dedinje", Belgrade, Serbia;
[3]Department of Computer and Electrical Engineering and Computer Science, FAU, FL, USA;
[4]Clinic for Hematology, University Clinical Center of Serbia, Belgrade, Serbia;
[5]Faculty of Medicine, University of Belgrade.

Abstract

The stem cell (SC) compartment of the human organism is a heterogeneous group of cells, which can be divided into embryonic, fetal, and adult "tissue-specific" / committed cell types. Embryonic SCs (ESCs) – as the only "authentic" pluripotent SCs – are capable of differentiating into every cell type of endoderm, ectoderm, or mesoderm. Fetal liver-derived SCs – as well as ESCs – can be transplanted into an individual without being rejected since they have little (to none) of "immune-response-triggering" proteins (HLA-antigens) on their surface. Adult SCs are at a superior maturation stage – but they are able of making identical copies of themselves (well-balanced self-renewal) and have extensive potential for proliferation and differentiation. Typically, these SCs produce cell types of the tissue in which they reside.

Recent studies have documented that some primitive adult "tissue-specific" SCs – which are in bone marrow (BM) and in some "non-hematopoietic" compartments – have also nearly "unlimited" biological potential. These cells – including very small embryonic-like (VSEL) and induced pluripotent stem cells (iPSCs) – have the ability to "switch" into other/all cellular lineages. These SCs are clinically applicable for "conventional" SC-transplants (BM repopulation with hematopoietic reconstitution) and "cell-based therapies" in the fields of regenerative medicine (due to "inter-systemic" SC-plasticity).

This paper aims to recapitulate facts related to conceptual, experimental, and practical aspects of SC biological significance, ex vivo graft engineering, and clinical use in SC transplants (hematopoietic reconstitution) and regenerative medicine (organ repair).

Keywords: Stem cells, harvesting, processing, cryopreservation, transplantation

Sažetak

Odeljak matičnih ćelija (MĆ) humanog organizma je heterogena grupa ćelija koju je moguće podeliti na embrionalne, fetalne i adultne "tkivno-specifične" tipove ćelija. Embrionalne MĆ (EMĆ) – kao jedino "autentične" pluripotentne MĆ – su sposobne da se diferentuju u sve ćelijske tipove endoderma, ektoderma ili mezoderma. MĆ poreklom iz fetalne jetre, slično EMĆ, mogu biti transplantovane bez rizika odbacivanja jer na svojoj površini imaju malo ili nemaju proteine (antigene HLA), odgovorne za "indukciju" imunološkog odgovora. Adultne MĆ su u odmaklijoj fazi maturacije, ali mogu da produkuju sebi identične ćelije (uravnoteženo samoobnavljanje), uz veliki potencijal proliferacije i diferentovanja. Tipično, ove MĆ stvaraju tipove ćelija tkiva u kojem one borave.

Skorašnje studije su dokumentovale da neke primitivne adultne "tkivno-specifične" MĆ koje se nalaze u kostnoj srži (KS) i u nekim "nehematopoetskim" odeljcima, takođe mogu imati skoro "neograničen" biološki potencijal. Ove ćelije, uključujući veoma male, embrionalnim slične (VSEL) i indukovane pluripotentne MĆ (iPMĆ), imaju svojstvo prelaska/prebacivanja ("switching") u druge/sve ćelijske linije. Ove MĆ su klinički primenljive za "konvencionalnu" transplantaciju (repopulacija KS sa rekonstitucijom hematopoeze) i za "ćelijsku-terapiju" u oblastima regenerativne medicine (usled "intersistemske" plastičnosti).

Cilj ovog rada je da rekapitulira podatke vezane za konceptualne, eksperimentalne i praktične aspekte biološkog značaja MĆ, ex vivo graft-inženjeringa i njihove kliničke primene u transplantacionoj (rekonstitucija hematopoeze) i regenerativnoj medicini (oporavak organa).

Ključne reči: matične ćelije, prikupljanje, procesiranje, krioprezervacija, transplantacija

Introduction

Stem cells (SCs) are "key cells" in the human body "working" as immature precursors which produce a large number (proliferation) of committed progenitors and heterogeneous morphologically recognizable mature cells (differentiation). Pluripotent SCs (PSCs) could be defined as cells with a unique potential for self-renewal – that is an option to reproduce themselves or create new cells for a long time without changing – to maintain and replenish their own entity in any "tissue-generating" systems (1–3).

The aim of this paper is to recapitulate facts related to conceptual and practical aspects of SC biological implications, some *ex vivo* graft manipulations, as well as the clinical use of SCs in "conventional" transplants (hematopoietic reconstitution) and regenerative medicine (SC-plasticity). Besides, the aim of this article is to summarize our data connecting to the evaluation of cell harvesting, processing, and cryopreservation protocols.

Stem cell hemobiology

Hematopoietic SCs (HSCs) are immature cells that are developing into all blood cells. HSCs are found in bone marrow (BM) and peripheral blood (PB), thus also named blood SCs. Since these cells express CD34 antigen – they are called CD34+ cells, too. A minor compartment of CD45+/CD34+ cells – with typical size and intracellular granularity – in accordance with the ISHAGE protocol represents authentic or "true" SCs and is named SCish. More primitive HSCs expresses also CD90 antigen and considered as CD90+SCish (CD45+/CD34+/CD90+) subtype (2, 4–6). In the clinical setting, the quantity and quality of applied CD90+SCish cells could be predicted BM repopulation (white blood cell and platelet recovery) after SC-transplants (4).

Cellular events mentioned above (self-renewal, differentiation, proliferation, migration, or apoptosis) are balanced with specific intrinsic genetic pathways that are subject to regulation by extrinsic signals – such as cytokines secreted by stromal cells – from the extracellular matrix and microenvironment in which SCs reside (2–4). Due to SC self-renewal ability, after dividing into "progeny-cells" – one of the "daughter-cell" continue the original nature of the "mother-cell" (renewing the persistent entity of PSCs), while the other one produces progenitors and lastly mature cells ("commitment program") (2, 3). Thus, it is a skillful regular maneuver or "trick" and one which works.

From embryonic to induced pluripotent stem cells

Within SC entity there are different cellular categories, such as embryonic SCs (ESCs), fetal and adult or "tissue-specific" cells – including very small embryonic-like (VSEL), mesenchymal/stromal SCs (MSCs), as well as induced PSCs (iPSCs) (2, 6–10).

Human ESCs are initially isolated/expanded from the inner cell mass (ICM) of the blastocyst, which subsequently forms the embryo (7). Only ESCs are authentic or natural totipotent SCs. They are able to differentiate into any cellular lineages of all three germ layers in the human body – that is endoderm, ectoderm, and mesoderm. The most immature fetal SCs (as well as ESCs) can be transplanted into an individual without being rejected. This is because they have little to none of "immune-response-triggering" proteins (HLA-antigens) on their membrane surface – but after the 12th gestational week, fetal SCs acquire these proteins. Recent studies have documented that some "tissue-specific" SCs have similar "unlimited" biological potential to ESCs (2, 5–7).

Generally, adult SCs are at a more advanced stage of development. They are thought to reside in a specific area of tissues ("niche") where they may remain inactive ("non-dividing") for a long time until they are activated by some disease or tissue injury. These "niches" can be found in the BM, blood vessels, fat tissue, skeletal muscles, skin, liver, etc. Very primitive SCs in the adults (having also relatively high-level biological capacity) are typically limited in their "regenerative potential" to the tissues in which they reside (2, 4–6).

Therefore, the SC compartment displays pluripotential and plays a central role in organogenesis of embryonic (ESCs and the most primitive fetal SCs) and tissue/organ homeostasis and regeneration (adult SCs). The ESC partition, as well as some very primitive "tissue-specific" SCs (including VSEL and iPSCs) have the potential for "switching" into all/other cell lineages ("inter-systemic" SC-plasticity). Consequently, they are clinically applicable for SC transplants and cell therapy in the field of regenerative medicine (2, 5, 11–13).

MSCs derive from mesoderm and they are important for making or repairing skeletal tissues. These cells can trans-differentiate into a variety of cell types, including osteoblasts, chondrocytes, myocytes and adipocytes. With age and/or disease, they mainly convert into fat cells. MSCs have high upcoming therapeutic possibilities and safety character, too (2, 5, 6).

The original concept of SC-plasticity was revised by Ratajczak et al. (8). They confirmed that BM (in addition to HSC) contains a heterogeneous population of "non-hematopoietic" SCs – named VSEL cells – which express several markers typical for PSCs. Additionally, VSELs have similar or the same ultrastructure and protein markers as ESCs. Thus, these cells are in adult BM, but also in some "non-hematopoietic" compartments and they are responsible or committed for trans-differentiation into various somatic cell lineages or tissue types from more than one germ layer. VSELs could be also mobilized into PB following stress and tissue damages (2, 8).

The phrase SC entity includes recently discovered iPSCs, generated using a reprogramming process ("induced pluripotency") too (9, 10). Immature iPSCs were produced by ectopic expression of genes for reprogramming an adult somatic cell. iPSCs are similar (or equivalent) to ESCs since comparative gene expression analyses, miRNA expression and DNA methylation confirmed no evident differences between the two cell types. The discovery and conception of iPSCs have opened up further possibilities in the fields of regenerative medicine, disease modeling, and drug testing – as an innovative "cellular tool" (10).

Stem cells in preclinical settings

Hematopoietic tissue was the first and most investigated "tissue-generating" (cytopoietic) system – in adults, BM is the "home organ" of HSC. Areas in which immature SC compartments and their "cellular-derivatives" have possible applications are: a) "conventional" SC-transplant – a standard tool for complete, long-term, and stable BM repopulation and hematopoietic reconstitution; b) regenerative medicine – PSCs can be used for tissue repair or damaged cell replace; c) cellular physiology/biology – PSCs or SC-derived cells give systems for exploration of normal/typical cellular development; d) disease research – PSCs or SC-derived cells are practical for modeling of pathological conditions or disorders; e) innovative medication – PSCs or PSC-derived cells are "skillful" instrument and system for new (experimental) drug testing (11–15).

SCs can be collected by aspirations from BM (historically the first SC source) and by mononuclear cell (MNC) harvesting from PB using apheresis (adult transplant settings) after mobilization, as well as by processing from umbilical cord blood (UCB; pediatric settings). The target volume of collected BM aspirate is 10 – 15 mL per kg of donor body mass (kgbm). SC harvesting from PB is less invasive collection method, with higher cell yield and rapid hematopoietic reconstruction, as well as inferior transplant-related morbidity. Due to the mentioned reasons, the number of patients treated by PB-derived SCs is ever-increasing worldwide (2–6).

Cryopreservation of SCs consists of the next steps: 1) graft processing – MNC separation and red blood cell depletion (BM aspirate); 2) equilibration and freezing – cell exposure to the cryoprotective agent and following uncontrolled-rate or controlled-rate cooling/freezing; 3) cell storage – typically at -140±10°C (mechanical freezer or steam of nitrogen) or at -196°C (liquid nitrogen); 4) cell thawing in a water bath at 37±3 °C (2). Our early cryo-investigations confirmed the best cell recovery of very primitive SCs when the controlled-rate freezing (with compensation of the released fusion heat) procedure and 10% dimethyl sulfoxide (DMSO) were combined (16).

Stem cells in clinical setting

SCs guarantee steady-state homeostasis in all "tissue-generating" (including hematopoietic) systems and they are capable of providing complete and long-term BM repopulation following SC-transplant in patients with partially or completely injured hematopoiesis. Concisely, "conventional" SC-transplant involves myeloablative treatment by intensive radio-chemotherapy followed by (re)infusion of harvested cells in order to eliminate the basic disease. A similar procedure with reduced-intensity conditioning (RIC) can be offered to patients who are disqualified for a high-dose (conditioning) regimen because of their age or co-morbidities. Applied SCs result in BM repopulation (engraftment) and long-term and complete hematopoietic reconstitution, associated with patients' overall recovery. SC-transplants are a standard and optimized treatment for a variety of hematologic malignancies, benign blood diseases, severe combined immunodeficiency (SCID), and metabolic or autoimmune disorders (e.g. multiple sclerosis). The SC-transplant efficacy depends on cellular parameters – quantity and viability (clonogenicity) of infused immature SCs (CD45+/CD34+/CD90+ subtype) and committed progenitors – type and intensity of conditioning regimen, patients' age and comorbidities (2, 6).

SC-transplants were used for the treatment of our patients with acute lymphoblastic and non-lymphoblastic leukemia (ALL and ANL), chronic myeloid leukemia (CML), multiple myeloma (MM), Hodgkin and non-Hodgkin lymphoma (HL and NHL), as well as patients with extragonadal non-seminal germ cell tumors, severe aplastic anemia (SAA), and multiple sclerosis. Hematopoietic reconstitution was obtained on the 9.4th vs. 15.9th day (granulocytes) and the 13.1th vs. 17.5th day (platelets) when PB vs. BM-derived SCs was compared. The SC-transplant efficacy depends on the type of disease, its stage, its sensitivity to chemotherapy, the patient's age, and their general health status, as well as the degree of HLA-matching (2, 4–6, 11).

The phenomenon of the SC multipotency and "inter-systemic" plasticity, which have been newly discovered, could also lead to a potential application of autologous cells in the field of regenerative medicine – for tissue/organ repair or regeneration. Namely, immature SCs (VSEL, MSCs, or iPSCs) are capable of colonizing damaged tissues with subsequent "switching" into the "host-organ" somatic cellular lineages, such as cardiomyocytes, hepatocytes, chondrocytes, including collateral vessel formation or neovascularization too (8–13).

Our results confirmed that treatment of acute ST-elevation myocardial infarction (STEMI) with intracoronary injection (cardiology) of MNCs with SCs (MNC/SCs), collected from the patients' activated (primed by G-CSF) BM was effective and safe. The left ventricular ejection fraction (LVEF) was improved by approximately 6% in the 4-month follow-up period. However, long-term positive LVEF effects were moderate. Besides, initial results in cardiac surgery (Coronary Artery Bypass Grafting – CABG) followed by MNC/SC intramyocardial implantation showed the superiority of this therapeutic approach. The LVEF was improved (5.0 ± 4.2%) and better-quality functional capacity was confirmed using the "6-minute walk test" (6-months follow-up period). Cardiovascular mortality was also lower during the 5-year follow-up period in these patients vs. the control group (CABG alone). Treatments were safe – no reinfarction, heart failure, or other adverse events were detected (11–13).

SC-transplant is a standard treatment for hematological, immune-mediated, and certain metabolic disorders. The use of cellular or subcellular (molecular-genetic) investigating and therapeutic systems in the area of SCs could be implemented in innovative components of personalized medicine or precision medicine. Explicitly, due to the expansion of new tools derived from "omics technology" – initially intended to determine and characterize some cellular biomolecules – transplant medicine is gradually incoming into the area of precision medicine designed to optimize medical benefits using molecular-genetic profiling (15, 17, 18).

In regenerative medicine, experimental and clinical data regarding stem/stromal cell therapy or bio-cellular treatments imply the existence of enhanced tissue/organ self-regeneration capacity due to cell potential for proliferation, differentiation, and "inter-systemic" plasticity. The most effective "self-healing" options include the targeted cell (ESCs, VSEL, MSCs, or iPSCs) placing, but also placement of extracellular matrix or proteins (laminin, collagen or fibronectin), "pro-regenerative" cytokines or growth factors, signal proteins, as well as compounds/substances critical to wound healing (19, 20).

Therefore, a growing SC practice has become a very active, promising, and attractive research area for transplant and regenerative medicine. However, to date, these "cell-based therapies" used to improve "conventional" transplant efficacy and tissue regeneration and wound healing – including personalized or precision medicine – remain partially "speculative" and additional cellular research in the next years will attempt to find some answers.

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SPECIFICS OF COLLECTION, PROCESSING AND THERAPEUTIC USE OF BLOOD AND CHEMOPRODUCTS IN COVID-19 PANDEMIC CONDITIONS

Branislava Belić
Academy of Medical Sciences of the Serbian Medical Association, Belgrade, Serbia

Abstract

Organization of the collection, processing and therapeutic application of chemoproducts introduced some changes due to the COVID-19 pandemic. Preventive measures are recommended to reduce infection risk and transmission. Transfusion treatments must be continuous and safe, despite a decreased number of the healthy population that can donate blood and voluntary blood donors, as a consequence of introduced public health measures. In order to prevent the transmission of the COVID-19 infection, additional measures for blood donors are implemented to ensure a sufficient amount of safe blood for treatment. The changes were made in the selection of blood donors to improve monitoring. During the pandemic, authorized transfusion services in cooperation with national regulatory bodies are obliged to ensure blood collection for all clinical needs, maintain the safety of voluntary blood donors, and employees, and reduce the possibility of virus transmission. Recommendations were made for voluntary blood donors who received COVID-19 vaccines, and measures were introduced to prevent virus transmission. The COVID-19 pandemic brought significant changes in the work of the transfusion service, but even in such specific circumstances, the blood transfusion service in Serbia fulfilled its basic task and provided sufficient amounts of blood and blood components, necessary for the treatment of the patients.

Keywords: blood transfusion, COVID-19 pandemic

Sažetak

Specifičnosti u organizaciji prikupljanja, prerade i terapijske primene hemoprodukata nastale su zbog pojave pandemije COVID-19. Preporučene su preventivne mere za smanjenje rizika nastanka i prenošenja ove infekcije. Transfuziološko lečenje mora da bude kontinuirano i sigurno, iako je smanjen broj zdrave populacije koja može dati krvi smanjen odziv dobrovoljnih davalaca krvi, zbog uticaja javno-zdravstvenih mera koje se preduzimaju. S ciljem sprečavanja prenošenja COVID-19 infekcije, za davaoce krvi su implementirane dodatne mere kako bi seobezbedile dovoljne količine bezbedne krvi za transfuziološko lečenje. Izmene su nastale kod izbora davalaca krvi, a cilj je pojačanje nadzora u novonastaloj situaciji. U toku pandemije ovlašćene transfuziološke službesu u obavezi da u saradnji sa nacionalnim regulatornim telima osiguraju prikupljanje krvi i obezbede sve kliničke potrebe, održe bezbednost dobrovoljnih davalaca krvi, zaposlenih u službama transfuzije krvi i smanje mogućnost prenošenja virusa putem transfuzije krvi. Sačinjene su preporuke za dobrovoljne davaoce krvi koji su primili vakcine protiv COVID-19 i uvedene su mere s ciljem sprečavanja prenošenja COVID-19. Pandemija COVID-19 je donela značajne izmene u radu transfuziološke službe, ali i u tako specifičnim okolnostima službi transfuzije krvi u Srbiji je ispunila svoj osnovni zadatak i obezbedila dovoljne količine krvi i komponenata krvi, neophodnih za lečenjeobolelih.

Ključne reči: transfuzijakrvi, pandemija COVID-19

Blood transfusion is one of the vital branches of medicine and is necessary for caring for the injured and treating the sick. The spread of the virus and the COVID-19 pandemic, which occurred in the world at the end of 2019 and continues today, significantly contributed to the introduction of special specificities in the organization and processing of blood, the supply of blood components, the safe therapeutic application of chemoproducts and the maintenance of stable supplies and reserves of blood components in the Blood Transfusion Service of Serbia.

The process of providing a sufficient number of blood units, which are collected from voluntary donors, is very complex, and unfavorable and unplanned factors often occur, such as bad weather conditions, vacations, infectious diseases, and epidemics. The limited expiration date of some blood components, the specifics of component storage, and the impossibility of predicting the needs of a particular type, blood type, and amount of components make the blood reserve management system complex, which is one of the most important tasks of the transfusion service in its daily work, and especially, in case of occurrence, such as the COVID-19 epidemic.

It is known that SARS-CoV-2 has a long incubation period (1–14 days, average of 5–6 days) and causes asymptomatic infection in a large number of patients, which represents a major problem for the selection of blood donors and the safety of transfusion (1). Symptoms of COVID-19 infection include fever, dry cough, fatigue, malaise, muscle aches, and difficulty breathing, which can lead to acute respiratory failure and fatal outcomes. Asymptomatic infection is also a big problem in the fight against the spread of the virus (2, 3).

With the beginning of the COVID-19 pandemic, precise recommendations and measures were adopted, which refer to the criteria for the temporary rejection of blood donors during the COVID-19 pandemic. The Republican Expert Commission for Blood Transfusion of the Ministry of Health of the Republic of Serbia, according to the recommendations of the European Center for Disease Control (ECDC), which introduced measures for blood donors in order to prevent the transmission of COVID-19, issued information for blood donors, and they refer to a warning to donors that do not apply for blood donation if they have traveled outside of Serbia in the last 28 days, if they have had a cold, cough and sneeze, elevated body temperature

and if they have been in contact with a sick person with the symptoms that resemble a coronavirus infection. Blood donors were reminded of their obligation to notify the authorized transfusion institution where they donated blood within 14 days after donating blood, in case of signs of an infectious respiratory disease. This so-called "post-donation information" or feedback on the health status of a voluntary blood donor within a period of 14 days from donating blood is of great importance for the safety of transfusion in the conditions of the COVID-19 pandemic. Some countries have introduced temporary storage of blood in quarantine for 14 days, and if there is no information about the donor's illness from a COVID-19 infection after donating blood, blood components (erythrocytes, fresh frozen plasma) are released from quarantine after 14 days (4-7). The European School of Transfusion Medicine (ESTM) has adopted an algorithm according to which if there is a sudden appearance of symptoms or suspicion of a COVID-19 infection and the donor informs the transfusion service about the positive result of the nasopharyngeal swab within 14 days of donating blood, all present labile blood components should be destroyed in stock, and if they have been previously transfused, it is necessary to inform the administration of the clinic where the transfused patient is lying (8). In accordance with the recommendations of the FDA and the AABB, a Recommendation was made for the procedure with voluntary blood donors who received the COVID-19 vaccine.

Although to date not a single case of SARS-CoV-2 blood transmission has been recorded, the pandemic has caused serious problems and brought great challenges to the supply of blood components. In addition to the constant need for transfusion treatment, the need for transfusion treatment arose in patients with COVID-19 infection, and with the spread of the pandemic, the reserves of blood and blood components were reduced, which is a consequence of the measures introduced in the fight against the spread of the COVID-19 pandemic (9).

There is no evidence that the transmission of the COVID-19 virus is carried out through blood and blood components, but some countries have introduced mandatory NAT testing for SARS-CoV-2 as part of the blood screening test. Considering that pathogen inactivation of plasma and platelets allows a 3–6 log reduction of SARS-CoV-2 and MERS-CoV, some countries have decided to introduce some of the methods of pathogen inactivation. In the conditions of the COVID-19 pandemic, the inactivation of pathogens in blood components can significantly contribute to greater transfusion safety, but in our country, as well as in a small number of countries in the world, it is not applied in routine practice and rapid implementation is a big task with numerous risks. However, in the midst of a pandemic or the potential worsening of a large-scale epidemiological situation, pathogen inactivation plays a vital role in maintaining stable blood supplies and safe transfusion (10). Special measures in blood transfusion services have been introduced in the organization of mobile teams and collection sites, disposal of medical waste, examination of potential donors, and mandatory body temperature measurement. Measures have been taken to temporarily store blood in quarantine for 14 days after collection, and special attention is focused on stock management of blood components and creating a collection plan, in order to avoid shortages of certain blood components or expiration of the shelf life of preserved blood or blood components.

Like other European countries, we have started the Anti-COVID-19 Plasma Project, which involves the motivation and recruitment of convalescents, people who have successfully fought the SARS-CoV2 virus, to donate plasma from people who have suffered from COVID-19. A certain number of units of convalescent plasma were collected and a part was used for the treatment of patients with COVID 19 infection. In the course of 2021, the WHO advised that the blood plasma of people who have recovered from the COVID-19 infection should not be used to treat the sick, because the available data showed that such treatment does not improve the chances of survival and does not reduce the need for a respirator.

In addition to the above measures, constant changes to the work plan are necessary for pandemic conditions, collecting a sufficient amount of blood for the needs of clinics, and at the same time maintaining the safety of voluntary blood donors and employees of the blood transfusion service (11). The main task of the transfusion service is to ensure the least possible transmission of the virus through transfusion, although it is known that there is a small risk of transmission of the SARS-CoV-2 virus through blood. The temporary storage of blood in quarantine for 14 days after the collection was introduced. Special attention is paid to the efficient management of blood component stocks and the development of a blood collection plan, in order to avoid shortages of certain blood components or their expiry date. The COVID-19 pandemic has caused major problems in the supply of blood components. In addition to the continuous need for all blood components (erythrocytes, plasma, platelets) for the treatment of oncological, hematological, and gynecological patients, in the case of trauma, emergency operations, or transplantation, the need for transfusion treatment has arisen patients with COVID-19 infection.

Conclusion

The COVID-19 pandemic has brought significant changes and specifics in the work of the transfusion service. Bearing in mind that the pandemic is still ongoing, it is necessary that the work of the transfusion service continues with the recommendations and new knowledge gained related to the infection. In the conditions of the COVID-19 pandemic, good cooperation of blood transfusion services with national regulatory bodies, public health institutes, and clinical centers is necessary, constant changes to the work plan in pandemic conditions and collection of a sufficient amount of blood and at the same time maintaining the safety of voluntary blood donors and employees in blood transfusion service. The main task of the transfusion service is to ensure the lowest possible level of transmission of the virus through transfusion, although the risk of transmission of the SARS-CoV-2 virus through blood is very small.

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WHAT HAVE WE LEARNED FROM THE COVID-19 CONVALESCENT PLASMA CAMPAIGN?

Primož Rožman, Katerina Jazbec, Klemen Žiberna,
Urška Rahne Potokar, Maja Černilec, Petra Jovanovič, Sonja Vuletić, Polonca Mali
Zavod RS za transfuzijsko medicino, Ljubljana, Slovenija

Abstract

Anti-SARS-CoV-2 neutralizing antibodies (nAbs) can neutralize the virus and reduce the viral load in patients with COVID-19, which renders COVID-19 convalescent plasma (CCP) interesting for therapy. However, international studies have shown that using CCP does not meet therapeutic expectations. A possible reason for poor efficiency is the eventual content of undesirable substances in CCP units, such as a) acute phase inflammatory factors with pathological hemostasis factors; b) cytokines; c) free DNA and RNA; e) irregular autoantibodies; f) extracellular membrane vesicles, and g) other soluble factors that cause (dis)regulation of the immune response. In 2020 and 2021, we collected approximately 4000 hyperimmune units of CCP with high titers of nAbs. We checked CCP units with increased titers of nAbs for the presence of undesirable substances. Our initial results showed that the vaccination largely increased the titers of nAbs, that the ABO blood group status did not influence the titer of Abs, and that the high titer of nAbs can be deduced based on a simple serological test, not demanding expensive neutralization assays neither the clinical and demographic data. Further metabolic and immunological factors in the CCP units, as well as the clinical outcomes of their application, are currently still being investigated.

Keywords: Hyperimmune plasma collection; COVID-19 disease, quality control

Introduction

The hyperimmune convalescent COVID-19 plasma (CCP) with anti-SARS-CoV-2 antibodies became an appealing source of therapy early after the start of the COVID-19 pandemic in 2020. The promising prospect was that the antibodies present in CCP units could neutralize the SARS-CoV-2 virus contributing to its clearance from the patient(1, 2). Several initial studies reported a beneficial effect of CCP treatment with no severe side effects (3-6). However, several parallel studies and larger international trials such as RECOVERY and REMAP-CAP did not show a reduction in mortality or improvement in clinical outcomes (7-11).

A possible reason for the poor efficiency of CCP could be the presence of undesirable substances in CCP units, such as a) acute phase inflammatory factors with pathological hemostasis factors; b) cytokines; c) free DNA and RNA; e) irregular autoantibodies; f) extracellular membrane vesicles; and g) other soluble factors that cause (dis)regulation of the immune response. Therefore, we checked the CCP units with high titers of nAbs for the presence of various metabolites compared with fresh frozen plasma (FFP) from healthy volunteers collected before the onset of the COVID-19 pandemic.

In 2020 - 2021 we collected 4614 hyperimmune units of CCP with high titers of neutralizing antibodies (nAbs) during 3200 sessions. Only 328 high titer units were later released for a clinical trial in 158 patients. Besides the testing of undesired substances, we aimed to establish whether the vaccination increased the titers of nAbs, what is the influence of the ABO blood group on the titer of nAbs, and find a supplement for the expensive neutralization assays.

Initial results

The first scientific question was whether we could predict which CCP units contain high levels of nAbs without an expensive neutralizing test. Shortly, since the standard neutralizing tests (NTs) used for determining appropriate CCP donors are costly and take several days, we explored whether more straightforward high-throughput serology tests could replace them. With 1302 CCP donors after PCR-confirmed COVID-19 infection, we built four multiple logistic regression models evaluating the relationships of their demographic data, COVID-19 symptoms, results of various serological testing, the period between disease and donation, and COVID-19 vaccination status. The analysis of the four models showed that the chemiluminescent microparticle assay (CMIA) for the quantitative determination of IgG Abs to the RBD of the S1 subunit of the SARS-CoV-2 spike protein was enough to predict the CCP units with a high NAb titer. CCP donors with respective results >6000 AU/ml SARS-CoV-2 IgG had a high probability of attaining sufficient NAb titers. Including additional variables such as donor demographics, clinical symptoms, or time of donation into a particular predictive model did not significantly increase its sensitivity and specificity. This confirmed that a simple quantitative serological determination of anti-SARS-CoV-2 antibodies alone is satisfactory for recruiting CCP donors with high titer NAbs(Jazbec et al. - submitted).

The second scientific question that could be answered quickly was whether the ABO blood group of the CCP donors influences the level of nAbs. The association of the ABO blood group with COVID-19 disease has been confirmed previously by several studies, with the blood group A patients being more susceptible and prone to a more severe clinical course of the disease. Besides, several authors also addressed the association of ABO-types and the levels of anti-SARS-CoV-2 antibodies in convalescents, primarily supporting the theory that the non-O blood group convalescents present higher levels of anti-SARS-CoV-2 antibodies. We quantified the anti-SARS-CoV-2 antibody levels in 3187 CCP plasma donors with three

commercial serological and one standard neutralizing antibody test. Most donors had undergone a mild form of the disease and the median time of sampling was 66 days after diagnosis. We found that the ABO blood group type does not influence the level of SARS-CoV-2 antibody response in COVID-19 convalescent plasma donors (12).

Conclusion

Several unanswered questions in COVID-19 biology are connected with the use of the CCP for therapy. The questions are whether CCP could be supplemented with polyspecific immunoglobulins, with specific anti-SARS-CoV-2 immunoglobulins, and whether there is a rationale for using monoclonal antibodies (MAbs). Yet another unsolved problem is the onset of new COVID-19 variants of concern (VOC), such as Delta and Omicron, and their resistance to the Abs against older variants of the virus. Another question is the role of vaccination against SARS-CoV-2 that can result in modified specificity and content of immunoglobulins, which pertains both to the patients and the convalescent donors. Some latest data show that CCP collected in 2020 is unlikely to be effective against current VOCs. COVID-19 variants also seem to escape the action of polyspecific immune globulins (13). Similarly, novel SARS-CoV-2 variants of concern (VOC) Delta and Omicron can escape some anti-Spike MAbs, making COVID-19 convalescent plasma (CCP) again a potential frontline treatment (14).

We concentrated on the question of CCP quality. CPP could contain bioactive molecules produced in response to the SARS-CoV-2 virus, which could affect the plasma recipient. Therefore we decided to define the composition and concentration of biochemical substances, hemostatic and thrombotic factors, plasma cytokines, chemokines and growth factors, extracellular DNA and RNA composition, and extracellular microvesicles in the plasma of COVID-19 convalescent plasma donors. These potentially undesirable factors in the CCP and the clinical outcomes of the recipients of CCP are being further investigated.

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CLIMATE CHANGE AND BLOOD SAFETY

Dragoslav Domanović
European Blood Alliance

Among the various effects that climate change can have on physical, biological, and human systems, extreme weather events and disasters, changes in infectious diseases and human health, and population movements are likely to have a significant impact on blood supply. We used a narrative review of reports and experiences from climate-induced events to highlight direct or indirect climate change impacts on the blood supply aiming to raise awareness of the potential threats posed by climate change and encourage blood establishments to prepare for their occurrence. Experiences from former disasters have shown that the disruption of the local or regional blood distribution system caused by compromised traffic is the main reason for blood supply failure during weather disasters. The long-term effects of climate change may induce changes in pathogens, the spatial distribution of infectious diseases, their annual/seasonal cycles, incidence, severity, and emergence that may threaten the infectious safety of blood supply. Migrants may occasionally introduce infectious diseases and trigger a disease outbreak in the destination country which may threaten blood safety. Since minority groups and immigrants are frequently under-represented as blood donors, it may cause difficulties in providing blood for a population with specific blood types.
Keywords: climate change, blood safety, migration

Sažetak
Među različitim efektima koje klimatske promene mogu da imaju na fizičke, biološke i ljudske sisteme, ekstremni vremenski događaji i katastrofe, promene u zaraznim bolestima i kretanja populacije mogu značajno da utiču na snabdevanje krvlju. Koristili smo narativni pregled i zveštaj, a i iskustava o klimatskim događajima da bi smo istakli direktne ili indirektne uticaje klimatskih promena na snabdevanje krvlju, s ciljem da podignemo svest o potencijalnim pretnjama koje predstavljaju klimatske promene i podstaknemo ustanove za transfuziju da se pripreme za njihovu pojavu. Iskustva iz ranijih katastrofa su pokazala da je poremećaj lokalnog i liregionalnog sistema distribucije krvi uzrokovan kompromitovanim saobraćajem glavni razlog za prekid snabdevanja krvlju tokom vremenskih nepogoda. Dugoročni efekti klimatskih promena mogu izazvati i promene u patogenima, prostornoj distribuciji zaraznih bolesti, njihovim godišnjim/sezonskim ciklusima, učestalosti, ozbiljnosti i pojavljivanju koje mogu ugroziti bezbednost snabdevanja krvlju. Migranti mogu povremeno da unesu zarazne bolesti i izazovu izbijanje bolesti u zemlji odredišta koja može ugroziti bezbednost krvi. Pošto su manjinske grupe i imigranti često nedovoljno zastupljeni kao davaoci krvi, to može izazvati poteškoće u obezbeđivanju krvi za populaciju sa retkim krvnim grupama.
Ključne reči: klimatske promene, bezbednost krvi, migracije

Introduction

According to the Intergovernmental Panel on Climate Change report for 2021, there is no doubt that human activities have warmed the atmosphere, the ocean, and the land leading to unprecedented climate changes (1). Due to global warming in the last decades, the occurrence of extreme weather events such as heatwaves, heavy precipitation, droughts, and tropical cyclones over most land areas across the world is increasing (2). It appears that among the various effects that climate change can have on physical, biological, and human systems, extreme weather events and disasters, changes in infectious diseases and human health, and population movements are likely to have a significant impact on blood supply. Our aim is to raise awareness of the potential threats posed by climate change, analyse their impact on blood supply, and encourage blood establishments to prepare for their occurrence while adapting their activities in support of reducing greenhouse gas emissions.

Methods

Although, climate research is usually interdisciplinary and often involves the development of climate impact models, here we used a narrative review of reports and experiences from climate-induced events to highlight direct or indirect climate change impacts on the blood supply.

Extreme weather events and disasters

Climate change is expected to increase the frequency, intensity, spatial extent, duration, and impacts of extreme weather events, to the magnitude of disasters. In 2021, the number of recorded disaster events and the annual average of economic losses was higher than the annual average in the previous two decades (3). By negatively affecting human life, infrastructure, communications, transportation, industry, and buildings, disasters may directly or indirectly affect the blood supply chain. Generally, disaster situations may cause disruptions in blood supply due to the demand surge or supply failure (4). Mass casualties requiring a sudden need of much larger amount of blood than usual are rarely associated with weather disasters, although the death toll can be high. Local or regional blood establishments are usually able to cover transfusion needs in the disaster area. Demand for blood in large disaster situations has mainly been determined by the number of injured who survived long enough to be presented for care and the rate of blood used in providing that care. To cope with such an emergent demand surge, blood establishments might experience an abrupt influx of large numbers of donors, requiring the accelerated drawing of blood. Such a strong community response to blood donation, especially in non-affected areas, may, however,

result in an over-collection of blood. On the other hand, impaired infrastructure and technologies may directly cause supply failure by restricting or eliminating the ability of blood establishments to collect, screen, process, and distribute products or by preventing or hampering the local population from donating or accessing available blood components. Experiences from former disasters have shown that the disruption of the local or regional blood distribution system caused by compromised traffic is the main reason for blood supply failure during weather disasters (4).

Changes in the infectious disease epidemiology

The long−term effects of climate change may induce changes in pathogens, the spatial distribution of infectious diseases, their annual/seasonal cycles, incidence, severity, and emergence. Changed pathogens or infectious diseases may be undetected during blood donor selection or screening of donated blood, leading to pathogen/disease transmission to transfusion recipients. Changes in climate can directly influence the survival, reproduction, and life cycle of pathogens, or indirectly, by affecting the habitat, environment, or competitors of pathogens. As a result, not only the quantity or virulence but also the geographic and seasonal distributions of pathogens may change. The systematic review of the literature on the 100 human and 100 animal pathogens with the greatest health burden showed that approximately 63% of the pathogens assessed were climate-sensitive and among those 82% were receptive to primary drivers (rainfall, temperature,) (5). An impact on zoonotic and vector-borne pathogens includes range shifts; changes in the population density and prevalence of the pathogen in the host or vector population that may lead to increased contact of infected animal hosts and vectors with humans or with other hosts and vectors, or changes in the pathogen load, the rates of pathogen reproduction, replication, or development in hosts or vectors that can lead to an increased likelihood that human contact with host or vector would result in pathogen transmission (6). Direct effects of climate change can be observed in the mosquito life cycle where the temperature and rainfalls have an impact on development and reproduction in the aquatic phase, while in the terrestrial phase the temperature and humidity may affect mosquito activity including transmission. The temperature may also impact the mosquito's extrinsic incubation period (7). Climate change can influence the geographical distribution of pathogens by expanding existing and creating new areas where tropical arthropod-borne diseases like WNV in Europe, dengue, chikungunya, and Zika worldwide (8). In a study that analysed a database of 335 emerging infectious diseases (EID) 'events' that occurred between 1940 and 2004, EID showed non-random global patterns and have risen significantly over time. According to the study, zoonoses are dominant covering 60.3% of the EIDs mostly originating in wildlife (9). The recent emergence of coronaviruses (SARS-CoV-1 and 2 MERS-CoV), Zika, hepatitis e, and influenza shows that a trend of increasing occurrence of EID continues.

Population movements

In the globalization era, human movements are part of the dynamic global process of moving biota, along with plants, animals, microorganisms, and other materials. These movements are increasing in numbers and speeds showing a diversity of destinations and purposes. As a type of movement, migration, is influenced by a combination of global economic, environmental, political, and social factors: either in a migrant's country of origin (push factors) or in the country of destination (pull factors). Many push factors for migration, like crop failure, famine, pollution, and natural disasters, are influenced by climate change (10). In 2019, there were an estimated 2.7 million immigrants to the EU from non-EU countries and about 1.2 million people emigrated from the EU to a country outside the EU. In addition, 1.4 million people previously residing in one EU Member State migrated to another Member State (11). However, the burden of infectious diseases among migrants and the general population of the destination country may differ. Thus, from the blood safety perspective, migrants originating from countries where some infectious diseases are endemic may occasionally introduce infectious diseases and trigger a disease outbreak in the destination country. When migrants became blood donors, some of them may have chronic asymptomatic diseases like Chagas that can be transmitted through blood transfusion. Minority groups and migrants are frequently under-represented as blood donors. Data from some European countries show a significant difference in blood donation between non-migrant and immigrant populations (12,13,). This situation may threaten the adequacy of blood supply in providing blood for a population with specific blood types (14).

Conclusion

Among various effects that climate change can have on physical, biological, and human systems, it is likely that extreme weather events and disasters, changes in infectious diseases epidemiology and population movements can have a significant impact on the blood supply. Thus, these climate change effects should be closely monitored, analysed, and considered in developing preparedness plans for maintaining the safety and adequacy of blood supply.

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AVAILABLE, SAFE AND QUALITY TRANSFUSION TREATMENT – LOGIC OF PROFESSIONAL AND ATYPICAL BUSINESS MANAGEMENT

Marina Samardzija[1, 2]
[1]Clinical Institute for Transfusion Medicine, University Hospital Osijek, Croatia
[2]School of Medicine Osijek, University J.J. Strossmayer in Osijek, Croatia

Blood has a status of the national good. The health system is a strategic part of the economy in many countries. Hospitals, in an economic sense, can be treated as business entities with atypical business characteristics. The hospital business is of a hybrid type and combines the logic of business management and social availability that is legally conditioned. Transfusion medicine is a specific medical profession that unites science, technology, and society as a whole, and touches all medical branches, economy, law, ethics, etc. Required knowledge and business management skills are different depending on the management level.

Transfusion medicine in Croatia is financed from the state budget, which is the main source of macroeconomic and financial instability. Because of the risk of transfusion-related side effects, this medical profession is more regulated by laws, regulations, and medical standards than any other medical profession.

Health law is still not a specially recognized branch of the law, and the subject of health law, in its entirety, is of interest to the Republic of Croatia, which is performed as a public service and according to the professional medical doctrine of healthcare workers. The principles of health care in Croatia are contained in the Act on health care and the Act on the Protection of Patients` Rights and include three principles: comprehensiveness, continuity, and availability of health care. These are the principles that are also used in the transfusion treatment of patients.

Keywords: transfusion medicine, economic aspects, legal aspects

Health is a fundamental human right that has a great role and significance in the quality of human resources.

The health of a nation contributes to the well-being of society and has a major impact on the economic competitiveness of the national economy. The health system is also a strategic part of the economy in many countries.

Transfusion medicine is a specific medical profession that combines science, technology, and society as a whole, and touches all medical branches, economy, law, ethics, etc.

The required knowledge and management skills are different depending on the management level.

Management levels are divided into central (strategic, political, and planning), middle (organizational, regional, and local), and active (operational, implementation), and the relationship of the necessary share of clinical and managerial skills changes at these three management levels.

The reorganization of the transfusion service in the Republic of Croatia began a decade ago without complete pre-analytical information about operational solutions and their effects, which created an unstable environment, mainly for authorized institutions that deal in the collection and production of blood products (blood banks), which are still part of the hospital system.

State-owned Croatian hospitals are an important and cost-intensive part of the public sector

healthcare system. The focus of the economic perspective is on the search for rational and profitable activities for each business entity.

Hospitals in the economic sense can be treated as business entities with atypical business characteristics.

The operation of hospitals is of a hybrid type and combines the logic of business management and social availability which is legally conditioned. All input costs have a market rate value (in transfusion medicine, only the raw material is "free"), and the prices of hospital services are determined by non-market valuation. Blood has the status of a public good.

In 1963, Kenneth Arrow was the first to clearly define the conceptual differences between health and other goods. The production and consumption of health are characterized by exceptional state regulation, uncertainty woven into the system at different levels (costs, revenues, prices, possible savings, measurement of effects, etc.), asymmetric information is strongly present (patient-doctor, patient-insurance company), the existence of barriers to entering the market and the existence of externalities.

Economic research on healthcare in the Republic of Croatia is rare due to the limited availability of data, and closed systems and because, historically and traditionally, healthcare is discussed by experts from the medical profession, which causes problems in communication with economic experts.

The health care system in the Republic of Croatia has been announcing reforms and/or their implementation for a long time. These reforms are implemented in each country within the framework of national economic opportunities and existing institutional limitations and there is no single international recipe for successful healthcare reform. In public health policy – politics choose, and the state finances allow the model of public health care. Adaptation of the domestic healthcare system to good, foreign practices often does not result in equally successful solutions. The specificity of the institutional environment creates the need for its own adaptation, and this adaptation can be innovative, but it does not have to be economically

efficient at the same time. More recent analyses (Hall and Jones, 2004, Nordhaus, 2003) show that the increase in health expenditures reflects a natural course of economic development (the wealthier the environment, the more people spend on health maintenance, the constant development of medical technologies, a greater number of the aging population is medically treated and the increase in the number of chronic diseases). In Croatia, health expenditures did not grow faster than the entire economy.

Transfusion medicine in Croatia is financed from the state budget, which is the main source of macroeconomic and financial instability. How to slow down the growth of healthcare expenditures without reducing the quality and scope of health services is a very complex issue.

Healthcare institutions that produce blood products must comply with laws and professional standards and apply the requirements of good processing practice. In Croatia, blood, blood products, and plasma derivatives are legally equated with drugs, and liability for harmful side effects that are caused during transfusion treatment due to incorrect handling or transfusion (due to ignorance or negligence) is borne by the health institution where the patient is treated.

In every treatment, there is a probability of side effects and damage, and the unwritten rule is that the greater the benefit from the treatment, the more acceptable the risk of side effects. Because of the danger of side effects, transfusion activity is more regulated by laws, regulations, and medical standards than any other medical profession. Health law is still not a specially recognized branch of the law, and the subject of health law, in its entirety, is of interest to the Republic of Croatia, which is performed as a public service and according to the professional medical doctrine of healthcare workers.

Ethics in transfusion medicine is complex because there are three subjects (donor, patient, and doctor). The patients are looking for a sufficient number of blood products, they want as many donors as possible, and they don't think about the interests of the donor and whether they are allowed to give blood. The doctor must ensure a sufficient number of blood products and must not harm the donor or the patient.

The principles of health care in Croatia are contained in the Health Care Act and the Act on the protection of patients' rights and include three principles: comprehensiveness, continuity, and availability of health care. These are the principles that are also applied in transfusion treatment for all the people residing in the territory of the Republic of Croatia, from diagnosis to the completion of treatment, with equal treatment conditions for all healthcare users.

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MODERN TOOLS IN IMMUNOHAEMATOLOGY

Erwin A. Scharberg[1,2]
[1]Institute of Transfusion Medicine and Immunohaematology Baden-Baden, Germany
[2]German Red Cross Blood Service Baden-Wuerttemberg-Hessen

Abstract

The testing of red cell antigens and the detection and identification of antibodies to red cell antigens are the most important and challenging issues in transfusion medicine. They are critical to providing patients with compatible blood products. Frequent problems in the pre-transfusion diagnostics are unspecific reactions in patients with free warm and/or cold autoantibodies, HLA-antibodies, antibodies to high and low prevalence antigens, multiple antibodies with similar serological behavior, antibodies to antigens which are not declared on the antigen tables of the identification panels and the therapeutic use of monoclonal antibodies. To solve these problems different serological test methods, as well as extended phenotyping and genotyping of the patient for red cell antigens, are used. To identify difficult antibodies rare blood cells are necessary. The enzyme treatment of the red cells, absorption and elution techniques, and the use of recombinant blood group antigens are also part of the diagnostics. In complex cases, a combination of different methods and techniques is needed.

Keywords: blood group antigens, blood group genotyping, recombinant blood group proteins

Antigen Typing

The testing of red cell antigens in blood donors and blood recipients is the basic and most important part of pre-transfusion diagnostics. Depending on the national guidelines the testing includes different mandatory typing ranging from ABO only up to ABO, RhD, RhCcEe, K, and the RhD genotyping of serologically RhD negative donors. Testing of additional blood group antigens in blood donors and recipients is needed to provide compatible blood products for patients with clinically significant red cell antibodies. There are 381 red cell antigens recognized by the ISBT Working Party on Red Cell Immunogenetics and Blood Group Terminology [1].

The red cell antigen testing is performed by a variety of serological methods mostly using the hemagglutination tests. The testing has different significance for blood donors and recipients. Because of possible false negative reactions with weak or partial antigens, the typing of blood donors requires more sensitive techniques and reagents. For typing the ABO, RhD, RhCcEe, K, Fy(a/b), Jk(a/b), S, s, M, and N monoclonal IgM sera have become standard reagents. However, for the very most antigens, no certified commercial sera are available [2].

In the last two decades, molecular DNA typing of blood group alleles has become available for routine. Providing genotypes gives essential information in predicting the phenotype of red cell antigens when serological testing is not possible because of reagent and technical limitations or in pre-transfused patients [3, 4].

Antibody Detection and Identification

The second essential part of immunohaematology is the detection and identification of antibodies to red cell antigens. It is one of the most important and challenging issues in transfusion medicine. In the routine, it is impossible to find antibodies to all known antigens. The most important scope is to detect and identify clinically significant antibodies and to provide the patients with compatible blood products.

Frequent Problems in the Diagnostics and the Solutions

Unspecific reactions in patients with free warm and/or cold autoantibodies: The most important focus in these patients is to rule out underlying alloantobodies.
The use of different techniques (gel, tube, solid phase), pre-warming of reagents, enzyme treatment (papain, bromelain, etc.) and auto- and/or alloadsorption with enzyme-treated red cells are the most helpful and promising methods to get rid of this frequent annoying technical problem.

HLA-antibodies:

They are not significant for red cell transfusions and pregnancies but when cross-reacting with red cells they can cause unclear positive reactions in antibody screen and identification testing or cross-matches. HLA-antibodies are significant for platelet transfusions and can reduce the survival time of platelets. The very most patients with HLA-antibodies (more than 90%) are women with a pregnancy history. The HLA-antibody testing of a patient's plasma is the best direct confirmation method.

Antibodies to high prevalence antigens:

The identification of these antibodies and the exclusion of additional underlying alloantibodies are the most challenging issues of pre-transfusion diagnostics. Usually, the testing is possible in reference laboratories only. The most important tools are libraries of frozen rare test red cells, which are negative for high prevalence antigens, and a collection of anti-sera to high prevalence antigens. These reagents are not commercially available and require participation in international exchange programs like SCARF (Serum, Cells, and Rare Fluids Exchange Program). In the last decade, recombinant blood group antigens (rBGA) have become available (table 1). In many cases, they are extremely useful to neutralize antibodies to a number of high prevalence antigens [5], [6], [7].

Antibodies to low prevalence antigens:

They are rarely found by case because the standard antibody screening and identification panels usually do not contain red cells positive for low prevalence antigens. They do not cause problems in providing patients with compatible red cells but they can be important and dangerous when undetected in pregnancies and in countries not performing cross-matches [8], [9].

Multiple antibodies with similar serological behavior

The presence of common antibodies to several antigens in one patient can be a serious diagnostic problem imitating antibodies to high prevalence antigens. Ruling out additional antibodies and providing compatible blood can get very difficult. Serological and/or molecular blood group typing of the patient are the most useful tool to identify the antibodies.

Antibodies to antigens that are not declared on the antigen tables of the identification panels:

The commercial antibody identification panels usually contain red cells typed for 25 to 30 antigens only. However, there are 381 presently recognized red cell antigens. In some cases, it is impossible to identify a specifically reacting antibody fitting no pattern on the antigen tables. “Classical” specificities are antibodies to Dombrock, Knops, Cost, Cartwright, Colten, Scianna, Chido, Rodger, etc. antigens. The use of genotyped test cells in antibody identification panels extends the range of detectable antibody specificities, accelerates antibody identification, and improves pre-transfusion diagnostics [10], [11].

Therapy with monoclonal antibodies (anti-CD38, anti-CD47):

The successful implementation of monoclonal antibodies for therapy of diseases like multiple myeloma has caused serious problems for pre-transfusion diagnostics because some of the antibodies (anti-CD38, anti-CD47) react with all test cells in antibody testing and cause positive cross-matches. To provide compatible blood products it is recommended to perform an extended serological or molecular typing of the patient for the most clinically significant antigens (RhD,C,c,E,e,, K, Fy(a/b), Jk(a/b), S, s) and if possible to provide matched red cell units.

DDT-treated red cells still carry most red cell antigens but they are CD38 negative. DDT-treated antibody screening and cross-matches help to exclude underlying alloantibodies in the patient’s plasma. The use of serologically typed red cells of other patients who usually get CD38 negative after a few weeks of treatment is also extremely useful.

Conclusion

The modern tools in immunohaematology consist of different serological test methods as well as extended phenotyping and genotyping of the patient for red cell antigens. To identify difficult antibodies rare blood cells are necessary, which are not commercially available. The enzyme treatment of the red cells, absorption and elution techniques, and the use of recombinant blood group antigens are also part of the diagnostics. In complex cases mostly the combination of different methods and techniques is needed.

Table 1. Available Recombinant Blood Group Antigens (rBGA

Chido(a)	R_Ch(a)	**C4B*3**
CROM/DAF	R_CROM	Cr(a+), Tc(a), **Dra+**, Esa+, IFC+, WES(b), UMC+, GUTI+, SERF+, CROZ+, CROV+, ZENA+, CRAM+, CROK+, CORS+
Dombrock(a)	R_Do(a)	**Do(a)**, Hy+, Jo(a+), DOLG+, DOYA+, DOMR+, DOLC+, DODE+
Dombrock(b)	R_Do(b)	**Do(b)**, Hy+, Jo(a+), DOLG+, DOYA+, DOMR+, DOLC+, DODE+
Duffy(a)	R_Fy(a)	**Fy(a)**, Fy6
Duffy(b)	R_Fy(b)	**Fy(b)**, Fy6
Kell-Kp(b)-Js(a)	R_grKba	Js(a), K12+, Ul(a-), K19+, TOU+, K23-, K13+, K22+, K11, **Kp(b),** RAZ+, VLAN+, **K**, K14/24, K18+, KASH+, KELP+, KYO-, KHUL+, KTIM+, KUCI+, KANT+, KETI+, KALT+, VONG+
Indian(b)	R_In(b)	**In(b)**, INFI+, INJA+, INRA+, INSL+
JMH	R_JMH	**JMH1**, JMH2, JMH3, JMH4, JMH5, JMH6
Cellano-Kp(b)-Js(a)	R_klkba	Js(a), K12+, Ul(a-), K19+, TOU+, K23-, K13+, K22+, K11, **Kp(b)**, RAZ+, VLAN+, **k,** K14/24, K18+, KASH+, KELP+, KYO-, KHUL+, KTIM+, KUCI+, KANT+, KETI+, KALT+, VONG+
Landsteiner-Wiener(a)	R_LW(a)	**LW(a)**
Rodgers(a)	R_Rg(a)	**C4A*3**
Sciannа1	R_Sc1	**Sc1**, Rd-, SCAN+, STAR+, SCER+
Xg(a)	R_Xg(a)	**Xg(a)**
Cartwright(a)	R_Yt(a)	**Yt(a)**, YTEG+, YTLI+, YTOT+
Kn(a)/DACY NEU	R_CR1_2	**Kn(a)**, McC(a), Sl(a), Sl3+, KCAM+, Yk(a), DACY
YCAD NEU	R_YCAD	YCAD
Lutheran(a)/Au(a) NEU	R_Lu(a)_2	**Lu(a)**, Lu4+, Lu5+, Lu6, Lu8, Lu12+, Lu13+, Lu16+, Lu17+, Lu20+, Lu21+, LURC+, Lu7+, Lu23, Lu24, Lu25, Lu27, Lu18
Lutheran(b)/Au(b) NEU	R_Lu(b)_2	**Lu(b)**, Lu4+, Lu5+, Lu6, Lu8, Lu12+, Lu13+, Lu16+, Lu17+, Lu20+, Lu21+, LURC+, Lu7+, Lu23, Lu24, Lu25, Lu27, **Lu19**

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NEW BLOOD GROUPS SYSTEMS AND ANTIGENS RECOGNIZED BY THE ISBT FROM 2019 TO 2021

Christoph Gassner[1, 2]
[1]Institute of Translational Medicine, Private University in the Principality of Liechtenstein, Triesen, Liechtenstein
[2]Institute of Clinical Molecular Biology, Christian-Albrechts-University, Kiel, Germany

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Conflict of interest statement
CG acts as a consultant to inno-train Diagnostik GmbH, Kronbergi.T., Germany. Procedures for the molecular detection of *GYPB* deletions for S-s-U- phenotype diagnostics have been granted as a European patent (EP 3 545 102 B1). Similar content patent US application is pending.

Abstract
The International Society of Blood Transfusion (ISBT) Working Party (WP) for Red Cell Immunogenetics and Blood Group Terminology (RCI & BGT) [1] is responsible for the ratification and naming of blood group systems and antigens.

With the detection of at least one natural human alloantibody directed against an erythrocyte antigen and the description of the causative DNA polymorphism on a gene different from all other genes encoding antigens of existing blood group systems, the core criteria [1] for the recognition of a candidate new blood group system by the WP are fulfilled. Similarly, new blood group antigens of existent systems are defined using the same criteria on known genes.[1]

Since the last report in 2018 [2], the WP has held four business meetings until June 2021. All 27 members (as of August 2022) and researchers who wanted to present new blood group systems or antigens were invited to the WP business meetings. Their observations were discussed and the systems and antigens were finally approved or rejected. This manuscript summarises the ratification of seven new blood group systems and 15 new antigens from existent systems by the WP from 2019 to June 2021.

Keywords:blood groups, red cell antigens, terminology, genetics, genomics

New Blood Group Systems 2019 to 2021
Seven new blood group systems were recognized by the WP and added to the existing 36 from 2019 to 2021.

System 037: KANNO
An antibody to a high-prevalence antigen, designated KANNO, was first identified in 1991 in a Japanese woman with a history of pregnancy.[3] Genome Wide Association Studies (GWAS) defined single nucleotide variants (SNVs) in four unrelated individuals with anti-KANNO on the *PRNP* gene, which were absent in 415 healthy Japanese. The causal variant is defined by rs1800014, c.655G>A on PRNP resulting in p.Glu219Lys, which has a frequency of 5.8% in Japanese, but is only rarely observed among Black Africans and Europeans.[4]

System 038: SID
The chemical basis of the Sd^{a}antigen was known to be a terminal trisaccharide and the candidate synthetase gene *B4GALNT2* had been cloned in 2003. Nevertheless, the genetic basis for the Sd(a−) phenotype remained unknown. Only 2-4% of Caucasians are truly negative and can make anti-Sd^a. The most common variant observed was rs7224888:C, c.1396T>C causing a homozygous p.Cys466Arg change in six of nine investigated Sd(a−) individuals.[5]

System 039: CTL2
Compatibility testing showed five unrelated subjects from Morocco and one female patient from Europe lacking a high-prevalence antigen on Red Blood Cells (RBC). Whole Exome and Sanger sequencing identified a c.1192C>A, p.Pro398Thr Single Nucleotide Variant (SNV) located on the *SLC44A2* gene (also known as *CTL2*) in all Moroccan samples.[6] The European subject exhibited a large deletion of the *SLC44A2* gene. The protein encoded by the *SLC44A*2 gene also carries HNA-3 (Human Neutrophil Antigen).

System 40: PEL

PEL– RBCs have been found only in four unrelated French-Canadian families from the province of Quebec. Integrated genomic and proteomic studies pinpointed ABCC4 as the likely candidate protein for PEL antigen expression. All PEL- cases showed a large, homozygous deletion of the *ABCC4* gene with the same breakpoint in all PEL− cases. [7]

System 041: MAM

Severe or even fatal Haemolytic Disease of the Fetus and Newborn (HDFN) has been reported in MAM negative individuals. Whole Exome and Sanger sequencing from ten MAM− subjects revealed *EMP3* as a candidate gene for the expression of MAM. A total of four different allelic/haplotypic mutant variants were identified in MAM– individuals: a total gene deletion, two different single-exon deletions, and a most frequently observed substitution, creating a stop codon with a frequency of 0.017%.[8]

System 042: EMM

The new blood group system EMM was reported independently by two teams.[9,10] Antibodies to a high-prevalence antigen, Emm, were first described in 1987. Using Whole Exome Sequencing, both teams identified a variety of different loss of function mutations in the *PIGG* gene, e.g. a 2 bp deletion, c.2624_2625delTA, a c.640C>T (p. His214Tyr), and deletions of exons 2-3, exon 6, and exons 7-9.[9,10] The PIGG enzyme is involved in the synthesis of the GPI protein anchor in the red cell membrane.

System 043: ABCC1

An antibody to an unknown high-prevalence red cell antigen was detected in a young Brazilian man.[11] Parents of the proband were first degree cousins. Whole Exome Sequencing, is defined a homozygous large deletion encompassing five exons in the *ABCC1* gene in the proband and the compatible sibling.

New Blood Group Antigens in Existing Blood Group Systems 2019 to 2021

Fifteen new blood group antigens were recognized in total by the WP from 2019 to 2021 and added to existing blood group systems (Table 1).[12 -24] These included high- and low-prevalence antigens. Of note, low-prevalence antigen SUMI (ISBT 002050)is the 50th MNS antigen to be ratified by the WP.[12] Serologic screening revealed that 23 of 541.522 Japanese individuals (0.0042%) were SUMI+. CETW (ISBT 002063), located on *RHCE* was shown on the RBC of two indigenous Australian individuals. The new KACY and YCAD of the Knops blood group system represent two antithetical antigens with alloimmunizations against them difficult to interpret.[21]Besides the Kg antigen (previously in the 700 series), all other new antigens represented *de novo* discoveries.[24] Of note, commercially available soluble recombinant proteins are more and more becoming invaluable diagnostic tools for the specification of allo-antibodies, both in routine and scientific applications.

Conclusion

Considering the described new blood group systems and antigens, the ISBT recognized 378 antigens of which 345 were clustered within 43 blood group systems by the end of June 2021. It is of note that advances in genomic, proteomic, and cellular technologies are contributing to this current wave of discoveries. This is contributing to both *de novo* discoveries and resolving antigens previously listed in the ISBT 200, 700, and 901 series. The ongoing recognition of new blood group systems and antigens underscores the diverse and complex biology of the red cell membrane. The curation of blood group systems, antigens, and associated alleles is of clinical significance to provide accurate typing and reporting for both donors and patients in the transfusion and antenatal settings.

Table 1. New blood group antigens ratified by the ISBT Working Party Red Cell Immunogenetics and Blood Group Terminology from 2019 until June 2021.

BG System	ISBT Antigen Number	Alternat. Name	Antigen Prevalence	Allele Name	Gene	Molecular Basis	Protein Change	SNV (rs-number)	Ref.
MNS	ISBT 00250	SUMI	Low	*GYPA*50*	*GYPA*	*c.91A>C*	p.Thr31Pro	pending	[12]
RH	ISBT 00463	CETW	Low	*RHCE*open*	*RHCE*	*c.486C>G*	p.Asn162Lys	rs199725473	[in press]
LU	ISBT 00528	LUNU	High	*LU*02.-28*	*BCAM*	*c.121G>A*	p.Val41Met	rs957795435	[13]
LU	ISBT 00529	LURA	High	*LU*02.-29*	*BCAM*	*c.1351A>C*	p.Lys451Gln	rs28399630	[14]
DI	ISBT 01023	DIST	Low	*DI*02.23*	*SLC4A1*	*c.1447G>A*	p.Gly483Ser	rs544557335	[15]
SC	ISBT 01308	SCAR	High	*SC*01.–08*	*ERMAP*	*c.424C>G*	p.Gln142Glu	pending	[16]
SC	ISBT 01309	SCAC	High	*SC*01.–09*	*ERMAP*	*c.217C>T, c.219C>T*	p.Arg73Cys, p.Arg73Cys	rs149787850, rs33954154	[17]
GE	ISBT 02012	GECT	High	*GE*01.–13*	*GYPC*	*c.59C>T*	p.Pro20Leu	rs143216051	[18]
GE	ISBT 02013	GEAR	High	*GE*01.–14*	*GYPC*	*c.333A>C, c.118G>A*	silent, p.Gly40Arg	rs1050967, rs772372126	[19]
KN	ISBT 02210	KDAS	average	*KN*01.10*	*CR1*	*c.4843A>G*	p.Ile1615Val	rs6691117	[20]
KN	ISBT 02211	DACY	average	*KN*01*	*CR1*	*c.3623A*	p.His1208	rs2274567	[21]
KN	ISBT 02212	YCAD	average	*KN*01.12*	*CR1*	*c.3623A>G*	p.His1208Arg	rs 2274567	[21]
JMH	ISBT 02607	JMHN	High	*JMH*01.–07*	*SEMA7A*	*c.709G>A, c.1545A>G, c.1865G>A*	p.Asp237Asn, p.Gln515Gln, p.Arg622His	rs140707085, rs741761, rs140128092	[22]
JMH	ISBT 02608	JMHA	High	*JMH*01.–08*	*SEMA7A*	*c.507C>T, c.556G>A, c.1545A>G*	p.Tyr169Tyr, p.Glu186Lys, p.Gln515Gln	rs2075589, rs572867366, rs741761	[23]
RHAG	ISBT 03005	Kg	Low	*RHAG*01.–03*	*RHAG*	*c.490A>C*	p.Lys164Gln	rs144305805	[24]

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BLOOD COMPONENTS-OLD CHALLENGES NEW APPROACH

Vesna Libek
Blood transfusion service, Clinical Hospital Center Zemun

Abstract

There are higher demands for blood component therapy and simultaneously regular donor populations aging. At the same time, there is an increasing lack of platelet concentrates (PC). The PC supply could be improved through expansion of the apheresis pool donors, and improvement in component processing and storage that result in a longer platelet shelf life in additive solutions.

To show our 13 years of continuous improvement in the automation of blood processing to increase efficiency, eliminate human errors and avoid deviations associated with multiple manual steps.

The components' adequate quality and their complete utilization are done through automation, from collection to separation, continual education of staff, and implementation of SOP and GMP. The initial step of blood collection on automatic scales through automation in processing leads to standardized platelet concentrates from the BC system.

Donation time on automatic scales was 5.99 ± 1.22 seconds; the level of F II 95.56 ± 23.34 %; F V 84.96 ± 15.76 %; F VII 102.89± 11.67 %; F VIII 105.94 ± 30.67 % and AT 89.23 ± 19.75 in plasma components immediately after processing and before freezing. On automatic separators, processed PC from T&B blood bags had average190, 39x109 Plt/unit and from T&T average 102, 08x109Plt/unit. pH in Plt concentrates, on the sixth day of the stocking period was an average 7,41.

Automation has become a milestone in the optimization of blood processing due to standardization and traceability, increasing the quality of blood components and minimizing procedural errors.

Keywords: automation, blood processing, safety

Sažetak

Postoji povećanje zahteva za terapijom komponentama krvi uz istovremeno starenje aktivne populacije donora. Istovremeno nedostaje sve više koncentrata trombocita (KT). Snabdevanje KT može se obezbediti kroz povećanje broja donora afereznih trombocita i poboljšanjem procesiranja komponenata i produžetak vremena **čuvanja** KT u aditivnim solucijama.

Prikaz našeg iskustva u toku 13 godina neprestanog poboljšanja u automatizaciji procesiranja krvi, s ciljem povećanja efikasnosti, eliminaciji ljudskih grešaka i izbegavanju odstupanja zbog višestrukih manuelnih koraka.

Komponente zahtevanog kvaliteta i potpune iskoristljivosti se dobijaju kroz automatizaciju, od kolekcije do separacije, kontinuiranom edukacijom osoblja i uvođenjem SOP-ova i GMP. Inicijalni korak, kolekcija krvi na automatskim vagicama mešalicama sa automatizacijom u precesiranju, vodi standardizovanim KT iz ``buffy coat``-a (BC).

Trajanje donacije na automatskim vagicama mešalicama je 5,99 ± 1,22 sekunde; nivo F II 95,56 ± 23,34%; F V 84,96 ± 15,76%; F VII 102,89 ± 11,67%; F VIII 105,94 ± 30,67% i AT 89,23 ± 19,75 u komponenti plazme odmah posle procesiranja, a pre zamrzavanja. KT procesirani na automatskim separatorima iz T&B kesa u proseku su imali 190, 39x10^9Tr/jedinica iz T&T kesa u proseku 102, 08x10^9Tr/jedinici. ***Šestog dana skladištenja pH u KT je bio prosečno 7,41.***

Automatizacija je oslonac optimizacije procesiranja krvi kako zbog standardizacije i sledljivosti, istovremeno povećavajući kvalitet komponenata i minimizirajući proceduralne greške.

Ključne reči: automatizacija, procesiranje, sigurnost

Contemporary transfusion medicine is a synergy of basic and clinical transfusiology. The up-to-date diagnostic procedures are guidelines in clinical transfusion medicine for well-chosen blood component therapy for the best benefit of patients. If the double helix is an icon of the modern age where is the story of blood components processing development (1, 2)?

According to the World Health Organization (WHO), more than 117 million whole blood (WB) units are collected annually worldwide, 42% in highly developed countries which represent 16% of the world population (3). There are higher demands for blood component therapy and the aging donor population. Hemoglobin (Hb)-based oxygen (O2) carriers (HBOCs) are being developed as alternatives to red blood cells and blood when these products are unavailable (4). A possible alternative is also the production of red cells from adult progenitor cells and progenitor cells from the belly button. These in vitro available methods cannot provide sustainable red cell supplies (5).

At the same time, the likelihood of critical platelet shortages is increasing. The platelet supply could be improved through the expansion of the apheresis donor pool, and improvement in component processing and storage that result in a longer platelet shelf-life in additive solutions (6).

Whole blood collected units are processed by centrifugation, filtration, and freezing. Introducing a component collection by apheresis, there was a great improvement in patient therapy, its quality as in adequate providing demanded components.

Blood components are standardized according to regulatory guidelines of the Council of Europe (7). Automation of blood processing has been aimed at increasing efficiency, eliminating human errors, and avoiding deviations associated with multiple manual steps which can get medical staff tired (8, 9, 10).

There are 81 million blood units transfused all over the world every year and there is a constant search for balance between the implementation of PBM (Patient blood management), individual and evidence-based access to patients, and

blood component therapy (1).PBM and the continuous improvement in blood processing can overcome demographic changes in the world, new arbovirus infections, discrepancies in blood donation numbers, and the high demand for specific blood components. The component's adequate quality and its complete utilization are done through automation, from collection to separation, continuous medical education of the staff, and implementation of SOP (Standard operative procedure) and GMP (Good manufacturing practice) (11).

The initial step in blood processing depends on the choice of blood bag's structure, with "inline filters" for whole blood or erythrocytes, with additive solution and adequate blood bags plastic. Long-term exposure to DEHP (2-ethylhexyl phthalate) and its metabolite from blood bags plastic, can influence multi-transfused patients (12).

The best choice in the initial step of blood collection is to use automatic scales with direct complete data transfer to a computer system (flow rate, duration of the donation), that enables initial quality control of donated blood. In a research Libek et al. Vox Sang (2014) 107:1:109, all controlled elements were in consent with quality control: donation time 5,99 ± 1,22 seconds; level of F II 95,56 ± 23,34 %; F V 84,96 ± 15,76 %; F VII 102,89 ± 11,67 %; F VIII 105,94 ± 30,67 % and AT 89,23 ± 19,75 in plasma components immediately after processing and before freezing (13).

Continuous temperature control in both, the transport chain and during processing, with "data loggers", temperature indicators, is necessary. Donated blood should be cooled for further processing on cooling plates with butanediol wax.

Blood components could be processed from whole blood through centrifugation, or collected by apheresis method. Centrifugation conditions and initial filtration of whole blood dictate further processing. The requested quality can be achieved by adapting all these parameters. Implementation of top-bottom blood bags, automation in processing standardized blood components is achieved and better efficiency in work (14).

The most prevalent system for blood processing in the last decades, in Europe, has been the semi-automated buffy coat system, for platelet concentrate components. This blood components production process requires numerous repetitive and time-consuming steps. By automation, this can be avoided, as well as potential human errors, and some deviation because of many manual steps (15,16). With added pathogen inactivation, the blood components' safety is improved.

The data in a study about platelet concentrate processed from T&B and T&T blood bags showed that there were no significant differences in platelet quantity, either in PC from T&B or from T&T blood bags (from T&B 190, 39 X109 Plt/ unit and from T&T 102, 08 X109 Plt /unit. Bacteriological control was negative in each tested unit (1,33% of all processed units) (11).

The study of measuring pH in Plt concentrates on the sixth day of the stocking period (average 7, 41) bothpCO2 and pO2, indicated that there was no significant accumulation of anaerobic metabolic products. That is one reason for recommending a prolonged stock period of Plt concentrates, more than 5 days in additive solutions with bacteriological control (17).

Refrigerated platelets, stored at 1° to 6°C, have the potential to improve patient safety and health status by improving hemostatic effectiveness in actively bleeding patients, and decreasing the risk of bacterial contamination while concurrently allowing Plt concentrates for a longer storage period of 14 days (18). The stable donor apheresis platelet pool combined with pathogen reduction of platelet components enables safe therapy for patients.

In the past decades, we have adopted increased levels of automation. More recently, a fully automated system able to process simultaneously, with a single centrifugation step (for example, Reveos, Terumo BCT), whole blood units into plasma units, red blood cell (RBC) concentrates, interim platelet units (IPU), and residual bags of white blood cells (WBCs). After this separation steps, further modification is enabled like RBC filtration, pooling of 4 to 6IPU with adding additive solution, and filtration of such platelet concentrate. Simultaneously quality residual plasma is obtained, which can be used for further fractionation so the constantly growing demands for blood derivates in Europe can be satisfied (6).

Good quality equipment ("blast shock" freezers, irradiation component devices, pathogen reduction devices, sterile connection) with the utilization of different additive solutions allows the processing of quality and standardized modified blood components in a completely closed system. Complete hemovigilance of all processed components is enabled by archiving samples of all donated whole blood units or apheresis components (13–17).

Automation has become a milestone in the optimization of blood processing due to standardization and traceability, increasing the quality of blood components, and minimizing procedural errors. Continual education of medical technicians can be carried out by equipment usage or by"online"(e-learning). The synergy of automation and staff skills in processing enable also the clinical efficiency in the therapy with blood components.

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PREVENTION, IDENTIFICATION AND MANAGEMENT OF INFECTION CAUSED BY THE COVID-19 PANDEMIC IN HEALTHCARE INSTITUTIONS

Olivera Savić, Biljana Martinović
Blood transfusion Institute of Serbia, Belgrade

Abstract

World history records many epidemics/pandemics. Respecting the legal regulations in the Institute for Blood Transfusion of Serbia (IBTS), established the Commission for Hospital Infections. Becoming the first health institution that drafted the Act on risk assessment at the workplace and in the working environment, IBTS's action plan for measures and activities was to maintain continuity and functionality in the conditions of the 2009 influenza pandemic. A formed Tim that created the aforementioned documents was obliged to monitor the emergence of new harms.

In 2019, during the infection with a new type of virus WHO, EBA, ECDC, and the Institute of Public Health regularly sent information and instructions about how to act. Prevention, identification, and management of infection were performed in relation to providers (employees) and recipients of services (VBD and patients).

Measures were taken to prevent contact, physical separation of work teams, and controlled movements for everyone in the institution were implemented. The use of protective equipment was introduced for all categories. Disinfection of the blood path and patient reception area was carried out once a day. Once a week, the entire institution was disinfected, twice by specialized units. The reporting of the sick and the implementation of isolation measures became mandatory. The level of the protective equipment and the frequency of disinfection were changing during the pandemic.

Keywords: risk management, Action Plan

Sažetak

Istorija sveta beleži brojne epidemije/pandemije. Poštujući pozitivne zakonske propise u Institutu za transfuziju krvi Srbije (ITKS) formirana je Komisija za bolničke infekcije. ITKS je bio prva zdravstvena ustanova koja je izradila Akt o proceni rizika na radnom mestu i u radnoj okolini, Akcioni plan ITKS za mere i aktivnosti na održavanju kontinuiteta i funkcionalnosti u uslovima pandemije gripa 2009. Formiran je Tim za izradu pomenutih dokumenata i praćenje pojave novih štetnosti i opasnosti.

Krajem 2019. godine registrovana je infekcija novim tipom virusa. SZO, EBA, ECDC i Institut za javno zdravlje redovno su slali informacije, uputstva o postupanju u novonastaloj situaciji. Prevencija, identifikacija i upravljanje infekcijom obavljana je u odnosu na davaoce (zaposlene) i primaoce usluga (DDK i pacijenti).

Preduzete su mere radi sprečavanja kontakata, fizičkog odvajanja timova za rad, kontrolisanog kretanja zaposlenih i stranaka krozustanovu. Uvedeno je korišćenje zaštitne opreme za sve kategorije, svakodnevno je obavljana dezinfekcija svih radnih i pomoćnih prostorija puta krvi i prijema pacijenata, jednom nedeljno dezinfekcija se sprovodila u celoj ustanovi, nakon završenog radnog procesa. U dva navrata je obavljena dezinfekcija od strane specijalizovane jedinice. Uvedeno je prijavljivanje obolelih i sprovođenje mera izolacije. Nivo zaštitne opreme, učestalost dezinfekcije se menjao tokom trajanja pandemije.

Ključne reči: upravljanje opasnostima, akcioni plan

Quality management within an institution implies controlled and documented management of work processes, but also employee protection and preservation of the working and living environment. As a working principle, the P (plan) D (do) C (check) A (act) method (1) is most often applied (1).

World history records many epidemics/pandemics, from the plague of Thucydides in 430 BC to MERS (2012-2020). Mass outbreaks of infectious diseases and their transmissions are associated with wars, that is, with large population migrations. The end of the 20th and the beginning of the 21st century were marked by wars, and thus by mass and frequent migrations of the population, there was an increase in the number of businesses, tourism, and travel, so it could be expected that some new agent would spread rapidly.

Respecting the legal regulations in the Institute for Blood Transfusion of Serbia (IBTS), the Commission for Hospital Infections was established in 2006. Becoming the first health institution that drafted the Act on risk assessment at the workplace and in the working environment, IBTS's action plan for measures and activities was to maintain continuity and functionality in the conditions of the 2009 influenza pandemic. A formed Tim that created the aforementioned documents was obliged to monitor the emergence of new harms, but also to monitor the measures of eliminating, reducing, and preventing risks (2, 3).

In 2019, the infection with a new type of virus SARS Cov-2 was registered. In March 2020, WHO declared a pandemic, and the Government of Serbia declared a state of emergency. Together with EBA, ECDC, and the Institute of Public Health, WHO regularly sent information, and instructions about how to act (4). Prevention, identification, and management of infection were performed in relation to providers (employees) and recipients of services (VBD and patients).

An effective and accurate risk assessment must be based on accurate data and it is necessary to determine adequate and proportionate action. It is necessary to take into account:

- the extent of the spread of the COVID-19 infection in the country,
- the level of circulation in the community,
- the work of the local epidemiological service,
- the quality of the health care system,
- readiness of public health for an adequate response (5).

Every epidemic, including this one, has the potential to lead to a reduced supply of blood and blood components and to negatively affect the entire Transfusion Service (6).

As a first step, IBTS created a plan of measures to prevent the spread of the epidemic of the infectious disease COVID-19. In order to ensure adequate personal protection of the agents, it was necessary to determine the level of danger. The level of risk, partly, depends on the need for close contact with people known or suspected to be infected with SARS-CoV-2, or the need for repeated or prolonged contact with people known or suspected to be infected with SARS-CoV-2. Jobs can be very high risk, medium risk, and low risk (6).

Employees who work on the collection of blood and blood components cannot be described as health workers in the traditional sense, since they work with healthy people. Donors are healthy people; they don't come to donate blood if they don't feel well (7). Blood collection jobs generally fall under the lower risk of exposure. For this category, in addition to standard precautions against blood-borne pathogens (8, 9), basic procedures are recommended: washing hands, covering coughs, cleaning surfaces, and disinfecting hands, tissues, and waste containers (10). Patients who come to IBTS are outpatients with health problems of a non-infectious nature, such as determination of blood group (pregnant women, preparations for surgical interventions), disorders of coagulation and humoral immunity, and HLA typing. These are the patients in relation to which protection is applied for VBD (10, 11). Infection with the SARS-CoV-2 virus can be transmitted between employees who work together, ergo, are in contact with each other, so protective measures must also be applied in areas where there are no service users (rest area) (3, 11).

At IBTS, measures were taken to prevent contact, physical separation of work teams, and controlled movement of employees and parties through the institution. Some European transfusion services were able to introduce appointments, which unfortunately we, in Serbia, could not. Reception of VBD who came to the institution was done. The reception was also carried out at mobile collection points with the application of prescribed protection measures. Patients came at scheduled times (e.g. INR control), submitted already taken samples, and if they came to IBTS, minimal detention was organized and only in the area of the Reception Laboratory.

The use of personal protective equipment was introduced for all categories. Disinfection of all working and auxiliary rooms for blood and patient reception was carried out every day, and disinfection was carried out in the entire institution once a week after the work process had been completed. Disinfection was carried out by a specialized unit on two occasions. The reporting of the sick and the implementation of isolation measures were introduced. Personal protection measures and the frequency of disinfection were changing during the pandemic. The specific measure of protection was and is the administration of a vaccine (12). Wearing masks remains obligatory in all health institutions, including authorized transfusion institutions such as IBTS.

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QUALITY MANAGEMENT IN TRANSFUSION MEDICINE

Marina Ferenac Kiš[1,2]
[1] Clinical Institute of Transfusion Medicine, University Hospital Osijek, Croatia
[2] Faculty of Medicine, Josip JurajStrossmayer University of Osijek, Croatia

Abstract
Transfusion medicine is an important part of modern health care. Transfusion services ensure the availability and quality of blood and blood products for patients. In order to assure the efficacy, quality, and safety of blood components, a robust quality management system is essential. The quality system should cover all aspects of transfusion service activities and assure full traceability from vein to vein. Benefits of a documented quality management system include meeting the customer's and organization's requirements, ensuring compliance with regulations, and providing cost- and resource-efficient obtained products and services. Major components of QMS in transfusion medicine are personnel and organization. premises, equipment, and materials change control, validation, documentation, collection, manufacture, labeling, product release, storage and distribution, traceability, non-conformance, and audit. In transfusion medicine established QMS undeniably increases the safety and quality of the transfusion process so to obtain safe and high-quality products QMS is essential.
Keywords: transfusion medicine, quality management system

Sažetak
Transfuzijska medicina važan je dio suvremene zdravstvene zaštite. Transfuzijske službe osiguravaju dostupnost i kvalitetu krvi i krvnih pripravaka za pacijente. Kako bi se osigurala učinkovitost, kvaliteta i sigurnost krvnih pripravaka, nužan je robustan sustav upravljanja kvalitetom. Sustav kvalitete trebao bi pokriti sve aspekte aktivnosti transfuzijske službe i osigurati potpunu sljedivost od vene do vene. Prednosti dokumentiranog sustava upravljanja kvalitetom uključuju ispunjavanje zahtjeva korisnika i organizacije, osiguravanje usklađenosti s propisima i osiguravanje proizvoda i usluga koji su učinkoviti u smislu troškova i resursa. Glavne komponente sustava upravljanja kvalitetom u transfuzijskoj medicini su: kadrovi i organizacija, prostori, oprema i materijali, kontrola promjena, validacija, dokumentacija, prikupljanje, proizvodnja, označavanje, puštanje proizvoda u promet, skladištenje i distribucija, sljedivost, upravljanje nesukladnostima i auditi. U transfuzijskoj medicini, uspostavljen sustav kvalitete nedvojbeno povećava sigurnost i kvalitetu cjelokupnog transfuzijskog procesa stoga je neophodan za dobivanje sigurnih i kvalitetnih krvnih pripravaka.
Ključne reči: transfuzijska medicina, sistem upravljanja kvalitetom

Transfusion medicine is an important part of modern health care. It bridges the healthy community with the bedside in hospitals. There is no equally valuable substitute for blood so it is the responsibility of the national blood service to ensure the availability and quality of blood and blood products for patients. In order to assure the efficacy, quality, and safety of blood components, a robust quality management system (QMS) is essential. A quality management system is a formalized system that documents processes, procedures, and responsibilities for achieving quality policies and objectives. Established QMS coordinates and directs an organization's activities to achieve the final goal - to meet regulatory and customer requirements, and continuously improve its competence and productivity.

The history of quality management begins in medieval times with the organized unions - guilds where master craftsman developed strict rules for product and service quality and maintained a form of quality control by inspecting goods before sale. It continued and developed in the industrial revolution, where quality was ensured through skilled workers and auditing systems. Nowadays, QMS data are analyzed using statistical techniques to see whether a process is stable and displayed in stylish forms like control charts. Today's international standards that specify requirements for a quality management system are shaped into a group of documents detailing the QMS in ISO 9001:2015. The development of transfusion medicine started at the beginning of the 20th century but Quality Management in transfusion has received attention several decades ago with the appearance of transfusion transmissible diseases and haemovigilance.

Every blood transfusion service should develop an effective QMS to ensure that all products are safe, clinically effective, and of proper and consistent quality. The quality system should cover all aspects of transfusion service activities and assure full traceability, from the concern for blood donors to the blood products administration. Benefits of a documented quality management system include meeting the customer's and organization's requirements, ensuring compliance with regulations, and providing cost- and resource-efficient obtained products and services. The basis of a QMS is both quality assurance and quality control. Quality assurance is an activity that recognizes defects in the process by ensuring that methods and processes are implemented correctly. Quality control activities focus on the examination of the quality of the end products and verifying that the products meet the defined quality standards.

Major components of QMS in transfusion medicine are:

Personnel must be trained and educated and the blood establishment must ensure adequate resources to attain the required standards which include equipment, consumables, work areas, utilities, etc. Premises must suit the activities to be carried out

(donation area, collection area, testing, and processing areas, storage areas, waste disposal area). Equipment and materials. Equipment must be validated, calibrated, and maintained for the intended purpose. Reagents and materials are from approved suppliers with documented requirements. Change control must be in place to ensure that changes are evaluated and made only if they provide benefits to the organization which results in benefits for patients and donors. Validation provides assurance that critical aspects of a process are in control and increase the probability of uniform product quality. Documentation provides clear instructions on what to do and prevents errors that may result from spoken communication. Collection must have procedures for safe donor identification, and ensure that each donation can be linked to the collection and processing system into which it was collected and/or processed. Manufacturers must have defined procedures in order to obtain products or services of the required quality and quality control process to confirm that products meet their pre-defined specifications. Labeling must unmistakably identify the type of content, and comply with the labeling and traceability requirements. Product release must ensure a safe and secure system to prevent release until all mandatory requirements have been fulfilled. Storage and distribution must ensure quality during the entire storage. Traceability must be maintained from the donor to the patient. Non-conformance (deviations, complaints, SARE) must be documented, and carefully investigated for constant improvement. Audit (self-inspection) is a key driver in the continual improvement of QMS, ensuring compliance with regulatory and technical requirements, as well as organizational competence.

Although it can be seen as complicated and highly demanding, once established, QMS undeniably increases the safety of the transfusion process. In EU countries, blood transfusion services have immense support from numerous legislative acts and guidelines that assist in the implementation and maintenance of robust QMS. However, quality is expensive so, in non-western countries with lower state gross income, challenges can be: restricted financial resources, limited human resources (work overload), expensive maintenance of equipment, and inability to have stock of consumables. Nevertheless, in transfusion medicine, in order to achieve continual quality improvement and deliver safe and high-quality products, QMS is essential.

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THE IMPORTANCE OF LEADERSHIP IN HEALTHCARE: APPROACH IN TRANSFUSION MEDICINE

Nevenka Bujandrić[1, 2]
[1]Blood Transfusion Institute Vojvodina, Novi Sad, Serbia
[2]The Faculty of Medicine Novi Sad, University of Novi Sad, Serbia

Abstract

Continuous supply of a sufficient amount of safe blood to patients is a joint effort of all team members in the Blood Transfusion Institute of Vojvodina: from medical technicians to administrative staff. Due to the humanity of donors, the staff makes an effort to fulfill the donor's highest-level needs. Managers are responsible for staff training and performance, leading them by example. Along these lines, despite the workload, employees share enthusiasm at work and a willingness to improve. Good qualities of managers and appropriate management styles are important in achieving goals. The specific tasks of a manager are interpersonal, informational, and decisive. In order to manage effectively, managers must have the appropriate skills: conceptual, human, and technical. Managers at all levels perform 4 functions: planning, organizing, leading, and controlling.

And while managers focus on managing tasks and achieving results, a leader inspires and motivates employees. Leadership development must be integrated longitudinally throughout a physician's career. Effective leadership is essential in healthcare organizations and involves developing a leadership culture where formal and informal leaders work together. Top management support for talent has a positive impact on organizational culture, job satisfaction, and commitment, and is the key to organizational competitiveness. An integrative model of managerial and medical leadership as well as the promotion of women to higher positions in healthcare are proving to be a useful way to increase the efficiency of the healthcare system.

Keywords: institutional management teams, office management,transfusion medicine

Sažetak

Neprekidno snabdevanje pacijenata dovoljnom količinom bezbedne krvi zajednički je napor svih članova tima Zavoda za transfuziju krvi Vojvodine, od medicinskih tehničara do administrativnog osoblja. Zbog humanosti davalaca osoblje se trudi da ispuni sve njihove potrebe. Menadžeri su odgovorni za obuku i učinak osoblja, vodeći ih svojim primerom. U tom smislu, uprkos opterećenju poslom, zaposleni dele radni entuzijazam i spremnost da se usavršavaju. U postizanju ciljeva važni su dobri kvaliteti menadžera i odgovarajući stil upravljanja. Specifični zadaci menadžera su međuljudski, informativni i odlučujući. Da bi efikasno upravljali, menadžeri moraju imati odgovarajuće veštine: konceptualne, ljudske i tehničke. Menadžeri na svim nivoima obavljaju 4 funkcije: planiranje, organizovanje, vođenje i kontrolu.

I dok se menadžeri fokusiraju na upravljanje zadacima i postizanje rezultata, lider inspiriše i motiviše zaposlene. Razvoj liderstva mora biti integrisan longitudinalno tokom karijere lekara. Efikasno vođstvo je od suštinskog značaja u zdravstvenim organizacijama i uključuje razvijanje liderske kulture u kojoj formalni i neformalni lideri rade zajedno. Podrška vrhunskog menadžmenta talentima ima pozitivan uticaj na organizacionu kulturu, zadovoljstvo poslom i posvećenost, i ključ je za organizacionu konkurentnost. Integrativni model menadžerskog i medicinskog liderstva, kao i unapređenje žena na više pozicije u zdravstvu, pokazuju se kao koristan način povećanja efikasnosti zdravstvenog sistema.

Ključne reči: institucionalni menadžment timovi, kancelarijski menadžment, transfuzijska medicina

Blood Transfusion Institute of Vojvodina collects blood from voluntary donors who, with their humane gesture, make it possible to improve the health of patients who need blood. In addition, the Blood Transfusion Institute of Vojvodina is constantly looking for better ways to minimize blood waste and maximize the usability of donated blood units. It's a collaborative effort where every team member has a role to play: from the medical technicians to the administrative staff. Employees in the blood donor motivation, blood collection, processing, and testing departments, take responsibility for ensuring a continuous supply of a sufficient amount of safe blood to meet patient needs. Because of the humanity that donors express through the act of donating blood, employees put the donors first and ensure that donors have a positive experience for the time of blood donation as well as a positive attitude towards donating blood again in the future. Teams of employees ensure that blood is collected in accordance with legal regulations and that it is stored and delivered safely. Managers are responsible for ensuring that staff is trained to meet safety objectives with appropriate performance. Managers must lead teams by example so that employees are flexible with occasional irregular or extended working hours. The most important thing is that despite the workload, all employees share enthusiasm for providing blood units and are ready to participate in improvement. Good qualities of managers and leaders and appropriate management style will be important in achieving these goals. In a friendly and supportive environment, employees will enjoy their roles.

The managers focus on planning, organizing, and coordinating resources (infrastructure and employees), supervising daily work processes, and planning finances and budget of the institution - managing tasks and achievement of results. The leaders are observing the environment in a wider framework. They, on the other hand, inspire, motivate and influence the employees, encouraging them to work and achieve their goals. Research conducted in Turkey and Great Britain has shown that for the successful introduction of Total Quality Management (TQM) in healthcare, the mediating role of the highest

level of management is necessary as well as employee support [1-2]. Studies conducted in the United States have shown that leadership is a key catalyst in encouraging the improvement of knowledge, skills, and abilities of employees resulting in improving performance, characteristic of organizations with a strong human resources culture [3].

Pounder et al., investigating the competencies and personal characteristics of leaders, emphasize that there is a need for greater training in the field of management competencies within the public health sector of developing countries [4]. Competences that a medical doctor acquires during the specialization in transfusion medicine include medical knowledge (transfusiology, hematology, hemostasis, etc.), laboratory skills, practical work (motivation, recruitment, and selection of donors, apheresis procedures, testing and processing of blood, screening antibodies, HLA testing, blood supply management, researching the problems of transfused patients, etc.), active cooperation in programs of scientific research/clinical research, participation in publications in peer-reviewed scientific journals and at national meetings, symposia, seminars, etc., knowledge of national laws, regulations and standards that apply to transfusion medicine as well as regulations and guides from other countries (FDA, AABB) and others. Around the world, physicians are generally accepted as leaders of clinical teams, while their role as organizational and system leaders varies considerably [5]. Till et al., reviewing UK perspectives in this area, recommend that leadership development must be integrated longitudinally throughout a physician's career. Due to the nature of their work, doctors of medicine in transfusion institutions have become team leaders already at the beginning of their careers, so it is important that management education is included in their education as soon as possible. Managers at all levels perform each of the 4 functions: 1. Planning - identification and selection of goals and course of action that determine the efficiency and strategy of the organization; 2. Organizing - grouping people into departments according to tasks, determining the line of authority and responsibility of members in a way that will coordinate and motivate employees to work together to achieve goals; 3. Leadership - helping employees understand their role in achieving goals; 4. Controlling - monitoring of individuals, departments, and organizations in order to assess the success of achieving goals and corrective measures for improvement [6]. Top management support for talent has a positive impact on both organizational culture and job satisfaction, as well as the commitment of career changers, but is also key to organizational competitiveness [7]. The manager, due to the position he occupies, represents the organization to other groups, both inside and outside of the company, and performs a set of specific roles: 1. Interpersonal - coordination and communication with employees (gives guidelines and goals, trains, advises, encourages performance, connects people); 2. Informational - obtaining and transmitting information needed for managing the organization, analysis of information, and use of information for positive influence on people in the organization and outside it; 3. Decisional - planning strategy and using resources to achieve goals (deciding on new projects to start and invest; responsibility for managing an unexpected event; assigning resources to departments, setting budgets, negotiating solutions between managers, unions, service users, etc.) [8]. Effective leadership is essential in healthcare organizations and involves developing a leadership culture where formal and informal leaders work together [9].

In order to manage effectively, managers should have appropriate skills: 1. Conceptual - the ability to analyze the situation and find cause and effect; 2. Human - the ability to understand, change, lead and control people's behavior; 3. Technical - specific knowledge needed to perform the task (e.g. marketing, accounting, etc.). Skills are improved through training, reading, and practice. Different levels of managers require a different level of each of the listed skills [10].

Good managers: 1. Create an environment for cooperation - employees feel heard, respected, and valued, so there is support and mutual trust in a team that works together. The manager encourages people by showing passion and positivity towards their work, delegates tasks, and encourages communication and feedback through regular meetings; 2. They are focused on the development of people - they help employees to progress, to use their interests and talents, to discover and remove obstacles so that employees can work at their best; 3. They are excellent communicators - they set clear expectations, they are transparent, they establish guidelines for giving and receiving feedback, everyone can express concerns, opinions, and ideas, they ask for help, and they are open; 4. They have the influence of a leader - they make every employee feel valued and thus motivate them, to learn together with their team, and work for improvement. For example, in the establishment of evidence-based healthcare practice provision, top managers through their influence on middle managers can significantly influence the implementation of innovative practices by frontline healthcare staff [11].

Leadership is one of the most frequently researched phenomena in management because both the positive and negative influences of the leader on the performance of the organization are easily observable. The basic question was what makes a leader, that is, what separates a leader from a non-leader? The first studies focused on the personal qualities that leaders have that "ordinary people" do not have, under the assumption that some people are "born leaders". It was established that there are qualities that all leaders have (intelligence, openness, self-confidence, initiative, energy, resourcefulness), but also that there are no qualities that only leaders have. Belsen and colleagues also investigated the promotion of women to higher positions in healthcare in a joint leadership model with different and overlapping roles, as a way to increase the efficiency of the healthcare system [12]. A group of UK authors also looked at the shared leadership model and the attitudes, barriers, and needs of clinical and non-clinical managers who share leadership responsibilities in the UK National Health Service. They conclude that leadership development programs are necessary for leaders, whether they are aspiring, emerging, or already established [13]. Savage and colleagues investigated the coexistence of managerial and medical logic in management, also concluding that an integrative leadership model would be useful [14]. A study by American authors follows the development of leadership over time by analyzing the limitations of the leaders' own subjectivity on their perspectives as well as the limitations set by accepted social norms and role models [15].

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EMERGENCY PREOPERATIVE PREPARATION AND MANAGEMENT OF MAJOR HEMORRHAGIC EVENTS IN PATIENTS TREATED WITH DIRECT ORAL ANTICOAGULANT DRUGS

Nebojša Antonijević[1,2], Dušan Petrović[3], Čedomir Uštević[4],Nikola Gosnjić[5], Jovana Klać[1], Ana Ušćumlić[1,2], Ivan Ranković[2,6], Lazar Travica[1], Dragan Matić[1,2], Tina Novaković[7], Nebojša Savić[7], Vladimir Kanjuh[8]

[1]Clinic of cardiology, University Clinical Centre of Serbia
[2]School of Medicine, University of Belgrade
[3]Center for radiology imaging and magnetic resonance, University Clinical Centre of Serbia
[4]Special hospital for rehabilitation "Termal" Vrdnik
[5]Faculty of Pharmacy, University of Belgrade
[6] Clinic of gastroenterohepatology, University Clinical Centre of Serbia
[7] Transfusiology department, Clinic of vascular and endovascular surgery, University Clinical Centre of Serbia
[8] Board on Cardiovascular Pathology, Serbian Academy of Sciences and Arts

Summary

Considering the increasingly frequent use of DOAC, there is a need to adopt the most adequate algorithm for the perioperative preparation of patients for elective and emergency surgical interventions. Perioperative preparation is personalized based on the urgency of intervention, risk of bleeding due to the intervention itself, comorbidities of the patient, type of antithrombotic therapy, time of consumption of DOAC, especially renal function, and other clinical parameters. Special attention is paid to the application of adequate measures of local hemostasis, which include the application of various modalities of fibrin glue, endoscopic, and endovascular invasive radiological procedures. In case of rapid neutralization of the effects of dabigtran, the direct antidote idarucizimab can be used, while andexanet alfa is used as an antidote for factor X coagulation inhibitors, which, unlike idarucizimab, is currently only indicated for use in life-threatening bleeding. In vital indications, special laboratory diagnostics are used, particularly ROTEM, especially the Clot-Pro apparatus, specific tests for evaluating the effects of DOAK (anti-factor Xa assays, dTT test, ECT tests, as well as standard biochemical analysis).

Significant (major) bleeding is registered in less than 4% of patients treated with direct oral anticoagulants (DOAC) and is accompanied by an increased degree of mortality. After establishing the patient's hemodynamic stability, local hemostasis measures are applied, as well as medical charcoal if the drug was ingested within 2 hours, whereas additional risk factors for bleeding such as hypertension are controlled. In life-threatening bleeding, the use of direct antidotes is preferred, but in practice, relatively good results are achieved with the use of 4-PCC (prothrombin complex concentrate) or aPCC (activated PCC). Along with laboratory monitoring, antifibrinolytics, cryoprecipitate, and other transfusion derivatives still have their place.

The teamwork of all members of the bleeding team, including endoscopists, interventional radiologists and surgeons, biochemists, and transfusion specialists, is a prerequisite for the successful treatment of vitally endangered patients previously treated with DOAC.

Keywords: direct oral anticoagulants, DOAC, perioperative management, bleeding

HITNA PREOPERATIVNA PRIPREMA I ZBRINJAVANJE VELIKIH HEMORAGIJSKIH DOGAĐAJA KOD BOLESNIKA LEČENIH ANTIKOAGULANTNIM LEKOVIMA

Sažetak

S obzirom na sve češću upotrebu direktnih oralnih antikoagulantnih lekova (DOAK) postoji potreba za usvajanjem najadekvatnijeg algoritma perioperativne pripreme bolesnika za elektivne i hitne hirurške intervencije. Perioperativna priprema se personalizuje na osnovu hitnosti intervencije, rizika od krvarenja zbog same intervencije, komorbiditeta bolesnika, vrste antitrombotske terapije, vremena konzumiranja DOAK-a, a posebno renalne funkcije i drugih kliničkih parametara. Posebna pažnja se obraća na primenu adekvatnih mera lokalne hemostaze koje uključuju primenu raznih modaliteta fibrinskog lepka, endoskopskih i endovaskularnih invazivnih radioloških procedura. U slučaju brzog neutralisanja dejstva dabigatrana može se primeniti direktni antidot idarucizimab, dok je antidot za inhibitore faktora X koagulacije andeksanet alfa, za razliku od idarucizimaba za sada indikovan samo za primenu u životno opasnim krvarenjima. U vitalnim indikacijama od velike pomoći za izbor hemostiptika se koristi specijalna laboratorijska dijagnostika, naročito ROTEM, posebno Clot-Pro aparat, specifični testovi za procenu dejstva DOAK-a (anti-faktor Xa eseji, dTT test, ECT testovi, kao i standardna biohemijska analitika).

Značajna (*major*) krvarenja registruju se u <4% kod bolesnika lečenih direktnim oralnim antikoagulansima (DOAK) i praćena su povećanim stepenom mortaliteta. Posle uspostavljanja hemodinamske stabilnosti bolesnika, primenjuju se mere lokalne hemostaze, medicinski ugalj ako je lek ingestiran u roku od 2h, kontrolišu se dodatni faktori rizika za krvarenje kao hipertenzija. U životno opasnim krvarenjima prednost ima primena direktnih antidota, ali se u praksi solidni rezultati postižu primenom 4-PCC (koncentrata protrombinskog kompleksa) ili aPCC (*activated PCC*). Uz laboratorijski monitoring svoje mesto i dalje imaju antifibrilitici, krioprecipitat i drugi transfuzijski derivati.

Timski rad svih članova tima za krvarenja, uključujući endoskopiste, interventne radiologe i hirurge, biohemičare, transfuziologe, preduslov je za uspešno lečenje vitalno ugroženih bolesnika prethodno lečenih DOAK-om.

Ključne reči: direktni oralni antikoagulansi, perioperativno zbrinjavanje, krvarenje

Considering the increasing population of patients treated with anticoagulant therapy with direct oral anticoagulants (DOAC), the issue of perioperative preparation of patients for elective and urgent surgical interventions in those who use these drugs is of utmost importance (1). It is estimated that as many as 15-20% of patients annually treated with DOAC will require a certain surgical or interventional procedure, and that up to 4% of patients treated with DOAC will manifest a significant (major) hemorrhagic complication within one year of DOAC introduction (1,2).

Before defining the perioperative anticoagulant regimen, it is necessary to assess the ischemic or thromboembolic risk for each patient individually (for example CHA_2DS_2VASc score which defines high risk for values greater than 4), risk of bleeding (for example HAS-BLED score with values above 3 defines the risk of bleeding), as well as the intrinsic risk of a particular intervention (minimal, low/moderate or high) (1-8).

For patients with **minimal risk of bleeding** (with a 30-day risk of bleeding ~0%), either no discontinuation of anticoagulants is required in the perioperative period, or short-term discontinuation of DOAC may be decided (i.e. on the day of the procedure). Procedures with minimal risk of bleeding includecataract surgery with phacoemulsification, uncomplicated dental extraction in persons with good dentition and absence of gingivitis, endoscopic resection of polyps on the colon, coronary angiography via femoral access (1), but also minor dermatological procedures, pacemaker, and cardioverter defibrillator implantation, arthrocentesis, thoracentesis, paracentesis, joint injections in which continuation of DOAC or minimal (one-day) interruption of therapy is advised (6,7,8). Other authors divide procedures into those with a low or high risk of bleeding. Procedures with a low risk of bleeding (<1.5%) according to MacDougall K and Oprea DA include the following: cataract surgery, extraction of up to two teeth, biopsies, and minor procedures on the skin (excision of cancer, nevus, keratosis, premalignant lesions), as well as endoscopic gastroenterology procedures (with or without mucosal biopsy), ERCP without sphincterectomy, endoscopic ultrasound without aspiration biopsy and permanent pacemaker implantation or pacemaker battery change, coronary angiography with radial access (3,4).

In **low to moderate bleeding risk** operations (with a 30-day bleeding risk of 0-2%), such asuncomplicated inguinal hernia operations, laparoscopic cholecystectomy, arthroscopy, lymph node biopsies or skin biopsies or bronchoscopic biopsies, bone marrow biopsies and non-cataract eye surgery, femoral access coronary angiography, gastrointestinal endoscopy with biopsy, laparoscopic cholecystectomy, hemorrhoid surgery, discontinuation and postoperative introduction of DOAC therapy is advised in relation to low hemorrhagic risk (1-8).

Operations with a **high risk of bleeding** (with a 30-day risk of bleeding >2% or interventions in vulnerable areas) require a sufficiently long period of discontinuation of DOAC so that a minimal residual anticoagulant effect is present during the operation itself with a prolonged postoperative period of re-introduction of DOAC. (1). High-risk procedures (>1.5% or in vulnerable areas) according to MacDougall K and Oprea DA include major intracranial or neuraxial surgery (spinal or epidural) or anesthesia, major thoracic, cardiovascular surgery, abdominopelvic surgery, major orthopedic surgery, head surgery and neck, reconstructive surgery (plastic surgery), facial surgery, extremity surgery, but also major skin procedures such as wide excision of melanoma, polypectomy >1cm, endoscopic mucosal and submucosal dissection, aspiration biopsy guided by endoscopic ultrasound, laparoscopic surgery, nephrectomy, kidney biopsy, percutaneous drainage of liver or gallbladder abscess or other aggressive manipulations with the implantation of drains or dilatation, Hickman catheter placement, lumbar puncture, periorbital surgery, vitreoretinal surgery, etc. There are controversial data on the risk of bleeding during needle electromyography and variceal ligation. (3-9). High-risk interventions include extensive tissue injuries as well as any major surgery lasting more than 45 minutes (7).

When planning the perioperative regimen, it should be kept in mind that DOACs have a maximum anticoagulant effect 2-4 hours after administration, and that the perioperative period of discontinuation of DOACs generally includes 4 to 5 elimination half-lives ($T_{1/2}$) of each individual DOAC, and that $T_{1/2}$ of DOAC is generally 9-14h (17h), which corresponds to an interval of 60-68h from the last dose of DOAC, so that before surgery there would be a state without residual or minimal anticoagulant effect (1,6). It is very important, especially for drugs that are predominantly excreted by the kidneys (dabigatran), to evaluate renal function, as well as to take into account the use of drugs that inhibit CYP3A4 or P-glycoprotein pathways (verapamil) that interfere with the clearance of DOAK (1). It is known that certain drugs (aspirin, certain non-steroidal anti-rheumatic drugs such as ibuprofen, indomethacin, naproxen) as well as dietary supplements (vitamin E, fish oil, omega 3 factor, selenium, ginger, ginseng, garlic, ginkgo biloba) can increase risk of bleeding (5).

In patients using **apixaban and rivaroxaban** and who are considered for an elective surgical procedure, it is advised to stop the drug, one day for low/moderate risk interventions; two days before high hemorrhagic risk surgery (1). In patients taking dabigatran, it is suggested to discontinue the drug one to four days before surgery (1). The perioperative regimen of patients on **dabigatran** implies optimization in relation to renal function, so a one-day interruption of therapy is advised in patients with operations with low to moderate hemorrhagic risk and creatinine clearance ($CrCl \geq 50$ mL/min); two-day discontinuation of dabigatran in those with $CrCl \geq 50$ mL/min with defined minor to moderate bleeding; also two days in those with planned high hemorrhagic risk operations and preserved renal function ($CrCl \geq 50$ mL/min), while a minimal four-day interruption of dabigatran therapy is recommended in patients with high hemorrhagic risk and CrCl<50ml/min. According to Oprea DA, dabigatran should be discontinued for 4 to 5 days in patients with normal renal function and for 6 days in those with reduced renal function, while rivaroxaban is recommended to be discontinued for 3 days before surgery (4).

In patients whose DOAC therapy was interrupted due to an elective surgical procedure, it is recommended to **re-introduce DOAC** in an interval shorter than 24h in patients with a low/moderate risk of bleeding, and 48-72h after operations with a high hemorrhagic risk (1). In the case of high hemorrhagic risk, re-introduction of DOAK in an interval of less than 24 hours,

but in a reduced dose, can be considered (6,7). According to ESC recommendations from 2022, DOAC is re-introduced at an interval of more than 6 hours in patients with a minor risk of bleeding, in patients with a low risk of bleeding, the introduction of DOAC is considered in the evening hours, while in patients with a high hemorrhagic risk, the re-introduction of DOAC is advised for more than 48-72h after surgery (9). Mandatory preoperative routine coagulation tests are not advised in patients who are planning to discontinue DOAK for an elective surgical procedure (1).

When preparing patients under DOAK therapy for **urgent surgical procedures** (within 24 hours), (e.g. hip fractures), it is recommended to perform the necessary laboratory tests, noting that PT (INR) and aPTT are insufficiently sensitive to define the residual anticoagulant effect (1). DOAK calibrated anti Xa level analysis is recommended for apixaban, rivaroxaban, edoxaban, and dilute thrombin time or ecarin clotting time for dabigatran (1).

Algorithms have been prepared for the reversal of the anticoagulant effect of DOAC, depending on whether the operation should be performed immediately (immediately), within a few minutes; urgent (within a few hours); or time-limited within a few hours (10). In the event that DOAC was ingested within 2 hours of admission, it is recommended to administer medical charcoal in a dose of 25-100 g orally (10-15). In the case that it is necessary to perform surgery immediately, the use of the antidote for dabigatran idarucizimab is advised, with the note that the antidote for Xa inhibitors, andexanet, has not been tested for the time being to prepare patients with DOAK for emergency operations (9,10). If a specific antidote is not available, it is advised to use the non-specific hemostatic agent prothrombin complex concentrate (PCC), which has been shown to reduce life-threatening bleeding with factor X inhibitors (8, 9, 10, 11,15). Activated PCC can normalize abnormal coagulation tests induced by DOAK therapy. Also, if necessary, antifibrinolytic therapy with transexamic acid can be applied, and in the case of dabigatran, hemodialysis. In some cases, the positive effect of recombinant factor VIIa was demonstrated (8-10).

Newer studies recommend the use of the CytoSorb hemoabsorption device to reduce rivaroxaban, apixaban and dabigatran levels in the blood. (11, 12. 13).

Principles of management of bleeding in patients with DOAK

Significant (major) bleeding is registered in 2%-3.5% of patients treated with direct oral anticoagulants (DOAC) and is accompanied by an increased degree of mortality (14-18).

Bleeding management measures in patients treated with DOAK are specially designed for patients with non-life-threatening major bleeding and include the application of local hemostasis, fluid replacement, transfusions of erythrocytes, platelets, antifibrinolytics, medical charcoal, desmopressin, with a note that freshly frozen plasma is included as plasma expanders and not into reversal agents (16, 17). Life-threatening bleeding requires the use of direct antidotes (idarucizimab and andexanat alfa) and as another option 4-PCC and aPCC (16, 17). After establishing the patient's hemodynamic stability, local hemostasis measures are applied, as well as medical charcoal if the drug was ingested within 2 hours, and additional risk factors for bleeding such as hypertension are controlled. In the absence of a direct antidote in patients with life-threatening bleeding, the use of 4-PCC is, based on our experience and literature data, a valid therapeutic option, with the note that when using 4-PCC, the results are less effective in patients with intracranial hemorrhages (14). The use of PCC normalizes the hemostatic parameters of standard, specific tests for DOAK monitoring as well as tests obtained by ROTEM analysis (14,18). Good results in the treatment of major bleeding using PCC in patients who received rivaroxaban or apixaban were registered in 65%, moderate in 20% of cases and weak in 15% of cases (14,15). It is possible that the combination of 4-PCC with tranexamic acid and fibrinogen concentrate improves the results of the treatment of significant bleeding in patients receiving rivaroxaban (16). Thromboembolic events are registered slightly more often with andexanate alfa (up to 10.7%) than with idarucizimab (3.8%), while thromboembolic complications with the use of 4-PCC are registered up to 4.3% (14,15).

The teamwork of all members of the bleeding team, including endoscopists, interventional radiologists and surgeons, biochemists, and transfusion specialists, is a prerequisite for the successful treatment of vitally endangered patients previously treated with DOAC.

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TRANSFUSION TRANSMITTED DISEASES: HOW WE STARTED, WHERE WE ARE TODAY AND FUTURE TRENDS

Dušan Vučetić[1,2], Dragana Gojkov[1], Nemanja Borovčanin[1], Zorana Kozić[1], Irina Maslovarić[3], Ivana Drvenica[3],Vesna Ilić[3]

[1] Institute for Transfusiology and Hemobiology of Military Medical Academy, Belgrade, Serbia;
[2] Faculty of Medicine of the Military Medical Academy, University of Defense, Belgrade, Serbia;
[3] Institute for Medical Research, University of Belgrade, Belgrade, Serbia

Abstract

The Food and Drug Administration introduced testing for antibodies to Treponema pallidum in the 1950s. In the 1960s the first assay for detecting hepatitis B surface antigen (HBsAg) was approved, while hepatitis C testing was started in the 1990s. The discovery of the human immunodeficiency virus (HIV) and the rapid implementation of anti-HIV antibody testing in 1985, led to a dramatic decrease in the number of transfusion-transmitted HIV cases. Significant improvement of serologic test detecting antibodies to TTIs causative agents and subsequent implementation of testing for HIV-1 p24 antigen, p22 HCV antigen, and testing for nucleic acids (NAT), further reduced the number of virus transmission by transfusion. Individual donation testing (NAT-ID), detecting circulating virus nucleic acids (RNA and DNA), shortened the window period for HIV to 5.6, for HCV to 4.9 days, and for hepatitis B to 20 days. Most of the commercially available serological screening assays are enzyme immune (EIA) or chemiluminescent (ChLIA) - combined antigen and antibody tests. The prevalence of TTIs among Serbian blood donors is very low, 0.087% for HBV, 0.064% for HCV, 0.013% for HIV, and 0.04% for syphilis. Good donor selection and applying of sensitive serological and molecular testing are two critical elements to ensure maximal blood safety.

Keywords: transfusion, viruses, blood testing

Sažetak

Američka Uprava za hranu i lekove (FDA) uvela je testiranje na prisustvo antitela na Treponemu pallidum 1950. godine. Tokom šezdesetih godina odobren je prvi test za detekciju površinskog antigena hepatitisa B (HBsAg), dok je testiranje za hepatitis C uvedeno devedesetih godina. Otkriće virusa humane imunodeficijencije (HIV) i uvođenje testiranja na prisutvo antitela na HIV 1985. doveli su do dramatičnog smanjenja broja slučajeva HIV-a prenetih transfuzijom. Poboljšanja osetljivosti svih seroloških testova za detekciju antitela na navedene viruse i naknadno uvedeno testiranje na HIV-1 p24 antigen, p22 HCV antigen i testiranje na prisustvo nukleinskih kiselina (NAT), dodatno su smanjili broj prenosa virusa putem transfuzija. Individualno testiranje (NAT-ID) koje dokazuje prisustvo cirkulišućih virusnih nukleinskih kiselina (RNK i DNK), omogućilo je da se HIV detektuje za 5,6 dana, HCV za 4,9, a hepatitis B 20 dana nakon infekcije. Većina komercijalno dostupnih seroloških skrining testova su enzimsko imuni (EIA) ili, najnoviji, hemiluminiscentni (ChLIA) – kombinovani testovi na antigen i antitela. Prevalencija TTI među davaocima krvi u Srbiji je veoma niska, 0,087% za HBV, 0,064% za HCV, 0,013% za HIV i 0,04% za sifilis. Dobra selekcija donora i što je moguće osetljivija serološka i molekularna ispitivanja su dva kritična elementa za obezbeđivanje maksimalno bezbedne krvi.

Ključne reči: transfuzija, virusi, testiranje krvi

The Food and Drug Administration (FDA) introduced testing for antibodies to Treponema pallidum in the 1950s as the first test to prevent transfusion-transmitted infections (TTIs) (1). During the sixties of the last century, the finding that posttransfusion hepatitis (PTH) is strongly associated with the transfusion of blood from paid donors, led to the development of the first assay for detecting the hepatitis B surface antigen (HBsAg) (2). HCV antibody testing was implemented during the 1990s when the hepatitis C virus (HCV) was cloned and identified as the causative agent of hepatitis C infection (3). The discovery of the human immunodeficiency virus (HIV) as the causative agent of AIDS and the rapid implementation of antibody testing in 1985 led to a dramatic decrease in the number of transfusion-transmitted HIV cases, especially in the hemophilia population (4). Improvements in serologic test detecting antibodies to antigens of TTIs causative agents and subsequent implementation of HIV-1 p24 antigen testing, HCV antigen testing, and testing for viral TTIs nucleic acids (NAT), further reduced the number of virus transmission by transfusion, and now it is not possible to determine the risks by prospective clinical studies, but only by theoretical mathematic model.

The primary cause of residual transmissions refers to an early infection period, when the blood donor is at the infection "window period" (WP), the period before the serological test detected antibodies to TTIs agents. However, since there is no test that can detect an infectious agent immediately after acquiring the infection, the phenomenon of WP persists, and if the donation is made within the WP, TTIs infected blood can enter the blood supply. By applying the technique for detection of circulating virus nucleic acids (NAT-ID - individual donation testing), WP for HIV is 5.6 days, for HCV 4.9 days, and for HBV 20 days (5). The average WP for TTIs nuclear acid testing in mini-pool PCR (MP) for HIV is 9 days, and for HCV is 7.4 days. WP for detection of HBsAg is a minimum of 30 to 38 days (6).

A variety of last-generation, serological assays for detecting antibodies to TTIs agents, exist in the market. Repeated testing with enzyme immunoassays (EIA) and chemiluminescence immunoassays (CHLIA) represents the first step in blood screening necessary to identify presumptive TTIs antibody-positive samples. To confirm if the positive result reflects real

infections or represents false positivity, more specific serological "confirmatory tests" (recombinant western/immune blot) are performed. It is important to note that, regardless of the results of confirmatory or complementary testing, the blood unit showing repeated positive reactions by screening serological tests is removed from the blood supply.

By applying modern technologies new generation of serological antibody detection tests and combined antigen and antibody tests with sensitivity closer to that of NAT-PCR (nucleic acid amplification test) have been developed.

The NAT-PCR technique, which involves nucleic acid extraction from the donor plasma, followed by amplification and detection of virus genetic sequences, is used for the primary screening of blood donors for HBV-DNA, HCV-RNA, and HIV-RNA in developed countries (7). This technology can be regarded as expensive, but its implementation significantly improves public health (8). The problem still exists in developing countries where TTIs incidence is higher than in developed countries, but where the implementation of NAT-PCR screening is not possible due to the high cost of the tests.

NAT-PCR must be constantly refined by molecular surveillance of novel nucleotide sequences, as infectious agents constantly evolve and modify their genomes by point mutations and recombinations. This problem has just been pointed out by the failure of available NAT-PCR (qualitative tests) to detect rare HIV mutants (9), and particularly HCV genotypes (10). Interestingly, the problem is more pronounced with quantification tests that enumerate certain HCV genotypes and HIV RNA copies (11). Due to the application of such "inappropriate tests", some TTIs remain undetected. For example, such testing leads to HBV transmission in South Africa, despite the simultaneous administration of serological tests and ID-PCR (12).

Two factors can influence the reliability of NAT-PCR screening. The first factor affecting the results of NAT-PCR is the detection sensitivity of MP-NAT-PCR. If the sensitivity is lower than the number of copies of the virus nucleic acid in the tested sample the results are often false-negative. This factor affecting the test results is of great importance for viruses with slow replication such as HBV. To resolve this problem, screening with highly sensitive MP-NAT-PCR, with MP-NAT-PCR that detects as small as possible blood samples, or with a more sensitive ID-NAT-PCR test is recommended. The second factor affecting the results of NAT-PCR is a mutation in viral RNA. In HIV infection, viral RNA is transcribed into DNA by the catalytic activity of enzyme reverse transcriptase. The replication error occurring during this transcription could not be corrected because reverse transcriptase does not participate in any mechanisms of nucleic acid repair. Therefore, researchers are permanently struggling to perform tests based on the amplification/detection of at least two conserved regions in the HIV-1 genome. In the context of mentioned insufficient test reliability, it is important to emphasize that any transfusion of more than 5 ml of plasma from an individual with a viral load of below 200 copies/ml, could lead to HIV transmission (13).

Among mandatory tested TTIs causative agents, HBV represents the most complex infectious agent whose structure significantly influences the results of laboratory tests. The best solution for resolving the problem of HBV testing represents triple HBV screening i.e., anti-HBc, HBsAg, and HBV-DNA testing. The presence of circulating HBV DNA in the absence of detectable HBV surface antigen (HBsAg), excluding the window period, is a characteristic of occult HBV infection (OBI). OBI is characterized by low and fluctuating viral load (≤ 100 IU/mL), often resulting in intermittent DNA detection. Most individuals with OBI have detectable anti-HBc, and about 50% of them have both anti-HBc and anti-HBs. A small proportion of OBIs have anti-HBs as the only serological marker, while others lacking serological markers are referred to as „primary OBI" (14). HBV transmission originating from OBI blood donors ranges from 2 to 48%, but a higher viral load and the absence of anti-HBs antibodies were related to an increased risk of transmission. Plasma volume correlated with the transmission risk, and also the infectious dose, initially estimated at 100 IU has recently been revised downward to ~3 IU [15].

The prevalence of TTIs among blood donors in Serbia in the period 2005-2017, was 0.087% for HBV, 0.064% for HCV, 0.013% for HIV, and 0.04% for syphilis which can be described as very low (16). Although military personnel might have an increased risk of having TTIs, the prevalence of TTIs among Serbian blood donors who donated blood to the Military Medical Academy in Belgrade was also very low (0.2% for HBV, 0.12% for HCV, 0.005% for HIV and 0.06% for syphilis (17). Over the period 2005-2017, it was recorded a declining trend in the prevalence of HBV and HCV infection, while the prevalence of HIV and syphilis remained unchanged (16, 17).

Testing for anti-HTLV-I/HTLV-II, Trypanosoma cruzi, West Nile virus, and Zika virus are not mandatory but are necessary in areas where these infectious agents are endemic. In a patient in Japan, the first evidence of direct donor-to-recipient transmission of hepatitis E (HEV), was reported. Since then, several cases of TT-HEV infections have been reported worldwide, (France, UK) which points out a necessity for more prevalent testing procedures in blood banks (18). To this day, there has not been a single reported case that SARS-CoV-2 could be transmitted by blood transfusion (19).

Donor selection (improved questionnaire) and blood testing are two critical elements of screening. Testing should be performed precisely and in accordance with the manufacturer's instructions. Also, a system for quarantine storage of positive blood products should exist. Nowadays, the real risk of transmission of mandatory tested infectious agents by donated blood is very low. However, it is very important to monitor the emergence of new TTIs and to introduce methods for their detection as early as possible. Pathogen inactivation may, in the future, provide some degree of protection against pathogens for which no tests are available. Since the supply of maximum safe blood and blood products is imperative, the goal to be pursued is the introduction of individual NAT-PCR and serologic tests with maximum analytical and clinical sensitivity.

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Introduction lecture / Uvodno predavanje UV 8

BLOOD DONATION IN A CRISIS

Milica Jovičić
Clinical Hospital Center "Dr Dragiša Mišović-Dedinje",
Belgrade, Serbia

Abstract

The COVID-19 pandemic is just one in a series of crises that affected the transfusion service in Serbia and the world. The basic task of our service is to provide a sufficient quantity of safe blood to all patients at all times. A constant deficiency of blood globally is a great challenge and despite advances made in medical science, there is no adequate blood replacement. Continuous provision of blood supply depends solely on blood donors, healthy individuals, aged 18 to 65. Every year the number and complexity of healthcare procedures in need of transfusion increase, however, every year the global population, especially in the Republic of Serbia becomes older. The role of transfusion service is even more difficult, challenging, and demanding in a crisis.

Keywords: crisis, blood donors

Sažetak

Pandemija Covid-19 je samo jedna u nizu kriza sa kojima se suočila transfuziološka služba u Srbiji i celom svetu. Osnovni zadatak naše službe je da u svakom trenutku obezbedimo dovoljne količine bezbedne krvi za sve pacijente. Stalni nedostatak krvi za transfuziju u celom svetu veliki je izazov i uprkos velikim naprecima u medicini ne postoji adekvatna zamena za krv. Obezbeđivanje kontinuiranih potreba za komponentama krvi oslanja se isključivo na davaoce krvi, zdrave osobe starosti 18–65 godina. Iz godine u godinu povećava se broj i složenost zdravstvenih procedura koje zahtevaju transfuziju krvi, ali i svake godine svetska, a posebno populacija Republike Srbije postaje sve starija. Uloga transfuziološke službe u vremenima krize je još teža, izazovnija i zahtevnija.

Ključne reči: kriza, davaoci krvi

The original meaning of the word crisis is an opinion, evaluation, or a decision, but nowadays it denotes a problematic, breaking point connected with the need to make a decision. In consideration of the last two decades, the COVID-19 pandemic is only one in a series of crises that affected the transfusion service in the Republic of Serbia, where it was necessary to act quickly and appropriately. Starting from the crises caused by sanctions and bombing, through the financial crisis, the crisis in the transfusion service reorganization, as well as everyday crisis situations dealt with and solved, the COVID-19 pandemic has contributed to the difficulty of our operations.

The main responsibility of our service is to provide a sufficient quantity of safe blood to all patients at all times, taking care of the safety of blood donors/blood components and employees during the pandemic. Although transfusion service was not part of the first line of defense in the battle against the new coronavirus, solutions needed to be found quickly and changed conditions in the selection of blood donors, the characteristics of SARS-CoV-2 infection for patients in the need of transfusion therapy monitored and priorities set for the component administration to reduce the effect of blood deficiency.

Continuous blood deficiency globally is a great challenge and despite advances in medical science, there is still no adequate blood replacement. Continuous provision of blood supply depends solely on blood donors. Even in periods of abundance and locations characterized by high resources such as the United States of America, blood supply is a limited resource maintained by the hard work of transfusion service and the Red Cross. The pandemic has contributed additionally to the system overload subjected to stress constantly, which resulted in a deficiency of all blood components and making difficult decisions regarding the actual needs of each patient (1). Based on the data from the American Red Cross, since the outbreak of the pandemic the usual two-week supply has been reduced to a day or two-day supply, with the announcement made about the biggest blood deficiency in the last ten years (2).

Many countries experienced the financial crisis of 2008, which resulted in an increase in the unemployment rate, a decrease in income, and a deterioration of all economic trends. All mentioned has affected the population's quality of life, living standard, mental state, as well as all other aspects of daily life. However, research by Greek authors showed that although the economic crisis affected the life of blood donors it has not impacted the donation frequency (3). It has been proven that volunteering and helping others can reduce stress, with blood donation being one form of volunteering. Besides, volunteering can activate people, develop new skills and provide team spirit, especially through social media (4).

The reorganization of the transfusion service in the Republic of Serbia brought many changes which affected the donors' response. As experienced by countries that underwent the reorganization, it should take three to five years to recover from the drop in donor numbers caused by dissatisfaction and changes in the operations made by the transfusion service.

Successful operation of transfusion service, but also the entire healthcare system, where almost every patient is a potential blood recipient, is based on altruism, solidarity, and civic responsibility of every individual in a society. During a crisis, society calls individuals to assume an active role in important activities and there are numerous experiences of increased readiness by individuals to help after a disaster. (5). In case of large-scale misfortunes and natural disasters, the donors' response may very often exceed the needs, especially given the fact that a large number of new donors registered. However,

the COVID-19 pandemic is much different from other crisis situations described in the literature and showcased many new characteristics. Primarily, it is a long-term crisis affecting everyone and poses a direct threat to the health of every individual. The pandemic has had a negative impact on the willingness to help others, especially in terms of blood donation. While in case of a disaster the individuals would feel the need to help the victims, a sense of personal moral obligation to give aid to others may be reduced if they have been affected by the crisis. The end of the current pandemic is still unknown and the results of the research indicate a significant decrease in personal responsibility and moral obligation. This is alarming because the more time passes the less likely it is the blood donors will return. (6) With the dying down of each wave, from transfusion service is expected high level of preparedness in terms of blood and blood components to be used in delayed operative procedures and treatments. This is the reason for the extreme significance of Patient Blood Management (PBM), or the importance of adequate blood use, decrease in the number of unnecessary blood and blood component transfusion, as well as mandatory PBM implementation globally (7). Instead of transfusion being the default decision based on a specific hemoglobin value, PBM can stop blood transfusion long before it is even considered by pointing out that blood is a valuable resource (8). Publication by the World Health Organization as of 2021 'The Urgent Need to Implement PBM' is a call to transform the awareness of importance into implementation as soon as possible around the world.

The only source of blood is found in voluntary blood donors, healthy individuals of age 18 to 65. Every year the number and complexity of healthcare procedures in need of blood transfusion increase, however, every year the global population becomes older. Serbia has a specific position as being among the oldest population in the world, where the average age is 43.4 years, and according to official data every fifth person in Serbia is older than 65, therefore cannot be a blood donor.

Based on the data provided by the Blood Transfusion Institute of Serbia, in the period from 1991 to 2021, the annual quantity of blood units collected was between 510353 (in 1994) and 78 749 (in 2018). Since 1991 the greatest quantity of blood units was collected at the Institute's site in 2021, namely 27466 blood units, mostly due to the efforts made during the pandemic, limited movement, and fear, to speak in the media on daily basis about the importance of blood donation and to raise awareness of individuals, companies, but also health workers.

The role of transfusion service is even more difficult, challenging, and demanding during the crisis. Our responsibility and obligation are to implement knowledge and make an effort to collect as many blood units as possible, but also to stop any irrational use of blood and blood components because only in such a manner blood will always be available to those in need in future and throughout new crisis situations, which will likely be ever greater.

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BLOOD TRANSFUSION SAFETY IN THE COVID-19 ERA: IT ALL STARTS WITH A VOLUNTARY BLOOD DONOR

Ana Antić
Blood Transfusion Institute Niš, Serbia

Abstract

At the end of 2019 and during 2020, the world was faced with the COVID-19 pandemic, which from its very beginning had a significant impact on the supply of blood components and the safety of transfusion. Data show that voluntary blood donation during the COVID-19 pandemic was dramatically reduced by 40-67%. For this reason, the transfusion services had to react quickly to the new conditions, which meant continuous public calls for voluntary blood donation through the media and social networks, together with assurances about safety at the collection point and compliance with prescribed measures aimed at suppressing the COVID-19 pandemic. Precise recommendations have been adopted related to the criteria for the temporary rejection of blood donors during the COVID-19 pandemic, the organization of mobile teams and collection points, the disposal of medical waste, the examination of potential donors and the mandatory measurement of body temperature.

The safety of voluntary donors, staff and patients receiving transfusions of blood products is the main goal of authorized transfusion institutions in the era of the COVID-19 pandemic.Special attention should be paid to preparing a work plan in pandemic conditions, ensuring blood collection in quantities that meet clinical needs, and achieving the highest level of safety at work.

Keywords: COVID-19, voluntary donor, safe transfusion

Sažetak

Krajem 2019. i tokom 2020. godine svet se suočio sa pandemijom COVID-19, koja je od samog početka imala značajan uticaj na snabdevanje komponentama krvi i bezbednost transfuzije. Podaci pokazuju da je dobrovoljno davanje krvi tokom pandemije COVID-19 dramatično smanjeno za 40–67%. Zbog toga su transfuziološke službe morale brzo da reaguju na novonastale uslove, što je podrazumevalo kontinuirane javne pozive za dobrovoljno davanje krvi putem medija i društvenih mreža, uz uveravanja o bezbednosti na mestu prikupljanja krvi i poštovanju propisanih mera s ciljem suzbijanja COVID-19 pandemije. Usvojene su precizne preporuke koje se odnose na kriterijume za privremeno odbijanje davalaca krvi tokom pandemije COVID-19, organizaciju mobilnih ekipa i mesta prikupljanja.

Bezbednost dobrovoljnih davalaca, osoblja i pacijenata koji primaju transfuziju krvnih komponenata glavni je cilj ovlašćenih transfuzioloških ustanova u eri pandemije COVID-19. Posebnu pažnju treba posvetiti izradi plana rada u uslovima pandemije, obezbeđivanju prikupljanja krvi u količinama koje zadovoljavaju kliničke potrebe i postizanju najvišeg stepena bezbednosti na radu.

Ključne reči: COVID-19, dobrovoljni davalac, bezbedna transfuzija

Although no cases of SARS-CoV-2 transmission via transfusion of blood and blood components have been reported to date, the COVID-19 pandemic has caused widespread instability in the global health system, including the operation of transfusion services and the supply of blood components. The pandemic has brought numerous challenges in maintaining stable blood reserves, considering that the social, as well as a large number of activities of the health system, have moved from their usual ones to activities that are oriented towards the suppression of the spread of the virus and the treatment of the sick (1). Potential blood donors have become confused, worried, and insufficiently informed about donating blood during the pandemic, while on the other hand, the measures to prevent the spread of the pandemic, such as the "stay at home" campaign, "lockdown" and the restriction of public gatherings made it difficult to organize voluntary blood donation actions. On the other hand, in addition to the continuous need for all blood components for the treatment of oncological, hematological, and gynecological patients, in case of trauma, emergency operations or transplantation, there was also the need for transfusion treatment for patients with COVID-19 infection. For this reason, the transfusion services had to react quickly to the new conditions, which meant adopting a national approach for the purpose of coherence and coordination of voluntary blood donation, taking into account all the specific factors of the local environment and the need for transfusion. This type of approach was intended to ensure public confidence in the safety and efficiency of the supply of blood components, as well as the support of all stakeholders in the blood supply system. Transfusion services were included in national teams responsible for a timely response to the current epidemiological situation, and have also developed, implemented, and realized blood collection plans in the conditions of the COVID-19 pandemic (2,3).

Data show that voluntary blood donation during the COVID-19 pandemic was dramatically reduced by 40-67%, especially in countries where movement restrictions were in force (4). As a result of the "lockdown" and "stay at home" campaigns were canceled in advance of scheduled blood donation campaigns, schools and universities were closed, a large number of people switched to working from home, all public activities were significantly reduced, which altogether had a great impact on the number of blood units collected. In order to solve this problem, continuous public calls for voluntary blood donation through the media and social networks, together with assurances about safety at the collection point and compliance with prescribed measures aimed at suppressing the COVID-19 pandemic, were of key importance (5).

The strategy for protection against the transmission of the SARS-CoV-2 virus at the collection site involves the implementation of public health measures and recommendations to prevent the spread of the COVID-19 pandemic, which includes screening for symptoms related to COVID-19 infection, social distancing, hand hygiene, use of personal protective equipment and hygiene workspace (6). Potential blood donors are advised to make an appointment or schedule blood donation in advance, not to come in large groups, and not to bring companions to the collection site. Their body temperature must be measured before entering the collection site, as well as to comply with all prescribed measures in the fight against pandemics (wearing a protective mask, washing and disinfecting hands with alcohol). The first step in the organization of blood collection during a pandemic is the education of potential donors about the criteria for self-exclusion from donating blood based on risk factors for transmission of the SARS-CoV-2 virus and clinical symptoms of infection. Screening of potential blood donors involves a thorough anamnesis taken from the donor with special emphasis on travel and contact history, as well as symptoms of suspected COVID-19 infection or colds. People with elevated body temperature, symptoms of a dry cough, or symptoms of suspected COVID-19 infection are refused to donate blood. In addition, donors with confirmed SARS-CoV-2 virus after the withdrawal of symptoms or a negative result of repeated PCR testing, as well as donors who had contact with a person with confirmed SARS-CoV-2 or are returning from a high-risk area are refused to donate blood for a period of at least 14 days (1–3).

An important place in maintaining transfusion safety in the conditions of the COVID-19 pandemic is the "post-donation information", feedback on the health condition of the voluntary blood donor within a period of 14 days from donating blood (7). Donors are advised that it is necessary to provide the transfusion service with information about their health, especially about the occurrence of elevated body temperature or symptoms of respiratory infection, by phone, email, or another form of communication within that period. According to the adopted algorithm, if there is a sudden appearance of symptoms that are suspicious of a COVID-19 infection and the donor informs the transfusion service about the positive result of the nasopharyngeal swab within 14 days of donating blood, it is necessary to destroy all labile blood components if are present in stock, and if they have already been previously transfused, it is necessary to inform the management of the clinic where the transfused patient is being treated (8).

In order to protect the health of voluntary blood donors and reduce the theoretical risk of transmission of the vaccine agent to transfusion recipients, the World Health Organization has adopted criteria related to the acceptance or exclusion of potential blood donors depending on the type of vaccine used against the COVID-19 infection. Recipients of SARS-CoV-2 vaccines that do not contain a live virus and feel well can donate blood immediately, without delay, while recipients of vaccines with a live virus (vector or attenuated virus) are refused to donate blood for at least two weeks.

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DIAGNOSTIC AND PROGNOSTIC VALUE OF IMMUNOHAEMATOLOGICAL TESTING IN CURRENT TRANSFUSION CLINICAL PRACTICE

Snežana Jovanović Srzentić[1], Ivana Radović[1], Anka Vlatković[1], Jelena Dmitrović[2]
[1] Department of Immunohaematology, Blood Transfusion Institute of Serbia, (BTIS), Belgrade, Serbia
[2] Department for HLA typing , Blood Transfusion Institute of Serbia, (BTIS), Belgrade, Serbia

Abstract

Proper decision to give a blood transfusion mainly depends on careful consideration of the risks against benefits in enabling safe blood transfusion and/or hematopoietic tissue transplantation. Immunohaematological testing is based on the reactions of antigens on red cells and antibodies in plasma and is usually divided into two groups: pretransfusion testing and perinatal testing. The aim of this paper is to present the role of immunohaematological testing in current transfusion clinical practice.

Diagnostic and prognostic value of a wide spectrum of immunohaematological testing in the pretransfusion investigation, during pregnancy and peritransplantation phase, are discussed in this lecture. The importance of molecular typing in current immunohaematological diagnostic and prognostic laboratory practice is also highlighted. Some of the results of serologic and molecular immunohaematological testing in the BTIS are presented.

In conclusion, immunohaematological tests represent an essential part of patient blood management, regarding their significant diagnostic and prognostic value in providing appropriate and safe blood components for transfusion and transplantation.

Keywords: immunohaematological testing, transfusion practice

Sažetak

Pravilna odluka o transfuziji krvi uglavnom zavisi od pažljivog razdvajanja rizika od koristi u omogućavanju bezbedne transfuzije krvi i/ili transplantacije hematopoetskih ćelija. Imunohematološko testiranje se zasniva na reakcijama antigena na eritrocitima i antitela u plazmi i obično se deli u dve grupe: pretransfuziono testiranje i perinatalno testiranje. Cilj ovog rada je da se prikaže uloga imunohematološkog ispitivanja u savremenoj transfuzionoj kliničkoj praksi.

Dijagnostička i prognostička vrednost širokog spektra imunohematoloških ispitivanja u pretransfuzionom ispitivanju, tokom trudnoće i peritransplantacione faze razmatraju se u ovom predavanju. Takođe je istaknut značaj molekularne tipizacije u aktuelnoj imunohematološkoj dijagnostičkoj i prognostičkoj laboratorijskoj praksi. Prikazani su neki od rezultata seroloških i molekularnih imunohematoloških ispitivanja u ITKS.

Zaključno, imunohematološki testovi predstavljaju suštinski deo upravljanja krvlju pacijenata, s obzirom na njihovu značajnu dijagnostički i prognostičku vrednost u obezbeđivanju odgovarajućih i bezbednih komponenata krvi za transfuziju i transplantaciju.

Ključne reči: imunohematološka ispitivanja, transfuziološka praksa

Introduction

Proper decision to give a blood transfusion mainly depends on careful consideration of the risks against benefits in enabling safe blood transfusion and/or hematopoietic tissue transplantation. Immunohaematological testing is based on the reactions of antigens on red cells and antibodies in plasma and is usually divided into two groups: pretransfusion testing and perinatal testing. A number of immunohaematological techniques are available for the detection and identification of antibodies in the patient's plasma, from conventional tubes and gel to more complex absorption and elution techniques to advanced molecular techniques. These techniques are suitable to identify if the antigen is present in the patient's red cells. Allo and autoantibodies against red cells have the potential of causing hemolytic transfusion reactions and could provoke challenges in compatibility testing regarding the provision of compatible blood for transfusion. All mentioned tests have the same aim to prevent undesired immunologic reactions after transfusion, transplantation, and during pregnancy.

Immunohaematological testing in various clinical settings

Pretransfusion immunohaematological testing

Regarding the importance of immunohaematological laboratory procedures, the effective development and maintenance of satisfactory standards in pretransfusion testing require a structured approach to adopting a quality management system. The guidelines for pretransfusion compatibility testing in blood transfusion laboratories by the British Committee for Standards in Hematology define the laboratory processes and procedures accepted in the largest number of countries in the world. They include quality management in pretransfusion tests, blood sampling, appropriate documentation, determination of blood groups of the ABO and RhD antigen systems, screening and identification of antibodies, selection of appropriate red cells for transfusion, examination and issuance of red cells in emergency situations and reporting of posttransfusion reactions. It is necessary for blood transfusion services in all countries to have guidelines for pretransfusion testing with valid recommendations for all segments and procedures, in order to enable the safe transfusion of blood components to all patients. Pretransfusion testing was performed for 2106 patients at the Department for pretransfusion testing and blood distribution of BTIS. In 68 recipients specific novel IgG red cell antibodies were discovered in the period from March 15th to August 31st, 2022. Red cell antibody screening in BTIS was additionally performed for 448 neonatology patients in the same period. Red

cell Ats were detected in 5 (1.1%) neonates. Defined specificities were: 2 cases each (40.0%) of anti-c and anti-D and one case (20%) of anti-K At . Both children with anti-c At had Rh phenotype CcDee. Children with anti-D and anti-K At were antigen-negative.

For specified groups of patients who are dependent on long-term transfusion support (malignant hemopathias, certain malignant tumors, thalassemias, hemoglobinopathies, sicle cell anemias), Dutch authors recommend the prophilactic matching for C, E, c, e, K and Jka antigens as the most efficient way for preventing alloimmunization. In Germany, this approach is applied to all women of childbearing age and girls, as a standard.

Immunohaematological testing in pregnancy

All pregnant women should perform immunohaematological testing for ABO and RhD antigens and screening tests for the detection of irregular red blood cell antibodies at the initial prenatal visit. Women with a history of clinically significant red cell antibodies or immunizing events, such as blood transfusions, complications in pregnancy, and diagnostic procedures like amniocentesis or chorionic villous sampling require additional antibody testing during the second to third trimester regardless of their RhD status. At the Department for immunohaematology of BTIS 6138, antibody screening tests were performed in 2020 and 6237 in 2021 (both two-stage enzyme technique and indirect antiglobulin test); in 2020. 167 pregnant women with positive screening tests and the presence of 1 or more red cell antibodies, in 2021, 175 pregnant women had positive screening tests, with the presence of 1 or more red cell antibodies.

If the mother forms antiplatelet IgG antibodies, they may cross the placenta and cause thrombocytopenia in the fetus. Both parents of an infant with suspected FNAIT should be tested, including genotyping for human platelet antigen (HPA) genes that have been associated with FNAIT. Maternal screening for specific anti-platelet antibodies is also recommended for diagnosis of this condition along with genotyping of an infant blood sample for the particular HPA genes, if possible. At the Department for immunohaematology of BTIS HPA antigen genotyping for diagnosis of FNAIT was performed in 10 cases, and incompatibility in HPA antigens between father and mother was proven in 8 cases.

Direct antiglobulin test (DAT) in immunohaematological and clinical practice

In clinical practice, the DAT is an important diagnostic laboratory procedure for the investigation of autoimmune hemolytic anemia (AIHA), hemolytic disease of the newborn (HDN), drug-induced immune hemolytic anemia (DIHA), and hemolytic transfusion reactions. Determination of ABO/RhD antigen and DAT from cord blood samples are considered standard procedures and are performed in many hospitals for all newborns.

It was found that DAT is not a diagnostic parameter that can predict the severity of hemolytic disease and is therefore not justified for routine screening.

In 31 (10.4%) neonates with non-O blood types, the presence of ABO class IgG isohemagglutinins was determined. Anti-A was detected in 22 (71.0%) and anti-B in 9 (29.0%) neonates. In 4 (12.9%) cases DAT was positive. In one case, anti-A was demonstrated only in the eluate from DAT-positive red cells.

Immunohaematological testing in peritransplantation phase

Immunohaematological tests are of great importance in hematopoietic stem cell transplantation (HSCT). Transplantations with major, minor, or bidirectional ABO incompatibility are commonly performed. Therefore, special guidelines need to be followed while selecting the blood components, considering the ABO and RhD compatibility and blood component processing in all three periods of HSCT. Red cell chimerism after HSC transplantation is monitored, particularly considering a precise timely detection of the patient's blood group change to the donor's blood group – for the proper administration of the correct blood product to these patients. Because of that, in the second period, from 4+ days is necessary to perform weekly monitoring of ABO IgM/IgG antibodies, by direct antiglobulin test of the patient RBC and indirect antiglobulin test of patient serum.

Molecular immunohaematologucal testing

Molecular techniques are increasingly used in immunohaematology in order to determine the RhD variant as well as another antigen status of the patients and to resolve complex problems of alloimmunization, especially when the DAT of the patient is positive. An AABB and American College of Pathologists Joint Working Group provided recommendations for genotyping of pregnant women in 2015. The proposed algorithm was formed based on the results of manual or automated testing. Individuals with serological results which suggest weak or undetermined RhD status are candidates for genotyping. Individuals who have weak D type 1, 2, 3, and 4.0 were considered not at risk for alloimmunization and are not candidates for RhD immunoprophylaxis. On the FluoVista device, using the Fluogene PCR-SSP method, with a fluorescent reading of the results (FluoGene® Inno-train Diagnostik GmbH, Germany), in the period from 2020 to 2022, 22 samples of RhD-negative persons, whose phenotype had C and or E antigen, as well as 20 persons with serologically weak D antigen, were examined. D weak type 1 and type 3 were proven in 10 cases each.

Conclusion

Patient blood management is, by definition, an evidence-based, multidisciplinary team approach to optimizing the care of patients who may need a transfusion. It focuses on measures to avoid blood transfusions, as well as on the proper use of blood components when they are necessary. Immunohaematological tests represent an essential part of patient blood management because they have significant diagnostic and prognostic value in providing appropriate and safe blood components for transfusion and transplantation.

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ALGORITHM OF AUTOMATED IMMUNOHAEMATOLOGY TESTING

Sanja Bogdanović
Blood Transfusion Institute of Vojvodina, Novi Sad, Serbia

Abstract

Immunohaematology testing is essential in transfusion medicine in testing blood samples of blood donors, patients, pregnant women, newborns, and other subjects. It can be performed classically in a test tube and automatically in an analyzer. The term "automation" in laboratory medicine describes a process in which one or more laboratory analyzers perform a large number of analyzes with minimal involvement of laboratory staff. Automation immunohaematology testing has led to the standardization of work and more objective and reproducible results compared to the classic test-tube technique. Also, human errors such as sample identification, recording/overwriting data about the subject, and test results had reduced. The progress and development of automation should use maximum aid in work. Automation seems to be a perfect substitute for human work but educated, trained personnel are essential in a laboratory, and a complete replacement is not possible.

Keywords:Automation, Quality Improvement, Laboratory

Sažetak

Imunohematološko testiranje ima veliki značaj u transfuzionoj medicini u ispitivanju uzoraka krvi davalaca krvi, bolesnika, trudnica, novorođenčadi i ostalih ispitanika, a može se izvoditi klasično u epruveti i automatskom metodom u analizatoru. Naziv „automatizacija“ u laboratorijskoj medicini se koristi za opisivanje procesa u kojem jedan ili više laboratorijskih analizatora izvodi veliki broj analiza uz minimalno učešće laboratorijskog osoblja. Automatizacija imunohematološkog testiranja je dovela do standardizacije rada, te objektivnijih i reproducibilnijih rezultata u odnosu na klasičan rad metodom u epruveti. Takođe, smanjen je broj ljudskih grešaka, kao što su identifikacija uzorka, zapisivanje/prepisivanje podataka o ispitaniku, te o rezultatima testiranja. Napredak i razvitak automatizacije treba iskoristiti kao maksimalnu pomoć pri radu, ali koliko god se automatizacija činila savršenom zamenom za rad čoveka, moramo biti svesni da bez edukovanog i osposobljenog osoblja laboratorijski posao nije moguć.

Ključne reči: automatizacija, unapređenje kvaliteta, laboratorija

Introduction

Immunohaematology testing is essential in transfusion medicine in testing blood samples of blood donors, patients, pregnant women, newborns, and other subjects. It can be performed classically in a test tube and automatically in an analyzer [1]. This article will present the algorithm of automated immunohaematology testing of blood samples and technological advances.

Automation in immunohaematology

The term "automation" in laboratory medicine describes a process in which one or more laboratory analyzers perform a large number of analyzes with minimal involvement of laboratory staff. Automation in immunohaematology testing is a significant measure to decrease the risk of potential error and establish blood safety [2,3].

Manual tube testing is still the Gold Standard in immunohaematology, but it has numerous disadvantages, especially in high throughput laboratories:

a.Variability of the concentration of red cell suspension affects the ratio of antigens and antibodies.
b. Elution of low-affinity antibodies during centrifugation.
c. Variation in reading and interpreting agglutination reaction.
d. Human errors.
e. D*eficit of* skilled staff

Automation of immunohaematology testing provides multiple advantages, such as:

a. The barcode system prevents sample identification errors.
b. Prevention of human errors in performing tests and subjective variations during reading and interpretation of results.
c. Prevention of transcription errors while documenting the results.
d. Improving objectivity, reproducibility, and storage and retrieval of results of immunohaematology tests.
e. Improving traceability of all variables during testing including samples, reagents, and operating staff.
f. It reduces manual input and therefore results in staff economy.
g.High throughput devices with lesser turnaround time improve the quality of services in large tertiary care settings [2,4].

Techniques and platforms of automated immunohaematology testing

Commonly used techniques are column agglutination technique (CAT), Solid Phase Red Cell Adherence Assay (SPRCA), and erythrocyte magnetized technique (EMT). They bring about an improvement in the quality of testing and the reproducibility of results. Fully automated platforms are available for forward and reverse ABO blood grouping, red cell antibody screening

and identification, cross matching, Rh and K phenotyping, etc. They are manufactured by: Biorad (Swiss), Diagast (France), Ortho Clinical Diagnostics (Johnson and Johnson, USA), Immucor (USA), Grifols (USA). These systems differ in their technical specifications, throughput, turn-around time, sample loading operation etc.

The CAT system consists of a plastic card with six to eight inbuilt microtubes. The microtubes have a wide reaction chamber in the upper part, while the lower part contains either a clear gel (Biorad and Grifols) or a glass microbead matrix (Ortho Clinical Diagnostics). SPRCA is a technique in which one of the components of an antigen-antibody reaction is immobilized onto a solid medium (microplate) and after reaction with a free antigen/antibody, the endpoint of the reaction is indicated by the use of red cells, which may be a part of the antigen-antibody reaction or may be added as indicator cells (Immucor). EMT technology is based on the magnetization of RBCs. Paramagnetic particles are adsorbed onto the surface of RBCs (Diagast) [5–8].

Installation and validation of equipment

The implementation of a Quality Management System helps to reduce the number of technical, and more often procedural, errors made in laboratories. These include quality assurance measures such as the use of standard operating procedures, staff training, periodic assessment of the technical competence of staff, documentation and validation of techniques, reagents, and equipment, procedures that monitor day-to-day reproducibility of test results, and methods to detect errors in analytical procedures. This should include a section on validation that describes the organization's validation policy which should comply with the regulatory requirements applicable in the country of use. All immunohaematology systems need validation before implementation. The system should not be used without proper validation of the results [1,9–11].

Automation of immunohaematology testing in Blood Transfusion Institute of Vojvodina

Blood Transfusion Institute of Vojvodina (BTIV) 2014 introduced automated immunohaematology testing of blood donors samples for forward and reverse ABO blood grouping, screening of irregular red cell antibody, Rh and K phenotyping on IH-1000 (Biorad) and added it 2015 Qwalys 3 (Diagast). Since 2016 is introduced automated immunohaematology testing of patients, pregnant women, and other subjects for forward and reverse ABO blood grouping, and direct and indirect immunoglobulin tests on IH-500 (Biorad). In May 2020 is introduced the algorithm of automated immunohaematology testing of patients, pregnant women, and other subjects which includes the discovery of a weak and partial variant of DVI antigen. In case of discrepant results according to the type of discrepancy between DVI- and DVI+, molecular testing of DVI antigen is indicated. All automated immunohaematology systems and algorithms are validated before implementation regarding standard operating procedures of the Quality Management System.

Future technologies

The serological techniques currently used in conjunction with evolving typing technologies (e.g. DNA Typing of Red Cell Antigens) can be of great value for safe blood transfusion [12]. There is an evolution in the development of new technologies, including electronic crossmatch in patients with negative antibody screens and a supply of uncrossing matched blood through vending machines away from the blood bank [13,14].

Conclusion

Therefore continuous scientific progress coupled with automation and computerization is the future requirement for maintaining the highest degree of quality in the blood bank. The progress and development of automation should use for maximum aid in work. Automation seems to be a perfect substitute for human work but educated, trained personnel are essential in a laboratory, and a complete replacement is not possible.

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CLINICAL MONITORING AND TREATMENT OF ALLOIMMUNIZED PREGNANT WOMEN IN TRANSFUSION

Ivana Pešić Stevanović[1], Marika Ljubenov[1], Željko Miković[1,2], Dejan Filimonović[1,2], Svetlana Ristić[1], Snežana Srzentić[3], Maja Pantić[1]

[1]Clinic of gynecology and obstetrics"Narodni Front", Belgrade
[2]Medical School, University of Belgrade
[3] Blood Transfusion Institute of Serbia

Abstract

Control and medical treatment of alloimmunized pregnant women are based on immunohaematological monitoring in a specialized center. The gold standard in the treatment of fetal anemia and hydrops is the use of intrauterine transfusion (IUT).

Sudy objective was to present experiences in the application of IUT in fetal anemia and their outcome in the period from July 1st/2018 to July 1st/2022 in GAK "Narodni front" in Belgrade.

Retrospectively all cases of alloimmunized pregnant women in the specified period were considered. The specificity of pregnant women's immune antibodies, their titer before the first transfusion, gestational week, serial ultrasound examinations, and the outcome of the mentioned procedure were monitored.

In the mentioned period, 54 intrauterine transfusions were performed: three intraperitoneal (5%) and 51 intravascular transfusions (95%) in 18 fetuses (18 pregnant women). Three fetuses (17%) had a severe form of hydrops before the first transfusion, five (28%) had mild, and ten fetuses were without hydrops (55%). The highest score of incidence of IUT was in RhDalloimmunized pregnant women. The highest anti-D antibody titer before the first IUT was 2048, the lowest 64. The median IUT was 3 per fetus with a range of 1-7. The mean gestational week was 29 gw with a range of 16-37 gw. The gestational week at the first intrauterine transfusion was 16-32 gw. The hematocrit of the applied blood units was 69-80%. The value of the blood volume used was 20-135 ml. The number of performed IUT before 20 gw was two (11%) and after 34 gw 10 (55%). Hematological values were monitored before and after IUT. A healthy newborn was born to 10 (56%) pregnant women, and 7 (39%) newborns had anemia that required transfusions after birth. After the intervention, after 7 days, intrauterine death occurred in 1 fetus (5%).

In conclusion, IUT is the therapy of choice in severe fetal anemia caused by alloimmunization. Although it is invasive, it ensures a high percentage of survival because it is performed in a safe and secure way. Alloimmunized pregnant women should be referred to a specialized center before the development of hydrops.

Keywords: intrauterine transfusion, alloimmunization, fetal anemia

Sažetak

Kontrola i lečenje aloimunizovanih trudnica zasniva se na imunohematološkom praćenju u specijalizovanom centru. Zlatni standard u lečenju fetalnih anemija i hidropsa je primena intrauterine transfuzije (IUT).

PCilj rada je prikazati naša iskustva u primeni IUT kod fetalnih anemija i njihov ishod u periodu od 01.07.2018. do 01.07.2022. godine u GAK „Narodni front" u Beogradu.

U ovoj retrospektivnoj studiji razmatrani su svi slučajevi aloimunizovanih trudnica u navedenom periodu. Praćena je specifičnost imunih antitela trudnica, njihov titar pre prve transfuzije, gestaciona starost, serijski ultrazvučni pregledi i ishod navedene procedure.

U navedenom periodu izvedene su 54 intrauterine transfuzije: tri intraperitonealne (5%) i 51 intravaskularna transfuzija (95%) kod 18 fetusa (18 trudnica). Tri fetusa (17%) su imala težu formu hidropsa pre prve transfuzije, pet (28%) blagu, 10 fetusa je bilo bez hidropsa (55%). Najveća zastupljenost IUT bila je kod RhD aloimunizovanih trudnica. Najveći titar anti-D antitela pre prve IUT bio je 2 048, najniži 64. Medijana IUT je tri po fetusu sa rasponom od 1 do 7. Srednja gestacijska starost bila je 29 ng u rasponu 16–37. ng. Starost gestacije pri prvoj IUT bila je 16–32. ng. Hematokrit primenjenih jedinica krvi bio je 69–80%. Primenjen je volumen krvi 20–135 ml. Broj izvedenih IUT pre 20. ng je bio dve (11%), a posle 34. ng 10 (55%). Praćene su hematološke vrednosti krvne slike pre i posle IUT. Zdravo novorođenče rodilo je 10 (56%) trudnica, 7 (39%) novorođenčeta je imalo anemiju koja je zahtevala primenu transfuzija nakon rođenja. Nakon 7 dana posle intervencije kod 1 fetusa (5%) nastala je intrauterina smrt.

U zaključku moguće je reći da IUT predstavlja terapiju izbora kod teških anemija fetusa izazvanih aloimunizacijom. Iako je invazivna, ona obezbeđuje visoki procenat preživljavanja jer se izvodi na bezbedan i siguran način. Aloimunizovane trudnice treba uputiti u specijalizovani centar pre razvoja hidropsa.

Ključne reči: intrauterina transfuzija, aloimunizacija, fetalna anemija

Introduction

Alloimmunization occurs as a result of the reaction of the pregnant woman's immune system to erythrocytes antigens of the fetus, by the production of antibodies of the IgG class. The result of this perinatal process is fetal anemia and hemolytic disease of the fetus/newborn (HBFN). A pregnant woman can be alloimmunized by blood transfusion or as a result of fetomaternal bleeding during childbirth, trauma, spontaneous or caused by abortion, ectopic pregnancy or invasive obstetric

procedure(1). Follow-up of alloimmunized pregnant women is based on immunohaematological testing as well as numerous ultrasound checks of the biophysical profile of the fetus, thickness of the placenta, also by doppler sonography measurements of the maximum systole flow through the fetal artery of the cerebral media ACM (middle cerebral artery peak systolic volume - MCA PSV). All of this is used for diagnoses of fetal endangerment, anemia or fetal hydrops (1,2). The study goal was to present experiences in the use of IUT in fetal anemia and their outcome in the period from July 2018 to July 2022. In the Clinic of Obstetrics and Gynecology "Narodni Front", in Belgrade.

Methods

In this retrospective study, all alloimmunized pregnant women were a part of the research study in the following period of time. The monitoring included: specificity of the mother's immune antibodies, the titer before the first transfusion, gestational age, frequent ultrasound examinations, and the outcome.

All reports of IUT, alloimmunization, intrapartum, postpartum and neonatal data were collected from an electronic database (ZIS, Delphyn), as well as from protocols for IUT, discharge lists or by contacts of neonatologists and transfusiologists from the institutions where newborns were referred for further treatment.

Intrauterine transfusion technique

During the research, three obstetricians applied IUT under ultrasound control. Pregnant women were prescribed Diazepam 10 mg i.m. or i.v. 30 minutes before the performance. For IUT a 21 G needle was used. After the introduction of the needle, the first sample was taken for transfusion and analysis of blood tests. The fetal blood count was analyzed by a Horibo Microsemi hematology analyzer.The volume of the IUT was calculated using the formula (4,6). IUT was performed by inserting a needle into an umbilical cord vein closer to the root of the placenta, into its intrahepatic course or by the choice of the gynecologist. After completion of IUT, another blood sample was taken to confirm transfusion procedures. In some cases, blood was transfused into the peritoneal cavity as an adjunct to intravascular IUT transfusion. This reduces the direct cardiovascular load of the fetus or extends the period until the next procedure. The birth was usually planned 2 weeks after the last one IUT.

Results

In the research period, a total of 54 intrauterine transfusions (IUT) were conducted: 3 intraperitoneal (5%) and 51 (95%) intravascular transfusions in 18 pregnant women and 18 fetuses. Representation of specific antibodies: anti-D (n= 8), anti-D+C (n= 3), anti-D+C+G (n=1), anti-c+K (n= 1), anti- D+E+Jka + Lea (n=1), anti-D+ C+Jka (n= 1), anti-D+E +Jka (n= 1), anti-K (n= 2)Three fetuses (17%) had a severe form.of hydrops in the first transfusion, 5 (28%) were mild, ten fetuses were without hydrops (55%). The greatest prevalence of IUT was in RhD-alloimunized pregnant women. The highest titer of the anti-D antibody was 2048, and the lowest was 64. During the research period, the median IUT was 3 per fetus with a range from 1-7. The mean gestational week was 29 gw in the range from 16-37 gw. The gestational week at the first intrauterine transfusion was from16 to 32 ng. Hct of the applied unit of blood was from 69% to 80%.

Administered blood volume was between 20 and 135ml. The number of performed IUT before 20 ng was two (11%) and after 34 ng 10 (55%). Co-hematological values before and after IUT were monitored. Mean hemoglobin and hematocrit levels before transfusion were significantly lower in hydrops than in non-hydrops fetuses Hgb 51 vs. 83 and 19% vs. 26%. Healthy newborns were born to 10 (56%) pregnant women, and 7 (39%) newborns had anemia that required postpartum transfusions. Adverse events included 1 emergency cesarean section immediately after IUT at 32ng and 1 premature delivery within 7 days after IUT. After 7 days of the intervention, intrauterine death occurred in one (5%) fetus.

Discussion

The application of intrauterine transfusions (IUT) is used in the treatment of severe fetal anemia. Direct intravascular transfusion to the fetus via the umbilical vein is the gold standard for the treatment of severe forms of HBV (2, 5). Hydrops fetalis is defined as mild when there are ascites (with or without pericardial effusion), and severe when marked ascites, pericardial effusion, enlarged liver, and edema are present skin (1, 7). There is a large number of publications in the literature about different diagnostic methods and HBFN therapy as well as about the condition of newborns with hemolytic disease (1, 2, 5). However, the main method of treatment of HBFN, IUT is the subject of several papers (6, 8, 9).

Earlier, for the diagnosis of fetal anemia, it was used amniocentesis, today anemia is assessed by doppler measurement of MCA PSV, which is converted to multiples of the median (MoM) (7) MCA PSV above 1.5 MoM is an indication for IUT. The sonographic feature of fetal hydrops is also an indication of fetal blood sampling-cordocentesis. A fetus with a hemoglobin value of at least two standard deviations (SD) below mean values for gestational age at fetal blood sampling was considered anemic (7).

Intraperitoneal transfusion is used in endangered fetuses in early pregnancy. In IUT, ORhD-negative erythrocytes, antigen-negative against which the corresponding anti-erythrocyte antibody present in the circulation of the pregnant woman, cytomegalovirus-negative and leukocyte-reduced (filtered), irradiated with 25 Gy, stored for up to 5 days from the day of the collection are used. It is recommended that the hematocrit (Hct) of the applied unit of erythrocytes for IUT is 70-80% (5, 8). The amount of applied IUT depends on the volume of blood in the placenta of the fetus, the fetal hematocrit, and the hematocrit of the donor (6, 8).

Adverse events related to the procedure can be mild (transient contractions requiring tocolysis and transient bleeding from the puncture) and severe (membrane rupture or intrauterine transection) within seven days, emergency section, fetal distress within 24 hours after the procedure, fetal and neonatal death (5).

In our series of 54 IUTs, 95% of the performed procedures passed without complications and adverse events, while in one fetus (5%) fetal death occurred 7 days after the procedure. Neonatal morbidity is mainly associated with hematological

complications and the consequences of premature birth (10). Some European researchers, in publications from 1988 to 2012, described perinatal mortality of 4.7%, while the complication rate associated with the procedure was 7.6% (4). Early gestational week at the first transfusion is another significant risk factor for complications related to the procedure, especially because performing IUT before 22 gw is particularly challenging (9). In our work, there was no perinatal mortality, which can be explained by the fact that regular screening of antibodies enabled timely referral of the pregnant woman to a tertiary center, reducing the percentage of hydrops fetuses. Despite our significant work, the overall mortality and complication rates observed in our study were comparable to those reported in other studies published in the literature (9, 10).

Conclusion

Intrauterine transfusion is the therapy of choice in severe fetal anemia caused by alloimmunization. Although it is an invasive method, it provides a high percentage of survival because it is performed in a safe and secure way. Pregnant women with alloimmunization should refer to a specialized center before the development of hydrops.

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ROLE OF THERAPEUTIC PLASMA EXCHANGE IN THE TREATMENT OF ACUTE RHEUMATIC CONDITIONS

Aleksandra Antovic[1, 2]
[1]Karolinska Institutet, Department of Medicine Solna, Division of Rheumatology, Stockholm, Sweden;
[2]Karolinska University Hospital, Unit of Rheumatology, Stockholm, Sweden

Abstract

Catastrophic antiphospholipid syndrome (CAPS) is a severe autoimmune condition characterized by numerous thrombotic lesions, occurring within a short period of time and leading to multiple organ failures. The pathognomonic sign of CAPS is triple positivity for antiphospholipid antibodies in high titers. Although CAPS patients represent less than 1% of all patients with antiphospholipid syndrome, they are usually in a life-threatening medical situation that requires high clinical awareness. Mortality rates are still very high, around 40%. Therapeutic plasma exchange (TPE) is frequently used as a part of combination therapy for CAPS (anticoagulants, steroids, and TPE) improving the survival rate in patients with CAPS up to 25%. TPE is a valuable therapeutic and well-tolerated procedure, with proven efficacy in the elimination of disease-specific antibodies from the plasma of patients with autoimmune conditions. Thus, the use of this technique, along with anticoagulation and if needed pharmacological immunosuppression, should be considered for the acute management of patients presenting with this life-threatening condition.

Keywords: Plasma exchange, antiphospholipid syndrome, ANCA-associated vasculitis.

Catastrophic antiphospholipid syndrome (CAPS)

The range of pathological features of the antiphospholipid syndrome (APS) includes thrombosis in the arterial and venous blood vessels as well as capillaries, together with obstetric morbidity in the presence of antiphospholipid antibodies (aPL) (1,2). According to the classifications criteria (1), the persistent presence of medium to high titers of aPL comprises antibodies against cardiolipin (aCL), β2glycoproteinI (anti-β2GPI), or positivity to lupus anticoagulant (LA).

Catastrophic antiphospholipid syndrome (CAPS) constitutes < 1% of all APS cases, though with 30-50% mortality. CAPS is a dramatic severe 'thrombotic storm', with thrombotic lesions in multiple locations occurring within a short period of time. A pathognomonic sign of CAPS is s.c. triple positivity for aPL. International consensus criteria from 2003 (3) state that for classification of a definite CAPS diagnosis, four criteria have to be fulfilled: (i) involvement of three or more organ systems, (ii) presentation within a week, (iii) biopsy confirming small vessel occlusion in at least one organ and (iv) aPL positivity. Patients may however present with acute APS-related symptoms, but do not fulfill all four criteria. In these cases, they should, depending on symptoms, be considered probable CAPS and be treated accordingly.

Small vessel occlusions dominate the clinical CAPS picture, but thromboses in large vessels may also occur. A major source of knowledge about CAPS comes from the CAPS registry, an online registry that has collected more than 500 international case reports. Information on initiating and descriptive factors, treatments, and outcomes is collected in this registry (https:// ontocrf.grupocostaisa.com/ web/caps), and all who care for these patients are asked to report their cases. The last updated cumulative data state that the average age at diagnosis is 38 and 69% are female. The most common organs to be affected are kidneys (73%), lungs (60%), brain (56%), heart (50%), and skin (47%). Mortality rates have declined over the years but are still very high, 37%. A key observation is that precipitating factors, 'a second hit', especially infections (49%), but also surgery (17%), malignancies (16%), contraceptives (10%), and pregnancy-related complications (8%), precede CAPS in a majority of cases. Patients with autoimmune diseases, especially SLE, were overrepresented (40%) and these patients had a more severe prognosis (4).

Treatment of CAPS

Importantly, all CAPS patients should be subject to intensive multidisciplinary care. Presentation is often within emergency medicine, and it is important to exclude other conditions with similar symptoms such as infections and sepsis with associated disseminated intravascular coagulation (DIC), heparin-induced thrombocytopenia (HIT), thrombotic thrombocytopenic purpura (TTP) and hemolysis, elevated liver enzymes and low platelet count (HELLP) syndrome during pregnancy (5).

The compiled data from the CAPS registry demonstrate the best outcome for patients who received a combined therapeutic approach, including anticoagulation, plasma exchange, and/or intravenous immunoglobulin (IVIG) and glucocorticoids (5,6). It is also important to promptly treat/correct all triggering factors such as infections.

Therapeutic plasma exchange (TPE)

Therapeutic plasma exchange (TPE) is effective in treating immune diseases by physically eliminating disease-specific free antibodies from the plasma (7). This technique has been used for the first time in systemic lupus erythematosus (SLE) in 1974 (8).

Due to the rarity of the disease and in the absence of well-designed randomized controlled trials, the American Society for Apheresis (ASFA) assigned category 2, grade 2C for the TPE to treat the CAPS (9). TPE is, therefore, considered a second-line treatment for CAPS.

Though, given the known benefits of TPE in the treatment of microangiopathies, as well as the proven pathogenicity of antiphospholipid antibodies, TPE has been used as a part of combination therapy for CAPS (10, 11). Retrospective studies have shown survival of 77.8% among patients treated with the triple therapy (anticoagulants, steroids, and TPE), compared to 55.4% of patients who did not receive TPE (11). The treatment protocol for CAPS at the Karolinska University Hospital includes TPE and is frequently used.

TPE is a relatively safe and well-tolerated procedure. In a large survey by McLeod et al, the overall incidence of adverse effects associated with TPE was 4.75% of mostly reversible adverse effects (12). The incidence of selected specific adverse events was: transfusion reaction 1.6%; vasovagal nausea and/or vomiting 1.2%; systolic blood pressure <80mmHg 0.4%; respiratory distress 0.3%; tetany or seizure 0.2%; and chills or rigors 0.2%. One possible way to decrease the further risk of transfusion reaction induced by exposure to plasma used as a replacement is the use of 5% serum albumin.

Conclusion

CAPS is a severe medical condition characterized by a thrombotic storm and high levels of circulating aPL antibodies. In the absence of randomized clinical trials, no treatment is yet considered optimal for this disease and the mortality is still high. TPE is a valuable therapeutic and well-tolerated procedure, with proven efficacy in the elimination of disease-specific antibodies from the plasma of patients with autoimmune conditions. TPE has shown reasonable therapeutic benefits and improved survival for patients with CAPS. Therefore, the use of this technique, along with anticoagulation and if needed pharmacological immunosuppression, should be considered for the acute management of patients presenting with this life-threatening condition.

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CONVALESCENT PLASMA IN TREATMENT OF COVID-19

Rada M. Grubovic Rastvorceva[1,2]
[1]Institute for Transfusion Medicine of RNM, Skopje, North Macedonia
[2] Faculty of Medical Sciences, University Goce Delcev, North Macedonia

Abstract

COVID-19 convalescent plasma (CCP) is the second most frequent investigational medicinal product evaluated in COVID-19-related clinical trials and increasing interest in this form of immunotherapy is documented by the fact that more than 140 clinical trials specifically evaluating CCP in COVID-19 have been registered to date worldwide. Despite the variability in the certainty of the evidence, mostly related to the risk of bias and inconsistency, there is a growing body of evidence supporting the efficacy of high-titer CCP in reducing progression to severe disease and decreasing mortality in in patients with early COVID-19 and low WHO scores. The safety of CCP has been confirmed in multiple studies, with the largest data set supporting a high safety profile coming from the US Expanded Access Program. Based on our experience, the use of CCP in hospitalized COVID-19 patients in North Macedonia was characterized by high safety and efficacy, when administered early in the disease course with high titer of antibodies, particularly in patients with moderate disease. Further studies are needed to identify the subset of patients that would most benefit from it and to elucidate the optimal dose.

Keywords: convalescent plasma, COVID19, SARS-CoV-2

The COVID-19 pandemic is a significant threat to public health. The disease, which has spread to 225 countries worldwide with more than 596 million confirmed cases, has caused over 6.5 million deaths. Clinicians and researchers have struggled to develop effective therapeutic protocols to treat and contain the spread of COVID-19 and more than 300 drugs have been or are being investigated under clinical trials in different parts of the world. Based on its historic success for a variety of infectious diseases and its overall safety, COVID-19 convalescent plasma (CCP) has been employed as a treatment for COVID-19 since nearly the beginning of the pandemic. CCP is readily available as soon as the first convalescent can donate plasma, affordable and deployable even in resource-poor countries. Randomized controlled trials (RCTs) of CCP have shown a consistent trend. To be effective, the CCP product must have sufficient titers of neutralizing antibodies (nAb) and be used at an early stage of the infection. Use of CCP with low (or no) levels of nAb or in patients who are at later stages where the disease process is driven by an overactive inflammatory response is not effective. CCP is the second most frequent investigational medicinal product evaluated in COVID-19-related clinical trials and increasing interest in this form of immunotherapy is documented by the fact that more than 140 clinical trials specifically evaluating CCP in COVID-19 have been registered to date worldwide. There is a growing body of evidence supporting the efficacy of high-titer CCP in reducing the progression to severe disease and decreasing mortality in inpatients with early COVID-19 and low WHO scores. Our results showed improvement in clinical findings in the investigated group of patients, with an increase of 32.3% in oxygenation-free days 24 hours after CCP transfusion and an increase of 58.5% in oxygenation-free days 7 days after CCP transfusion, and accordingly apparent improvement in WHO clinical progression scores. The overall mortality rate in our cohort (11.6%) is similar to that reported in recent real-life studies performed on large cohorts of hospitalized COVID-19 patients and comparable to figures reported in most previous studies on CCP. There were no deaths after receiving CCP transfusion in patients with a WHO score of 3 (mortality 0/65; 0%) and in patients treated in the first 7 days of illness. Mortality in patients belonging to WHO disease progression score 4 was 4.6% (3/65). A systematic review by Franchini M et al. highlights a mortality reduction in CCP over standard therapy when administered early and at high titer, without increased adverse reactions, despite the variability in the certainty of the evidence, mostly related to the risk of bias and inconsistency. A similar finding, i.e., a strong inverse correlation between CCP use and mortality per hospital admission, was also observed in a publication reporting the US experience on Expanded Access Program (EAP) use of CCP in approximately 500,000 patients. On the other hand, there have been a large number of well-executed clinical trials, such as RECOVERY, REMAPCAP, or CONCOR-1 that did not find CCP to be beneficial, albeit in advanced COVID-19. While it was not known at the time of their design, many of these studies of CCP focused, disproportionately, on populations (i.e., late-stage COVID-19) and interventions (low-titer CCP) that are now known to be suboptimal or ineffective for passive antibody-based therapy, whereby early administration of high-titer plasma is critical. As an example, a subgroup analysis of the RECOVERY data for patients without the use of corticosteroids (indicative of earlier disease stage) showed a trend toward fewer deaths at 28 days in the CCP versus the control groups (19% vs. 24%, respectively). There was a similar observation in patients that did not receive respiratory support and received CCP early after disease onset. There are several explanations for the discrepancy between mortality rates observed in real-life studies and in RCTs, many of which failed to show a reduction in mortality, and some discontinued for futility. These include the fact that CCP is not pharmaceutical but rather an artisanal product (it is produced at transfusion centers), and nAb titer and absolute content in the cumulative volume varies widely. Additionally, differences in study design, patients` characteristics, and disease severity could have played a role. Nevertheless, when subgroup analyses were restricted to the early use of high-titer CCP, most of the published RCTs showed signals of CCP efficacy, including reductions in mortality. Other studies have demonstrated that CCP treatment can benefit immunocompromised patients as well as outpatients. Another important finding of our study is that CCP therapy was a safe treatment with no serious adverse

events among the 189 CCP units transfused. The safety of CCP has been confirmed in multiple studies, with the largest data set supporting a high safety profile coming from the US Expanded Access Program, which initially reported on 5,000 then 20,000, and most recently on 100,000 CCP recipients. Factors associated with worse outcomes in this study were increased age and stay in the intensive care unit, i.e. more advanced disease. These findings are in accordance with other studies. The clinical characteristics of non–survivors included adult males, A blood group, overweight (mostly obese), with comorbidities and hypertension as the most common, which is in line with the other studies. Blood group A may be associated with a higher risk of SARS-CoV-2 infection along with severe disease. According to a prognostic study by Park H et al., based on data from the COMPILE study, patients with preexisting conditions (diabetes, cardiovascular and pulmonary disease), with blood type A or AB, and at early COVID-19 stage (low baseline WHO scores) were expected to benefit most from CCP. The main limitation of our study is that we did not have a control group of patients. Nonetheless, the result from this study demonstrated safety (no serious adverse events) and suggested efficacy, especially if given in the first 7 days and to patients with mild to moderate disease (i.e. WHO scores 3 and 4 on the WHO 8-score disease progression scale). Our results with CCP use in RNM are consistent with and supportive of findings in other parts of the world. The COVID-19 pandemic is still present worldwide and new waves of the disease are occurring, even in countries where the population has been vaccinated, due to the emergence of new variants and the decreasing efficacy of existing vaccines. Therefore, patients with a high risk of morbidity and mortality should be identified early in order to administer the best treatments available before they progress to severe disease. While old CCP stocks are no longer effective at neutralizing Omicron, nowadays CCP is largely available from regular donors who are likely to be also triple vaccinated. The concurrence of these 2 conditions creates heterologous immunity, which is extremely helpful at a time when the Omicron BA.2 and BA.4/BA.5 sublineages have defeated most of the anti-Spike monoclonal antibodies authorized so far. While fractionated plasma products (e.g. hyperimmune globulin, monoclonal antibodies) and/or vaccination may offer durable therapeutic options, human anti–SARS–CoV-2 plasma is the only therapeutic strategy that is immediately available for use to prevent and treat COVID-19, especially in low and middle-income countries where availability of more expensive drugs is limited. The other major advantage is versatility, with the potential for CCP to respond to emerging variants. Niches for CCP treatment of COVID-19 include outpatients who are at high risk for disease progression, hospitalized patients who do not have SARS-CoV-2 antibodies detected at admission or have preexisting immunosuppression and chronically infected patients, as recently recommended by AABB and FDA guidance. This study suggests that CCP may be as effective as other antibody-based and small-chemical antivirals, especially if given early in the disease course and with a high titer of antibodies. CCP can be helpful in selected patients with COVID-19 and further studies are needed to identify the subset of patients that would most benefit from it and to elucidate the optimal dose. In conclusion, based on our experience, the use of CCP in hospitalized COVID-19 patients was characterized by high safety and efficacy, when administered early in the disease course with high titer of antibodies, particularly in patients with moderate disease.

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ALLOGENEIC STEM CELL TRANSPLANTATION AS A THERAPEUTIC CHALLENGE

Milena Todorović Balint[1,2], Nada Kraguljac Kurtović[1],
Dijana Šefer[1], Irena Đunić[1,2], Marija Dinić[3], Bela Balint[3,4]

[1]Clinic for Hematology,University Clinical Center of Serbia, Belgrade, Serbia;
[2]Faculty of Medicine, University of Belgrade, Serbia;
[3]Department for Therapeutic Apheresis Procedures, University Clinical Center of Serbia;
[4]Department of Medical Sciences, Serbian Academy of Sciences and Arts, Serbia;
[5]Institute of Cardiovascular Diseases "Dedinje", Belgrade, Serbia

Abstract

Historically, the concept of bone marrow transplantation as a therapeutic modality arose from the idea of scientists after World War II who tried to reverse the effects of radiation on people who survived the atomic bomb explosion in Japan. The first basic research focused on preclinical animal models with total-body irradiation with spleen protection.

Implementation of HLA histocompatibility between donor and recipient with improved conditioning and graft-versus-host disease (GvHD) prophylaxis, allowed successful transplantations in aplastic anaemia and leukemia.

A clear correlation between the occurrence of GvHD and the risk of relapse established the existence of the graft-versus-leukemia (GvL) effect induced by donor T-cells, which led to the application of donor lymphocyte infusion (DLI) after stem cell transplantation in patients who relapsed. In the late 1980s, the introduction of G-CSF mobilized peripheral blood stem cells to enable faster engraftment. Since only 30% of the patients have an HLA-identical sibling donor, unrelated donor registries provide a pool of about 30 million people. The expansion of haploidentical stem cell transplantation offers the concept that every patient could have a potential donor. The growing tendency of using reduced intensity conditioning regimen decreased non-relapse mortality.

The main focus is on reducing the risk of relapse by developing strategies to monitor minimal residual disease including novel drugs in pre and post-transplant clinical settings.

Keywords: allogeneic stem cell transplantation, history, current principles

Sažetak

Istorijski gledano, koncept transplantacije kostne srži kao terapijskog modaliteta nastaje na temelju ideje naučnika nakon Drugog svetskog rata koji su pokušali da ponište efekte zračenja na ljudima koji su preživeli eksploziju atomske bombe u Japanu. Prva bazična istraživanja su se fokusirala na pretkliničke životinjske modele sazračenjem celog tela uz zaštitu slezine.

Implementacija HLA histokompatibilnosti između donora i primaoca uz poboljšanu profilaksu bolesti kalema protiv domaćima (graft-versus-host disease − GvHD), omogućila je uspešne transplantacije kod aplastične anemije i leukemije.

Jasna korelacija između pojave GvHD i rizika od relapsa utvrdila je postojanje efekta graft-versus-leukemia (GvL) izazvanog T-ćelijama donora, što je dovelo do primene infuzije donorskih limfocita (DLI) nakon transplantacije matičnih ćelija kod pacijenata koji su imali recidiv. Krajem 1980-ih uvođenje G-CSF-om mobilisanih matičnih ćelija periferne krvi omogućilo je njihov brži "engraftment". S obzirom da samo 30% pacijenata ima HLA identičnog srodnog donora, postoje registri nesrodnih davalaca matičnih ćelija koji broje oko 30 miliona ljudi. Ekspanzija haploidentičnih transplantacija matičnih ćelija nudi koncept da svaki pacijent može imati potencijalnog donora. Rastuća tendencija korišćenja režima kondicioniranja smanjenog intenziteta smanjila je mortalitet nevezan za relaps bolesti.

Glavni fokus je na smanjenju rizika od relapsa razvojem strategija za praćenje minimalne rezidualne bolesti uključujući nove terapijske agense primenjene pre i posle transplantacije.

Ključne reči: alogena transplantacija matičnihćelija, istorijat, aktuelni principi

Historical overview and current principles

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) has advanced from a treatment that was proclaimed dead in the 1960s to a standard treatment option for otherwise lethal malignant and non-malignant blood disorders. Nowadays about 20,000 allo-HSCT are performed within Europe annually and the numbers are increasing. The main indications are myeloid leukemia, acute lymphoblastic leukemia, and myelodysplastic syndrome. Also, it is a standard treatment for many immunodeficiency states, and metabolic disorders to date, about 1.5 million hematopoietic cell transplants have been performed in more than 1500 transplantation centers worldwide (1).

One of the limitations in early allo-HCT was that only 30% of patients had HLA-identical siblings who could be donors. In order to overcome that limitation, and assisted by an increasing understanding of the genetics of the HLA region, along with improved HLA-typing techniques, unrelated donor registries were established in the 1980s that collected HLA data from unrelated volunteer donors, first in the UK with the Anthony Nolan Foundation, in the United States with the National Marrow Donor Registry, and then other national registries (1). For Caucasian patients, the probability of finding HLA matched unrelated donor is about 80%, and this percentage drops intensely for patients from ethnic groups (2). In order to provide a potentially curative option for these patients, transplant methods have been developed to use grafts either from unrelated

umbilical cord blood (UCB) or from HLA-haploidentical donors. Such donors can be found for 95% of transplant candidates regardless of age and ethnic background (1).

Also, in 1995, G-CSF-mobilized peripheral blood hematopoietic stem cells (HSC) were introduced, and nowadays they are the predominant graft source for patients with hematologic malignancies (3). Since peripheral blood HSC caused more chronic graft versus host disease (GvHD), bone marrow remained the preferred source of stem cells for patients with non-malignant diseases such as severe aplastic anemia.

An important step forward was the introduction of less toxic conditioning regimens of reduced intensity (RIC) which led to the expansion of allo-HSCT for older patients in the past two decades (4). This therapeutic postulate is of great importance since most hematologic malignancies happen to occur in older years.

The immune effect of allo-HSCT was presented by the interactions between immunocompetent donor T cells and tumor cells in mediating a graft versus tumor (GvT) or graft versus leukemia (GvL) effect. It was supported by an increased rate of relapse in allo-HSCT from which T cells have been removed (T-cell depletion), with an inverse correlation between relapse rate and severity of GvHD (5). Finally, the most convincing evidence for a T cell-mediated GvL effect originates from the examination that infusion of donor lymphocyte infusion (DLI) per se i.e. without the second conditioning regimen, can treat leukemia relapse successfully after allogeneic HSCT (6). The infusion of DLI sustained cytogenetic and molecular remissions. Over time it became obvious that a significant part of the curative potential of allo-HSCT was directly cause by GvL effect.

Also, major advances in infectious disease prevention and treatment were made in the 1990s, including using acyclovir to prevent herpes simplex and varicella zoster virus reactivation, monitoring for cytomegalovirus (CMV) reactivation and, once reactivation occurred, preventing CMV disease with ganciclovir or foscarnet, preventing Pneumocystis Jirovecii infections with sulfamethoxazole and trimethoprim, and introducing more effective anti-fungal agents and antibiotics (1).

However, non-relapse mortality caused by infections, GvHD, or toxicity induced by the conditioning regimen still remains a major problem. Numerous preclinical and clinical research was done to reduce the toxicity of the conditioning by using so RIC regimens or non-myeloablative (NMA) conditioning with low-dose TBI as well as the development of new forms of GVHD prophylaxis by including also mTOR inhibitors and other forms of T-cell depletion such as alemtuzumab or ATG. It was also observed a dramatic reduction in liver GvHD with the standard use of ursodeoxycholic acid in two las decades (7).

The concept of conditioning regimens is to be intensified to the upper limit of tolerability in order to optimize tumor cell kill, so it was began realized that intensive, myeloablative (MAC) regimens, including cyclophosphamide/TBI or busulfan/cyclophosphamide were too toxic for elderly patients or for those with comorbid conditions.

Also, the use of post-transplant cyclophosphamide (post-Cy) in order to make in vivo T cell depletion after haploidentical transplantation improved significantly patients outcomes, and it was widely used since 2008 (8).

The introduction of the HCT comorbidity index (HCT-CI) in 2005 simplified assessments of results between transplant centers, and has served as an important decision-making tool for choosing optimal transplant regimens (9).

Obstacles and perspectives

Disease relapse, poor graft function (PGF), GvHD, and infections are the main causes of transplant failures, and can seriously compromise the whole transplant procedure. Strategies for the prevention and treatment of these serious complications are in the focus in the past decades.

The novel CMV prophylaxis with letermovir dropped the incidence of CMV reactivation which could be one of the main causes of PGF (10). Namely, CMV positivity before HCT has remained an adverse risk factor despite monitoring for CMV reactivation and pre-emptive therapy in case of reactivation.

Another recent development has been the introduction of JAK2 inhibitor ruxolitinib for the treatment of steroid-refractory acute GvHD (11) in addition to the role of mesenchymal stem cells that have low immunogenicity and strong immunomodulatory effect. Extracorporeal photopheresis (ECP) has been used as an off-label second-line treatment for cutaneous steroid-refractory acute and chronic GvHD since the early 2000s, with variable success (1).

In high-risk acute leukemia such as FLT3-ITD AML, encouraging results have been reported with maintenance therapy after allo-HCT. Namely, a randomized, prospective trial in 204 patients conditioned with busulfan/cyclophosphamide showed significantly less relapse with post-HCT sorafenib compared to controls (1-year relapse 7% vs. 24.5%) and improved leukemia-free and overall survival (12). Early results of the RADIUS study showed that midostaurin reduced post- HCT relapse in FLT3-mutated AML patients, 145, as well as gliteritinib in a post-allo-maintenance setting (13).

Novel CAR-T cell therapy can be used as a “bridge” to allo-HCT from 2018 (14).

Finally, monitoring of minimal residual disease before and after allo-HSCT could be an adequate tool for assessment of disease status, and indicator for appropriate therapy.

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INDICATIONS FOR HEMATOPOIETIC STEM CELL TRANSPLANTATION IN CHILDREN

Dragana Vujić
Maternal and Child Health Care Institute of Serbia "Dr Vukan Čupić"

Apstract

Hematopoietic stem cell transplantation (HSCT) is a standard therapy for numerous congenital and acquired diseases, and for some, it is the only possible treatment. Standard indications for the use of hematopoietic stem cells have been clearly defined for several decades. HSCT is standard therapy in children who suffer from acute leukemia high-risk group or relapse, chronic myeloid leukemia resistant to tyrosine kinase inhibitors, juvenile myelomonocytic leukemia, myelodysplastic syndrome, lymphomas resistant to therapy or in relapse, thalassemia major, sickle cell disease, inborn marrow failure syndromes, metachromatic leukodystrophy, peroxisomal storage diseases, severe aplastic anemia, some forms of congenital immunodeficiency, osteopetrosis and some solid tumors. The use of hematopoietic stem cells in the treatment of children suffering from diabetes mellitus type I, cerebral palsy, hypoxic-ischemic encephalopathy, or autism spectrum disorders can only be carried out through registered clinical studies.

Keywords: transplantation, children, indications

Sažetak

Transplantacija hematopoetskih matičnih ćelija (Hematopoietic Stem Cell Transplantation − HSCT) je standardna terapija za brojne urođene i stečene bolesti, a za neke je i jedini mogući način tretmana. Standardne indikacije za kliničku upotrebu hematopoetskih matičnih ćelija definisane su već nekoliko decenija. HSCT je standardna terapija kod visoko-rizične grupe dece obolele od akutne leukemije ili visokim rizikom relapsa bolesti, zatim hronične mijeloidne leukemije koji ne reaguju na primenu inhibitora tirozin kinaze, juvenilne mijelomonocitne leukemije, mijelodisplaznog sindroma, limfoma otpornih na hemioterapiju ili u relapsu, talasemije major, bolesti srpastih ćelija, sindroma urođene insuficijencije kostne srži, metahromatske leukodistrofije, peroksizomalne bolesti, teške aplastične anemije, nekih oblika urođene imunodeficijencije, osteopetroze i nekih solidnih tumora. Primena matičnih ćelija hematopoeze u lečenju dece obolele od dijabetes melitusa tipa I, cerebralne paralize, hipoksično-ishemijske encefalopatije ili poremećaja iz spektra autizma može se sprovoditi samo putem registrovanih kliničkih studija.

Ključne reči: transplantacija, deca, indikacije

Six decades ago ideas on the treatment of congenital immunodeficiencies and leukemia by hematopoietic stem cell transplantation (HSCT) were accompanied by great skepticism, great enthusiasm, and numerous disappointments. Most of the patients in whom, in this early period of transplant medicine, HSCT was performed were in the terminal phase of their disease and died before adequate evaluation. And when there was a successful acceptance of the graft, death soon occurred due to infection or graft-versus-host disease, since there was no possibility of tissue typing in that period. The first successful transplants were performed in 1968 in children with congenital immunodeficiencies, boys suffering from severe combined immunodeficiency, and a boy suffering from Wiskott-Aldrich syndrome.

Thanks to a better understanding of the pathophysiological mechanisms of complications that occur after HSCT, new knowledge in the field of immunology, pharmacology, molecular biology, the introduction of new drugs for the prevention and treatment of early and late complications of HSCT, knowledge from pharmacology about toxicity and maximum doses of cytostatics, the development of cryobiology, the introduction new methods of processing hematopoiesis stem cells, development of supportive therapy, improved psychological support and the formation and development of the world registry of voluntary donors of hematopoietic stem cells have resulted in better survival and a better quality of life in transplanted patients.

For many years, standard indications for HSCT in children have been defined, as well as the type of transplantation that will be performed, the best conditioned dependingon the diagnosis, as well as the availability of the donor in allogeneic hematopoietic stem cell transplantation. HSCT is a standard therapy for only some congenital and acquired diseases of the lymphohematopoietic system and solid tumors. Today, when making a decision about HSCT, it is justified to follow the recommendations of the European Group for Blood and Marrow Transplantation (EBMT) and the American Society of Transplantation and Cellular Therapy (ASTCT) (Table 1).

Since the early 2000s, we have increasingly witnessed the application of hematopoietic stem cells in the so-called non-hematopoietic indications. As it is a developing therapy, it is crucial that it is carried out exclusively within the framework of carefully designed clinical studies, which are based on strict ethical principles. It is necessary to look at all the benefits of the application of hematopoiesis stem cells beyond standard indications, but also to be critical of side effects, which can be the immediate cause of death (Table 2 - clinical studies registered at www.clinicaltrials.gov).

Table 1: Indications for hematopoietic stem cell transplantation in children (taken and adapted from: Snowden JA, Sánchez-Ortega I, Corbacioglu S, Basak GW, Chabannon C, de la Camara R, Dolstra H, Duarte RF, Glass B, Greco R, Lankester AC , Mohty M, Neven B, de Latour RP, Pedrazzoli P, Peric Z, Yakoub-Agha I, Sureda A, Kröger N; European Society for Blood and Marrow Transplantation (EBMT). Indications for haematopoietic cell transplantation for hematological diseases, solid tumors and immune disorders: current practice in Europe, 2022. Bone Marrow Transplant 2022; 57:1217-39).

Table 1. EBMT and ASTCT recommendations for HSCT

Disease	Disease status and subtypes	Identical sibling donor	Match unrelated donor	Alternativ donor (haploidentical, cord blood, mismatch unrelated donor	autologous
AML	CR 1, LR[1]	GNR/II	GNR/II	GNR/III	GNR/II
	CR1, HR, VHR[1]	S/II	S/II	CO/II	GNR/II
	CR2	S/II	S/II	S/II	GNR/II
	>CR2	CO/II	CO/II	CO/II	GNR/II
LLA	CR 1, LR[1]	GNR/II	GNR/II	GNR/III	GNR/II
	CR1, HR, VHR[1]	S/II	S/II	CO/II	GNR/II
	CR2	S/II	S/II	CO/II	GNR/II
	>CR2	S/II	S/II	CO/II	GNR/II
CML	1st CP, failing 2nd or 3rd line TKI S/II S/II CO/ II GNR/III Ac- celerated phase, blast crisis or >1st CP	S/II S/II	S/II S/II	CO/II CO/II	GNR/III GNR/III
JCML		S/II	S/II	CO/II	GNR/III
NHL	CR1, NR	GNR/II	GNR/II	GNR/II	GNR/II
	CR1, VR	CO/II	CO/II	CO/II	CO/II
	CR2	S/II	S/II	CO/II	CO/II
HL	CR1	GNR/II	GNR/II	GNR/II	GNR/II
	prvi recidiv, CR2	CO/II	CO/III	CO/III	S/II
Primary ID	SCID	S/II	S/II	S/II	NA
	NON-SCID PID	S/II	S/II	S/II ili CO/II	NA
	primary HLH	S/II	S/II	S/II	NA
	other PID	S/II	S/II	CO/II	NA
MPS [2]	MPS-1H	S/II	S/II	S/II	NA
	Wolman disease	CO/III	CO/III	CO/III	NA
	MPSII-VI	CO/II	CO/II	CO/II	NA
	MLD	S/II	S/II	CO/II	NA
PSD	X-ALD	S/II	S/II	CO/II	NA
thalassae- mia and SCD		S/II	CO/II	CO/II	NA

osteopetroza		S/II	S/II	S/II	NA
IBMFS		S/II	S/II	CO/II	NA
acquired SAA		S/II	S/II	CO/II	NA
germ cell tumours		CO/II	CO/II	CO/II	CO/II
Sa Ewing (HR or >CT 1)		D/II	D/III	D/III	S/II
soft tissue sarcoma (high risk or >CR1)		D/II	D/II	D/III	CO/II
osteogenic sarcoma		GNR/III	GNR/III	GNR/III	D/II
neuroblastoma HR or >CT 1		CO/II	CO/II	D/III	S/II
brain tumours		GNR/III	GNR/III	GNR/III	CO/II
Tu Wilms >CT1		GNR/III	GNR/III	GNR/III	CO/II
AD	Including monogenic AD	CO/II	CO/II	CO/II	CO/II

AD − autoimmune disorders, ALL − acute lymphoblastic leukaemia, Allo − allogeneic transplantation, AML − acute myeloid leukaemia, Auto − autologous transplantation, CML − chronic myelogenous leukaemia, CO − clinical option (can be carried after careful assessment of risks and benefits), CR1, CR 2 − first, second complete remission, D − developmental, GNR − generally not recommended, HL − Hodgkin lymphoma, HSCT − haematopoietic stem cell transplantation, IBMFS − inborn marrow failure syndromes, ID − immunodeficiency, JMML − juvenile myelomonocytic leukaemia, MDS − myelodysplastic syndromes, MLD − metachromatic leukodystrophy, MMAD − mismatched alternative donors (cord blood, haploidentical and mismatched unrelated donors), MPS − mucopolysaccharidosis, MSD − matched sibling donor, MUD − well-matched unrelated donor (8/8, 10/10, or 9/10 if mismatched is in DQB1), PSD − peroxisomal storage diseases, S − standard of care (generally indicated in suitable patients), SAA − severe aplastic anaemia, SCD − sickle cell disease (high risk), SCID − severe combined immunodeficiencies, X-ALD − X-linked adrenoleukodystrophy. 1-categories are based on number of white blood cells, cytogenetics and molecular markers at diagnosis and time to achieve remission; 2- for Wolman disease, MPSII and VII, decision is individualised after expert evaluation

Table 2: Clinical studies on the use of stem cells in children
(taken and adapted from www.clinicaltrial.gov)

Disease	Number of registred clinical trials	Study status
diabetes mellitus type I	20	8 complited (for 1 available results), 1 withdrawn, 8 unkonowen status, 18 phase I or II, 2 phase III (unknowen status)
8 complited (for 1 cerebral palsy hypoxic-ischemic encephalop-athy	29	11 completed (for 2 available results) 2 withdrawn, 1 suspended, 7 unknown, 5 in recruitment, 2 not available completed study results: 2 in phase I, 2 in phase I/ II, 4 in phase II, 1 in phase 1 and for 2 unavailable data on the study phase
hypoxic-ischemic encephalopathy	5	2 studies-unknowen status, 1 withdrawn, 1 recruiting, 1 active study in phase 1

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NEW APPROACHES OF TRANSFUSION SUPPORT OF HEMATOLOGICAL DISORDERS USING FRESH FROZEN PLASMA, CRYOPRECIPITATES, IMMUNOGLOBULINS AND CLOTTING FACTORS CONCENTRATES

Miodrag Vučić[1,2], Ana Antić[3], Jelena Vučić[4], Irena Ćojbašić[1,2]
[1]Haematology, Allergology and Clinical Immunology Clinic, University Clinical Center Niš, Serbia
[2]University of Niš, Faculty of Medicine Niš, Serbia
[3]Blood Transfusion Institute Niš, Serbia
[4]Clinic for Children`s Internal Diseases, University Clinical Center Niš, Serbia

Abstract

Transfusion support is often one of the most important factors in the treatment of numerous congenital and acquired hematological diseases. It is especially those resulting in a disorder in the composition of plasma proteins with consequent disruption of hemostasis, and impaired immune response. Numerous novelties in the preparation of existing and the emergence of new chemoproducts in recent years have significantly improved the therapeutic outcome in hematological patients. The most used chemoproducts are, in addition to plasma and cryoprecipitate, immunoglobulins, plasma of convalescents who are in the recovery phase from infectious diseases, as well as the use of procoagulant and anticoagulant factors, and in a past few years, monoclonal antibodies.

Keywords: transfusion support, fresh frozen plasma, immunoglobulins

Sažetak

Transfuziološka potpora je često jedan od najvažnijih faktora u postupku lečenja brojnih urođenih i stečenih hematoloških bolesti. To se naročito odnosi na one koji za posledicu imaju poremećaj u sastavu proteina plazme, sa posledičnim poremećajem hemostaze i poremećen imunološki odgovor. Brojne novine u pripremi postojećih i pojava novih hemoprodukata poslednjih godina, značajno su unapredile terapijski ishod kod hematoloških pacijenata. Najviše korišćeni hemoprodukti su pored plazme i krioprecipitat, imunoglobulini, plazma rekonvalescenata koji su u fazi oporavka od infektivnih bolesti, kao i upotreba prokoagulantnih i antikoagulantnih faktora, a u skorije vreme i monoklonskih antitela.

Ključne reči: transfuziološka potpora, sveža zamrznuta plazma, imunoglobulini

Use of plasma transfusion for treating hematologic diseases

Plasma is a hemoproduct containing coagulation factors, albumins, immunoglobulins, proteins, lipids, and other biological mediators. Plasma-derived products currently available for transfusion include fresh frozen plasma (SSP-FFP), plasma frozen within 24 hours (PF24), thawed plasma (TP), liquid plasma (LP), and solvent detergent plasma (SDP). Indications for use are in bleeding patients requiring multiple coagulation factor replacement due to liver disease, disseminated intravascular coagulation [DIC]); massive transfusion; warfarin intoxication; therapeutic plasma exchange in thrombotic thrombocytopenic purpura (TTP); in congenital or acquired deficiency of coagulation factors when concentrates of specific factors are unavailable; and rare specific plasma protein deficits. Current guidelines for plasma transfusion in patients with coagulopathy suggest giving only when specific therapy or factor concentrate is inappropriate or unavailable [1].

One of the main indications for SSP is during intoxication with warfarin or related vitamin K antagonists (VKA), and for patients who are bleeding or undergoing urgent invasive procedures and who only need a temporary reversal of the effect of warfarin. Recently developed 4-factor prothrombin concentrate complex. (4F-PCC) is currently considered optimal for the treatment of warfarin intoxication compared to plasma, as it corrects INR values faster with a smaller volume of injected product [2, 3].

Finally, patients with TTP constitute an important group of patients receiving SSP or cryoprecipitate-poor plasma transfusion or plasmapheresis to replace the vWF-cleaving protease, ADAMTS13. While acquired TTP still requires plasmapheresis as therapy, the recombinant protein rADAMTS13 (BAKS930) is currently in phase III clinical trials for use in patients with congenital TTP [4].

Use of covalescent plasma

The plasma of patients recovering from recent acute viral diseases contains neutralizing antibodies that mediate the immune removal of the virus. The plasma of convalescents has been used safely in numerous infectious diseases so far. It has recently been used in patients with COVID-19 (SARS-CoV-2 virus) [5]. There is evidence of a favorable effect of plasma on convalescents in more severe forms of the disease, but it is necessary to conduct a larger number of clinical trials to confirm this thesis.

Use of cryoprecipitate in hematologic diseases

Cryoprecipitate contains fibrinogen, factor VIII, factor XIII, von Willebrand factor, and fibronectin. It has been routinely

used to treat hemophilia A and deficiencies of various coagulation factors. However, its use is increasingly limited to the treatment of hemorrhage with the development of a deficiency of individual coagulation factors. Although there are no definitive criteria for prescribing cryoprecipitate, general recommendations advise its use in patients who are bleeding, when fibrinogen levels are less than 100 mg/dL, or who have developed DIC. Cryoprecipitate is primarily used as a concentrated source of fibrinogen in the case of acquired fibrinogen deficiencies: massive blood loss due to trauma, hemorrhagic obstetric complications, liver transplantation, and DIC [6].

The use of immunoglobulins in hematologic diseases

Immunoglobulins are used as replacement therapy in primary or secondary immunodeficiencies or as specific therapy against certain pathogens as "hyperimmune" globulin. Furthermore, immunoglobulins can target Fc receptors of the reticuloendothelial system, which explains their use in conditions such as immune thrombocytopenic purpura (ITP). IVIG therapy can reduce the incidence of bacterial infections in hematologic malignancies, such as chronic lymphocytic leukemia, multiple myeloma, and graft-versus-host disease in patients with allogeneic bone marrow transplantation. The use of IVIG in autoimmune diseases has shown different results. Immune thrombocytopenia (ITP) is the primary indication for the use of IVIG. This treatment combined with high-dose corticosteroids can rapidly increase the platelet count in hours when a rapid increase in platelets is needed. Recent data indicate potential new trends in the use of immunoglobulins with their subcutaneous administration in patients with immunodeficiencies. [7].

Use of clotting factor concentrate in hematologic disease

The most commonly used concentrated factors are F VIII and F IX in the treatment of hemophilia A and B. Today, the latest generation of recombinant factors with reduced immunogenicity dominates. In recent years, gene therapy has shown great progress in the treatment of hemophilia. In addition, a unique alternative to factor VIII has emerged: emicizumab, a bispecific chimeric monoclonal antibody, which mimics the cofactor activity of factor VIII by causing factor IXa to attach to factor X, thereby enabling clot formation in the absence of F VIII [8, 9].

Fibrinogen concentrate is now widely used in the treatment of numerous congenital or acquired deficiencies.

Prothrombin is available as a multi-factor concentrate, called prothrombin complex concentrate, and exists in 2 forms: 3-factor PCC (3F-PCC) consisting of factors II (prothrombin), IX and X, as well as protein C and S, and 4-factor PCC (4F-PCC) which additionally contains factor VII. Its indication is currently only for emergency reversal of VKA-warfarin in adults with acute major bleeding; however, there are multiple uses including reversal of direct oral anticoagulants or emergency surgery, treatment of bleeding in congenital deficiencies of any of the coagulation factors found in PCC (vitamin K-dependent factors), prophylactic use to reduce perioperative bleeding, and decrease the need for transfusion and in traumatic bleeding with FFP to correct coagulopathy [10].

Recombinant activated factor VII (rFVIIa) has long been available, with indications for the treatment of bleeding episodes and perioperative management in adults and children with hemophilia A or B with inhibitors (or acquired hemophilia), congenital Factor VII deficiency, and Glanzmann's thrombasthenia with refractoriness to platelet transfusion [11].

Conclusion

Plasma and plasma derivatives are still the most commonly used chemo products in the treatment of various congenital and acquired hematological disorders. The use of plasma and cryoprecipitate is most often used in the treatment of bleeding episodes and in the treatment of complex coagulopathies such as DIK. With the development of synthetic ADAMTS-13 products, they are expected to take the place of plasma in the treatment of congenital TTP. The administration of immunoglobulin is essential in conditions of humoral immunodeficiency, ITP, as well as in numerous autoimmune disorders. In recent years, significant progress has been made in the production of plasma factors, and new recombinant procoagulant and anticoagulant plasma proteins have appeared. It is expected that in the coming period, recombinant factors and the appearance of monoclonal antibodies will further improve the treatment of numerous hematological and hemostatic disorders.

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ROLE OF PLATELETS IN GYNECOLOGY AND OBSTETRICS OTHER THAN HAEMOSTATIC

Ljubinka Nikolić
Clinic for Gynecology and Obstetrics,
University Clinical Center of Serbia, Belgrade, Serbia

Abstract

Platelets are the smallest blood cells of discoid or round shape and are cytoplasmic fragments of megakaryocytes. Platelets contain 3 types of granules: alpha granules, dense granules, and lysosomes. Granules secrete growth factors, coagulation factors, cytokines, and numerous proteolytic enzymes. The basic and most investigated role of platelets is in the process of hemostasis. The aim of this paper is to point to other recognized platelet functions unrelated to hemostasis.

The less-known platelet functions becoming a subject of interest with the development of applied science. Platelets participate in inflammation by releasing proinflammatory mediators (CD154, CD40L). CD40L accelerates releasing RANTES protein leading to intensified activation of T-lymphocytes. Complement activation via P selectin, platelet generates an immunomodulatory effect. During embryonic development, platelets allow blood and lymph vessel separation by activating CLE-2 receptor and PDPN ligand. Platelets alleviate migration and invasiveness of tumor cells and contribute to disease progression and development of metastases. Platelets have a significant role in innate and adaptive immunity. Platelets affect the maturation of follicles and oocytes and have an important role in the embryo implantation process and placentation.

The conclusion arises that platelets are not only participants in hemostasis, but that they play a significant role in inflammation, unspecific and specific body defending, tumor biology, embryonic development, and female reproductive system regulation.

Keywords: platelets, Inflammation, tumor, reproduction

Sažetak

Trombociti su najmanje ćelije krvi diskoidnog ili okruglog oblika i predstavljaju citoplazmatske fragmente megakariocita. Trombociti sadrže 3 vrste granula: alfa granule, guste granule i lizozome. Granule izlučuju faktore rasta, faktore koagulacije, citokine i brojne proteolitičke enzime. Osnovna i najistraženija uloga trombocita je u procesu hemostaze. Cilj ovog rada je da ukaže na druge prepoznate funkcije trombocita koje nisu povezane sa hemostazom.

Sa razvojem primenjene nauke predmet interesovanja postaju manje poznate funkcije trombocita. Trombociti učestvuju u zapaljenju oslobađanjem proinflamatornih medijatora (CD154, CD40L). CD40L ubrzava otpuštanje RANTES proteina dovodeći do pojačane aktivacije T-limfocita. Trombociti generišu imunomodulatorni efekat aktivacijom komplementa preko P selektina. Tokom embrionalnog razvoja, trombociti omogućavaju razdvajanje krvnih i limfnih sudova aktiviranjem CLE-2 receptora i PDPN liganda. Trombociti olakšavaju migraciju i invazivnost malignih ćelija, doprinose progresiji tumora i razvoju metastaza. Trombociti utiču na sazrevanje folikula i oocita i imaju važnu ulogu u procesu implantacije i placentacije embriona.

Nameće se zaključak da trombociti nisu samo učesnici u hemostazi, već da imaju značajnu ulogu u zapaljenju, nespecifičnoj i specifičnoj odbrani organizma, biologiji tumora, embrionalnom razvoju i regulaciji ženskog reproduktivnog sistema.

Ključne reči: trombociti, zapaljenje, tumor, reprodukcija, placentacija

Introduction

Platelets are the smallest blood cells of discoid or round shape and represent fragments of the cytoplasm of megakaryocytes. The volume of a mature platelet is about 6 cubic micrometers (6 μme3) with a diameter of 2 to 3 μm. In adults, there is a total of about 10e12 platelets in the circulation, which represents about 3% of the total blood volume, and 150-450x10e9/L. expressed as a concentration in a routine blood count. The lifespan of platelets in the circulation is 7-11 days. In order to maintain a constant number of platelets, more than 10e11 platelets are produced daily, and significantly more in case of bleeding. Platelets fulfill their role through active molecules located in membranes, in the cytoplasm, and in granules [1, 2, 3].

Platelets contain three types of granules:

• α-granules containing hundreds of bioactive proteins (fibrinogen, GPIIbIIIa, P-selectin (CD62P), vWF, coagulation factors, fibrinolytic factors, cytokines, growth factors such as PDGF, TGF-β, IL-1β, sCD40L, RANTES β -thromboglobulin/ NAP2, TF4/CXCL4, adhesion receptors, adhesion proteins). The constituents of α-granules can be soluble and located in the granule membrane. Soluble active ingredients of α-granules, in addition to their role in hemostasis, participate in inflammation and wound healing (Table 1) [2,4,5].

• dense granules containing energy-rich nucleotides (ADP, ATP, GTP, cAMP, UTP), catecholamines, serotonin, glutamate, histamine, pyrophosphate, and divalent cations [6].

• lysosomes containing many proteolytic enzymes

Secretion and release of granule contents is a key process in platelet activation, amplification of their activity, aggregation, and in thrombus stabilization. The enzyme system of platelets synthesizes prostaglandins from the phospholipids of the platelet membrane, where glycogen granules are the main source of energy [4, 6]. In addition, constituents of granules play an important

role in inflammation, non-specific defense of the organism, the process of wound healing, angiogenesis, atherosclerosis, and malignancy In a word, platelets participate in many physiological and pathophysiological processes [5, 7].

Table 1. Soluble α-granules constituents and their role

The role of soluble α-granules constituents		
Hemostasis	**Inflamation**	**Wound healing**
Fibrinogen	Complement component C3a	VEGF
Fibronectin	Complement component C4	EGF
Kininogen	CD40 Ligand/TNF SF 5	FGF
Plasmin	CCL5/RANTES	PDGF family
Plasminogen	Complement Factor H	Angiopoietin-1
Faktor II	CXCL1/GRO alpha/KC/CINC-1	Endostatin
Factor V	CXCL4/PF4	HGF
Factor XI	CCL3/MIP-1 alpha	IGF-1
Factor XIII	APRIL/TNF SF 13	TGF-beta 1
Angiostain	ADAMDEC.1	Latent TGF-beta bp 1
APLP-2	CCL2/JE/MCP-1	MMP-1,2,9
Laminin alpha 3/Laminin-5	CXCL5	SPARC
Laminin alpha-4	CXCL7/NAP-2	Protein disulfide isomerase
Laminin gamma 1	CXCL8/IL8	Thyimosin beta-4
Multimerin-1/EMILIN-4	CXCL12/SDF-1	TIMP.1,4

The basic and most investigated function of platelets is their role in hemostasis. Platelets fulfill their role through receptors [4, 8, 9].

Platelet receptors. Platelet membrane receptors have always been the focus of scientists' interest. Platelet receptors are also known as platelet agonists and each has its own specific activity [2, 7]. Platelet receptors are divided into receptors that participate in activation, amplification, and receptors that participate in stabilization.

Platelet receptors that participate in activation, adhesion, and aggregation are located on the surface of platelets or in the membrane.

The most known receptors at the surface of the platelets membrane are as follows:

- GPIb-IX-V complex, represents the receptor for the von Willebrand factor (vWF),
- thrombin, FXI, FXII, P-selectin, HK, Mac-1, and TSP-1. Its absence is known as BernardSoulier syndrome.
- GPVI receptor for collagen and laminin, belonging to the superfamily of immunoglobulin
- CD148
- Receptors found in the membrane of platelets:
- α2β1 – receptor for collagen
- αIIbβ3 – receptor for fibrinogen, fibrin, vWF, TSP-1, fibronectin, and vitronectin. Its deficiency leads to Glanzmann thrombasthenia
- α5β1 – receptor for fibronectin
- α6β1 – receptor for laminin
- αVβ3 – receptor for, fibronectin, fibrinogen,
- vWF, osteopontin
-

Receptors active in the amplification phase of platelet activities are found in platelet membranes. The most famous of them are:

- Receptor for ADP – P2Y1
- Thrombin receptor PAR1
- The receptor for platelet-activating factor (PAF) – PAF receptor
- Thromboxane receptor – tPA
- ATP receptor – P2X1
- TPO receptor – c-Mp1
- PDGF receptor

Platelet receptors active in the stabilization phase of platelet activity can be found in the membrane or reach the platelet membrane from α granules during the activation phase like P-selectin, CD36, PEAR1, PECAM-1, and PGI 2 receptor [2, 4, 7, 8].

1. The role of platelets in inflammation.

Platelets play an important role in inflammation due to their positive influence on the release of pro-inflammatory mediators: CD154, CD40 ligand (CD40L), and thromboxane (TXS). Platelet alpha-granules contain RANTES and inflammatory signaling molecules. Among them, CD154 has a special position, because platelets represent the main source of CD154, since CD154 contributes to most of these new platelet attributes. CD154, also known as CD40 ligand (CD40L), a member of the tumor necrosis factor (TNF) family, plays a central role in the immune response [2, 3, 9]. In response to proinflammatory agents, endothelial cells express the membrane chemokine fractalkine, otherwise not present in endothelial cells in healthy individuals. Fractalkine, on the other hand, via G-proteins induces exposure of P-selectin to platelets and further improves platelet adhesion to fibrinogen, one of the acute phase proteins, by means of GPIIbIIIa [10].

2. The role of platelets in innate and specific body defense

Another role of platelets, in addition to hemostasis, is the immunomodulatory effect. Platelets achieve this effect by activating complement via P selectin mediated by the Par4 receptor [11]. P-selectin, from alpha granules, activates neutrophils. Modern research shows that human umbilical vein endothelial cells, stimulated by tumor necrosis factor-α (TNF-α) and interferon - γ, greatly express the membrane chemokine fractalkine (CKS3CL1), which leads to a significant accumulation of leukocytes in the blood circulation. Animal model studies have shown that the role of platelets expressing the fractalkine receptor (CKS3CR1) is necessary for leukocyte adhesion to the endothelium. Fractalkine released from endothelial cells leads to the activation of adhered platelets, which consequently leads to platelet degranulation and the expression of P-selectin on the platelet membrane, which is necessary for leukocyte adhesion to the inflamed endothelium [11].

Soluble and membrane fractalkine can induce degranulation and expression of P-selectin on the platelet`s surface. The P-selectin formed in this way directly leads to the interaction of leukocytes and platelets, and in this way, platelets are involved in the elimination of pathogens [10, 11]. Activated platelets also express CD40L, which also exists in a soluble form. Soluble CD40L (sCD40L) is primarily produced by platelets after activation. It, additionally, activates platelets, which is manifested by morphological changes that are characteristic of αIIbβ3 (GPIIb/IIIa) activation, CD40L, in addition to the main receptor CD40, has several more receptors, among them αIIbβ3 α5β1, and αMβ2. CD40L and CD40 are expressed by a large number of immune cells, including monocytes, dendritic cells, and B lymphocytes, which influence the development of the acquired immune response. In the further course, the pairs of receptors and ligands (CD40/CD40L) represent costimulatory molecules that mediate the reaction between T and B lymphocytes and antigen-presenting cells (APC), whereby CD40L is expressed on activated T lymphocytes, and CD40 on B lymphocytes and APC [2, 3, 10].

3. The role of platelets in the development regulation of blood and lymphatic vessels

Various groups of researchers have obtained genetic confirmation of the role of platelets in the mechanism of regulation of vascular development. Research has shown that platelets are responsible for the separation of blood and lymphatic vessels by activating the CLE-2 receptor (C-type lectin receptor - CLEC-2) via podoplanin ligand (PDPN), which is found on lymphatic endothelial cells (LEC). PDPN and CLEC-2 are both transmembrane proteins and their expression in the membranes of associated cells is necessary for the direct contact of platelets and endothelial cells [20]. Platelet alpha granules are known to contain a number of angiogenic growth factors (Table 1). This theory supports the hypothesis that degranulation is a platelet activation mechanism that controls the growth of lymphatic vessels [12].

Interaction between platelets and LECs can be observed in major veins during LEC changes in PDPN expression. However, this interaction is not detected in the intestines, where there is also communication between blood and lymphatic vessels. The use of platelets as a means of marking the contact of blood vessels with lymphatic endothelial cells is justified, given that platelets are one of the few blood cells that do not extravasate or enter the lymphatic vessels even after trauma. How LEC-mediated platelet activation prevents the association of blood vessels and LECs remains unclear. The importance of these studies lies in the discovery that platelets play an important role in the embryogenesis of the vascular system that is not related to hemostasis [2, 12].

4. The role of platelets in tumor biology

Platelets have multiple roles in cancer progression. The procoagulant environment provided by platelets protects cancer cells from the immune system and thus allows cancer cells to proliferate leading to tumor growth. Platelets promote the migration and invasiveness of tumor cells, which leads to the formation of metastases. Research shows that in breast cancer and ovarian cancer, platelets increase the invasiveness of cancer cells, leading to disease progression. In addition, the same tumor cells show the ability to aggregate platelets, which increases the possibilities for the development of metastases. Platelet activation and regulation of other cells are controlled by thrombin via active G protein-coupled protease receptors. Research has shown that thrombin and its signaling pathways greatly contribute to tumor progression in the process of tumorigenesis and neoangiogenesis. Due to this fact, the routine application of anticoagulant therapy for malignant diseases is part of daily clinical practice with special caution due to the unstable procoagulability characteristic of both occult and confirmed malignant diseases [2, 4, 13].

5.1 The role of platelets in the regulation of the female reproductive system

Clinical and experimental research has shown that platelets affect the regulation of the hypothalamic-pituitary-ovarian system (axis). Hypothalamic gonadotropin-releasing hormone (GnRH) releases follicle-stimulating hormone (FSH) from the anterior lobe of the pituitary gland, induces and stimulates the maturation of follicles and oocytes, as well as the secretion of ovarian steroid hormones. During this period, follicular cells increase the production of platelet-activating factor (PAF). Platelets stimulated in this way accumulate in the follicular vessels surrounding the follicle and, due to the release of soluble

molecules (growth factors, mediators, chemokines, cytokines and neurotransmitters), locally lead to hormone secretion and oocyte maturation. Based on these findings, it is suggested that platelets are not only small participants but have a leading influence on complex regulatory systems that have several unclear mechanisms. Thus, platelets are much more corpuscular transmitters than participants in the process of hemostasis [14, 15].

5.2 The role of platelets in pregnancy (implantation and placentation)

Platelets play a major role in the formation of spiral arteries and trophoblasts. The process is still unknown. Platelets are thought to be activated by contact with thrombomodulin and the protein C receptor on the trophoblast. Trophoblast cells show the ability to activate coagulation in the vascular bed of the placenta. Another mode of action of platelets is immunomodulatory, by activating complement via the P-selectin receptor Par4 [10, 14]. Immunohistochemical staining with antibodies to P-selectin showed the presence of activated platelets in the decidua, in the area of maternal origin between the trophoblastic cells of the placenta and in the spiral arteries [14]. Conditions and disorders of increased platelet activity lead to trophoblast disorders, particularly visible in preeclampsia and HELLP syndrome (Hemolysis Elevated Liver Enzymes Low Platelet – HELLP). Fetal prothrombogenic genes can also locally activate maternal platelets leading to impaired placental development [14, 15].

Conclusion

Platelet function unrelated to hemostasis is becoming a subject of research along with the development of applied science. Platelets are actively involved in the inflammatory process by releasing proinflammatory mediators. Thrombocytes are actively involved in the non-specific and specific defense of the organism due to their immunomodulatory effects and activation of leukocytes. In addition, platelets play an important role in tumor biology. Activated platelets accelerate cancer progression and the development of metastases in many different ways. This role represents a new and important field for the action of new drugs. Receptors on platelets are the target for the application of many drugs with polytherapeutic effects. Their specific individual property is the basis for the development of personalized medicine, and a good knowledge of receptors on platelets enables the use of one drug as a polyindicative agent. Platelets play an important role in the development of the embryo and in the separation of blood and lymphatic vessels. Platelets influence hormone secretion and oocyte maturation by releasing growth factors, cytokines and neurotransmitters in the blood vessels around the ovarian follicle. Therefore, platelets are directly involved in the regulation of the female reproductive system. Considering platelets functions, a new spectrum of therapeutic effects is opened as fields of research that connect many immunological diseases, innate and acquired defense of the organism, neoangiogenesis, fertile functioning of women and maintenance of pregnancy.

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HLA ANTIBODIES IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

Zorana Andrić
Blood Transfusion Institute of Serbia,
Tissue Typing Department, Belgrade

Abstract

Finding of HLA match donor impacts the clinical outcome in allogenic haematopoetic stem cell transplantation (HSCT). By introducing transplantation with partially mismatched and haploidentical donors it is possible for most patients to find a suitable donor. Despite advances in HLA matching, graft failure due to the presence of donor-specific antibodies (DSA) remains a serious complication after HSCT. The role of the HLA laboratory supporting HSCT has expanded to provide HLA antibody detection and monitoring for the selection of compatible donors. Estimation of the presence or absence of circulating HLA antibodies and of their specificity and strength is crucial for the evaluation of immunological risk for mismatched donor selection, as well as for monitoring desensitization treatment. Nowadays, solid-phase immunoassays for screening and identification of DSA and cell-based crossmatch assays are commonly used to monitor patients' circulating HLA antibodies.

Keywords: hematopoietic stem cell transplantation, donor specific antibodies, donor selection

Sažetak

Pronalaženje odgovarajućeg davaoca utiče na klinički ishod u alogenoj transplantaciji matičnih ćelija hematopoeze (TMĆH). Uvođenjem transplantacija sa delimično podudarnim i haploidentičnim davaocem, omogućeno je da većina bolesnika ima odgovarajućeg davaoca. Uprkos napretku u određivanju HLA podudarnosti između bolesnika i davaoca, neprihvatanje/odbacivanje kalema zbog prisustva antitela specifičnih za davaoca (DSA) ostaje ozbiljna komplikacija nakon TMĆH. Uloga HLA laboratorija se proširila kako bi se omogućila detekcija i monitoring anti-HLA antitela za izbor kompatibilnih davaoca. Dokazivanje prisustva ili odsustva cirkulišućih anti-HLA antitela i njihove specifičnosti je ključna za procenu imunološkog rizika za izbor nepodudarnog davaoca, kao i za praćenje primenjenog protokola desenzibilizacije pre transplantacije. Za skrining i identifikaciju DSA danas se koristi Luminex tehnologija, kao i limfocitotoksični test za unakrsnu reakciju.

Ključne reči: transplantacija matičnih ćelija hematopoeze, donorska specifična antitela, selekcija donora

Hematopoietic stem cell transplantation (HSCT) is an established therapy for a wide range of malignant and non-malignant hematologic disorders. It is well known the importance of HLA matched between patient and donor in allogenic HSCT, so the best donor is a complete HLA-matched sibling donor, followed by matched unrelated donor. Transplantation with partially mismatched donors has been enabled, including mismatched unrelated donors, cord blood units, and relatives who share one HLA haplotype with the patient (haploidentical donor), so nowadays for almost all patients could be possible to find HLA acceptable donor. However, a new barrier to transplantation appeared due to the possible sensitization of patients for HSCT to the mismatched HLA antigens of the intended donors. The role of donor-specific antibodies (DSA) has been well analyzed in solid organ transplantations but has been recently recognized in HSCT as an important barrier against the successful engraftment of donor cells. Primary graft failure (PGF) could be a serious complication after transplantation in patients with DSA who were transplanted with mismatched donors. PGF is associated with very poor outcomes, either due to increased transplant-related mortality following infectious complications or early relapse in the absence of a functioning graft. The exact mechanism by which DSA causes graft failure or rejection in HSCT remains unclear. In general, antibody-mediated graft rejection may occur either by antibody-dependent cell-mediated cytotoxicity or complement-mediated cytotoxicity.

The overall strategy for overcoming the HLA antibody barrier to HSCT implies an identification of the patients with HLA antibodies and avoidance of donors carrying alloantigens against which the candidates are sensitized. Desensitization protocols to reduce circulating DSA may be a solution for cases in which a histocompatible donor is not available or in which the urgency of the transplant does not permit a wider search. In recent years, the role of the HLA laboratory in support of HSCT has expanded to include HLA antibody screening, monitoring, and assessment of the effectiveness of antibody reduction treatments. For this purpose, tools for estimation DSA are now part of routine testing in laboratories supporting HSCT.

HLA antibodies are formed after exposure to foreign HLA during pregnancies, transfusions, or solid organ transplantations. The prevalence of HLA antibodies in patients with hematologic malignancies can be up to 40% and DSAs were identified in up to 25% of HSCT recipients. As expected, it is highly dependent on the recipient's gender, with a very low prevalence in male recipients (5%) as compared with female recipients (86%).

A number of methods have been developed for the screening and identification of HLA antibodies. Generally, these methods are categorized into cell-based assays or solid-phase immunoassays.

The earliest technique for detection of HLA immunological compatibility and antibody screening was the complement-dependent cytotoxicity assay (CDC), in which antibodies in patient serum initiate the classical complement cascade following incubation with lymphocyte suspensions. The CDC assay could be used for antibody screening by using a panel of HLA-typed lymphocytes or for crossmatch using lymphocytes from a potential donor. The CDC could only detect antibodies capable of activating the complement cascade. Pre-treatment of sera with dithiothreitol (DTT) enables discrimination between IgG and IgM antibodies. The assay could be performed using unseparated lymphocytes from peripheral blood, lymph node, or

spleen which allows the detection preferentially of HLA class I antibodies. The introduction of cell separation techniques with cell-specific magnetic beads enabled the distinction between HLA class I expression on T cells and class II antibody express on B cells. However, the CDC assay has many disadvantages. It depends on the viability of lymphocytes, HLA specificity of antibodies in highly sensitized patients is not possible to differentiate, has relatively low sensitivity, and involves subjective analysis.

Introducing Luminex as solid-phase immunoassays in HLA laboratories has allowed a more complete analysis of HLA antibodies. In Luminex-based tests, HLA proteins are coated onto the surface of different fluorescently labeled microbeads. After incubation with serum, anti-IgG, conjugated with a fluorochrome, is added. HLA-bound antibodies are detected by a dual-laser flow analyzer on a Luminex platform. The level of HLA antibody binding to each bead is measured and recorded as relative mean fluorescent intensity (MFI).

There are three kinds of kit panels according to their targets: a) screening panels with antigens pooled from multiple cells, b) phenotype panels in which each bead population carries the entire Class I or Class II HLA proteins of a cell line derived from a single individual and c) single antigen bead (SAB) panels in which each bead population is coated with multiple copies of a single recombinant antigen. Screening panels are used for detecting the presence or absence of HLA antibodies. SAB panels cover the most common alleles of all HLA class I and II polymorphic loci and are used to define antibody specificity. HLA antibodies directed against the proteins produced by all 11 polymorphic HLA loci (HLA-A, HLA-B, HLA-C, HLA-DRB1, HLA-DRB3, HLA-DRB4, HLA-DRB5, HLA-DQA1, HLA-DQB1, HLA-DPA1, and HLA-DPB1) are used in this assay. They are the most sensitive and specific, but false-positive reactions due to protein denaturation ("cryptic epitopes") could be possible. In general, SAB has allowed for the detection and identification of HLA antibodies that were not previously detected by cellular assays and has enabled easier monitoring and improved resolution of HLA antibody profiles. Additionally, SAB assays have been modified to detect complement-fixing antibodies (C1q or C3d) in an effort to characterize antibody functionality. However, SAB is not a quantitative assay. SAB MFI values are not comparable across laboratories and MFI values are affected by lot-to-lot and inter-assay variability. Also, SAB beads generally carry a higher amount of HLA antigen relative to that found on cell surfaces, especially for HLA-Cw, DQ, and DP proteins.

The exact MFI threshold for permissible DSA has not been established but transplant centers have reported that low-level DSA may not affect engraftment, has not impacted patient survival, and represent a minimal risk for HSCT.

A patient may be sensitized but have no circulating antibodies at the time of assessment. For this reason, antibody levels must be monitored over time and in particular after sensitizing events such as transfusion of platelets or other blood products.

Several desensitization methods have been used to decrease total antibody load to levels that would permit successful donor stem cell engraftment. The strategies to desensitize patients with DSA include antibody removal by using plasmapheresis or immunoadsorption, antibody neutralization using intravenous immunoglobulin or with donor HLA antigens (platelet transfusions or irradiated "buffy coat"), inhibition of antibody production and inhibition of complement cascade. The most efficient protocol for desensitization and strategies for DSA monitoring have been under investigation.

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Introduction lecture / Uvodno predavanje UV 22

THE ROLE OF TRANSFUSION MEDICINE IN TRANSPLANTATION AND HEMATOPOIETIC STEM CELL THERAPY

Olivera Šerbić
Institute for Mother and Child Healthcare of Serbia "Dr Vukan Čupić"

Abstract

Hematopoietic stem cell transplantation (HSCT) is the most widely used type of cell therapy, which leads to the cure of many hematological and non-hematological diseases. In the last five years, the use of cell therapy for tissue regeneration and in the field of cancer immunology has been increasing. Transfusiologists and transfusion technicians are involved in all stages of HSCT and are an important part of the transplant team. Assessment and testing of donors before transplantation are essential processes that affect the quality and safety of the HSC donation. For the pediatric population, there are specific recommendations that take bioethical principles into account. In case of major ABO incompatibility and high isoagglutinin titer, it should be reduced by performing therapeutic plasma exchange to the recipient, or selective removal by in vivo immunoadsorption. Also, bone marrow is processed in apheresis systems to deplete red cells (Hct<5%) and reduce plasma volume. If the recipient has a higher body mass than the donor, multiple sources of MHC are combined. Regenerative medicine aims to replace or restore missing, dysfunctional, or damaged cells, tissues, and organs, and the types of therapy it uses are cell therapy, tissue engineering, and gene therapy. It is divided into prenatal and postnatal in pediatrics.

Keywords: Stem cell, Transfusion, Transplantation

Sažetak

Transplantacija matičnih ćelija hematopoeze (TMĆH) je najrasprostranjenija vrsta ćelijske terapije koja dovodi do izlečenja mnogih hematoloških i nehematoloških bolesti. Poslednjih pet godina u porastu je upotreba ćelijske terapije za regeneraciju tkiva i u oblasti imunologije kancera. Transfuziolozi i transfuziološki tehničari uključeni su u sve faze TMĆH i važan su deo tima za transplantaciju. Procena i testiranje davalaca pre transplantacije su suštinski procesi koji utiču na kvalitet i bezbednost donacije MĆH. Za pedijatrijsku populaciju postoje specifične preporuke koje uzimaju u obzir bioetičke principe. U slučaju major ABO nekompatibilnosti i visokog titra izoaglutinina, treba ga smanjiti sprovođenjem terapijske izmene plazme kod primaoca ili selektivnim uklanjanjem *in vivo* imunoadsorpcijom. Takođe, koštana srž se obrađuje u sistemima za aferezu radi deplecije eritrocita (Hct<5%) i da bi se smanjila zapremina plazme. Ako primalac ima veću telesnu masu od davaoca, kombinuje se više izvora MĆH. Regenerativna medicina ima za cilj da zameni ili obnovi nedostajuće, disfunkcionalne ili oštećene ćelije, tkiva i organe, a vrste terapije koje koristi su ćelijska terapija, tkivni inženjering i genska terapija. U pedijatriji se deli na prenatalnu i postnatalnu.

Ključne reči: matične ćelije, transfuzija, transplantacija

Hematopoietic stem cell transplantation (HSCT) is the most widely used type of cell therapy, which leads to the cure of many hematological and non-hematological diseases since its introduction as a procedure in practice in 1968. A significant increase in HSCT has been recorded in the last 30 years. In 1990. there were 143 transplant centers in 20 countries, in 2019; 700 centers in 51 countries (1). Also, in the last two decades, a significantly higher number of transplants were performed from HSC peripheral blood than from bone marrow (98% autologous and 79% allogeneic in Europe, and 86% allogeneic in the USA). In the last five years, the use of cell therapy for tissue regeneration and in the field of cancer immunology has been increasing, which represents new options in the treatment of malignancy (2). HSCT procedures are an example of a highly complex and sophisticated, expensive type of treatment, but with a wide field of application. HSCT some times associated with life-threatening complications, and therefore strict quality requirements are insisted for all resources participating in the HSCT procedure (3). Mandatory directives/laws of HSCT are prescribed by government regulatory bodies, e.g. FDA/US, and EU directives for tissue donation, and cell therapy products (4,5). Facultative standards are prescribed by non-governmental professional organizations and associations (Foundation for Accreditation of Cell Therapy - FACT/USA, Joint Accreditation Committee of the ISCT- JACIE/UK), although, their application is voluntary, they significantly contribute to better and safer work at HSCT (2,6). The implementation of the transplantation program requires good support and equipment of auxiliary structures: laboratories, blood banks, cryobiology units, and clinical consulting ambulances, therefore there are prescribed minimum conditions for the implementation of transplantation activities. Through strategic planning, the medical structures of tertiary health institutions that are predetermined to be established as transplant centers are strengthened (6,7). But, the most important role has the highly trained and experienced staff that builds the transplant team. Transfusiologists and transfusion technicians are involved in all stages of HSCT and are an important part of the transplant team (8). Assessment and testing of donors before transplantation are essential processes that affect the quality and safety of the HSC donation. For unrelated donors, the World Marrow Donor Association (WMDA) has published detailed recommendations with criteria for assessing health status (9). Guidelines and recommendations that are applied today and regularly updated (Worldwide Network for Blood and Marrow Transplantation - WBMT) are accepted by transplant centers in Europe, North America, Japan, Australia, and New Zealand (10). Eligibility criteria for related donors are less strict and vary significantly between centers (11). Children have been donors of HSC for sick relatives for decades. For the pediatric population, there are specific

recommendations that take bioethical principles into account. Related matched pediatric donors with known genetic mutations that could be transmitted to the recipient but with healthy bone marrow should be considered. Depending on whether carrying mutations (MDS, Glucose-6-PDHG) can cause a new disease in the recipient or slow and partial graft acceptance, a decision is made to continue the preparation of the donor or to search for a matching unrelated donor. If the recipient has a significantly higher body mass (BM) than the donor, multiple sources of MHC are combined (eg, apheresis and umbilical cord blood HSC if purposefully collected and cryopreserved) (12). According to WMDA recommendations, a physician who obtains informed consent from a parent must not be involved in the treatment of a sick relative recipient. According to the Declaration of Helsinki, neither the child's recipient nor the donor can be subjects of research in the field of HSCT (13). Transfusion medicine specialists are involved in the establishment and management of the National Register of Bone Marrow Donors of Serbia (RDKSS), finding a donor at the World Register of Voluntary Bone Marrow Donors (Bone Marrow Donors Worldwide - BMDW), HLA typing of patients, and potential related donors, cross-reaction (CDC test), examination of the presence of anti-HLA antibodies. They participate in the international cooperation of accepting HSC products who arrive from abroad for our patients, and collecting and sending HSC to European transplant centers if there is a matching unrelated donor from RDKSS (14). Pre-transplantation, it is basic to determine the ABO blood type and titer of isoagglutinin, DAT, antibody, and hemolysin screening of the donor and recipient of HSC, as well as the immunoserological erythrocyte phenotype of the recipient, if this is not possible due to polytransfusion, to perform a genotype. In case of major ABO incompatibility and high isoagglutinin titer, it should be reduced by performing therapeutic plasma exchange (TPE) to the recipient. Another strategy is the selective removal of anti-A and anti-B antibodies in vivo by immunoadsorption. The advantage of this technique is that there is no need for replacement fluid (albumin/FFP). In one TPE procedure changes 1-1.5 calculated plasma volume (CPV) and in the immunoadsorption procedure 2.5-3 CVP. If the bone marrow of a related matched donor is taken by biopsy in the operating room, he should be taking oral iron beforehand. A unit of autologous whole blood is usually collected 7 days before the HSCT. (15). Bone marrow is processed in apheresis systems to deplete red cells (Hct<5%) and reduce the plasma volume of the final product (18). Transfusion doctors give recommendations and make a plan to support the cellular components of blood in the transplanted patient (16). The central role of the transfusiologist and the transfusion technician is in the collection of autologous/allogeneic HSC by cytapheresis of mononuclear cells on a cell separator. The collected autologous peripheral HSC are frozen, and the allogeneic ones are further modified or administered unmodified to the patient. The recommendations of EBMT due to the COVID-19 epidemic are that all donors of HSC must be PCR antigen negative and all HSC products must be frozen before administration (17). Seven days after the application of bone marrow HSC, control of graft acceptance begins by monitoring changes in the ABO and RhD phenotype and the isoagglutinin titers. Post-transplantation, it is necessary to monitor the appearance of irregular antibodies and alloantibodies in the patient, as well as the appearance of refractoriness to platelet transfusions (19). A cell therapy product is defined as an infusion of HSC that after collection has been subjected to minimal processing and is related to the HSCT procedure, e.g. donor lymphocyte infusion. Cell products in which HSC/SC after collection are subjected to extensive manipulation - selection, expansion, or genetic modification represent Advanced therapy medicinal products (ATMPs). They are medicinal products for human use based on genes, tissues, or cells and must comply with EU Directive EC 1394/2007. These include chimeric antigen receptor T cells (CAR-T); in vitro selected and/or expanded T cells, cytokine-activated virus-specific T cells, cytokine-induced killer cells (CIK), regulatory T cells (TREGS), other genetically modified T cells except CAR-T, natural killer cells NK, dendritic cells, mesenchymal stromal cells, in vitro expanded CD34+ cells, and genetically modified CD34+ cells (20). CAR-T cells are a new class of cancer therapy in which autologous or allogeneic T cells are engineered to express a CAR that targets a specific tumor antigen. Two products are approved in Europe, tisagenlecleucel (for the treatment of refractory/relapsed acute lymphoblastic leukemia in children and young adults and refractory/relapsed diffuse large B-cell lymphoma) and axicabtagene ciloleucel (for the treatment of refractory/relapsed high-grade B-cell lymphoma) (21).

Regenerative medicine aims to replace or restore missing, dysfunctional, or damaged cells, tissues, and organs, and the types of therapy it uses are cell therapy, tissue engineering, and gene therapy. Pediatric regenerative medicine is divided into prenatal and postnatal. Prenatally, intrauterine transplantation (IUTp) introduces MHC, genes or gene-modified MHC, mesenchymal cells (MCC), and a combination of HSC and MCC. The procedure is used for congenital diseases for which there has been no therapy until now. Although IUTp represents a biomedical, technological, and ethical challenge, it also has multiple advantages. The therapy starts before the child's birth, the fetus has 10x less BM, so a smaller number of MĆH is needed, the remaining cells can be used postnatally as a booster transplant if necessary. Due to the existence of the Foramen ovale and ductus arteriosus, the infusion of MHC into the umbilical vein bypasses the fetal lungs and there is no sequestration of HSC in the microvasculature of the lungs as it is postnatally. The immune system of the fetus is immature, in the phase of recognizing its own antigens, and even recognizes donor cells as its own, immune tolerance to HSC develops, and graft acceptance occurs without the need for myeloablation and immunosuppression. The proliferation of fetal cells enables the migration of HSC to different anatomical departments and thus more comprehensive implantation of donor cells. The procedure has the greatest psychological effect on the parents because instead of terminating the pregnancy after IUTp and cure, they get a healthy newborn. Several papers have been published on the treatment of B thalassemia, Osteogenesis imperfecta, and SCID (Severe combined immunodeficiency). IUTp procedures carry risks from the cellular product itself and from the method of administration. Success depends on fetal gestation, route of administration, competition with host cells, immaturity of niches, and fetal, and maternal immunity. Alloimmunization of the mother can begin after the transplantation of donor HSC and the transfer of alloantibodies through the placenta to the fetus can affect the outcome of the whole IUTp. The International Society for Fetal Transplantation and Immunology (IFeTIS) is concerned with defining best practices for IUTp in terms of monitoring and safety of the fetus and mother as well as a series of ethical dilemmas. (22). Postnatally, gene, cell therapy, and new niche-based technology and their combinations enable structural and functional reconstitution of the complex hierarchy of cells, tissues, and organs. The greatest success with this therapy was recorded in pediatrics in wound healing due to the high regenerative capacity and undamaged peripheral circulation compared to adults (23).

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CONTEMPORARY ASPECTS OF COVID-19 PLASMA DONATION

Jasmina Grujić[1,2], Pavle Banović[3,4]
[1]Blood Transfusion Institute of Vojvodina, Novi Sad, Serbia
[2]Department of Internal Medicine, Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia
[3]Department of Prevention of Rabies and Other Infectious Diseases, Pasteur Institute Novi Sad, Novi Sad, Serbia
[4]Department of Microbiology with Parasitology and Immunology, Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia

Abstract

Passive immunotherapy with convalescent plasma (CP), a common therapeutic treatment throughout history, has been actualized during recent infectious disease outbreaks. Although it appeared promising, data from multiple clinical studies that evaluated the use of convalescent COVID-19 plasma (CCP) delivered mixed results, suggesting interference of different factors that should be addressed; in the first place - collection and administration of CCP plasma with high neutralization potency. Our research on local CCP donors revealed that high anti-SARS-CoV-2 antibody titer is linked with male gender, older age groups and more severe form of COVID-19. We made collaboration with Pasteur Institute of Novi Sad and implemented standard neutralization assay for super-analysis of CCP donations that passed current threshold on ELISA test. Established inter-institutional collaboration, gained experience and lessons learned will be essential in facing future pandemic threats and emerging diseases.

Keywords: COVID-19 Serological Testing,Neutralization Tests; SARS-CoV-2

Sažetak

Pasivna imunoterapija korišćenjem rekonvalescentne plazme (RP) tokom istorije bila je široko rasprostranjena i ponovo aktuelizovana tokom prethodnih epidemija. Iako je primena RP tokom pandemije COVID-19 inicijalno bila obećavajuća, više kliničkih studija koje su analizirale upotrebu RP dale su kontradiktorne rezultate. Kao jedan od glavnih problema izdvojeni su sakupljanje i administracija RP sa visokim titrom antitela. Iskustva Zavoda za transfuziju krvi Vojvodine pokazala su da su davaoci RP sa visokim titrom antitela muške osobe, starijeg doba koji su se oporavili od težih formi bolesti COVID-19. Ostvarena saradnja sa Pasterovim zavodom Novi Sad omogućava uvođenje neutralizacionog testa za donacije plazme koje ELISA testiranjem pokažu zadovoljavajući indeks antitela. Uspostavljena međuinstitucionalna saradnja, stečeno iskustvo i naučene lekcije biće od suštinskog značaja za suočavanje sa budućim globalnim pretnjama pandemije i pojavom nepoznatih bolesti.

Ključne reči: COVID-19 serološko testiranje, neutralizacioni test, SARS-CoV-2

Introduction

Coronavirus disease 2019 (COVID-19), the highly contagious viral illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was recognized as a pandemic by the World Health Organization (WHO) in March 2020. It caused the emergence of a global world health crisis resulting in more than 6.5 million deaths worldwide as of August 2022 [1]. The earliest genomic identification was done from virus samples from five patients in Wuhan. The sequences were found to share: 79.6% similarity to SARS-CoV, 50% to MERS-CoV, and 96.2% to bat Coronavirus (BatCoV RaTG13). These discoveries led to the conclusion of the possibility of an intermediate host for viruses, possibly pangolins [2].

The proteins that define SARS-CoV-2 are nucleocapsid (N), membrane (M), envelope (E), and spike (S) proteins [3]. The S protein consists of two subunits S1 and S2 and mediates the entry of the virus into host cells. Although the respiratory system is the principal target for SARS-CoV-2, the virus can affect other major organ systems such as the gastrointestinal tract, hepatobiliary, cardiovascular, renal, and central nervous system. The SARS-CoV-2 pandemic overwhelmed healthcare systems, resulting in loss of lives, prolonged recovery followed by post-COVID-19 syndrome, and a negative impact on the global economy.

Like other RNA viruses, SARS-CoV-2 has a tendency to evolve and develop mutations over time. Several variants of SARS-CoV-2 have been described, among which only a few are considered as variants of concern (VOCs) by the WHO, given their impact on global public health (i.e., Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), Delta (B.1.617.2) and Omicron (B.1.1.529)) [4].

Initially, the understanding of COVID-19 and its therapeutic options were limited, but progress has been made, which resulted in the development of novel medications and vaccines. A variety of therapeutic options are currently available, including antiviral drugs (e.g., molnupiravir, nirmatrelvir, remdesivir), anti-inflammatory drugs (e.g., dexamethasone), immunomodulatory agents (e.g., baricitinib, tocilizumab) and anti-SARS-CoV-2 monoclonal antibodies (e.g., bamlanivimab/etesevimab, casirivimab/imdevimab) [5]. The administration of convalescent plasma (CP) has been known since the end of the 19th century, and it has been successfully used in previous viral disease outbreaks worldwide (Severe acute respiratory syndrome, Middle East respiratory syndrome, Ebola Virus Disease) (6). Although it appeared promising, data from multiple

clinical studies that evaluated the use of COVID-19 convalescent plasma (CCP) delivered mixed results, suggesting interference of different factors that need to be addressed (6).

Objective

The aim of this editorial is to demonstrate our experiences derived from the establishment of the ambulance for the collection of COVID-19 convalescent plasma at the Blood Transfusion Institute of Vojvodina (BTIV). In addition, we will report our results from studies (i) examining demographic factors associated with donors of high titer CCP, and (ii) comparing "in-house" neutralization assay with commercial ELISA for suitability to identify high titer CCP donors, in cooperation with Pasteur Institute Novi Sad.

Our experience

Technical adjustments and adaptation to CCP collection procedures

In order to adapt to the newly developing situation, it was essential to reorganize the work of BTIV Apheresis ambulance. In addition to the acquisition of sets compatible with devices Haemonetics MCS+ for apheresis procedures, it was crucial to obtain more devices to process the excessive number of donors per day. Existing staff had skills with apheresis procedures but needed to take additional training courses regarding CCP plasmapheresis. All mandatory preventive measures concerning COVID-19 were applied. Potential CCP donors were contacted directly in cooperation with the Institute for Public Health of Vojvodina. Staff training was carried out focusing on the maintenance of motivation in blood donors, and how to conduct a conversation and motivate convalescents to report to BTIV and donate CCP.

Determination of factors related to higher anti-SARS-CoV-2 Ab titer in CCP donors from Vojvodina Autonomous Province

We conducted research to determine a possible correlation between anti-SARS-CoV-2 IgG and demographic and clinical parameters in CCP donors (7). Individuals were characterized according to age, gender, comorbidities, COVID-19 severity, ABO blood type, and RhD factor. From 468 candidates tested with COVID-19 ELISA IgG (Vircell S.L, Granada, Spain), 420 reached the threshold value (420/468; 89.74%) of anti-SARS-CoV-2 IgG reactivity. Subjects who had an Antibody index >6 were qualified for inclusion in the National CCP donation program. Further statistical analysis showed that male individuals ($p = 0.034$), older age groups ($p < 0.001$), existence of hypertension ($p = 0.008$), and severe COVID-19 ($p = 0.000$) are linked with higher levels of anti-SARS-CoV-2 IgG. The link between age and anti-SARS-CoV-2 seroreactivity is possibly due to several factors, considering that older persons are more susceptible to hypertension and severe form of COVID-19. The same findings in relation to age were also found in studies conducted in Germany, Brazil, the USA, England, and Austria [8,9]. Considering gender as a factor related to the higher reactivity of anti-SARS-CoV-2 IgG, it was suggested that male sex hormones could have a stimulatory effect on humoral immune response, thus mechanism is still unclear [10]. Stronger antibody response in CCP donors recovered from severe COVID-19 was also detected in multiple studies in Japan, the USA, China, and Denmark [11,12]. And finally, hypertension was found as only comorbidity related to higher anti-SARS-CoV-2 reactivity in our study population. These findings directed us to a more refined CCP donor selection, thus additional studies were needed to assess the neutralization potency of CCP collected from our donors with high anti-SARS-CoV-2 IgG reactivity.

Is current ELISA test threshold sufficient for acceptance of CCP donors?

The gold standard for the detection of neutralizing antibodies is to perform neutralizing assay (Nta). Due to the biosafety requirements, access to Nta is limited to highly specialized laboratories. For that reason, anti-SARS-CoV-2 antibody detection is widely carried out by ELISA instead of the gold standard despite its limitations, including lower specificity. Another limitation of ELISA is that commercial assays are mostly based on the Wuhan variant, while Nta can be modified to be performed with SARS-CoV-2 variant that circulates in examined population. In addition, ELISAs can detect total antibodies or specific antibodies directed toward one of the structural proteins (e.g., S, N, etc.) but they are not able to quantify levels of neutralizing antibodies, which is one of the crucial factors for CCP treatment success [13].

In order to assess the suitability of ELISA assay for inclusion individuals in the National CCP donation program, we tested 23 serum and plasma samples from CCP donor candidates in the same time via COVID-19 ELISA IgG (Vircell S.L, Granada, Spain) and Nta developed in Pasteur Institute Novi Sad, where SARS-CoV-2 strain SI-4265/20, D614G (acquired from Institute for Microbiology and Immunology, Ljubljana, Slovenia) was used as a challenge. Neutralization of 50 TCID50 virus units in titer of 1:320 was considered as a threshold for CCP donor acceptance, as proposed by several previous studies [14-15].

From a total of 23 samples, an Antibody index higher than 6 was detected in 22 (22/23; 95.65%), while only 9 samples showed a neutralizing titer of 1:320 or higher (9/21; 39.13%). In order to validate "in-house" Nta, we compared COVID-19 ELISA IgG values with a titer of neutralizing antibodies, where a positive correlation was found $r(23) = 0.474$, $p = 0.017$. According to our findings, there is a possibility that a great number of CCP donations was not containing a high level of anti-SARS-CoV-2 neutralizing antibodies, despite the high antibody index shown by ELISA. Therefore, the therapeutic effect of CCP accepted with the current ELISA threshold recommendation is highly questionable.

Conclusion

Based on our experience, direct communication with COVID-19 convalescents results in high motivation of the population and consequent provision of a sufficient amount of CCP. Based on demographic data and antibody values of ELISA, we propose a specific CCP donor profile that will possibly allow us to acquire plasma with the highest antibody titer. In order to assure that only high-potency CCP will be administered to COVID-19 patients in need, we propose the implementation of gold standard neutralization assay for super-analysis of CCP donations that pass the current threshold on ELISA assay, through collaboration with Pasteur Institute Novi Sad. Established inter-institutional collaboration, gained experience, and lessons learned will be essential in facing future pandemic threats and emerging diseases.

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THERAPEUTIC PLASMA EXCANGE IN DISABLING RELAPSES IN MULTIPLE SCLEROSIS AND NEUROMYELITIS OPTICA SPECTRUM DISORDER –TREATMENT CONTROVERSIES

Marija Dinić[1], Bela Balint[2], OliveraTamaš[3]
[1]University Clinical Center of Serbia, Belgrade, Serbia
[2]Department of Medical Sciences, Serbian Academy of Sciences and Art, Serbia
[3]Clinic for Neurology, University Clinical Center of Serbia, Belgrade

Abstract

Inflammatory demyelinating diseases of the central nervous system (CNS) are the result of a disorder of the immune system instigated by infectious or environmental factors in genetically predisposed individuals. They are a heterogeneous group of diseases presented by clinical symptoms and signs of brain, spinal cord, and optic nerve damage. The spectrum of inflammatory demyelinating CNS diseases are multiple sclerosis (MS), variants of MS (Balo, Marburg, Schilder's disease), acute disseminated encephalomyelitis (Adem), NMO spectrum of diseases (NMOSD), and diseases associated with myelin oligodendrocyte glycoprotein (MOG) antibodies. According to its course, these diseases can be "monophasic" or relapsing. The aim of this paper is an overview of current opinions (presentation of clinical studies) and overview of our experiences.

In addition to immunosuppressive therapy, therapeutic plasma exchange (TPE) has proved to be an effective type of immunotherapy for these diseases, especially in their acute phase, as a therapy for severe relapse, but also as second-line therapy (especially in some cases of relapsed NMOSD) and a little more than five decades of self-administered immunotherapy or in combination with other treatments. TPE is a non-specific, non-selective method of removing the circulating agents from plasma, which is an assumed pathophysiological substrate in the development and expression of disease. The TPE is an interventional procedure during which the plasma is extracted from other circulating blood elements and the volume of plasma recovered is then substituted by crystalloid solutions, albumin solutions or plasma.

Our results, in a large group of MS patients, confirmed that TPE is an effective and safe procedure in the treatment of severe MS relapses.

Keywords: therapeutic plasma exchange, relapse, multiple sclerosis

Sažetak

Inflamatorne demijelinizacione bolesti centralnog nervnog sistema (CNS) nastaju kao posledica poremećaja imunološkog sistema koji je podstaknut infektivnim faktorima ili faktorima spoljne sredine kod genetski predisponiranih osoba. Predstavljaju heterogenu grupu oboljenja koja se prezentuje u kliničkim simptomima i znacima oštećenja mozga, kičmene moždine i optičkog nerva. Spektar inflamatornih demijelinizacionih bolesti CNS čine: multipla skleroza (MS), varijante MS (Balo, Marburg, Schilderova bolest), akutni diseminovani encefalomijelitis (ADEM), NMO spektar bolesti (NMOSD) i bolesti udružene sa mijelin oligodendrocitni glikoprotein (MOG) antitelima – (MOGAD). Prema svom toku, ove bolesti mogu biti monofazne ili relapsne.Cilj ovog rada je pregled i prikaz dosadašnjih stavova (evaluacijom kliničkih studija), uz prikaz naših iskustava.

Pored imunosupresivne terapije, imajući u vidu da su ove bolesti u osnovi autoimune prirode, terapijska izmena plazme (TIP) se pokazala kao efikasan vid imunoterapije ovih oboljenja, pre svega u njihovoj akutnoj fazi, kao terapija teškog relapsa, ali i kao terapija druge linije (posebno u pojednim slučajevima relapsne NMOSD) i primenjuje se nešto više od pet decenija samostalno ili u kombinaciji sa drugim vidovima lečenja.Terapijska izmena plazme (TIP) je nespecifična, neselektivna metoda uklanjanja cirkulišućeg agensa iz plazme koji predstavlja pretpostavljeni patofiziološki supstrat u razvoju i ispoljavanju bolesti. Terapijska izmena plazme predstavlja interventnu proceduru tokom koje se plazma izdvaja od ostalih elemenata krvi u cirkulaciji, a izdvojeni volumen plazme se potom supstituiše kristaloidnim rastvorima, rastvorima albumina ili plazmom.

Naši rezultati, u relativno velikoj grupibolesnika sa MS, potvrdili su da je TPE efikasna i sigurna procedura u lečenju teških recidiva MS.

Ključne reči: terapijska izmena plazme, relaps, multipla skleroza.

Inflammatory demyelinating CNS diseases

Inflammatory demyelinating diseases of the central nervous system (CNS) are the result of a dysfunction with following disorder of immune system initiated by infectious or environmental factors in predisposed individuals. They are a heterogeneous group of diseases presented by clinical symptoms and signs of brain, spinal cord and optic nerve damages. The spectrum of inflammatory demyelinating CNS diseases is multiple sclerosis (MS), variants of MS (Balo, Marburg, Schilder's disease), acute disseminated encephalomyelitis (Adem), NMO spectrum of diseases (NMOSD) and diseases associated with myelin oligodendrocyte glycoprotein (MOG) antibodies (1, 2).

According to its course, these diseases can be "monophasic" or relapsing. Severe relapse means: a) high degree of incapacity; b) incapability of patient to take care of himself; c) inability to perform basic life activities; d) incapacity for work and e) need for hospitalization. Clinical manifestations of severe relapses include high-level paresis and/or plegia, ataxia of the torso and extremities, as well as sensory ataxia, amaurosis, bulbar damage, internuclear ophthalmoplegia, paralysis of the eyes, etc (3, 4).

Myelin oligodendrocyte glycoprotein antibody-associated disorders (MOGAD) have been widely recognized as a distinct clinical entity only in the last decade, following the development of reliable cell-based assays using full-length human MOG as the target antigen They encompass monophasic and relapsing presentations of central demyelization. Within the neuromyelitis optica phenotype, optic neuritis is more common than transverse myelitis. The clinical spectrum has since expanded to include brainstem and cortical encephalitis (5, 6).

In comparison to aquaporin-4 antibody-positive neuromyelitis optica spectrum disorders (AQP4-Ab NMOSD), relapse is less common. Approximately half of MOGAD patients may have monophasic disease, but some experience frequent relapses despite immunosuppressive therapy. The value of antibody titers in predicting relapse is not yet fully understood. Overall, motor and visual disability outcomes seem better in MOGAD than in AQP4-Ab NMOSD (7).

Therapeutic plasma exchange

The idea of cleaning blood from toxic substances belongs to Fleig, who launched it in 1910. In 1914, Abel-Rountree and Turner tried to put in place an artificial kidney. As a therapeutic method or as a method for plasma extraction, plasmapheresis can be performed with adequate devices and kits by two procedures: by blood centrifugation or using blood filtration (8−10).

Extracting a large volume of plasma in a short time (500 − 600 mL) without affecting the oxiphoric function (restoration of the circulation of red blood cells) has intensified and developed plasmapheresis as an essential attribute in the therapeutic arsenal of many illnesses, speeding up, healing or bringing to normal the functions of organs, of the body physiology as a whole. Therapeutic plasma exchange is a therapeutic procedure in which the blood of the patient is removed and passed through a medical device that separates out and removes the plasma from the other blood components, which are returned to the patient (11−14).

Therapeutic plasmapheresis has large therapeutic and prophylactic potential as it can be used both in emergencies and in substantive treatments, in intoxications, dyslipidemias, allergies, organ deficiency, but also for the treatment of different autoimmune diseases, such as MS, Guillain-Barré syndrome (GBS), systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), etc (5−10, 13). The next group of indications (e.g. transplants in development) is that for which there is the least clinical experience and where additional basic research is needed to precisely define the role and effectiveness of transplantation (9, 10). An example would be some autoimmune diseases (e.g.MS) in case of the use of autologous stem cell (SC) transplantation. Thus, transplantation provides a complete and long-term reconstitution of the hematopoietic system following myeloablative or immunoablative conditioning − seldom following myelosuppressive pretreatment or conditioning regimens of reduced intensity (RIC) or other bone marrow damage that threatens the patient's life (10).

Nowadays, the basic mechanisms of the therapeutic action of apheresis are recognized and generally accepted. Accordingly, TPE makes extracorporeal immunomodulation (9, 10):

- Removal of pathogenic auto-antibodies, complement, immune complexes, and cytokines;
- Unblock of the mononuclear phagocyte system (MPS);
- Immunomodulation by influencing the ratio antigen/antibody in circulation;
- Modulation of solubility of immune complexes;
- Modification of activation of T lymphocyte subsets (shift according to Th2 response).

Therapeutic apheresis (primarily TPE) is an aggressive procedure, which directly intervenes in the circulation of patients and therefore can be accompanied by adverse events and side effects. In order to reduce them to the smallest possible extent, special criteria are applied for the selection of donors and patients. In addition, permanent monitoring of appropriate biological parameters is carried out, along with clinical monitoring of persons who are scheduled for apheresis (9).

There are some potential side effects of TPE, such as complications of the venepuncture, local infection, thrombosis, hypotension, dizziness, collapse, hypocalcaemia (with perioral paresthesia), hypo-fibrinogenemia (cryoprecipitate replacement), hypoalbuminemia (albumin replacement), as well as risk of infection, sepsis, embolism and cardiac arrest (9, 10).

In certain conditions and situations, the use of TPE is "unworkable", impossible or contraindicated. The most significant and common contraindications would be the following (10):

- Inadequate access to peripheral pathway and inability to tolerate central venous catheter;
- Hemodynamically severely unstable patients;
- Patients allergic to fresh frozen plasma or albumin(depends on the type of procedure, i.e. replacement fluid category);
- Patients with severe hypocalcaemia are at risk of worsening or provocation the condition due to the use of citrate to prevent blood clotting.

Special and unique criteria and/or recommendations for TPE treatment of inflammatory demyelinating diseases should be divided into those that are effective in the acute phase and those that are useful in the chronic phase of the disorder (15). Consequently, in the acute phase of the disease, TPE is used in the treatment of severe relapses in patients with multiple sclerosis, as second-line therapy (mono or add-on therapy).Also, TPE is used as relapse therapy in patients with NMO spectrum as the first line of therapy with or without concomitant administration of high doses of corticosteroid therapy. In addition, TPE is used in cases of side effects of immunomodulatory therapy, bearing in mind that it accelerates the removal of monoclonal antibodies (natalizumab) in the presence of progressive multifocal leukoencephalopathy or in need of replacement therapy. On the other hand, in chronic phase of the disease, TPE is used in patients with NMO spectrum as a maintenance therapy (16).

Finally, it should be highlighted that our results show the same effectiveness of TPE therapy in the treatment of different immunoneurological disorders (9−12). Namely, on Clinic for Neurology of the UCCS, TPE was performed as a second-line treatment of severe relapses of multiple sclerosis (MS) that don't respond to standard steroid therapy. The objective of our study was to evaluate the effectiveness and safety of TPE in severe relapses of MS in a cohort of patients treated at Neurology Clinic, CCS, Belgrade, from 2007 until 2018.

This retrospective study included 131 MS patients: 13% with clinically isolated syndrome suggestive of MS, 68% with relapsing-remitting MS, 17% with secondary progressive, 5% with primary progressive MS and 1 patient who had Marburg type of MS. Mean age was 39.5 yrs (range 19–79 yrs), 72% women. "Pulse"corticosteroid treatment was used before TPE in 88% of patients. The mean maximal EDSS score during the relapse was 6.0 (range 2.0–10.0). After TPE, 66% patients showed a marked to moderate clinical improvement, 22% showed mild improvement and in 12% there was no improvement. Mean EDSS, one month and 6 months after TPE was identical (4.0), and was significantly lower in comparison with maximal EDSS during the relapse (6.0) ($p < .001$). Multivariate regression analysis showed that early initiation of TPE (OR 0.98, 95% confidence interval [CI] 0.97−0.99) and lower maximal EDSS during relapse (OR 0.63, 95% CI 0.41−0.96) were significantly associated with better treatment response after 6-month follow-up. Adverse events occurred in 17% of patients, none of which was serious.

Thus, our study, in a large cohort of MS patients, provides additional support to the notion that TPE is an effective and safe procedure in the treatment of severe MS relapses.

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USMENE PREZENTACIJE - SAŽECI
ORAL PRESENTATIONS - ABSTRACTS

HOTEL CROWNE PLAZA
Beograd, Srbija / Belgrade, Serbia
9-12. novembar 2022. / November 9th-12th 2022

UP 1

PRIPREMA I PRIMENA JEDINICA KONCENTROVANIH TROBOCITA ČUVANIH U ADITIVNOM RASTVORU TRI GODINE ISKUSTVA

Vučetić D[1,2], Gojkov D[1], Borovčanin N[1], Vojvodić D[2,3].
[1]Institut za transfuziologiju i hemobiologiju Vojnomedicinska akademija, [2]Univerzitet odbrane, Medicinski fakultet Vojnomedicinska akademija, Beograd, [2,3]Institut za medicinska istraživanja Vojnomedicinska akademija, Beograd, Srbija.

Uvod: Aditivni rastvori za trombocite (PAS) razvijeni su 1980-ih da bi u jedinicama koncentrovanih trombocita bilo što manje plazme, jer se smatraloa da plazma sadrži štetne enzime koji su izazvali lezije trombocita tokom skladištenja.
Cilj: Istražiti razlike u prosečnom broju filtriranih trombocita dobijenih iz četiri „buffy-coata“ koji su uskladišteni u aditivnom rastvoru (SSP+) korišćenjem „top&bottom“ kesa, i filtriranih trombocita uskladištenih u plazmi dobijenih iz četiri buffy-coat-a korišćenjem različitih - petostrukih kesa (top&top).
Metoda: Deset jedinica krvi (450±45 mL) je prikupljeno u petostrukim kesama tkz.”top&bottom“ (Macopharma, Francuska), dok je drugih deset jedinica krvi prikupljeno u petostruke kese “top&top” (TH, Kina). Buffy-coat su dobijeni iz cele krvi, najkasnije dva sata nakon uzimanja, tokom 10 minuta centrifugiranja na 3.890 g (Hettich, Nemačka) i dodatno odvojeni automatskim ćelijskim procesorom Luksomatik (LMB, Nemačka). Nakon toga, korišćenjem „sistema voza“, četiri buffy-coata (dobijena iz ”top&bottom“ kesa) identične ABO grupe i 250 mL SSP+ su uliveni u jednu kesu, dalje centrifugirani na 747 g tokom 5 minuta, a nakon odvajanja trombocita, filtrirani kroz trombocitne filtere (Terumo, Japan). Buffy-coat (četiri) dobijeni iz ”top&top“ kesa su centrifugirani na 377 g tokom 5 minuta i obrađeni na istom procesoru, trombociti su sakupljeni u jednu kesu i filtrirani. Broj trombocita je određen analizatorom (Coulter, SAD).
Rezultati: Prosečan broj filtriranih trombocita u aditivnom rastvoru bio je $2,3x10^{11}$, a u TH kesama $1,9x10^{11}$. Prosečna zapremina trombocita aditivnom rastvoru je bila 340 mL, a u plazmi 290 mL. Tokom tri godine nije zabeležen nijedan slučaj alergijskih reakcija, febrilnih nehemolitičkih transfuzijskih reakcija, imunološke inkompatibilnosti ili prenošenja virusnih infekcija.
Zaključak: Prinos koncentrovanih filtrovanih trombocita iz “top&bottom” kesa je viši u odnosu na trombocite dobijene iz “top&top” kesa.

UP 1

THE PREPARATION AND APPLICATION OF CONCENTRATED PLATELET UNITS STORED IN AN ADDITIVE SOLUTION - THREE YEARS OF EXPERIENCE

Vučetić D[1,2], Gojkov D[1], Borovčanin N[1], Vojvodić D[2,3].
[1]Institute for transfusiology and hemobiology of Military Medical Academy, [2]University of Defence, Faculty of Medicine of the Military Medical Academy, Belgrade, [2,3]Institute for Medical Research of Military Medical Academy, Belgrade, Serbia.

Background: Platelet additive solutions (PASs) were developed in the 1980s to have as little plasma as possible in a platelet concentrate, as plasma was suspected to contain harmful enzymes that caused the platelet storage lesion.
Aim: To investigate differences in the number of collected filtered platelets obtained from four buffy-coats stored in additive solution (SSP+) using top&bottom bags, and filtered platelets collected from four buffy-coat using different - quintuple bags (top&top) stored in plasma.
Method: Ten blood units (450±45 mL) were collected into quintuple top&bottom plastic bag systems (Macopharma, France) while another ten blood units were collected in quintuple top&top blood bags (TH, China). The buffy coats were isolated from whole blood, no later than 2 hours after the collection, by 10 minutes of centrifugation at 3,890 g (Hettich, Germany) and additionally separated with an automatic cell processor LUXOmatic V2 (LMB, Germany). After that, using “train system”, four buffy-coats (derived from top&bottom bags) of an identical ABO group, and 250 mL of SSP+ were collected in one bag, further centrifugated at 747 g for 5 minutes, and after platelet separation, filtered through platelet filters (Terumo, Japan). Buffy-coats (four) derived from top&top bags were centrifuged at 377 g for 5 minutes and processed on the same processor, platelets collected in one bag and filtered. The platelet counts were determined by an analyser (Coulter, USA).
Results: The average number of filtered platelets in the additive solution was $2.3x10^{11}$, but in TH bags was $1.9\ x10^{11}$. The average volume of platelets in additive solution was 340 mL but in plasma was 290 mL. During three years, we did not have any case of allergic reactions, febrile non-hemolytic transfusion reactions, immunologic incompatibility or transmission of viral infections.
Conclusion: The yield of concentrated filtered platelets from “top&bottom” bags is higher compared to platelets obtained from “top&top” bags.

UP 2

UTICAJ VREMENA INAKTIVACIJE PATOGENA PRIMENOM RIBOFLAVINA I ULTRAVIOLETNOG ZRAČENJA NA INTEGRITET KONSTITUENATA PLAZME U ZAMRZNUTOJ SVEŽOJ PLAZMI

Gojkov D[1], Balint B[2,3,4,5], Vojvodić D[4,6], Dejanović B[7], Vučetić D[1,4]
[1]Institut za transfuziologiju i hemobiologiju VMA, Beograd, Srbija, [2]Institut za kardiovaskularne bolesti “Dedinje”, Beograd, Srbija; [3]Univerzitet u Beogradu, Institut za medicinska istraživanja, Beograd, Srbija; [4]Univerzitet Odbrane, Medicinski fakultet Ministarstva Odbrane, Beograd, Srbija; [5]Srpska akademija nauka i umetnosti, Odeljenje medicinskih nauka, Beograd, Srbija; [6]Institut za medicinska istraživanja VMA, Beograd, Srbija; [7]Institut za medicinsku biohemiju VMA, Beograd, Srbija

Uvod: Tretman zamrznute sveže plazme (ZSP) riboflavinom i ultravioletnim zračenjem inhibira replikaciju nukleinskih kiselina patogena i leukocita. Sistem za redukciju patogena Mirasol (Mirasol-PRT) se koristi za inaktivaciju pojedinačnih jedinica ZSP i trombocita, koje su posle toga spremne za neposrednu kliničku upotrebu.
Cilj: Poređenje efekta Mirasol-PRT sistema na sadržaj proteina u ZSP ako se ona „inaktiviše” neposredno posle izdvajanja iz jedinice cele krvi, a pre skladištenja i ukoliko je tretirana nakon skladištenja u zamrznutom stanju, tj. posle odmrzavanja, a neposredno pre aplikacije.
Materijal i metode: Jedinice plazme izdvojene iz cele krvi centrifugiranjem su: a) inaktivisane i zamrznute - prethodna inaktivacija [PI] ili kontrolna grupa i b) odmah zamrznute, a posle određenog vremena, odmrznute i inaktivisane - naknadna inaktivacija [NI] - eksperimentalna grupa. Inaktivacija je urađena Mirasol-PRT sistemom. Ispitivani su biohemijski parametri: urea, kreatinin, ukupni bilirubin, trigliceridi , holesterol, kalijum, natrijum, gvožđe, aspartat-aminotransferaza, alanin-aminotransferaza, gama glutamil-transpeptidaza, laktat-dehidrogenaza, osmotski pritisak, ukupni proteini i albumini; imunski parametri (IgM, IgG, IgA i komponente komplementa C3 i C4, uz aktivnost CH50) i prokoagulantni (FII, FV, FVII, FVIII, FIX, FX) i inhibitorni (AT-III, protein C, protein S i α2-antiplazmin) faktori hemostaze.
Rezultati: Nema značajne promene u finalnim koncentracijama biohemijskih parametara – proteina, imunoglobulina i ostalih konstituenata u obema grupama. Očekivano sniženje nivoa faktora koagulacije prisutno je u obe grupe. Najzad, utvrđen je dobar oporavak inhibitora koagulacije bez značajnijih razlika između grupa osim za AT-III koji ima bolji oporavak u eksperimentalnoj grupi.
Zaključak: Naknadna inaktivacija ZSP, prema potrebama pacijenata, tj. odgovarajućih krvnih grupa, nije inferiorna u odnosu na klasičan način prethodne inaktivacije koja podrazumeva nasumično izabrane jedinice. Ovakav protokol bi značajno smanjio troškove primene relativno skupe tehnologije, jer bi se ZSP inaktivisala ciljano, za konkretnog bolesnika, a izbegla bi se mogućnost odbacivanja prethodno inaktivisanih jedinica plazme u slučaju da na testiranju budu pozitivne na markere transfuzijom prenosivih infekcija.

UP 2

INFLUENCE OF TIME OF PATHOGEN INACTIVATION WITH RIBOFLAVIN AND UV LIGHT ON PLASMA PROTEINS IN FRESH FROZEN PLASMA

Gojkov D[1], Balint B[2,3,4,5], Vojvodić D[4,6], Dejanović B[7], Vučetić D[1,4]
[1]Institute for transfusiology and hemobiology MMA,Belgrade, Serbia; [2]Institute for Cardiovascular Diseases “Dedinje”, Belgrade, Serbia; [3]University of Belgrade, Institute for Medical Research, Belgrade, Serbia; [4]University of Defence, Faculty of Medicine of the Military Medical Academy, Belgrade, Serbia; [5]Serbian Academy of Sciences and Arts, Department of Medical Sciences, Belgrade, Serbia; 6Institute for Medical Research MMA, Belgrade, Serbia [7]Institute for Medical Biochemistry, MMA, Belgrade, Serbia

Introduction: Treatment of frozen fresh plasma (FFP) with riboflavin and ultraviolet radiation inhibits the replication of nucleic acids of pathogens and leukocytes. The Mirasol Pathogen Reduction System (Mirasol-PRT) is used to inactivate individual FFP units and platelets, making then ready for immediate clinical use.
Goal: Compare the effect of the Mirasol-PRT system on the protein content in FFP "inactivated" immediately after separation from whole blood, before storage and treated after storage in a frozen state, after thawing.
Materials and methods: Plasma units separated from whole blood by centrifugation are: a) inactivated and frozen - previous inactivation or control group and b) immediately frozen, and after a certain time, thawed and inactivated - subsequent inactivation or experimental group. Inactivation was performed with Mirasol-PRT system. The following biochemical parameters were tested: urea, creatinine, total bilirubin, triglycerides, cholesterol, potassium, sodium, iron, aspartate-aminotransferase, alanine-aminotransferase, gamma-glutamyl transpeptidase, lactate dehydrogenase, osmotic pressure, total proteins and albumin; immune parameters (IgM, IgG, IgA) and complement components C3 and C4, with CH50 activity and procoagulant (FII, FV, FVII, FVIII, FIX, FX) and anticoagulant (antithrombin III, protein C, protein S and α2-antiplasmin) factors.
Results: There is no significant change in the final concentrations of biochemical parameters - proteins, immunoglobulins and other constituents in both groups. The expected decrease in coagulation factor levels is present in both groups. Finally, good recovery of natural inhibitors was found without significant differences between groups except for AT-III which recovery is better in experimental group.
Conclusion: We have shown that the subsequent inactivation of FFP, according to the needs of patients, ie. the appropriate blood groups, is not inferior to the classical method of previous inactivation. Such a protocol would significantly reduce the cost and avoid the possibility of rejecting previously inactivated plasma units in case they are positive for markers of transfusion transmitted infections.

UP 3

ODRŽAVANJE ZALIHA KOMPONENTI KRVI U ZAVODU ZA TRANSFUZIJU KRVI VOJVODINE

Klašnja J.[1], Bujandrić N.[1,2], Grujić J.[1,2], Budakov- Obradović Z.[1,2], Gulan Z.[1]
[1]*Blood Transfusion Institute of Vojvodina, Novi Sad, Serbia*
[2]*Faculty of Medicine, University of Novi Sad, Serbia*

Uvod: Broj donacija krvi širom sveta je u konstantnom padu. Sa druge strane, potrebe za krvlju i krvnim produktima su svake godine sve veće. Mnogo studija je analiziralo odgovarajuću upotrebu zamrznute sveže plazme (ZSP), kao i efikasnost transfuzije ZSP. Zamrznuta sveža plazma predstavlja zapreminu plazme izdvojenu iz jedne jedinice cele krvi 6-8 sati nakon kolekcije i brzo zamrznuta na temperaturi od − 20°C (ili nižoj) u odgovarajućim zamrzivačima.
Cilj rada: Cilj ove studije je bio da se ispita poboljšanje kvaliteta u vezi sa proizvodnjom, potrošnjom i brojem odbačenih jedinica ZSP u Zavodu za transfuziju krvi Vojvodine (ZZTKV).
Materijal i metode: Retrospektivnom studijom je analiziran period od januara do decembra 2021. godine u ZZTKV, najvećem distributeru krvi i krvnih produkata u Vojvodini (za 8 bolničkih banki krvi i 19 bolnica). Relevantni podaci su dobijeni iz informacionog sistema ZZTKV. Podaci su analizirani prema proizvodnji, potrošnji i količini odbačenih jedinica ZSP.
Rezultati: Tokom perioda istraživanja prikupljeno je ukupno 43073 jedinica krvi od kojih je napravljeno 34831 (80,86%) jedinica ZSP. Za terapijsku upotrebu je iskorišćeno 19556/34831 (56,14%), dok je 15275/34831 (43,86%) odbačeno. Glavni razlozi za odbacivanje ZSP bili su:
lipemični produkti 58,75%, tehničke greške 37,7%, i pozitivni rezultati testiranja na transmisivne bolesti (0,91%). Ostale pripremljene komponente bile su: 4099 jedinica krioprecipitata, 3917 jedinica ZSP bez krioprecipitata, 88 dečijih doza ZSP.
Najveći potrošaci ZSP su bili Klinički centar Vojvodine (30%), bolničke banke u Vrbasu (14,2%), Zrenjaninu (13,9%). Usled zastarelosti nije izdato 0,16% jedinica.
Zaključak: Razlog povećanog broja donacija lipemične plazme predstavlja činjenica da se u Vojvodini konzumira tradicionalna hrana bogata masnoćama. Edukacija davalaca krvi može da podstakne da se stvore zdravije navike ishrane. Smanjen broj tehničkih greški može se postići boljom opremom (centrifuge, separatori), kao i pažljivim rukovanjem napravljenim produktima krvi.
Ključne reči: Plazma, Davaoci krvi, Hiperlipidemija

UP 3

MAINTAINING STOCK OF BLOOD COMPONENTS IN BLOOD TRANSFUSION INSTITUTE OF VOJVODINA

Klašnja J.[1], Bujandrić N.[1,2], Grujić J.[1,2], Budakov- Obradović Z.[1,2], Gulan Z.[1]
[1]*Blood Transfusion Institute of Vojvodina, Novi Sad, Serbia*
[2]*Faculty of Medicine, University of Novi Sad, Serbia*

Introduction: Number of blood donations worldwide is continually decreasing. On the other hand, need for blood and blood products is increasing every year. Many studies analysed appropriate use of fresh frozen plasma (FFP) as well as efficacy of FFP transfusions. FFP must be separated from whole blood within 6 to 8 hours of collection and then frozen at − 20°C (or below) in a blood bank freezer.
Aim: Aim of this study was to examine a quality improvement addressing FFP production, consumption and discarded FFP at the Blood Transfusion Institute of Vojvodina (BTIV).
Material and methods: This retrospective study was conducted from January to December 2021st at the BTIV, the top provider of blood components in Vojvodina (for 8 blood banks and 19 hospitals). Relevant data were extracted from the information system BTIV. Data regarding FFP production, consumption and discard was reviewed.
Results: During this period 43073 units of blood were collected and 34831 (80.86%) units of FFP were made. For therapeutic purposes 19556/34831 (56.14%) units were used, while 15275/34831 (43.86%) units were discarded. Main reasons for discard were: lipemic plasma products (58.75%), errors in production (37.7%), and positive test results on transmissive diseases (0.91%). Other blood components were: 4099 cryoprecipitate units, 3917 FFP units without cryoprecipitate, 88 FFP children units. Top users of the FFP were Clinical Center of Vojvodina (30%), hospital blood bank in Vrbas (14.2%) and Zrenjanin (13.9%). A small percentage (0.16%) of the FFP were not used due to expired date of the products.
Conclusion: The reason for increased numbers of lipemic plasma donations is probably traditional high-fat food in Vojvodina. Blood donors education may encourage them towards healthy diet. Decrease of technical errors can be achieved by use of better equipment (centrifuges, separators) as well as careful handling of FFP units.
Key words: Plasma; Blood Donors; Hyperlipidemias.

UP 4

PRIPREMA KOMPONENATA KRVI U VREME PANDEMIJE COVID-19 U ODNOSU NA DVOGODIŠNJI PERIOD PRE PANDEMIJE

Mijović S, J. Anđelić, V. Savović, S. Radević
Institut za transfuziju krvi Srbije

Uvod: Odeljenje za pripremu komponenata krvi vrši prijem, trijažu jedinica cele krvi, pripremu komponenata krvi (KK), čuvanje i distribuciju, kako bi se obezbedile dovoljne količine sigurne krvi/produkata za potrebe lečenja bolesnika.
Cilj: Analiza podataka o pripremljenim KK za period 2018–2019. godine u odnosu na ukupan broj prikupljenih i pripremljenih KK za vreme pandemije Covid-19, 2020–2021. godine.
Materijal i metode: Retrospektivna analiza podataka prikupljenih 156 990 jedinica cele krvi (CK) u 2018-2019. godini, a u periodu pandemije 2020-2021. godine prikupljeno je 123 858 jedinica CK, kada je vršeno i preuzimanje anti-Covid plazme.
Rezultati: U periodu 2018–2019. godine prikupljeno je 156 990 jedinica CK: u K4 kese 88%, u K5 9,9%, u K2 od 450ml u 2%. Od primljenih jedinica CK proizvedene su 363 296 komponenata krvi: resuspendovani eritrociti osiromašeni Le i Tr; eritrociti filtrirani prethodno; deplazmatisana krv; koncentrati trombocita iz buffy coat-a; komponente zamrznute sveže plazma; krioprecipitat. U periodu 2020–2021. godine od prikupljenih 123 858 jedinica CK uzete: u K4 kese 83%, K5 16% i K2 2,3%, proizvedene su 311 101 jedinice KK. U vreme pandemije Covid-19 uzeto je 21,1% manje jedinica CK u odnosu na period pre pandemije, samim tim je smanjen broj pripremljenih komponenata krvi.
Od 11.04.2020. godine iz ITKS preuzete su 4 137 jedinica anti-Covid 19 plazme.
Zaključak: Pandemija Covid-19 uticala je na smanjenje broja prikupljenih jedinica CK u 2020. i 2021. godini za 21,1% u odnosu na navedeni period pre pandemije. Bez obzira na ovaj smanjen broj pripremljenih komponenata krvi uspevali smo da obezbedimo dovoljan broj adekvatnih komponenata krvi i anti-Covid plazme za potrebe lečenja bolesnika.
Ključne reči: komponente krvi, pandemija, anti-Covid plazma

UP 4

BLOOD COMPONENTS PREPARATION DURING THE COVID-19 PANDEMIC COMPARED TO TWO YEARS BEFORE

Mijović S, J. Anđelić, V. Savović, S. Radević
Blood Transfusion Institute of Serbia (BTIS), Belgrade, Serbia

Introduction: The Blood Processing Department is in charge of the receipt and triage of whole blood (WB) units and the preparation of blood components (BC), their storage and distribution in order to ensure sufficient quantities of safe blood/products for the needs of patient treatment.
Objective: Data review of prepared BC for the period 2018-2019 compared to the total number of collected and prepared BC during the Covid-19 pandemic, 2020-2021.
Material and Methods: Retrospective data analysis of 156 990 WB units for the period 2018-2019 and 123 858 WB units during the pandemic period 2020-2021, when anti-Covid convalescent plasma was also collected.
Results: During 2018-2019, 156 990 WB units were collected: 88% in K4 bags; 9.9% in K5; 2% in K2 450ml bags. From the received WB units, 363 296 BC were produced: resuspended erythrocytes depleted of Le and Tr; pre-filtered erythrocytes; deplasmated blood; buffy coat derived platelet concentrates; frozen fresh plasma components; cryoprecipitate. During 2020-2021, 83% of the collected 123 858 units of WB were in K4 bags; 16% in K5 and 2.3% in K2 bags; 311 101 BC units were produced. During the pandemic 21.1% fewer WB units were taken compared to the period before the pandemic, thus reducing the number of prepared BC.
Since 11.4.2020, 4 137 anti-Covid plasma units were received from BTIS.
Conclusion: The Covid-19 pandemic has affected and reduced the number of BC units in 2020 and 2021; 21.1% less compared to the specified period before the pandemic. Regardless of the reduced number, we have managed to secure sufficient quantities of adequate BC and anti-Covid plasma units for patient treatment needs.
Keywords: blood components, pandemic, anti-Covid plasma

UP 5

OUR EXPERIENCE WITH PREPARING CONVALESCENT PLASMA IN THE INSTITUTE OF TRANSFUSION MEDICINE AT REPUBLIC OF NORTH MACEDONIA, REGIONAL CENTRE BITOLA

Stojanova Vilos L[1], Stojanovska Z., Dimitrova D., Balalovska L., Jolevska M.[1], Useini S., Grubovic R.[2]
[1]. ITM of RNM - Regional Centre Bitola, [2]. ITM of RNM

Introduction: The pandemic COVID 19 opened new fields of investigation and work in the field of
transfusion medicine. Convalescent plasma (Cpl) appears as a new blood product and a challenge for us, the transfusion medicine workers.
Aim: To show work volume and logistics in preparing Cpl in Regional Centre (RC) Bitola from december 2020 to end of 2021.
Materials and methods: In the beginning, it was supposed to be a national project performed by the Institute of Transfusion Medicine (ITM) in Skopje. But it came out that it was too big of a project to be performed only by ITM Skopje. So, after a few months, RC Bitola stood out with independent work. We used the same laboratory for estimating antibodies at the Centre for Immune, Molecular and Genetic Investigation (CIMGI) at RNM. The protocol for giving blood for Cpl was that potential donors could be every healthy person who had beaten COVID 19 in the last one to three months. It was agreed that only neutralisation Receptor Binding Domain (RBD) - IgG antibodies, above five units were acceptable for Cpl. And we accepted results only from CIMGI at RNM. The protocol for regrouting BD for Cpl involved two actions. First we tested blood count, biochemical examination, blood type and RBD antibodies. At the same time a smear was taken from the blood donor`s throat and nose for PCR test. After a few mounts the protocol was changed, simplified, with only blood count and amount of RBD antibodies.
Every BD filled in two questionnaires. One for ordinary blood donation and another for the covid history of the BD. The issuance of Cpl was on demand from the clinicians. Defrosted Cpl was issued to the patient, along with two forms, one for the clinician and another for the patient. The form for the clinician should be performed at the end of hospitalisation in covid centres. The form for the patient was an informed consent form. We made a register of issued Cpl which contains all the important information about the Cpl and patients who received it.
Results: A number of 465 BD were accepted for Cpl in RC Bitola. 258 BD gave blood in the Service of Transfusion Medicine (STM) Bitola, 178 BD in STM Prilep and 34 BD in STM Ohrid. STM Bitola issued 252 Cpl along with the forms. Only 56 of the 252 forms were completed. It was understandable, considering the amount of work that our colleagues had in the covid centres.
Conclusion: With our efforts we made a meaningful contribution to the fight against COVID 19.

UP 5

UP 6

PRIPREMA I PRIMENA TROMBOCITNOG GELA U LEČENJU HRONIČNIH RANA

Gojkov D[1], Milićević S[2], Abazović Dž[3], Vučetić D[1]
[1]Institut za transfuziologiju i hemobiologiju VMA, [2]Klinika za plastičnu hirurgiju i opekotine VMA, Beograd, Srbija, [3]Klinika Renova, Beograd.

Uvod: Trombociti sadrže brojne faktore rasta, citokine i hemokine koji su aktivno uključeni u spontano zarastanje rana i značajno poboljšavaju oporavak kože i vaskularizaciju. Unapređen nivo bezbednosti transfuzije doprineo je široj upotrebi alogenih krvnih produkata i nudi nove terapijske opcije za pacijente koji ne mogu da se podvrgnu autolognoj donaciji krvi.
Cilj: Procena kliničke efikasnost alogenog trombocitnog gela (TG) pripremljenog standardnim procedurama iz koncentrata trombocita (KT) dobijenih iz Buffy coat-a (BK).
Metoda: Trombociti izdvojeni iz Buffy coat (KT-BK) su dobijeni od davalaca krvi identične ABO grupe, negativnih na bolesti koje se prenose transfuzijom. Jedinice sa brojem trombocita od najmanje 1000 x 10^3/µl podeljene su na doze od 15 ml i zamrznute na -80°C do upotrebe, maksimalno 6 meseci.
Da bi se dobila jedinica TG, zamrznuta doza KT-BK je odmrznuta na 37°C i aktivirana alogenim trombinom (domaće proizvonje) i kalcijum glukonatom. Rastvor aktivatora je aseptički ubrizgan u kesicu i, nakon mešanja, ostavljen je da odstoji na 22-25°C tokom 20-30 minuta, koliko je potrebno za spontano geliranje.
Rezultati: Hronična rana je lečena aplikacijom TG jednom ili dve puta nedeljno, u zavisnosti od kliničkog odgovora i stanja rane. Za prvog pacijenta lečenog na ovaj način (dijametar rane 15 x 6cm, dubina 1cm), primenjeno je ukupno 26 jedinica trombocitnog gela tokom 12 aplikacija. Posle tri meseca, hronična rana je potpuno zarasla i pacijent je otpušten kući.
Zaključak: Faktori zarastanja rana koji potiču od trombocita bili su jedan od prvih i najefikasnijih proizvoda dobijenih od trombocita koji su uspešno korišćeni za lokalni tretman kožnih lezija. Nova vrsta pripreme trombocitnog gela omogućava primenu alogenog TG za lečenje hroničnih rana kod veoma starih, slabo pokretnih pacijenata kod kojih primena produkata od autologne krvi nije moguća.

UP 6

PREPARATION AND APPLICATION OF PLATELET GEL IN THE TREATMENT OF CHRONIC WOUNDS

Gojkov D[1], Milićević S[2], Kozarski J[2], Đorđević B[2], Stepić N[2], Abazović Dž[3], Vučetić D[1],
[1]Institute for transfusiology and hemobiology of Military Medical Academy, [2]Clinic for Plastic Surgery and Burns of Military Medical Academy, Belgrade, Serbia, [3]Renova Clinic, Belgrade.

Background: Platelets contain a number of growth factors, cytokines and chemokines actively involved in spontaneous wound healing and significantly improve dermal repair and vascularization. Improved level of transfusion safety has contributed to the use of allogeneic blood products and offers novel therapeutic options for patients who cannot easily undergo autologous blood processing.
Aim: We evaluated the clinical efficacy of allogeneic platelet gel (PG) prepared with standard blood banking procedures from routine platelet concentrates (PCs) obtained from buffy coats.
Method: Buffy coat derived platelets (BC-PC) were obtained from blood donors of an identical ABO group, negative for transfusion-transmitted diseases. Units with a platelet count of minimum 1000x 10^3/µL, were subdivide into 15 mL aliquots and frozen in a -80°C until use, for a maximum of 6 months.
To obtain the PG units, a frozen BC-PC aliquot was thawed at 37°C and activated with homemade allogeneic thrombin and calcium gluconate. The activator solution was injected aseptically into the bag and, after mixing, was let to rest at 22-25°C for 20-30 min, allowing for gelation to occur spontaneously.
Results: Chronic wound was treated with one or two PG applications per week, according to the clinical response and state of the wounds. The first patient with the chronic wound (diameter 15 x 6cm, 1cm depth), was treated during 12 platelet gel applications. A total of 26 platelet gel units were applied. After three months, the chronic wound was completely healed and the patient was discharged home.
Conclusion: Platelet-derived wound healing factors were one of the first and most effective platelet-derived products successfully used for topical treatment of skin lesions. This novel kind of preparing platelet gel supports the efficacy and feasibility of allogeneic PG to treat chronic wounds in very elderly hypomobile patients for whom autologous blood processing was not possible.

UP 7

IMPLEMENTATION OF A TOTAL QUALITY SYSTEM IN THE INSTITUTE FOR TRANSFUSION MEDICINE IN REPUBLIC OF NORTH MACEDONIA

Petkovikj E[1], Stojkoska S[1], Grubovic Rastvorceva R[1], Daskalovska Khan D[1], Neceva V[1], Stankovic D[1], Shterjanovski M[1], Shorova M[2], Jolevska M[3], Vilos L[3], Ibraimi M[4], Useini S[1].

1 Institute for Transfusion medicine, Skopje, Republic of North Macedonia
2 Regional Center for Transfusion medicine, Shtip, Republic of North Macedonia
3 Regional Center for Transfusion medicine, Bitola, Republic of North Macedonia
4 Regional Center for Transfusion medicine, Tetovo, Republic of North Macedonia

Introduction: Increased progress in the transfusion medicine and technology have enabled the implementation of Quality Management System as critically important in order to increase the efficacy, quality and safety of the blood and blood components.
Aim: Aim of this paper is to show our experience in the implementation of the total quality system (TQS) in the Institute for Transfusion medicine in Republic of North Macedonia (ITM-RNM).
Materials and methods: The TQS includes policy, organizational structure, responsibilities, processes, procedures and resources established by the management to achieve and maintain quality.
Results: ITM-RNM is working according the actual national legislative, the law for blood safety (Official Gazette, September 2007) and by-laws for safe and quality collection, processing and testing of blood, storage and distribution of the blood components. ITM-RNM owns a unified system of working standards, procedures and equipment. The Quality Assurance and Quality Control (QAQC) department in ITM analyzes the total number of blood donations, processed blood components, the incidence of transfusion transmitted infection, the number of recalled components, number of reported serious adverse events and reactions; revises Quality manual (according ISO 9001:2015) and standard operational procedures; registers of non-conformities; undertakes corrective and preventive measures, internal and external audits, ISO 9001:2015 accreditation and reaccreditation, EDQM audits.
Conclusions: A quality system should ensure that no part of the transfusion chain is lacking in quality. TQS implies complex management of the risk and safety in blood establishments involved in collection, testing, processing, storage and distribution of blood and blood components, as well as in hospital departments where these blood components are transfused to patients.
Key words: Total Quality Management; Transfusion Medicine; Blood Transfusion.

UP 7

UP 8

PRIMENA ROTACIONE TROMBELASTOMETRIJE U PRAĆENJU HEMOSTAZE KOD KRITIČNO OBOLELIH COVID-19 BOLESNIKA SA SEPSOM

Kulić A[1], Libek V[1], Todorović-Balint M[2], Kovač M[3]
[1]*Služba za transfuziju krvi KBC Zemun, Beograd, Srbija*
[2]*Klinika za hematologiju KCS, Beograd, Srbija*
[3]*Institut za transfuziju krvi Srbije, Beograd, Srbija*

UVOD: Karakteristike COVID-19 koagulopatije (CAC) pokazuju određene razlike u odnosu na koagulopatiju povezanu sa bakterijskom sepsom i DIK-om. Koagulopatija uzrokovana COVID-19 infekcijom je kombinacija DIK-a niskog stepena i plućne trombotične mikroangiopatije što dovodi do mulitisistemske disfunkcije organa. Rotaciona trombelastometrija (TEM) je point of care metoda koja daje informacije o inicijaciji koagulacije, polimerizaciji fibrina, čvrstoći ugruška i fibrinolizi.
CILJ: Cilj istraživanja je bio da se primenom TEM-a odredi vrsta poremećaja hemostaze, kao i parametri koji su od značaja u identifikaciji CAC-a.
MATERIJAL I METODE: U istraživanje je uključeno 30 COVID-19 bolesnika sa sepsom u KBC Zemun od 01.11.2020. do 30.04.2021. godine. TEM je urađen na automatskom analizatoru ClotPro®Haemonetics. Za definisanje koagulopatije korišćena su tri testa: EX-test, AP-test, FIB-test i parametri: CT(vreme koagulacije), CFT(vreme formiranja krvnog ugruška) i MCF(maksimalna čvrstoća krvnog ugruška).
REZULTATI: Skraćeno CFT u EX testu i povišeni MCF u EX i FIB testu (hiperokoagulabilnost) registrovani su kod 6 (20%) bolesnika. Hipokoagulabilnost je bila prisutna kod 19 (63,3%) bolesnika sa značajnim produženjem CT-a i CFT-a u svim testovima. Utvrđena je statistički značajna povezanost ($p<0,05$) trombocitopenije i CFT-a sa smanjenim hemostaznim kapacitetom. Kod 13(43.3%) bolesnika MCF u FIB-testu je bio snižen, a u EX-testu kod 17(56,7%). Hiperfibrinoliza manjeg stepena bila je prisutna kod 7(23,3%) bolesnika. Parametri TEM-a od značaja za definisanje CAC-a u EX-testu je A20 (amplituda krive 20 minuta nakon formiranja krvnog ugruška), a u FIB-testu MCF i A20. Veće amplitude merenja su ukazivale na hiperkoagulaciju i trombozu, a manje na hipokoagulaciju i potencijalni DIK. 19(63.3%) bolesnika sa smrtnim ishodom su imali statistički značajno produženo CFT u EX-testu u odnosu na 11 (36.7%) preživelih bolesnika.
ZAKLJUČAK: Monitoring CAC-aTEM metodom pokazuje širok spektar poremećaja od hiper do hipokoagulabilnosti. Zajedno sa standardnim testovima hemostaze, ova metoda može biti korisna za praćenje dinamičnih promena u hemostazi kod kritično obolelih COVID-19 bolesnika.
KLJUČNE REČI: COVID-19 koagulopatija, rotaciona trombelastometrija, sepsa

UP 8

HEMOSTASIS MONITORING WITH ROTATION THROMBELASTOMETRY IN CRITICALLY ILL COVID-19 PATIENTS WITH SEPSIS

Kulić A[1], Libek V[1], Todorović-Balint M[2], Kovač M[3]
[1]*Blood bank Department CHC Zemun, Belgrade, Serbia*
[2]*Clinic of hematology Universety Clinical Center of Serbia, Belgrade, Sebia*
[3]*Blood transfusion Institute of Serbia,Belgrade,Serbia*

BACKGROUND: The characteristics of COVID-19 coagulopathy (CAC) show some differences compared to coagulopathy associated with bacterial sepsis and disseminated intravascular coagulation (DIC). CAC is a combination of low-grade DIC and pulmonary thrombotic microangiopathy leading to multisystem organ dysfunction.Rotational thrombelastometry (TEM) is a point-of-care method that provides information on coagulation initiation, fibrin polymerization, clot strength, and fibrinolysis.
AIM: Our investigationdetermined the type of haemostasis disorders using rotation thrombelastometry, as well as the parameters that are important in the identification of CAC.
MATERIAL AND METHODS: In CHC Zemun, in the period from 01.11.2022. to 30.04.2022. thirty (30) COVID-19 patients with sepsis were included in the research. TEM was performed on a point of care automatic analyzer (ClotPro®Haemonetics). We used three tests to define hemostasis disorders: EX-test, AP-test, FIB-test with parameters: CT (coagulation time), CFT (clot formation time) and MCF (maximum clot firmness).
RESULTS: Shortened CFT in EX test and elevated MCF in EX and FIB test (hypercoagulability) were registered in 6(20%) patients. Hypocoagulability was present in 19(63.3%) patients with significanly prolonged of CT and CFT in all tests. In these patients we discovered a statistically significant association ($p<0.05$) of thrombocytopenia and CFT with reduced hemostatic capacity. In the FIB-test MCF was reduced in 13(43.3%) patients, and in the EX-test in 17(56.7%) patients. Hyperfibrinolysis was present in 7(23.3%) patients. TEM parameters important for defining CAC in EX-test are A20 (amplitude of the curve 20 minutes after blood clot formation), and in FIB-test MCF and A20 parameters. Higher amplitudes of measurements indicated hypercoagulation and thrombosis, and lower amplitudes indicated hypocoagulation and potential DIC. 19(63.3%) patients with a fatal outcome had statistically significantly prolonged CFT in the EX-test compared to 11(36.7%) surviving patients.
CONCLUSION: Monitoring of CAC using TEM method shows a wide range of disorders from hypercoagulation to hypocoagulation. Together with standard coagulation tests, this method is useful for monitoring dynamic changes in haemostasis in critically ill COVID-19 patients.
KEY WORDS:COVID-19 coagulopathy, rotational thrombelastometry, sepsis

UP 9

POREMEĆAJI HEMOSTAZE KOD BOLESNIKA OBOLELIH OD CIROZE JETRE PRAĆENI ROTEM-OM

Dinić R, Mijović L, Životić B, Štrbac N,Mladenović N, Šoškić T, Lukić V
Urgentni centar, Univerzitetski Klinički Centar Srbije, Beograd, Srbija

Uvod: Jetra sintetiše, modifikuje i inaktiviše većinu enzima i drugih proteina koji učestvuju u procesu koagulacije. Oštećena hepatična funkcija može dovesti do poremećaja sinteze koagulacionih proteina i njihovog kvalitativnog i kvantitativnog deficita. Poremećena funkcija jetre neretko se komplikuje oštećenjem rada drugih organa, remećenjem homestatskih i hemodinamskih mehanizama kao i sklonošću ka infekciji. To utiče da fini balans hemostaze biva pomeren ka krvarenju ili pak ka trombozi.
Cilj rada: Uloga ROTEM-a u proceni koagulacionog statusa kod bolesnika sa završnom fazom ciroze jetre.
Materijal i metode: Retrospektivna analiza rezultata koagulacionog testiranja na ROTEM aparatu 152 bolesnika u završnoj fazi ciroze jetre u periodu januar 2018. - januar 2022. godine.
Rezultati: Testiranje je sprovedeno kod 152 bolesnika , 106 muškaraca i 46 žena prosečne starosti 56,7 godina, koji su lečeni na Odeljenju intenzivne nege. Rezultati EKSTEM-a i FIBTEM-a kod 51 (33.55%) bolesnika bili su unutar referentnih opsega, što ukazuje na to da je bolest bila stabilna. Produženo vreme formiranja ugruška uočeno je kod 24 (15.78%) bolesnika, prema CTu EXTEM testa. Dva pacijenta su pokazala samo umereni nedostatak fibrinogena mereno FIBTEM-om, dok je kod 33 (21,71%) bolesnika registrovana blaga trombocitopenija i snižena aktivnost trombocita. Kod 30 (19.73%) bolesnika otkriven je globalni poremećaj hemostaze, sa deficijencijom fibrinogena ispod 1 g / L, kao i poremećenim brojem i aktivnošću trombocita. Patološka fibrinoliza je bila prisutna kod 12 (7,89%)pacijenata ML EKSTEM> 15%.Preko trećine bolesnika(38,43%) je imalo stabilnu bolest bez poremećaja hemostaze dok je 25% bolesnika imalo globalni poremećaj koagulacije.
Zaključak: Viskoelastični testovi, kao što je ROTEM®, omogućuju dinamičku procenu celog procesa koagulacije i daju bolju ilustraciju interakcija između pro- i antikoagulantnih faktora, kao i trombocita. Adekvatna hemostatska terapija vođena rezultatima ROTEM-a omogućava brzu, doziranu i pravovremenu terapiju kod krvavljenja kao i ciljanu i usmerenu terapiju komponentama krvi.
Ključne reči: hemostaza, Rotem, ciroza jetre

UP 9

COAGULATION DISORDERS IN PATIENTS WITH CIRRHOSIS HEPATIS MONITORED BY ROTEM

Dinić R, Mijović L, Životić B, Štrbac N, Mladenović N, Šoškić T, Lukić V
University Clinical Center of Serbia, Belgrade, Serbia

Backgraund:In deranged hepatic function such as liver cirrhosis there is a reduced synthesis of procoagulants and endogenous anticoagulants, however, extrahepatically synthesized hemostatic and fibrinolytic factors are disproportionately affected. Also, there are many concomitant factors, such as hemodynamic changes, other organs affection, namely kidney, and predisposition to infection, that shift the balance towards either bleeding or thrombosis.
Aim:The aim of our study was evaluation of the ROTEM results obtained in the monitoring of the patients with end stage liver cirrhosis.
Metods: From January 2018 till January 2022, in 152 patients in the end stage of liver cirrhosis,
106 male and 46 female(med.age 56.7), were admitted to the internal intensive care unit.
ROTEM tests EXTEM and FIBTEM were performed in order to follow the haemostasis parameters. In all of them, based on obtained results, adequate doses of haemostatic therapy were administered. All ROTEM results and the applied therapy were evaluated.
Results: EXTEM and FIBTEM results of 51 (33.55%) patients were within reference ranges, suggesting that disease was stable. Prolonged clotting formation time was observed in 24 (15.78%) patients, according to CT extem. Two patient showed only a moderate fibrinogen deficiency measured by FIBTEM, while in 33 (21,71%)patients, only moderate platelet count and activity were registered. In 30 (19.73%) patients, complete haemostasis disorder was detected, associated with fibrinogen deficiency below 1 g/l, as well as disordered count and activity of platelets. ML EXTEM > 15% , Patological fibrinolysis was present in 12 (7,89%) patients.
Conclusion: Viscoelastic tests ,such as ROTEM®, allow dynamic assessment of the entire coagulation process and provide a better illustration of the interactions between pro- and anticoagulants as well as platelets.Adequate haemostatic therapy based on the obtained ROTEM methods enables quick and timely reaction to bleeding as well as appropriate consumption of blood components.
Key words: Haemostasis, Rotem, Cirrhosis hepatis

UP 10

AKTIVNOST FAKTORA VIII KOD BOLESNIKA U ODNOSU NA TIP TROMBOZE I FAKTORE RIZIKA ZA TROMBOZU, STAROST I KOMORBIDITET

Basarić D[1], Saračević M[1], Bosnić V[1], Vlatković A[1], Tomić B[2], Kovač M[1,3]
[1]Institut za transfuziju krvi Srbije, Odeljenje za ispitivane poremećaja hemostaze, Beograd,Srbija
[2]Institut za molekularnu genetiku i genetičko inženjerstvo ,Univerzitet u Beogradu, Beograd,
[3]Medicinski Fakultet Univezitet u Beogradu, Beograd, Srbija

Uvod: Povećana aktivnost faktora VIII (FVIII) se pokazala kao nezavisan faktor rizika za duboku vensku trombozu (DVT) i plućnu emboliju. Poznato je da povećani nivoi FVIII sami po sebi nisu dovoljni da izazovu trombozu, međutim povećanje FVIII sa drugim faktorima rizika može doprineti povećanju rizika za trombozu.
Cilj rada: Procena nivoa FVIII u odnosu na tip tromboze i faktore rizika bolesnika kao što su starost i komorbiditeti.
Materijal i metode: U ispitivanje je uključen 441 bolesnik koji je upućen na testiranje na trombofiliju u periodu (januar 2010. – decembar 2020). Bolesnici kod kojih je prva tromboza nastala pre 50. godine života su bili obuhvaćeni ispitivanjem. Podaci o bolesnicima koji su korišćeni u statističkim analizama prikupljeni su iz našeg registra za trombofiliju.
Rezultati: Broj ispitanika sa povišenim FVIII preko 1,5 IU/mL je isti bez obzira na vrstu tromboze. Aktivnost FVIII počinje da raste već nakon 40. godine života i dostiže srednje vrednosti od 1,45 IU/mL blizu "cut off" vrednosti (1,5 IU/mL) pokazujući statistički značajnu razliku u poređenju sa onima ispod 40. godina; P=0,001. Pridružene bolesti nisu imale uticaja na povećanje FVIII osim bolesti štitaste žlezde i maligniteta. U navedenim bolestima dobijena je prosečna vrednost FVIII od 1,82 (0,79) odnosno 1,65 (0,43).
Zaključak: Na aktivnost FVIII značajno utiče starost. Tip tromboze i komorbidne bolesti osim bolesti štitaste žlezde i maligniteta nisu imale uticaja na nivo FVIII.
Ključne reči: aktivnost faktora VIII, tip tromboze, starost

UP 10

FACTOR VIII ACTIVITY IN RELATION TO THE TYPE OF THROMBOSIS AND PATIENT'S RISK FACTORS FOR THROMBOSIS, AGE AND COMORBIDITY

Basaric D[1], Saracevic M[1], Bosnic V[1], Vlatkovic A[1], Tomic B[2], Kovac M[1,3]
[1]Blood Transfusion Institute of Serbia, Hemostasis Department, Belgrade, Serbia
[2]Institute of Molecular Genetics and Genetic Engineering, University of Belgrade, Belgrade,
[3]Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Objective. Elevated factor VIII (FVIII) has been shown to be an independent risk factor for deep venous thrombosis (DVT) and pulmonary embolism. It has been suggested that increased FVIII levels by itself is insufficient to cause thrombosis, however, increased FVIII with other risk factors could increases the risk of thrombosis.
The aim of the study was to evaluate the FVIII level with regard to the type of thrombosis and patient's risk factors such as age or comorbidity.
Materials and methods. In total 441 patients who were referred for thrombophilia testing in the period (January 2010 - December 2020) were included in the study. The patients who developed their first thrombosis before the age of 50 were eligible for the study. The patients data that was used in statistical analyses were collected from our thrombophilia register.
Results. The number of the subjects with increased FVIII over 1.5 IU/mL is equal regardless of the thrombosis type. FVIII activity already begins to increase over 40 years of age and reaches the mean values of 1.45 IU/mL close to the cut off (1.5 IU/mL), showing a statistically significant difference compared to those under 40, P = 0.001. Comorbidities other than thyroid disease or malignancy had no influence on the increase in FVIII. In the mentioned conditions, the average FVIII of 1.82 (0.79) respectively 1.65 (0.43) were obtained.
Conclusion. FVIII activity is significantly affected by the age. Thrombosis type and comorbid diseases other than thyroid disease and malignancy had no effect on FVIII.

Keywords: Factor VIII activity, thrombosis type, age

UP 11

MARKERI KOAGULACIJE – PREDIKTORI PREŽIVLJANJA OBOLELIH OD SARS-COV 2 INFEKCIJE?

Milenković M[1,2], Kovač M[3], Hadžibegović A[1], Petrović K[1], Stanisavljević J[1,2], Šijan Đ[1], Rović I[1], Zdravković M[2,4]
[1]Univerzitetski klinički centar Srbije, Beograd
[2]Medicinski fakultet Univerziteta u Beogradu
[3]Institut za transfuziju krvi Srbije, Beograd
[4]Kliničko bolnički centar ,,Bežanijska kosa", Beograd

Uvod: SARS-CoV 2(severe acute respiratory syndrome coronavirus 2)pokreće prekomerni nesvrsishodni imuno-hemostatski odgovor koji izaziva brojne komplikacije, kao što su: tromboze, oštećenje tkiva, akutna povreda pluća, akutni respiratorni distres sindrom (ARDS), diseminovana intravaskularna koagulacija (DIK) i sindrom multiorganske disfunkcije (The Multiple Organ Dysfunction Syndrome - MODS), te je neophodno COVID-19 posmatrati ne samo kao respiratorno, već i kao multisistemsko oboljenje. Koagulopatija koja se javlja u skolupu COVID 19 karakteriše se jednim hiperkoagulabilnim stanjem, sa većom učestalošću tromboza. Indikatori takve koagulopatije su pre svega povišene vrednosti D-dimera, promene na nivou broja trombocita, zatim protrombinskog vremena, vrednostima fibrinogena, antitrombina, faktora VIII, kao i aktivnosti von Willebrand-ovog faktora.
Cilj rada: Ispitivanje prognostičkog značaja određivanja markera koagulacije, i to INR, aPTT, fibrinogena i D-dimera, kod bolesnika sa teškom kliničkom slikom SARS-CoV 2 infekcije.
Materijal i metode: Istraživanje je obuhvatilo 146 bolesnika sa postavljenom dijagnozom COVID-19 koji su lečeni u Jedinici intenzivnog lečenja u periodu juna i jula 2020. godine. Uvidom u medicinsku dokumentaciju Kliničko bolničkog centra „Bežanijska kosa" retrospektivno su analizirani podaci ispitanika , vrednosti INR, aPTT, fibrinogena, D-dimera i ishodi obolenja.
Rezultati:Tokom lečenja 82 pacijenta je preminulo (56.2%), od toga 58 osoba muškog (70,7%) i 24 ženskog pola (29.3%), dok je 64 otpušteno sa lečenja (43.8%). U pogledu ishoda oboljenja, značajno više vrednosti D-dimera na prijemu u JIL, zabeležene su kod osoba koje su u toku lečenja preminule 888 (1226,5)ng/ml u odnosu na osobe koje su otpuštene sa lečenja 666 (1207,3) ng/ml (p=0,03). Razlike nisu uočene među ostalim parametrima (INR, aPTT, fibrinogen). Korišćenjem Kaplan-Meier krive preživljajvanja i log-rank testa pokazano je da D-dimer viši od ili jednak 760 ng/ml je statistički značajan prediktor bolničkog smrtnog ishoda (p=0,04).
Zaključak: Vrednosti D-dimera veće od 760ng/ml izmerene na prijemu u JIL, povezane su sa većom smrtnošću od COVID-19.
Ključne reči: COVID-19;d-dimer, preživljavanje

UP 11

COAGULATION MARKERS - PREDICTORS OF SURVIVAL IN PATIENTS WITH SARS-COV 2 INFECTION?

Milenković M[1,2], Kovač M[3], Hadžibegović A[1], Petrović K[1], Stanisavljević J[1,2], Šijan Đ[1], Rović I[1], Zdravković M[2,4]
[1]University Clinical Centre of Serbia, Belgrade, Serbia
[2]Faculty of Medicine, University of Belgrade, Belgrade, Serbia
[3]Blood Transfusion Institute of Serbia, Belgrade, Serbia
[4]University Clinical Hospital Center Bezanijska Kosa, Belgrade, Serbia

Introduction: SARS-CoV 2(severe acute respiratory syndrome coronavirus 2) triggers an excessive inappropriate immune-hemostatic response that causes numerous complications, such as: thrombosis, tissue damage, acute lung injury, acute respiratory distress syndrome (ARDS), disseminated intravascular coagulation (DIC) and multiorgan dysfunction syndrome (MODS), therefore it is necessary to approach to COVID-19 not only as a respiratory, but as a multisystem disease. The coagulopathy that occurs in COVID-19 patients is characterized by hypercoagulable state, with a higher frequency of thrombosis. Indicators of such coagulopathy are primarily elevated D-dimer values, changes in platelet count, then prothrombin time, fibrinogen, antithrombin, factor VIII and von Willebrand factor activity.
Aim: Examining the prognostic significance of coagulation markers, INR, aPTT, fibrinogen and D-dimer, in patients with a severe clinical presentation of SARS-CoV 2 infection.
Material and methods: The research included 146 patients diagnosed with COVID-19 who were treated in the Intensive Care Unit during June and July 2020. By inspecting the medical documentation of the "Bežanijska Kosa" Clinical Hospital Center, the mortality of the subjects, INR, aPTT, fibrinogen, D-dimer values and disease outcomes were retrospectively analyzed.
Results: During treatment 82 patients died (56.2%), of which 58 were male (70.7%) and 24 female (29.3%), while 64 were discharged from treatment (43.8%). Regarding the outcome of the disease, significantly higher D-dimer values on admission to the ICU were recorded in patients who died during treatment 888(1226.5)ng/ml compared to persons who were discharged from hospital 666(1207.3)ng/ml (p=0.03). No differences were observed among other parameters (INR, aPTT, fibrinogen). Using the Kaplan-Meier survival curve and the log-rank test, it was shown that D-dimer higher than or equal to 760ng/ml is a statistically significant predictor of in-hospital death (p=0.04).
Conclusion: D-dimer value greater than 760ng/ml measured at ICU admission is associated with higher mortality from COVID-19.
Keywords: COVID-19; D-dimer; survival

UP 12

REZULTATI BOLNIČKE BANKE KRVI KBC" DR DRAGIŠA MIŠOVIĆ - DEDINJE"U DIJAGNOSTICI I TERAPIJI TRUDNICA OBOLELIH OD COVID-19

Stojković S, Janković-Oreščanin B, Jovičić M, Mihajlović S, Đukić V
KBC"Dr Dragiša Mišović-Dedinje",Beograd

UVOD: KBC "Dr Dragiša Mišović-Dedinje"je od početka pandemije Covid-19 u Republici Srbiji bio uključen u lečenje najteže obolelih pacijenata, što je donelo mnoge izazove i nepoznanice. Bolnica za ginekologiju i akušerstvo od marta 2020. godine zbrinjava i Covid pozitivne trudnice, koje su kao osetljiva populacija imale značajno povećan nadzor u dijagnostici i terapiji koagulopatskih i/ili tromboembolijskih komplikacija, gde je primena POC testova hemostaze bila od neprocenjive pomoći.
CILJ RADA: Prikaz rezultata bolničke banke krvi (BBK) u dijagnostici i terapiji trudnica sa poremećajima hemostaze i komplikacijama Covid-19 infekcije.
MATERIJAL I METODE: U periodu od marta 2020. do septembra 2022. hospitalizovano je 564 trudnica sa potvrđenim Covid-19 i obavljeno 367 porođaja. Retrospektivno su analizirani podaci za 26 trudnica kojima su pored standardnih rađenii POC testovi hemostaze.
REZULTATI: U BBK su rađeni testovi standardne hemostaze (APTT, PT, D-dimer, AT, anti-Xa) , a kod njih 26 i POC testovi. U posmatranom period urađeno je 146 testova tromboelastografije i 114 Multiplate testova. Od 18 trudnica koje nisu imale peripartalno krvarenje, u POC testovima 10 je pokazalo trend prema hiperkoagulabilnosti, 4 nedostatak trombocita, 1 deficit fibrinogena , a 3 udružen deficit fibrinogena i trombocitopeniju. Od 8 trudnica koje su imale postpartalno krvarenje,u POC testovima 1 je imala nedostatak trombocita, 5 udruženi deficit fibrinogena i trombocitopeniju,1 normalne POC testove, a 1 deficit faktora unutrašnjeg puta za koju je bilo potrebno dodatno ispitivanje u referentnoj laboratoriji i utvrđeno postojanje stečene hemofilije.
ZAKLJUČAK: BBK je izvodeći POC testove hemostaze značajno poboljšala svoju ulogu u pripremi za porođaj kao i u vođenju postpartalne transfuzione terapije, u dobroj multidisiciplinarnoj saradnji kako stučnjaka KBC" Dr Dragiša Mišović-Dedinje"tako i iskusnih transfuziologa iz drugih ustanova, da bi omogućila pravovremenu odgovoarajuću hemostatsku i/ilitransfuzionu terapiju za sve trudnice.
KLJUČNE REČI: Covid-19,trudnice, POC testovi

UP 12

RESULTS OF THE HOSPITAL BLOOD BANK IN CHC "DR DRAGISA MISOVIC-DEDNJE" IN THE DIAGNOSIS AND THERAPY OF PREGNANT WOMEN INFECTED WITH COVID-19

Stojković S, Janković-Oreščanin B, Jovičić M, Mihajlović S, Đukić V
CHC "Dr Dragisa Misovic-Dedinje", Belgrade, Serbia

INTRODUCTION: CHC "Dr Dragiša Mišović-Dedinje" has been involved in the treatment of the most seriously ill patients since the beginning of the Covid-19 pandemic in the Republic of Serbia, which brought many challenges and unknowns. Since March 2020, the Hospital for Gynecology and Obstetrics has also been caring for Covid-positive pregnant women, a usually sensitive population.
AIM: Presentation of the results of the hospital blood bank (HBB) in the diagnosis and therapy of pregnant women with hemostasis disorders and complications of Covid-19.
MATERIAL AND METHODS:In the period from March 2020 to September 2022, 564 pregnant women with confirmed Covid-19 were hospitalized and 367 deliveries were performed. Data for 26 pregnant women, who underwent POC hemostasis tests in addition to the standard ones were retrospectively analyzed.
RESULTS: Standard hemostasis tests were performed in HBB, and 26 of them also underwent POC tests. In the observed period, 146 thromboelastography tests and 114 Multiplate tests were performed. Out of 18 pregnant women who did not have peripartum bleeding, in POC tests 10 showed a trend towards hypercoagulability, 4 lack of platelets, 1 fibrinogen deficiency, and 3 combined fibrinogen deficiency and thrombocytopenia. Out of 8 pregnant women who had postpartum bleeding, in POC tests 1 had platelet deficiency, 5 had combined fibrinogen deficiency and thrombocytopenia, 1 had normal POC tests, and 1 had intrinsic pathway factor deficiency for which additional testing in the reference laboratory was required and the existence of acquired hemophilia was established.
CONCLUSION: By performing POC hemostasis tests, HBB significantly improved its role in the preparation for childbirth as well as in the management of post-partum transfusion therapy in order to enable timely and appropriate hemostatic and/or transfusion therapy for all pregnant women.
KEY WORDS: Covid-19, pregnant women, POC tests

UP 13

DIMEROMANIJA

Petrović M.
Zavod za transfuzijukrvi Niš, Srbija

Uvod: D-dimer je jasan marker razgradnje fibrina, pa je samim tim verodostojan pokazatelj koagulacionih poremećaja koji prate Kovid infekciju. S obzirom da se gotovo rutinski radi u pojedinim fazama kovida, eskalacijom broja obolelih u 2021.godini je i broj urađenih analiza drastično uvećan.
Cilj rada: Prikaz pacijentkinje i analize D-dimera toku i nakon prebolele infekcije Covid 19
Rezultati: Jedan pacijent je prosečno radio 0,8 D-dimera u jeku pandemije, a maksimalni broj provera kod težih slučajeva Kovid koagulopatija dugotrajno lečenih derivatima heparina i oralnom antikoagulantnom terapijom nije prelazio 12. Slučaj pacijentkinje J.J. (49 godina), koja je anamnestički pozitivna na psihičke smetnje, radila je ovu analizu, delom po nalogu vaskularnog hirurga, kao i izabranog lekara, a dobrim delom i na lični zahtev ukupno 48 puta u periodu od 14 meseci nakon preležane blage forme Kovida. 40 rezultata bilo je u laborararatorijskim granicama (do 230 ng/mL), 6 rezultata bilo je u klinički prihvatljivim granicama (do 500 ng/mL) a samo dva nalaza neposredno nakon obolevanja bila su povišena (644 i 780 ng/mL). Pacijentkinja je u početku bila na niskomolekularnom heparinu 10 dana, anakon toga, što po nalogu lekara a kasnije i samoinicijativno na antiagregacionoj terapiji –Aspirin protect (100mg dnevno).
Zaključak: Kovid je povezao transfuzijsku medicinu sa skoro svim granama medicine pa čak i psihijatrijom. Potrebna je bolja koordinacija između lekara i pacijenata da bi se izbegle pojave ovakvih grubih zloupotreba određenih medicinskih analiza.
Ključne reči: D- dimer, Kovid 19

UP 13

DIMEROMANIA

Petrović M.
Blood transfusion center Nis, Serbia

Introduction:D-dimer is obvious and significant fibrin degradation marker, as well as trustworthy indicator of coagulation disorders caused by Covid infection. It is almost routinely checked in different Covid infection phases of disease. Highly increased number of infected in 2021 was followed by highly increased number of D-dimer laboratory testings.
Aim: Presentation of the patient and D-dimer analysis during and after recovering from the Covid 19 infection
Results: Averagepandemia numbers were 0,8 D-dimers per patient.Maximal recorded number was 12 checks for one patient with more severe form of illness,until patient J.J(49 years)appeared.Her medical history reveal 48 D-dimer checks in period of 14 months after her covid illness,mostly asked by her doctors,but great deal were asked by herself without justifiedindication,triggered by her mental state confirmed with medicament she used.Level of her D-dimer was mostly normal (40 samples lower than 230 ng/mL), clinically acceptable (6 samples lower than 500 ng/mL) and only two results, immediately after disease were higher(644 and 780 ng/mL).Patient was treated with LMWH ten days after infection, with Aspirine 100mg once a day, first period on doctors prescription and later self-initiated.
Conclusion:As we have witnessed,covid have created correlation between all medical branches even psihiatry. Better coordination between doctors and patients is necessary,in order to avoid apperaring of rough abuse of certain medical services.
Key words: D- dimer, Covid 19

UP 14

REZULTATI NAT TESTIRANJA U SRBIJI OD JULA 2019. DO JULA 2022. GODINE

Antonijević I., Kovačević M., Nedeljković M., Stamenić Lj., Damjanović V., Dukić M.
Institut za transfuziju krvi Srbije

UVOD: Glavni cilj transfuzioloških službi je obezbeđivanje i snabdevanje „sigurnom“ krvi svih primalaca. U tu svrhu, uveden je NAT (Nucleic Acid amplification Technique) – molekularna tehnika za direktnu detekciju genetskog materijala virusa. Tehnologija NAT koja se koristi u Srbiji, zasniva se na korišćenju lančane reakcije polimeraze – PCR, kojom se umnožava genetski materijal virusa do količine potrebne za detekciju, detektujući ga ranije nego druge skrining metode i na taj način smanjujući „window“ period za HBV, HCV, HIV.
CILJ: Analiza rezultata NAT testiranja dobrovoljnih davalaca krvi (DDK) u Institutu za transfuziju krvi Srbije (ITKS) i rezultata rađenih za 7 centara u Republici Srbiji.
METODE: Retrospektivna analiza NAT testiranja na transfuzijom prenosive bolesti uključila je period jul 2019. – jul 2022. godine. Testiranje je sprovedeno u minipulu od po 6 uzoraka. Rezultati za testirane 542 041 jedinice krvi dobrovoljnih davalaca krvi uzeti su iz informacionog sistema ITKS.
REZULTATI: Od ukupno 542 041 jedinice krvi testirane u navedenom periodu otkriveno je 218 HBV NAT pozitivnih uzoraka, od čega ih je 63 bilo „samo NAT“ pozitivno, a ostalih 155 bili su pozitivni NAT i serološki. Registrovano je i ukupno 69 HCV NAT pozitivnih jedinica, od čega su 2 jedinice „samo NAT“ pozitivne, a ostalih 66 su pozitivne NAT i serološki. Pozitivnost i serološkim i NAT testiranjem pokazale su 23 HIV NAT pozitivne jedinice DDK.
ZAKLJUČAK: Dobijeni rezultati ukazuju na opravdanost NAT testiranja jedinica DDK. Na taj način postignut je viši nivo bezbednosti krvi i krvnih produkata imajući u vidu da su 63 jedinice bile „samo NAT“ pozitivne na HBV, a 2 jedinice na HCV.
Međutim, rizik od prenošenja infekcije transfuzijom krvi ne može biti u potpunosti eliminisan zbog eventualno niskog nivoa markera virusnog genoma koji su nedektabilni za postojeće testove, zbog odsustva markera infekcije u periodu prozora ili zbog mogućnosti laboratorijske greške pri samom testiranju.

Ključne reči: NAT, minipul, bezbednost
Način izlaganja: usmeno

UP 14

RESULTS OF NAT TESTING IN SERBIA FROM JULY 2019 TO JULY 2022

Antonijević I., Kovačević M., Nedeljković M., Stamenić Lj., Damjanović V., Dukić M.
National Blood Transfusion Institute of Serbia

INTRODUCTION: The main goal of transfusion services is to ensure and supply "safe" blood to all recipients. For this purpose, NAT (Nucleic Acid Amplification Technique) –a molecular technique was introduced for the direct detection of the genetic material of the virus. The NAT technology used in Serbia is based on the use of polymerase chain reaction - PCR, which multiplies the genetic material of the virus to the amount required for detection, detecting it earlier than other screening methods and thus reducing the "window" period for HBV, HCV , HIV.
OBJECTIVE: Analysis of the results of NAT testing of blood donors (BD) at the National Blood Transfusion Institute of Serbia (NBTI) and the results of 7 centers in the Republic of Serbia.
METHODS: A retrospective analysis of NAT testing for a transfusion-transmitted disease included the period July 2019 - July 2022. Testing was conducted in a minipool of 6 samples. The results for the tested 542,041 units of blood from BD were taken from the information system of NBTI.
RESULTS: Out of a total of 542,041 units of blood tested in the mentioned period, 218 HBV NAT positive samples were detected, of which 63 were "only NAT" positive, and the other 155 were NAT and serologically positive. A total of 69 HCV NAT positive units were registered, of which 2 units were "only NAT" positive, and the other 66 were NAT and serologically positive. 23 HIV NAT positive units of BD showed positivity by both serological and NAT testing.
CONCLUSION: The obtained results indicate the justification of NAT testing of BD units. In this way, a higher level of safety of blood and blood products was achieved, bearing in mind that 63 units were "only NAT" positive for HBV, and 2 units for HCV.
However, the risk of transmission of infection by blood transfusion cannot be completely eliminated due to possibly low levels of viral genome markers that are undetectable by existing tests, due to the absence of infection markers in the window period, or due to the possibility of laboratory error during the testing itself.

Keywords: NAT, minipool, security
Mode of presentation: oral

UP 15

OSMOMESEČNO ISKUSTVO VOJNOMEDICINSKE AKADEMIJE U NAT SKRININGU VIRUSA KOJI SE PRENOSE TRANSFUZIJOM

Kozic Z[1], Gojkov D[1], Đurić-Petković D[2], Vučetić D[1,3]
[1]Institut za transfuziologiju i hemobiologiju Vojnomedicinske akademije, Beograd
[2]Institut za mikrobiologiju Vojnomedicinske akademije, Beograd
[3]Medicinski fakultet, Vojnomedicinska akademija, Univerzitet odbrane, Beograd, Srbija

SAŽETAK
Uvod: Visoko specifično i osetljivo NAT-TMA testiranje na tri virusa HIV (HIV-1, HIV-2), HCV i HBV, značajno je za bezbednost komponenti krvi. Zbog toga je ove godine Institut za transfuziologiju i hemobiologiju Vojnomedicinske akademije u Beogradu uveo individualno (ID)-NAT testiranje, kao obavezno za sve davaoce krvi. Posle osam meseci, predstavljamo rezultate evaluacije performansi test skrininga.
Metode: Od januara do avgusta tekuće godine, prikupljeno je ukupno 5279 donacija i testirano na HIV-1, HIV-2, HCV i HBV pomoću Procleix Ultrio Elite Assay-a, na platformi Procleix Panther (Grifols). Prvobitno reaktivni (IR)-NAT uzorci su u triplikatu podvrgnuti ponovljenom testiranju u dve nezavisne serije, a ako su i tada bili više puta reaktivni (RR), rađen je diskriminatorni NAT (dNAT) test i potvrdni test RT-PCR-om. Samo ako su sva tri testa ostala negativna (kao i anti-HBc za HBV), testirani produkti su mogli da se koriste.
Rezultati: Od 5279 testiranih uzoraka, 3 (0,06%) su bila RR u NAT-u. Bila su reaktivna 2 (66,67%) HBV, 1 (33,33%) HCV i nijedan HIV reaktivan (HIV-1, HIV-2). Kod jednog od 2 HBV reaktivna uzorka, utvrđena je 1 okultna HBV infekcija (OBI).
Zaključak: Zahvaljujući razvoju NAT tehnologije, bezbednost komponenti krvi je značajno povećana. Uvođenjem Individualnog skrininga nukleinskih kiselina uzročnika infekcija koje se prenose putem krvi (HIV-1, HIV-2, HCV i HBV), poboljšana je bezbednost krvi u Srbiji. Tokom ovih osam meseci, pored hiljada potvrđenih negativnih uzoraka, otkrivena su i tri pozitivna uzorka, sa otkrivenom jednom okultnom HBV infekcijom kod davaoca.

Ključne reči: NAT testiranje, Infekcije koje se prenose transfuzijom, Testiranje nukleinske kiseline

UP 15

EIGHT-MONTHS EXPERIENCE IN NAT SCREENING OF TRANSFUSION TRANSMITTED VIRUSES IN MILITARY MEDICAL ACADEMY

Kozić Z[1], Gojkov D[1], Đurić-Petković D[2], Vučetić D[1,3]
[1] Institute for transfusiology and hemobiology of the Military Medical Academy, Belgrade
[2] Institute for microbiology of the Military Medical Academy, Belgrade
[3] Faculty of Medicine, Military Medical Academy, University of Defence, Belgrade, Serbia

Keywords:NAT-testing, Transfusion-transmitted infections,Nucleic acid testing

Abstract
Introduction: A highly specific and sensitive NAT-TMA testing for three viruses HIV (HIV-1, HIV-2), HCV and HBV, are significant for the safety of blood components. Therefore, this year, Institute for transfusiology and hemobiology of the Military Medical Academy in Belgrade, implemented individual donation (ID)-NAT testing, as a mandatory for all blood donors. After eight months, this are the results of the evaluation of test screening performance.
Methods: From January to August current year, a total of 5279 donations were collected and screened for HIV-1, HIV-2, HCV and HBV using the Procleix Ultrio Elite Assay on the Procleix Panther (Grifols) platform. Initially reactive (IR)-NAT samples were subjected to repeat testing in triplicate in two independent runs, and if repeatedly reactive (RR), discriminatory NAT (dNAT) assay was performed and confirmed by RT-PCR. Only when all three tests remained negative (anti-HBc for HBV, too), the products were released.
Results: From the 5279 samples tested, 3 (0.06%) were RR in NAT. There were 2 (66.67%) HBV, 1 (33.33%) HCV reactive and none HIV reactive (HIV-1, HIV-2). Out of these 2 HBV reactive, 1 occult HBV infections (OBI) were determined.
Conclusion: Thanks to the development of NAT technology, the safety of blood components has substantially increased. The implementation of nucleic acid screening for blood transmissible infections (HIV-1, HIV-2, HCV and HBV), has improved blood safety in Serbia. During these eight months, in addition to thousands of samples confirmed negative, three positive samples were detected, with 1 occult HBV donations identified.

UP 16

RAZREŠAVANJE PONOVLJENO POZITIVNIH REZULTATA SEROLOŠKOG HIV TESTIRANJA SA BIO-RAD GEENIUS HIV 1/2 POTVRDNIM TESTOM KOD DOBROVOLJNIH DAVALACA KRVI

Beronja M[1], Ademović Sazdanić D[1], Bujandrić N[1,2]
Zavod za transfuziju krvi Vojvodine, Novi Sad, Srbija
Medicinski fakultet Novi Sad, Univerzitet u Novom Sadu, Srbija

Uvod: U cilju bezbednosti svaka jedinica krvi se obavezno testira na transfuzijom prenosive bolesti (hepatitis B, hepatitis C, virus humane imunodeficijencije - HIV i sifilis). Prisustvo HIV-a testira se serološki (anti-HIV1/2 i HIV1 antigen), kao i molekularno - tehnikom umnožavanja nukleinske kiseline (NAT: HIV1/2-RNA). Pri donošenju odluke o rezultatu seroloških testa problem predstavljaju „neodređeni" rezultati – rezultati ispod granične vrednosti ali značajno viši u odnosu na ostale rezultate u testiranoj seriji uzoraka, kao i ponovljeno reaktivni rezultati.
Cilj rada: Konfirmacija neodređenih i ponovljeno reaktivnih rezultata seroloških testiranja dobijenih na LIAISON XL MUREX HIV Ab/Ag i imunohromatografskim potvrdnim testom - Geenius ™ HIV 1/2 Confirmatory Assay, kod dobrovoljnih davalaca krvi (DDK) u Zavodu za transfuziju krvi Vojvodine.
Materijal i metode: Test LIAISON XL MUREX HIV Ab/Ag, DiaSorin, Saluggia, Italy (CLIA - ChemiLuminescent ImmunoAssays) uveden je u rad Zavoda jula 2021. godine. Nakon 6 meseci korišćenja 20 neodređenih i ponovljeno reaktivnih rezultata sa ovog testa dodatno su testirani potvrdnim imunohromatografskim testom: 10 uzoraka sa signal-to-cutoff (S/CO) od 0.65-0.99, 10 uzoraka sa S/CO 1-6,6. Svi uzorci su bili nereaktivni pri serološkom testiranju testom drugog proizvođača (Abbott, Alnity™ S) kao i pri molekularnom testiranju. Svih 20 uzoraka testirano je imunohromatografskim potvrdnim testom - Geenius ™ HIV 1/2 Confirmatory Assay (Bio-Rad, France).
Rezultati: Svi testirani uzorci čiji rezultati su bili „neodređeni" ili reaktivni pri testiranju sa- LIAISON XL MUREX HIV Ab/Ag bili su negativni pri testiranju sa Bio-Rad Geenius HIV 1/2 potvrdnim testom.
Zaključak: Test Geenius je jednostavan i brz dodatni test, efikasan u razrešavanju ponovljeno pozitivnih rezultata pri serološkom skrinigu DDK na prisustvo HIV infekcije.
Ključne reči: HIV testiranje, serološki testovi, davaoci krvi

UP 16

RESOLUTION OF REPEATEDLY POSITIVE RESULTS OF SEROLOGY HIV TESTING WITH THE BIO-RAD GEENIUS HIV 1/2 CONFIRMATION TEST IN VOLUNTARY BLOOD DONORS

Beronja M[1], Ademović Sazdanić D[1], Bujandrić N[1,2]
Blood Transfusion Institute of Vojvodina, Novi Sad, Serbia
Faculty of Medicine, University of Novi Sad, Serbia

Introduction: Each unit of donated blood must be tested for transfusion-transmissible diseases (hepatitis B, hepatitis C, human immunodeficiency virus - HIV and syphilis). The presence of HIV is tested serologically (anti-HIV1/2 and HIV1 antigen), as well as molecularly - using the nucleic acid amplification technique (NAT: HIV1/2-RNA). Resolving the results of serological testing, the problem is to define "indeterminate" results - results below the threshold value but significantly higher than the other results in the tested series of samples, as well as repeatedly reactive results.
Objective: Confirmation of indeterminate and repeatedly reactive results of serological testing with the LIAISON XL MUREX HIV Ab/Ag and immunochromatographic confirmatory test - Geenius ™ HIV 1/2 Confirmatory Assay, in voluntary blood donors (VBD) at the Blood Transfusion Institute of Vojvodina.
Material and methods: LIAISON XL MUREX HIV Ab/Ag test, DiaSorin, Saluggia, Italy (CLIA - ChemiLuminescent ImmunoAssays) was introduced into the work of the Institute in July 2021. After 6 months of use, 20 indeterminate and repeatedly reactive results from this test were additionally tested with a confirmatory immunochromatographic test: 10 samples with signal-to-cutoff (S/CO) of 0.65-0.99, 10 samples with S/CO 1-6.6. All samples were non-reactive in serological testing by another manufacturer's test (Abbott, Alinity™ S) as well as in molecular testing. All 20 samples were tested with an immunochromatographic confirmatory test - Geenius ™ HIV 1/2 Confirmatory Assay (Bio-Rad, France).
Results: All tested samples that were "indeterminate" or reactive when tested with LIAISON XL MUREX HIV Ab/Ag were negative when tested with Bio-Rad Geenius HIV 1/2 (confirmatory test.
Conclusion: The Geenius test is a simple and quick additional test, effective in resolving repeatedly positive results during serological screening of VBD for the presence of HIV infection.
Key words: HIV testing, serological tests, blood donors

UP 17

PROCENA DIJAGNOSTIČKIX KARAKTERISTIKA BRZOG IMUNOXRO-MATOGRAFSKOG TESTA ZA DETEKCIJU ANTITELA NA VIRUS XEPATITISA CE KOD DOBROVOLJNIX DAVALACA KRVI

Vučetić D.[1,2], Maslovarić I.[3], Gojkov D.[1], Kozić Z. [4], Marković D.[3], Drvenica I.[3], Kovačić M.[3], Ilić V.[3]
[1]Institute for Transfusiology and Haemobiology, Military Medical Academy, Belgrade, Serbia
[2]Faculty of Medicine, Military Medical Academy, University of Defence, Belgrade, Serbia
[3]Institute for Medical Research, National Institute of Republic of Serbia, University of Belgrade, Belgrade, Serbia
[4]Institute of Medical Research, Military Medical Academy, Belgrade, Serbia

Uvod: Brzi imunohromatografski testovi (ICH) nemaju široku primenu za detekciju prisustva antitela na HCV antigene u krvi dobrovoljnih davalaca.
Materijal i metode: Dijagnostičke karakteristike ICH testa (Geenius HCV Supplemental Assay) smo procenili na osnovu detekcije anti-HCV antitela u 62 seruma dobrovoljnih davalaca krvi u čijoj krvi je prisustvo ovih antitela prethodno detektovano barem jednim od četiri serološka testa (imunohemiluminescentni test (ICL), dva imunoenzimska testa (EIA) i vestern blot).
Rezultati: Kod 19 (31%) seruma ICH testom su detektovana anti-HCV antitela, a njihovo prisustvo je potvrđeno i vestern blotom. ICH je 5% seruma okarakterisao kao nedeterminisane, a 24% uzoraka koji su okarakterisani kao negativni su pokazali reaktivnost u vestern blotu. Većina ICH pozitivnih seruma je reagovala sa antigenima kapsida i NS3 antigenom, 63% je reagovalo sa NS4, a 47% sa NS5 antigenom, pri čemu je primećeno šest obrazaca reaktivnosti. κ analizom je pokazano dobro slaganje rezultata ICH testa i oba EIA, kao i rezultata ICH testa i vestern blota ($0,61<\kappa\leq 0,80$), dok je slaganje rezultata ICH i ICL testova bilo slabo. Takođe je pokazano skoro potpuno slaganje ICH testa i vestern blota u reaktivnosti prema antigenima kapsida, dok je slaganje u reaktivnosti prema ostalim HCV antigenima bilo nešto slabije. Istovremeno prisustvo HCV RNK i anti-HCV antitela detektabilnih ICH testom je nađeno u 23% seruma. Jedan RNK pozitivan serum je ICH testom i jednim EIA okarakterisan kao anti-HCV negativan (serološki prozor). Isti uzorak je ICL testom identifikovan kao anti-HCV pozitivan, a vestern blotom kako nedeterminisan. Specifičnost, pozitivna prediktivna vrednost osetljivost i negativna prediktivna vrednost ICH testa su bile visoke (>95%).
Zaključak: Dobijeni rezultati ukazuju da analizirani ICH test ima prihvatljive dijagnostičke karakteristike, a rezultati dobijeni ovim testim pokazuju značajan stepen saglasnosti sa tri od četiri ispitivana serološka testa za detekciju anti-HCV antitela. Primećene razlike u rezultatima primenjenih testova zahtevaju da budu objašnjene u narednim studijama.

Ključne reči: Virus Xepatitisa Ce, Serološko testiranje, imunohromatografski testovi.
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UP 17

EVALUATION OF DIAGNOSTIC PERFORMANCES OF A RAPID IMMUNO-CHROMATOGRAPHY TEST FOR DETECTION OF ANTIBODIES TO HEPATITIS C VIRUS IN DONATED BLOOD

Vučetić D.[1,2], Maslovarić I.[3], Gojkov D.[1], Kozić Z. [4], Marković D.[3], Drvenica I.[3], Kovačić M.[3], Ilić V.[3]
[1]Institute for Transfusiology and Haemobiology, Military Medical Academy, Belgrade, Serbia
[2]Faculty of Medicine, Military Medical Academy, University of Defence, Belgrade, Serbia
[3]Institute for Medical Research, National Institute of Republic of Serbia, University of Belgrade, Belgrade, Serbia
[4]Institute of Medical Research, Military Medical Academy, Belgrade, Serbia

Introduction: Rapid immunechromatography tests (ICH) are not widely used for the screening of donated blood for the presence of antibodies to HCV antigens.
Introduction: With a rapid immunochromatography (ICH) test (Geenius HCV Supplemental Assay), we analysed the presence of anti-HCV antibodies in 62 blood donors' sera with anti-HCV reactivity, previously detected with at least one of four serology tests (chemiluminescent immunoassay (ICL), two enzyme immunoassays (EIA), and western blot (WB)).
Results: ICH test identified 19 (31%) sera as anti-HCV antibodies positive, and the positivity was confirmed with WB. With ICH test 5% sera were found indeterminate, and 24% of samples were found negative with ICH test, but reactive in WB. Most of ICH positive sera recognized capsid and NS3 antigens, 63% reacted with NS4, and 47% with NS5 antigen. Six patterns of anti-HCV antibodies reactivity with HCV antigens were observed. Kappa analysis showed substantial agreement between ICH and both EIA and ICH and WB ($0.61< \text{kappa}\leq 0.80$), but slight agreement between ICH and ICL. In addition, we detected almost perfect agreement between WB and ICH in the reactivity with capsid antigen(s), and substantial or moderate agreement in the reactivity with other HCV antigens. Simultaneous presence of HCV RNA and ICH detectable anti-HCV antibodies was found in 23% sera. One HCV RNA positive serum was identified as anti-HCV antibodies negative (window period) with ICH and one of EIAs, but as anti-HCV positive with ICL and other EIA, and as indeterminate with WB. The ICH test specificity, positive predictive value, sensitivity, and negative predictive value were high (>95%).
Conclusion: The results obtained indicate that the ICH test has acceptable diagnostic characteristics and shows good agreement with three of the four serological tests detecting of anti-HCV antibodies. However, we observed some differences between the applied tests that require to be explained in future studies.
Key words: Hepatitis C virus, Serological testing; rapid immunochromatography tests
Acknowledgement: This work was supported by the Ministry of Education, Science and Technological Development of the Republic of Serbia (contract number 451-03-9/2021-14/200015 with Institute for Medical Research University of Belgrade, University of Belgrade) and Ministry of Defence of Republic of Serbia.

UP 18

DOBROVOLjNO DAVALAŠTVO KRVI – IZAZOVI TOKOM PANDEMIJE KOVIDA

Rodić I., Knežević M.
Institut za transfuziju krvi Srbije, Beograd, Srbija

Uvod: Zakon o transfuzijskoj medicini, donet 2017. podrazumevao je sa početkom primene od 2019. značajne organizacione promene u oblasti promocije, motivacije, edukacije i organizacije akcija dobrovoljnog davanja krvi. Uz prilagođavanje novom konceptu rada, suočili smo se sa dodatnim izazovom - pandemijom kovida.
Cilj rada: Prikaz promotivnih aktivnosti, modela edukacije, koncepta organizacije akcija u periodu januar 2020.– jun 2022. koji su doprineli da se u vanrednim uslovima obezbede dovoljne rezerve krvi.
Materijal i metode: Komparacija sa konceptom rada u 2019., kvalitativna analiza uvedenih inovacija i efekat primenjenih aktivnosti u praksi.
Rezultati: Aktivnosti su realizovane u skladu sa tokom pandemije, uz stalno prisustvo na terenu i obaveštavanje građana o značajnim informacijama. U 2019. od 70 240 jedinica krvi 35% je prikupljeno u školama, fakultetima, institucijama i kompanijama. Prelaskom na on line nastavu i rad od kuće, akcije su organizovane samo u lokalnoj zajednici. Realizovane su tradicionalne kampanje i obeleženi Nacionalni i Svetski dan davalaca. Podršku su pružili Srpska pravoslavna crkva i patrijarh Porfirije, sportska društva, poznate ličnosti i udruženja pacijenata Nurdor i Leuka. Edukacija je organizovana u okviru on line nastave i kroz grupe studenata volontera. Priznanja „Šampion solidarnosti" i plakete za najuspešnije sredine uručene su u sredinama dobitnika. Donacijama smo obezbedili promo bilborde, brendiranje vozila gradskog prevoza u Beogradu i izradu murala „Put krvi" u Institutu. U saradnji sa Xemofarmom pokrenuta je kampanja „Izvuci AS iz rukava". Uz podršku medija, intenzivirali smo i promociju na društvenim mrežama, kao osnovni vid komunikacije sa mladima. U 2020. prikupljeno je 17%, a 2021. 6.7% manje jedinica krvi u odnosu na 2019. U prvih šest meseci 2022. uprkos najvećem broju zaraženih prikupljeno je 1.7% jedinica krvi više u odnosu na isti period 2019.
Zaključak: Realizacija navedenih aktivnosti i poverenje redovnih davalaca i građana doprineli su visokoj motivisanosti za redovno davanje krvi tokom pandemije.
Ključne reči: promocija, informisanje, edukacija

UP 18

VOLUNTARY BLOOD DONATION – CHALLENGES DURING THE COVID-19 PANDEMIC

Rodić I., Knežević M.
Blood Transfusion Institute of Serbia, Belgrade, Serbia

Introduction: The transfusion medicine law, brought in 2017 and put into practice in 2019 brought significant change in the fields of promotion, motivation, education and organisation of blood drives. Besides having to adapt to a novel work concept, we have faced an additional challenge – the Covid-19 pandemic.
Goal: Showcase of promotional activities, education models, concept of blood drive organisation between January 2020 and June 2022 which have enabled amassing adequate blood reserves in extraordinary circumstances.
Material and Methods: Comparison with the work concept in 2019, qualitative analysis of introduced innovations and the effect of introduced activities in practice.
Results: The activities have been realised in accordance with the course of the pandemic, with constant presence on field and informing citisens on important updates. In 2019 from the 70 240 collected blood units, 35% was collected in schools, universities, institutions and companies. Following the transfer to online educational models and work from home, blood drives were only organised in local communities. Traditional campaigns have been realised and the National and World Blood Donor Day have been celebrated during this period. Support to these activities has been given by the Serbian Orthodox Church and the Patriarch Porfirije, sports associations, celebrities and patient associations Nurdor and Leuka. Education missions have been organised through the online classes model and groups of student volunteers. Accolades, "Champion of Solidarity" and plaques for the most successful communities were awarded. Promotional billboards, branded public transport vehicles in Belgrade and a "Blood Transfer Chain" mural in the Institute were enabled through donations. In cooperation with Hemofarm a campaign "Play your ace!" was started. With support from media, we have increased promotion on social media, as the main means of communication for young people. In comparison to 2019, 17% and 6.7% less blood units were collected in 2020 and 2021 respectively. In the first 6 months of 2022, despite the highest number of positive cases, 1.7% more blood units were collected than in the same period of 2019.
Conclusion: Realisation of described activities and the trust of regular donors and citisens has led to high motivation for regular blood donation during the pandemic.
Key Words: promotion, information, education

UP 19

UP 19

CHALLENGES TO THE TRANSFUSION SYSTEM IN COLLECTING BLOOD AND BLOOD COMPONENTS - PRESENTATION OF THE EXPERIENCE OF THE REGIONAL CENTER FOR TRANSFUSION HEMATOLOGY – VARNA

Zhanina Yordanova Ivanova Z.
RCTH Varna, Bulgaria

The transfusion system faces a number of challenges not only in Bulgaria, but also on a global scale. A significant challenge in recent years has been COVID-19, which has had a pronounced negative effect on our blood collection across the country. There is an urgent need to develop innovative ways to recruit and retain voluntary blood donors. The purpose of the present study is to present the experience of the Regional Center for Transfusion Hematology - Varna with the challenges related to the collection of blood and blood components. To achieve the goal, a detailed analysis of the transfusion system in the country was made, and the main shortcomings were identified. The results of the present study showed that the COVID-19 pandemic had a negative impact on blood collection, not only in terms of reducing the number of donors, but also in terms of the emerging needs for a new type of blood components. It was necessary to take anti-epidemic measures, as well as to create different algorithms for behavior in situations of persons in contact with COVID-19 or even in contact with infected persons. This is accompanied by constant fear and tension both in the staff of the RCTH and in relation to the donors. Additionally, new requirements arise for donors in order to provide the convalescent plasma necessary for the treatment of seriously ill patients. As a result of the analysis, a strategy for recruitment and retention of voluntary blood donors is presented.

Key words: challenges, transfusion system, strategy, blood center, blood donation

UP 20

DONACIJA KRVI U LOKALNOJ ZAJEDNICI – TRADICIJA I BUDUĆNOST PRIČA KOJA TRAJE

Libek V, Djurdjević J, Strugar A, Gojković I, Kulić A.
Služba za transfuziologiju KBC Zemun

Uvod: Kako motivisati ljude da postanu davaoci krvi? Nema čarobnog odgovora. Savremene generacije mladih ljudi, X, milenijalci, Z i alfa generacija, su specifične na svoj način. Porast novih arbovirusnih infekcija, starenje populacije, nedostatak mladih davalaca krvi i istovremeni porast potreba za odredjenim komponentama krvi zahteva kontinuiran rad na promociji davalaštva krvi.
Služba za transfuziologiju KBC Zemun već 70 godina neprekidno prikuplja, procesira i testira krv od do sada preko 83 350 registrovanih davalaca kvi. Kontinuirana kolekcija tokom cele godine je imperativ za dobro organizovanu Nacionalnu službu transfuzije. Podrška organizacije Crvenog krsta na nacionalnom i lokalnom nivou, i podrška lokalne zajednice omogućava regrutovanje novih i zadržavanje stalnih davalaca krvi.
Cilj rada: Prikaz načina regrutacije novih davaoca krvi i zadržavanja starih, uz istovremenu edukaciju mladih generacija zdravim stilovima života u lokalnoj zajednici.
Materijal i metode: Više od 40 godina se deca predškolskog i školskog uzrasta zajedno sa volonterima Crvenog krsta Zemun, uz podršku lokalne zajednice na manifestaciji „ Krv znači život“ na obalama Dunava, upoznaju sa značajem doniranja krvi. Motivaciona kampanja sa više od 400 dece Zemuna, slavi Nacionalni dan davalaca krvi, crtajući na obali Dunava na ovu temu. Poruke humanosti posetioce motiviše za doniranje krvi na mobilnoj sesiji. Deca se upoznaju sa procesom donacije krvi a davaoci uživaju u jedriličarskoj manifestaciji „Trka za svaku kap krvi“.
Rezultati: Zemun kao jedna od 17 opština Beograda, sa 10,13% stanovnika Beograda, prikupila je u periodu od 2011. do 2021. godine od 12,70% do 16,82% od ukupno prikupljenih jedinica krvi u Beogradu i doprinela radu svih zdravstvenih ustanova na njegovoj teritoriji.
Zaključak: Tradicionalne i nove metode, u komunikaciji i motivaciji raznih generacija uz podršku lokalne samouprave, su imperativ u širenju ideje davalaštva krvi. Budućnost pronalaženja novih puteva do saznanja o neophodnosti doniranja krvi, je možda i povezivanje svih gradova na medjunarodnoj reci Dunav u slavljenju davaoca krvi na sličan način.
Ključne reči: donacija krvi, motivacija, deca

UP 20

COMMUNITY MOTIVATION FOR BLOOD DONATION – TRADITION AND FUTURE NEVER ENDING STORY

Libek V, Djurdjević J, Strugar A, Gojković I, Kulić A.
Blood transfusion service CHC Zemun

Abstract Introduction: How to motivate people to donate blood? There is no magic answer. New generation of young people, X, millenials, Z and alpha generation are specific in their own way. Rising of new arbovirus infections, older population, lack of young blood donors and at the same time increasing demands for particular blood components requires continuous work on blood donation promotion.
BTS CHC Zemun has been continuously for 70 years collecting, processing and testing blood from more than 83 350 registered blood donors. The continuous collection through the whole year is imperative for well-organized NBTS. The support of Red Cross organization, on the national and local level, and support of local community allows the recruitment of new blood donors and retaining the old ones.
Aims: To show means of new blood donors recruitment and retaining regular blood donors and simultaneously teaching new generations safe lifestyle in local community.
Material and methods: For over 40 years we introduce small children, together with the volunteers of Red Cross Zemun and with the support of local community, in the manifestation “Blood means life” on the bankside of Danube, with the importance of blood donation. Motivation campaign through entertaining over 400 children from the Zemun Municipality celebrates National blood donor day. Painting on the riverbank leaves messages of humanity and motivates people to donate blood in an organized mobile session nearby. Children are introduced to the donation process and donors enjoy a sailing race- „Race for every blood drop “.
Results: Zemun, as one of the 17 Belgrade municipalities, has 10, 13% of the all capital city inhabitants. From this area in a period from 2011. to 2021. the average number of collected unit was between 12, 70% - 16.82% of all collected units in Belgrade. This was a great support for health care institution in this area.
Conclusion: Tradition with embracing new methods of communication and motivation for different generation, with support of local community, is imperative in spreading blood donation idea. This is the way to show, once more, our appreciation to the regular blood donors. Connection of all cities on the reiver Danube and celebrating blood donors in a similar way may be the future of this continuous work of finding new paths to human awareness for blood donation.
Key words: blood donation, motivation, children

UP 21

PRISUSTVO U MEDIJIMA KAO VAŽAN SEGMENT PROMOCIJE KULTURE DAVALAŠTVA KRVI

Knežević M, Rodić I.
Institut za transfuziju krvi Srbije, Beograd, Srbija

UVOD: Prisustvo u medijima predstavnika Instituta za transfuziju krvi Srbije (ITKS) je važan segment u radu na omasovljavanju davalaštva krvi, koji omogućava da prava informacija stigne do šire populacije i doprinese većem odzivu davalaca krvi.
CILj RADA: Prikaz efikasnosti medijskih i promotivnih aktivnosti tokom 2020., 2021. i u prvoj polovini 2022. koje su doprinele prikupljanju dovoljnih količine krvi i komponenata krvi za zbrinjavanje pacijenata kojima je krv lek, u izazovnom periodu sa kojim smo se suočili zbog pandemije virusa kovid 19.
MATERIJAL I METODE: Poređenje sa ranijim načinom rada u promotivnim i medijskim aktivnostima i kvalitativna analiza uvedenih inovacija sa ciljem ostvarenja većeg broja davanja krvi.
REZULTATI: Svakodnevne servisne informacije o mestu i vremenu održavanja akcija davanja krvi objavljivane su u svim medijima, štampanim, elektronskim i inernet izdanjima. Svakog meseca imali smo gostovanja na nacionalnim medijima, u prvih šest meseci ove godine više od 100 uključenja iz ITKS i sa terena, više od 150 objava tekstova u štampanim medijima i preko 500 objava na internet portalima. Podrška poznatih ličnosti, udruženja, organizacija i institucija bila je od neprocenjive važnosti. Različite kampanje, kao noviteti u radu, pojačane aktivnosti na društvenim mrežama, otvaranje profila ITKS na Instagramu približile su sugrađanima ideju značaja davanja krvi za celo društvo i uticali su na povećanje broja davalaca krvi.
ZAKLjUČAK: Rad na promociji, uvođenje novina i podrška medija, doprineli su stabilnom prilivu krvi tokom ovog perioda. Za prvih šest meseci u 2022. bilo je 35 617 davanja krvi, što je 23.5% više u odnosu na isti period 2020. i 11.4% više u odnosu na isti period 2021. Mediji su redovno izveštavali o aktivnostima ITKS, najavljivali događaje koje smo organizovali i objavljivali apele upućene našim sugrađanima.
KLjUČNE REČI: mediji, promocija, informisanje.

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SENCE IN MEDIA AS AN IMPORTANT SEGMENT OF BLOOD DONATION CULTURE PROMOTION

Knežević M, Rodić I.
Blood Transfusion Institute of Serbia, Belgrade, Serbia

INTRODUCTION: Presence in media of the representatives of the Blood Transfusion Institute of Serbia (BTIS) is an important segment of increasing blood donation rates, which enable the right information to reach the wider population and lead to higher responsiveness from blood donors.
GOAL: Showcase of the effectiveness of media and promotional activities during 2020, 2021 and the first half of 2022 which have contributed to the collection of adequate blood and blood component reserves for patients in the challenging period of the Covid-19 pandemic.
MATERIAL AND METHODS: Comparison with earlier work methodology in promotional and media activities and qualitative analysis of introduced innovations with the goal of increasing the blood donation rate.
RESULTS: Everyday practical information on the time and place of blood drives were announced in all media (printed, electronic and web editions). Every month we had regular guest spots on national media programs: in the first 6 months of this year, more than 100 broadcasts from BTIS and field, more than 150 released articles in printed media and more than 500 posts on web portals. Support from celebrities, associations, organisations and institutions was of immeasurable importance. Different campaigns, as well as new work methodologies, increased social media activity and opening the BTIS profile on Instagram have made the importance of blood donation more approachable to the entire populace and have influenced the increased number of blood donors.
CONCLUSION: Working on promotions, introducing novelties and media support have contributed to a stable blood income during this period. During the first 6 months of 2022, a total number of 35 617 blood donations was recorded, which is higher by 23.5% and 11.4% in comparison to the same period of 2020 and 2021 respectively. Media outlets have regularly reported on the activities of BTIS, announcing events under our organisation and releasing blood drive calls directed to our fellow citisens.
KEY WORDS: media, promotion, information

UP 22

PROMOCIJA DAVALAŠTVA MATIČNIH ĆELIJA HEMATOPOEZE KROZ NACIONALNU KAMPANJU

Blagojević G, Lako-Šoškić B, Lesjak S, Andrić Z.
Odeljenje za tipizaciju tkiva, Institut za transfuziju krvi Srbije

Uvod: Registar davalaca matičnih ćelija hematopoeze (MĆH) Srbije omogućava pronalazak davaoca za bolesnike kojima je neophodna transplantacija, a koji nemaju podudarnog davaoca u svojoj porodici. Za oko 10% bolesnika nije moguće pronaći odgovarajućeg davaoca, zbog toga je bilo neophodno pokretanje nacionalne kampanje sa ciljem povećanja broja davalaca. Cilj rada je prikaz aktivnosti koje su omogućavale podizanje svesti o značaju omasovljavanja nacionalnog registra i povećanja broja novoprijavljenih davalaca. Materijal i metode: Decembra 2021. Registar davalaca MĆH Srbije je pokrenuo jednogodišnju nacionalnu kampanju, uz stručnu podršku nemačkog registra, a pod pokroviteljstvom Ministarstva zdravlja RS, za povećanje broja davalaca kroz: organizovanje akcija na terenu putem mobilnih ekipa Instituta za transfuziju krvi Srbije (ITKS), organizovanje akcija podržanih od strane bolesnika, konferencija za štampu, angažovanje poznatih ličnosti za promociju i izradu spota, TV i radio gostovanja, izradu sajta, podizanje društvenih mreža, angažovanje volontera za promociju, učešće u Letnjoj kampanji ITKS-a. Kampanja se sprovodi u saradnji sa ekipama ITKS-a, Udruženjem za borbu protiv akutnih leukemija "Leuka" i Crvenim krstom Srbije. Rezultati: U prvih 8 meseci, organizovano je 8 akcija koje su podržane od strane transplantiranih ili bolesnika koji čekaju transplantaciju, na kojima je Registru pristupilo 1200 novih davalaca. U okviru akcija za dobrovoljno davanje krvi Registru je pristupilo u julu 204, a u avgustu 317 davalaca. Bilo je 32 gostovanja stručnog osoblja u radio i televizijskim emisijama, 380 medijskih objava, 73 interaktivne objave na Instagramu i Facebook-u sa preko 12000 pregleda. Osmišljen je novi slogan kampanje " Osloni se na mene" i izrađen sajt. Od početka godine , 1866 davalaca je pristupilo Registru što odgovara ranijem trogodišnjem proseku. Zaključak: Pokretanje nacionalne kampanje je dovelo do značajnog povećanja broja novoprijavljenih davalaca u Registru davalaca MĆH Srbije.
Ključne reči: Registar davalaca matičnih ćelija hematopoeze Srbije, davalac, nacionalna kampanja

UP 22

PROMOTION OF HEMATOPOIETIC STEM CELL DONATION AS A NATIONAL CAMPAIGN

Blagojević G, Lako-Šoškić B, Lesjak S, Andrić Z.
Tissue Typing Department, Blood Transfusion Institute of Serbia

Introduction: Serbian Bone Marrow Donor Registry (SBMDR) enables finding donors for patients who need transplantation, and whose matching donor couldn't be found in their family. For 10% of patients wasn't possible to find a matched donor and that was the reason why it was necessary to launch a national campaign with the goal to increase the number of donors. The aim of this paper is to present the activities that provided increasing public awareness of the importance of transplantation. Material and methods: SBMDR with the professional support of the German Registry, and Ministry of Health, RS, launched a one-year national campaign in December 2021. The purpose of this campaign is to increase the number of donors by organizing mobile teams of Blood Transfusion Institute of Serbia (BTIS) all across the country; patient drives, press conferences, and celebrity engagement for promotion, and videos production, TV and radio guest appearances; website development, online advertisements, social networking; volunteers' engagement and participation in the Summer Campaign. The campaign is carried out in cooperation with BTIS , Association "Leuka" and the Serbian Red Cross. Results: In the first 8 months, 8 patient drives were organized, which led to that 1200 new donors. There were 521 donors joined by BTIS actions. There were 32 TV and radio, 380 social media publications, 73 Instagram and Facebook announcements.
The campaign's slogan "Lean on me" and a website were created. Since the beginning of the year, 1,866 donors have joined the Register, which was to the previous three-year average. Conclusion: The launch of the national campaign led to a significant increase in the newly registered number of donors in the SBMDR.
Keywords: Serbian Bone Marrow Donor Registry, Stem Cell Donor, a National Campaign

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MOTIVES AND INCENTIVES FOR BLOOD DONATION

Terzieva K[1,2], Popov R[1], Borisova T[1]
[1]*Center of Transfusion Hematology, Military Medical Academy, Sofia, Bulgaria*
[2]*Laboratory of Transfusion Hematology, National Hospital of Cardiology, Sofia, Bulgaria*

Introduction: The Center of Transfusion Hematology in Military Medical Academy (MMA), Sofia, Bulgaria performs all activities in the transfusion chain – from blood donation to delivering blood components for clinical use. Nonremunerated voluntary blood donation is the basis of safe blood and blood components. It is recommended by the World Health Organization and the Council of Europe.
Aim: To present a study of the attitude towards blood donation among military servicemen of the Bulgarian army as well as the strong and weak motives and incentives for nonremunerated voluntary blood donation.
Material and methods: A survey was conducted with a questionnaire gathering information about the attitude and incentives for blood donation.
Results: One third of the MMA blood donors are military servicemen. Blood donations are organized annually in military formations as part of the campaign "Be one of us! Donate blood– save a life!". Military servicemen are ready for voluntary and unpaid blood donation. The main motives for blood donation among them are altruism, social responsibility and duty in combination with advanced feeling of belonging and collegiality and increasing the sense of self-efficacy. It was found that weak incentives for donating blood are reciprocity, paid leave, medical tests, snacks, ect.
Conclusion: Against the backdrop of a global trend of the need for blood and blood components increasing, a number of countries report a decrease in the number of blood donations, especially since the beginning of the COVID – 19 pandemic. Blood donations remain as the only way to provide blood and blood components and it is a challenge for blood centers to maintain a sufficient level of blood donation. The knowledge and study of psychological factors that stimulate a blood donation attitude is extremely important for the recruitment, retention and management of blood donors.
Keywords: blood donation, motives and incentives for blood donation, recruitment and retention of blood donors

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UP 24

VOLONTARY BLOOD DONATION DURING THE PANDEMIC COVID- 19

Stojić D, Istatkov J, Kovač M.
The Blood Transfusion Institute of Serbia

Introduction: During the pandemic and the introduction of emergency measures, it was difficult to organize any gatherings including blood collection. Employees in the blood collection department organize work in the blood collection hall and in the field, in accordance with the newly created situation, in order to prevent infection among employees and blood donors.
Aim: presentation of all measures and activities carried out as part of work during the pandemic.
Materials and methods: All activities were analyzed in accordance with the procedures introduced during the pandemic in relation to recommendations of the Ministry of Health and Crisis Staff of Republic of Serbia.
Results: General measures – prevention measures in the hall and in the field: disinfection of surfaces, keeping distance, wearing protective equipment, body temperature measurement of employees and donors.
Measures during the examination of the donor: the examination of the donor included everything related to the infection by COVID 19 (coughing, sore throat, temperature, loss of sense of smell, muscle pain, headache, diarrhea, difficulty breathing).The appearance of any symptom was contraindication for donating blood.
Measures for donors who resided abroad: new rules which were related to the ban of donating blood upon returning from abroad and delay period after vaccination.
Measures for donors who were infected with COVID 19: due to the lack of clear criteria for donors infected with COVID 19 at the beginning of pandemic, doctors were guided by the existing criteria for infectious diseases. The delay in donating blood depended on severity of the clinical picture, duration of hospitalization and the presence of complications (neurological, cardiological, thrombosis ,pulmonary fibrosis). Reasons for permanent rejection of donors are ischemia of myocardium and CNS.
Conclusion: The influence of social-epidemiological aspect – fear, limited movement, the transition to online classes and working from home, made it difficult for us to work and led to a drop in the of number blood donations. However, in addition to all difficult circumstances caused by the pandemic and with the necessity of introducing new measures, BITS managed to collect and provide a sufficient number of blood units for the COVID hospitals and emergency interventions.
Key words: pandemic, blood donors, prevention measures

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ISTRAŽIVANJE O ZADOVOLJSTVU DOBROVOLJNIH DAVALACA KRVI (TOKOM PANDEMIJE COVID-19)

Miladinović Lj.[1], Čukić M.[1], Raič M.[1], Mihajlović M.[2], Bogdanović N.[3], Savić A.[4], Todorović J.[5], Mijatović D.[6]
[1]Crveni krst Srbije, Beograd
[2]Opšta bolnica Valjevo, Valjevo
[3]Crveni krst Kragujevac, Kragujevac
[4]Crveni krst Niš, Niš
[5]Crveni krst Kosova i Metohije, Kosovska Mitrovica
[6]Crveni krst Vojvodine, Novi Sad

Uvod
Obezbeđivanje dovoljnih količina krvi je u velikom broju zemalja povereno Crvenom krstu. Kroz razvijenu mrežu rad počiva na volonterskom angažovanju, humanističkim vrednostima i solidarnosti među ljudima. Crveni krst Srbije, odredbama Zakona o Crvenom krstu Srbije (član 7 tačka 4.), ima javno ovlašćenje za poslove motivacije građana za dobrovoljno davanje krvi i organizacije i sprovođenje akcija dobrovoljnog davanja krvi u saradnji sa ovlašćenim transfuzijskim ustanovama.U specifičnim uslovima pandemije bilo je neophodno obezbediti dobar odziv te je mišljenje davalaca procenjeno presudnim.
Cilj rada
Utvrditi nivo zadovoljstva davalaca krvi uslovima, bezbednošću i informisanošću u uslovima COVID 19 da bi se ubuduće preduzeli konkretni koraci koji će uticati na povećanje zadovoljstva, bezbednosti i informisanosti davalaca krvi u Srbiji.
Istraživanje je usmereno ka davaocima krvi koji krv daju u prostorijama Crvenog krsta, transfuziomobilu i slično. Poseban osvrt je usmeren ka brizi o zdravlju i davanju krvi u okolnostima pandemije.
Materijal i metod
Kroz Microsoft365 Forms, napravljen je upitnik koji se skeniranjem QR koda pametnim telefonom preuzima i popunjava onlajn na samoj akciji, a odgovori se generišu u realnom vremenu. Davaoci su dobili obaveštenje da je upitnik anoniman i imali mogućnost da se opredele da li će učestvovati u istraživanju.
Uzorak čini 2.962 davalaca na akcijama organizovanim u 45 organizacija Crvenog krsta u periodu od 7. februara do 31.marta 2022. Ukupno je 94% njih dalo krv a 6% je odbijeno. Najveći broj ispitanika,76% izjasnio se da najčešće daje krv u lokalnoj zajednici što je porast u odnosu na period pre pandemije.
Zaključak
Dobrovoljni davaoci su tokom pandemije bili oprezniji pri odluci da daju krv, petina je u nekom trenutku i odustala. Čak 10% njih je odgovorilo da ne zna tačno zna kome da se obrati u vezi pitanja o davanju krvi tokom pandemije. Veoma su zainteresovani za svoje zdravlje, čak 78% ispitanika bi volelo da o svom zdravlju dobija više informacija.
Ključne reči
#davalaštvo #crvenikrst #istraživanje

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RESEARCH ON BLOOD DONOR SATISFACTION (DURING THE COVID 19 PANDEMIC)

Miladinović Lj.[1], Čukić M.[1], Raič M.[1], Mihajlović M.[2], Bogdanović N.[3], Savić A.[4], Todorović J.[5], Mijatović D.[6]
[1]Crveni krst Srbije, Beograd
[2]Opšta bolnica Valjevo, Valjevo
[3]Crveni krst Kragujevac, Kragujevac
[4]Crveni krst Niš, Niš
[5]Crveni krst Kosova i Metohije, Kosovska Mitrovica
[6]Crveni krst Vojvodine, Novi Sad

Background
The blood management is reffered to the Red Cross organization in the large number of countries worldwide. The Red Cross of Serbia trough it's developed humanitarian and volunteer network has public powers in blood management referred by the Law on the Red Cross of Serbia (article 7. bulletin 4) During promotion, recruitment and retention and blood drive logistics organization, the Red Cross of Serbia cooperates with the blood establishments in the country. In order to continue to give blood during the pandemic, donor opinion was crucial.
Project goal
To understand the blood donor satisfaction considering conditions, safety and level of provided information during pandemic, in order to improve their satisfation, safety and level of shared information.
The targeted blood donor population: blood donors giving blood out of the blood establishments. The focus of the research was towards donor care and giving blood during pandemic.
Methods and materials
By scanning the QR code at blood drive, blood donors with their smartphones reached the anonimous questioner deciding wether they are willing to participate or not. The blood donors answers were instantly generated by the Microsoft365 Forms aplication.
From Febryary7 to March 31 2022, 2.962 blood donors participated in the reasearch at the blood drives organized by the 45 Red Cross branches . In total, 94% gave blood and 6% were not eligible. Majority, 76% of the blood donors confirmed that the most common venues where they give blood are local blood drives. This represents an encrease, comparing to the period before the pandemic.
Conclusion
During the pandemic, the blood donors often hesitated to donate blood, 20% in some moment postponed their donation. In total, 10% blood donors answered that they are not sure to whom to address for the answers about giving blood and pandemic. Blood donors are extremely interested in donor care, 78% of them would like to receive more information about their health.
Key words #blood #redcross #reasearch

UP 26

REZULTATI PRIKUPLJANJA ANTI-COVID-19 PLAZME U INSTITUTU ZA TRANSFUZIJU KRVI SRBIJE

Bosnić V, Obrenović M, Vavić N, Špuran Z, Miljuš D, Miletić G, Andrić Z, Mijucić V.

Uvod: Zbog velike brzine širenja virusa SARS-CoV-2, nepostojanja specifične terapije na početku pandemije, pristupilo se prikupljanju plazme od rekonvalescenata, smatrajući da specifična antitela iz plazme mogu da novoobolelima pruže pasivnu, privremenu zaštitu.
Cilj rada je da se prikažu rezultati prikupljanja anti-COVID-19 plazme u Institutu za transfuziju krvi Srbije (ITKS) automatizovanom metodom-plazmaferezom.
Materijal i metode: Retrospektivno su analizirani struktura davalaca anti-COVID-19 plazme prema polu i broju donacija, razlozi za trajno i privremeno odbijanje za davanje, broj plazmafereza, neželjene reakcije kod davalaca plazme za period od 11.04.2020-06.09.2021. godine. Podaci su dobijeni iz Informacionog sistema ITKS-a. Obavljen je 2001 telefonski, trijažni razgovor sa potencijalnim davaocima.
Rezultati: Na osnovu anamneze trajno je odbijeno 937 (46,8%), privremeno 210 (10,5%), a 854 (42,7%) je ispunilo kriterijume da dođu na testiranje (fizikalni pregled i laboratorijsko testiranje) u ITKS. Na testiranju u ITKS-u je zbog neadekvatnih vena odbijeno 33 (3,8%), na lekarskom pregledu 36 (4,2%), neadekvatnih rezultata kompletne krvne slike 92 (10,8%), neadekvatnih biohemijskih parametara 116 (13,7%) i zbog pozitivnih markera na transfuzijske transmisivne bolesti 4 davaoca (0,5%). Ukupno je 573 davalaca ispunilo kriterijume za davanje plazme, muškaraca 433 (75,6%), žena 140 (24,4). Urađeno je 1800 plazmafereza, prikupljeno 3576 jedinica anti-COVID-19 plazme. Prekinuto je 12 procedura (0,7%), od čega 9 (0,5%) zbog hematoma, 3 (0,2%) zbog vazovagalnih reakcija. U proseku je bilo 3,2 davanja plazme po davaocu, 253 davalaca doniralo je plazmu jedanput, dva puta njih 107, tri puta 55, dok je 5 davalaca doniralo plazmu 14 puta.
Zaključak: Veliki broj trajno i privremeno odbijenih davalaca govori o zdravstvenom stanju davalaca u post-COVID periodu. Za sada nema studije o efikasnosti primene rekonvalescentne plazme u Srbiji.
Ključne reči: COVID-19, anti-COVID-19 plazma, plazmafereza

UP 26

RESULTS OF ANTI-COVID-19 PLASMA COLLECTION IN THE BLOOD TRANSFUSION INSTITUTE OF SERBIA

Bosnić V, Obrenović M, Vavić N, Špuran Z, Miljuš D, Miletić G, Andrić Z, Mijucić V.

Introduction: Due to rapid spread of SARS-CoV-2 virus and lack of specific therapy at the beginning of the pandemic, convalescent plasma was collected, assuming that specific antibodies in plasma could provide passive, temporary protection to infected patients.
Objective: Presenting results of anti-COVID-19 plasma collection at the Blood Transfusion Institute of Serbia (BTIS) using the automated plasmapheresis method.
Materials and methods: Retrospective analysis of gender structure of anti-COVID-19 plasma donors, number of donations, rejection reasons, number of plasmaphereses and adverse reactions, in the period April 11, 2020 - September 6, 2021. The data were obtained from BTIS Information System. Total of 2001 telephone triage interviews were conducted with potential donors.
Results: Based on anamnesis, 937 (46.8%) potential donors were rejected permanently, 210 (10.5%) temporarily, while 854 (42.7%) met criteria for physical examination and laboratory testing at the BTIS. Upon testing at the BTIS, 33 (3.8%) potential donors were rejected due to inadequate veins, 36 (4.2%) after medical examination, 92 (10.8%) due to inadequate blood test results, 116 (13.7%) due to inadequate biochemical parameters, and 4 (0,5%) due to positive markers for transfusion transmissible diseases. Out of 573 donors, 433 were men (75.6%), and 140 women (24.4%). Total of 3576 anti-COVID-19 plasma units were collected from 1800 plasmaphereses. Twelve procedures (0.7%) were terminated prematurely, out of which 9 (0.5%) due to hematoma, and 3 (0.2%) due to vasovagal reactions. On average, there were 3.2 plasma donations per donor (253 donors donated plasma once, 107 twice, 55 three times, and 5 donors 14 times).
Conclusion: Large number of permanently and temporarily rejected donors testify about the health status of donors in the post-COVID period. Currently, there is no study on the effectiveness of the application of convalescent plasma in Serbia.
Keywords: COVID-19, anti-COVID-19 plasma, plasmapheresis

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EVALUATION OF REASONS FOR DEFERRAL OF COVID-19 CONVALESCENT PLASMA DONORS

Useini S[1], Grubovic Rastvorceva R[1, 2], E Petkovic[1], M Shorova[1,2, 3], Ismani E[1,4], Vilos L[1,5], Stojanoska Z[1,5] , Brnjarcevska T[6], Petlichkovski A[6]
[1]Institute for Transfusion Medicine of RNM, Skopje, N. Macedonia , [2]Faculty of Medical Sciences, University Goce Delcev, N. Macedonia [3]Regional Center for Transfusion Medicine – Stip, N. Macedonia Regional Center for Transfusion Medicine - Tetovo, N.Macedonia, [5]Regional Center for Transfusion Medicine – Bitola, N. Macedonia, 6Institute for Immunobiology and Human Genetics, N. Macedonia

Background: Taking into consideration historic success of convalescent plasma in prophylaxis and treatment of various infectious diseases over the century and expansion of COVID-19 pandemics, we started the COVID-19 convalescent plasma (CCP) program in our country. Aims: The aim of our study was to evaluate reasons for deferral of the COVID-19 convalescent plasma (CCP) donors. Materials and Methods: This is a prospective study organized in the Institute for Transfusion Medicine of Republic of North Macedonia since 30 April 2020 till July 2021. CCP donors eligible for donation were donors without a history of blood transfusion, female donors who have never been pregnant, or who have been tested and found negative for anti-HLA antibodies, age 18-65, in good health that fulfill all other criteria for regular blood donors. All potential donor were tested for: negative RTPCR for SARSCoV-2 before donation, anti-SARS-CoV-2 antibodies, anti-HLA antibodies (where applicable), blood count, blood group, TTI and biochemistry. Antibody testing was performed at the Institute for Immunobiology and Human Genetics in Skopje using CLIA method with Snibe Maglumi SARS-CoV-2 S-RBD IgG with IgG cut-off for CCP donation larger than 5 AU/ml (cut-off for regular positive result was larger than 1 AU/ml). All donors signed inform consent for donation and inclusion in the study. Results: There were 1462 potential CCP donors, of which 762(52.1%) did not fulfill criteria for CCP donation, 424(55.6%) women and 338(44.4%) men . There were 454(59.6%) potential CCP donors that did not have enough antiSARS-CoV-2 S-RBD IgG antibodies (Ab), of which 223(49.1%) had Ab concentration less than 1AU/ml (29.3% of all deferred donors) and 231(50.9%) had Ab concentration between 1 and 5AU/ml (30.3% of all deferred donors). In this subgroup of deferred donors, there were 227 women (50%) and 227 men (50%), with mean age 37.2±10.1 (range 18- 63). There were statistical significant correlation between the gender and the Ab concentration less than 1AU/ml and from 1 to 5AU/ml (Pearson Chi-square: 3.88667, df=1, p=0.048671). Multiple regression analysis showed that gender is independently associated with the Ab concentration, OR=1.4495 (95%CI 1.0016-2.0976), i.e. male gender increases the chance for increased Ab concentration for one and a half times. According to the age group, the majority of deferred CCP donors, because of low Ab concentration, are in the age group from 30 till 39(39.6%), followed by age group from 40 till 49(23.8%), and least deferred donors were in 50 and above age group (13.2%). The most of these deferred donors were treated at home, 451(99.3%) and had symptoms 240(52.9%). Distribution according to blood group in CCP donors deferred due to low Ab concentration was: blood group A - 182(40.1%), blood group O – 153(33.7%), blood group B – 69(15.1%) and blood group AB – 42(9.3%). In the whole investigated group, 65 (8.5%) potential donors were deferred because of low hemoglobin level (less than 12.5g/dl for women and less than 13.5g/dl for men), 26 (3.4%) were deferred because of positive TTI markers and 102 (13.4%) women of the total number of deferred donors were deferred because of presence of HLA antibodies (i.e. 24% of investigated women). Summary / Conclusions: There is large percentage of deferred CCP donors mostly because of low Ab concentration, presence of HLA antibodies and low hemoglobin level, but starting of COVID-19 convalescent plasma program was a big success for our institution and our country and helped a lot of patients.
Keywords: COVID-19 convalescent plasma, antibodies concentration, donor deferral

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NAJČEŠĆI RAZLOZI ODBIJANJA DAVALACA KRVI U INSTITUTU ZA TRANSFUZIJU KRVI SRBIJE U PERIODU OD 01.01.2018 GODINE DO 31.12.2021 GODINE

Stanojević N, Obradović S, Radivojev B, Kuljic V, Stojneva Istatkov J..
Institut za transfuziju krvi Srbije, Beograd, Srbija

Uvod: Dostupnost bezbedne krvi i krvnih produkata je kritična komponenta u poboljšanju zdravstvene zaštite. Dobrovoljno davanje krvi treba da bude bezbedan i siguran proces kako za primaoca tako i za davaoca. Ukoliko postoji rizik po zdravlje, davaoci se odbijaju prema Pravilniku o davaocima i komponentama krvi, privremeno ili trajno.
Cilj rada: Prikazati najčešće privremene i trajne kontraindikacija za davanje krvi u periodu od četiri godine.
Materijal i metode: Retrospektivnom metodom, iz jedinstvenog informacionog sistema Instituta, analizirano je 326 212 potencijalnih davalaca krvi u periodu od 01.01.2018 do 31.12.2021 godine. Selekcija davalaca krvi vršena je na osnovu popunjenog upitnika, određivanja nivoa hemoglobina, anamneze i fizikalnog pregleda. Grupisani su uzroci i određene učestalosti odbijanja.
Rezultati: Od ukupnog broja davalaca u ispitivanom periodu, privremeno je odbijeno 42 516 (13%) a trajno odbijeno 2082 (0.9%) davalaca. Najčešći razlozi za privremeno odbijanje davalaca su niske vrednosti hemoglobina (32,6%), hipotenzija (4,8%), lakše infektivne bolesti (4,1%), akutne alergije (3,7%), poremećaji srčanog ritma (3,7%), benigna hipertenzija (3,2%). Najčešći razlozi za trajno odbijanje davalaca su astma (1,0%), hipo ili hipertireoza (0,9%), psorijaza (0,7%).
Zaključak: Rezultati studije su pokazali da su najčešći razlozi za privremeno odbijanje davalaca nizak nivo hemoglobina, neadekvatan arterijski pritisak, sezonske prehlade i sezonske alrgije. Svakom davaocu treba dati temeljno obrazlozenje razloga odbijanja i jasne smernice za rešavanje zdravstvenog problema.
Ključne reči: davaoci krvi, kontraindikacije za davanje krvi, selekcija davalaca krvi

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THE MOST COMMON REASONS FOR DEFFERAL OF BLOOD DONOR IN BLOOD TRANSFUSIONE INSTITUTE OF SERBIA FROM 01.01.2018 TO 31.12.2021

Stanojević N, Obradović S, Radivojev B, Kuljic V, Stojneva Istatkov J.
Blood Transfusion Institute of Serbia, Belgrade, Serbia

INTRODUCTION: The availability of safe blood and blood products is a critical component in improving health care. Voluntary blood donation should be a safe and secure process for both the recipient and the donor. If there is a health risk, donors are rejected according to the Rulebook on donors and blood components, temporarily or permanently.
OBJECTIVE: Show the most common temporary and permanent contradictions for blood donation over a period of four years.
MATERIALS AND METHODS: By retrospective method, from the Institute's unique information system, 326,212 potential blood donors were analyzed from 01.01.2018 to 31.12.2021 and determined the causes and frequencies of rejection. The selection of blood donors was conducted on the basis of a completed questionnaire, determining hemoglobin levels, anamnesis and physical examination.
RESULTS: Out of the total number of donors in the examined period, 42,516 (13%) were temporarily rejected and 2082 (0.9%) of donors were permanently rejected. The most common reasons for temporary rejection of donors were low hemoglobin level (32.6%), hypotension (4.8%), mild infectious diseases (4.1%), acute allergies (3.7%), heart rhythm disorders (3.7%), benign hypertension (3.2%). The most common reasons for permanent rejection of donors were asthma (1.0%), hypo or hyperthyreosis (0.9%), psoriasis (0.7%).
CONCLUSION: The results of the study showed that the most common reasons for temporary rejection of donor were low levels of hemoglobin, inadequate arterial pressure, seasonal colds and seasonal allergies. Each donor should be given a rational explanation for the reasons of the rejection and clear guidelines for solving the health problem.
Keywords: blood donors, blood donation contradictions, selection of blood donors

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RIJETKE RHD VARIJANTE KOD DAVALACA KRVI

Guzijan G[1], Lilić M[2], Jovanović-Srzentić S[3], Milosavić M[1], Veselka Ćejić[1], Selak-Đukelić B[1], Mitrović S[1]

[1] Zavod za transfuzijsku medicinu Republike Srpske, Banja Luka, BiH

[2] Odjel za bioligiju, Sveućilište Josipa Jurja Strossmayera u Osijeku, Osijek, Hrvatska

[3] Institut za transfuziju krvi Srbije, Beograd, Srbija

UVOD: Različite varijante Rh gena kod donora kada nisu otkrivene mogu uzrokovati aloimunizaciju kod RhD-negativnih primalaca.

CILJ:Cilj istraživanja bio je otkriti karakteristične molekularne mehanizme za RhD-negativan fenotip kod davalaca krvi.

MATERIJALI I METODE: DNK je izolovana od 600 serološki RhD-negativnih nesrodnih davalaca krvi sa C+ i/ili E+, koji rutinski daju krv u Zavodu za transfuzijsku medicinu Republike Srpske. Molekularno testiranje je uključivalo početni skrining za RHD, skeniranje RHD eksona, određivanje klinički najrelevantnijih slabih RHD alela. Korišteni FluoGene testovi zasnovani su na PCR-SSP (prajmeri specifični za PCR sekvencu) sa evaluacijom rezultata očitavanjem fluorescencije na instrumentu FluoVista (Inno-train Diagnostik). Svi uzorci sa RHD varijantom su naknadno ispitani tehnikom adsorpcije/elucije (humani anti-D – u kućnoj proizvodnji, eluiran DiaCidel rastvorom za kiselo eluiranje, Bio-Rad Laboratories) kako bi se potvrdila ili odbacila DEL ekspresija dotičnog RHD alel.

REZULTATI: Kod 5/600 (0,83%) davalaca krvi utvrđena su ukupno tri različita RHD alela – RHD*01N.03, RHD*01EL.44 (RHD*DEL44) i RHD*05.05 (RHD*DV.5).

Četiri davaoca sa rijetkim hibridnim alelima (RHD*01N.03 i RHD*01EL.44) su naknadno potvrđena kao RhD-pozitivna adsorpcijom/elucijom, čime je potvrđena ekspresija DEL fenotipa ovih alela. Oba alela se obično tumače kao da imaju RhD negativnu ekspresiju. Alel RHD*01N.03 ima strukturu RHD*D-CE(2-9)-D, što sugerira da bi se tipično trebao ponašati kao nulti alel. Iako je RHD*DEL44 zapravo katalogiziran kao alel DEL od strane ISBT, njegov DEL fenotip potvrđen je tek izvorno u Kini, a tek nedavno u Hrvatskoj.

ZAKLJUČAK:Naši rezultati pokazuju potrebu za molekularnim pojašnjenjem RhD-negativnog fenotipa kod C+ i/ili E+ davalaca krvi. Posebno je za hibridne alele imperativ da se utvrdi da li oni eksprimiraju RhD antigen, a ne da se podrazumjevano preuzme njegov RhD-negativni fenotip, s obzirom na mogućnost aloimunizacije.

Ključne riječi: molekularno testiranje, serološki RhD-negativan fenotip

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RARE RHD VARIANTS IN BLOOD DONORS

Guzijan G[1], Lilić M[2], Jovanović-Srzentić S[3], Milosavić M[1], Veselka Ćejić[1], Selak-Đukelić B[1], Mitrović S[1]

[1] Institute for Transfusion Medicine of Republika Srpska, Banja Luka, Bosnia and Herzegovina

[2] Department of Biology, Josip Juraj Strossmayer University of Osijek,Osijek,Croatia

[3] Head of the Department of Immunohaematology Blood Transfusion Institute of Serbia

INTRODUCTION: Different variants of RH genes in donors when undetected can cause alloimmunisation in RhD-negative recipients.

AIM:The aim of the study was to detect distinctive molecular mechanisms for RhD-negative phenotype within donors.

MATERIALS AND METHODS:DNA was isolated from 600 serologically RhD-negative unrelated blood donors with C+ and/or E+ who routinely donate blood at Institute for transfusion medicine of Republika Srpska. Molecular testing included initial screening for RHD, RHD exon scanning, determination of clinically most relevant weak RHD alleles. The FluoGene assays used are based on PCR-SSP (PCR-sequence specific primers) with the results evaluation by fluorescence reading on the FluoVista instrument (Inno-train Diagnostik). All the samples with an RHD variant were subsequently examined by adsorption/elution technique (human anti-D – in house production, eluted by DiaCidel solution for acid elution, Bio-Rad Laboratories) in order to confirm or dismiss the DEL expression of the respective RHD allele.

RESULTS: In 5/600 (0.83%) donors in total three different RHD alleles were determined – RHD*01N.03, RHD*01EL.44 (RHD*DEL44) and RHD*05.05 (RHD*DV.5).

Four donors with the rare hybrid alleles (RHD*01N.03 and RHD*01EL.44) were afterwards confirmed as RhD-positive by adsorption/elution, thus confirming the DEL phenotype expression of these alleles. Both alleles are commonly interpreted as having an RhD negative expression. The RHD*01N.03 allele has a structure of RHD*D-CE(2-9)-D, which suggests it should typically behave as a null allele. Although RHD*DEL44 is actually catalogued as the DEL allele by ISBT, its DEL phenotype was confirmed only originally in China and just recently in Croatia.

CONSLUSION:Our results demonstrate the need for molecular clarification of RhD-negative phenotype in C+ and/or E+ donors. Especially for hybrid alleles it is imperative to determine whether they express the RhD antigen and not to assume its RhD-negative phenotype by default, considering the possibility of alloimmunisation in the RhD-negative recipients.

KEY WORDS: molecular testing, serologically RhD-negative phenotypes

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UNCOMMON RH VARIANTS IN BLOOD DONORS

Lilić M[1], Jaklin G[2], Gojčeta K[3], Raos M[4], Golubić-Ćepulić B[5]

[1] Josip Juraj Strossmayer University of Osijek, Osijek, Croatia

[2] Department for Transfusion Medicine, General Hospital Varaždin, Varaždin, Croatia

[3] Clinical Department for Transfusion Medicine and Transplantation Biology, University Hospital Centre Zagreb, University of Applied Health Sciences, Zagreb, Croatia

[4] Clinical Department for Transfusion Medicine and Transplantation Biology, University Hospital Centre Zagreb, University of Applied Health Sciences, Zagreb, School of Medicine,University of Zagreb, Zagreb, Croatia

[5] Clinical Department for Transfusion Medicine and Transplantation Biology, University Hospital Centre Zagreb, Zagreb, Croatia

University of Applied Health Sciences, Zagreb, Croatia

School of Medicine,University of Zagreb, Zagreb, Croatia

University Department of Health Studies, University of Split, Split, Croatia

INTRODUCTION:There are around 600 genes coding for antigens of the Rh system. Most of them could cause alloimmunization, which should be prevented by their confirmation. AIM:This was a population-based study within the blood donors from northwestern Croatia, with the intention to describe the Rh variants, their frequencies and haplotypes.

MATERIALS AND METHODS:The two-year prospective study included two groups of healthy unrelated regular blood donors: serologically RhD-negative (N=704) and serologically weak D (N=31). All donors are residents of the two northernmost counties in Croatia (Međimurje and Varaždin).Molecular testing for Rh variants was performed by qPCR (FluoGene) on the FluoQube qPCR instrument. TheRHD zygosity was determined for samples with anyRHD exon reactivity. This subset of donors was subsequently examined also for the presence of RhD epitopes by adsorption/elution technique.

RESULTS:In RhD-negative donor group, in addition to the RHD deletion (702/704, 99,72%), the following DEL alleles were encountered within two hemizygous Ccee donors (0,28%): RHD*01EL.44(RHD*DEL44) and RHD*01EL.32 (RHD*DEL32). One RH negative sample exhibited some RHD sequence from a hybrid allele at RHCE locus of the structure RHCE*D(1)-CE.These three samples revealed also the presence of RhD epitopes in erythrocyte membrane, including the RHD negative donor with the hybrid RHCE allele.Eight RHD alleles were distinguished within the serologically weak D group, the most frequent one being RHD*01W.1.Special recognition is warranted for the RHD*01W.40 allele, whose associated haplotype was unambigously disclosed as Dce for the first time.CONCLUSION:The DEL phenotype of the RHD*01EL.44expression is described for the first time in the population of European origin and, more globally, outside of China.The allele RHCE*D(1)-CE was sporadically reported in China and Slovenia until now. This research distinctively unveiled the RhD epitope(s) presence in the RHD negative donor carrying that allele.Molecular testing of donor populations enables safer transfusions. It can prevent unwelcome immunization of genuinely RhD-negative recipients by an RhD-positive blood product.

Key words: blood groups, Rh system, RHD, molecular typing, RhD variants

UP 31

ULOGA MOLEKULARNOG TESTIRANJA U REŠAVANJU SEROLOŠKIH IMUNOHEMATOLOŠKIH PROBLEMA

Radović I[1], Vlatković A[1], Šerbić O[2], Kuzmanović M[2], Jovanović Srzentić S[1]
[1] Institut za transfuziju krvi Srbije, Beograd, Srbija
[2] Institut za zdravstvenu zaštitu majke i deta Srbije „dr Vukan Čupić“, Beograd, Srbija

Uvod: Politransfundovani pacijenti predstavljaju izazov u imunohematološkom testiranju iz nekoliko razloga. Često su imunizovani protiv više eritrocitnih antigena, pa je potrebno testiranje i sa više panela test eritrocita (Er) u cilju dokazivanja svih prisutnih specifičnosti, a titar antitela (At) se menja tokom vremena u zavisnosti od antigene stimulacije. Istovremeno prisustvo populacija Er primaoca i više davaoca otežava tipizaciju. Pojedini fenotipovi se ne mogu pouzdano razlikovati serološkim metodama.
Prikaz slučaja: Sa Instituta za zdravstvenu zaštitu majke i deta „dr Vukan Čupić“ upućen je 14.12.2021. uzorak deteta, crne rase, sa dijagnozom srpaste anemije radi identifikacije At. Pacijent je primao transfuzije u julu i septembru iste godine, a prethodno je transfundovan i u drugoj ustanovi.
Identifikacija At rađena u gelu na Coombs Anti-IgG karticama sa ID-DiaPanel Er (BioRad Laboratories, Inc.) pokazala je prisustvo anti-E i anti-Fya . Pretragom informacionog sistema ustanovljeno da je ranije identifikovano anti-C i suspektno anti-K. Tipizacijom Er utvrđen fenotip ccDee Fy(a-,b-). Iz novog uzorka izolovana DNK i urađen RBC-FluoGene vERYfy eXtend, RBC-FluoGene vERYfy i RBC-FluoGene CDE test na aparatu FluoVista (Inno-train Diagnostik, Germany). FluoGene metod je zasnovan na PCR-SSP-u sa „end point“ detekcijom fluorescentnog signala. Detektovane su sledeće alele klinički značajnih sistema: RHD D, RHCE c, e, KEL-02, JK-01, JK-02, FY-02N.01, GYPA-01, GYPA-02, GYPB-03, GYPB-03N.03. Dokazana je homozigotnost za Duffy null alelu, koja je karakteristična za crnu rasu u pojedinim regijama.
Za transfuziju je preporučena primena E-negativnih, C-negativnih, K-negativih i Fya-negativnih Er.
Zaključak: Primenom moleklarne genotipizacije, objašnjen je neuobičajen serološki nalaz i stečen uvid u prisutne alele drugih klinički značajnih krvnogrupnih sistema. Proširenu genotip omogućava siguran izbor kompatibilne krvi za pacijente na hroničnom programu transfuzije.
Ključne reči: genotipizacija eritrocitnih antigena, imunohematološko testiranje, PCR-SSP

UP 31

THE ROLE OF MOLECULAR TESTING IN SOLVING SEROLOGICAL IMMUNOHAEMATOLOGICAL PROBLEMS

Radović I[1], Vlatković A[1], Šerbić O[2], Kuzmanović M[2], Jovanović Srzentić S[1]
[1] Blood transfusion institute of Serbia, Belgrade, Serbia
[2] Institute for Mother and Child Health Care of Serbia „dr Vukan Čupić“, Belgrade, Serbia

Introduction: Polytransfused patients present a challenge in immunohaematological testing for several reasons. They are often immunized against multiple erythrocyte antigens, so testing with multiple erythrocyte test panels (Er) is required in order to identify all present specificities, and the antibody (Ab) titer changes over time depending on antigenic stimulation. The simultaneous presence of recipient and multiple donor Er populations makes typing difficult. Certain phenotypes cannot be reliably distinguished by serological methods.
Case report: A sample of a child, of a black race, diagnosed with sickle cell anemia was sent from the Institute for Health Care of Mother and Child "Dr. Vukan Čupić" on December 14th 2021 for the identification of Ab. The patient received transfusions in July and September of the same year, and was previously transfused in another institution.
In-gel identification of Ab on Coombs Anti-IgG cards with Er ID-DiaPanel BioRad Laboratories, Inc. showed the presence of anti-E and anti-Fya. A search of the information system established that anti-C and suspected anti-K were previously identified. Typing Er determined the phenotype ccDee Fy(a-,b-). DNA was isolated from the new sample and the RBC-FluoGene vERYfy eXtend, RBC-FluoGene vERYfy and RBC-FluoGene CDE tests were performed on the FluoVista device (Inno-train Diagnostik, Germany). The FluoGene method is based on PCR-SSP with end point detection of the fluorescent signal. The following alleles of clinically significant systems were detected: RHD D, RHCE c, e, KEL-02, JK-01, JK-02, FY-02N.01, GYPA-01, GYPA-02, GYPB-03, GYPB-03N.03. Homozygosity for the Duffy null allele, which is characteristic of the black race in certain regions, was proven.
The use of E-negative, C-negative, K-negative and Fya-negative Er is recommended for transfusion.
Conclusion: By applying molecular genotyping, an unusual serological finding was explained and insight into the present alleles of other clinically significant blood group systems was gained. Extended genotyping allows safe selection of compatible blood for patients on a chronic transfusion program.
Key words: genotyping of erythrocyte antigens, immunohaematological testing, PCR-SSP

UP 32

UP 32

PERSISTENT ANTIGEN A AFTER ABO INCOMPATIBLE HEMATOPOIETIC STEM CELL TRANSPLANTATION IN CHILDREN

Andrić B[1], Radonjić Z[1], Šerbić O[1,2], Vujić D[2,1], Zečević Z[2,1], Simić M[1],Gobeljić B[1], Jovanović-Srzentić S[3,2]
1 Mother and Child Health Care Institute of Serbia „Dr Vukan Čupić“, Belgrade
2 University of Belgrade, Faculty of Medicine, Belgrade
3 Blood Transfusion Institute of Serbia, Belgrade

Introduction: In the setting of allogeneic hematopoietic stem cell transplantation (HSCT), red blood cells (RBCs) are produced by donor-derived hematopoietic stem cells after HSCT, which express carbohydrates based on the donor's ABO gene. The recipient's ABO blood type ultimately changes to the donor's ABO blood type after ABO-incompatible (ABOi) HSCT. In contrast, most non-hematopoietic tissues retain expression of the patient's original blood group for life, and these antigens may adsorb from the plasma onto the donor-derived RBCs which causes the presence of persistent patient A- and/or B-antigen in the clinical laboratory, despite 100% white cell donor chimerism.
Aim: To present a serological and molecular findings in three children with persistent antigen A after minor ABOi HSCT.
Material and methods: For the immunohaematological monitoring we used automatic technique (IH-500) and gel card method. The Fluogene method on the FluoVista device was used for molecular testing. We performed adsorbtion-elution study using tube and gel method for third patient.
Results: First case M.M. was the 6-year-old girl, A, RhD+, with T-cell acute lymphoblastic leukemia (ALL), transplanted with bone marrow (BM) from HLA-matched unrelated donor (MUD) O, RhD+. Second, M.A. was the 16-year-old boy, A, RhD+, with B-cell ALL transplanted with BM MUD O, RhD+. Third case was Š.I. the 8-year-old girl, A, BRhD- with ALL transplanted with a BM from HLA-matched related donor BRhD+. The presence of persistent antigen A was registered in all patients six months after HSCT, despite excellent chimerism (98-100%). Molecular typing proved the presence of ABO*01 allele only in first and second patients, and the presence of ABO*01 and ABO*B in third, which indicates that the donor's blood groups were accepted in all patients.
Conclusion: Adsorption of recipient antigens onto donor RBCs adds another level of complexity to the interpretation of the ABO group, and this may have implications for blood component support and clinical decision-making.
Key words: persistent antigen, transplantation, children

UP 33

MOGUĆNOST DETEKCIJE SLABOG RhD ANTIGENA TEHNIKOM „ČVRSTE FAZE" NA NEOIRIS AUTOMATSKOM IMUNOHEMATOLOŠKOM SISTEMU

Dukić Novaković M, Stamenić Lj, Damjanović V, Djilas I, Krsmanović S, Kosović S.
Institut za transfuziju krvi Srbije, Beograd

Uvod:Antigen D je najjači imunogen, među antigenima Rhesus sistema i u odnosu na ostale antigene drugih krvno grupnih sistema. Zbog izuzetnog kiničkog značaja, određivanje RhD antigena je obavezn imunohematološo ispitivanje kod svih davalaca i primalaca krvi i predstavlja izazov u svakodnevnoj transfuziološkoj praksi.
Cilj rada: Tromesečno retrospektivno praćenje rezultata određivanja RhD antigena, kod dobrovoljnih davalaca krvi Instituta za transfuziju krvi Srbije (ITKS), kod kojih je u rutinskom radu pri određivanju RhD antigena dobijen negativan rezultat.
Materijal i metodi: U studiju je uključeno 2529 uzoraka krvi RhD-negativnih davalaca. Pored rutinskog testiranja, ovi uzorci su testirani i testom "weak D" korišćenjem Capture R select i Novaclone anti-D reagensa, tehnikom u mikroploči na aparatu NEOIris.
Rezultati:U ITKS, testiranje krvne grupe ABO/RhD dobrovoljnim davaocima krvi, rutinski se obavlja tehnikom u mikroploči na automatskim platformama. Svim RhD-negativnim-davaocimasa-C ili E antigenom, dodatno se proverava nalaz RhD antigena tehnikom u gelu. Testom „weak D" testirano je ukupno 2529 uzoraka RhD-negativnih davalaca. Rh fenotip Ccddee je određen kod 137 davalaca (5,4 %), ccddEe kod 41 (1,6 %), CCddee kod 2 (0,08 %), CcddEe kod 2 (0,08 %), preostali ispitani davaoci su bili ccddee.Za tri testirana uzorka krvi dobijeni su nepodudarni rezultati ispitivanja RhD antigena (0,12 %).Kod sva tri davaoca RhD antigen serološki je dokazan tehnikom adsorpcije i elucije. Ove davaoce je potrebno dalje ispitivati molekularnom tehnikom radi preciznog određivanja RhD statusa.
Zaključak: Trenutan način testiranja ne omogućava otkrivanje svih slabih D fenotipova . Sprovedeno ispitivanje ukazuje da je Capture R select /Novaclone Anti-D "weak test" osetljiviji od drugih rutinskih metoda u detekciji slabijih varijanti RhD antigena. Problemi u testiranju RhD antigena mogu se prevazići kombinacijom seroloških ispitivanja i molekularnih tehnika.
Ključne reči: davaoci krvi, weak D, molekularna ispitivanja

UP 33

POSSIBILITY OF WEAK D ANTIGEN DETECTION BY THE "SOLID PHASE" TEHNIQUE ON THE NEOIRIS AUTOMATIC SYSTEM

Dukić Novaković M, Stamenić Lj, Damjanović V, Djilas I, Krsmanović S, Kosović S.
Blood Transfusion Institute of Serbia, Belgrade

Introduction: Antigen D is the strongest immunogen, not only among Rhesus system antigens,but also among antigens of all other blood group systems. Due to its great clinical importance,RhD antigen determination is a mandatory immunohaematological test for all blood donors and recipients, representing a constant challenge in daily transfusion practice.

Aim: Quarterly retrospective monitoring of RhD antigen determination results in voluntary blood donors at the National Blood Transfusion Institute of Serbia (NBTI), in which RhD negative result was obrtained.
Material and methodology: Study involving 2529 blood samples from RhD negative donors. In addition to routine testing, these samples were also tested with the "weak D" test using Capture R select and Novaclone Anti-D reagents by microplate technique on the NEO Iris device.
Results: Determination of ABO/RhD blood group of voluntary blood donorsat the NBTI is routinely performed using microplate technique on the automatic platforms. All Rh D-negative donors with C or E antigene are further checked for thepresence of RhD antigen using gel technique. A total of 2529 donor blood samples, routinely determined as RhD-negative, were tested with the "weak D" test. In 137 donors, Rh phenotype was determined as Ccddee (5.4%),ccddEe in 41 (1.6%), CCddee in 2 (0.08%) andCcddEe in 2 (0.08%). Remaining tested donors were ccddee. RhD antigen test results showed discrepancy in three blood samples (0.12%). In all three donors, RhD antigen serologically was proven by adsorption and elution technique. Those donors needed to be further investigated using molecular technique to accurately determine RhD status.
Conclusion: Current testing mode does not identify all weak D phenotypes. The conducted test indicates that Capture R select / Novaclone Anti-D "weak test" is more sensitive than other routine methods for detecting weaker RhD antigen variants. Problems with RhD antigen testing can be overcome by a combination of serological testing and molecular techniques.
Keywords: blood donors, weak D, molecular typing

UP 34

REZULTATI ISPITIVANJA SKRININGA ANTITELA NA APARATIMA QWALIS1 I NEO IRIS U PERIODU OD 01.07.2016. GODINE DO 30.06.2022. GODINE

Stamenić Lj.[1], Dukić Novaković M[1], Jovičić M[2], Antonijević I[1], Damjanović V[1], Đilas I[1]
[1] Institut za transfuziju krvi Srbije, Beograd, Srbija2, KBC Dr Dragiša Mišović-Dedinje, Beograd, Srbija

UVOD: Otkrivanje klinički značajnih antitela u plazmi dobrovoljnih davalaca krvi (DDK) je od velike važnosti, jer ta antitela mogu dovesti do nastanka hemolizne transfuzijske reakcije kod pacijenta. Pri testiranju jedinica krvi uz određivanje krvne grupe i RhD fenotipa,obavezno je i testiranje skrininga iregularnih antitela.
CILJ RADA: Prikaz i analiza rezultata testiranja skrininga iregularnih antitela kod dobrovoljnih davalaca krvi (DDK) u Institutu za transfuziju krvi Srbije (ITKS), u periodu od 1.07.2016–1.07.2022.godine.
METODI RADA: Analizirani su podaci o broju urađenih skrininga iregularnih antitela na automatskim analizatorima (Qwalis1 i Neo Iris). Skrining iregularnih antitela se radi u mikrotitarskoj ploči metodom indirektnog antiglobulinskog testa, uz upotrebu komercijalnih test eritrocita. Kod pozitivnih rezultata, identifikacija antitela obavljala se manuelno metodom u gelu i metodom u epruveti, uz upotrebu komercijalnih test eritrocita radi utvrđivanja specifičnosti antitela.
REZULTATI: U periodu od šest godina skrining iregularnih antitela urađen je za 433838 uzoraka dobrovoljnih davalaca krvi, afereznih trombocita i rekonvalescentne Covid plazme. Broj preliminarno pozitivnih skrininga iregularnih antitela je 1583 (0,36%), od tog broja nakon ponavljanja i identifikacije kod 861 DDK skrining iregularnih antitela je negativan (54%). Kod 722 DDK identifikovana su sledeća antitela : papainska antitela neutvrđene specifičnosti identifikovana su kod 214 DDK (29,6%), hladna antitela neutvrđene specifičnosti identifikovana su kod 147 DDK (20,3%). Klinički značajna antitela su identifikovana kod 361 DDK (50 %), od toga je anti D je identifikovano kod 71 DDK (20%), anti K kod 64 DDK (18 %), anti E kod 37 DDK (10 %), anti c kod 11 DDK (3 %), anti C kod 6 DDK (1,6 %), anti e kod 4 DDK (1,1%), anti M kod 44 DDK (12%). Ostala klinički značajna antitela učestvuju u manjem procentu identifikacija.
ZAKLJUČAK: Testiranje na automatskim analizatorima Qwalis1 i Neo Iris podiglo je osetljivost testiranja i doprinelo većoj bezbednosti primenjene krvi i produkata od krvi pacijentima.

Ključne reči: automatizacija, skrining, identifikacija.

UP 34

RESULTS OF ANTIBODY SCREENING ON THE QWALIS1 AND NEO IRIS DEVICES IN THE PERIOD 01.07.2016 TO 30.06.2022.

Stamenić Lj.[1], Dukić Novaković M[1], Jovičić M[2], Antonijević I[1], Damjanović V[1], Đilas I[1]
[1] Blood Transfusion Institute of Serbia, Donor Testing Department, Belgrade, Serbia
[2] Clinical Hospital Centar Dr. Dragiša Mišović-Dedinje, Belgrade, Serbia

INTRODUCTION: The detection of clinically significant antibodies in the plasma of voluntary blood donors (VBD) is of great importance, because these antibodies can lead to a hemolytic transfusion reaction in the patient. When testing blood units in addition to determining the blood group and RhD phenotype, it is also mandatory to test the presence of irregular antibodies.
OBJECTIVE OF THE WORK: Presentation and analysis of the results of irregular antibody screening in voluntary blood donors (VBD) at the Blood Transfusion Institute of Serbia (BTIS), in the period from July 1, 2016 to July 1, 2022.
METHODS: Total number of irregular antibody screenings, performed on automatic analyzers (Qwalis1 and Neo Iris) were analyzed. Screening of irregular antibodies is done in a microtiter plate using the indirect antiglobulin test method, using commercial test erythrocytes. In the case of positive results, antibody identification was performed manually using the gel method and the test tube method, with commercial test erythrocytes to determine the specificity of the antibody.
RESULTS: In a period of six years, irregular antibody screening was performed for 433 838 samples of voluntary blood donors, apheresis platelets and convalescent Covid plasma. The number of preliminary positive irregular antibody screenings is 1583 (0.36%), after repetition and identification, 861 irregular antibody screenings were negative (54%). At 722 VBD the following antibodies were identified: papain antibodies of undetermined specificity were identified in 214 VBD (29,6%), cold antibodies of undetermined specificity were identified in 147 VBD (20,3%). Clinically significant antibodies were identified in 361 VBD (50%), of which anti D was identified in 71 VBD (20%), anti K in 64 VBD (18%), anti E in 37 VBD (10%), anti c in 11 VBD(3%), anti C in 6 VBD (1,6%), anti e in 4 VBD (1,1%), anti M in 44 VBD (12%). Other clinically significant antibodies participate in a smaller percentage of identifications.
CONCLUSION: Testing on automatic analyzers Qwalis1 and Neo Iris increased the sensitivity of testing and contributed to greater safety of administered blood and blood products to patients.

Keywords: automation, screening, identification.

UP 35

POVEZANOST ABO KRVNO GRUPNOG SISTEMA SA NIVOOM IgG ANTI-KOVID ANTITELA KOD DAVALACA REKONVALESCENTNE PLAZME

Korać N[1], Andrić Z[1], Milin J[2], Blagojević G[1],Vavić N[1],Jovičić M[3], Bosnić V[1], Mijucić V[1]
[1] Institut za transfuziju krvi Srbije, Beograd
[2] Katedra za medicinsku statistiku i informatiku,Medicinski fakultet Univerziteta u Beogradu
[3] Kliničko bolnički centar Dr "Dragiša Mišović", Beograd

Uvod: Određene studije u kojima je ispitivana povezanost SARS-CoV-2 infekcije sa ABO krvno grupnim sistemom, su pokazale da osobe krvne grupe O ređe oboljevaju, u odnosu na osobe drugih krvnih grupa. U dosadašnjim studijama takođe je pokazano, da nivo IgG anti-kovid antitela nakon infekcije,korelira sa godinama, muškim polom i težinom bolesti, ali je povezanost sa ABO krvno grupnim sistemom nepoznata.Cilj rada: Ispitivana je povezanost ABO krvno grupnog sistema sa nivoom IgG anti-kovid anitela kod davalaca rekonvalescentne plazme nakon preležane infekcije. Metod: Ispitivani su davaoci uzrasta od 18 do 40 godina, TM iznad 60 kg, bez komorbiditeta. Svim davaocima na prvom pregledu određena je krvna grupa u ABO sistemu metodom u mikroploča na aparatu Qwalys 3 i NeoIris. Nivo IgG antitela meren je testom Covid-19 Elisa IgG Vircell i prikazan je indeksom. Indeks IgG>6 je bio pozitivan, IgG 4-6 indeterminantan, IgG<4 negativan. Rezultati:Ispitivanjem je obuhvaćeno 748 dobrovoljnih davalaca rekonvalescentne plazme, koji su preležali COVID-19 infekciju ili su imali ranije određen pozitivan test IgG anti-covid antitela. Davaoca muškog pola bilo je 523 (69.9%), ženskog pola 225 (30.1%). Davaoca krvne grupe O bilo je 236 (31.5%), krvne grupe A 345 (46.1%), krvne grupe AB 52 (6.9%), krvne grupe B 116 (15.5%). Srednja vrednost indeksa antitela kod davalaca krvne grupe 0 bila je 22.26 (7.99-41.17), krvne grupe A bila je 17.43 (6.92-36.03), krvne grupe AB bila je 23.14 (10.54-35.11), a krvne grupe B 19.44 (6.66-39.29). Najviši nivo indeksa antitela je zabeležena kod davalaca krvne grupe AB, razlika je bila blizu konvencionalnog nivoa značajnosti (p=0.096). Zaključak: Davaoci krvne grupe AB imaju višu srednju vrednost indeksa antitela. Potrebne su studije na većem broju pacijenata kako bi se utvrdila povezanost krvne grupe i nivoa IgG anti-kovid antitela.
Ključne reči: ABO krvno grupni sistem, antitela, SARS-CoV-2 infekcija

UP 35

ASSOCIATION OF THE ABO BLOOD GROUP SYSTEM WITH THE LEVEL OF IgG ANTI-COVID ANTIBODIES IN DONORS OF CONVALESCENT PLASMA

Korać N[1], Andrić Z[1], Milin J[2], Blagojević G[1], Vavić N[1], Jovicic M[3], Bosnić V[1], Mijucić V[1]
[1] Institute for Blood Transfusion of Serbia, Belgrade
[2]Department for medical statistics and informatics, Faculty of Medicine, University of Belgrade,
[3]Clinical Hospital Center "Dr Dragiša Mišović",Belgrade

Certain studies investigating the association of SARS-CoV-2 infection with the ABO blood group system, have shown that people with blood group O are less often infected than people with other blood groups. Previous studies have also shown that the level of IgG anti-covid antibodies after infection correlates with age, male gender and the severity of the disease, but the connection with the ABO blood group system is unknown. The association of the ABO blood group system with the level of IgG anti-covid antibodies in donors of convalescent plasma after a prolonged infection was investigated. The examined donors had 18- 40 years, a body mass above 60 kg and no comorbidities. At the first examination, blood group of donors was determined in the ABO system using the microplate method on the Qwalys 3 and NeoIris devices. The level of IgG antibodies was measured by the Covid-19 Elisa IgG Vircell test and is shown as an index. The index IgG>6 was positive, IgG 4-6 indeterminate, IgG<4 negative. The study included 748 voluntary donors of convalescent plasma, who had undergone a COVID-19 infection or had previously determined a positive IgG anti-covid antibody test. There were 523 male donors (69.9%), 225 female donors (30.1%). There were 236 donors of blood group O (31.5%), blood group A 345 (46.1%), blood group AB 52 (6.9%), blood group B 116 (15.5%). The mean value of the antibody index in blood group O donors was 22.26 (7.99-41.17), blood group A was 17.43 (6.92-36.03), blood group AB was 23.14 (10.54-35.11), and blood group B 19.44 (6.66- 39.29). The highest level of antibody index was recorded in donors of blood group AB, the difference was close to the conventional level of significance (p=0.096). AB blood group donors have a higher mean value of antibody index. Studies on a larger number of patients are needed to determine the association between blood type and IgG anti-covid antibody levels.
Key words: ABO blood group system, antibodies, SARS-CoV-2 infection

UP 36

PREVALENCA ANTIERITROCITNIH ANTITELA U KLINIČKO BOLNIČKOM CENTRU ZVEZDARA

Borovinić J, Komatina B, Paunović M.
Kliničko bolnički centar Zvezdara, Beograd, Srbija

Uvod: Aloimunizacija eritrocitnim antigenima predstavlja razvoj antitela nakon izlaganja stranim eritrocitima tokom transfuzije, transplantacije ili trudnoće. Multitransfundovani pacijenti imaju veliki rizik za aloimunizaciju i nastanak više antieritrocitnih antitela. Prisustvo aloantitela može dovesti do kasne hemolizne ili serološke transfuzijske reakcije i otežati pronalazak kompatibilne jedinice krvi za buduće transfuzije.
Cilj: Prikaz i analiza rezultata identifikacije antieritrocitnih antitela u šestogodišnjem periodu.
Materijal i metode: Podaci su dobijeni retrospektivnom analizom perioda od 01.01.2016. do 31.12.2021. Izvor podataka su imunohematološki protokoli Službe za snadbevanje krvlju i krvnim produktima KBC Zvezdara i zdravstveni informacioni sistem Heliant. Skrining i identifikacija antitela rađeni su gel metodom sa komercijalnim test eritrocitima Serascan Diana 2, Serascan Diana 3 i Identisera Diana/Extend P panelom (Grifols, Barcelona, Spain).
Rezultati: U ispitivanom periodu imunohematološki je testirano 9880 pacijenata. Otkriveno je 265 iregularnih antitela kod 232 pacijenta, od toga 165 (71,1%) ženskog i 67 (28.9%) muškog pola. Najučestalije specifično antitelo je anti-K (22,64%), potom slede anti-E (16,6%), anti-D (14.34%), anti-Jka (5,28%), anti-M (4,91%), anti-c (4,53%), anti-C (4,15%) i anti-Fya (4,15%). Kod 27 pacijenata otkrivena su 2 aloantitela. Najčešće kombinacije aloantitela su anti-D+anti-C (6 pacijenata) i anti-E+anti-K (5 pacijenata). Tri pacijenta su imala 3 aloantitela (anti-D+anti-C+anti-K, anti-D+anti-K+anti-Jka, anti-E+anti-Cw+ anti-K). Antitela neutvrđene specifičnosti nađena su kod 43 pacijenata.
Zaključak: U našem istraživanju najčešća antieritrocitna antitela su iz Rh i Kell krvnogrupnih sistema (64,15%). Određivanje Rh(C,c,E,e) i Kell fenotipa pacijenata i dobrovoljnih davaoca krvi i transfuzija podudarnih jedinica eritrocita može značajno smanjiti učestalost antieritrocitnih antitela.
Ključne reči: aloimunizacija, aloantitela, identifikacija

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PREVALENCE OF ANTIERYTHROCYTE ANTIBODIES IN ZVEZDARA UNIVERSITY MEDICAL CENTER

Borovinić J, Komatina B, Paunović M.
Zvezdara University Medical Center, Belgrade, Serbia

Introduction: Red blood cell (RBC) alloimmunization is defined as the development of antibodies after exposure to foreign RBC due to transfusion, transplantation or pregnancy. Multi-transfused patients have high risk of alloimmunization and development of multiple anti-erythrocyte antibodies. The presence of alloantibodies can result in delayed hemolytic or serological transfusion reactions and may make finding of compatible RBC units difficult.
Objective: To present and analyze results of anti-erythrocyte identification over a period of six years.
Materials and methods: A retrospective analysis of the period from 01.01.2016. to 31.12.2021. Data collection was made from the immunohaematology protocols of the Department of supply of blood and blood products and health information system Heliant. Antibody screening and identification were performed by gel method with commercial test erythrocyte reagents Serascan Diana 2, Serascan Diana 3 and Identisera Diana/Extend panel (Grifols, Barcelona, Spain).
Results: During the study period, in 9880 patients immunohaematology tests were performed. A total of 265 irregular antibodies were discovered in 232 patients, 165 (71,1%) female and 67 (28.9%) male. The most common alloantibody was anti-K (22,64%), followed by anti-E (16,6%), anti-D (14.34%), anti-Jka (5,28%), anti-M (4,91%), anti-c (4,53%), anti-C (4,15%) and anti-Fya (4,15%). In 27 patients we found 2 associated alloantibodies. The most frequent combinations were anti-D+anti-C (6 patients) and anti-E+anti-K (5 patients). Three patients had 3 associated alloantibodies (anti-D+anti-C+anti-K, anti-D+anti-K+anti-Jka, anti-E+anti-Cw+ anti-K). Antibodies of undetermined specificity were found in 43 patients.
Conclusion: We observed that the most frequent anti-erythrocyte antibodies are directed towards Rh and Kell blood group systems (64,15%). Performing Rh(C,c,E,c) and Kell phenotyping for the patients and blood donors with antigen matching transfusions can significantly reduce alloantibodies frequency.
Keywords: alloimmunization, alloantibodies, identification

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HAEMOLYTIC TRANSFUSION REACTION DUE TO ANTI-Jka – CASE REPORT

Velkova E[1], Srzentic S[2], Hristova A[1], Makarovska- Bojadzieva T[1], Dejanova Ilijevska V[1], Petkovic E[1], Ristovska E[1], Todorovski B[1]
[1] *Institute for Transfusion Medicine of North Macedonia*
[2] *Institute for Blood Transfusion of Serbia*

Introduction: Kidd blood group system has a special importance in transfusion medicine as the antibodies to Kidd antigens tend to go down to undetectable levels but show an anamnestic response on exposure through pregnancy or blood transfusion and cause hemolytic transfusion reaction, most commonly delayed transfusion reaction.
Aim: We report a patient who developed alloantibodies to 'Kidda' antigen leading to delayed hemolytic transfusion reaction.
Material and methods: The patient, female, 5 years old, diagnosed as Anemia Cooley, blood groups O, Rh(D)-positive. Until 4 months ago, stable without the need of transfusion, when in last 4 months she received 5 transfusions of red blood cells (RBC's). Pretransfusion tests were negative each time. After the last transfusion Hb begin to drop rapidly. After 15 days the need of transfusion arose again, antibody screenings were: indirect antiglobulin test (IAT) negative, enzyme 1+,direct antiglobulin test (DAT) and autoantibodies 3+ positive,cross match (CM) with two units of O Rh+ RBC's were negative. We performed additional tests: identification in IAT was negative, with enzyme were non-interpretable, acid elution and identification on 37°C show presence of anti-Jka antibody. Serologic phenotype and PCR typing of Jka antigen showed negative result for the patient and positive for both units of RBC's, which were previouly negative.
Conclusion: The antibody was the cause of an delayed hemolytic reaction associated with the transfusion of Jk (a+) blood units. We emphasize the steps for detecting these antibodies and the precautions to be taken once these antibodies are identified.
Key words: alloimmunization, anti Jka, delayed hemolytic transfusion reaction

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SIGNIFICANCE OF RHD GENOTYPING IN PRENATAL RHIG PROPHYLAXIS

Velkova E, Makarovska-Bojadzieva T, Hristova-Dimceva A, Dejanova-Ilijevska V, Petkovic E, Ristovska E, Drakulevska S, Todorovski B.
Institute for transfusion medicine of North Macedonia
Skopje
North Macedonia

Aim: Genotyping can reduced antenatal use of RhIG, safe reserve of RhD-negative blood and improve the management of high risk sensibilised pregnancies.
Material and methods: All pregnant women were tested for ABO, RhD, Rh phenotype, K and screening of alloantibodies in the first trimester of pregnancy. Pregnant women who have the DVI phenotype are typed as D−negative. Pregnant women, 50 in total, with weak expression of D, with score<2+, including those with DEL phenotype, were tested with a panel of D monoclonal antibodies, commercial kit (ID-Partial RhD Typing Set, Bio Rad)), or by molecular testing (Ready Gene RBC ABO, CDE, Dweak, Inno Train), for RhD variants. The results that we have obtained showed that 17 samples were RhD-negative and 33 samples showed results for weak D: weak D Type1 (60,6%),Type 2 (12,2%),Type 3 (24,2%) and only 1 pregnant woman was RhD Type 4. The research also included 30 pregnant women in whom the RhD fetal status had been detected by noninvasive technique from the mother's plasma, by Real time PCR method. Obtained results for fetalRhD status demonstrate that 9 fetuses were RhD- negative and 21RhD-positive.
Conclusion: In our study only 3% of RhD-negative mothers needed RhIG prophylaxis, and 97% were weak D variants 1-3 that we can consider as RhD-positive and we provide RhIG antenatal prophylaxis in 97% unnecessarily. Subsequently they can be transfused with RhD-positive blood and save a stock of RhD-negative blood. The advantage of RhD fetal status is avoiding prophylaxis in 30% of RhD negative, sensibilised pregnant women can be saved from unnecessary testing, since there is no risk of HBFN.
Key words: noninvasive RhD genotyping in pregnancy, RhIG prophylaxis

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SEROLOŠKA I MOLEKULARNA IMUNOHEMATOLOŠKA TESTIRANJA U PREVENCIJI I DIJAGNOSTICI RhD IMUNIZACIJE U TRUDNOĆI

Vlatković A., Jovanović Srzentić S., Radović I.
Institut za transfuziju krvi Srbije, Beograd, Srbija

Uvod: Prema sadašnjim preporukama, na prvu imunohamatološku kontrolu svaka trudnica bi trebalo da dođe već od 12. nedelje trudnoće da bi se utvrdila krvna grupa u ABO i Rh i eventualno prisustvo antitela. U situacijama kada postoje nepodudarnosti u rezultatima serološkog ispitivanja RhD antigena ili je prisutan serološki slab D fenotip (Dweak), neophodno je uraditi molekularno ispitivanje prisustva D alele, da bi se dala pravovremena i odgovarajuća preporuka za primenu RhD imunoprofilakse.
Cilj rada:Utvrditi prisustvo varijanti D antigena u populaciji trudnica.
Materijal i metod:U Institutu za transfuziju krvi Srbije, na Odeljenju za imunohematološka ispitivanja, izvršena je analiza podataka molekularnih ispitivanja za period 2020.- 2022. godine.
Ispitivanje RhD fenotipa se radi metodom u epruveti sa monoklonskim anti-D test serumima (IgM i mešavinom IgM i IgG, ImuMed) humanog porekla, uz eventualnu upotrebu antihumanog globulina i tehnike indirektnog antiglobulinskog testa (IAT), u slučaju izostale ili slabe aglutinacije. Za potvrdu Dweak se koriste anti-IgG rabbit kartice i monoklonski IgG anti-D test serum (BioRad).
Molekularna ispitivanja prisustva RHD alele se vrše na izolovanoj DNK trudnica koje su serološki bile RhD-negativne, a u Rh fenotipu imale C i/ili E i onih koje su imale serološki slab oblik D antigena PCR-SSP metodom (RBC-FluoGene D weak/variant, FluoGene® Inno-train Diagnostik GmbH, Germany).
Rezultati: Od 2020. godine testirano je ukupno 42 trudnice, od kojih su 22 serološki bile RhD- negativne, a u Rh fenotipu imale C i/ili E i 20 koje su imale Dweak. Ni kod jedne trudnice,koje su serološki bile RhD-negativne, a u Rh fenotipu imale C i/ili E, molekularnom metodom nije utvrđeno prisustvo RHD alele, a kod trudnica koje su imale serološki slab oblik D antigena, 10 je imalo Dweak tip 1 a 10 tip 2.
Zaključak:Molekularna ispitivanja RhD genotipa su važna ne samo za donošenje odluke o neophodnosti primene RhD imunoprofilakse, već i racionalne primene RhD-negativne krvi.
Ključne reči: RhD imunoprofilaksa, molekularna testiranja, slabi D

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SEROLOGICAL AND MOLECULAR IMMUNOHAEMATOLOGICAL TESTING IN THE PREVENTION AND DIAGNOSIS OF RhD IMMUNIZATION IN PREGNANCY

Vlatković A., Jovanović Srzentić S., Radović I.
Blood Transfusion Institute of Serbia, Belgrade, Serbia

Introduction: According to current recommendations, every pregnant woman should come for the first check-up around the 12th week of pregnancy to determine the in ABO and Rh blood group and presence of antibodies. In situations where there are inconsistencies in the results of serological testing of RhD or there is a serologically weak D phenotype (Dweak), it is necessary to perform molecular testing for presence of D allele, in order to give adequate recommendation for RhD immunoprophylaxis.
Aim: Determining presence of D antigen variants in the population of pregnant women.
Material and method: In Blood Transfusion Institute of Serbia, at the Department for Immunohaematological Testing, analysis of molecular testing data for the period 2020.-2022. was performed.
RhD phenotype is tested using the test tube method with monoclonal anti-D test serums (IgM and IgM/IgG, ImuMed) of human origin with antihuman globulin and the indirect antiglobulin test (IAT) in case of weak or absent agglutination. Anti-IgG rabbit cards and monoclonal IgG anti-D test serum (BioRad) are used to confirm Dweak.
Molecular testing for presence of RHD alleles are performed on DNA isolated from pregnant women who were serologically RhD-negative and have C and/or E in Rh phenotype, and those who had a serologically weak form of D antigen using PCR-SSP method (RBC-FluoGene Dweak/variant, FluoGene® Inno-train Diagnostik GmbH, Germany).
Results: From year 2020, a total of 42 pregnant women were tested, 22 of whom were serologically RhD-negative, and had C and/or E in Rh phenotype and 20 who had Dweak phenotype. In none of the pregnant women, who were serologically RhD-negative, and had C and/or E in the Rh phenotype, was RHD allele determined by the molecular method, and among the pregnant women who had Dweak phenotype, 10 had type 1 and 10 type 2.
Conclusion: RhD genotyping will not only determine accurate management of RhD immunoprophylaxis but will also rationalize use of RhD-negative blood.

Key words: RhD immunoprophylaxis, molecular testing, Dweak

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POTVRDA ANTI-G ANTITIJELA KOD NOVOROĐENČETA SA POZITIVNIM DIREKTNIM ANTIGLOBULINSKIM TESTOM - PRIKAZ SLUČAJA

Vučinić S, Praštalo-Grubiša M, Zonjić J, Šćepanović T, Rašović G, Cvijović A.
Zavod za transfuziju krvi Crne Gore (ZTKCG), Podgorica, Crna Gora

Uvod: Anti-G antitijelo se dokazuje tehnikom dvostruke adsorpcije i elucije ili jednostepenom adsorpcijom i elucijom sa R2R2 ili r'r eritrocitima uz obaveznu "D-diferencijaciju". Anti-G antitijelo najčešće ne dovodi do HBFN, a ako se javi HBFN, ona je sa blažom kliničkom slikom čak i kada je DAT novorođenčeta pozitivan.
Cilj: Prikazati prvu potvrdu anti-G antitijela kod novorođenčeta sa pozitivnim DAT-om.
Prikaz slučaja: Trudnica starosti 36 godina, četvrta trudnoća, uredno sprovedena RhD imunoprofilaksa u predhodnim trudnoćama, tri Rh- pozitivna djeteta. Prenatalnim skriningom u trećem mjesecu četvrte trudnoće identifikovana su anti-D + C aloantitijela, titar anti-D bio je veći od titra anti-C, ali oba ispod kritičnih vrijednosti za HBFN. Nije rađena "G-diferencijacija". Suprug trudnice je A, RhD+, CcDEe, K+.U 4. i 5. kontroli antitijela titar anti-D i anti-C je bio izjednačen, a potom u 6. kontroli titar anti-D je bio manji od titra anti-C. Postupkom dvostruke adsorpcije i elucije dokazano je anti-G aloantitijelo. O rezultatu identifikacije obaviješten je ginekolog i data je preporuka za RhD imunoprofilaksu.Trudnica je porođena prirodnim putem , krvna grupa novorođenčeta je A+,CcDee, K+, sa pozitivnim DAT 3+ gel metodom. U serumu novorođenčeta enzimskom tehnikom je identifikovano anti-G, IAT je bio negativan, a identifikacijom eluata sa eritrocita novorođenčeta kao i identifikacijom eluata sa r'r eritrocita nakon adsorpcije eluata novorođenčeta na r'r eritrocite potvrđeno je anti-G antitijelo. Novorođenče je bilo bez kliničkih i laboratorijskih pokazatelja hemolizne bolesti .
Zaključak: Diferencijacija D+C od anti-G ili G+C u prenatalnoj dijagnostici kod aloimunizovanih trudnica je bitna zbog adekvatnog vođenja trudnoće, kliničke prognoze HBFN i primjene RhD imunoprofilakse RhD- negativnim trudnicama.
Ključne riječi: anti-G antitijelo, DAT, adsorbcija i elucija, identifikacija antitijela

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CONFIRMATION OF ANTI-G ANTIBODIES IN A NEWBORN WITH A POSITIVE DIRECT ANTIGLOBULIN TEST - CASE REPORT

Vucinic S, Prastalo-Grubisa M, Zonjic J, Scepanovic T, Rasovic G, Cvijovic A.
Institute for Blood Transfusion of Montenegro, Podgorica, Montenegro

Introduction: Anti-G antibody is proven by double adsorption and elution technique or single step adsorption and elution with R2R2 or r'r erythrocytes with mandatory "D-differentiation". The anti-G antibody most often does not lead to HDFN, and if HDFN occurs, it has a milder clinical picture even when the newborn's DAT is positive.
Objective: To present the first confirmation of anti-G antibody in a DAT-positive newborn.
Case report: Pregnant woman, 36 years old, fourth pregnancy, properly administered RhD immunoprophylaxis in previous pregnancies, three RhD-positive children. Prenatal screening in the third month of the fourth pregnancy identified D + C alloantibodies, the anti-D titer was higher than the anti-C titer, but both were below the critical values for HDFN. "G-differentiation" was not performed.
The pregnant woman's husband is A+,CcDEe, K+.
In the 4th and 5th antibody controls, the titers of anti-D and anti-C were equal, and then in the 6th control, the anti-D titer was lower than the anti-C titer.
Anti-G alloantibody was demonstrated by double adsorption and elution procedure. The gynecologist was informed about the result of the identification and a recommendation was given for RhD immunoprophylaxis.
The pregnant woman had natural childbirth , the blood group of the newborn is A+, CcDee, K+ with a positive DAT 3+ in gel method. Anti-G was identified in the newborn's serum using an enzymatic technique, the IAT was negative, and the identification of the eluate from the newborn's erythrocytes, as well as the identification of the eluate from r'r erythrocytes after adsorption of the newborn's eluate on r'r erythrocytes, confirmed the anti-G antibody.
The newborn was without clinical and laboratory indicators of hemolytic disease.
Conclusion: Differentiation of anti-D+C from anti-G or from G+ C in prenatal diagnosis in alloimmunized pregnant women is important for adequate management of pregnancy, clinical prognosis of HDFN and application of RhD immunoprophylaxis to RhD-negative pregnant women.
Key words: anti-G antibody, DAT, adsorption and elution, antibody identification

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ABO HEMOLITIČKA BOLEST NOVOROĐENČETA A2B KRVNE GRUPE S NEGATIVNIM DIREKTNIM COOMBS TESTOM , MAJKE B KRVNE GRUPE – PRIKAZ SLUČAJA

Ivana Talić Drlje, Anita Primorac Marić
Transfuzijski centar, Sveučilišna klinička bolnica Mostar, Bosna i Hercegovina

Uvod: ABO hemolitička bolest novorođenčeta (HBN) je najčešći uzrok hemolize eritrocita novorođenčeta. Iako u 15-20% svih trudnoća postoji ABO inkompatibilnost majke i fetusa najčešće se HBN javlja ukoliko je majka krvne grupe O, a novorođenče A ili B.
Materijali i metode: Imunohematološko testiranje učinjeno je tehnikom u mikrogel kartici proizvođača Grifols. Molekularno određivanje krvne grupe određeno je metodom PCR-SSP na uređaju FluoVista upotrebom kita RBC-Fluogene ABO.
Prikaz slučaja: U svibnju 2022. godine zaprimljen je uzorak muškog novorođenčeta gestacijske dobi 28+5/7 tjedana, koje je po porodu hospitalizirano u Jedinici intenzivnog liječenja zbog neonatalne sepse i intrakranijalnog krvarenja. Treći dan života zbog snižene vrijednosti hemoglobina indicirano je transfuzijsko liječenje. Imunohematološkim testiranjem određena je krvna grupa AB-poz; Ccee; Cw-negativan; K-neg; direktni Coombs test (DCT) negativan. Urađena interrakcija s dozom krvi AB-poz., je bila pozitivna (DCT doze negativan). Isti rezultat interakcije dobili smo i sa dozama krvne grupe AB-neg, A-poz. i A-neg. Interakcija s dozom krvi B-poz. i B-neg. krvne grupe bila je negativna.Takav rezultat pobudio je sumnju u ABO HBN uzrokovanu majčinim anti-A antitijelima. Rezultati testiranja majke su: krvna grupa B-neg., ccee, K-neg, ICT-negativan. Molekularnim testiranjem uzorka krvi novorođenčeta odredi se A2B krvna grupa, što objašnjava negativan DCT polispecifičnim AHG testom. Zbog sumnje na postojanje anti-A antitijela uradi se monospecifični IgG DCT koji je pozitivan, a elucijom se dokaže postojanje anti-A antitijela.
Zaključak: Iako u literaturi postoji dosta podataka koji nas obavezuju na imunohematološko testiranje novorođenčadi majki O krvne grupe, zbog povišenog IgG titra anti-A i anti-B antitijela, ovim prikazom želimo skrenuti pozornost na mogućnost razvoja ABO HBN i kod majki koje su krvne grupe A i B. U ovom slučaju je ABO HBN bilo teže dokazati zbog postojanja podgrupe A2B kod novorođenčeta.
Ključne riječi: ABO HBN; anti-A antitijela; direktni Coombs test

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UVOĐENJE NOVE METODE TESTIRANJA ANTITROMBOCITNIH ANTITELA U DIJAGNOSTICI FETALNE I NEONATALNE ALOIMUNE TROMBOCITOPENIJE

Dmitrović J., Dukić T., Srzentić Jovanović S.,Andrić Z.
Institut za transfuziju krvi Srbije

Uvod: Fetalna i neonatalna aloimuna trombocitopenija (FNAIT) je stanje uzrokovano destrukcijom fetalnih trombocita. Nastaje usled imunizacije majke i stvaranja antitela usmerenih na fetalne antigene nasleđene od oca. Nakon isključenja drugih uzroka trombocitopenije, u dijagnostici ovog stanja od značaja je testiranje seruma na prisustvo antitrombocitnih antitela. Od 2021. godine na Odeljenju za tipizaciju tkiva, Instituta za transfuziju krvi Srbije, uvedena je i validirana metoda za dokazivanje prisustva i utvrđivanja specifičnosti antitrombocitnih antitela (anti-HPA).
Cilj rada: Prikaz prvih rezultata uvođenja nove metode u testiranju seruma ispitanika sa sumnjom na FNAIT.
Materijal i metode: U periodu od jula 2021. do avgusta 2022. godine, testirano je 27 seruma trudnica, porodilja, fetusa, neonatusa i žena koje se pripremaju za predstojeću trudnoću. Za detekciju antitela u serumu ispitanika primenjen je Lifecodes Pak Lx kvalitativni imunoesej (Immucor) zasnovan na principu Luminex 200 platforme. Za interpretaciju rezultata korišćen je sofver MATCHIT! Platelet Ab.
Rezultati: Od ukupnog broja testiranih ispitanika bilo je 8 (30%) trudnica sa ultrazvučno dijagnostikovanim promenama ploda, 6 (22%) žena nakon porođaja ili pobačaja, 10 (37%) neonatusa, 2 (7%) žene u pripremnoj fazi za narednu trudnoću i 1 fetus. Anti-HPA antitela detektovana su u 15% slučajeva (u serumima 2 trudnice i 2 neonatusa). Od toga, kod jedne trudnice dokazano je prisustvo klinički najznačajnijeg anti-HPA-1a antitela.
Zaključak: Uvedena metoda omogućava pouzdano otkrivanje klinički najznačajnijih anti-HPA antitela, što doprinosi dijagnozi FNAIT-a i važno je za praćenje svake naredne trudnoće. Pravovremeno otkrivanje HPA-1a negativnih trudnica primenom antenatalnog HPA screeninga bila bi najbolja strategija u prevenciji FNAIT-a.
Ključne reči: Antitrombocitna antitela, FNAIT, Luminex metoda

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IMPLEMENTATION OF A NEW METHOD FOR PLATELET ANTIBODIES TESTING IN THE DIAGNOSIS OF FETAL AND NEONATAL ALLOIMMUNE THROMBOCYTOPENIA

Dmitrović J, Dukić T, Srzentić Jovanović S, Andrić Z.
Blood Transfusion Institute of Serbia

Introduction: Fetal and neonatal alloimmune thrombocytopenia (FNAIT) is a condition caused by the destruction of fetal platelets. It occurs as a result of maternal immunization and the formation of antibodies directed against fetal platelet antigens inherited from the father. After excluding other causes of thrombocytopenia, serum testing for the presence of platelet antibodies is important in the diagnosis of this condition. Since 2021, the Tissue Typing Department, Blood Transfusion Institute of Serbia, has introduced and validated a method for screening and identification of platelet antibodies (anti-HPA).
The Aim: Presentation of the first sera testing results of patients with suspected FNAIT, after the implementation of the new method. Material and methods: During the period from July 2021 to August 2022, 27 sera of pregnant women, postpartal women, fetuses, neonates and women preparing for an upcoming pregnancy were tested. The Lifecodes Pak Lx qualitative immunoassay (Immucor) based on the principle of the Luminex 200 platform, was used to detect antibodies in the sera of the subjects. The software MATCHIT! Platelet Ab was used to interpret the results. Results: Out of the total number of tested subjects, there were 8 (30%) pregnant women with ultrasound-diagnosed fetal changes, 6 (22%) women after childbirth or miscarriage, 10 (37%) neonates, 2 (7%) women preparing for the next pregnancy and 1 fetus. Anti-HPA antibodies were detected in 15% of cases (in the sera of 2 pregnant women and 2 neonates). Out of this, the presence of the most clinically significant anti-HPA-1a antibody was demonstrated in one pregnant woman. Conclusion: The introduced method enables the reliable detection of clinically significant anti-HPA antibodies, which contributes to the diagnosis of FNAIT and is important for monitoring each subsequent pregnancy. Timely detection of HPA-1a negative pregnant women using antenatal HPA screening would be the best strategy in the prevention of FNAIT.
Key words: Platelet antibodies, FNAIT, Luminex method

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IDENTIFIKACIJA MULTIPLIH ANTITIJELA I ANTITIJELA NA ANTIGEN VELIKE UČESTALOSTI KOD ALOIMUNIZOVANE TRUDNICE –PRIKAZ SLUČAJA

Praštalo-Grubiša M, Rašović G, Vučinić S, Šćepanović T, Cvijović A, Zonjić J.
Zavod za transfuziju krvi Crne Gore

Uvod:Aloimunizacija u trudnoći nosi rizik za nastanak HBFN, može da pravi problem u određivanju specifičnosti antitijela i pravovremenom obezbjeđivanju krvi za majku i/ili novorođenče, naročito kada su prisutna multipla antitijela i/ili antitijelo na antigen velike učestalosti.
Cilj:Izvještavanje o prvom slučaju fetomaternalne eritrocitne nekompatibilnosti koja je posledica prisustva multiplih aloantitijela i antitijela na antigen visoke učestalosti u serumu trudnice.
Prikaz slučaja: Trudnica, 31 godina, druga trudnoća, 38.n.g. upućena je u Klinički Centar Crne Gore zbog daljeg praćenja i porođaja, nakon otkrivenog pozitivnog indirektnog antiglobulinskog testa u skriningu. Identifikacija antitijela i pozitivna interreakcija sa kompatibilnim eritrocitim adonora,ukazivala je na multipla antitijela i na antitijelo protiv antigena velike učestalosti. Trudnica je ubrzo i porođena , novorođenče je bilo O, RhD+, DAT pozitivan. Identifikacijom eluata nakon adsorbcije seruma porodilje na odgovarajuće eritrocite donora, kao i identifikacijom seruma novorođenčeta i eluata sa eritrocita novorođenčeta, utvrđeno je prisustvo aloantitijela specifičnosti anti–D, anti- E i anti–Jka, a anti-S i anti-K nijesu mogla biti isključena . Uzorci porodilje, novorođenčeta i oca djeteta su poslani u Međunarodnu referentnu laboratoriju za krvne grupe u Bristolu gdje je identifikovano anti-Yta antitijelo i potvrđeno prisustvo anti-D, anti- E, anti–Jka, i anti-S aloantitijela. Isključeno je prisustvo anti-K. Sprovedena je genotipizacija sva tri uzorka kojom je utvrđeno da su novorođenče i otac pozitivni na sve antigene koji odgovaraju antitijelima majke. Utvrđeno je da porodilja ima heterozigotnu mutaciju (c.1057C>A) koja je karakteristična za YT*A/B genotip, što bi predviđalo Yt (a+b+) fenotip. Međutim, otkrivena je i dodatna heterozigotna nova mutacija (c.1364G>A), za koju se predpostavlja da utišava alel YT*A. To dovodi do Yt(a-b+) fenotipa i istovremene proizvodnje aloanti-Yta.
Zaključak: Multipla aloantitijela kao i antitijelo protiv antigena velike učestalosti predstavljaju izazov za svaku IH laboratoriju. Ključno za uspješno rešavanje identifikacije multiplih antitijela u serumu pacijenta je dobro poznavanje karakteristika antieritrocitnih antitijela i antigena, studiozan pristup problemu i podrška referentnih laboratorija.
Ključne riječi: multipla aloantitijela, antigeni velike učestalosti, DAT, IAT

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IDENTIFICATION OF MULTIPLE ANTIBODIES AND HIGH-FREQUENCY ANTIGEN ANTIBODIES IN AN ALLOIMMUNIZED PREGNANT WOMAN - CASE REPORT

Praštalo-Grubiša M, Rašović G, Vučinić S, Šćepanović T, Cvijović A, Zonjić J.
Institute for Blood Transfusion of Montenegro

Introduction: Alloimmunization during pregnancy, apart from the risk of developing HBFN, can create a problem in determining the specificity of the antibodies and providing timely blood for the mother and/or the newborn.
Objective: Reporting the first case of fetomaternal erythrocyte incompatibility resulting from the presence of multiple alloantibodies and high-frequency antigen antibodies in the serum of a pregnant woman.
Case report: Pregnant woman, 31 years old, second pregnancy, 38 week of gestation she was referred to the Clinical Center of Montenegro, after a positive indirect antiglobulin test was detected. Antibody identification and positive interaction with compatible donor erythrocytes indicated multiple antibodies and an antibody against a high-frequency antigen. The pregnant woman soon gave birth, the newborn was O, RhD+, DAT positive. The identification of eluates after the adsorption of the mother's serum on the appropriate donor erythrocytes, as well as the identification of the newborn's serum and eluate from the newborn's erythrocytes, determined the presence of alloantibodies of anti-D, anti-E and anti-Jka specificity, and anti-S and anti-K could not be excluded. Samples from the mother, the newborn, and the child's father were sent to the International Blood Group Reference Laboratory in Bristol where anti-Yta antibody was identified and the presence of anti-D, anti-E, anti-Jka, and anti-S alloantibodies were confirmed. The presence of anti-K was excluded. Genotyping determined that the newborn and the father were positive for all antigens corresponding to the mother's antibodies. The parturient was found to have a heterozygous mutation (c.1057C>A) characteristic of the YT*A/B genotype, which would predict a Yt (a+b+) phenotype. However, an additional heterozygous new mutation (c.1364G>A) was detected, which we hypothesize silences the YT*A allele. This results in a Yt(a-b+) phenotype and concomitant production of alloanti-Yta.
Conclusion:The key to successfully solving the identification of multiple antibodies in the patient's serum is a good knowledge of the characteristics of antierythrocyte antibodies and antigens, a studious approach to the problem and the support of reference laboratories.
Key words: multiple antibodies, high-frequency antigen, DAT, IAT

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AN EXAMPLE OF ANTI-M ANTIBODY IN THE MN INFANT

Radonjić Z[1], Andrić B[1], Krasić S[1], Radović I[2]
[1]Mother and Child Health Care Institute of Serbia "Dr Vukan Čupić", Belgrade
[2]Blood Transfusion Institute of Serbia, Belgrade

Introduction: The MNS blood group system is second only to the Rh blood group system in its complexity. Antigens in the MNS system are fully developed at birth, and some have been shown to be present on red cells quite early in fetal life. Anti-M is detected frequently as a saline antibody if testing is done at room temperature. Antibodies to antigens in the MNS blood group system are often "naturally occurring" and if they do not react at 37°C can be ignored in transfusion practice. At least 17 cases of anti-M occurring as an autoantibody have been reported since the original description by Fletcher and Zmijewski in 1970.
Patient and methods: We describe the MN male infant whose plasma contains the anti-M antibody.
Results: The antibody showed marked dosage effect and reacted most strongly at 4oC and at room temperature as well as in the indirect antiglobulin phase of testing. We discuss the results of the blood bank serologic evaluations and clinical consequences.
Conclusion: Autoanti-M antibody may not be such a rare entity but rather may be underdiagnosed.
Key words: autoantibody, MNS blood group system

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PRIPRAVCI I PACIJENTI U 2022.GODINI

Đozo A.
Zavod za transfuzijsku medicinu FBiH, Sarajevo, Bosna i Hercegovina

Uvod: Transfuzijsko liječenje je konstanta, bez obzira na sve okolnosti i dešavanja na lokalnom i globalnom planu. Banke krvi se, stoga, konstantno suočavaju sa jednakim izazovima, a to je, kako obezbijediti dovoljne količine kvalitetnih i sigurnih pripravaka za svakog pacijenta u pravo vrijeme. Dostupnost podataka o karakteristikama pacijenata koji primaju krvne pripravke, kao i o vrsti i količini izdatih jedinica, ključni su u sistemu obezbjeđenja zaliha i distribucije krvnih pripravaka.
Cilj: Cilj je bio prikazati pacijente za koje je Zavod za transfuzijsku medicinu Federacije Bosne i Hercegovine izdao krvne pripravke u periodu januar- avgust 2022.god, kao i vrstu i količinu izdatih krvnih pripravaka.
Materijal i metode: Ispitivanje je bilo retrospektivno u smislu analize podataka o količini i vrsti izdatih krvnih pripravka iz Zavoda za transfuzijsku medicinu FBiH u periodu od 01. januara do 31. avgusta 2022.god. Također su analizirani podaci o pacijentima i bolničkim odjelima sa kojih su zahtijevani krvni pripravci. Navedeni podaci su dobiveni iz zavodskog Informacionog sistema Renovatio.
Rezultati: U navedenom periodu izdato je 17 344 krvnih pripravaka za 2399 pacijenata. Od ukupnog broja izdatih pripravaka koncentrata eritrocita je izdato 7987, jedinica svježe smrznuta plazme 5369 i 3988 koncentrata trombocita. 26% pripravaka izdato je za Hematološku kliniku, 12% za Kardiovaskularnu hirurgiju, 11,8% za Intenzivnu njegu, te 8,2% za Ortopedsko- traumatološku kliniku. Među pacijentima, 49% su bili muškarci, a 51% žene. Prosječna životna dob pacijenata iznosila je 47,9 godina.
Zaključak: Rezultati ispitivanja su pokazali da je prisutan trend povećanja potrošnje krvnih pripravaka u odnosu na isti period prošle godine za 12%, za 8% više pacijenata. Skoro 1/3 krvnih pripravaka izdata je za pacijente sa malignim oboljenjima, a slijede pacijenti Klinike za kardiovaskularnu hirurgiju. Za hirurške odjele i Odjel intenzivne njege izdato je 44,5 % koncentrata eritrocita od ukupnog broja izdatih jedinica. Raspodjela utrošenih jedinica krvi, uglavnom, odgovara podacima iz drugih centara.
Ključne riječi: transfuzija krvnih pripravaka, pacijenti, odjeli

UP 45

PRODUCTS AND RECIPIENTS IN 2022.

Đozo A.
Blood Transfusion Institute of Federation of Bosnia and Herzegovina Sarajevo, Bosnia and Herzegovina

Abstract
Introduction: Blood transfusion therapy is the Constant, regardless of all circumstances and events on the local and global level. Blood banks, therefore, constantly face the same challenges, how to provide sufficient supplies of high-quality and safe blood products for each patient at the right time. Availability of epidemiologic data on recipients of blood products, as well on type and numbers of blood products issued, is crucial for demand planning and policy development in the blood supply and delivery system.
Aim: The aim of this study was to present patients for whom the blood products were issued in the period January-August 2022, as well as the type and number of blood products issued.
Methods: We performed a retrospective analysis of products issued from Blood Transfusion Instiute of Federation of Bosnia and Herzegovina between 1 January 2022 and 31 August 2022. Data on patients and hospital wards from which blood products were requested were also analyzed. The above data were obtained from the Institut's Renovatio Information System.
Results: During the study period there were 17,344 blood products issued to 2,399 patients. Of the total number of products issued, 7,987 were red cells units, 5,369 units of fresh frozen plasma and 3,988 platelet concentrates. 26% of the products were issued for the hematology department, 12% for cardiovascular surgery, 11.8% for intensive care unit, and 8.2% for the orthopedic-trauma center. Among the patients, 49% were male and 51% were female. The mediane age of the transfused patients was 47.9 years.
Conclusion: The study results showed that there is a trend of increasing of the blood products usage compared to the same period in 2021 by 12% more products issued for 8% more patients. Almost 1/3 of blood products were issued for patients with malignant diseases, followed by patients in the cardiovascular surgery department. About 44,5% of all red cells units were transfused in the intensive care unit and surgical departments.Our data corresponds to results obtained from the other centers.
Key words: blood transfusion, recipients, products, hospital wards

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PROCJENA TRANSFUZIJSKOG LIJEČENJA PRIMJENOM ROTACIJSKE TROMBOELASTOMETRIJE U KARDIOKIRURŠKIM OPERACIJAMA

Knežević J, Kraljević I.
Sveučilišna klinička bolnica Mostar,Bosna i Hercegovina

Uvod: Kardiokirurški zahvati na srcu uz uporabu stroja za izvan tjelesnu cirkulaciju (EKC) smatraju se kirurškim zahvatima s visokim rizikom za ekscesivno krvarenje. Ekscesivno krvarenje nakon kardiokirurškog zahvata uz upotrebu EKC uređaja predstavlja važan uzrok morbiditeta i mortaliteta kardiokirurških bolesnika. Poremećaji hemostaze uvjetovani EKC-om i samim kirurškim zahvatom imaju multifaktorijalnu etiologiju, kao što je gubitak reaktivnosti trombocita, potrošnja faktora koagulacije, hemodilucija radi ispunjavanja cijevi EKC sistema kristaloidnim otopinama.
Cilj:je utvrđivanje može li se procjenom visokoelastičnih svojstava krvnog ugruška stratificirati bolesnike prema riziku za poslijeoperacijsko krvarenje. Cilj je utvrditi predikcijsku sposobnost rezultata rotacijske tromboelastometrije u procjeni rizika krvarenja bolesnika, ispitati kako se prediktabilnost mijenja kroz točke mjerenja i u kojoj točci je snažnija.
Materijal i metode: U skupinu ispitanika uključeni su svi bolesnici koji se podvrgavaju kardiokirurškoj operaciji na otvorenom srcu upotrebom (EKC). Bolesnici su prema intenzitetu krvarenja podijeljeni na dvije skupine sa i bez ekscesivnoga krvarenja. Prediktabilnost svrstavanja u jednu od dvije grupe utvrđivana je pomoću testova rotacijske tromboelastometrije. U cilju perioperacijske evaluacije visokoelastičnih svojstava krvnog ugruška uzorkovanje krvi s provođenjem testa rotacione tromboelastometrije izvedeno je u 2 točke mjerenja: TI točka mjerenja predstavlja fazu indukcije anestezije i T2 točka mjerenja predstavlja vrijeme od 15 minuta nakon aplikacije protamina i neutralizacije heparina,
Rezultati: Istraživanje je pokazalo kako je rotacijska tromboelastometrija koristan test u stratifikaciji rizika ekscesivnog krvarenja nakon elektivnih kardiokirurških operacija. Najsnažniji prediktori ekscesivnog krvarenja bili su testovi provedeni u točki T2 kada su nam nalazi rotacijske tromboelastometrije (Intem,Heptem,Extem i Fibtem testovi) signaliziraju povećanje potrošnje prokoagulantnih krvnih pripravaka..
Zaključak: Tromboelastometrija je metoda koja daje dobru procjenu krvarenja u kardiokirurških bolesnika
Ključne riječi: tromboelastometrija, krvarenje , pripravci

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ASSESSMENT OF TRANSFUSION TREATMENT USING ROTARY THROMBOELASTOMETRY IN CARDIOSURGICAL SURGERY

Knežević J, Kraljević I.
University Clinical Hospital Mostar, Bosnia and Herzegovina

Introduction: Cardiosurgical interventions on the heart with the use of a machine for extracorporeal circulation (ECC) are considered surgical procedures with a high risk for excessive bleeding. Excessively bleeding after cardiac surgery with the use of an ECC device is an important cause morbidity and mortality of cardiac surgery patients. Disorders of hemostasis caused by ECC-om and the surgical procedure itself have a multifactorial etiology, such as loss reactivity of platelets, consumption of coagulation factors, hemodilution to fill tubes ECC system with crystalloid solutions.
The goal: is to determine whether it is possible to evaluate the highly elastic properties of a blood clot to stratify patients according to risk for postoperative bleeding. The goal is to determine predictive ability of rotational thromboelastometry results in the assessment of bleeding risk patient, to examine how the predictability changes through the measurement points and at which point it is stronger.
Material and methods: The group of subjects included all patients undergoing surgery open-heart cardiac surgery using (ECC). Patients are according to intensity bleeding divided into two groups with and with out excessive bleeding. Predictability classification into one of the two groups was determined using rotary tests thromboelastometry. In order to perioperatively evaluate the highly elastic properties of blood clot blood sampling with a rotational thromboelastometry test was performed in the 2nd measurement points: TI measurement point represents the induction phase of anesthesia and T2 measurement point represents the time of 15 minutes after protamine application and heparin neutralization,
Results: The research showed that rotational thromboelastometry is a useful test in risk stratification of excessive bleeding after elective cardiac surgery. The most powerful predictors of excessive bleeding were the tests performed at the T2 point when wethe results of rotational thromboelastometry (Intem, Heptem, Extem and Fibtem tests) signal increasing consumption of procoagulant blood products.
Conclusion: Thromboelastometry is a method that gives a good assessment of bleeding in cardiac surgery patients.
Key words: thromboelastometry, bleeding, preparations

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ULOGA BOLNIČKE BANKE KRVI U KOVID BOLNICI

Vasiljević-Jovanović B[1], Zdravković M[1,2], Crnokrak B[1,2], Branković M.[1,2]
[1] KBC"Bežanijska kosa", Beograd
[2] Medicinski fakultet, Univerzitet u Beogradu

Uvod: U globalnoj borbi protiv KOVID-19 pandemije, značajnu ulogu imajubolničke banke krvi. Inicijalno, službama transfuzije nije dat veliki značaj. U fokusu su bile ovlašćene transfuzijskeustanove zbog drastično smanjenog broja davalaca krvi, kao i pitanja vezanih za bezbednost transfuzije i mogućnosti transmisije SARS-KoV-2. Prema EU Direktivamaupravljanje bolničkim rezervama krvi je jedna od najvažnijihodgovornostibolničke banke krvi (BB)i od neprocenjivog je značaja za zdravlje i bezbednost pacijenta. Pandemijaje donela nove izazove i testirala spremnostBBda očuva adekvatne zalihe krviu uslovima njene smanjene dostupnosti, kao i da omogući efikasnu, pravičnu raspodelu krvi u skladu sa prioritetima.U dijagnostici i zbrinjavanju poremećaja hemostaze kod bolesnika obolelih od KOVID-19, Point of care metode dobile su na značaju, kao iosnovni principi sistema Patient Blood Managementa usmerena hemoterapija i optimizacija potrošnje krvi.
Cilj rada:Prikaz primene krvnih komponenata (KK) isprovedenih imunohematoloških testiranjau 2020.god., prvoj godini pandemije, u odnosu pre-KOVID 2019 godinu.
Materijal i metode:Analiza je izvršena retrospektivno na osnovu podataka iz Protokola i Izveštaja o izvršenim imunohematološkim testiranjima Bolničke banke krvi KBC"Bežanijska kosa".
Rezultati:Početkom KOVID-19 pandemijei ulaskomKBC"Bežanijska kosa" u sistem „KOVID-19 ustanova" smanjila se potrošnja KK kako zbogsmanjenog brojaelektivnih operacija, tako i zbogredukovane primene transfuzija kod pacijenata obolelih od KOVID-19. U toku 2019. god je izdato je 8059 KK, od toga 6010 koncetrata eritrocita(6010/8059). Takođe je sprovedeno 56017 različitih imunohematoloških testiranja. U prvoj godini pandemije brojizdatih koncetrata eritrocita smanjio se na 3006 (3006/ 6008 KK), a broj pretransfuzijskih testiranja na 33615. Nije prijavljen nijedan neželjeni događaj da pacijent nije primio neophodnu transfuziju.
Zaključak:U toku prve godine pandemije u KBC"Bežanijska kosa" smanjen je broj primenjenih transfuzija krvi.Zalihe krvi su takođe bile smanjene. Ipak, bolnička banka krvi je uspela da održi stabilne zalihe krvi i da uz racionalnu upotrebu krvi, koordinaciju i odgovarajuće odluke oko prioriteta transfuzijskog zbrinjavanja pacijenata, odgovori na zahteve kliničara.
Ključne reči: COVID-19, transfuzija krvi, Bolnička banka krvi

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THE ROLE OF THE BLOOD BANK IN THE COVID-19 HOSPITAL

Vasiljević-Jovanović B[1], Zdravković M[1,2], Crnokrak B[1,2], Branković M.[1,2]
[1] University Hospital Medical Center (UHMC) "Bežanijska Kosa", Belgrade
[2] Faculty of Medicine, University of Belgrade

Background: Hospital blood banks (BB) play an important role in the global fight against the COVID-19 pandemic. Initially, transfusion services were not given much importance. The focus was on the Blood establishments due to the drastically reduced number of blood donors, as well as issues related to transfusion safety and the possibility of SARS-KoV-2 transmission. According to EU Directives, the management of hospital blood reserves is one of the most important responsibilities of the BB and of inestimable importance for the patient's health and safety. The pandemic brought new challenges and tested the readiness of BB to preserve adequate blood supplies in the conditions of its reduced availability, as well as to enable efficient, fair distribution of blood in accordance with priorities. In the diagnosis and management of hemostasis disorders in patients suffering from COVID-19, Point of Care methods have gained importance, as have the basic principles of the Patient Blood Management system, guidedtransfusions and optimization of the use of blood.
Aim: To present the use of blood components (BC) and performed immunohaematology tests in 2020, the first year of the pandemic, compared to the pre-COVID 2019.
Material and methods: Retrospective analysis according to data from the Protocols and Reports on the performed immunohaematology tests of the UHMC "Bežanijska Kosa" Hospital blood bank.
Results: At the beginning of the COVID-19 pandemic and entry of UHMC "Bežanijskakosa" to the system of "COVID-19 institutions",thenumber of transfusions decreased in general due to the consequent suspension of elective surgeries, as well as thelow rateof blood utilization in COVID-19 patients. In the course of 2019, 8059 BCs were issued, of which 6010 were red blood cell concentrates (6010/8059). A total of 56017 different immunohaematology tests were performed. In the first year of the pandemic, the number ofred blood cell concentrates issued decreased to 3,006 (3006/ 6008 BC), and the number of pre-transfusion tests to 33615. No adverse event due to patient not receiving necessary transfusion was reported. Conclusion: During the first year of the pandemic, the rates of red blood cell transfusion administered in the UHMC "Bežanijskakosa" decreased. Blood supplies were also depleted. Nevertheless, the hospital's blood bank managed to maintain stable blood supplies and to respond to the demands of clinicians with rational blood use, coordination and appropriate decisions regarding the priorities corresponding to patient's individual requirements.
Keywords: COVID-19, blood transfusion, blood bank

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REKONVALESCENTNA SARS-COV2 PLAZMA – MODALITET LEČENJA KOD UMERENIH I SREDNJE TEŠKIH OBLIKA INFEKCIJE KORONA VIRUSOM

Vučetić D[1,2], Abazović Dž[3], Ostojić G[1,2], Gojkov D[1], Stanojević I[4], Šupić G[4], Vukosavljević M[5], Vojvodić D[4].
[1] Institut za transfuziologiju i hemobiologiju Vojnomedicinska akademija,
[2] Medicinski fakultet Univerziteta odbrane Beograd,
[3] Klinika Renova, Beograd, 4Institut za medicinska istraživanja, Vojnomedicinska akademija, Medicinski fakultet Univerziteta odbrane Beograd,
[5] Načelnik Vojnomedicinske akademije, Medicinski fakultet Univerziteta odbrane Beograd, Srbija.
Uvod: Pojava novog koronavirusa (Coronavirus 2 -SARS-CoV-2), je u celom svetu rezultovala pandemijom COVID-19. Upotreba rekonvalescentne plazme se nametnula kao jedan od efikasnih tretmana u lečenju.
Cilj: Napraviti sopstveni enzimoimuni test za detekciju antitela IgG, IgM i IgA klase na S1S2 i na nukleprotein virusa. Rekonvalescentnu plazmu sa najvišim titrom antitela izdvojiti manuelneom procedurom i primeniti u lečenju umerenih i srednje teških bolesnika tokom prvih tri do pet dana.
Materijal i metodi: Specifična anti-S1S2 SARS CoV2 antitela i antitela na nucleoprotein, su kvantifikovana pomoću ELISA "in house" kvantitativnog testa. Specifični SARS CoV2 S1S2 i SARS CoV2 nukleoprotein (Sino Biological, EU) antigeni su obloženi na polistirenskim jažicama. Sekundarna antitela su inkubirana nakon ciklusa ispiranja (kozji anti-humani IgG, IgA ili IgM Southern Biotech, SAD). Nakon inkubacije sa supstratom i zaustavljanja reakcije određena je optička gustina svakog uzorka na 450nm (Synergy HT, EU spektrofotometar). Koncentracija je određena na osnovu standardnih krivih dobijenih sa monoklonskim antitelima specifičnim za S1S2 ili nukleoprotein (Sino Biological, EU).
Rezultati: Nakon testiranja 868 uzoraka seruma, 290 (33,41%) je imalo zadovoljavajući titar anti-S1S2 SARS CoV2 IgG antitela. Cut-off vrednost je bio titar od 200 i takvih je bilo 139, titar preko 400 je imalo 96 davalaca, preko 600 je imalo 45 davalaca, preko 800 je bilo 8 davalaca i preko 1000 je bilo svega dva davaoca. Svi davaoci su preležali virusnu infekciju i nisu bili vakcinisani. Lečeno je 26 bolesnika davanjem po dve jedinice plazme u dva uzastopna dana (od 4 davaoca) i kod svih je u prvih 48 sati od početka terapije uočeno značajno poboljšanje u toku infekcije u svim parametrima.
Zaključak: Rekonvalescentna plazma data u prvim danima od pojave simptoma kod umerenih odnosno srednje teških oblika bolesti, dovodi do povlačenja tegoba kod svih inficiranih pacijenata. Plazmu je najbolje prikupiti najkasnije 90 dana nakon preležane infekcije.
Ključne reči: korona virus, rekonvalescentna plazma, antitela

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SARS-COV2 CONVALESCENT PLASMA – TREATMENT MODALITY FOR MODERATE AND MEDIUM SEVERE FORMS OF CORONA VIRUS INFECTION

Vučetić D[1,2], Abazović Dž[3], Ostojić G[1,2], Gojkov D[1], Stanojević I[4], Šupić G[4], Vukosavljević M[5], Vojvodić D[4].
[1] Institute for transfusiology and hemobiology of Military Medical Academy,
[2] Medical Faculty University of Defense Belgrade,
[3] Renova Clinic, Belgrade,
[4] Institute for Medical Research, Military Medical Academy, Medical Faculty University of Defense Belgrade,
[5] Director of Military Medical Academy, Medical Faculty University of Defense Belgrade, Serbia.
Background: The appearance of the new coronavirus (Coronavirus 2 -SARS-CoV-2) has resulted in the worldwide pandemic of COVID-19. The use of convalescent plasma has emerged as one of the most effective treatments.
Aim: Make own enzyme immunoassay for the detection of antibodies of the IgG, IgM and IgA class to S1S2 and the nucleoprotein of the virus. The convalescent plasma with the highest titer of antibodies is separated by a manual procedure and used in the treatment of moderate and moderately severe patients during the first three to five days.
Material and methods: Specific anti-S1S2 SARS CoV2 antibodies and nucleoprotein antibodies were quantified using an ELISA "in house" quantitative test. Specific SARS CoV2 S1S2 and SARS CoV2 nucleoprotein (Sino Biological, EU) antigens were coated on polystyrene wells. Secondary antibodies were incubated after a wash cycle (goat anti-human IgG, IgA or IgM Southern Biotech, USA). After incubation with the substrate and stopping the reaction, the optical density of each sample was determined at 450 nm (Synergy HT, EU spectrophotometer). The concentration was determined based on standard curves obtained with monoclonal antibodies specific for S1S2 or nucleoprotein (Sino Biological, EU).
Results: After testing 868 serum samples, 290 (33.41%) had a satisfactory anti-S1S2 SARS CoV2 IgG antibody titer. The cut-off value was a titer of 200 and there were 139 such, a titer over 400 had 96 donors, over 600 had 45 donors, over 800 there were 8 donors and over 1000 there were only two donors. All donors were suffering from a viral infection and had not been vaccinated. 26 patients were treated by giving two units of plasma in two consecutive days (from 4 donors) and in all of them, in the first 48 hours from the start of therapy, a significant improvement in the course of the infection was observed in all parameters.Conclusion: Convalescent plasma given in the first days after the onset of symptoms in moderate or medium-severe forms of the disease, leads to the withdrawal of symptoms in all infected patients. It is best to collect plasma no later than 90 days after the previous infection.
Key words: coronavirus, convalescent plasma, antibodies

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OSNOVNI PRINCIPI TRANSFUZIJE KRVI U RATU

Borovčanin N, Vučetić D.
Institut za transfuziologiju i hemobiologiju VMA, Beograd, Srbija

Uvod: Najznačajnije medicinsko dostignuće u prvom svetskom ratu je bila transfuzija krvi. Drugi svetski rat je važan zbog uvođenja transfuziološk eslužbe u obliku koji je sličan današnjoj službi, a hladni rat je vodio ka istraživanjima vezanim za primenu zamrznutih hemoprodukata. Tokom mnogobrojnih ratova širom sveta, razvijali su se i osnovni principi transfuzije krvi u ratu.
Materijal i metode: Analizirali smo različite radove i vodič kliničke prakse Združenog sistema traume (JTS): Prehospitalna transfuzija krvi da bi odredili koji su osnovni principi transfuzije krvi u ratu.
Rezultati: Obezbeđivanje smišljenog fleksibilnog plana za hitne situacije, standardizovanog programa banke krvi, upravljanja gubitkom krvi, skladištenja krvi i njenih produkata, „bezkrvna" hirurgija i strategije regrutovanja davalaca su veoma važni u savremenim ratovima. Mogućnos tsnabdevanja krvlju na lokalnom nivou je kritični faktor u takvim hitnim situacijama. Prehospitalni principi nadoknade tečnosti i davanja transfuzije su: brzo prepoznavanje životno ugrožavajućeg hemoragičnog šoka, prevencija hipotermije, kontrola krvarenja sredstvima za mehaničku hemostazu, nadoknada krvi, izbegavanje hipokalcijemije/nadoknada kalcijuma, izbegavanje nadoknade kristaloidima, davanje traneksamičke kiseline i ukoliko je to moguće korišćenje suve zamrznute plazme.
Zaključak: Davanje prehospitalne transfuzije krvi zahteva dovoljno treninga da bi svi bili adekvatno pripremljeni. Izvođenje što realističnije mogućeg treninga dovodi do poboljšanja u rezultatima lečenja traume u boničkim uslovima.
Ključne reči: transfuzija krvi, trauma, hemostaza.

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BASIC PRINCIPLES OF BLOOD TRANSFUSION IN WAR

Borovčanin N, Vučetić D.
Institute of transfusiology and hemobiology of MMA, Belgrade, Serbia

Introduction: The most medical advance of World War I was blood transfusion. The Second World War saw the introduction of the type of transfusion service with which we are familiar today, and with the advent of the cold war, led to research in frozen blood techniques. Along the multiple wars around the world, the development continued and resulted basic principles of blood transfusion in war.
Material and methods: We analized different articles and Joint Trauma System Clinical Practice Guideline: Prehospital Blood Transfusion to find what will be basic principles of blood transfusion in war.
Results: Providing a thoughtful flexible emergency plan, standardized blood bank program, blood loss management, blood storage and it products, bloodless surgery and donor recruitment strategies are very important in modern wars. Local blood supply considered as critical factor in conquering such emergencies. Prehospital principles of resuscitation and transfusion are: rapid recognition of life-threatening hemorrhagic shock, prevent hypothermia, hemorrhage control with mechanical hemostatic adjuncts, hemostatic resuscitation, avoid hypocalcemia/calcium replacement, avoid crystalloid resuscitation, tranexamic acid administration and consider source of freeze dried plasma.
Conclusion: Execution of prehospital blood transfusions requires sufficient training to adequately prepare. Conducting the most realistic training possible has been shown to improve in-hospital trauma team performance.
Key words: blood transfusion, trauma, hemostasis.

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PRIMENA TERAPIJSKE IZMENE PLAZME KOD BOLESNICE SA TROMBOTIČNOM TROMBOCITOPENIJSKOM PURPUROM KOMPLIKOVANOM PNEUMOKOKNOM SEPSOM I NEUROINFEKCIJOM

Kulić A[1], Libek V[1], Đurđević J[1], Strugar A[1], Gojković I[1], Cvetković Z[2], Ivanović A[2]
Služba za transfuziju krvi KBC Zemun, Beograd,Srbija[1]
Služba za hematologiju, Klinika za internu medicinu KBC Zemun, Beograd, Srbija[2]

UVOD: Kod određenog broja bolesnika sa trombotičnom trombocitopenijskom purpurom (TTP) dolazi do čestih egzacerbacija bolesti ili multiplih relapsa što zahteva povećan broj terapijskih izmena plazmi (TIP). Lečenje ovih pacijenata je tehnički zahtevno i često povezano sa ozbiljnim komplikacijama (infekcije, tromboze ili transfuzijske reakcije).
CILJ: Predstavljen je neočekivani klinički tok i lečenje bolesnice sa relapsirajućim TTP-om uzrokovanim bakterijskom neuroinfekcijom i penumokoknom sepsom.
MATERIJAL i METODE: Procedure TIP-a konitinuiranog tipa su izvođene na aparatu za aferezne procedure Spectra Optia (Terumo BCT).
REZULTATI: Bolesnica starosti 57 godina u akutnom konfuznom stanju hospitalizovana je u našoj ustanovi zbog sumnje na relaps TTP-a (trombociti 51x109/l), koji je incijalno lečen sa TIP-om, uz kortikosteriodnu terapiju (1,5 g/kgTT). U proseku se menjao 1,7 cirkulatorni volumen,a za nadoknadu je upotrebljena kriosupernatantna plazma. Nakon osme izmene došlo je do normalizacije broja trombocita (10x109/l -174x109/l). Kod desete procedure uočen je značajan pad broja trombocita (90x109/l). U terapijski protokol je uključen vinkristin koji je obustavljen zbog pozitivne hemokulture (koagulaza negativan stafilokok). U brisu femoralnog CVK izolovan je Proteus, a u sputumu Candida. I pored komplikacija sa venskim pristupom i prisutnim infekcijama bolesnica postiže kompletan terapijski odgovor nakon 18-tog TIP-a. Petnaest dana nakon otpusta bolesnica se ponovo hospitalizuje zbog pogoršanja kliničkog stanja. U kliničkoj slici su dominirali neurološki simptomi, a u laboratoriji trombocitopenija, retikulocitoza (6%), lekocitoza sa visokim CRP-om. Dominacija neurološke simptomatologije ukazivala je na postojanje bakterijske neuroinfekcije i zahtevala izvođenje lumbalne punkcije. Dobijanjem citološkog, biohemijskog i mikrobiološkog nalaza likvora započelo se sa empirijskom antibiotskom terapijom (Vankomicin, Meronem i Ampicilin). Istovremeno je u nalazu hemokulture izolovan Streptococcus pneumoniae osetljiv na primenjene antibiotike. Uz intezivne izmene plazme (ukupno pet), sa izmenama dva cirkulatorna volumena došlo je do oporavka broja trombocita (235x109/l), regresije neuroloških simptoma i normalizacije parametara zapaljenja i hemolize.
ZAKLJUČAK: Pravovremeno prepoznavanje i adekvatno lečenje komplikacija, kao i multidisciplinarni pristup bolesniku rezultuje povoljnim kliničkim ishodom TTP-a.
KLJUČNE REČI: terapijska izmena plazme, trombotična trombocitopenijska purpura, sepsa

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PLASMA EXCHAGE IN THROMBOTIC THROMBOCYTOPENIC PURPURA ASSOCIATED WITH NEUROINFECTION AND PNEUMOCOCCAL SEPSIS

Kulić A[1], Libek V[1], Đurđević J[1], Strugar A[1], Gojković I[1], Cvetković Z[2], Ivanović A[2]
Blood Bank Department CHC Zemun, Belgrade, Serbia[1]
Department of haematology CHC Zemun, Belgrade, Serbia[2]

BACKGROUND: Patients with thrombotic thromobocitopenic purpura (TTP) who developed relapses or persistent disease required multiple sessions of plasma exchange (PE). Their therapy is technically demanding and usually associated with serious complications (infection, thrombosis or transfuison reactions).
AIM: We present the treatment and unexpected clinical course of female patient with relapsing TTP associated with bacterial neuroinfection and pneumococcal sepsis.
MATERIAL AND METHODS: All sessions of PE were proceded with Spectra Optia Apheresis system (Terumo BCT).
RESULTS: A 57-year-old patient in an acute confused state was hospitalized in our institution due to suspected relapse of TTP (platelets 51x109/l), which was managed with PE and corticosteroid therapy (1.5 g/kg body weight). During PE sessions, 1, 7 plasma volumes were changed with cryosupernatant plasma as substitution. After 8th PE, the platelets were normalized (10x109/l -174x109/l). Significant drop in platelets number (90x109/l) was observed in 10th PE. In the therapeutic protocol vincristine was included, which was discontinued due to a positive blood culture (coagulase-negative staphylococcus). Proteus was isolated in the swab of femoral CVK and Candida in the sputum. Despite complications a complete therapeutic response was achieved after the 18th PE. Fifteen days after discharge, the patient was hospitalized again due to deterioration. Neurological symptoms were dominant both with thrombocytopenia, reticulocytosis (6%), and leukocytosis with high CRP. Neurological symptomatology indicated bacterial neuroinfection and required a lumbar puncture. After obtaining the cytological, biochemical and microbiological results of the cerebrospinal fluid, empiric antibiotic therapy (Vancomycin, Meronym and Ampicillin) was started. At the same time, in blood culture, Streptococcus pneumoniae was isolated, sensitive to the applied antibiotics. With intensive PE (five in total), changing two circulatory volumes recovery of platelet count was achieved (235x109/l), regression of neurological symptoms and normalization of inflammation and hemolysis parameters.
CONCLUSION:The prompt recognition and adeqate treatment of complications, as well as multidisciplinary apporach to the patient resulted in a favorable clinical outcome of TTP.
KEY WORDS: plasma exchange, thrombotic thromocytopenic purpura, sepsis

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UTICAJ I RASPODELA ABO KRVNIH GRUPA U COVID-19 INFEKCIJI

Radovanović J.
Služba za transfuzijologiju krvi KBC Zemun

Uvod: COVID-19 pandemija, uzrokovana SARS-CoV-2 virusom, izazvala je veliku nestabilnost u zdravstvenim sistemima. Njegovo brzo širenje i ogroman uticaj na sisteme zdravstvene zaštite učinili su da je prioritet identifikovanje potencijalnih faktora rizika povezanih sa infekcijom. Zato ovaj rad ima za cilj da utvrdi uticaj i povezanost između pripadnosti određenoj krvnoj grupi i sklonosti od infekcije virusom COVID-19.
Materijal i metoda rada
Retrospektivnom analizom obuhvaćeni su pacijenti koji su zbog infekcije virusom COVID-19 hospitalizovani u bolnici KBC Zemun 2020. godine. Podaci su prikupljeni na osnovu podataka u informacionom sistemu, protokola krvnih grupa i radnih protokola.
Rezultati
Od ukupnog broja hospitalizovanih pacijenata zaraženih virusom COVID-19 u bolnici KBC Zemun u periodu od 31.03.2020. do 04.11.2020.godine kod 411. pacijenata je odrađena krvna grupa. Raspodela krvnih grupa je bila sledeća: krvna grupa A je bila dominantna grupa sa ukupno 199 pacijenata (48,42%), zatim krvna grupa O prisutna kod 138 pacijenata (33,57%), B krvna grupa kod 48 pacijenata (11,68%) i krvna grupa AB kod 26 pacijenata (6,33%). Raspodela krvnih grupa pacijenta zaraženih virusom COVID-19 je procentualno približna raspodeli krvnih grupa opšte populacije.Veći procenat pacijenata sa krvom grupom A ukazuje na veću mogućnost nastanka infekcije virusom COVID-19 kod ljidi A krvne grupe u odnosu na ostale krvne grupe(O,B i AB).
Zaključak
ABO krvne grupe utiču na genetsku osetljivost domaćina na različite virusne bolesti i to se takođe može primeniti na SARS-Cov-2. Sama raspodela krvnih grupa nije imala veći uticaj u ishodu bolesti ,već u samoj mogućnosti zaraze COVID-19 virusom.
Ključne reči: ABO krvne grupe, COVID-19,KBC Zemun

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IMPACT AND DISTRIBUTION OF ABO BLOOD SYSTEM IN COVID-19 INFECTION

Radovanović J.
Zemun hospital

Introduction: The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has caused great instability in healthcare systems. His enormous impact on health care systems has made it a priority to identify potential risk factors associated with the infection. That is why this work wants to prove the influence and connection between belonging to a certain blood group and susceptibility to infection with the COVID-19 virus.
Material and method of work
The retrospective analysis included patients who were hospitalized at Zemun hospital in 2020 due to infection with the COVID-19 virus. Material were collected on the basis of data in the information system, blood types protocols and work protocols.
Results
From the total number of hospitalized patients infected with the COVID-19 virus in the Zemun hospital in the period from 03.31.2020.-04.11.2020. 411 patients had their blood type tested. The distribution of blood groups was : blood group A was the dominant group with a total of 199 patients (48.42%), followed by blood type O with 138 patients (33.57%), blood type B with 48 patients (11.68 %) and blood type AB with 26 patients (6.33%). The distribution of blood types of patients infected with the COVID-19 virus is similar to the distribution of blood types of the general population. A higher number of patients with blood type A indicates a greater possibility of infection with the virus COVID-19 in people of blood type A compared to other blood types (O, B and AB).
Conclusion
The role of ABO blood type in the development of symptomatic disease with a higher risk in subjects with blood type A and a protective effect of blood types B and O. Blood types do not seem, however, to play a role in susceptibility, progression to severe disease.
Key words: ABO blood types, COVID-19,Zemun hospital

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OVERVIEW OF TELEMEDICINE IN THE INSTITUTE FOR TRANSFUSION MEDICINE OF RNM

Useini S[1], Grubovic Rastvorceva R[1,2]
[1]*Institute for Transfusion Medicine of RNM, Skopje, N. Macedonia,*
[2]*Faculty of Medical Sciences, University Goce Delcev, N. Macedonia*

Background: Telemedicine is a service that is rapidly evolving to provide increased access to high-quality healthcare that is efficient and cost-effective. Aim: The shortage of specialist transfusion doctors as well as the age structure of the doctors employed at the Institute of Transfusion Medicine of Republic of North Macedonia has imposed the need to find a concept that will provide efficient operation of Transfusion Medicine Centers and Services over the years. At the same time, it was imperative to reduce the involvement of doctors in duties and regularities and to unify the way of working in all places. Materials and Methods: After the creation of the VPN (Virtual Private Network) LogMeIn Hamachi was completed and the translation of the remote-validation software into Macedonian was also completed, the first telemedicine system was installed in the Transfusion Medicine Service - Specialty Hospital for Surgery Saint Naum Ohridski in March 2013. After completing installation in 3 Centers and 17 Transfusion Medicine Services, from 01 October 2018 telemedicine is in full use in our country. In July 2019, an installation was also made at the Resen Health Service. A regional separation was made of 4 regions according to which each of the doctors in the region validated the results elsewhere in the region where they belonged. Results: Each of the Transfusion Medicine Centers and Services works the same way. The following tests are performed: 1. Blood group with reverse grouping; 2. Blood group for newborns; 3. Antibody screening with a commercial set of erythrocytes I-II; 4. Blood Test Profile consisting of: Donor Blood Type Confirmation, Patient Blood Type Confirmation, Patient Antibody Screening, Cross-match. Unification of work, unified report, archive of validated tests with images and information who has completed and validated the test, remote inspection and interpretation of pre-transfusion tests, rapid and efficient blood delivery, 24 hour doctor availability, especially in less available services with few doctors and cost savings are the major benefits of introducing telemedicine in our country. Simple analysis system for improving analysis' work processes, work organization and so on. There are more than 110.000 validated results in the whole country through the telemedicine system in 2021, of which 2/3 are in working hours (from 8 to 15 h) and 1/3 after 15 h. Just over 35% of validated results are in the region that gravitates towards the Regional Transfusion Center Bitola. Conclusions: The use of telemedicine has a strong impact on the improved and timely transfusion service for patients, improved organization and rationalization of work in the Institute for Transfusion Medicine of RNM and on substantial cost.
Keywords: telemedicine, transfusion medicine, work organization

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HEPCIDIN IN PHILADELPHIA-CHROMOSOME NEGATIVE MYELOPROLIFERATIVE NEOPLASMS – A SINGLE CENTER EXPERIENCE

Cvetković Z[1,2], Libek V[3], Novković A[1], Kulić A[3], Marinković G[1], Strugar A[3]
[1] *Department of Hematology Clinic for Internal medicine, Clinical Hospital Center Zemun, Belgrade, Serbia, e-mail zcvetkovic06@gmail.com*
[2] *Faculty of Medicine, University of Belgrade, Belgrade, Serbia*
[3] *Department of Transfusiology Clinical Hospital Center Zemun, Belgrade, Serbia*

Introduction: Philadelphia-chormosome negative Myeloproliferative neoplasms (MPN: Polycythemia vera -PV, Essential thrombocythemia -ET and Primary myelofibrosis -PMF) are rare, heterogeneous group of clonal hematopoietic stem cell disorders, characterized by increased proliferation of one or more myeloid lineages in the bone marrow, and the presence of phenotype-driver mutations of the intracellular cytokine-signaling molecule JAK2 (Janus kinase 2) leading to increased pluripotent stem cell sensitivity to erythropoietin (Epo). Under physiological conditions of stimulated erythropoiesis, the synthesis of hepcidin, the key regulatory protein in iron homeostasis, is suppressed.
Aim: To evaluate the relationship between parameters of blood count, iron metabolism, Epo and hepcidin concentrations in patients with MPN.
Material and methods: Total of 49 consecutive outpatients with MPN (27 male/22 female; mean age 63) were included in the study. Point mutation JAK2V617 was detected in 19/23(82.5%) PV pts, 11/18(61,1%) PMF pts and 2/6(33.3%) ET pts. Patients with clinical and laboratory signs of infection, anemia and other significant comorbidities were excluded from the study in order to avoid their impact on hepcidin level, which was also determined in control group of 27 healthy individuals.
Results: Hemoglobin concentration ($p<0.05$), hematocrit ($p<0.01$) and red blood cell count ($p<0.05$) were significantly higher in group of PV patients compared to the PMF and ET patients groups, while ferritin end Epo concentrations were significantly lower ($p<0,05$). Serum hepcidin level did not differ significantly between PV, PMF and ET groups ($p>0.05$), as well as there were no difference between MPN patients (8.37±15.24ng/l) and healthy control (8,5±10,12ng/l) ($p>0,05$). In MPN patients, symptomatic splenomegaly and thromboembolic events had no impact on hepcidin level ($p>0.05$).
Conclusion: According to our experience, the hepcidin is not suppressed by induced erythropoiesis in MPN indicating the need for further studies as the improvement upon the existing understanding of abnormal hepcidin production may lead to potential novel therapeutic target.
Key words: Polycythemia vera, Essential thrombocythemia, Primary myelofibrosis, erythropoiesis, hepcidin

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LUMINEX TEST NA BAZI PERLI ZA SIMULTANU DETEKCIJU HUMANIH TROMBOCITNIH I HUMANIH LEUKOCITNIH ANTITELA

Vojvodić S.[1,2], Ademović Sazdanić D.[2]
[1]*Univerzitet u Novom Sadu, Medicinski fakultet, Novi Sad*
[2]*Zavod za transfuziju krvi Vojvodine, Novi Sad*

Sažetak:
Uvod: Aloantitela protiv humanih trombocitnih antigena (HPA) i humanih antigena leukocita (HLA) su uključena u nekoliko imunološki posredovanih poremećaja trombocita. Detekcija ovih antitela je ključna u dijagnozi i lečenju refraktornosti na transfuziju trombocita, posttransfuzione purpure i fetalne i neonatalne aloimune trombocitopenije.
Cilj: Cilj ovog istraživanja bio je da se istovremeno detektuju anti-HLA i anti-HPA-1, -HPA-2, -HPA-3, -HPA-4, -HPA-5 i -GpIV antitela pomoću Luminex tehnologije na bazi mikroperli.
Materijal i metode: Metoda detekcije glikoprotein (GP) specifičnih HPA antitela na bazi mikroperli sa monoklonskim antitelima specifičnim za glikoproteine trombocita i molekule HLA I klase koji su odvojeno spojeni sa Luminex mikroperlama je korišćena u detekciji antitela. Uzorci seruma su prikupljeni od 234 pacijenta sa trombocitopenijom, 11 pacijenata sa aloimunom trombocitopenijom (NAIT) i 14 pacijenata sa refraktornošću na trombocite, za koje se sumnja da imaju antitela na HPA ili HLA I klasu i testirani PakLx testom sa Matchit softverom za interpretaciju rezultata.
Rezultati: Među 259 uzoraka, 72 su bila sa senzibilizacijom na HLA i/ili antigene trombocita (27,79%). Od 72 pozitivna uzorka, 29,16% su posedovala antitela na antigene HLA I klase, 45,83% antitela specifičnih za trombocite i 25 % uzoraka posedovalo je antitela na obe vrste isptivanih antigena. Anti-GPIIb/IIIa (HPA-1,-3,-4) i anti-GPIa/IIa (HPA-5) antitela, bila su najčešća među svim pozitivnim slučajevima sa prisutnim antitelima specifičnim za humane trombocitne antigene.
Zaključak: Metoda Luminex na bazi mikroperli u kombinaciji sa monoklonskim antitelima može se uspešno koristiti za detekciju HPA i HLA I klase antitela istovremeno, posebno sa visokom osetljivošću u detekciji anti-HPA antitela.

Ključne reči: Luminex test, HPA antitela, HLA antitela

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LUMINEX BEAD-BASED ASSAY FOR SIMULTANEOUS DETECTION OF HUMAN PLATELET AND HUMAN LEUKOCYTE ANTIBODIES

Vojvodić S.[1,2], Ademović Sazdanić D.[2]
[1]*University of Novi Sad, Faculty of Medicine, Novi Sad*
[2]*Institute for Blood transfusion of Vojvodina, Novi Sad*

Abstract:
Introduction: Alloantibodies against human platelet antigens (HPA) and human leukocyte antigens (HLA) are implicated in several immune-mediated platelet disorders. Detection of these antibodies is crucial in the diagnosis and management of refractoriness to platelet transfusions, post-transfusion purpura and fetal and neonatal alloimmune thrombocytopenia.
Aim: The aim of this study was to simultaneously detect anti-HLA and anti-HPA-1, -HPA-2, -HPA-3,-HPA-4, -HPA-5 and -GpIV antibodies with Luminex microbeads technology.
Material and methods: Bead-based glycoprotein (GP) specific HPA antibody detection method with monoclonal antibodies specific for platelet glycoproteins and HLA I Class molecules which were separately coupled to the Luminex microbeads was undertaken for screening of antibodies. Sera samples were collected from 234 patients with thrombocytopenia, 11 neonatal alloimmune thrombocytopenia (NAIT) patients and 14 platelet refractoriness patients, suspected of having HPA or HLA antibodies and tested by PakLx assay with Matchit Platelet Antibody Software for the interpretation of results.
Results: Among the 259 samples, 72 were sensitized to HLA and /or HPA (27,79%).The 72 positive samples consisted of 29,16% of HLA I Class antibodies, 45,83% of platelet-specific antibodies, and 25% consisted of both. Anti-GPIIb/IIIa positive (HPA-1,-3,-4) and anti-GPIa/IIa positive (HPA-5) were the most frequent among all the platelet-specific antibody positive cases.
Conclusion: Luminex microbeads coupled with monoclonal antibodies could be successfully used to detect HPA and HLA antibodies simultaneously, especially with high sensitivity in detecting HPA antibodies.

Keywords: Luminex assay, HPA antibodies, HLA antibodies

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AFEREZNO PRIKUPLJANJE MATIČNIH ĆELIJA HEMATOPOEZE ZA POTREBE AUTOLOGNE I ALOGENE TRANSPLANTACIJE KOŠTANE SRŽI U UKC TUZLA

Delic Custendil S, Poliklinika za transfuziologiju
Univerzitetsko-klinički centar Tuzla, Bosna i Hercegovina

Uvod: Transplantacija matičnih ćelija hematopoeze (MĆH) predstavlja jedan od modaliteta lečenja raznih vrsta malignih i nemalignih hematoloških obolenja. Time se veliki broj dosada neizlečivih bolesti može staviti pod kontrolu, uvodeći bolesnika u fazu remisije, čime se pobolšava kvalitete života i daje šansa za izlečenje. Poliklinika za transfuziologiju permanentno je jedina koja na području cele države izvodi ovaj tip procedura.
Ciljevi: Prikaz preseka stanja programa afereznog prikupljanja MĆH od početka 2005. do kraja 2021. godine prezentovanjem broja afereznih procedura i evaluacijom prikupljenih MĆH i mononuklearnih ćelija (MNĆ), kroz definisani period.
Materijal i metode: Retrospektivnom studijom analizirane su 254 aferezne procedure, koje su rađene pacijentima obolelim od malignih hematoloških bolesti hospitalizovanim na Hematološkoj klinici UKC Tuzla. Među pacijentima žena je bilo 97 (38,2%) i 157 (61,8%) muškaraca, životne dobi od 17 do 65 godina. Aferezni produkti namenjeni za autolognu transplantaciju su bili podvrgnuti programiranoj kriokonzervaciji sa kriporotektorom 10% DMSO te uskladišteni na temperaturi od -1400 C. Aferezni produkti namenjeni za alogenu transplantaciju su transfundirani neposredno nakon procedure prikupljanja MĆH, u slučaju minor ABO-nepodudarnosti, dodatno je vršeno centrifugiranje suspenzije MĆH sa maksimalnom redukcijom antitela usmerenih protiv eritrocitnih antigena primaoca. Uspešnost prikupljenog afereznog produkta je merena brojem CD 34 + ćelija i MNĆ.
Rezultati: Tokom analiziranog perioda urađene su 254 aferezne procedure prikupljanja MĆH, od kojih je 230 bilo za potrebe autologne transplantacije, a 24 za alogene transplantacije. U cilju prikupljanja odgovarajućeg broja CD34+ ćelija, ukupno 50 autolognih aferenih procedura je urađeno u dva akta, a dvije procedure u tri akta. Tokom afereznog prikupljanja vršeno je procesiranje krvi velikog volumena (3-4). Uspješnost prikupljanja je procenjivana prinosom MNĆ po kg tjelesne težine. Srednja vrijednost prikupljenih MNĆ iznosila je 4,7 x108/kgTT, a srednja vrijednost CD34+ nakon procedure 3,8 x 106/kgTT.
Zaključak: Procesiranjem većeg volumena krvi dobija se veći broj CD34+ ćelija. Zadovoljavajući prinos CD34+ MĆH i MNĆ ostvaren prikazanim programom afereznog prikupljanja MĆH, osnova je za procenu uspešnosti transplantacije.

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APHERESIS COLLECTION OF HEMATOPOIETIC STEM CELLS FOR AUTOLOGOUS AND ALLOGENEOUS BONE MARROW TRANSPLANTATIONS IN UCC TUZLA

Delic Custendil S, Polyclinic of Transfusion Medicine
University-Clinical Center Tuzla, Bosna and Hercegovina

Transplantation of hematopoietic stem cells (HSC) is one of the modalities of treatment of various types of malignant and non-malignant hematological diseases. In this way, a large number of previously incurable diseases can be brought under control, introducing the patient into the phase of remission, which improves the quality of life and gives a chance for curative. The Polyclinic of Transfusion Medicine is permanently the only one in the entire country that performs this type of procedure.
Objectives: An overview of the program of apheresis collection of HSC from the beginning of 2005 to the end of 2021 by presenting the number of apheresis procedures and evaluation of the collected HSC and mononuclear cells (MNC) throughout the defined period.
Materials and methods: A retrospective study analyzed 254 apheresis procedures performed on patients suffering from malignant hematological diseases, hospitalized at the Hematology Clinic of the UCC Tuzla. There were 97 (38.2%) female patients, and 157 (61.8%) male patients, aged 17 to 65 years. Apheresis products intended for autologous transplantation were subjected to programmed cryopreservation with a cryoprotectant of 10% DMSO and stored at a temperature of -1400 C. Apheresis products intended for allogeneic transplantation were transfused immediately after the procedure of HSC collection, in case of minor ABO-incompatibility, additional centrifugation suspension of HSC was performed with maximum reduction of antibodies directed against erythrocyte antigens of the recipient. The success of the collected apheresis product was measured by the number of CD 34+ of cells and PBMC.
Results: During the analyzed period, 254 apheresis procedures were performed to collect HSC, out of which 230 were for autologous transplantation, and 24 for allogeneic transplantation. In order to collect the appropriate number of CD34+cells, a total of 50 autologous afferent procedures were performed in two acts, and two procedures in three acts. During the apheresis collection, a large volume of blood was processed (3-4). The success of the collection was evaluated by the yield of HSC per kg of body weight. The mean value of the collected HSC was 4.7 x 108/kgbwt, and the mean value of CD34+ after the procedure was 3.8 x 106/kgbwt.
Conclusion: By processing a larger volume of blood, a larger number of CD34+ cells is obtained. The satisfactory yield of CD34+ HSC and PBMC achieved by the shown HSC apheresis collection program is the basis for evaluating the success of transplantation.

UP 56

ASSESSMENT RATIONALITY OF BLOOD USE IN PATIENTS UNDERGOING ELECTIVE UROLOGY SURGICAL PROCEDURES AT UNIVERSITY CLINICAL CENTER OF SERBIA

Lukić V.
Emergency room, University clinical center of Serbia

Introduction Patient blood management (PBM) is a multidisciplinary approach to treating patients and includes correction of low total erythrocyte mass and preoperative anemia, reduction of perioperative blood loss and application of a restrictive threshold model in transfusion indications. In order to improve PBM, a special system of requiring and testing blood units has been developed, which defines the maximum number of allogeneic erythrocyte components necessary for certain surgical interventions.
Key words: patient blood management, MSBOS
Goals The aim of the study was to evaluate the rationality of erythrocyte consumption during surgical interventions at the Urology Clinic of the Clinical Center of Serbia (Clinic).
Methods The retrospective study followed 617 patients, 185 women and 432 men aged 45 to 75 years. During the research, the consumption of erythrocytes was monitored in relation to the primary indication, i.e. the type of surgery, comorbidities, preoperative hemoglobin values, values of coagulation tests and applied therapy.
Results The study showed that at the Clinic, the overall C: T ratio was 4.2, which corresponds to 24% of transfused units in relation to the number of cross matches performed. No statistically significant difference between the sexes was observed, while a statistically significant difference in the average related to the age was observed between the subjects in whom there was irrational (64.65 ± 9.49 years) and those in whom there was a rational use of erythrocytes. There was a statistically significant difference in the frequency of different primary diagnoses according to the International Classification of Diseases as well as in relation to the values of hemoglobin and prothrombin time between the group with rational and irrational use of erythrocytes.
Conclusion The obtained data show that it is necessary to introduce a PBM system at the clinic, to revise the existing protocols for erythrocyte demand according to indications, as well as to improve patient preparation in order to minimize the use of allogeneic erythrocytes.

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BOLESNICI SA SPECIFIČNIM AUTOIMUNIM ANTIERITROCITNIM ANTITELIMA U PERIODU 1.1.2016-31.12.2019. GODINE – REZULTATI, TRANSFUZIJSKO LEČENJE I PRIKAZ SLUČAJA

Mladenović N, Mijović L, Životić B, Štrbac N, Radovan D, Lukić V, Šoškić T.
Odsek za pretransfuziona testiranja i hemovigilancu Urgentnog centra Univerzitetskog kliničkog centra Srbije (UCUKC)

Uvod: Autoimuna antieritrocitna antitela reaguju sa antigenima sopstvenih eritrocita. Češće su nespecifična, ali mogu imati jasnu krvnogrupnu određenost – specifična autoimuna antitela.
Cilj: Analiza rezultata identifikacija antieritrocitnih antitela obavljenih u četvorogodišnjem periodu u kojima su otkrivena autoimuna antitela određene specifičnosti, i prikaz načina transfuzijskog zbrinjavanja ovih pacijenata uz prezentaciju jednog slučaja.
Metod i materijal: Retrospektivna studija obuhvata period od 1.1.2016-31.12.2019. i prikazuje analizu podataka preuzetih iz pisanih protokola i elektronske baze podataka UCUKCS o 125954 pacijenata za koje je pripremana krv za transfuziju. Identifikacije antieritrocitnih antitela na +37ºC obavljene su metodom u gelu: a) na Bio Rad anti IgG rabbit Liss/Coombs karticama uz primenu komercijalnih ID-BioRad Panel test cells eritrocita; ili b) na BioRad NaCl/enzyme karticama zajedno sa BioRad test eritrocitima obradjenih papainom. Identifikacije na +22ºC izvršena su metodomu epruveti sa Rea Cel test eritrocitima. Antigeni na eritrocitima bolesnika i kesa krvi tipizirani su metodom u epruveti sa test serumima različitih proizvodžača.
Rezultati: Tokom navedenog perioda za 125954 pacijenata ukupno je uradjeno 248162 testa interreakcije s ciljem odabira odgovarajućih jedinica eritrocita za transfuziju. Od tog broja bolesnika kod njih 27 (0,02%) otkrivena su ukupno 33 specifična autoantitela: autoanti e 23 (70%), autoanti C 6 (18%), i po dva autoanti D i autanti c (6%). 6 pacijenata je imalo po dva autoantitela različite specifičnosti. Kod 5 (18,5%) politransfundovanih bolesnika autoantitelo je bilo u sklopu kompleksnih imunizacija (tri ili više alo i autoantitela). Najviše pacijenata sa autoantitelima bilo je sa hematoonkološkim dijagnozama (52%). Samo 2 pacijenta razvila su i aloantitelo na drugi antigen istog fenotipa posle transfuzija eritrocita (autoanti e i aloanti E).
Zaključak: Autoantitela respektovana su isto kao aloantitela, odnosno za transfuziju se primenjivala kompatibilna antigen negativna krv. Eritrociti sa pozitivnim testom interreakcije koristili su se isključivo kada drugog izbora nije bilo, a nikada unapred s razlogom prevencije aloimunizacije drugim antigenima.
Ključne reči: autoantitela, aloantitela, identifikacija antieritrocitnih antitela, transfuzija

UP 57

PATIENTS WITH SPECIFIC AUTOIMMUNE ANTIERYTHROCYTE ANTIBODIES IN THE PERIOD 1.1.2016-31.12.2019. YEARS - RESULTS, TRANSFUSION TREATMENT AND CASE REPORT

Mladenović N, Mijović L, Životić B, Štrbac N, Radovan D, Lukić V, Šoškić T.
Department for pre-transfusion testing and hemovigilance of the Emergency Center of the University Clinical Center of Serbia (UCUKCS)

Introduction: Autoimmune anti-erythrocyte antibodies react with antigens of one's own erythrocytes. More often they are non-specific, but they can have a clear blood group determination - specific autoimmune antibodies
Objective: Analysis of the results of the identification of antierythrocyte antibodies were done on four-year period in which autoimmune antibodies of a certain specificity were detected, and presentation of the transfusion treatment of these patients with the presentation of one case.
Method and material: The retrospective study covers the period from January, 1st 2016. to December, 31st 2019. and shows an analysis of data taken from written protocols and the UCUKCS electronic database on 125,954 patients for whom blood was prepared for transfusion. Identification of antierythrocyte antibodies at +37ºC was performed using the gel method: a) on Bio Rad anti IgG rabbit Liss/Coombs cards using the commercial ID-BioRad Panel test cells erythrocytes; or b) on BioRad NaCl/enzyme cards together with BioRad papain-treated test erythrocytes.
Results: During the mentioned period, a total of 248,162 interaction tests were performed for 125,954 patients with the aim of selecting appropriate units of erythrocytes for transfusion. In 27 of that number of patients (0.02%), a total of 33 specific autoantibodies were detected: autoanti e 23 (70%), autoanti C 6 (18%), autoanti D 2 (6%) and autoanti c 2 (6%). Six (22,2%) patients each had two autoantibodies of different specificities. In 5 (18.5%) polytransfused patients, the autoantibody was part of complex immunizations. Only 2 patients also developed alloantibody to another antigen of the same phenotype after erythrocyte transfusions (autoanti e and alloanti E).
Conclusion: Autoantibodies were respected in the same way as alloantibodies, i.e. compatible antigen-negative blood was used for transfusion. Erythrocytes with a positive interaction test were used exclusively when there was no other choice, and never for the reason of prevention of alloimmunization with other antigen.
Key words: autoantibodies, alloantibodies, identification of antierythrocyte antibodies, transfusion

UP 58

UTICAJ INTRAOPERATIVNOG SPAŠAVANJA KRVI NA PREVENCIJU POSTOPERATIVNE ANEMIJE KOD OPERACIJE ZAMENE KOLENA

Matić S, Mihajlović M.

Uvod: Prema definiciji udruženja za naprednim upravljanjem krvi (Society for Advanced Blood Management-SABM), Patient Blood management (PBM) je „Pravovremena primena hiruških i medicinskih mera zasnovanih na dokazima, koji održavaju nivo hemoglobina, optimizuju hemostazu i smanjuju krvarenje u cilju poboljšanja pacijentovog oporavka". Prema vremenu pripreme razlikujemo preoperativne, intraoperativne i postoperativne mere.
Cilj: Prikazati kako primena intraoperativnog spašavanja krvi (ISK) može sprečiti pojavu anemije kod ortopedskih pacijenta sa operacijom kolena
Materijal i metod : U retrospektivnoj studiji iz informacionog sitema Heliant i bolničkih protokola ortopedije i Bolničke banke krvi dobijeni su podaci o lečenju pacijenata na odeljenju ortopedije za 2014 i 2019.godinu. Ukupan broj ispitanika je podeljen na kontrolnu-50 pacijenta (operisanih 2014.) i eksperimentalnu-52 pacijenta (operisanih 2019.godine.)
Rezultati: Procenjeno neposredno intraoperativno krvarenje u kontrolnoj grupi je iznosilo 438.33 ± 284.29 ml, dok je u ispitivanoj grupi iznosilo 308.66 ± 172.14 ml. Ukupno je primenjeno 27 jedinica krvi za 15 pacijenata kontrolne grupu bolesnika od 50 pacijenata. U eksperimentalnoj grupi ni jedan pacijent nije primao preparate eritrocita. Od ukupno 52 pacijenta eksperimentalne grupe kod kojih je vršeno ISK prosečno je vraćeno 152,76 ml autologne krvi.
Diskusija: Za sprrečavanje anemije neophodno je primeniti osim intraoperativnog spašavanja krvi i ostale mere koncepta PBM i to korigovanje preoperativne anemije preparatima intravenskog gvožđa, intraoperativne gubitke što više smanjiti primenom hiruških tehnika i antifibrinolitika, i primeniti restriktivnu transfuzijsku strategiju u postoperativnom periodu i smanjiti količinu krvi koja se uzima za laboratorijske analize.
Zaključak: Analiza naših rezultata pokazala je da primena metode ISK pri operacijama artroplastike kolena: značajno smanjuje primenu alogene krvi, značajno smanjuje postoperativni pad hemoglobin i samim tim pojavu postoperativne anemije. Primena koncepta PBM može sprećiti pojavu postoperativne anemije i pored manje primene krvi i krvnih derivata.

Ključne reči: Intraoperativno spašavanje krvi, operacija zamene kolena, anemija

UP 58

IMPACT OF INTRAOPERATIVE CELL SALVAGE FOR PREVENTING POSTOPERATIVE ANEMIA IN PATIENTS WITH TOTAL KNEE ARTHROPLASTY

Matić S, Mihajlović M.

Introduction: According to definition of Society for Advanced Blood Management (SABM) , Patient Blood Management (PBM) is „ is a patient-centered, systematic, evidence-based approach to improve patient outcomes by managing and preserving the patient's own blood, while promoting patient safety and empowerment." By timing of action, the measurements we can divide to preoperative, intraoperative and postoperative measurements.
The Aim: To assess how Intraoperative Cell Salvage (ICS) measurements can prevent postoperative anemia in patints with total knee arthroplasty.
Material and methods: In observational, retrospective study, from Hospital Informatical System „Heliant", and protocols of blood bank and otrhopaedic departments, we collect data from patients from 2014 to 2019 year. Total number of patients was divided to control group (50 patients, operated in 2014.) and experimental group (52 patients, operated in 2019.)
Results: Estimted intraoperative blood loss in control group was 438.33 ± 284.29 ml, in experimental group was 308.66 ± 172.14 ml. In total 27 units of red blood cells was given in control group, in experimental group none of patients receive red blood cells. For 52 patents in experimental group, in average there was 152,76 autologous blood returned during operation.
Discussion: For preventing postoperative anemia, except ICS, there is mandatory to apply other methods of PBM such as : correcting of preoperative anemia with intravenous iron therapy, minimize blood loss with blood sparing tecniques, using of antifibrinolytic therapy, restrictive transfusion strategy in postoprative period and less blood withdrowal for laboratory analyses.
Conclusion: Analysis of our results has shown that ICS method: significantly reduce number of allogeneic blood units applied, significantly reduce postoperative hemoglobin values drop, and reduce postoperative anemia. Introducing PBM concept can reduce postoperative anemia even with less number of blood products applied.

Key words: Intraoperative Blood Cell Salvage, Total knee arthroplasty, anemia

UP 59

POZITIVAN EFEKAT PRIMENE ERITROCITA O KRVNE GRUPE U AB PLAZMI U ODNOSU NA CELU KRV O KRVNE GRUPE U INTRAUTERINOJ TRANSFUZIJI – PRIKAZ SLUČAJA

Rajković D, Stojanović N, Crvenkov T, Zdelar Stojanović Lj, Petrović B, Nikolić Lj.
Klinika za ginekologiju i akušerstvo, Univerzitetski klinički centar Srbije, Beograd, Srbija

UVOD. Intrauterina transfuzija (IUT) je vid fetalne terapije i predstavlja terapiju izbora kod hemolitičke bolesti fetusa i novorođenčeta. IUT se može izvesti intraperitonealno, intravaskularno i intrakardijalno. IUT može biti rana, pre 20. nedelje gestacije (NG) i kasna nakon 20. NG. Mi prikazujemo slučaj kasne intrauterine intravaskularne transfuzije (IUIVT).
PRIKAZ SLUČAJA. U našu kliniku primljena je trudnica starosti 29 godina, u 24. NG druge, spontano nastale trudnoće, komplikovane Rh senzibilizacijom i stanjem nakon spontanog pobačaja. Krvna grupa majke je A RhD-, fenotip Ccddee, Fy(a+b-), Jk(a-b+), P1+, Lu(a-b+), MNss, Le(a+b+). Na početku trudnoće pri rutinskoj kontroli antitela identifikovano je anti-D u titru 128 i anti-E u tragu. U 22/23. NG dolazi do porasta titra na 1024. Nalaz na IgG1 i IgG3 je bio pozitivan u razblaženju, u odnosu 1:100. Na osnovu ultrazvučnog nalaza, opšteg stanja fetusa i naglog porasta titra antitela odlučeno je da se sprovede IUIVT. Prva IUIVT izvedena je u 25. NG, inicijalni hematokrit (Hct) fetusa iznosio je 16%. Dato je 40 ml O RhD- krvi (Hct-78%), a završni Hct fetusa bio je 40%. Fenotip fetusa: ARhD+, CcDwee, DAT 4+. Druga IUIVT je izvedena nakon 7 dana, inicijalni Hct fetusa 19%, na osnovu čega je procenjeno da je dnevni pad Hct iznosio 3%. Dato je 49ml O RhD- krvi(Hct-74%), postignut je završni Hct fetusa od 40%. Pre treće IUIVT titar anti-D je bio 16384. Treća IUIVT je izvedena nakon 14 dana, inicijalni Hct 18%, procenjeno je da je dnevni pad Hct iznosio 1,5%. Dato je 57ml O RhD- (Hct-80%), završni Hct fetusa bio je 40%. Četvrta IUIVT je izvedena nakon 14 dana, inicijalni Hct <10%, procenjeno je da je dnevni pad Hct bio 2,14%. Dato je 82ml O RhD- eritrocita u AB plazmi (Hct-67%), postignut je završni Hct fetusa od 28%. Pre pete IUIVT titar anti-D je bio 32768. Peta IUIVT je izvedena nakon 6 dana, inicijalni Hct 23%, procenjeni dnevni pad Hct iznosi 0,8%. Dato je 67ml O RhD- krvi (Hct-82%) , završni Hct fetusa bio je 40%. Nakon pete IUIVT DAT fetusa je negativan. Šesta IUVT je izvedena nakon 8 dana, inicijalni Hct 19%, procenjeni dnevni pad Hct iznosio je 1,25%. Dato je 49ml O RhD- krvi (Hct-78%) , postignut je završni Hct fetusa od 40%. U 34/35. NG Carskim rezom , rodjeno je živo žensko dete, telesne mase 2490g, Ap 7/8. Vrednost bilirubina u prvom času je bila 83.4umol/l, a Hct 31,2%, zbog čega je primenjena eksangvino transfuzija. Nakon hospitalizacije od 23 dana na KGA, dete se otpušta u dobrom opštem stanju.
ZAKLJUČAK. U prikazanom slučaju IUIVT primena eritrocita O krvne grupe u AB plazmi imala je najmanji prosečni dnevni pad Hct (0,8%), što govori u prilog pozitivnom efektu primene kompatibilnih eritrocita O krvne grupe u AB plazmi u odnosu na celu krv O krvne grupe u IUT.
KLJUČNE REČI. HBFN, IUIVT, transfuzija

UP 59

POSITIVE EFFECT OF THE APPLICATION OF O BLOOD GROUP ERYTHROCYTES IN AB PLASMA IN REGARD TO WHOLE BLOOD OF O BLOOD GROUP IN INTRAUTERINE TRANSFUSION-CASE REPORT

Rajković D, Stojanović N, Crvenkov T, Zdelar Stojanović Lj, Petrović B, Nikolić Lj.
Clinic for Gynecology and Obstretrics, University Clinical Center of Serbia, Belgrade

INTRODUCTION. Intrauterine transfusion (IUT) is therapy of choice for hemolytic disease of the fetus/newborn (HDFN). IUT can be perfomed intraperitoneally, intravascularly and intracardiacally. IUT can be early, before 20th week of gestation (GW), and late after 20th GW. We are showing the case of late intrauterine intravascular transfusion (IUIVT).
CASE REPORT. A 29-year old pregnant woman was admitted to our hospital at 24th week of gestation at her second, spontaneous pregnancy complicated with Rh sensitization and condition after spontaneous abortion. Blood group was A RhD-, phenotype Ccddee, Fy(a+b-), Jk(a-b+), P1+, Lu(a-b+), MNss, Le(a+b+). At a routine checkup anti-D titer was 128 and anti-E on the trail. At 22th/23th GW titer increased to 1024. At admission both IgG1 and IgG3 was positive in a dilution 1:100. Based on ultrasound findings and antibody titer it was indicated an IUIVT. First IUIVT was performed at 25th GW. Initial fetal hematocrit (Hct) was 16%. It was given 40 ml of O R D- blood (Hct-78%). A hematocrit of 40% was achieved. Fetal phenotype: A RhD+, CcDwee, DAT 4+. Second IUIVT was performed after 7 days, initial Hct was 19%. The estimated daily drop of Hct was 3%. It was given 49 ml of ORhD- blood with Hct 74% and finial fetal Hct was 40%. Before third IUIVT anti-D titer was 16384. Third IUIVT was performed after 14 days, initial Hct was 18%, so daily drop of Hct was 1.5%. It was given 57 ml of ORhD – blood with Hct 80%, final fetal Hct was 40%. Fourth IUIVT was performed after 14 days. Initial Hct was <10%, so the estimated daily drop of Hct was 2.14%. It was given 82 ml of O RhD- erythrocytes in AB plasma (Hct-67%), final fetal Hct was 28%. Before fifth IUIVT anti-D titer was 32768. Fifth IUIVT was performed after 6 days. Initial Hct was 23%, so the estimated daily drop of Hct amounted 0.8%. It was given 67 ml of O RhD- blood (Hct-82%) and final Hct of the fetus was 40%. After the fifth IUVT DAT of the fetus was negative. Sixth IUIVT was performed after 8 days, initial Hct was 19%. The Hct daily drop was 1.25%. It was given 49 ml of 0 RhD- blood (Hct-78%) and final fetal Hct was 40%. In 34th/35th GW a live female child was born by Caesarean section, body weight was 2490 g, Apgar score 7/8. The first hour bilirubin was 83.4 umol/l, and Hct 31.2%, so exchange transfusion was applied. After 23 days of hospitalization the child discharged in good general condition.
CONCLUSION. In the presented case of IUIVT application of O blood group erythrocytes in AB plasma had the smallest average daily drop of Hct (0.8%), The results are in favor of a positive effect of compatible O blood group erythrocytes in AB plasma in regards to whole blood O blood group in IUT.
KEY WORDS. HDFN, IUIVT, transfusion

UP 60

ZNAČAJ UTVRĐIVANJA PODKLASE IMUNOGLOBULINA G U PROCENI RIZIKA ZA RAZVOJ HEMOLITIČKE BOLESTI NOVOROĐENČETA-PRIKAZ SLUČAJA

Zdelar Stojanović Lj, Crvenkov T, Rajković D, Petrović B, Nikolić Lj.
Hematološka laboratorija sa transfuzijom krvi, Klinika za ginekologiju i akušerstvo, Univerzitetski klinički centar Srbije, Beograd, Srbija

Uvod. Godinama je RhD - trudnicama praćen nivo antitela i bilirubina u amnionskoj tečnosti. Ugroženost ploda procenjivana je na osnovu Lajlijeve krive (Liley) i titra antieritrocitnih antitela. Titar antitela i ultrazvučni nalaz (UZ) i dalje predstavlja standardni protokol za procenu fetalne anemije i stepena hemoličke bolesti fetusa/novorođenčeta (HBFN). Prikaz slučaja. Trudnica starosti 24 godine, ORhD-, javila se u petom mesecu prve, spontano nastale trudnoće, kontrolisane u Domu zdravlja, urednog toka. Negirala je prethodnu primenu transfuzije, pobačaje, hronična oboljenja, operacije i primenu RhD profilakse. Antieritrocitna antitela su prvi put detektovana u 32. nedelji gestacije i to: anti-D+C u IgM i IgG klasi, a enzimski su detektovana antitela čija se specifičnost nije mogla utvrditi. Titar anti-D je bio 8. Antitela su zatim kontrolisana na dve nedelje. Nakon mesec dana identifikovano je anti-Jka antitelo. Finalni nalaz antitela je Anti-D+C+Jka, titar anti-D iznosio je 16. UZ fetusa tokom cele trudnoće uredan, bez znakova anemije ploda. Trudnica je negirala tegobe tokom trudnoće. Poslednji utvrđen titar anti-D iznosio je 64, zbog čega smo odredili podklase IgG da bismo procenili potrebu za eksangvino transfuzijom (EST). Potklase IgG1 i IgG3 su bile negativne. Porođena carskim rezom. Rođeno je terminsko žensko dete sa Apgar skorom 8/9 telesne mase 3470g, krvne grupe O RhD+ uz pozitivan nalaz DAT 3+. Potklase IgG1 i IgG3 su i kod deteta bile negativne. Elucijom eritrocita deteta ustanovili smo Anti-D+C+Jka. U prvom času nakon rođenja bilirubin je iznosio 37 umol/L, a hemoglobin 145 g/l, tako da nije bilo potrebe za transfuzijom i EST. Majka i dete su otpušteni u dobrom opštem stanju. Zaključak.Određivanje antitela IgG1 i IgG3 potklase se u ovom slučaju pokazalo kao dobar dijanostički parameter, koji bi mogao imati značaja u planiranju EST i pripremi krvi. Za uspešno zbrinjavanje HBFN bitna je saradnja ginekologa-akušera, pedijatra i transfuziologa.

Ključne reči. Hemolitička bolest fetusa i novorođenčeta, podklase imunoglobulina G, transfuzija

UP 60

THE SIGNIFICANCE OF DETERMINING THE SUBCLASS OF IMMUNOGLOBULIN G IN ASSESSING THE RISK FOR THE DEVELOPMENT OF HEMOLYTIC DISEASE OF THE NEWBORN - CASE REPORT

Zdelar Stojanović Lj, Crvenkov T, Rajković D, Petrović B, Nikolić Lj.
Hematology Laboratory with Blood Transfusion, Clinic for Gynecology and Obstetrics, University Clinical Center of Serbia, Belgrade, Serbia

Introduction. For years, the levels of antibodies and bilirubin in amniotic fluid were analysed in RhD- pregnant women. The risk of the fetus/newborn was assessed on the basis of the Liley curve and titer of antierythrocyte antibodies. Antibody titers and ultrasonography (US) remain the standard protocol for the evaluation of fetal anemia and severity of hemolytic disease of the fetus/newborn (HBFN).
Case presentation. A 24-year-old pregnant woman, O RhD-, presented in the fifth month of her first spontaneously occurring pregnancy, regularly checked in Health center. She denied previous abortions, administration of transfusion, chronic diseases, operations and application of RhD prophylaxis. Antierythrocyte antibodies were detected for the first time in the 32nd week of gestation: anti-D+C in the IgM and IgG class, and antibodies of undetermined specificity were detected by enzime metods. Anti-D titer was 8. Antibodies were then controlled every two weeks. After a month anti-Jka antibody was identified. The final antibody finding was Anti-D+C+Jka, the anti-D titer was 16. US of the fetus throughout the pregnancy was normal, without signs of fetal anemia. The pregnant woman denied any complaints during pregnancy. The last determined anti-D titer was 64, which is why we performed IgG subclasses to assess the need for exchange transfusion(ET). Subclasses IgG1 and IgG3 were negative. Caesarean section was done. The female child was born with Apgar score 8/9, body weight was 3470g, blood group O RhD+ with a positive DAT 3+ finding. IgG1 and IgG3 were also negative in the child. By elution of the child's erythrocytes, we established Anti-D+C+Jka. In the first hour after birth, bilirubin was 37 umol/L, and hemoglobin was 145 g/l, so there was no need for transfusion or ET. Mother and child were discharged in good general condition.
Conclusion. Determination of IgG1 and IgG3 subclass antibodies proved to be good diagnostic parameter in this case, which can be important in planning ET and preparation of blood. Important part of successful treatment of HBFN is cooperation of gynecologist-obstetricians, pediatricians and transfusion specialists.
Key words. Hemolytic disease of the fetus and newborn, immunoglobulin G subclasses, transfusion

UP 61

PRIMJENA TRANSFUZIJE KRVI U LIJEČENJU PACIJENATA SA PROKSIMALNIM PRELOMOM OKRAJKA FEMURA

Milić S.
Zavod za transfuzijsku medicinu RS, služba Foča

Uvod: Učestalost primjene transfuzija krvi kod operativnog zbrinjavanja preloma proksimalnog okrajka femura. Očekuje se da su pacijenti sa prelomom proksimalnog okrajka femura primili više transfuzija krvi kod nižih vrijednosti hemoglobina (Hb) i eritrocita (Er) na prijemu, kod prisustva udruženih oboljenja, i starije životne dobi.
Cilj rada: Osnovni cilj istraživanja je analiza rezultata dobijenih liječenjem transfuzijom krvi kod preloma proksimalnog okrajka femura.
Materijal i metode: Istraživanje je sprovedeno kao deskriptivno – retrospektivna studija. U ispitivanju su uključeni pacijenti sa prelomom proksimalnog okrajka femura, koji su hospitalizovani i hirurški zbrinuti u Ortopedskoj službi Univerzitetske bolnice Foča u peridu od 01. 01. 2007. – 31. 12. 2017. godine.
Rezultati: Liječenje transfuzijom krvi operativno zbrinutih pacijenata sa prelomom proksimalnog okrajka femura je neophodna. Perioperativni gubitak krvi iznosi 800 do 2000 ml krvi. Veći broj transfuzija krvi su primili stariji pacijenti, žene, i koji su imali preoperativno niže vrijednosti Hb, hematokrita (Htc) i Er na prijemu, kao i koji imaju udružena oboljenja, pacijenti u opštoj endotrahealnoj anesteziji, i, kojima je operacija trajala duže. Najveći broj primjenjene transfuzije krvi je krvna grupa (kg) 0+.
Zaključak: Od 553 ispitanika transfuziju krvi nije primilo samo 49 ispitanika. Jednu transfuziju krvi je primilo 279 ispitanika, 194 je primilo od 2 – 5 transfuzija, a preostalih 31 ispitanik je primio više transfuzija krvi (6 – 52).
Ključne riječi: transfuzija, hemoglobin, eritrociti.

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APPLICATION OF BLOOD TRANSFUSION IN THE TREATMENT OF PATIENTS WITH PROXIMAL FEMURAL FRACTURES

Milić S.
Institute for Transfusion Medicine of the RS, Foča service

Introduction: The frequency of blood transfusions in the operative management of fractures of the proximal femur. It is expected that patients with a fracture of the proximal end of the femur received more blood transfusions with lower values of hemoglobin (Hb) and erythrocytes (Er) at admission, in the presence of associated diseases, and older age.
The aim of the work: The main aim of the research is the analysis of the results obtained by blood transfusion treatment for fractures of the proximal end of the femur.

Material and methods: The research was conducted as a descriptive - retrospective study. The study included patients with a fracture of the proximal end of the femur, who were hospitalized and treated surgically in the Orthopedic Department of the Foča University Hospital in the period from January 1, 2007 to December 31, 2017.
Results: Blood transfusion treatment of operatively treated patients with a fracture of the proximal femur is necessary. Perioperative blood loss amounts to 800 to 2000 ml of blood. A greater number of blood transfusions were received by older patients, women and those who had preoperatively lower values of Hb, hematocrit (Htc) and Er on admission, as well as those who have associated diseases, patients under general endotracheal anesthesia, and whose surgery lasted longer. The largest number of applied blood transfusions is blood group (kg) 0+.

Conclusion: Out of 553 subjects, only 49 subjects did not receive a blood transfusion. 279 respondents received one blood transfusion, 194 received 2-5 transfusions, and the remaining 31 respondents received multiple blood transfusions (6-52).
Key words: transfusion, hemoglobin, erythrocytes

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POTKLASE IMUNOGLOBULINA G U PROCENI POTREBE ZA EKSANGVINO TRANSFUZIJOM NOVOROĐENČETA

Crvenkov T, Zdelar Stojanović Lj, Rajković D, Petrović B, Nikolić Lj.
Hematološka laboratorija sa transfuzijom krvi, Klinika za ginekologiju i akušerstvo, Univerzitetski klinički centar Srbije, Beograd, Srbija

Uvod. Hemolitička bolest fetusa i novorođenčeta (HBFN) nastaje nakon transplacentarnogprolaska antieritrocitnih IgG antitela majke i posledičnog razaranja eritrocita ploda. Težina kliničke slike HBFN procenjuje se na osnovu kliničkih i biohemijskih parametara, kao i titra antieritrocitnih antitela. Titar ≥32 smatra se značajnim, premda su u literaturi opisani slučajevi gde i veći titar nije doveo do HBFN. Istraživanja su ukazala da su za razvoj HBFN usled senzibilizacije odgovorne potklase imunoglobulina G, IgG1 i IgG3.
Cilj.Ukazati na značaj određivanja IgG1 i IgG3 u proceni težine kliničke slike HBFN i potrebe za eksangvino transfuzijom (EST).
Materijal i metode.Retrospektivno su analizirani podaci iz protokola za određivanje krvnih grupa, interreakcija, antitela i porođaja u periodu od 1.1.2022. do 31.8.2022. Za određivanje potklasa IgG1 i IgG3 koristili smo ID–Card IgG1/G3 proizvođača Bio-Rad.
Rezultati.U periodu od osam meseci Carskim rezom je porođeno 1160 žena, a 1811 žena porodilo se prirodnim putem, ukupno 2971 porođaj. Antitela su detektovana i identifikovana kod 64 trudnice, što predstavlja 2,15% od ukupnog broja porođenih žena. Titar antitela ≥32 razvilo je 6 trudnica odnosno 9,38% od ukupnog broja senzibilisanih trudnica i 0,2% od ukupnog broja porođenih žena. Kod ovih 6 žena i njihove novorođenčadi određivane su potklase IgG1 i IgG3. Samo kod jedne porodilje i njenog novorođenčeta detektovan je pozitivan nalaz na IgG1 i IgG3, u razblaženju 1:100. EST je bilo neophodno primeniti kod prethodno pomenutog novorođenčeta što predstavlja 0,034% u odnosu na ukupan broj porođaja. Novorođenčad čije su majke imale titar antitela iznad 32 a negativan nalaz IgG1 i IgG3, u našem slučaju nisu zahtevala EST.
Zaključak.Pozitivan nalaz na IgG1 i IgG3 u razblaženju ≥1:100 pokazao se kao koristan parametar u proceni potrebe za EST, čime se omogućava pravovremeno planiranje i priprema krvi za EST, u saradnji sa ovlašćenim transfuziološkim ustanovama. Za uspešno zbrinjavanje HBFN neophodan je multidisciplinarni pristup i saradnja između ginekologa-akušera, pedijatara i transfuziologa.
Ključne reči. Hemolitička bolest fetusa i novorođenčeta, eksangvino transfuzija, potklase imunoglobulina G

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SUBCLASSES OF IMMUNOGLOBULIN G IN THE ASSESSMENT OF THE NEED FOR EXCHANGE TRANSFUSION OF NEWBORNS

Crvenkov T, Zdelar Stojanovic Lj, Rajkovic D, Petrovic B, Nikolic Lj.
Laboratory for Hematology and Blood Transfusion, Clinic for Gynecology and Obstetrics, University Clinical Center of Serbia, Belgrade, Serbia

Introduction.Hemolytic disease of the fetus and newborn (HDFN) occurs after the transplacental passage of anti-erythrocyte IgG antibodies of the mother and the destruction of fetal erythrocytes. The severity of HDFN is assessed based on clinical and biochemical parameters and the titer of antierythrocyte antibodies. The titer ≥32 is considered significant, although cases have been described in the literature where even a higher titer did not lead to HDFN. Research has shown that the subclasses of immunoglobulin G, IgG1 and IgG3 are responsible for the development of HDFN due to sensitization.
Objective.To indicate the importance of determining the IgG subclasses in assessing the severity of HDFN and the need for exchange transfusion (ET).
Material and methods.Data from the transfusion protocols were retrospectively analyzed in the period from 1/1/2022 until 31/8/2022. To determine the IgG1 and IgG3 subclasses, we used the ID-Card IgG1/G3 produced by Bio-Rad.
Results.Out of 2971 births, 1160 women gave birth by Caesarean Section, and 1811 women gave birth naturally. Antibodies were identified in 64 pregnant women, which represents 2.15% of the total number of births. Antibody titer ≥32 was found in 6 pregnant women, 9.38% of the total number of sensitized women and 0.2% of the total number of women who gave birth. These 6 women and their newborns were tested for IgG1 and IgG3. Only one mother and her newborn were tested positive for IgG1 and IgG3 at a dilution of 1:100. It was necessary to administer ET to the previously mentioned newborn, which represents 0.034% of the total number of births. Infants whose mothers had an antibody titer above 32 and a negative test for IgG1 and IgG3 did not require ET in our case.
Conclusion.A positive finding on IgG1 and IgG3 in a dilution ≥1:100 proved to be a useful parameter in assessing the need for ET, which enables timely planning and preparation of blood for ET, in cooperation with authorized transfusion institutions. The multidisciplinary approach and cooperation between gynecologist-obstetricians, pediatricians and transfusion specialists are necessary for the successful care of HBFN.
Keywords. Hemolytic disease of the fetus and newborn, exchange transfusion, immunoglobulin G subclasses

UP 63

TERAPIJSKA IZMENA PLAZME KOD PACIJENATA SA INSUFICIJENCIJOM JETRE

Milić A[1], Dinić M[1], Milutinović S[1], Miljuš D[2]
[1] Urgentni centar UKCS
[2] Institut za tranfuziju krvi Srbije

Uvod: Akutna insuficijencija jetre kao i akutizacija hronične bolesti zajedno sa multiorganskom disfunkcijom spadaju u vitalno ugrožavajuća stanja. Pored standardne simptomatske medikamentozne terapije sprovode se i terapijske izmene plazme (TIP). Ciljevi TIP su redukcija nivoa bilirubina, amonijaka i drugih toksina, ALT, AST, fertina i drugih proinflamatornih medijatora, ali i korekcija narušene hemostaze. Zbog toga se smatraju terapijama koje omogućavaju preživljavanje bolesnika do postizanja remisije ili pronalaska organa za transplataciju.
Cilj: Prikaz i analiza procedura TIP kod pacijenata sa akutnom insuficijencijom jetre sprovedenih od janurara 2020. do avgusta 2022. godine
Metod: Retrospektivna analiza podataka dobijenih iz protokola Odseka za terapijske aferezne procedure u periodu od 1. januara 2020. do 30. avgusta 2022.
Rezultati: U posmatranom periodu 59 pacijenata sa akutnom insuficijencijom ili akutizacijom hronične insuficijencije jetre tretirano je TIP. Ukupno je urađeno 419 procedura. Broj procedura po pacijentu je varirao od jedne pa do 109, a prosečno 6 procedura po pacijentu. Bilo je 40 muškaraca i 19 žena. Najmlađi pacijent je imao 20 godina, a najstariji 66 godina. Zahvaljujući TIP uspešnu transplantaciju su dočekala 3 pacijenta. Sve tri transplantacije su obavljene u inostranstvu.
Zaključak: Terapijska izmena plazme je sigurna i dobro tolerisana procedura koja bez obzira što dovodi do biohemijskih poboljšanja ne dovodi do smanjenja smrtnosti ali se može smatrati metodom koja premošćava period do transplantacije jetre.
Ključne reči: insuficijencija jetre, terapijska izmena plazme, transplatacija jetre

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PLASMA EXCHANGE IN PATIENTS WITH LIVER FAILURE

Milić A[1], Dinić M[1], Milutinović S[1], Miljuš D[2]
[1] Emergency Center, University Clinical Center of Serbia, Belgrade
[2] Institute of blood transfusion of Serbia, Belgrade

Introduction: Acute liver insufficiency as well as acute exacerbation of chronic disease together with multiorgan dysfunction lead to life-threatening condition. In addition to standard symptomatic drug therapy are carried out and plasma exchange (pe). The goal of pe are reduction of level of bilirubin, ammonia, other toxins, alt, ast, ferritin and other proinflammatory mediators, but also the correction of demaged hemostasis. For this reason they are considered therapies that enable the survival of the patients until achieving remission or funding an organ for transplantation.
Aim: Review and analysis of pe procedures in patients with liver failure performed from January of 2020. to August of 2022.
Metodology: A retrospective analysis of data obtained from protocol of Department for therapeutic apheresis procedures in the period of the 1st January of 2020 to the 30th Avgust of 2022.
Results: In the observed period 59 patients with acute insufficiency or acute exacerbation of chronical liver insufficiency were treated with plasma exchange. Total is done 419 procedures. The number of procedures varied from 1 to 109 and the average was done 6 procedure per patient. There were 40 men and 19 woman. The youngest patient was 20 years old and the oldest was 66 years old. Thanks to tpe 3 patients received a successful transpalntation of liver. All of them were performed abroad.
Conclusions: Plasma exchange is safe and well tolerated procedure that despite leading to biochemical improvements does not reduce mortality but can be considered a method that bridges the period until transplantation of liver.
Keywords: liver failure, plasma exchange, transplantation of liver

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SAFETY AND EFFICACY OF APHERESIS COLLECTION OF PERIPHERAL BLOOD HEMATOPOIETIC STEM CELLS IN HEMATOLOGIC PATIENTS AND HEALTY DONORS

Grubovic Rastvorceva R[1,2], Useini S[1], Georgievski B[3], Petkovikj E[1], Pivkova Veljanovska A[3], Hristova Dimceva A[1], Grubovic M[1]
[1] *Institute for Transfusion Medicine of RNM, Skopje, N. Macedonia*
[2] *Faculty for Medical Sciences, University Goce Delcev, N. Macedonia*
[3] *University Clinic of Hematology, Skopje, N. Macedonia*

Background: Peripheral blood stem cells (PBSC) are preferred source for 99% autologous and 79% of allogeneic hematopoietic stem cell transplantation (SCT). Optimal donor and recipient outcomes require maximized stem cell collection efficiency and minimized non-target cell contamination. The aim of our study is to present our experience with collecting of mobilized PBSC in hematologic patients and healthy donors. Material and Method: This is a retrospective study performed in the Institute for Transfusion Medicine of Republic of North Macedonia and University Clinic for Hematology; the data was obtained from our database for period from 2000 till 2022. All patients were fully informed on the donation procedure and signed an informed consent for donation. Minimum dose required to ensure successful and sustained engraftment was 2x106/kg CD34+ cells and/or 2x108/kg mono-nucleated cells (MNC). PBSC collection was performed with continuous flow cell separator Baxter C53000, COBE Spectra and Terumo BCT Spectra Optia using conventional-volume apheresis processing the 2 - 2.5 total blood volumes per apheresis. A femoral catheter was used for collection of PBSC and Acid Citrate Dextrose formula A (ACD-A) is used for anticoagulation. Mobilization regimens included granulocyte colony-stimulating factor (G-CSF) alone or combination of G-CSF and disease-specific chemotherapy. Results: There were 977 apheresis collections of PBSC in total, of which 792 (81%) performed in 448 hematologic patients (aged 16-65) and 185 procedures (19%) performed in 120 healthy donors, mostly siblings of the treated patient, including 5 unrelated voluntary donors (aged 16-63). The single procedure usually took 180-270 minutes and the volume of collected stem cells was 50-400 ml. The needed number of MNC and CD34+ cells was successfully collected by 1.8 apheresis in autologous donors and 1.5 apheresis in allogeneic donors. Apheresis procedures were generally well tolerated. The only adverse effects were bone pain, as reaction of G-CSF and numbness of the extremities as reaction of ACD-A, which occur rarely and were very mild. The main indications for autologous stem cell transplantation in our patients were: multiple myeloma - 229 (51.1%), acute myeloid leukemia 83 (18.5%), non-Hodgkin lymphoma – 61 (13.6%), Hodgkin disease – 60 (13.4%), acute lymphoblastic leukemia – 11 patients (2.5%), chronic lymphoblastic leukemia – 3 patients (0.7%) and 1 patient with Ewing Sarcoma (0.2%), while indications for allogeneic SCT were: acute myeloid leukemia - 67 patient (55.8%), acute lymphoblastic leukemia - 17 patients (14.2%), chronic myeloid leukemia – 9 patients (7.5%), severe aplastic anemia – 7 patient (5.8%), myeloproliferative disorders – 6 patients (5%), myelofibrosis – 5 patients (4.2%), non-Hodgkin lymphoma – 4 patient (3.3%), multiple myeloma – 3 patients (2.5%) and one patient with Hodgkin disease and chronic lymphoblastic leukemia. Conclusion: An adequate hematopoietic stem cell collection is fundamental for successful stem cell transplantation.

Keywords: peripheral blood stem cells, apheresis collection, hematopoietic stem cell transplantation

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POLIMORFIZAM HLA KOD MALIGNIH HEMOPATIJA ZA KOJE JE INDIKOVANA TRANSPLANTACIJA MATIČNIH ĆELIJA HEMATOPOEZE

Kačaki N., Blagojević G., Jovanović B., Miladinović Ž., Andrić Z.
Odeljenje za tipizaciju tkiva, Institut za transfuziju krvi Srbije

Uvod: Polimorfizam predstavlja pojavu alelomorfnih oblika gena u populaciji sa učestalošću većom od 1%. HLA gene odlikuje ekstremno visok stepen polimorfizma, odnosno stotine alelnih varijanti koje segregiraju u prirodnim populacijama. Analize polimorfizama imaju praktičnu primenu u transplantaciji matičnih ćelija hematopoeze kao i u ispitivanju udruženosti sa bolestima. Cilj: Ustanoviti polimorfizam HLA kod obolelih od malignih hemopatija, potencijalnu razliku u učestalosti ispitivanih alela kod bolesnika sa mijeloidnim i limfoblastnim neoplazmama. Materijal i metode: Retrospektivnom analizom obuhvaćeno je 410 bolesnika. Uzorci DNK su izolovani ručnom metodom (Qiagen) i automatskom (Maxwell). Tipizacija HLA je rađena upotrebom molekularne tehnike prajmera specifičnih za sekvencu (PCR – SSP, Olerup). Rezultati: Ukupno je dokazano 289 alela, od toga u mijeloidnoj 150, a u limfoblastnoj grupi 139 alela. Najčešće zastupljeni aleli (iznad 10%) u mijeloidnoj grupi su: A*02:01 (28,9%), A*01:01 (14,45%), A*03:01 (12,69%), A*24:02 (10,35%), B*51:01 (13,08%), C*07:01 (16,79%), C*04:01(12,89%), C*12:03 (12,89%), C*02:02 (11,32%), DRB1*11:04 (12,10%), DRB1*16:01 (11,91%), DQB1*03:01 (24,60%), DQB1*05:02 (13,67%), DQB1*05:01 (12,5%). U limfoblastnoj grupi najčešći aleli su: A*02:01 (31,16%), A*01:01 (15,90%), A*24:02 (13,31%), B*51:01(11,36%), C*07:01 (15,90%), C*04:01(15,58%), C*12:03 (14,28%), DRB1*16:01 (11,68%), DQB1*03:01 (20,12%), DQB1*05:02 (13,63%), DQB1*05:01 (11,03%).Nema statistički značajane razlike u distribuciji alela između ispitivanih grupa ($p<.0,05$), kao ni sa poznatim rezultatima zdrave populacije Srbije. Alel A*03:01 se procentualno češće javljao u grupi mijelodnih neoplazmi (12,69% vs 7,79%), razlika nije dostigla statističku značajnost. Zaključak: Prvi put je pokazan polimorfizam kod bolesnika sa malignim hemopatijama. Daljim studijama na većem broju bolesnika bi se eventualno pokazao uticaj HLA polimorfizma na dijagnozu i patogenezu malignih hemopatija, kao i lociranje gena podložnosti.

Ključne reči: polimorfizam, HLA tipizacija, maligne hemopatije

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HLA POLYMORPHISM IN MALIGNANT HEMOPATHIES FOR WHICH HEMATOPOSIS STEM CELL TRANSPLANTATION IS INDICATED

Kačaki N., Blagojević G., Jovanović B., Miladinović Ž., Andrić Z.
Tissue Typing Department, Blood Transfusion Institute of Serbia

Introduction:Polymorphism represents the occurrence of allelomorphic forms of genes in the population with a frequency greater than 1%. HLA genes are characterized by an extremely high degree of polymorphism, i.e. hundreds of allelic variants that segregate in natural populations. Analyzes of polymorphisms have a practical application in hematopoietic stem cell transplantation and examining associations with diseases. Aim: To establish the HLA polymorphism in patients with malignant hemopathies, the potential difference in the frequency of the examined alleles in patients with myeloid and lymphoblastic neoplasms. Material and methods: 410 patients were included in the retrospective analysis. DNA samples were isolated by manual method (Qiagen) and automatic method (Maxwell). HLA typing was done using the molecular technique of sequence-specific primers (PCR - SSP, Olerup). Results: A total of 289 alleles were proven: 150 in the myeloid group, and 139 alleles in the lymphoblastic group. The most frequently represented alleles (above 10%) in the myeloid group are: A*02:01 (28,9%), A*01:01 (14,45%), A*03:01 (12,69%), A*24:02 (10,35%), B*51:01 (13,08%), C*07:01 (16,79%), C*04:01(12,89%), C*12:03 (12,89%), C*02:02 (11,32%), DRB1*11:04 (12,10%), DRB1*16:01 (11,91%), DQB1*03:01 (24,60%), DQB1*05:02 (13,67%), DQB1*05:01 (12,5%). In the lymphoblastic group, the most common alleles are: A*02:01 (31,16%), A*01:01 (15,90%), A*24:02 (13,31%), B*51:01(11,36%), C*07:01 (15,90%), C*04:01(15,58%), C*12:03 (14,28%), DRB1*16:01 (11,68%), DQB1*03:01 (20,12%), DQB1*05:02 (13,63%), DQB1*05:01 (11,03%). There is no statistically significant difference in the distribution of alleles between the examined groups ($p<.0.05$), and results of the healthy population of Serbia. The A*03:01 allele was more frequent in the group of myeloid neoplasms (12.69% vs 7.79%), the difference did not reach statistical significance. Conclusion:Polymorphism was demonstrated for the first time in patients with malignant hemopathies. Further studies on a larger number of patients would eventually show the influence of HLA polymorphism on the diagnosis and pathogenesis of malignant hemopathies, as well as the location of susceptibility genes.

Key words: polymorphism, HLA typing, malignant hemopathies

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ANALIZA NENAMENSKOG I NAMENSKOG DAVANJA AFEREZNIH TROMBOCITA U INSTITUTU ZA TRANSFUZIJU KRVI SRBIJE

Bosnić V, Vavić N, Andrić Z, Jovanović-Srzentić S, Špuran Z, Gogić Z, Obrenović M, Miljuš D.
Institut za transfuziju krvi Srbije, Beograd

Uvod: Na Odeljenju za donorske afereze prikupljaju se aferezni trombociti uglavnom namenjeni hemato-onkološkim bolesnicima.2012. godine počinje formiranje Registra davalaca afereznih trombocita (RDAT). Njega čine nenamenski davaoci koji su dali pisanu saglasnost da se iz uzorka njihove krvi mogu izvoditi dodatne analize (tipizacija HLA i HPA antigena) kako bi se u slučaju refraktarnosti ili aloimunizacije kod bolesnika ili kada nema namenskih davalaca oni pozivali da doniraju trombocite.
Cilj rada je da se prikaže struktura davanja afereznih trombocita u Institutu za transfuziju krvi Srbije (ITKS).
Meterijal i metode: Urađena je retrospektivna analiza broja nenamenskih i namenskih trombocitafereza za period od 2014-2022. godine, broja nenamenskih davalaca u RDAT i urađenih tipizacija HLA i HPA antigena.
Rezultati: Od 2014-2020. god. broj trombocitafereza je bio od 1533-2609, u proseku 2042, procenat nenamenskog davanja od 20% do 30%, u proseku 26,4%. Tokom 2021. i do septembra 2022. godine broj trombocitafereza je bio 2796, odnosno 1868. Nenamenskih trombocitafereza je bilo 1148 (42%) u 2021. godini i 782 (42%) u 2022. godini. U 2022. godini urađene su 323 trombocitafereze za pedijatrijske bolesnike, 176 (55%) od nenamenskih davalaca. Ukupan broj davalaca u RDAT do septembra 2022. godine je 1422, kod 204 davaoca urađena je tipizacija HLA antigena, kod 82 HPA antigena. Za 11 pacijenata sa refraktarnošću na transfuzije trombocita pretraživanjem RDAT pronađeni kompatibilni davaoci.
Zaključak: U 2021. i 2022. godini beleži se porast broja nenamenskih trombocitafereza. Treba povećati broj davalaca u RDAT, sve davaoce iz RDAT treba tipizirati na HLA i HPA antigene, kako bi bolesnici primili adekvatnu i pravovremenu transfuziju trombocita.
Ključne reči: Registar davalaca afereznih trombocita, trombocitafereza, nenamenski davaoci

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ANALYSIS OF UNINTENDED AND INTENDED APHERESIS PLATELETS DONATIONS AT THE BLOOD TRANSFUSION INSTITUTE OF SERBIA

Bosnić V, Vavić N, Andrić Z, Jovanović-Srzentić S, Špuran Z, Gogić Z, Obrenović M, Miljuš D.
Blood Transfusion Institute of Serbia, Belgrade

Introduction: Department for Donor apheresis collects apheresis platelets, mostly for hemato-oncologic patients. In 2012 the formation of Registry of apheresis platelets donors (RAPD) began. It consists of unintended donors who have given written consent that additional analyzes can be performed from blood sample (HLA and HPA antigen typing) so they can be invited to donate platelets in case of refractoriness or alloimmunization in patients or when there are no intended donors.
The aim of the paper is to present the structure of donations of apheresis platelets at The Blood Transfusion Institute of Serbia (BTIS).
Material and methods: A retrospective analysis of unintended and intended plateletpheresis was performed for the period 2014-2022, the number of unintended donors in RAPD and the typing of HLA and HPA antigens.
Results: From 2014-2020. there were 1533-2609 plateletpheresis, on average 2042, the percentage of unintended donations was from 20% to 30%, on average 26.4%. During 2021 and until September 2022, the number of plateletpheresis was 2796 and 1868, respectively. There were 1148 (42%) unintended plateletpheresis in 2021 and 782 (42%) in 2022. In 2022, 323 plateletpheresis were performed for pediatric patients, 176 (55%) were unintended. The total number of donors in RAPD until September 2022 is 1,422, HLA antigen typing was done in 204 donors, HPA antigen in 82. For 11 patients with refractoriness to platelet transfusions, compatible donors were found by searching RAPD.
Conclusion: In 2021 and 2022, there is an increase in number of unintended plateletepheresis. The number of donors in RAPD should be increased, all donors from RDAT should be typed for HLA and HPA antigens, so patients receive adequate and timely transfusion of platelets.
Key words: Registry of apheresis platelets donors, plateletpheresis, unintended donors

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NEŽELJENI DOGAĐAJI KOD DAVALACA REKONVALESCENTNE ANTI- COVID 19 PLAZME U VOJVODINI, SRBIJA

Zorana Budakov Obradović[1,2], Nevenka Bujandrić[1,2], Jasmina Grujić[1,2] ,Jelena Klašnja[1]
[1] *Blood Transfusion Institute Vojvodina, Novi Sad, Serbia*
[2] *The Faculty of Medicine Novi Sad, University of Novi Sad, Serbia*

Uvod: Tokom pandemije Covid 19 virusom, sistem prikupljanja krvi, dovodi do pomeranja pažnje sa dobrovoljnog davaoca krvi (DDK) na dobrovoljnog neplaćenog davaoca plazme (DDP). Rekonvalescentna anti- Covid 19 plazma je sakupljana od davalaca nakon preležane infekcije SARS-CoV-2 virusom.
Cilj rada: odrediti demografske karakteristike, incidencu i tip neželjene reakcije kod davalaca rekovalescentne anti- Covid 19 plazme u AP Vojvodini.
Materijal i metode: Retrospektivna studija neželjenih događaja povezanih sa donorskom afereznom peocedurom- plazmaferezom sprovedena je u Zavodu za transfuziju krvi Vojvodine u Novom Sadu u periodu od 05.05.2020. do 21.02.2022. godine.
Rezultati: Za davanje plazme prijavilo se 1147 osoba koje su prebolele Covid 19 infekciju: 1019 (88,83%) koje nisu nikad davale krv (ne-DDK) i 28 (11,17%) sa iskustvom davanja krvi (DDK). Među prijavljenima bilo je 870 (75,87%) muškaraca i 277 (24,13%) žena. Među 1032/1147 (90%) davaoca plazme bilo je: 970 (94,06%) ne-DDK i 62 (5,94%) DDK; 836 (81,01%) muškaraca i 196 (18,99%) žena. Među 115/1147 (10%) odbijenih bilo je: 90 (78,20%) ne-DDK i 25 (21,80%) DDK; 75 (65,41%) muškaraca i 40 (34,59%) žena. U posmatranom periodu urađeno je 2332 procedure u toku kojih su se kod 34 (1,46%) davalaca javile neželjene reakcije: 21 (61,77%) ne-DDK i 13 (38,23%) DDK; 22 (64,71%) muškarca i 12 (35,29%) žena. Neželjene reakcije su se javile kod jedne (2,94%) osobe, pre izvođenja procedure, kod 27 (79,41%) u toku i kod šest (17,65%) posle završetka procedure. Neželjene reakcije kod DDP su bile: kolaps vene 6, preznojavanje 12, slabost 14, mučnina 5, povraćanje 2, trnjenje usana 2, kolaps 12.
Zaključak: Donorska plazmafereza je generalno sigurna i bezbedna aferezna procedura. Visoka motivacija, adekvatna selekcija i odabir davalaca, kao i odgovarajuća priprema efikasni su u smanjenju broja neželjenih reakcija.
Ključne reči: Plazma; Rekovalescentna anti- Covid 19 plazma; Davaoci krvi.

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ADVERSE EVENTS AMONG CONVALESCENT ANTI- COVID 19 PLASMA DONOR IN VOJVODINA, SERBIA

Zorana Budakov Obradović[1,2], Nevenka Bujandrić[1,2], Jasmina Grujić[1,2] ,Jelena Klašnja[1]
[1] *Blood Transfusion Institute Vojvodina, Novi Sad, Serbia*
[2] *The Faculty of Medicine Novi Sad, University of Novi Sad, Serbia*

Introduction: During the COVID-19 pandemic, donor system experienced a simple shift of attention from the voluntary blood donor (BD) to the voluntary unpaid plasma donor. Convalescent plasma were collected from individuals who have recovered from SARS-CoV-2 infection.
Aim: to determine demographic characteristics, incidence and type of adverse events (AEs) among convalescent plasma donors in AP Vojvodina.
Material and methods: A retrospective study of AEs associated with donor plazmapheresis was conducted in the Blood Transfusion Institute of Vojvodina over the period from Maj 5, 2020 through january 22, 2022 year.
Results: 1147 patients who have recovered from COVID-19 applied to donate plasma: 1019 (88.83%) with non blood donation experience (never blood NBD) and 28 (11.17%) with blood experience (BD); 870 (75.87%) men and 277 (24.13%) women. Among 1032/1147 (67.03%) plasma donors there were 970 (94.06%) NBD and 62 (5.94%) BD; 836 (81.01%) men and 196 (18.99%) women. Among 115/1147 (10%) rejected persons there were 90 (78.20%) NBD and 25 (21.80%) BD; 75 (65.41%) men and 40 (34.59%) women. In the observed period were done 2332 procedure during AEs were identified in 34 (1.46%) donors: 21 (61.77%) NBD and 13 (38.23%) BD; 22 (64.71%) men and 12 (35.29%) women;. AEs occurred: before the procedure 1 (2.94%), during plazmapheresis 27 (79.41%), and after the procedure 6 (17.65%). Six donors had collapsed veins, 12 sweating, 14 weakness, 5 nausea, 2 vomiting, 2 tingling lips, and 12 collaps.
Conclusion: Donor plazmapheresis is a generally safe apheresis procedure. High motivation, adequate selection and good preparation of the donor are effective in reducing the number of AEs.
Keywords: Plasma; Recovalescent anti- Covid 19 plasma; Blood Donors.

UP 68

APHERESIS COLLECTION OF SINGLE DONOR PLATELETS IN THE INSTITUTE FOR TRANSFUSION MEDICINE OF RNM

Useini S[1], Grubovic Rastvorceva R[1,2], Petkovic E[1], Muaremoska Useini S[3], Muaremoska Kanzoska L[4].
[1] *Institute for Transfusion Medicine of RNM, Skopje, N. Macedonia,*
[2] *Faculty of Medical Sciences, University Goce Delcev, N. Macedonia,*
[3] *Special Hospital for Gynecology and Obstetrics - Mother Theresa, Skopje, N. Macedonia*
[4] *University Clinic for Children Disease, Skopje, N. Macedonia*

Background: Apheresis collected platelet concentrate is preferable in terms of reducing the risks of adverse reactions in platelet transfusion when compared to random donor platelet concentrates. The aim of our study is to present our experience in apheresis collection of single donor platelets. Material and Methods: This is a retrospective study performed in the Institute for Transfusion Medicine of RNM from 2010 till 2022. All donors were fully informed on the donation procedure and signed an informed consent for donation. The optimal platelet count that we want to achieve was ≥ 3.0x1011. Minimum preapheresis platelet count in donors requested before the apheresis collection was 150.000/µl. Platelet collection was performed using flow cell separators Haemonetics MCS+ and Teruno BCT Trima Accel. Acid Citrate Dextrose formula A was used for anticoagulation. Results: There were 2269 apheresis platelet collections in total, mean 189 per year. There were 49 apheresis collections in 2010, 66 in 2011, 78 in 2012, 97 in 2013, 105 in 2014, 108 in 2015, 120 in 2016, 208 in 2017, 356 in 2018, 364 in 2019, 300 in 2020 and 418 collections in 2021. The number of plateletpheresis is increasing each year; especially in the last 5 years when 73% of procedures was performed. Median precollection platelet count of donors was 275.000/µl, with range from 180.000/µl to 397.000/µl. Male were 77% and females were 23%. The single procedure usually took 45-70 minutes. The mean platelet count collected was 4.8x1011, range 3-6.5x1011. The mean processed blood volume was 3284ml and mean used ACD-A was 353ml. Mean total volume of collected product was 382ml. The adverse effects included vein perforation and the numbness of the extremities as reaction of ACD-A (hypocalcemia), which occur rarely and was very mild. Conclusions: The collected platelet count was more than the wanted optimum platelet count.
Keywords: apheresis collection, single donor platelets, platheletpheresis

UP 68

POSTER PREZENTACIJE
POSTER PRESENTATIONS

HOTEL CROWNE PLAZA
Beograd, Srbija / Belgrade, Serbia
9-12. novembar 2022. / November 9th-12th 2022

PP 001

OVERVIEW OF BLOOD DONATIONS IN BLOOD TRANSFUSION SERVICE IN GENERAL HOSPITAL – STRUGA IN PERIOD PRE AND DURING COVID-19 PANDEMIC

Kochovska C[1,2], Grubovic Rastvorceva R[2,3], Useini S[2]
[1] *Blood Transfusion Service – Struga,*
[2] *PHI Institute for Transfusion Medicine of RNM, Skopje, N. Macedonia,*
[3] *Faculty of Medical Sciences, University Goce Delcev, N. Macedonia*

Background: Adequate and safe availability of blood has become a significant concern worldwide as COVID-19 pandemic began. The aim of this paper is to review the blood donation in the Blood Transfusion Service in "General Hospital"-Struga (BTS-Struga) in the period pre and during COVID-19 pandemic, in order to see the effects of COVID-19 on the process of blood donation. Material and Methods: The materials used were retrospective monthly reports from the BTS-Struga including mobile teams from 2018 to 2021. Blood donors were analyzed by first-time donation, gender, occupation, ethnicity, reason of deferral etc. Results: BTS-Struga participated with 1448 donations (62.5%) in 2018, 1357 donations (59.8%) in 2019, 1163 donations (68.9%) in 2020 and 1271 donations (63.4%) in 2021 of total blood donation in Struga municipality. Most of the donors were Macedonian 43% followed by 37% Albanian. There were a constantly lower percentage of female donors 11% in our municipality, compared to the state average of 20%. The most of the donors were employed 83%, unemployed 15%, and low 2% were secondary school and college students, as an effect of online learning in the schools and universities during the pandemic. Before the pandemic the blood donation was performed only in in BTS-Struga premises, but with the beginning of pandemic 25% blood donations were performed at the mobile sites. Rejected donors were 1.4% and the most common reason of deferral was hypotension and hypertension. The percentage of family blood donors was 9.5% and first-time donors 16%, which significantly increased during the peak of the pandemic period 2020-2021. We started to collect COVID-19 convalescent plasma as well. Conclusion: BTS-Struga managed to maintain the number of blood donors, despite the small drop when the COVID-19 pandemic began, which contributed to a continuous flow of blood products and meeting the patient's needs.
Keywords: blood donation, COVID-19, blood donors

PP 001

PP 002

TRENDS IN PREDONATION BLOOD DONOR DEFERRAL CHARACTERISTICS IN BLOOD TRANSFUSION DEPARTMENT STRUMICA

Stambolieva D.
Transfusion department Strumica

Background: Blood transfusion service is the vital part of modern health care system without which efficient medical care is not possible. Safe blood supply and transfusion is one of the major issues in transfusion medicine. Potential blood donors may not be able donate blood for several reasons either related to donors own health or risk to the recipient. To ensure safe transfusion, it is paramount that all blood donors are in good health. This leads to shortage of blood donors and necessitates understanding and analyzing the cause of deferral in potential blood donors.
Aim: To evaluate the rate and major reasons of blood donor deferrals
Material and method: A retrospective study- to analyze the causes of blood donor deferrals' over a period of two years from January 2020 till December 2021. Donor eligibility criteria were followed according to the National guidelines for blood donation. Donors deferred were analyzed according to their age, sex, type of donor, type of deferral and reasons for deferral.
Result: Of 2992 blood donors who came to donate blood, 95 % were eligible for donation (2834), 5% were deferred (158). The deferral rate among male population (101/2317 blood donors- 4, 35%) and female population (57/517 blood donors- 11%) were observed. Temporary deferral was significantly more common than the permanent deferral (93% vs. 7%) Leading causes of deferral were anemia (45 causes-28%), Covid 19 vaccine (most in 2021 year, 33 causes -21%), hypertension (32 causes - 20%) tattoo and piercing (18 causes-11%), taking antibiotics (16 causes- 10%), underweight ant under 17 years old (14 causes -8,9%).The leading causes of male donor deferral were anemia , hypertension and vaccine, where among female donors it was anemia, underweight and vaccine.
Anemia was the most common cause of temporal deferral, whereas HbsAg confirmatory positive test was the primary reason of permanent deferral .Maximum deferrals were seen in the age group of 40-60 years (110 causes-69%)
Conclusion: Studying the profile of blood donors, will help us to identify selection of the donor population which could be targeted to increase the pool of voluntary blood donors and also to guide and provide the essential database for the policy design and program implementation
Key words: blood donor,deferrals,safe transfusion

PP 002

PP 003

BLOOD DONATION IN REGIONAL CENTER FOR TRANSFUSION MEDICINE IN TETOVO FROM 2020 TO 2021

Ismani Xhemaili E[1,2], Grubovic Rastvorceva R[2,3], Useini S[2], Ismani E[1,2]

[1] *Regional Center for Transfusion Medicine – Tetovo, N. Macedonia,*
[2] *Institute for Transfusion Medicine of RNM, Skopje, N. Macedonia,*
[3] *Faculty of Medical Sciences, University GoceDelcev, N. Macedonia*

Introduction:Although the municipality of Tetovo has a great tradition inblood donation, the last two years were very challenging due to pandemic. Aim:The purpose of our work is to make a comparison of blood donation in 2020 and 2021in Tetovo.Material and methods:Data was obtained from the blood donations reports in the Regional Center for Transfusion Medicine – Tetovo(RCTM-Tetovo) from 2020 to 2021, including donations with mobile teams. Results:There were 2239 blood donations in 2020 - 1724 (76,99%) in the RCTM-Tetovo and 1178 (25.13%) with mobile teams. There were1762 (78.69%) voluntary and477 (21.30%)familyblood donors, 2058 (91.91%) males and167 (7.45%)females, 1916 (85.57%) employed, 219 (9.78%)not employed,49 (2.18%)high school students, 46 (2.05%)university students and7 (0.31%) retired. According to ethnicity the most of them were Albanians 1107 (49.44%), followed by Macedonians 961 (42.92%) and others 38 (1.69%). There were 137 (6.12%) deferred donors.There were 2448 blood donations in 2021- 1785 (72.91%) inRCTM-Tetovo and 663 (27.08%)with mobile teams. There were 1966 (80.31%) voluntary and 482 (19.68%) family blood donations, 2181 (89.09%) males and 267 (10.90%) females. According to social status they were employed 2022 (82.59%),not employed 175 (7.14%), high school students117 (4.77%), university students 122 (4.98%),retired 12 (0.49%). According to ethnicity there were 1493 (60.98%) Albanian blood donors,926 (37.82%) Macedonianand 29 (1.18%)others. There were 187 (7.63%) deferred donors.Conclusion:The blood supply in RCTM-Tetovo was stabile with slight increase in 2021. There was an increase in the percentage of Albanian blood donors and both, high school and university students in 2021, as well. This was achieved with great effort of our personnel,motivation on many fronts including lectures,presentations,sticking posters in many frequent places in the city and etc.
Keywords: blood donation, COVID-19 pandemic, blood donors

PP 003

PP 004

FEMALE BLOOD DONORS IN THE ISTITUTE FOR TRANSFUSION MEDICINE OF RSM

Ismani E [1,2], Grubovic Rastvorceva R[2,3], Useini S[2], Ismani Xhemaili E[1,2]
[1] *Regional Center for Transfusion Medicine – Tetovo, N. Macedonia,*
[2] *Institute for Transfusion Medicine of RNM, Skopje, N. Macedonia,*
[3] *Faculty of Medical Sciences, University Goce Delcev, N. Macedonia*

Introduction: Gender studies are very limited in the transfusion field, whether considered broadly or with specific regards to the selection, management and retention of donors. Therefore, it seemed important to compare the presence of women among blood donors in different parts of our country and examine the roles that gender is reported to play in the donation of blood in order to identify possible implications for communication and management of donors. Aim: To evaluate the percentage of female blood donors in the voluntary blood donation process in different parts of North Macedonia in 2020 and 2021. Material and Methods: Retrospective analysis was performed on data collected from the annual reports and Information system E-Delphyn at Institute for Transfusion Medicine of RNM. Results: There were in total 45084 blood donation in N. Macedonia in 2020, of which 16.7% (7520) were females. According to the different parts of the country where they donate blood, their distribution was as following: 18% (4508/25014) in the Institute for Transfusion Medicine – Skopje, 16.7% (1105/6627) in Regional Center for Transfusion Medicine (RCTM) – Stip, 16.5% (1358/8234) in RCTM – Bitola and 10.5% (549/5209) in RCTM – Tetovo. There were in total 50906 blood donation in N. Macedonia in 2021, of which 17.71% (9013) were females. According to the different parts of the country where they donate blood, their distribution was as following: 19.7% (5804/29366) in the Institute for Transfusion Medicine – Skopje, 17.6% (1304/7392) in RCTM – Stip, 15.7% (1302/8286) in RCTM – Bitola and 10.3% (603/5862) in RCTM – Tetovo. Conclusion: Presented data showed that the percentage of female blood donors is around 17% in general and only in RCTM – Tetovo the percentage of female blood donors is around 10% in both years. More targeted blood promoting activities are needed to motivate female donors and to encourage this particular category to donate blood.
Keywords: blood donation, women blood donors, donors' management

PP 004

PP 005

EVALUATION OF BLOOD DONATION IN MACEDONIA

Andonov G, Nikoloska I, Useini S, Apostolovska R, Makarovska Bojadjieva T, Velkova E,Trajkova J, Ristovska E, Grubovik Rastvorceva R
Institute of transfusion medicine, Skopje, RN Macedonia

Introduction: Republic of North Macedonia (RNM) has tri Regional centers (RC) for transfusion medicine (Bitola, Shtip and Tetovo), blood donor departments in other towns, and one Institute for transfusion medicine (ITM) in Skopje .
Aim: The aim of this abstract is to evaluate blood donation in 2021.
Material and method: We analyzed data from blood donor departments and form the donor information system.
Results. In RNM, 50 906 blood units were collected in 2021. In ITM-Skopje, 29277 blood units were donated from which 54% were collected by Mobile teams for blood collection (MTBC) and 46% were collected in premises of ITM. From all donations, 26149 (89, %) were Macedonian, 2342 (8,0%) were Albanian and 820 (2,8%) were other nationality (ON). In RC Bitola, from 8328 blood units 5945 (70, 2%) were donated in premises of RC Bitola and 2437 (29%) were collected by MTBC. From all donations, 7769 (92, 6%) were Macedonian, 327(4%) were Albanian and 286 (3,2%) were ON. In RC Shtip, from 7550 blood units 4590 (60, 8%) were donated in premises of RC Shtip and 2960 (39, 2%) were collected by MTBC. From all donations 7550 (96.8%) were Macedonian, 20 (0.2%) were Albanians and 218 (3%) were ON. In RC Tetovo, 5697 blood units were donated from which 4622 (81, 1%) were donated in premises of RC Tetovo and 1075 (18, 9%) were collected by MTBC. From all donations, 2696 (47, 3%) were Macedonian, 2666 (46,7%) were Albanian and 335 (6%) were ON. The overall ethnic distribution of blood donors is: Macedonian-86,3%, Albaninan-10,3% and ON-3,3%.
Conclusion. In all RC blood donation take place mainly in premises of the transfusion centers, while in ITM-Skopje the proportion of donated blood at the blood donation department and collected by mobile teams is almost the same. There is difference in the ethnic distribution of blood donors among the blood transfusion centers which is related to the place of living.
Key word: blood donation, mobile team

PP 005

PP 006

OVERVIEW OF BLOOD DONATIONS IN BLOOD TRANSFUSION SERVICE -GOSTIVAR IN THE PERIOD OF 2019 - 2020

Xheladini I[1,2], Grubovic Rastvorceva R[2,3], Useini S.[2]

[1] *Blood Transfusion Service – Gostivar, N. Macedonia*
[2] *Institute for Transfusion Medicine of RNM, Skopje, N. Macedonia,*
[3] *Faculty of Medical Sciences, University Goce Delcev, N. Macedonia*

Background: Blood donation is a vital part of worldwide healthcare. Aims: Our aim was to compare the number of blood donations in 2019 (before the COVID2019 pandemic) and blood donations in 2020 during pandemic in Blood Transfusion Service in Gostivar (BTS-Gostivar). Materials and Methods: Data was taken from the monthly and yearly reports of blood donations in BTS-Gostivar for the years 2019-2020, including donations with mobile teams. Donors were analyzed according to gender, age, occupation, nationality, the types of blood donation, and etc. Results: There were 1108 blood donations in 2019 and 1007 donations in 2020, of which 76.4% (847/1108 donations) in BTS premises and 23.5% (261/1108) with mobile teams in 2019, and 84.7% donations in BTS premises (853/1007) and 17% with mobile teams (172 /1007) in 2020. There were 85.1% male donors and 14.8% females in 2019 and 88.8% males and 12.9% females in 2020, with slight decrease in female blood donors. According to ethnical distribution there was a decrease in Macedonian blood donors (41% in 2020 vs. 48% in 2019) and increase in Albanian blood donors (44.4% in 2020 vs. 35% in 2019). There was a significant increase in first-time donors, 23% in 2020 compared to 15% in 2019. Total number of deferred donors was 10.1% in 2019 and 5.1% in 2020. There were no family donations in 2019, but with the start of pandemic in 2020, there were 11.9% family donors (91/1007). There was significant decrease of young blood donors (high school students and university students) 2.58% in 2020, compared to 6.14% in 2019, due to on-line learning during pandemic. Conclusions: The COVID-19 pandemic has led to a reduction of blood related activities in the region, but our BTS-Gostivar manages to keep stabile blood supply.
Keywords: blood donation, COVID-19-19 pandemic, blood donors

PP 006

PP 007

DODATNA LABORATORIJSKA ISPITIVANJA DOBROVOLJNIH DAVALACA UKLJUČENIH U PROJEKAT PRIKUPLJANJA ANTI –COVID PLAZME

Jagličić I., Mitrović M., Vujović J., Bosnć V., Mijucić V, Savić O.
Institut za transfuziju krvi Srbije, Beograd

U početku pandemije SARS CoV-2 virusa nisu postojali specifični antivirusni lekovi pa je primena plazme COVID-19 rekonvalescenata bila logican izbor u terapiji. U ITKS je brzo nakon proglašenja epedimije, započeo Projekat prikupljanja i primene anti-COVID 19 plazme. Postoji dosta radova koji se bave analizom prisustva anti-fosfolipidnih antitela kod COVID pacijenata i osoba koje su preležale COVID infekciju. Rezultati ovih ispitivanja su veoma nehomogeni. Cilj rada je bio da se utvrdi zastupljenost anti-kardiolipinskih (aCl-At) i anti-beta2 glikopritein1 antitela (ab2GP1-At) u populaciji davalaca anti-COVID –19 plazme. U Laboratoriji za biohemijska i imunohemijska ispitivanja analizirali smo serume 347 davoca anti-COVID plazme (starosti 26-45 godina, oba pola) na prisuatvo aCl-At i ab2GP- At. Uzorci davalaca su u laboratoriju stizali na ispitivanje osnovnih i proširenih biohemijskih (ukupni proteini, analiza funkcija jetre, CRP) i imunohemijskih parametara (elektroforeza proteine i koncentracija IgG), a u sklopu kontrole zdravlja davalaca. Uzorkovanje je vršeno 1-5 meseci posle infekcije koja je bila potvđena PCR testom. aCl-At i ab2GP1 su odeđivana ELISA tehnikom. Biohemijsjke analize su rađene na analizatoru MINDRAY BS120, elektroforeza proteina je metodom po Tiseliusu, a koncentracija IgG imuno-nefelometrijom. aCl i ab2GP1 antitela bila su prisutna kod 16 davalaca (4.61%). Kod 12 davalaca je identifikovano po jedno At (2 aClIgM, 4 aClIgG, 5 ab2IgM, 1 ab2IgG) i kod 4 dva antitela (aClIgM i ab2IgM 2, po jedan aClIgG i ab2IgG i aClIgM i aClIgG). Biohemijski parametara ovih 16 davalaca su pokazala povišen AST i ALT kod 3, a od njih su dva isključena sa programa zbog povišenog CRP. Koncentracije IgG su bile u granicma normale. Elektroforeza proteina je pokazivala povećanje intenziteta prealbumina kod 7 davalaca, alpha zone kod 3 davaoca i gamma zone kod 7 od 16 davaoca. Dobijeni rezultati su u skladu sa podacima iz literatute i našim ranijim ispitivanjma prisustva Cl-At i ab2GP1-At u domaćoj zdravoj populaciji.

Ključne reči: antikardiolipinska antitela, anti-beta2 glikopritein1 antitela, anti-COVID plazma,

PP 007

ADDITIONAL LABORATORY EXAMINATIONS OF VOLUNTARY DONORS INCLUDED IN ANTI-COVID PLASMA COLLECTION PROJECT

Jagličić I., Mitrović, M., Vujović J, Bosnć V, Mijucić V, Savić O.
Institute for Blood Transfusion of Serbia, Belgrade

At the beginning of the pandemic, there were no specific antiviral drugs or a vaccine, so the use of plasma from COVID-19 convalescents was imposed. In BTIS, after the announcement of the epidemic, the project of collection and administration of anti-COVID 19 plasma started. Papers about the analysis of the presence of anti-phospholipid antibodies in COVID patients and COVID convalescents are very inhomogeneous. The aim of the study was to show that the prevalence of anti-cardiolipin (aCl-Ab) and anti-beta2 glycoprotein1 antibodies (ab2GP1-AB) in the population of anti-COVID-19 plasma. Biochemical and immunochemical laboratory, analyzed serums of 347 anti-Covid plasma donors (aged 26-45 years, both sexes) for the presence of aCl-Ab and ab2GP-Ab. Samples were analized for basic and extended biochemical (total proteins, liver function analysis, CRP) and immunochemical parameters (protein electrophoresis and IgG concentration). Sampling was performed 1-5 months after the infection, which would be confirmed by PCR test. aCl-Ab and ab2GP1-Ab were determined by ELISA technique. Biochemical analyzes were performed on a MINDRAY BS120 analyzer, protein electrophoresis was performed using the Tiselius method, and IgG concentration was performed using immuno-nephelometry. aCl and ab2GP1 antibodies were present in 16 donors (4.61%) In 12 donors one Ab was identified (2 aClIgM, 4 aClIgG, 5 ab2IgM, 1 ab2IgG) and in 4 two antibodies (aClIgM and ab2IgM) 2, one each aClIgG and ab2IgG and aClIgM and aClIgG. Biochemical parameters of these donors showed elevated AST and ALT (3). Two of them were excluded from the program due to elevated CRP. IgG concentrations were within normal limits. Protein electrophoresis showed increased intensity of prealbumin in 7 donors, alpha zone in 3 donors and gamma zone in 7out of 16 donors. The obtained results are in accordance with the data from the literature and our earlier tests aCl-Ab and ab2GP1-Ab in the local healthy population

Key words: anticardiolipin antibodies, anti-beta2 glycoprotein1 antibodies, anti-COVID plasma,

PP 008

NAMENSKO DAVANJE KRVI - PODSTICAJ I IZAZOV TOKOM PANDEMIJE

Šurbevski M[1], Šurbevska Boneva B[2], Taškovska M.[1]
[1] JZU GOB "8mi. Septembar"
[2] Institut za plućne bolesti i tuberkulozu, Skoplje

Uvod: Početkom marta 2020. godine u celoj zemlji je proglašeno vanredno stanje zbog brzog širenja pandemije izazvane virusom Kovid-19, koje je trajalo do marta 2022. godine. U tom periodu, broj obolelih i umrlih bio je značajno veći u odnosu na prethodnih godina. Da bismo obezbedili adekvatno i redovno snabdevanje krvlju i krvnim proizvodima, izradili smo plan i jasno definisali aktivnosti transfuziološke službe u našoj ustanovi. Ovo je obuhvatilo niz mera koje se odnose na dobrovoljne davaoce krvi: način i vreme poziva, izolaciju, organizaciju rada i kriterijume za izbor davalaca.
Cilj rada: predstaviti naše rezultate i način prikupljanja krvi i pripreme krvnih produkata tokom pandemije.
Materijal i metode: Analizirali smo broj redovnih i namenskih davalaca krvi za period od 01.03.2020 do 01.03.2022. Dobijene podatke uporedili smo sa istim periodom pre pandemije.
Rezultati: U periodu pandemije prikupljeno je ukupno 3098 jedinica krvi, od čega je 318 jedinica uzeto od namenskih davalaca. Izdato je 2977 jedinica deplazmirane krvi i 3098 doza SSP. U istom periodu pre pandemije, od 01. februara 2018. do 01. marta 2020. uzeto je 4.619 jedinica krvi, od čega su 603 jedinice bile od namenskih davalaca.
Diskusija: Tokom pandemije smanjene su planirane i elektivne hirurške intervencije. Kao rezultat toga, potreba za krvlju i krvnim derivatima je značajno smanjena. Zbog specifičnih uslova rada i preventivnih mera, smanjen je broj dobrovoljnih davalaca krvi. Preduzete su sve mere za zaštitu dobrovoljnih davalaca i redovno snabdevanje krvlju i krvnim derivatima. Ukupan broj prikupljenih jedinica krvi u ispitivanom periodu manji je za 1521 (-33%) u odnosu na isti period pre pandemije. Procenat namenskih davalaca krvi tokom pandemije bio je 10,3 %, dok je u prethodnom periodu taj procenat iznosio 13 %.
Zaključak: Tokom pandemije smanjen je broj elektivnih hirurških zahvata. Zbog vanrednog stanja, očekivali smo dugoročno smanjenje broja dobrovoljnih davalaca krvi (DDK). Ne postoji značajna razlika u procentu namenskih davalaca krvi tokom ili pre pandemije. Međutim, namenski davaoci su od velikog značaja, posebno kada postoji manjak krvi i krvnih komponenata retkih krvnih grupa.

Ključne reči: davaoci krvi, epidemija, namenski davaoci krvi

PP 008

DEDICATED BLOOD DONATION - STIMULATION AND CHALLENGE DURING THE PANDEMIC

Shurbevski M.[1], Shurbevska Boneva B[2], Tashkovska M[1]
[1] JZU GOB "8-mi Septemvri"
[2] Institute for Lung Diseases and Tuberculosis Skopje

Introduction: At the beginning of March 2020, a state of emergency was declared in the entire country due to the rapid spread of the Covid-19, which lasted until March 2022. During this period the number of patients and mortality were significantly higher than in previous years. For an adequate and regular supply of blood and blood products, we created a plan and clearly defined the activities of the transfusion service in our institution. This included a number of procedures related to voluntary donors: method and time of calling, isolation, organization of actions and criteria for selection of donors.
The goal of our paper: to present our results and the way blood is collected and the preparation of blood products during the pandemic.
Material and methods: We analyzed the number of regular and dedicated blood donors for the period from March 1, 2020 to March 1, 2022. We compared these data with the same period beforethe epidemic.
Results: During the pandemic period, we collected a total of 3098 units of blood, of which 318 units were taken from dedicated donors. 2977 units of deplasmated blood and 3098 doses of FFP wereissued. In the same period before the pandemic, from February 1, 2018 to March 1, 2020, 4,619 units of blood were taken, of which 603 units were from dedicated donors.
Discussion: During the pandemic, planned and elective surgical interventions were reduced, and the need for blood and blood derivatives was significantly reduced. Due to specific working conditions and preventive measures, the number of voluntary blood donors has decreased. All measures have been taken for the protection of voluntary donors and the regular supply of blood and blood derivatives. The total number of blood units collected in the forementioned period was 1521, (- 33%) less than in the same period before the epidemic. The percentage of dedicated donors during the pandemic was 10.3%, while in the previous period that percentage was 13%. There is no significant statistical difference in dedicated donors before and during the pandemic.
Conclusion: During the pandemic, the number of elective surgical procedures decreased. Due to the state of emergency, we expected a reduced number of voluntary blood donors (VBD) in the long term. There is no significant difference in the percentage of dedicated donors during or outside the pandemic. Nevertheless, the importance of dedicated donors is great, especially when there is a shortage of blood and blood components of rare blood groups.

Key words: blood donors, epidemic, dedicated donors

PP 009

ZNANJE, STAVOVI, PREPREKE I MOTIVACIJA ZA DAVANJE KRVI KOD STUDENTSKE POPULACIJE U VOJVODINI

Kocić N, Budakov Obradović Z, Bujandrić N, Grujić J, Bežanović M.
Zavod za transfuziju krvi Vojvodine, Novi Sad, Srbija

SAŽETAK
Uvod: Smanjene zalihe krvi predstavljaju globalni problem, praćen negativnim trendom broja prikupljenih jedinica krvi. Problem zahteva uspostavljanje efektivne promocije davalaštva krvi. Podsticanje davalaca da daju krv je efikasnije kada su poznati njihovo znanje, stavovi, motivacioni faktori i potencijalne prepreke za davanje krvi.
Cilj rada: Ispitati postojanje razlika u znanju i stavovima o dobrovoljnom davanju krvi između redovnih i novih davalaca krvi studentske populacije Vojvodine, kao i potencijalne barijere i motivacione faktore za davanje krvi.
Materijal i metode: Prospektivna studija sprovedena je u studentskoj populaciji Univerziteta u Novom Sadu u periodu od 01. maja do 31. jula 2022. godine. Podaci su prikupljeni putem specijalno dizajniranog upitnika sa 22 pitanja, podeljena u četiri grupe (stavovi, znanje, motivacija i potencijalne prepreke).
Rezultati: Istraživanjem je obuhvaćeno 500 studenata, 297 (59,4%) muškog i 203 (40,6%) ženskog pola. Među njima je bilo 224 (44,8%) redovna i 276 (55,2%) novih davalaca krvi. U obe grupe su utvrđeni: dobro znanje o davalaštvu (78,6%); pozitivan stav o davanju krvi (82%); glavni motivacioni faktori: pomoć osobama kojima je krv potrebna (67%), hitan apel medija za davanje krvi (18,5%), davanje krvi članovima porodice/prijateljima (11%); potencijalne prepreke: strah od igle (40,2%), strah od neželjenih reakcija nakon davanja krvi (22,6%), nedostatak podsticaja za davanje krvi (21,8%). Utvrđena je statistički značajna razlika u znanju i stavovima između redovnih i novih davalaca ($p < 0,05$). Pomoć onima kojima je krv potrebna bio je statistički značajniji motiv kod redovnih davalaca ($p < 0,05$). Strah od neželjene reakcije bio je statistički značajnija barijera kod redovnih davalaca ($p < 0,05$).
Zaključak: Ova studija pokazuje da studentska populacija ima relativno dobro znanje i povoljan stav o dobrovoljnom davalaštvu krvi. Promotivne aktivnosti zasnovane na ovom istraživanju doprineće otklanjanju barijera za davanje krvi kao i podizanju svesti studenata o davanju krvi kao humanom i visoko moralnom činu.
Ključne reči: Davaoci krvi; Motivacija; Studenti

PP 009

KNOWLEDGE, ATTITUDE, BARRIERS AND MOTIVATIONS REGARDING BLOOD DONATION AMONG THE STUDENT POPULATION IN VOJVODINE

Kocić N, Budakov Obradović Z, Bujandrić N, Grujić J, Bežanović M.
Blood Transfusion Institute Vojvodina, Novi Sad, Serbia

ABSTRACT
Introduction: Reduced blood supplies are recognized as a world-wide problem, accompanied by decreasing trend of blood collection. The problem requires the establishment of effective blood donor (BD) promotion. Encouraging BD to donate blood is more effective when their knowledge, attitudes, motivational factors and potential barriers to donating are known.
Aim: To analyze of knowledge and attitudes about voluntary blood donation between regular and first time BD of the student population of Vojvodina, potential barriers and motivational factors for blood donation.
Material and Methods: The prospective study was conducted in student population of the University of Novi Sad in the period from May 1 to July 31, 2022. Data were collected through a specially designed questionnaire with 22 questions, divided into four groups (attitudes, knowledge, motivation, potential barriers).
Results: The research included 500 students, 297(59.4%) male and 203(40.6%) female. Among them were 224(44.8%) regular and 276(55.2%) first time BD. In both groups, the following were found: good knowledge about donating (78.6%); positive attitude towards donating (82%); main motivating factors: helping people who need blood (67%), urgent media appeal to give blood (18.5%), donating blood to family/friend members (11%); potential barriers to donating blood: fear of needles (40.2%), fear of adverse reactions after donating blood (22.6%), lack of incentive to donate blood (21.8%). A statistically significant difference was found towards knowledge and attitudes in regular and first time BD ($p< 0.05$). Helping those who need blood had statistically significant correlation with regular BD ($p< 0.05$). Fear of adverse reaction was statistically significant barrier among regular BD ($p< 0.05$).
Conclusion: This study suggests that student population has relatively good knowledge and favorable attitude about blood donation. Promotional activities based on research will contribute to removing barriers to donating blood and contribute to raising student's awareness of donating blood as a humane and highly moral act.
Keywords: Blood Donors; Motivation; Students

PP 010

ZADOVOLJSTVO DOBROVOLJNIH DAVALACA KRVI U INSTITUTU ZA TRANSFUZIJU KRVI SRBIJE U PERIODU 2018-2021.

Savvas Radević, S. Jovanović, V. Kuljić, J. Stojneva Istatkov
Institut za transfuziju krvi Srbije

Uvod: Zadovoljstvo dobrovoljnih davalaca krvi (DDK) je jedan od najvažnijih faktora regrutovanja novih i zadržavanja redovnih DDK. Institut za transfuziju krvi Srbije (ITKS) je decembra 2018, 2019. i 2021. godine sproveo anketu među DDK na Odeljenju za prikupljanje krvi i komponenata krvi po proceduri ITKP 069 „Praćenje i merenje zadovoljstva korisnika". Zbog pandemije „COVID-19" anketa nije bila sprovedena u 2020. godini. Cilj: Cilj studije je evidentiranje izazova i pronalaženje mogućih solucija radi povećanja zadovoljstva i broja kako redovnih DDK tako i novo-registrovanih DDK. Materijal i metode: U toku jedne radne nedelje anonimnom anketom po završetku procedure prikupljanja krvi su obuhvaćeni DDK na svim radnim mestima prikupljanja krvi ITKS. Analizirana je i knjiga utisaka u Odeljenju za prikupljanje krvi ITKS i evidentirane pohvale, primedbe i sugestije DDK. Rezultati: Na izuzetno visokom procentu se zadržava profesionalizam i ljubaznost osoblja pri dolasku DDK (2018 – 99%; 2019 – 98,51%; 2021 – 99,61%), tokom davanja krvi (97%; 99%; 99,61%), kao i po završetku davanja (99%; 98,26%; 99,22%). Ističe se blagi porast ispitanika koji prvi put daju krv 2021. godine (18%; 16.67%; 23,35%). Evidentirali smo i visok procenat i blagi porast u 2021. godini DDK koji će sigurno i nadalje davati krv (95%; 93,53%; 96,50%). Knjiga utisaka beleži veći broj pohvala u odnosu na sugestije (2018 – 63 pohvale i 13 sugestija; 2019 – 64 i 16; 2021 – 32 i 1). Zaključak: Rezultati ankete ukazuju da su DDK u toku 2018-2021. godine bili zadovoljni kvalitetom rada osoblja ITKS. U visokom procentu iskazano je zadovoljstvo ljubaznošću i profesionalizmom zaposlenih. Od primedbi i sugestija najviše je bilo pohvala ali ima i primedbi na nedostatak parking prostora ispred Instituta kao i nedostatak majica i nedostatak zahvalnih obroka. Rešavanjem navedenih primedbi doprinećemo regrutovanju novih i zadržavanju redovnih DDK.

Ključne reči: Davanje krvi, Dobrovoljni davaoci krvi, Zadovoljstvo, Anketa

PP 010

VOLUNTARY BLOOD DONORS' SATISFACTION AT THE BLOOD TRANSFUSION INSTITUTE OF SERBIA FOR THE PERIOD 2018-2021

Savvas Radevic, S. Jovanović, V. Kuljić, J. Stojneva Istatkov
Blood Transfusion Institute of Serbia

Introduction: The satisfaction of voluntary (non-remunerated) blood donors (VBD) is one of the most important factors in the recruitment of new and retention of regular VBD. In December 2018, 2019 and 2021, the Blood Transfusion Institute of Serbia (BTIS) conducted a survey at the Department for collection of blood and blood components according to ITKP 069 procedure "User satisfaction monitoring and evaluation". Due to the "COVID-19" pandemic, the survey was not conducted in 2020. Objective: The aim is to identify challenges and find possible solutions to increase satisfaction and number of both regular VBD and newly-registered VBD. Material and methods: During one working week, we conducted an anonymous survey with VBD after completing the blood collection procedure at all BTIS blood collection workplaces. The impressions book at the Hall of BTIS was also analysed; praises, remarks and suggestions of DDK were recorded. Results: Staff professionalism and courtesy is maintained at an extremely high percentage upon VBD arrival (2018 – 99%; 2019 – 98.51%; 2021–99.61%), during blood donation (97%; 99%; 99.61%) and at the end of the process (99%; 98.26%; 99.22%). A slight increase in respondents who donate blood for the first time in 2021 (18%; 16.67%; 23.35%) is highlighted. Moreover, we recorded a high percentage and a slight increase in 2021 of VBD who will certainly continue to donate blood (95%; 93.53%; 96.50%). The impressions book records a higher number of praises than remarks (2018 – 63 praises and 13 remarks; 2019 – 64 and 16; 2021 – 32 and 1). Conclusion: The results of the survey indicate that the VBD in the period of 2018-2021 were satisfied with the quality of work. A high percentage expressed satisfaction with the employees' courtesy and professionalism. Most comments were praises, but there were also remarks about lack of Institute parking spaces, T-shirts and complimentary meals. By solving these, we may contribute to the recruitment of new and retention of regular VBD.

Keywords: Blood donation, Voluntary blood donors, Satisfaction, Survey

PP 011

NEŽELJENE REAKCIJE KOD DOBROVOLJNIH DAVALACA CELE KRVI U VOJVODINI TOKOM 2021. GODINE

Bežanović M, Bujandrić N, Budakov Obradović Z, Kocić N, Grujić J.
Zavod za transfuziju krvi Vojvodine, Novi Sad, Srbija.

Uvod: Dobrovoljni davaoci krvi, u većini slučajeva, dobro tolerišu postupak davanja cele krvi, međutim, povremeno se mogu javiti neželjene reakcije. Neželjene reakcije kod davalaca često imaju negativan uticaj na njihov ponovni dolazak, stoga osoblje transfuzioloških ustanova mora biti edukovano i adekvatno obučeno da iste prepozna i zbrine davaoce krvi koji pre, tokom ili nakon procedure dožive neželjene reakcije. Incidencija neželjenih reakcija iznosi oko 1%.
Cilj rada: Utvrditi učestalost i težinu neželjenih reakcija koje su se javile kod davalaca krvi na teritoriji Vojvodine, analizirati uzrast i profil davalaca kod kojih su prepoznate, ukazati na moguću prevenciju neželjenih reakcija.
Materijal i metode: Retrospektivna studija analizirala je zapise o neželjenim reakcijama kod davalaca cele krvi u Zavodu za transfuziju krvi Vojvodine, u periodu od 1.1. do 31. 12. 2021. godine. Iz informacionog sistema Zavoda dobijeni su demografski podaci o davaocima. Podaci su analizirani prema težini neželjenih reakcija (slabe, srednje teške, teške).
Rezultati: Tokom perioda studije bilo je 43 075 donacija krvi. Pri 603 (1,4%) donaciji je došlo do neželjene reakcije kod davalaca. Incidencija je bila 2 na 100 donacija. Davaoci koji su doživeli neželjene događaje imali su 26,0 ± 6,8 godina, 403 (66,8%) ispitanika su činili muškarci, a 203 (33,2%) žene, dok je prvi put davalo krv 495 (82,1%). Kod 483 (80%) davalaca javila se vazovagalna reakcija, 151 (25%) je imalo mučninu, 72 (12%) je doživelo sinkopu, 36 (6%) je razvilo hiperventilaciju, 12 (2%) je imalo hematom. Gubitak svesti, zastoj srca i konvulzije se nisu javljali. Kod višestrukih davalaca, neželjeni efekti su se značajno manje javljali ($p<0,05$).
Zaključak: Iako je broj davalaca sa neželjenim reakcijama u našoj ustanovi nizak, neophodno je njihovo praćenje, promptno reagovati u slučaju njihove pojave i rizike nastanka svesti na minimum, prvenstveno kroz edukaciju i pripremu davalaca za postupak davanja cele krvi.
Ključne reči: Davaoci krvi; Hemovigilanca; Nesvestica.

PP 011

ADVERSE REACTIONS IN VOLUNTARY WHOLE BLOOD DONORS IN VOJVODINA DURING 2021

Bežanović M, Bujandrić N, Budakov Obradović Z, Kocić N, Grujić J.
Blood Transfusion Institute Vojvodina, Novi Sad, Serbia.

Introduction: Blood donors (BDs), in most cases, tolerate the whole blood donation procedure well, however, occasionally adverse reactions (ARs) may occur. ARs with donors often have a negative impact on their return, therefore, the staff of transfusion institutions must be educated and properly trained to recognize and take care of BDs who experience them before, during or after the procedure. The incidence of ARs is about 1%.
Aim: To determine the frequency and severity of ARs that occurred among BDs in the territory of Vojvodina, analyze the age and profile of donors in whom they were recognized, indicate possible prevention of ARs.
Material and methods: A retrospective study analyzed the records of ARs among whole BDs at the Blood Transfusion Institute Vojvodina, from January 1, until December 31, 2021. Demographic data on donors were obtained from the Institute's information system. The data were analyzed according to the severity of ARs (mild, moderate, severe).
Results: During the study period 43 075 persons donated whole blood. The ARs were identified in 603 (1,4%) BDs. The incidence was 2 in every 100 donations. BDs who suffered ARs were 26,0 ± 6,8 years old, 403 (66,8%) were male, 203 (33,2%) were female, while 495 (82,1%) donated blood for the first time. In 483 (80%) BDs vasovagal reaction occurred, 151 (25%) experienced nausea, 72 (12%) suffered syncope, 36 (6%) developed hyperventilation, 12 (2%) gained hematoma. Loss of consciousness, cardiac arrest and convulsions were not reported. In multiple BDs, ARs were significantly less frequent ($p<0,05$).
Conclusion: Although the number of donors with ARs in our institution is low, it is necessary to monitor them, react promptly in case of their occurrence and minimize the risks of occurrence, primarily through education and preparation of donors for the whole blood donation procedure.
Key words: Blood donors; Haemovigilance; Fainting.

PP 012

NEŽELJENE REAKCIJE U TOKU DAVANJA KRVI U INSTITUTU ZA TRANSFUZIJU KRVI SRBIJE U PERIODU OD 01.01.2018. DO 31.12.2021.

Isaković V, Jovanović S, Jovanovic S, Kuljic V, Stojneva-Istatkov J.
Institut za transfuziju krvi Srbije, Beograd, Srbija

Uvod: Dobrovoljno davanje krvi smatra se bezbednom procedurom. U nekim slučajevima se mogu dogoditi neželjene reakcije različite težine u toku ili nakon davanja krvi, koje se mogu podeliti u tri grupe: blage, srednje teške i teške. Takođe, pokazano je da je veća učestalost neželjenih reakcija kod novih davalaca i kod žena.
Cilj rada: Cilj ovog rada je bio utvrđivanje učestalosti neželjenih reakcija kod dobrovoljnih davalaca krvi u odnosu na njihovu težinu, definisanje tipa, identifikovanje davalaca kod kojih se one češće javljaju, unapređenje mera za njihovu prevenciju.
Materijal i metode: Deskriptivna studija za period od 1.1.2018. do 31.12.2021. U studiju je uključeno 280851 dobrovoljnih davanja krvi. Podaci o neželjenim reakcijama preuzeti su iz baze podataka ITKS.
Rezultati: Prijavljeno je 2405 neželjenih reakcija kod 280851 davanja krvi, tako da je ukupna incidenca 0,86%, odnosno javi se 8,6 neželjenih reakcija kod 1000 davanja. Blage reakcije čine 88,67%, srednje teške 11,21% i teške 0,12% od ukupnog broja neželjenih reakcija. Takođe, relativno su slične incidence broja novih davalaca i broja žena u odnosu na ukupan broj neželjenih reakcija u odnosu na broj davalaca po zabeleženoj godini.
Zaključak: Rezultati studije pokazuju relativnu konstantnost i nisku incidencu u broju neželjenih reakcija kod dobrovoljnih davalaca krvi. Preporučene mere, kao što su konzumiranje vode i drugih tečnosti, ali i razgovor sa davaocima radi skretanja misli sa njima pre davanja krvi pokazuju se kao bitni faktori za prevenciju neželjenih reakcija u toku i nakon davanja krvi.
Ključne reči: neželjene reakcije, dobrovoljni davalac, prevencija, mere.

PP 012

ADVERSE REACTIONS DURING VOLUNTARY BLOOD DONATION FROM 1.1.2018. TO 31.12.2021. AT THE BLOOD TRANSFUSION INSTITUTE OF SERBIA

Isakovic V, Jovanovic S, Jovanovic S, Kuljic V, Stojneva-Istatkov J.
Blood Transfusion Institute of Serbia, Belgrade, Serbia

Background: Voluntary blood donating is considered a safe procedure. In some cases adverse reactions may occur during or after blood donation. They can be divided into three groups: mild, moderate and severe. Also, it was previously shown that the adverse reactions occurred more frequently in new blood donors and in women.
Goal: The goal of this study was to estimate the frequency of adverse reactions in correlation to their type, definition of types of adverse reactions, the identification of voluntary donors who develop reactions more often, improving measures for their prevention.
Material and Methods: Descriptive study was conducted from 1.1.2018 to 31.12.2021. The study included 280851 voluntary blood donations. Data of adverse reactions were taken from the information system of the Blood Transfusion institute of Serbia.
Results: Out of 280851 donations, 2405 adverse reactions were reported, so the incidence was 0.86, or almost 8.6 adverse reactions per 1000 donations. Out of all adverse reactions, mild reactions occurred in 88.67%, moderate in 11.21% and severe in 0.12% of cases. Also, the incidence of new blood donations and the donations that were done by women are relatively similar to those within the total number of blood donations per year.
Conclusions: The results of this study show a relative consistency and low incidence in the number of adverse reactions in voluntary blood donating. Measures, such as taking water and other liquids as well as talking with donors in order to avoid thinking about donating blood are shown as important factors for the prevention of adverse reactions during or after blood donations.
Keywords: adverse reactions, voluntary blood donor, prevention, measures.

PP 013

TROMBOCITAFEREZE U INSTITUTU ZA TRANSFUZIJU KRVI SRBIJE – DA LI SMO NA DOBROM PUTU?

Gogić Z, Bosnić V, Vavić N, Špuran Z, Obrenović M, Miljuš D.
Institut za transfuziju krvi Srbije, Beograd

Uvod: Odeljenje za donorske afereze bavi se prikupljanjem afereznih trombocita. Od 2012. god. počinje formiranje Registra davalaca afereznih trombocita (RDAT) zbog malog broja adekvatnih, namenskih davalaca trombocita i sve većeg broja bolesnika koji primaju transfuzije. RDAT čine davaoci koji su dali pisanu saglasnost da se mogu pozivati po potrebi da doniraju trombocite.
Cilj rada: Prikazati udeo nenamenskih trombocitafereza u odnosu na ukupan broj trombocitafereza u Institutu za transfuziju krvi Srbije, kao i broj i strukturu davalaca u RDAT.
Materijal i metode: Analiziran je broj afereznih procedura – trombocitafereza za period od 2017–2022. godine, korišćenjem podataka Informacionog sistema Instituta za transfuziju krvi Srbije.
Rezultati: Tokom 2017. godine urađene su 1 754 trombocitafereze, nenamenskih je bilo 586 (33%); u 2018. godini od 1 921 trombocitafereze, nenamenskih je bilo 583 (30%); 2019. godine od 2 362 trombocitafereze, nenamenskih je 432 (25%), 2020. od ukupno 2 609, nenamenskih je 732 (28%); 2021. od 2 796, nenamenskih je bilo 1 148 (42%), i do septembra 2022. od 1 868 procedura, nenamenskih je 782 (42%). Ukupan broj davalaca u RDAT do septembra 2022. god je 1 422. Tokom 2021. god. u RDAT je pristupilo 106 davalaca: 70 od njih prethodno su bili namenski davaoci trombocita, 36 su bili dobrovoljni davaoci krvi (DDK). Tokom 2022. za RDAT se prijavilo 209 davalaca: od toga 142 nekada namenskih davalaca trombocita, 67 dobrovoljnih davalaca krvi.
Zaključak: Postoji porast nenamenskih trombocitafereza kao rezultat većeg broja davalaca u RDAT. Treba nastaviti sa širenjem RDAT kroz motivaciju dobrovoljnih davalaca krvi i regrutaciju namenskih davalaca trombocita sa ciljem da nenamensko davanje trombocita bude dominantno.
Ključne reči: Registar davalaca afereznih trombocita, aferezni trombociti, trombocitafereza

PP 013

PLATELETPHERESIS AT THE BLOOD TRANSFUSION INSTITUTE OF SERBIA - ARE WE ON THE RIGHT WAY?

Gogić Z, Bosnić V, Vavić N, Špuran Z, Obrenović M, Miljuš D.
Blood Transfusion Institute of Serbia, Belgrade

Introduction: Apheresis platelets are collected at the Department for donor apheresis. Due to a small number of adequate, intended platelet donors and the increasing number of patients receiving transfusions in 2012 begun the forming of the Registry of Apheresis Platelet Donors (RAPD). It consists of donors who have given written consent to be invited for donation of platelets if necessary.
The aim of the paper is to show: the share of unintended plateletpheresis in total number of plateletpheresis in The Blood Transfusion Institute of Serbia (BTIS), as well as the number and structure of donors in RDAT.
Material and methods: The number of apheresis procedures-plateletapheresis for the period 2017-2022 was analyzed, using data from the Information system of BTIS.
Results: During 2017, 1754 plateletpheresis were performed. Of these, 586 (33%) were unintended. In 2018, 583 out of 1,921 - 30% were unintended, in 2019 it was 432 (25%) out of 2,362, in 2020 - 732 (28%) out of 2,609, in 2021 - 1,148 (42%) out of 2,796, and until September 2022, 782 (42%) out of 1,868 procedures. The total number of donors in RAPD until September 2022 is 1422. During 2021. 106 donors joined RAPD: 70 of them were previously intended platelet donors, 36 were voluntary blood donors (VBD). During 2022. 209 donors applied for RAPD: 142 were former intended platelet donors, 67 VBD.
Conclusion: There is an increase in number of unintended plateletpheresis as a result of larger number of donors in RAPD. The expansion of RAPD should be continued through the motivation of VBD and the recruitment of intended platelet donors with the aim of making unintended plateletpheresis dominant.
Key words: Registry of apheresis platelets donors, apheresis platelets, plateletpheresis

PP 014

NOVI RAZLOZI KOJI DOVODE DO PRIVREMENOG ODBIJANJA DOBROVOLJNIH DAVAOCA KRVI

Ljuca A., Bradarić F.
Zavod za transfuzijsku medicinu Federacije Bosne i Hercegovine

Uvod
Sigurnost krvi je glavna briga u cijelom svijetu. Jedan od najvažnijih koraka koji se koriste da bi se osigurala sigurnost krvi je odabir davalaca krvi (u daljem tekstu ddk). Da bi se osigurala sigurnost krvi, potrebno je regrutovati sigurne davaoce, a davaoce visokog rizika odgoditi privremeno ili trajno.
Cilj rada
Cilj ovog istraživanja je utvrditi nove razloge odgađanja kod davaoca krvi koji imaju negativan uticaj kako na proces selekcije, tako i na opskrbu, jer se mnogi odgođeni davaoci ne vraćaju na ponovnu donaciju, ali ipak sam proces selekcije pridonosi sigurnosti krvnih komponenata.
Materijal i metode
Ova studija provedena je u Odjeljenju za kolekciju i proizvodnju pripravaka iz krvi. Analizirani su davaoci koji su prijavljeni za darivanje krvi u 2021. godini korištenjem informacionog sistema Renovatio .
Rezultati
Naši rezultati potvrđuju da novi razlog (hidžama) privremenog odbijanja ddk na kraći period doprinosi gubitku ddk nakon urađene hidžame 4/6 mjeseci, ograničava ddk da bira između hidžame i darivanja krvi. Od 16.749 osoba koje su se javile u 2021. godini za darivanje krvi, 2091 (12,4%) je odgođeno. Krv je uspjelo darovati 14.658 ddk (87,5%). Hidžama je zabilježena kod 127 ddk (6%) kao novi razlog zbog kojeg davaoci ne mogu pristupiti darivanju krvi.
Zaključak
Hidžama kao novi razlog privremenog vraćanja ddk koristi se kao metoda koja rješava mnoge zdravstvene tegobe. Izvodi se tako da se na kožu, na raznim mjestima po tijelu, postave posudice koje pomoću vakuma nakupljaju krv .Budući da hidžamu ne izvodi samo medicinski obučeno osoblje, postoji mogućnost infekcije upotrebom nožića i posudica, te narušavanja asepse.
Iz tog razloga hidžama se u transfuziji tretira kao akupunktura, pirsing, tetovaža, te zahtjeva privremeno odbijanje ddk.
Ključne riječi: hidžama, darivanje krvi, sigurna krv

PP 014

PP 015

COVID -19 I DAVALASTVO KRVI

Ivanovic B.
Zavod za transfuziju krvi Crne Gore , O.J. Berane

Uvod : Pandemija COVID-19 traje vise od dvije i po godine .
Zbog epidemioloskih mjera (socijalnog distanciranja , zabrane putovanja) , straha davalaca krvi (DK) od inficiranja , oboljevanja DK ,oboljevanja osoblja , moze doci do opasnosti smanjenja bezbednih zaliha krvi
Prvi slucajevi U Crnoj Gori su se pojavili u martu 2020 .god .
Cilj rada : je da prikaze kako se kretalo davalastvo krvi od godine pred i u toku prve 2 god. pandemije
Materijal i metode : Protokoli DK i izdatih jedinica krvnih komponenti za 2019 -2021 god
Rezultati : 2019 .god broj izdatih koncentrata eritrocita (KE) je bio 1466
2020 .god, 956 KE , 35 % manje u odnosu na. 2019 .
2021. god. je izdato 1329 KE , sto je manje 9, 5 % u odnosu na 2019 .
2019 .god. je uzeto od DK 1938 jedinica krvi (JK) , u 2020 .god. 1542 JK ,(smanjenje za 21 %) da bi se u 2021 .broj uzetih JK vratio na skoro identican broj (1924) u odnosu na 2019
Dobrovoljni DK su dali krv 2019 god 696 puta , 2020 god 574 puta , (sto je nize za 18 % ,u odnosu na 2019 god.) a 2021 god 642 puta , (nize za 7 % u odnosu na 2019 god)
U 2019 izvedene su 22 akcije dobrovoljnog davanja krvi , 2020 god . 8 akcija (smanjenje 74 %) , 2021 .god ,16 akcija (smanjenje za 27 %)
Zakljucak : Covid-19 pandemija je znatno poremetila rad transfuzionih sistema (TS). Pravovremenim reagovanjem i epidemioloskim mjerama negativni efekti na organizaciju i rad TS mogu se ublaziti i otkloniti

PP 015

PP 016

PREGLED DAVANJA KRVI U SLUŽBI TRANSFUZISKE MEDICINE U KOČANI U PERIODU OD 2019 DO 2021 GODINE

Angelova J., Dejanova-Ilijevska V., Makarovska –Bojadžieva T., Velkova E., Petkovik E., Ristovska E., Todorovski B.
Institut Transfuziske Medicine RS Makedonija

Uvod
Donošenjem nacionalnog programa za davalaštvo krvi kao nacionalni dokumenat, tačno su definisane uloge različitih sudeonika i nivne odgovornosti sa ciljom unapređenja kvalitete kliničke transfuziske prakse.
Cilj
Prikaz stanja sa davalaštvom krvi u STM Kočani u periodu 2019-2021 kroz analizu različitih ciljnih grupa sa akcenat na zaposlenih u privatnom naspram zaposlenih u javnom sektoru .
Materijal i metodi
Korišteni su podatci iz mesečnih izveštaja STM Kočani u periodu od 2019 do 2021 godine.Podaci dobijeni ovom analizom obrađeni su deskriptivnim statističkim metodama i prikazani tabelarno i grafički.
Rezultati
Ukupno darovanih jedinica krvi u STM Kočani od 2019 do 2021 godine je 1581, od čega 407 jedinica u 2019 godini, 539

jedinica u 2020 godini i 635 jedinica u 2021 godini. Od ukupnog broja davalaca, 1408 su muškarci (ili 89%) i 173 žene (ili 11%). 2019 godine, od ukupno 323 zaposlenih koji su darovali krv, 138 je iz javnog sektora, a 185 iz privatnog sektora. 2020 godine, od ukupno 407 zaposlenih, 200 je iz javnog sektora, a 207 iz privatnog sektora, dok je 2021 godine od 518 zaposlenih 132 iz javnog sektora, a čak 380 iz privatnog.
Zaključak
Iz navedenih podataka, akcenat treba staviti na ispunjenje nekoliko ciljeva, uključujući motivaciju zaposlene iz javnog sektora. Mobilizacija novih davalaca i zadržavanje postojećih je dugoročan i kontinuiran proces u koji treba stalno ulagati, jer kao dugoročni cilj treba postaviti trajnu motivaciju društva za proces davanja krvi.

ključne reči: davaoci krvi, privatni sektor, javni sektor

PP 016

REVIEW OF BLOOD DONATION IN THE SERVICE OF TRANSFUSION MEDICINE IN KOCHANI IN THE PERIOD FROM 2019 TO 2021

Angelova J., Dejanova-Ilijevska V., Makarovska-Bojadžieva T., Velkova E., Petkovic E., Ristovska E., Todorovski B.

Institute of Transfusion Medicine, RS Macedonia

Introduction
By adopting the national program for blood donation as a national document, the roles of various participants and their responsibilities were precisely defined with the aim of improving the quality of clinical transfusion practice.
Aim
Presentation of the state of blood donation in STM Kochani in the period 2019-2021 through the analysis of different target groups with an emphasis on employees in the private sector versus employees in the public sector.
Material
Data from the monthly reports of STM Kochani in the period from 2019 to 2021 were used.
METHODS
The data obtained from this analysis were processed using descriptive statistical methods and presented in tables and graphics.
Results
The total number of donated blood units in STM Kochani from 2019 to 2021 is 1581, of which 407 units in 2019, 539 units in 2020 and 635 units in 2021. From the total number of donors, 1408 are men (or 89%) and 173 are women (or 11%). In 2019, out of a total of 323 employees who donated blood, 138 were from the public sector, and 185 from the private sector. In 2020, out of a total of 407 employees, 200 are from the public sector, and 207 from the private sector, while in 2021, out of 518 employees, 132 are from the public sector, and as many as 380 from the private sector.
Conclusion
From the above data, emphasis should be placed on the fulfillment of several goals, including the motivation of employees from the public sector. The mobilization of new donors and the retention of existing ones is a long-term and continuous process that should be continuously invested in, because the long-term goal should be the permanent motivation of society for the blood donation process.

keywords: blood donors, private sector, public sector

PP 017

CONVALESCENT PLASMA DONORS IN THE REGIONAL CENTER FOR TRANSFUSION MEDICINE - SHTIP FOR PERIOD FROM MAY 2020 TO SEPTEMBER 2021

Stoileva M[1,2], Grubović Rastvorčeva R[2,3], Useini S[2] , Shorova M[1,2,3]
[1]*Regional Center for Transfusion Medicine – Shtip, N. Macedonia,*
[2] *Institute for Transfusion Medicine of RNM, Skopje, N. Macedonia,*
[3] *Faculty of Medical Sciences, University Goce Delcev, N. Macedonia*

Background: As the coronavirus disease (COVID-19) pandemic led to a global health crisis, there were limited treatment options and no prophylactic therapies. Convalescent plasma is quick to implement, potentially provides benefits, and has a good safety profile. Aim: Presentation of COVID-19 convalescent plasma (CCP) donors at the Regional Center for Transfusion Medicine - Shtip (RC Shtip) from May 2020 to September 2021. Materials and Methods: Data from monthly reports from RC Shtip for candidates and donors of convalescent plasma were analyzed by number of donations, gender, and reason for refusal, first donation and type of donation. Results: A total of 700 candidates registered to donate CCP and were tested, of which only 152 (21.71%) donated convalescent plasma, 66 (43.5%) women and 86 (56.5%) men. The largest percentage of candidates who did not donate (541) did not have a sufficient concentration of IgG antibodies - (517 candidates or 95.5%), while the other 4.5% were anemic, HLA +, positive for infectious markers, had a positive PCR when retested; or did not appear on the scheduled date for donation. There were 63 (41.5%) first-time donors and 89 (58.5%) have donated blood before, of which 15 (9.8%) donors donated in ITM in Skopje with apheresis procedure and 137 (90.2%) donated whole blood in RC Shtip. Conclusion: Considering the large number of registered potential convalescent plasma donors, only a small part of them donated plasma. Only 21.7% candidates had a sufficient concentration of neutralizing IgG antibodies, male donors predominate. A large number of the CCP donors were first-time donors, which is a very significant fact.
Keywords: COVID-19 convalescent plasma, blood donors, neutralizing IgG antibodies

PP 017

PP 018

ESTABLISHING COVID-19 CONVALESCENT PLASMA PROGRAM IN REPUBLIC OF NORTH MACEDONIA

Grubovic Rastvorceva R[1,2],Useini S[1], E Petkovic[1], M Shorova[1,2, 3], Ismani E[1,4], Vilos L[1,5], Stojanoska Z[1,5] , Brnjarcevska T[6], Petlichkovski A[6]
[1] *Institute for Transfusion Medicine of RNM, Skopje, N. Macedonia ,*
[2] *Faculty of Medical Sciences, University Goce Delcev, N. Macedonia*
[3] *Regional Center for Transfusion Medicine – Stip, N. Macedonia,*
[4] *Regional Center for Transfusion Medicine - Tetovo, N.Macedonia,*
[5] *Regional Center for Transfusion Medicine – Bitola, N. Macedonia,*
[6] *Institute for Immunobiology and Human Genetics, N. Macedonia*

Background: Taking into consideration the expansion of COVID-19 pandemics and previous safe and successful use of convalescent plasma, we started the COVID-19 convalescent plasma (CCP) program. Aims: The aim of our study is to show our experience with collecting the CCP in North Macedonia. Materials and Methods: This is a prospective study performed in the Institute for Transfusion Medicine of Republic of North Macedonia since 30 April 2020 till July 2021. Antibody testing was performed at the Institute for Immunobiology and Human Genetics in Skopje using CLIA method with Snibe Maglumi SARS-CoV-2 S-RBD IgG (quantitative) with IgG cut-off larger than 5 AU/ml. All potential donor were tested for: negative RT-PCR for SARSCoV-2 before donation, anti-SARS-CoV-2 antibodies, anti-HLA antibodies (where applicable), blood count, blood group, TTI and biochemistry. Preferred method for plasma collection was plasmapheresis which was performed with Terumo BCT Trima Accel and donation of whole blood, depending on the donor preference and venous access. All donors signed inform consent for donation and inclusion in the study. Results: There were 1476 potential CCP donors, but only 700(47.9%) donors fulfilled all the criteria and we obtained 793 units of CCP; 639 (80.6%) units from whole blood donors and 154(19.4%) CCP units from 61 plasmapheresis donors, 485(69.3%) males and 215(30.7%) females. All donors were non vaccinated. Mean age of the donors was 40 years (range 18-63). Mean value of SARSCoV-2 S-RBD IgG concentration was 31.05 AU/ml, (range from 5.1 AU/ml to >100 AU/ml), mean value of SARS-CoV-2 SRBD IgG in men was 37.6 AU/ml and 28.9 AU/ml in women ($p<0.05$). Distribution of CCP donors according to the ABO blood group was: 301 blood group A (43%) with median value of SARS-CoV-2 S-RBD IgG = 27.15 AU/ml, 220 blood group O (31.4%) median value of SARS-CoV-2 S-RBD IgG = 32.1 AU/ml, 116 blood group B (16.6%) median value of SARS-CoV-2 S-RBD IgG = 35.9 AU/ml and 63 donors had blood group AB (9%) median value of SARS-CoV-2 S-RBD IgG = 26.45 AU/ml. There were 69 donors that were previously hospitalized with mean value of SARS-CoV-2 S-RBD IgG = 48.6 AU/ml, and 629 that were treated at home with mean value of SARS-CoV-2 SRBD IgG = 29.1 AU/ml ($p<0.05$), of which 578 had symptoms with mean value of SARS-CoV-2 S-RBD IgG = 29.1 AU/ml and 51 were asymptomatic with mean value of SARS-CoV-2 S-RBD IgG = 29.3 AU/ml. The CCP donors had the following distribution according to the age: 125 donors in the 18-29 age group with median value of SARS-CoV-2 S-RBD IgG = 23.0 AU/ml, 200 donors in the 30-39 age group with mean value of SARSCoV-2 S-RBD IgG = 28.2AU/ml, 217 donors in the 40-49 age group with mean value of SARS-CoV-2 SRBD IgG= 32.9 AU/ml and 156 donors in the 50-63 age group mean value of SARS-CoV-2 SRBD IgG = 38.3 AU/ml ($p<0.05$). Conclusions: The collection procedures were safe and effective and collected CCP units were with high concentration and quality. The concentration of SARS-CoV-2 S-RBD IgG in CCP obtained from previously hospitalized patients was significantly larger than in ones that were treated at home. The concentration of SARS-CoV-2 S-RBD IgG was higher in men, in advanced age group and in donors with blood group B. The further studies are needed to clarify the impact of different variables on antibodies concentration/titer in donors. Starting of COVID-19 convalescent plasma program was a big success for our institution and our country and helped a lot of patients.
Keywords: COVID-19, convalescent plasma, antibodies' concentration

PP 018

PP 019

STRUKTURA KRVNIH GRUPA DOBROVOLJNIH DAVALACA KRVI OPŠTINE NIKŠIĆ

Dendić B.
Zavod za transfuziju krvi Crne Gore, O.J.Nikšić

Uvod: Krajem osamdesetih godina prošlog vijeka u Nikšiću je na Odjeljenju za transfuziju krvi formirana baza podataka davalaca krvi. Program je kreiran pomoću DOS operativnog sistema. Unošenje podataka u program je stornirano 2020. godine uvođenjem E-kartona.
Cilj rada: Prikazati strukturu krvnih grupa davalaca krvi opštine Nikšić
Materijal i metode: U bazi podataka se nalazi 18 957 davalaca krvi.Organizaciona jedinica Zavoda za transfuziju krvi- Nikšić pruža usluge građanima tri opštine (Nikšić, Plužine, Šavnik) što čini oko 80 000 stanovnika i jednu četvrtinu teritorije Crne Gore.
Rezultati: Od ispitivanog uzorka davalaca krvi (18 957) , njih 5893 je sa A-pozitivnom krvnom grupom namjenskih, a 1215 dobrovoljnih, ukupno 7108 (37.5 %) Sa krvnom grupom A-negativnom je registrovano 1511 namjenskih, a 213 dobrovoljnih, ukupno 1364 (7.2%)
Sa O-pozitivnom krvnom grupom je bilo 4611 namjenskih, a 909 dobrovoljnih davalaca krvi. Ukupno 5520 (29.0%) Njih 928 je upisano sa O-negativnom krvnom grupom namjenskih, a 187 dobrovoljnih davalaca krvi. Ukupno 1115 (5.9 %)
Sa B-pozitivnom krvnom grupom registrovano je 1780 namjenskih davalaca , a 477 dobrovoljnih. Ukupno 2257 (11.9%)Od B-negativnih davalaca krvi je bilo 348 namjenskih i 77 dobrovoljnih. Ukupno 425 (2.2 %)
Davalaca krvi sa AB-pozitivnom krvnom grupom je bilo 886 namjenskih, a 214 dobrovoljnih. Ukupno 1100 (5.8 %) Sa AB-negativnom krvnom grupom je registrovano 27 namjenskih, a 41 dobrovoljnih. Ukupno 68 (0.3%). Ukupno RhD-pozitivnih davalaca krvi ima 84.3 %
Ukupno Rh- negativnih davalaca krvi je 15.7 %:A krvna grupa- 44.7%, B krvna grupa-14 %,O krvna grupa-35 % I AB krvna grupa-6.3 %
Zaključak: Struktura ABO/RhD krvnih grupa davalaca krvi je u korelaciji sa njihovom distribucijom u opštoj populaciji Crne Gore.
Ključne riječi: ABO/RhD, davaoci krvi, distribucija

PP 019

THE STRUCTURE OF ABO/RHD BLOOD GROUPS IN THE MUNICIPALITY OF NIKSIC

Dendic B.
Institute for Blood Transfusion of Montenegro, O.J. Nikšić

Introduction: At the end of the eighties of the last century, a database of blood donors was formed at the Blood Transfusion Department in Nikšić. The program was created using the DOS operating system. Data entry into the program was canceled in 2020 with the introduction of E-cartons.
Aim: To show the structure of the blood groups of blood donors in the municipality of Nikšić
Material and methods : There are 18,957 blood donors in the database. The organizational unit of the Institute for Blood Transfusion - Nikšić provides services to the citizens of three municipalities (Nikšić, Plužine, Šavnik), which makes up about 80,000 inhabitants and one quarter of the territory of Montenegro.
Results: From the examined sample of blood donors (18,957), 5,893 of them are designated with A positive blood group, and 1,215 are voluntary. A total of 7108 (37.5 %) with negative blood group A, 1511 registered and 213 voluntary. Total 1364 (7.2%) There were 4,611 dedicated and 909 voluntary blood donors with O positive blood group. A total of 5,520 (29.0%) of them 928 were registered with O negative blood group as dedicated and 187 voluntary blood donors. Total 1115 (5.9%) 1780 dedicated donors and 477 voluntary donors were registered with B positive blood group. A total of 2257 (11.9%) of B negative blood donors were 348 designated and 77 voluntary. Total 425 (2.2 %).There were 886 dedicated and 214 voluntary blood donors with AB positive blood group. A total of 1100 (5.8 %) with AB negative blood group were registered, 27 dedicated and 41 voluntary. Total 68 (0.3%) Total RhD positive blood donors: 84.3%
Total RhD negative blood donors 15.7%:A blood group 44.7% ,B blood group 14%, O blood type 35%
I AB blood type 6.3 %
Conclusion: The structure of ABO/RhD blood groups of blood donors is correlated with the distribution of ABO/RhD groups in Montenegro as well as the general population.
Key words: blood donors, ABO/RhD, distribution

PP 020

SKRINING ANTITIJELA KOD RhD-NEGATIVNIH TRUDNICA, PERIOD 2010-2019, U SLUŽBI TRANSFUZIJE PRIJEDOR

Tatić Sevimli D.
Zavod za transfuzijsku medicine Republike Srpske, Prijedor, Bosna i Hercegovina, Služba transfuzije Prijedor

Uvod: Imunohematološka testiranja u trudnoći uključuju određivanje ABO, RhD krvnih grupa i blagovremeno otkrivanje antieritrocitnih antitijela, koja mogu da izazovu hemoliznu bolest novorođenčeta (HBN).
Cilj: Prikazati učestalost senzibilizacije i efikasnost prenatalne zaštite kod RhD-negativnih trudnica, na području koje pokriva služba Prijedor, Zavoda za transfuzijsku medicinu Republike Srpske.
Materijal i metode: Retrospektivna analiza dobijena je iz informacionog sistema i protokola RhD-negativnih trudnica prijedorske transfuzije. Skrining antitijela RhD-negativnih trudnica, rađen je enzimskom (bromelin) metodom i indirektnim antiglobulinskim testom u epruveti. Uzorci krvi trudnica s pozitivnim skriningom, slani su u centralnu laboratoriju u Banja Luku, radi identifikacije antitijela,metodom u gelu.
Rezultati: U periodu od 2010. do 2019. godine, testirano je 2.860 uzoraka RhD-negativnih trudnica skriningom antieritrocitnih antitijela. Od toga, 20 trudnica je u tom periodu imalo pozitivan skrining antitijela. Kod 11(55%) trudnica identifikovano je anti-D antitijelo, dvije trudnice bile su sa anti-E antitijelom (10%), dok je sedam antitijela bilo neutvrđene specifičnosti (35%). U analiziranom periodu, kod troje novorođenčadi, utvrđena je HBN, sa pozitivnim direktnim antiglobulinskim testom,uzrokovanim anti-D antitijelima. Sve trudnice su imale višestruke trudnoće koje nisu bile redovno kontrolisane i nisu primile anti-D imunoglobulin. Učestalost senzibilizacije na antigen D prema ovim podacima iznosi 0,38%.
Zaključak: Skrining antitijela u prenatalnoj zaštiti je važan u otkrivanju imunizacije i sprečavanju posljedica eventualne HBN. Uprkos višegodišnjoj primjeni RhD imunoprofilakse u našoj regiji,većina imunizacija su imunizacije RhD antigenom.Kako bi se doslijedno sprovela RhD imunoprofilaksa i obezbijedilo rađanje zdrave populacije, bitno je da saradnja transfuziološke i ginekološke službe bude na najvećem nivou.
Ključne riječi: skrining, antitijela, Rh inkopatibilija

PP 020

ANTIBODY SCREENING PREFORMED IN RhD-NEGATIVE PREGNANT WOMEN FROM 2010-2019.IN BLOOD TRANSFUSION SERVICE PRIJEDOR

Tatić Sevimli D.
Institute for Transfusion Medicine of Republic Of Srpska, Prijedor, Bosnia and Herzegovina

Introduction: Immunohaematology testing in pregnancy involves determining blood type and screening of anti-erythrocyte antibodies which might cause haemolytic disease in new born (HDN).
Aim: The aim of this study is to show the frequency of sensitization in pregnant women to Rh erythrocyte antigens and the efficiency of prenatal care in area covered by Prijedor Transfusion.
Materials and methods: Retrospective analysis was taken from information system and prenatal testing protocols. The screening of antibodies were performed by enzyme (bromelin) technique and an indirect antiglobulin test in a test tube. Blood samples with positive screening were sent to our referent laboratory at Institute for Transfusion Medicine in Banja Luka ,for confirmation and identification by gel card technology.
Results: During the period between 2010-2019, 2860 antibody screening analysis has been performed. Out of total, 20 pregnant women have had positive antibody screening. The identification of antibodies show that the anti-D antibody was found in 11 cases (55%).Two pregnant women was found anti-E antibody (10%) and 7 cases were antibodies of undetermined specificity(35%). In analysed period, 3 of the new born were developed symptoms of HDN with positive direct antiglobulin (coombs) test, caused by anti-D antibodies. All cases were women with multiple pregnancies, non-regularly controlled and did not receive anti D antiglobulin. According to this data, the frequency of sensitization to antigen D is 0,38%.
Conclusion: Antibody screening in prenatal care is crucial in antibody detection and HDN prevention. Despite yearly long RhD immunoprophylaxis in our region ,still the majority of immunizations are anti D immunizations. For consistent implementation of RhD immunoprophylaxis , there is a necessity of a better team work between gynaecology and transfusion departments.
Key words: screening, antibody, Rh immunization

PP 021

REZULTATI IDENTIFIKACIJE ANTIERITROCITNIH ANTITELA KOD PACIJENATA ODELJENJA ZA PRETRANSFUZIONA ISPITIVANJA, DISTRIBUCIJU KRVI I PRODUKATA OD KRVI I HEMOVIGILANCU INSTITUTA ZA TRANSFUZIJU KRVI SRBIJE

Nedeljković M., Korać N.,Radović I., Jovanović Srzentić S.
Institut za transfuziju krvi Srbije, Beograd

Uvod: Prema različitim studijama učestalost antieritrocitnih antitela (At) kod bolničkih pacijenata je oko 1%. Kod imunizovanih bolesnika, zbrinjavanje adekvatnim produktima krvi može biti odloženo jer indentifikacija At, kao i pronalaženje kompatibilne jedinice krvi mogu biti dugotrajni procesi. **Cilj:** Utvrditi učestalost i specifičnost antieritrocitnih At identifikovanih kod bolničkih pacijenata ispitivanih na Odeljenju za pretransfuziona ispitivanja, distribuciju krvi i produkata od krvi i hemovigilancu Instituta za transfuziju krvi Srbije.**Metode:** Urađena je retrospektivnom analiza podataka iz Protokola za identifikaciju antieritrocitnih At Odeljenja u period 15.03.2022-31.08.2022. Skrining i identifikacija At rađene su indirektnim Coombsovim testom metodom u gel kartici ili metodom u epruveti u NaCl medijumu uz korišćenje komercijalnih test eritrocita (BioRad).**Rezultati:** Od ukupno 3719 uzoraka bolesnika kod 99(2,6%) su identifikovana At. Bolesnika muškog pola bilo je 32(32,3%), ženskog pola 67(67.7%). Skrining je prethodno bio pozitivan kod 65(65.7%) bolesnika. Najčešće su bila identifikovana hladna antitela 38(38.4%). Topla autoantitela dokazana su kod 6(6.1%)bolesnika. Kod 55(55.5%) bolesnika detektovana su klinički značajna aloantitela, jedno ili više. Najčešće je bilo detektovano anti-K antitelo kod 14 (14.1%)bolesnika, zatim antitela iz Rh sistema: anti-E 11(11.1%), anti-D 9(9.1%), anti-c 5(5.1%), anti-C 3(3.0%). Od ostalih klinički značajnih At detektovana su anti-M 7(7.1%) i anti-Jka 4(4.0%). Sa učestalošću manjom od 2% bili su zastupljeni anti-Fya, anti-Fyb, anti-S, anti-Lea, anti-Leb. Antitela neutvrđene specifičnosti je imalo 5 (5.1%) bolesnika Za njih je postojao anamnestički podatak o prethodnoj terapiji monoklonskim antitelima.**Zaključak:** Kod najvećeg broja naših bolesnika detektovana su hladna antitela koja nisu bila klinički značajna. Od klinički značajnih antitela najveća je bila učestalost antieritrocitnih antitela iz Rh i Kell sistema,pa bi primena kompatibilne krvi u Kell i Rh sistemu kod bolesnika na hroničnoj transfuzionoj terapiji, sprečila imunizaciju.
Ključne reči: antieritrocitna antitela, imunohematološko testiranje, aloimunizacija

PP 021

RESULTS OF RED CELL ANTIBODIES IDENTIFICATION IN PATIENTS TESTED IN DEPARTMENT FOR PRETRANSFUSION TESTING, DISTRIBUTION OF BLOOD AND BLOOD COMPONENTS AND HEMOVIGILACE IN BLOOD TRANSFUSION INSTITUTE OF SERBIA

Nedeljković M, Korać N., Radović I., Jovanović Srzentić S.
Blood Transfusion Institute of Serbia, Belgrade

The prevalence of red blood cell antibodies (Ab) among hospital-based patients typically has averaged approximately 1 percent in various studies. In immunized patients, treatment with adequate blood products can be delayed because identification of Ab, as well as finding a compatible blood unit, can be long-term processes.The aim of this study was to determine the frequency and specificity of red blood cell Ab identified among hospital-based patients tested in Department for pretransfusion tesing, distribution of blood and blood components and hemovigilance in Blood Transfusion Institute of Serbia. A retrospective analysis from Protocol for identification of red blood cell Ab in Department was performed from 15 th March to August 2022.Screening and identification of Ab was performed by indirect Coombs test using gel card method, or test tube saline method with commercial test erythrocytes (BioRad). Antibodies were found in 99 patients(2.6%) of all 3719 samples. There were 32 (32.3%) male, 67 (67.7%) female patients. Screening was previously positive in 65 (65.7%) patients. The most frequently identified were cold antibodies in 38 (38.4%)patients. Warm autoantibodies were identified in 6 (6.1%) patients. Clinically significant one or more alloantibodies,were detected in 55 (55.5%) patients. The most common alloantibody was anti-K detected in 14 (14.1%) patients, and antibodies from Rh anti-E 11(11.1%), anti-D 9 (9.1%), anti-c 5 (5.1%), anti -C 3(3.0%). Other clinically significant Ab were anti-M 7(7.1%) and anti-Jka 4(4.0%). Anti-Fya, anti-Fyb, anti-S, anti-Lea, anti-Leb were identified with a frequency of less than 2%. Had antibodies of undetermined specificity 5 (5.1%) patients with history of treating with monoclonal antibodies. Clinically non significant cold antibodies have high prevalence in our patients. Among clinically significant antibodies, the most common were Rh and Kell antibodies, so the use of Kell and Rh compatible blood unit, in chronically transfused patients would prevent the immunization.

Key words: Red blood cell antibodies,immunohaematological testing, alloimmunization

PP 022

POŠTOVANJE PREPORUKA SAVREMENIH VODIČA ZA IMUNOHEMATOLOŠKA TESTIRANJA TRUDNICA – IMPERATIV DANAŠNJE GINEKOLOGIJE

Ljubenov M, Pešić Stevanović I, Ristić S.
Ginekološko-akušerska klinika „Narodni Front" Beograd, Srbija

UVOD: Imunohematološka ispitivanja su neophodna kod svih trudnica. Pravovremeno mogu da predvide i preveniraju potencijalnu hemoliznu bolest fetusa/novorođenčeta (HBFN).
CILJ:Pokazati na slučaju RhD-pozitivne trudnice značaj imunohematoloških testiranja.
MATERIJAL I METODE: Imunohematološke analize izvedene su na automatizovanom sistemu IH-500 (Bio-Rad), uz korišćenje odgovarajućih kartica sa gelom. Titar antitela rađen je u epruveti, korišćeni su Kell-pozitivni eritrociti i AHG reagens.
PRIKAZ SLUČAJA: Trudnica starosti 38 godina prvi put imunohematološki ispitana u 17. nedelji gestacije, A RhD-pozitivna, DAT/negativan, IAT/pozitivan; identifikacija: anti-Kell antitelo klase IgG, titar 32 u IAT. Nakon prvog živorođenog deteta i dva pobačaja (38. i 8. nedelja gestacije) imala je samo određenu krvnu grupu. U 21. nedelji utvrđen je porast titra anti-K antitela na 64 u IAT. U 25. nedelji ispitana je fetalna krv uzeta kordocentezom. Krvna grupa fetusa:A, RhD-pozitivna, Kell fenotip: K-k+.
DISKUSIJA: Testiranje trudnice izvedeno je prvi put po preporuci vodiča razvijenih zemalja. Antieritrocitno anti-K antitelo je imunoglobulin klase IgG i uzrokuje nastanak hemolizne bolesti fetusa/novorođenčeta (HBFN). Titar nije uvek u korelaciji sa težinom kliničke slike. Kell antigen je prisutan na progenitorima eritrocita u ranijem stadijumu eritropoeze od pojave antigena Rh sistema. Zato je bilirubin u amnionskoj tečnosti normalan, novorođenče nema žuticu, ali je prisutna anemija zbog supresije eritropoeze u kostnoj srži. Brzina protoka krvi kroz centralnu moždanu arteriju i Doppler fetoplacentne i uteroplacentne cirkulacije imaju izvesna ograničenja zbog individualne procene. Nepostojanje K antigena je isključilo sumnju na HBFN.
ZAKLJUČAK:Dijagnostika i lečenje HBFN zahtevaju dobru saradnju trudnice, ginekologa i transfuziološke laboratorije. Kako i kad alečiti ugroženi fetus bazirano je na proceni fetalne anemije i gestacijskoj starosti. Odre]ivanje titra antitela treba da bude usaglašeno u svim transfuzioloških ustanovama i standardiyovano uy pomoć jedne metode, zbog pravilnog praćenja dinamike njegovog porasta.
Ključne reči: imunizacija, anti-K antitelo, HBFN

PP 022

COMPLIANCE WITH THE RECOMMENDATIONS OF MODERN GUIDELINES FOR IMMUNOHAEMATOLOGICAL TESTING OF PREGNANT WOMEN- AN IMPERATIVE OF TODAY'S GYNECOLOGY

Ljubenov M, Pešić Stevanović I, Ristić S.
Clinic of gynecology and obstetrics „Narodni front", Beograd

Introduction: Immunohaematological tests can predict and prevent potential hemolytic disease of the fetus/newborn (HDFN) in time.
Goal: To demonstrate the importance of immunohaematological testing on the presented case of an RhD-positive pregnant woman.
Materials and methods:Immunohaematological analyzes were performed on an automated system IH-500 (Bio-Rad), using appropriate gel cards. Antibody titer was done in a test tube, antigen K - positive erythrocytes and AHG reagent were used.
Case report: A 38-year-old pregnant woman was examined immunohaematologically for the first time in the 17th week of gestation. Her blood group: ARhD-positive, DAT: negative, IAT: positive; identification: anti-K antibody of class IgG, titer 32. After the first birth and two miscarriages (38 and 8 weeks of gestation), she had only one specific blood group. In the 21st week, an increase in the anti-K antibody titer was 64. In the 25th week, the fetal blood taken by cordocentesis was examined. Fetal blood group: ARhD-positive, Kell phenotype: K-k+.
Discussion: The titer of anti-K antibody does not always correlate with the severity of the clinical picture of HDFN. Kell antigen is present on erythrocyte progenitors in an earlier stage of erythropoiesis than in the appearance of Rh system antigens. The amniotic fluid is normal, the newborn does not have jaundice, but anemia is present due to the suppression of erythropoiesis in the bone marrow. Velocity of blood flow through the central cerebral artery and doppler fetoplacental and uteroplacental circulation have some limitations due to individual assessment. The absence of K antigen excluded the suspicion of HDFN.
Conclusion: Diagnosis and treatment of HDFN require a good cooperation of the pregnant woman, gynecologist and transfusion laboratory. How and when to treat an endangered fetus is based on the assessment of fetal anemia and gestational age. Performing a titer of antibodies should be harmonized in all transfusion institutions due to proper method and monitoring of dynamics of its increase.
Key words: immunization, anti-K antibody, HDFN

PP 023

OD SMETNJI U ODREĐIVANJU KRVNE GRUPE ABO DO DIJAGNOZE X VEZANE AGAMAGLOBULINEMIJE (BRUTON) – PRIKAZ SLUČAJA

Vučinić S, Praštalo-Grubiša M, Zonjić J, Šćepanović T, Rašović G, Cvijović A
Zavod za transfuziju krvi Crne Gore (ZTKCG), Podgorica, Crna Gora

Uvod: Smetnje u određivanju krvnih grupa ABO sistema postoje kada rezultat testiranje eritrocita nije u saglasnosti sa rezultatom testiranja seruma. Serum ispitivanog uzorka može biti uzrok pogrešnog rezultata ABO testiranja kod pacijenata sa naslednom primarnom imunodeficijencijom kod koje prirodni izohemaglutinini ili nedostaju ili su prisutni u izrazito niskom titru a bolest se obično klinički manifestuje rekurentnim infekcijama sa inkapsuliranim bakterijama
Cilj: Prikazati kako smetnje u određivanju krvne grupe ABO mogu inicirati niz dijagnostičkih analiza i pregleda do postavljanja dijagnoze X vezane agamaglobulinemije (Bruton).
Prikaz slučaja: Dječak star 7 god. upućen je u ZTK radi određivanja krvne grupe u sklopu priprema za operaciju trećeg krajnika zbog čestih upala srednjeg uha. Pri određivanju krvne grupe postojale su smetnje u testiranju seruma po tipu nerazvijenih prirodnih anti-A i anti-B izohemaglutinina gel metodom i metodom u epruveti na 22°C. DAT i IAT su bili pozitivni.
Mjesec dana nakon operacije adenoida IH testiranja su pokazala identičan rezultat zbog čega je pacijent upućen hematologu. Nakon odrađenog imunofenotipa limfocita periferne krvi koji je ukazao na izrazito snižen relativni i apsolutni br.B limfocita odrađno je gensko ispitivanje. Molekularnogenetičkim ispitivanjem dokazana je mutacija u genu Bruton tirozin kinase (Btk) tj. X vezana agamaglobulinemija – Bruton.
Zaključak: Prepoznavanje i rešavanje smetnji pri određivanju krvnih grupa ABO uvijek je izazov za IH laboratoriju i obično podrazumijeva izvođenje i dodatnih IH testova. Ova testiranja mogu biti uvod u postavljanju dijagnoze nekih oboljenja hematopoeznog ili imunog sistema.
Ključne riječi: ABO testiranje, X vezana agamaglobulinemija (Bruton)

PP 023

FROM DISTURBANCES IN DETERMINING THE ABO BLOOD GROUP TO THE DIAGNOSIS OF X-LINKED AGAMMAGLOBULINEMIA (XLA-BRUTON) - CASE REPORT

Vucinic S, Prastalo-Grubisa M, Zonjic J, Scepanovic T, Rasovic G, Cvijovic A
Institute for Blood Transfusion of Montenegro, Podgorica, Montenegro

Introduction: Disturbances in determining the blood groups of the ABO system exist when the result of the erythrocyte test does not agree with the result of the serum test. The serum of the tested sample can be the cause of a wrong result of ABO testing in patients with hereditary primary immunodeficiency in which natural isohemagglutinins are either missing or present in an extremely low titer, and the disease is usually clinically manifested by recurrent infections with encapsulated bacteria.
Objective: To show how disturbances in the determination of the ABO blood group can initiate a series of diagnostic analyzes and examinations until the diagnosis of X-linked agammaglobulinemia (Bruton) is established.
Case report: A 7-year-old boy was referred to IBT for blood type determination as part of preparations for surgery on the third tonsil due to frequent middle ear infections When determining the blood group, there were obstacles in testing the serum due to undeveloped natural anti-A and anti-B isohemagglutinins using the gel method and the test tube method at 22C. DAT and IAT were positive.
One month after the adenoid surgery, IH tests showed an indentical result, which is why the patient was referred to a hematologist. After the immunophenotyping of peripheral blood lymphocytes, which indicated a markedly reduced relative and absolute number of B lymphocytes, a genetic test was performed. Molecular genetic testing proved a mutation in the Bruton tyrosine kinase (Btk) gene, i.e. X-linked agammaglobulinemia – Bruton.
Conclusion: Recognizing and solving disturbances when determining ABO blood groups is always a challenge for the IH laboratory and usually involves the performance of additional IH tests. These tests can be an introduction to the diagnosis of some diseases of the hematopoietic or immune system.
Key words: ABO testing, X-linked agammaglobulinemia (Bruton)

PP 024

DISCREPANT ABO BLOOD GROUP-CASE REPORT

Neziri Zeneli V, Dejanova Ilijevska V, Tashkovska M, Ismaili L, Acevska E, Petkovikj E, Makarovska Bojadjieva T, Ristovska E, Velkova E, Todorovski B

Institute for transfusion medicine, Skopje, RNMacedonia

Introduction: ABO blood group discrepancy indicate that the results of the erythrocyte test are not consistent with the results of the serum test, which is reflected in an unexpected positive or negative result in one or both procedures.
Aim: The aim of this study is to demonstrate the resolution of a weak subgroup of blood group A within the ABO system.
Materials and methods: Blood group was to be determined on a blood sample of a patient from the traumatology department. ABO blood group was determined by two methods, a plate test and a microagglutination method in a card (BioRad and Ortho Clinical Diagnostics). Tube test and molecular blood typing were used as additional methods.
Results: On a plate, erythrocytes showed no agglutination with either anti-A, anti-B or anti-AB reagent, so blood group was determined as O, RhD-positive. Microagglutination method showed negative agglutination with anti-A, anti-B, and anti-AB, while only a potent anti-B antibody at room temperature was detected in the serum, so a discrepancy has occurred. Patient serum and test RBC (A1 and B) were incubated for 30 minutes at +4oC degrees, using microagglutination method. No anti- A antibodies were detected. Blood group was also determined in tube with the same result (absence of A antigen and anti-A antibodies, macroscopically, with rare and inconclusive agglutinates microscopically). Further assessment was performed using molecular analyzes by PCR method. The results showed that the blood group is a weak subgroup of A antigen with Ax/O1 genotype.
Conclusion: We reported subgroup of A in a female patient, diagnosed through a mismatch between erythrocyte and serum (reverse) typing. Weak subgroups within ABO system are very rare and usually can be determined by adsorption and elution technique, but some cases, especially for more precise distinction molecular blood typing is required.

Keywords: ABO system, weak subgroups

PP 024

PP 025

ANALIZA REZULTATA SKRININGA ANTIERITROCITNIH ANTITIJELA PACIJENATA OPĆE BOLNICE U SARAJEVU- JEDNOGODIŠNJI PRIKAZ

Ašonja M[1], Đozo A[2].
[1] Opća bolnica "Prim. dr Abdulah Nakaš" Sarajevo, BiH
[2] Odsjek za transfuzijsku medicinu
Zavod za transfuzijsku medicine Federacije Bosne i Hercegovine, Sarajevo, BiH

Uvod: Skrining antitijela je jedan od osnovnih prijetransfuzijskih testova, u kome se pomoću eritrocita poznatog antigenskog sadržaja otkriva prisustvo iregularnih antitijela u serumu primaoca krvi. Antieritrocitna antitijela mogu biti prirodna ili nastati imunizacijom usljed transfuzije, trudnoće i transplantacije. Otkrivena antitijela treba identifikovati da bi se obezbijedili antigen-negativni eritrociti za transfuziju i spriječilo potencijalna hemoliza primaoca krvi.
Cilj rada: Prikazati analizu skrininga antieritrocitnih antitijela kod pacijenata u Općoj bolnici "Prim. dr Abdulah Nakaš" u Sarajevu kroz frekvencu, specifičnost i klinički značaj otkrivenih antitijela.
Materijal i metode: Skrining antitijela je urađen kod 2375 pacijenata metodom u gelu, uz korištenje "Type and screen" gel kartica proizvođača BioRad. Rezultati su praćeni u periodu od 01.04.2021.god. do 31.03.2022.god. Identifikacija antitijela iz uzoraka pacijenata sa pozitivnim skriningom antitijela je urađena u referentnoj ustanovi, Zavodu za transfuzijsku medicinu FBiH metodom u gelu, proizvođača BioRadi Grifols.
Rezultati: Pozitivan rezultat skrininga je dobijen kod 44 pacijenta. Specifična antitijela(35) su potvrđena u serumu 34 pacijenta. Kod četiri pacijentice je identifikovano pasivno uneseno anti D antitijelo. Prirodno prisutna ili stečena specifična antitijela su otkrivena kod 30 pacijenata, 23 žene i 7 muškaraca. Frekvenca u odnosu na broj ispitanika je bila: anti-D 10(0,42%), anti-E 6(0,25%), anti-e, anti-C i anti-c 2(0,08%), anti-Kell 4(0,16%), anti-M 3(0,12%), anti-Lea 2(0,08%), anti k, Jka, Fya, i P 1(0,04%), sa dva antitijela kod šest pacijenata(0,25%), i složenom imunizacijom (3) kod jednog(0,04%). Od kliničkih značajnih antitijela identifikovana su antitijela u sistemima: Rh, Kell, Duffy i Kidd, ukupno 1,17%.
Zaključak: Najveći broj otkrivenih antitijela, 75%, su klinički značajna. U imunohematološkom testiranju neophodno je odabrati najbolju metodu za skrining antitijela. Metoda u gelu, radi specifičnosti, senzitivnosti i dužine trajanja je omogućila otkrivanje i identifikaciju antitijela prije transfuzije, a rezultat je primjena fenotipski kompatibilne krvi pacijentima.
Ključne riječi: skrining antitijela, imunohematologija

PP 025

ANALYSES OF ERYTHROCYTE ANTIBODIES SCREENING RESULTS OF THE GENERAL HOSPITAL IN SARAJEVO PATIENTS - ONE YEAR REPORT

Ašonja M[1], Đozo A[2].
[1] General Hospital "Prim. Dr. Abdulah Nakaš" Sarajevo, Bosnia and Herzegovina, Department of Transfusion Medicine
[2] Institute for Transfusion Medicine of the Federation of Bosnia and Herzegovina, Sarajevo, BiH

Introduction: Antibody screening is one of the basic pre-transfusion tests, for detection of the irregular antibodies presence in the blood recipient's serum, using erythrocytes of known antigenic content. Erythrocyte antibodies can be natural or arise, through immunization due to transfusion, pregnancy and transplantation. Detected antibodies should be identified in order to provide antigen-negative erythrocytes for transfusion and prevent potential destruction of the recipient's erythrocytes.
The aim of the work: To show the analysis of erythrocyte antibody screening in patients of the General Hospital "Prim. Dr. Abdulah Nakaš" in Sarajevo through the frequency, specificity and clinical significance of the detected antibodies.
Material and methods: Antibody screening was performed in 2375 patients using the gel method, with "Type and screen" gel cards manufactured by BioRad. The results were monitored in the period from April 1, 2021. until March 31, 2022. The identification of antibodies from samples of patients with positive antibody screening was done in the reference institution, the Institute for Transfusion Medicine of FBiH using the gel method, manufactured by BioRad and Grifols.
Results: A positive screening result was obtained in 44 patients. Specific antibodies (35) were confirmed in the serum of 34 patients. Passively introduced anti-D antibody was identified in four patients. Naturally present or acquired specific antibodies were detected in 30 patients, 23 women and 7 men. The frequency in relation to the number of subjects was: anti D 10(0.42%), anti E 6(0.25%), anti e, anti C and anti c 2(0.08%), anti Kell 4(0 ,16%), anti M 3(0.12%), anti Lea 2(0.08%), anti k, Jka, Fya, and P 1(0.04%), with two antibodies in six patients(0 ,25%), and complex immunization (3) in one (0.04%). Of the clinically significant antibodies, antibodies in the following systems: Rh, Kell, Duffy and Kidd, 1,17% of total, were identified.
Conclusion: The largest number of detected antibodies, 75%, are clinically significant. In immunohaematological testing, it is necessary to choose the best method for antibody screening. The gel method, due to its specificity, sensitivity and length of time, enabled the detection and identification of antibodies before transfusion, and the result was the application of phenotypically compatible blood to our patients. Key words: antibody screening, immunohaematology

PP 026

RARE BLOOD GROUPS IN BLOOD DONORS

Makarovska Bojadjieva T, Velkova E, Dejanova Ilijevska V, Petkovik E, Ristovska E, Todorovski B, Tashkovska M, Petkovska Bozinovska A, Ismaili Lj.
Institute of Transfusion Medicine, Faculty of Medicine, Ss. Cyril and Methodius University in Skopje, Republic of North Macedonia

Background. The term rare blood group is defined as an absence of high-frequency antigen in general population, absence of multiple frequent antigens within a single blood group system or absence of multiple frequent antigens within different blood systems.
Aim. To perform extended red blood cell typing of Kpa, Kpb, Fya, Fyb, Jka, Jkb, S, s, Lua and Lub antigen, as well as to calculate antigen and phenotype frequency.
Material and methods. In 920 blood donors apart from the routine ABO, Rh and Kell antigen typing, extended typing of Kpa, Kpb, Fya, Fyb, Jka, Jkb, S, s, Lua, and Lub antigens was performed using specific sera, antihuman globulin and column agglutination technique. Weak ABO subgroups were determined using absorption elution method or molecular genotyping. Antigen and phenotype frequencies were calculated using statistics module from the donor information system.
Results. Weak ABO subgroups were identified in 0,009 % of the donors with the following phenotype and genotype frequency: A3 (0.004%), A3B (0.001%), AxO1 (0,0026%), AxB (0,001%). Rh system antigen frequency is as follows: D (85.79%), C (71.7%), c (76.0%), E (26.0%) and e (97.95%). Most common Rh phenotype is DCcee (32.7%) while the rarest one is ddCcEe (0.007%). The frequency of K and k antigen is 7.5% and 99.94% respectively. Phenotype (K+k-) is present in 21 (0.06%) of blood donors. The frequency of other clinically significant antigens is: 1.1% (Kpa), 100.0% (Kpb), 60.3% (Jka), 76.2% (Jkb), 65.5% (Fya), 79.5% (Fyb), 59.8% (S), 86.5 (s), 7.2% (Lua) and 92.8% (Lub). Most frequent phenotypes are Jk(a+b+) with 41.5%, Fy(a+b+) with 48.5%, Ss(S+ s+) with 46.3% and Lu(a-b+) with 92.8%. Fy(a-b-) phenotype was detected in 0.21% of blood donors.
Conclusion. Large scale blood group phenotyping and/or genotyping enables identification of blood donors with rare blood groups for patients with rare phenotypes, with antibodies to high-frequency antigens or with multiple antibodies to antigens within one or more blood group systems.
Key words:Rare blood group, antigen frequency

PP 026

PP 027

ANTIERITROCITNA ANTITIJELA DOKAZANA KOD TRUDNICA U ZAVODU ZA TRANSFUZIJSKU MEDICINU FEDERACIJE BOSNE I HERCEGOVINE,U PERIODU AVGUST 2021. DO AVGUST 2022. GODINE.

Vilić-Hasanović V. Musić E. Miličić V.
Zavod za transfuzijsku medicinu FBiH,Sarajevo BiH.
vildana.vilic-hasanovic@ztmfbih.ba

Uvod: Imunohematološka testiranja u trudnoći su nezaobilazni dio rutinske transfuziološke prakse.Tri su osnovna razloga ovih testiranja: 1)određivanje ili potvrda ranije određene krvne grupe ABO sistema i RhD antigena, kao i otkrivanje antieritrocitnih antitijela,koja mogu otežati pronalazak kompatibilne krvi za transfuziju; 2)Identifikacija trudnica,kojima je potrebna RhD imunoprofilaksa; 3)Pravovremeno otkrivanje i kontrola klinički značajnih antitijela,koja imaju potencijal da uzrokuju anemiju i/ili hemolitičku bolest fetusa/neonatusa.
Ciljevi: 1)Prikazati otkrivena antieritrocitna antitijela kod trudnica u ZTM FBiH,u periodu 01.08.2021. do 31.08.2022; 2)Analizirati rezultate dobijene imunohematološkim testiranjem trudnica i 3)Izvući zaključke o korelaciji s aktuelnim međunarodnim rezultatima.
Metode: Retrospektivna analiza podataka dobijenih iz elektronskih kartona pacijentica,Upitnika za trudnice i Protokola imunohematoloških testiranja. Skrining i identifikacija antieritrocitnih antitijela rađeni su IAT metodom,gel-tehnikom u mikrokarticama s AHG-om(Grifols i BioRad).
Rezultati: U ispitivanom periodu testirano je ukupno 2 611 trudnica.Kod 10 trudnica (0,38%) nađena su antitijela u IAT-u.Antitijela detektabilna samo enzimskom tehnikom nisu otkrivena u ispitivanom uzorku.Kod 8 trudnica otkrivena su samostalna antitijela utvrđene specifičnosti: anti-D 2(20%),anti-E 2(20%),te kod po jedne trudnice (10%) anti-K,anti-S,anti-Kpa,anti-Lea antitijela.Kod dvije trudnice (20%) dokazano je prisustvo udruženih antitijela-dva antitijela: anti-D,C 1 i anti-E,Lea 1.
Zaključak: Imunohematološkim testiranjima u antenatalnom i perinatalnom periodu smanjuje se nastanak i učestalost kliničkih oblika HBFN.Minimiziranje izloženosti žena u reproduktivnoj dobi inkompatibilnim eritrocitnim antigenima putem nepotrebnih transfuzija,smanjuje incidencu aloimunizacije i rizik od HBFN.Optimalna briga i nadzor nad trudnicama s trudnoćom u riziku,podrazumijeva multidisciplinarni pristup tima stručnjaka iz više medicinskih disciplina.Pravovremena i odgovarajuća komunikacija ima ključni značaj za uspješan završetak trudnoće.Komparacija rezultata sa prevalencom otkrivenih antitijela na globalnom nivou,ne govori o značajnim odstupanjima.
Ključne riječi: aloantitijelo,aloimunizacija,trudnoća.

PP 027

ANTIERYTHROCYTE ANTIBODIES ISOLATED IN PREGNANT WOMEN AT THE INSTITUTE FOR TRANSFUSION MEDICINE OF THE FEDERATION OF BOSNIA AND HERZEGOVINA, IN THE PERIOD AUGUST 2021. TO AUGUST 2022.

Vilić-Hasanović V. Musić E. Miličić V.
Institute for Transfusion Medicine FBiH, Sarajevo BiH.

Introduction: Immunohaematological tests in pregnancy are an indispensable part of routine transfusion practice.There are three basic reasons for these tests: 1)determination or confirmation of the previously determined blood group of the ABO system and RhD antigen,as well as the detection of antierythrocyte antibodies,which can make it difficult to find compatible blood for transfusion; 2) Identification of pregnant women who need RhD immunoprophylaxis; 3)Timely detection and control of clinically significant antibodies,which have the potential to cause anemia and/or hemolytic disease of the fetus/neonate.
Objectives: 1)To show detected anti-erythrocyte antibodies in pregnant women in ZTM FBiH,in the period 01.08.2021. until 31.08.2022; 2)Analyze the results obtained by immunohaematological testing of pregnant women and 3)Draw conclusions about the correlation with current international results.
Methods: Retrospective analysis of data obtained from electronic patient records,Questionnaire for pregnant women and Protocol of immunohaematological testing.Screening and identification of anti-erythrocyte antibodies were done by IAT method,gel-technique in microcards with AHG(Grifols and BioRad).
Results: In the examined period,a total of 2,611 pregnant women were tested. Antibodies were found in IAT in 10 pregnant women (0.38%).Antibodies detectable only by the enzymatic technique were not detected in the examined sample.Detached antibodies of established specificity were detected in 8 pregnant women: anti-D 2(20 %),anti-E 2(20 %),and in one pregnant woman (10 %) anti-K,anti-S,anti-Kpa,anti-Lea antibodies.In two pregnant women (20%),the presence of combined antibodies was proven-two antibodies:anti-D,C 1 and anti-E,Lea 1.
Conclusion: Immunohaematological testing in the antenatal and perinatal period reduces the occurrence and frequency of clinical forms of HBFN.Minimizing the exposure of women in reproductive age to incompatible erythrocyte antigens through unnecessary transfusions,reduces the incidence of alloimmunization and the risk of HBFN.Optimal care and monitoring of pregnant women with at-risk pregnancies,implies a multidisciplinary approach by a team of experts from several medical disciplines.Timely and appropriate communication is of great importance for the successful completion of pregnancy.Comparison of the results with the prevalence of detected antibodies on a global level,does not indicate significant deviations.
Key words: alloantibody,alloimmunization,pregnancy.

PP 028

TREATMENT OF ANEMIA IN A MOTHER WITH A RARE PHENOTYPE AND TWO ALLOANTIBODIES: ANTI-C AND ANTI-E - CASE STUDY

Jukić B, Udovčić D, Mitrović S, Kovačević B, Banjac D, Lončar Pejaković T.
Institute For Transfusion Medicine of The Republika Srpska, Banja Luka, Bosnia and Herzegovina

INTRODUCTION: Anemia is the most common medical complication in pregnancy. If the pregnancy is not controlled, this anemia can manifest itself during and after childbirth, thus directly endangering the life of the mother and potentially the newborn.
OBJECTIVE: To show how a woman who has just given birth was cared for when the presence of a rare phenotype and two alloantibodies were detected only after delivery.
MATERIALS AND METHODS: Since the frequency of this phenotype in the population is 2.10%, we had to type a large number of erythrocyte doses to find an antigen-negative match for therapy. Serotyping was performed manually on the plate, and negative doses were confirmed by the test tube method. Screening and identification of antibodies was done by the gel method on the IH-500 device with BioRad's erythrocyte panel.
RESULTS: Request for two blood doses arrived for the mother P.G. (born in 1987) with Hb values of 69, which required immediate correction. During the pre-transfusion examination, a positive screening was obtained and two alloantibodies were identified: anti-C and anti-e, clinically significant (blood type: ARhD+, phenotype ccEE). Out of a total of 103 serotyped blood doses, only four units were compatible, of which the mother received two doses. From this third unmonitored pregnancy, a male child was born, blood type: BRhD+ with a CcEe phenotype, while the DAT was negative on the third day after delivery when we finally recieved the newborn's sample. We found one blood dose of 0RhD-, phenotype ccEE. Although the child did not receive a transfusion, elevated bilirubin values were corrected by UV lamp therapy.
CONCLUSION: It is necessary to perform screening of antibodies in all pregnant women, not only RhD-, in order to avoid these situations and to allow timely preparation of appropriate serotyped blood doses in case of an emergency positive screening. In this way, the morbidity/mortality of both the mother and the child would be reduced.
Key words: alloimmunization, phenotype, serotyping

PP 028

ZBRINJAVANJE ANEMIJE KOD PORODILJE SA RIJETKIM FENOTIPOM I RAZVIJENA DVA ALOANTITIJELA: ANTI-C I ANTI-E-PRIKAZ SLUČAJA

Jukić B, Udovčić D, Mitrović S, Kovačević B. Banjac D.
Zavod Za Transfuzijsku Medicinu Republike Srpske, Banja Luka, Bosna i Hercegovina

UVOD: Anemija je najčešća medicinska komplikacija u trudnoći. Ako trudnoća još nije kontrolisana, ta anemija se ispolji kao problem tek tokom i poslije porođaja i tako direktno ugrozi život majke, a potencijalno i novorođenčeta.
CILJ: Prikazati kako je zbrinuta porodilja sa rijetkim fenotipom i dva aloantitijela koja su dokazana tek nakon poroda.
MATERIJAL I METODE: Pošto je učestalost ovog fenotipa u populaciji 2,10% morali smo tipizirati veliki broj doza eritrocita da bismo našli podudarne, antigen-negativne doze za terapiju. Tipizacija je rađena manuelno na pločici, a negativne doze potvrđivane su metodom u epruveti. Skrining i identifikacija antitijela su rađeni metodom u gelu na aparatu IH-500 BioRad-ovim panelom eritrocita.
REZULTATI: Zahtjev za dvije doze krvi za porodilju P.G. (1987. godište) je stigao sa vrijednostima Hb 69 koji je zahtijevao hitnu korekciju. Prilikom pretransfuzijskog ispitivanja dobije se pozitivan skrining i identifikuju se dva aloantitijela: anti-C i anti-e, klinički značajna (KG: ARhD+, fenotip ccEE). Od ukupno 103 tipizirane doze krvi, samo su četiri jedinice bile kompatibilne, od kojih je porodilja primila dvije doze. Iz ove treće nekontrolisane trudnoće rođeno je muško dijete, KG: BRhD+ sa fenotipom CcEe, a DAT je bio negativan trećeg dana po porodu kad smo konačno dobili uzorak djeteta. Pronašli smo jednu dozu krvi 0RhD-, fenotipa ccEE, ali dijete nije primilo transfuziju, već su povišene vrijednosti bilirubina korigovane terapijom UV lampom.
ZAKLJUČAK: Neophodno je kontrolisati skrining svih trudnica, a ne samo RhD- kako bismo izbjegli ovakve situacije i bili spremni sa odgovarajućim tipiziranim dozama krvi kod pozitivnog skrininga u hitnoći. Na taj način bi se smanjio morbiditet/mortalitet kako kod majke tako i kod djeteta.
Ključne riječi: aloimunizacija, fenotip, tipizacija

PP 029

IMMUNOHAEMATOLOGY TESTING PROBLEMS DUE TO ACTIVATION OF COMPLEMENT-CASE REPORT

Velkova E[1], Srzentic S[2], Makarovska-Bojadzieva T[1], Dejanova-Ilijevska V[1], Petkovic E[1], Ristovska E[1], Hristova-Dimceva A[1], Drakulevska S[1]
[1] *Institute for transfusion medicina of North Macedonia*
[2] *Blood transfusion institute of Serbija*

Background: C4d and C3d bind covalently to RBC (E-C4d, E-C3d) According to its immunochemical characteristics, AIHA can be classified as warm (WAIHA) or cold (CAIHA), based on the results of direct agglutinin test (DAT), depending on if the DAT is positive for IgG alone, or IgG and C3d.
Aim: Importance of complement activation in immunohaematology testing because it can bind complement that may be detected in antiglobulin tests, or enable the antibody to act as a haemolysin in vitro.
Case report: Patient female, 71 years old, from kardiosurgery department, no data for previous transfusions, blood group A Rh negative. Cross much with 8 units of RBC was negative, but screening for antibody (IAT, DAT, Enzyme) was positive in polispecific columna test-BioRad IgG,C3d. We assumed that positivity is as a result of anti-H antibody, as a result of O Blood group of the test RBC. To prove the anti-H we made CM with A1,A2 and O blood samples and we obtain the negative, 2+ positive and 3-4+ positive reaction respectively. So, the question was why DAT and autoantibody are positive. DAT in monoclonal ID showed positive reaction in IgG and C3d, and negative in IgM, IgA and C3c.
Conclusion The patient was sensibilised with anti-H antibody, Complement was activated do to undiagnosed AIHA . Recommendation is pretransfusion testing to do with monospecific IgG kolumna test.
Kee words: aloimunisation, polispecific IgG, C3d, AIHA

PP 029

PP 030

SEROPREVALENCA KRVLJU PRENOSIVIH BOLESTI U ZAVODU ZA TRANSFUZIJSKU MEDICINU FBIH: PERIOD 2016-2021. GODINA

Ćatović-Baralija E, Ahmetović-Karić G, Bradarić F, Đozo A.
Zavod za transfuzijsku medicinu FBiH, Sarajevo, BiH

Uvod:
Precizna procjena prevalence krvlju prenosivih bolesti je krucijalna za nadzor izbora dobrovoljnih davalaca krvi kao i njihovog odbijanja i praćenja epidemiološke situacije u zemlji.
Cilj studije je da se uradi procjena seroprevalence markera na krvlju prenosive bolesti kod dobrovoljnih davalaca krvi za period 2016-2021. godina.

Metode:
Uzorci krvi su testirani na: HBsAg, anti HCV, Combo Ag/Ab HIV i anti Syphilis (TP). U testiranju su upotrebljeni serološki testovi (CMIA, Architect SR2000 sistem, ABBOTT). Ponovljeno reaktivni uzorci testirani su potvrdnim testovima Western blot metodom (MIKROGEN recomLine HIV, HCV i TP, MIKROGEN GmbH), a za HBV rađena su dodatna testiranja potvrdnim testom (CMIA, Architect i1000 sistem, ABBOTT).

Rezultati:
Ukupan broj uzoraka dobrovoljnih davalaca krvi testiranih u periodu od 2016-2021.godine je 89.411. Posmatrajući broj ukupnih prikupljenih jedinica krvi tokom šest godina, najmanji broj je bio tokom pandemijske 2020. i 2021. godine. Testiranjem na TP nije zabilježena prijava potvrđeno pozitivnih u 2016. i 2021. godini, dok potvrđeno pozitivne nismo zabilježili ni za HCV tokom 2018., 2020. i 2021. godine, kao ni za HIV tokom 2018. i 2019. godine. Najveći broj ponovljeno reaktivnih (RR) uzoraka u ispitivanom periodu je bio na HCV(0,27-0,43%), a potvrđeno pozitivnih (CP) uzoraka na HBV(0,02-0,07%).

Zaključak:
Stopa prevalence markera na krvlju prenosive bolesti kod dobrovoljnih davalaca krvi tokom analiziranog perioda, bila je najviša za HBV, što može biti povezano sa rastom infekcije među opštom populacijom te dodatnom potrebom fokusiranja na strategije primarne prevencije.

Ključne riječi: Prevalenca, davaoci, krv

PP 030

PP 031

THE IMPORTED MALARIA – HOW TO PROTECT THE SAILORS?

Filipović S.
Institute for blood transfusion of Montenegro
Introduction: Imported malaria is a major problem of sailors or workers on oil platforms in the area of endemic malaria. In 87 countries of Latin America, Asia and sub-Saharan Africa, this parasitic disease is present.

Aim: To educate sailors, voluntary blood donors, about the risk of the possibility to get malaria and how to fight this dangerous parasitic disease in order to provide donation of safe blood.
Matherial and metods : Report of Europian Centre for control and prevention of disease, report of US Blood bank, maps of endemic area, report of Institute for public health of Montenegro.
Results: Problem of malaria issues involves: inadequate protection measures, vaccine lack, a large percentage of self-excluded donors, resistance of parasites on antimalarics, mosquito resistance on insecticide, irregular or lack of chemoprophilaxis, large prevalence of malaria areas.
Protection of sailors , potential blood donors, demands proper education of pupils and students of the sea school and faculty to apply ABCDE prevention (Awareness, Bites, Chemoprophylaxis, Diagnosis, Emergency).
Awareness that Plasmodim malariae is the most dangerous parasite, transmited through infected blood. In the errol-canned blood, the parasite remains treadable for up to 14 days. One case of transmission through fresh frozen plasma, applied 24 hours after freezing, is described.
Bites can be avoided by implementing measures of protection (stay in areas, repelent, deet, picardin, permetrin).
Chemoprophylaxis like using antimalaric drugs per schema: seven days before departure ,during stay and six weeks upon return.
Diagnosis of malaria is placed on the basis of epidemiological data and clinical images and confirmation with the laboratory analyses (PCR,Elisa,dipstick test).
Emergency and Self help to use antimalaric one-time three consecutive day.
Conclusion: The first case of the of malaria get through transfusion was reported in 1911. Since then 3000 cases have been documented, of wich 11 percent deadly. Part of developmental cycle of parasites is related to red blood cells which is why there is a possibility of transfering malaria by transfusion of blood components from infected donors. Correct and timely ABCDE prevention is the key in protection of sailors and providing safe blood.

PP 031

PP 032

PETOGODIŠNJA STUDIJA PRESEKA SEROPREVALENCE HCV INFEKCIJE KOD DOBROVOLJNIH DAVALACA KRVI U ZAVODU ZA TRANSFUZIJU KRVI VOJVODINE

Krga Milanović M[1], Grujić J[1,2], Gulan Z[1], Klašnja J[1]
[1] *Zavod za transfuziju krvi Vojvodine, Novi Sad*
[2] *Medicinski fakultet, Univerzitet u Novom Sadu*

Uvod: Prevencija prenosa uzročnika zaraznih bolesti putem transfuzije krvi (TPI) testiranjem uzoraka dobrovoljnih davalaca doprinosi obezbeđivanju kvalitetne i bezbedne primene krvi i krvnih komponenti. TPI predstavljaju jedan od najznačajnijih neželjenih efekata transfuzije krvi koji možemo sprečiti adekvatnim skriningom dobrovoljnih davalaca, odgovarajućim testiranjem i podizanjem svesti javnosti o značaju samoisključivanja iz procesa davanja krvi. Seroprevalencija TPI kod zdravih davalaca krvi indirektno odražava prevalence ovih infekcija u opštoj zdravoj populaciji.

Cilj rada: Prikaz HCV pozitivnih dobrovoljnih davalaca krvi (DDK) u periodu od 2017.do 2021.godine testiranih u Zavodu za transfuziju krvi Vojvodine (ZTKV). Analiza demografskih podataka HCV pozitivnih DDK, pruža naučnu osnovu za formulisanje strategija kontrole i mera prevencije prema ovim grupama, i igra ključnu ulogu u sprečavanju da zarazne bolesti uđu u lanac snabdevanja krvlju.

Materijal i metode: Retrospektivno su prikazani rezultati 194 425 jedinica krvi prikupljenih na teritoriji Vojvodine testiranih u ZTKV. Sve jedinice krvi dobrovoljnih davalaca krvi testirane su imunološkim testovima koji za detekciju patogen specifičnog antitela ili antigena u plazmi davaoca koriste enzimsku tehniku (ELISA –Enzyme-Linked ImmunoSorbent Assay) ili hemiluminiscenciju (CLIA – Chemiluminescence immunoassay). U slučaju ponovljenog reaktivnog rezultata jedinice krvi su isključene, a za potvrdu infekcije korišćen je potvrdni imunoblot test. Svi serološki pozitivni davaoci ispitani su i klinički potvrđeni na HCV infekciju. Od avgusta 2019.godine sve jedinice krvi se testiraju i tehnikom umnožavanja nukleinske kiseline (NAT).

Rezultati: U posmatranom periodu prikupljeno je u ZTKV ukupno 194 425 jedinica krvi, od toga tokom 2017.godine 26 772 jedinica krvi , 2 (0,008%) HCV pozitivnih davalaca ; 2018.godine 37 770, 6 HCV pozitivnih (0,016%) ; u 2019. godini od 47 669 bilo je 5 (0,012%); tokom 2020.godine od 39 139 bilo je 3 HCV pozitivnih (0,008%) a u 2021.godini od 43 075, 7 pozitivnih (0,016%). Među HCV pozitivnim DDK predominiraju osobe muškog pola (65%), starosne kategorije 36-45 (39%).

Zaključak: Naša studija prikazuje oscilirajući trend HCV prevalence tokom petogodišnjeg perioda koji se održava na niskom nivou. Potrebno je uložiti napore da se poveća svest i edukuje stanovništvo o smanjenju faktora rizika za HCV infekciju.

Ključne reči: Stopa prevalencije, TTI, davaoci krvi

PP 032

A FIVE YEAR CROSS-SECTIONAL STUDY ON HCV INFECTION SEROPREVALENCE IN VOLUNTARY BLOOD DONORS IN BLOOD TRANSFUSION INSTITUTE OF VOJVODINA

Krga Milanović M[1], Grujić J[1,2], Gulan Z[1], Klašnja J[1]
[1] *Blood Transfusion Institute of Vojvodine, Novi Sad*
[2] *Faculty of Medicine, University of Novi Sad*

Introduction: Transfusion-transmitted infections (TTIs) represent one of the most significant side effects of blood transfusion that can be prevented by adequate screening of voluntary blood donors (VBDs), appropriate testing and raising public awareness of the importance of self-exclusion from the blood donation process. The seroprevalence of TTI in healthy VBDs indirectly reflects the prevalence of these infections in the general healthy population.

Objective: Presentation of HCV positive VBDs in the period from 2017 to 2021 tested at the Blood Transfusion Institute of Vojvodina (BTIV). The analysis of demographic data of HCV-positive VBDs provides a scientific basis for control strategies and prevention measures for these groups, and plays a key role in preventing infectious diseases from entering the blood supply chain.

Material and methods: Retrospectively present the results of 194 425 blood units collected in the territory of Vojvodina and tested in BTIV. All VBDs units were tested with immunological tests for the detection of pathogen-specific antibodies or antigens in the donor's plasma using the enzyme technique (ELISA – Enzyme-Linked ImmunoSorbent Assay) or chemiluminescence (CLIA – Chemiluminescence immunoassay). In the case of a repeatedly reactive result, the blood units were excluded, and a confirmatory immunoblot test was used to confirm the infection. All serologically positive donors were examined and clinically confirmed for HCV infection. Since August 2019, all blood units are also tested with the nucleic acid amplification technique (NAT).

Results: In the observed period, a total of 194 425 units of blood were collected in BTIV, of which 26 772 blood units were collected in 2017 with 2 (0,008%) HCV positive donors; In 2018, 37 770 units and 6 HCV positive donors (0,016%) ; in 2019, out of 47 669 units, there were 5 HCV positive (0,012%); in 2020, out of 39 139, there were 3 HCV positive (0,008%), and in 2021, out of 43 075 units, 7 donors were positive (0,016%). Men predominate among HCV-positive VBDs (65%) while dominant age category is 36-45 (39%).

Conclusion: Our study shows an oscillating trend of HCV prevalence during a five-year period that maintained at a low level. Efforts should be made to increase awareness and educate the population about reducing risk factors for HCV infection.

Keywords: Prevalence rate, TTI's, Blood donors

PP 033

RESULTS OF CONFIRMATION TESTING IN VOLUNTEER BLOOD DONORS FOR MARKERS OF TRANSFUSION TRANSMISSION DISEASES

Damjanović V[1], Jovičić M[2], Antonijević I[1], Dukić Novaković M[1], Stamenić LJ[1]
[1] *Institute for Blood Transfusion of Serbia, Department for Testing and Control of Donor Blood, Belgrade, Serbia*
[2] *KBC Dr. Dragiša Mišović-Dedinje, Belgrade, Serbia*

Introduction: Confirmatory tests have a role in resolving the status of blood donors with reactive results of screening test and they are applied in reference laboratories.

Objective: Presentation and analysis of the results of serological, confirmatory and molecular testing-NAT (nucleic acid amplification testing) for markers of transfusion transmissible diseases (TTB) in voluntary blood donors (VBD).

Material and method: Data for the period January 2020 - December 2021 were analyzed. 129 272 DDK samples were tested for TTB using adopted standard operating procedures and in accordance with the basic testing algorithm (serology and NAT). For serological tests were used ELISA and chemiluminescence tests, and for NAT tests were used a minipool of 6 samples. Confirmatory testing (CT) was done with the Innolia score tests on the Tendigo/Fujirebio device.

Results: A total of 484 confirmatory tests were performed: for anti-HCV 213, anti-HIV 83 and anti-TP 188. A negative result was registered in 323 VBD, indeterminate 65 and positive results in 96. The highest number of registered indeterminate results was in the test of anti-TP 46, anti-HCV 17 and anti-HIV 2. The positive result of CT was determined in order: anti-TP 60, anti-HCV 29 and anti-HIV 7. In the observed period, the prevalence obtained for confirmatory testing: HCV 0.022; HIV 0.005 and TP 0.046. In 9 HCV PT positive samples, the results of NAT HCV testing were non-reactive.

Conclusion: The role of NAT testing significantly contributed to the safety of blood administration. Confirmatory testing for VBD is of crucial importance in order to resolve the status of blood donors, which enables VBD with negative results on CT and NAT to continue donating blood (69.73%), and VBD with positive and indeterminate results to report to competent institutions for further diagnosis and therapy.

Key words: confirmatory testing of VBD, prevalence, NAT.

PP 033

PP 034

ANALYSIS OF NONCONFORMITIES IN THE INSTITUTE FOR TRANSFUSION MEDICINE OF THE REPUBLIC OF NORTH MACEDONIA

Khan Daskalovska D, Petkovikj E, Stojkoska S, Stankovikj D, Shterjanovski M, Rastvorceva Grubovikj R, Useini S.
Institute for Transfusion Medicine of the Republic of North Macedonia

Introduction: The quality management system is a key link in the process of ensuring the quality and safety of blood and blood products. With the introduction of the Quality Management System, the Institute for Transfusion Medicine of the Republic of North Macedonia (ITM - RNM) is committed to consistent implementation of nonconformities management in all its activities.
Aim: The aim of this study was to analyze nonconformity reports (NCR) in the Quality Assurance and Quality Control (QAQC) Department at ITM – RNM and to identify the root causes of NCR.
Materials and methods: This is a retrospective analysis of the data from the NCR register in the QAQC department at ITM - RNM for the period from 2020 to 2021.
Results: There were reported 150 NCR in 2020 and 559 NCR in 2021. The most common NCR 2020/2021 were: incompletely filled blood bags 25 (16.6%) / 374 (66.9%), damaged fresh frozen plasma bag 33 (22%) /55 (9.8%), expired blood components 13 (8.6%) /3 (0.5%), inappropriate labeling (blood donor card, barcode, test tube) 11 (7.3%) / 14 (2.5%). During 2021 year 50 (5%) NCR were reported because of interface error between Hemoflow portable scale and mixers and the eDelphyn system. The other NCR is reported in very small numbers for various reasons. Compared to NCR in previous years (2015-37, 2016-29, 2017-31, 2018-20, 2019-61), a significant increasing trend is observed, which is due to the increased activity and commitment of the QAQC department at ITM - RNM.
Conclusions: During 2020 and 2021 the most frequently NCR were detected in the blood collection process in the ITM, and are most likely the result of human error, vasovagal reactions and inadequate veins. This result indicates a need for retraining and working strictly according to existing standard operating procedures (SOPs), as well as appropriate and professional IT support.
Key words: Quality Assurance, Health Care; Total Quality Management; Blood Banks.

PP 034

PP 035

ADVERSE TRANSFUSION REACTIONS –15 YEARS MACEDONIAN EXPERIENCE

Petkovikj E , Stojkoska S , Grubovic Rastvorceva R, Daskalovska Khan D , Velkova E, Makarovska Bojadzieva T , Dejanova V , Ristovska E, Todorovski B, Useini S.
Institute for Transfusion medicine of Republic of North Macedonia

Introduction: Haemovigilance is the systematic surveillance of adverse events, covering the whole transfusion chain from the collection of blood and blood components to the follow-up of transfusion recipients. Haemovigilance is used to identify and prevent occurrence or recurrence of transfusion related unwanted events to increase the safety and efficiency of blood transfusion.
Aim: The aim of this study was to analyze the adverse transfusion reactions (ATR) that were reported to the Quality Assurance and Quality Control (QAQC) Department in the Institute for Transfusion medicine of Republic of North Macedonia – Skopje.
Materials and methods: retrospective analysis of the reported ATR to the QAQC department in the period 2007-2021 from its monthly and yearly registries.
Results: The most frequent ATR were mild allergic and febrile non-haemolytical transfusion reactions with urticaria, fever and vomiting. In 2007 were 2 reported ATR (to Cryoprecipitate and Fresh Frozen Plasma (FFP)), in 2008 – 1(FFP), in 2009 – 1(FFP), in 2010 –1(FFP), 2011 – 3 (2 RBCSAGM and 1 F.VIII conc.), in 2012 - 1 (Cryoprecipitate), in 2013- 2 (RBC-SAGM and Cryoprecipitate), in 2014 – 1 (Cryoprecipitate), in 2015 – 1 (FFP), in 2018 - 4 (1-FFP and 3-RBC-SAGM), in 2019 – 3 (FFP), in 2020 - 4 (1-Platetelet concentrate, 3 RBC-SAGM) and in 2021 – 1 (RBC-SAGM). There was no mortality associated with blood transfusion in the last 15 years.
Conclusions: Important part of the haemovigilance is to report every adverse event related to transfusion of blood or blood component and evaluation of the report, equally as well as active feedback on all transfused units. The hospital transfusion committees have a key role in dealing with hemovigilance and risk management. Analysis of the reports for the blood components use, adverse transfusion reactions and the outcome of every single transfusion of blood components, will help us to decrease ATR.
Key words: Transfusion Reaction; Blood Safety; Blood Transfusion.

PP 035

PP 036

BIOCHAGA AND BIODIHYDROQUERCETIN IN PREVENTION, TREATMENT AND REHABILITATION OF BRAIN DISORDERS

Dimitrijevic G.
Institute for Blood transfusion of Vojvodina, Novi Sad, Serbia

Introduction: Biochaga (Inonotus Obliques) is a photogenic parasitic fungus growing on white birch trees and is known for its medicinal properties. In the USA it is classified as a dietary supplement and in Europe and Russia as a medicinal mushroom used for medicinal properties. In the USA it is classified as a dietary supplement and in Europe and Russia as a medicinal mushroom used for medicinal properties. Beta glucans is known to establish better intercellular communication. In neurology it is used for relieves stress and anxiety, establishes the transport of substances in the brain tissue after injuries and stroke, increases work capacity, life force, improves memory, fight insomnia.
Aim: The aim of this paper is to describe the use of Biochaga and Biodihydroquercetin, Siberian supplements that are very good for prevention, treatment and rehabilitation of brain disorders as well as to show their benefit to brain insults and some other disorders which are very common among elderly people in Serbia.
Materials and methods: The description of using those two extremely natural supplements (powder consistency) emphasizing that there are no side effects of using them.
Results: Biodihydroquercetin protects capillary blood vessel endothelial cells against corrosive compounds damage, increased vascular permeability, reduces blood viscosity, improves microcirculation. It promotes the establishment of microcirculation, improves metabolism of brain cells, and regulates the metabolism process of neurotransmitters and peroxidation reaction in the cerebral cortex, visual nerve and retinal neurons. In neurology it is used for neurasthenia, neuralgia, neuritis, radiculitis, Parkinson's disease, Alzheimer' s disease, headaches, migraine. "If you increase the breathing capacity, the flow of oxygen to the brain and other organs, you open the way to tens of thousands of closed capillaries, you will not encounter any disease that cannot be cured." (A.Zalmanov)
Conclusions: Biochaga and Biodihydroquercetin together are very useful and effective. Nobel prize winner Linus Pauling said: "Regular use of Dihydroquercetin can extend human life by 25 years ".
Key words: Dietary Supplements; beta-Glucans; Brain Diseases.

PP 036

PP 037

EXPERIENCE WITH THE HEPATITIS C VIRUS "TRACEBACK" PROCEDURE

Shorova M[1], Jovanova N[1], Grubovic-Rastvorceva R[2], Petkovik E2, Stambolieva D[1], Vilos L[3]
[1] *Regional Center for transfusion medicine Shtip, Republic of North Macedonia*
[2] *Institute for transfusion medicine, Skopje, Republic of North Macedonia*
[3] *Regional Center for transfusion medicine Bitola, Republic of North Macedonia*

Introduction: A traceback investigation is carried out by the Transfusion service after receiving a report of possible transfusion transmission infection following the transfusion of blood or blood components. The investigation requests retesting of archived blood samples if available from the Transfusion Service and/or testing of new blood samples, obtained from the suspected donor. Since last year, Institute for Transfusion Medicine in Skopje (ITM) has been performing PCR testing in order to reduce the pre-seroconversion window period for transfusion-relevant viruses.
Aim: The aim of this study was to investigate the results of blood donor TTI testing due to existing epidemiological indications of possible HCV transmission through blood components.
Materials and methods: At the request of a Public Health Center, a traceback procedure was performed, with the use of a computer database (e-Delphin). Inspection of the medical documentation was done, due to possibility transmission of HCV infection through blood components.
All blood donations collected at the blood centers and mobile units are tested with enzyme immunoassay (EIA) and NAT. NAT results from the testing site at ITM Skopje were distributed through the e-Delphin, a National transfusion IT system, to all 3 blood centers.
Results: During the inspection, it was determined that the person had been staying in the Clinical Hospital Shtip from 11.04.2022 to 21.04.2022. Patient received iv and im therapy, gastroscopy and a colonoscopy were performed, and on 13.04.2022, he received one dose of erythrocyte concentrate. After one month, an acute HCV infection appeared. First, we inspected the medical card of the donor whose blood was received by the person infected with HCV. All the tests performed at the time of donation were negative. We called him for a re-analysis, this time with the PCR technique. The results of the HCV antibody and HCV RNA testing were negative and undetectable.
Conclusions: The HCV traceback investigation showed that there was no evidence of HCV transmission from blood donor to recipient via blood. The choice of centralized NAT screening, the implementation of an IT transfusion network for the whole country, and the cooperation among 3 blood centers and ITM Skopje, have proved to be effective for improving blood transfusion safety.
Key words: Hepatitis C; Transfusion Reaction; Blood Safety.

PP 037

PP 038

BLOOD SUPPLY AND BLOOD INVENTORY MANAGEMENT

Makarovska Bojadjieva T[1], Velkova T[1], Ristovska E[1], Petkovik E[1], Dejanova Ilijevska V[1], Trajkova J[1], Ismaili Lj[1], Nikoloska I[1], Apostoloska R[1], Tashkovska M[2]
[1] *Institute of Transfusion Medicine, Faculty of Medicine, Ss. Cyril and Methodius University in Skopje, Republic of North Macedonia*
[2] *City General Hospital 8th September, Skopje, Republic of North Macedonia*

Introduction: Blood inventory management is the critical step between blood supply and the demand of patients for blood products which keeps a balance between the shortage and wastage of blood.
Aim: To evaluate blood inventory management and to propose practices that will ensure optimal blood supply with minimal wastage of blood.
Materials and methods: The number and phenotype ABO/D of red blood cells (RBC) and platelets (PLT) expired in 2019 was assessed using data from the donor information system.
Results: From the total of 50600 collected whole blood units 4500 (8.9%) were eliminated (2.7 % from the laboratory and 6.2% as unsuitable for production). The total stock during the study period was 46000 RBC and 28410 PLT. Out of them 44000 (95.5%) RBC and 24440 (86.1%) PLT were issued for clinical use. The rest of 2100 (4.5%) RBC and 3970 (13.9%) PLT were excluded after the expiration. The overall rate of produced, issued and expired was 126, 120 and 6 units/day for RBC and 78, 67 and 11 units/day for PLT. The percentage of produced, issued and expired component AB type was: for RBC 8.2%, 7.3%, 16%; for PLT 5.7%, 5.0%, 27%, with a significantly higher percentage of expired component for both RBC and PLT. The percentage of expired RhD negative RBC (25%) and RhD negative PLT (33%), especially of the O and AB blood group, was significantly greater in comparison to the produced RBC (14%) and PLT (11%), as well as the issued RBC (12%) and PLT (10%). In 2021, the amount of time-expired RBC waste was reduced to 2.9%, mostly due to the issuance of ABO non-identical but compatible units. The percentage of time-expired PLT remains the same (13.3%).
Conclusions: The study found a significantly greater proportion of expire group O RhD negative RBC and expire AB RhD negative PLT. Blood facilities should collaborate with the hospitals in setting indicators for monitoring the blood inventory in order to minimise waste of blood and to meet patients' needs for transfusion.
Key words: Erythrocytes; Platelet Transfusion; Blood Donors.

PP 038

PP 039

MICROBIOLOGICAL CONTROL OF PLATELET CONCENTRATE IN THE INSTITUTE FOR TRANSFUSION MEDICINE OF REPUBLIC OF NORTH MACEDONIA

Stojkoska S, Petkovikj E, Stankovic D, Shterjanovski M, Khan Daskalovska D, Grubovic Rastvorceva R, Useini S
Institute for Transfusion Medicine, Skopje, Republic of North Macedonia

Introduction: Ensuring safer practice in every stage of production blood and blood products in order to prevent contamination is a major challenge of transfusion services. Bacterial culture from platelet concentrates gives the best picture of contamination. Platelet concentrates carry greater risks of sepsis than other components because of their storage at room temperature.
Aim: To analyze the results of microbiological control of platelet concentrates using BacT /ALERT 3D.
Matherials and methods: This is a retrospective analysis of data from the register for "Microbiological analysis of sterility" in the Quality Assurance and Control Department at the Institute of Transfusion Medicine of the Republic of North Macedonia (ITM-RNM) in the period from 2015 to 2021. BacT /ALERT 3D was used for aerobic and anaerobic bacteriological cultivation since 04.11.2015.
Results: During the study period a total of 6907 microbiological control was performed, about 80-100 analyzes per month. In 2015-235, 2016-772, 2017-1336, 2018-866, 2019-1394, 2020-1057 and in 2021-1247 analyzes were made. The increasing trend in the performed analyzes had a drop in 2018 due to the renovation of the Department/microbiology laboratory ITM-RNM. A very small number of false positive results were found. Only one true positive result (staphylococcus vitulinus) was found in platelet concentrate, in 2017. Institute of Microbiology and Parasitology at the Faculty of Medicine - Skopje confirm the result. All blood components produced were removed from use.
Conclusions: The scientific-technological progress allowed a significant improvements in all segments of the transfusion process. Therefore, in the future, transfusion medicine will be directed towards the development of new techniques of inactivation of pathogens in blood components, as well as the search for alternative solutions for transfusion treatment.

Key words: Microbiology; Platelet Transfusion; Quality Control.

PP 039

PP 040

UPRAVLJANJE MEDICINSKIM OTPADOM NA ODELJENJU ZA PRIKUPLJANJE KRVI I KOMPONENATA KRVI

Vujnović M, Brkanović T, Radulović J, Radević S, Kuljić V,
Martinović B, Stojneva Istatkov J.
Institut za transfuziju krvi Srbije, Beograd

Uvod: Medicinski otpad je otpad koji nastaje pri pružanju zdravstvene zaštite ljudima. Upravljanje medicinskim otpadom je skup mera kojima je utvrđeno bezbedno razvrstavanje, pakovanje, skladištenje, transport i inaktivacija unutar ili van ustanove. Pravilnim upravljanjem otpadom povećava se bezbednost medicinskog osoblja, pacijenata i čitave zajednice, kao i doprinosi zaštiti i očuvanju životne sredine.
Cilj: Prikazati proces upravljanja medicinskim otpadom na Odeljenju za prikupljanje krvi i komponenata krvi Instituta za transfuziju krvi Srbije (ITKS).
Materijal i metode: Medicinski otpad nastao u toku rada Odeljenja za prikupljanje krvi i komponenata krvi ITKS se svakodnevno tretira u skladu sa procedurom ITKP116 - Upravljanje medicinskim otpadom. Na mestu nastanka otpada, na Odeljenju ili na terenu, vrši se njegovo razdvajanje i identifikacija u skladu sa SOP116/01 - Razvrstavanje medicinskog otpada na mestu nastanka. Otpad se sortira u kese ili kontejnere obeležene određenom bojom i sa oznakom koja sadrži osnovne informacije o vrsti, količini i generatoru otpada.
Rezultati: Tokom 2021. godine generisano je ukupno 4900 kg medicinskog otpada, od toga: 4478 kg igala sa zaštitom, PNC kesa, vakutajnera, vate (u žutim kesama); 370 kg rastvora bakar sulfata (u žutim kesama); 44 kg lanceta, vate, pasterovih pipeta (u posudama za oštre predmete). Uz odgovarajući formular na kome je navedena vrsta i količina otpada medicinski otpad je dostavljan na uništavanje. Dobru praksu upravljanja otpadom podržali su zdravstveni radnici i saradnici koji su znali šta se od njih očekuje, bili su motivisani i propisno obučeni za navedene aktivnosti. Postojala je adekvatna saradnja na svim nivoima zdravstvene ustanove po pomenutim pitanjima.
Zaključak: Pravilnim rukovanjem medicinskim otpadom i pridržavanjem uspostavljenih procedura na Odeljenju za prikupljanje krvi i komponenta krvi sprečava se nastanak infekcija koje se mogu preneti putem krvi i doprinosi zaštiti i unapređenju zdravlja populacije i očuvanju životne sredine.
Ključne reči: medicinski otpad, radno mesto, davaoci krvi.

PP 040

MANAGEMENT OF MEDICAL WASTE AT THE DEPARTMENT OF COLLECTION OF BLOOD AND BLOOD COMPONENTS

Vujnović M, Brkanović T, Radulović J, Radević S, Kuljić V,
Martinović B, Stojneva Istatkov J
Blood Transfusion Institute of Serbia, Belgrade

Introduction: Medical waste is defined as waste generated by health-care activities. Medical waste management is a set of measures that determine the safe sorting, packaging, storage, transport and inactivation inside or outside the facility. Proper waste management increases the safety of medical staff, patients and the entire community, as well as contributes to the protection and preservation of the environment.
Objective: To present the medical waste management at the Department of collection of blood and blood components (Department) of the Blood Transfusion Institute of Serbia (BTIS).
Methods: Medical waste generated in the course of the Department's work is daily treated according to the procedure ITKP 116 "Medical waste management". At the place of origin of waste, at the Department or during fieldwork, it is separated and identified in accordance with SOP116/01 "Medical waste sorting at the place of origin". The waste is sorted into bags or containers that are marked with a specific color, and with a label that contains basic information about the type, amount and the generator of the waste.
Results: During 2021, the Department generated a total of 4900 kg of medical waste: 4478 kg of needle with protective cap, PNC bags, vacutainers, medical cotton (in yellow bags), 370 kg of copper sulfate solution (in yellow bags) and 44 kg of sharp item containers with lancets, medical cotton, Pasteur pipettes. Medical waste was submitted for destruction with the appropriate form on which waste type and amount was specified. Efficient waste management practice was supported by health workers and associates who were fully aware of what was expected of them; were motivated and properly trained for the mentioned activities. There was adequate cooperation at all levels of the health institution on the aforementioned topics.
Conclusion: Proper handling of medical waste and adherence to established procedures at the Department prevents the occurrence of infections that can be transmitted through blood and contributes to the protection and improvement of the population's health along with the preservation of the environment.
Keywords: Medical Waste; Workplace; Blood Donors.

PP 041

MYTERM – NINE YEARS BETTER QUALITY HEALTH SYSTEM

Apostolovska R, Nikoloska I, Neceva V, Makarovska-Bojadzieva T,
Andonov G, Useini S
Institute for transfusion medicine, Skopje, Republic of North Macedonia

Introduction: The Ministry of Health of the Republic of North Macedonia in 2013 introduced a national electronic system for medical examinations appointments called "MyTerm". This system is a part of the National system for electronic health records which provides different services such are: E-Prescription of medicines, Electronic health insurance cards and electronic medical record of patient's history of health condition. This system allows patient's referral from General Practitioners and specialists. The system generates unique number for each patient with the exact day and time for regular appointed medical examination or creates an emergency appointment as that has validity for 24 h or a priority for 7 days, both without exact time. The provided services are electronically registered directly to Health Insurance Fund.
Aim: To evaluate of appointed and realized medical examinations of patients at the Institute for Transfusion Medicine (ITM) - Skopje that were registered trough "MyTerm" in 2021 (regular, emergency or priority).
Material and method: Retrospective study in which as material was used data from the electronic system from the Outpatient Department in ITM - Skopje, by access to a data base of "MyTerm". The number of appointed and realized medical examinations was analyzed.
Results: In 2021, from 88.636 appointments, 83.784 (94.5%) medical examinations were realized. There were 75.155 (89.7%) with regular appointments, 6.258 (7.5%) with emergency and 2.371 (2.8%) with priority appointments. The number of first medical and control examinations was 60.084 (71.7%) and 23.700 (28.3%) respectively. The average number of examined patients per day/per doctor was 32.
Conclusions: For 9 years, "Myterm" is very helpful tool for better organization of patient's flow within the medical institutions, better evidence of provided healthcare services and less waiting time for patients. This system also improves a communication among doctors at all levels of healthcare, the therapy given and medical history of the patient.
Key words: Medical Records; Appointments and Schedules; Health Priorities.

PP 041

PP 042

MAINTAINING THE QUALITY MANAGEMENT SYSTEM IN THE ISTITUTE FOR TRANSFUSION MEDICINE OF RNM

Grubovic Rastvorceva R[1,2], Useini S[1], Petkovic E[1], Stojkoska S[1], Daskalovska D[1], Ismani E[1], Shorova M[1,2], Todorovska E[1], Nikoloska I[1], Trajkova J[1], Todorovski B[1], Uzunovska T[1], Gorcaj L[1], Raka F[1], Ristovska E[1], Dejanova-Ilijevska V[1], Ortakovska S[1], Grubovic M[1].

[1] *Institute for Transfusion Medicine of RNM, Skopje, Republic of North Macedonia*

[2] *Faculty of Medical Sciences, University Goce Delcev, Republic of North Macedonia*

Introduction: The quality management is a continuous process, involving implementation, maintenance and improvement.

Aim: Study aim was to show our experience in maintaining the quality management system (QMS) in the Institute for Transfusion Medicine of Republic of North Macedonia (ITM-RNM).

Materials and methods: ITM-RNM is the main institution in charge of Blood Transfusion Service in our country, which is the national unified system. The QMS implementation across the whole of the institution and QMS maintaining were obtained through the establishing of the ISO standardization, working according to EU directives and the EDQM guidelines and implementing JACIE standards in the Stem Cell Collection Department. The two of our colleagues became the JACIE Inspectors. We had two audits from the EDQM auditors and an orientation visit from the independent JACIE inspector in order to improve our QMS.

Results: ITM-RNM was part of IPA project “Strengthening the Blood Supply System”, which put the basis for unification of blood transfusion standards and operating procedures in the whole country as well as set up essential education of blood transfusion personnel. There is a national regulatory framework in place and WHO and World Bank initiatives in Macedonia which support quality in health care and accreditation. Our personnel is continuously working in harmony with quality management standards, according to institutional standard operating procedures, which are regularly revised, followed by regular meetings, trainings and self-evaluation of the personnel. We are three times ISO accredited ISO 9001:2008 and ISO 9001:2015, and reaccredited in 2022.

Conclusion: Working with respect standards, following the rules and regular self-evaluations will help us to maintain the strong QMS. Every institution will benefit from a QMS that brings us into the line with international standards. Ensuring the quality of our services and products is essential to keep safe and strong blood transfusion service.

Keywords: Total Quality Management; Quality Assurance, Health Care; Blood Transfusion.

PP 042

PP 043

POVEZANOST ABO KRVNOGRUPNOG SISTEMA SA SARS-COV-2 INFEKCIJOM

Radonjić S[1] , Filipović S[2]
Zavod za transfuziju krvi Crne Gore, O.J.Bar[1]
Zavod za transfuziju krvi Crne Gore, O.J.Kotor[2]

Uvod
Pandemija Sars -CoV-2 utiče na društveni,ekonomski i zdravstveni život cijelog svijeta od kraja 2019. godine.
Cilj
Prikazati povezanost i potencijalnu ulogu ABO krvne grupe i oboljevanja od ovog virusa.
Materijal i metode
Ispitivali smo 1075 uzoraka krvi testiranih na ABO krvnu grupu osoba liječenih u barskoj bolnici na covid odjeljenju za region južnog Jadrana u 2020. godini.
Rezultati
Utvrđeno je da pacijenti sa krvnom grupom A, njih 422 (39,3%) imaju veću stopu infekcije u poređenju sa pacijentima sa krvnom grupom O, kojih je bilo 250 (23,3%).Osobe muškog pola (616 osoba) starije životne dobi (61 do 90god.), njih 476, koji imaju A krvnu grupu (207 osoba) su bili prijemčiviji za virus u odnosu na ženski pol.
Diskusija
Utvrđeno je da pacijenti sa A krvnom grupom imaju veću stopu infekcije u poređenju sa O krvnom grupom. Hipoteza o prisustvu anti-A antitijela,kao jednog od potencijalnih mehanizama , sugeriše da anti-A antitijela, koja su prisutna u plazmi O i B krvne grupe sprečavaju interreakciju između C proteina virusa i ACE2 na površini ćelije domaćina, imaju jacu zaštitnu ulogu i pripadaju IgG klasi.
Infekcija virusom po mehanizmu sličnom transfuziji kompatibilne krvi je druga hipoteza. Osobe koje imaju O krvnu grupu imaju najmanji rizik zaraze, mogu da zaraze osobe svih krvnih grupa, a mogu biti zaraženi samo od osoba koje imaju O krvnu grupu.
Zaključak
Potrebno je registrovati ABO krvne grupe svih zaraženih pacijenata radi izrade opsežnije studije o povezanosti ABO krvne grupe i oboljevanja, boljeg razimijevanja patofiziologije virusne infekcije i mogućnosti liječenja.
Ključne riječi: ABO krvne grupe, infekcija Covid-19

PP 043

THE CONNECTION OF THE ABO BLOOD GROUP SYSTEM WITH SARS COV-2 INFECTION

Radonjić D, Filipović S.
Institute for blood transfusion of Montenegro, Organizational unit Bar
Institute for blood transfusion of Montenegro, Organizational unit Kotor

Introduction
The pandemic Sars-CoV-2 affects the social,economic and health aspects of life of the whole word since the end of 2019 year.
The aim
Show the connection and potential role of ABO blood type and infection with Covid-19.
Material and method
We observed 1075 blood samples tested for the ABO blood group of persons treated for Covid-19 in the Bar hospital Department for the southern Adriatic region in 2020 year.
The results
It was determined that patients with blood group A, 422(39,3%)of them have a higher infection rate compared to patients with blood group O-250(23,3%) of them. Of 616 male persons, in older age (61 to 90 years old) were 476 of them;among them, patients of blood group A (207) are more susceptible to the virus compared to females.
Discussion
Patients with blood type A were found to have higher rates of infection compared to O blood type. Hypothesis of anti-A antibodies as one of the potential mechanisms, suggest that anti-A antibodies present in plasma of O and B blood group patients prevent interreaction between C protein virus and ACE2 on the surface on the host cell and have a protective role when belong to the IgG class. Infection of the virus under a mechanisms similar to a blood-compatible transfusion is another hypothesis.People who have O blood type have a lowest risk of infection, can infect people of all blood groups and they are infected only from persons of O blood group.
Conclusion
It is necessary to register blood groups of all infected patients for a more extensive study on the link between ABO blood groups and disease ,better understanding of the pathophysiology of viral infection and treatment possibilities.
Key words: ABO blood groups, Covid-19 infection

PP 044

POTROŠNJA KRVI I TRANSFUZIJSKE KOMPLIKACIJE KOD PACIJENATA SA MIJELODISPLASTIČNIM SINDROMOM LEČENIH AMBULANTNIM TRANSFUZIJAMA

Ratković Rangelov I, Petrović A, Rajković D, Zdelar Stojanović Lj, Crvenkov T, Nikolić Lj
Univerzitetski klinički centar Srbije, Beograd, Srbije

Uvod. Učestalost primene transfuzije kod pacijenata sa mijelodisplastičnim sindromom dovodi do poboljšanja kvaliteta života, neželjenih reakcija i komplikacija. Na primenu transfuzije eritrocita i trombocita utiču vreme postavljanje dijagnoze, primena antihemoragika, učestalost primene puliranih/ afereznih trombocita, eritrocita resususpendovanih osiromašenih leukocitima i trombocitima/filtriranih eritrocita.
Cilj je analiza potrošnje komponenata krvi i praćenje neželjenih reakcija.
Metode. Analizirane su vrednosti hemoglobina, trombocita, količina primenjenih eritrocita i trombocita pet pacijenata (3 ženskog i 2 muškog pola) starosti između 61-74 godine u periodu od 01.07.2021. do 30.06.2022.godine.
Rezultati. Pacijenti su prosečno godišnje primili po 37,4 jedinice (9215,2 mL) resuspendovanih eritrocita osiromašenih leukocitima i trombocitima i/ili filtriranih eritrocita, transfuzije trombocita 1016 ml (prosečno po pacijentu: 3 pula, 6 afereznih i 65 koncentrata trombocita iz buffy coat-a). Prosečne vrednosti hemoglobina su 73.2 g/L (raspon:44-87g/L), trombocita iznose 83x10e9/L (raspon:4-107x10e9/L). Na eritrocitne antigene identifikovana su: anti-Kell, anti-E, anti-c, papainska antitela, neidentifikovana antitela. Na trombocitima detektovana anti-HLA antitela klase I, anti-HPA-2b, anti-HPA-5b i anti-GPIIb/ IIIa antitela. Antitela su detektovana kod tri od pet pacijenata (dve osobe ženskog i jedna muškog pola , svi su A krvne grupe). Jedan ispitanika imao je burnu reakciju tokom primene transfuzije eritrocita u vidu jeze, drhtavice, temperature, hematoma i čvorova duž gornjih i donjih ekstremiteta. Četiri od pet ispitanika su bar jednom doživeli blažu transfuzijsku reakciju tokom ili nakon primene u vidu glavobolje, mučnine ili subfebrilne temperature.
Zaključak. Praćenjem pacijenata sa mijelodisplastičnim sindromom u Ambulantnoj transfuziji UKCS zaključeno je da restriktivni pristup u transfuziji smanjuje rizik od senzibilizacije, formiranja antitela, učestalosti neželjenih transfuzijskih reakcija. Da bi izabrali najkompatibilniju krv za naše pacijente koji su transfuziono zavisni, potrebno je uraditi proširenu fenotipizaciju eritrocita, a za transfuziju trombocita primenjivati tipizirane koncentrate trombocita u skladu sa prisutnim antitelima. Time bi smanjili rizik od nastajanja antitela, smanjili troškove pretransfuzionog testiranja i zbrinjavanja transfuzijskih reakcija.
Ključne reči: Transfuzija, Mijelodisplastični sindrom, Antitela

PP 044

BLOOD CONSUMPTION AND TRANSFUSION COMPLICATIONS IN PATIENTS WITH MYELODISPLASTIC SYNDROME TREATED WITH OUTPATIOTIC TRANSFUSIONS

Ratković Rangelov I, Petrovic A, Rajković D, Zdelar Stojanović Lj, Crvenkov T, Nikolic Lj
University Clinical Center of Serbia, Belgrade, Serbia

Introduction. Frequency of transfusion application in patients with myelodysplastic syndrome leads to improved quality of life, adverse reactions and complications.The application of erythrocyte and platelet transfusions is influenced by the timing of diagnosis, application of anti-heemoragiks, frequency of application of pulized/adhesive platelets, erythrocytes resuscitated with leukocytes and platelets/filtered erythrocytes.The goal is to analyze blood component consumption and monitor adverse reactions.
Methods. The values of hemoglobin, platelets, amount of applied erythrocytes and platelets of five patients (3 female and 2 male) were analyzed between 61-74 years between 01.07.2021.
Results. Patients received an average of 37.4 units (9215.2 mL) of resuscitated erythrocytes depleted by leukocytes and platelets and/or filtered erythrocytes annually, platelet transfusions 1016 ml (average per patient: 3 pulses, 6 affairs and 65 platelet concentrates from buffy coat.Average hemoglobin values are 73.2 g/L (range:44-87g/L), platelets are 83x10e9/L (range:4-107x10e9/L). Erythrocyte antigens have been identified: anti-Kell, anti-E, anti-c, papaya antibodies, unidentified antibodies. Anti-HLA antibodies class I, anti-HPA-2b, anti-HPA-5b and anti-GPIIb/IIIa antibodies were detected on platelets. Antibodies have been detected in three out of five patients (two people female and one male, all A blood groups).One respondent had a violent reaction during the application of erythrocyte transfusions in the form of hedgehosis, tremors, fever, hematoma and nodes along the upper and lower extremities. At least once, four out of five respondents experienced a mild transfusion reaction during or after application in the form of headaches, nausea or subfebrile temperature.
Conclusion. Monitoring of patients with myelodysplastic syndrome in the UKCS Ambulance Service found that restrictive approaches in transfusions reduce the risk of sensitization, antibody formation, frequency of unwanted transfusion reactions.In order to choose the most compatible blood for our patients who are transfusion-dependent, an extended phenotyping of erythrocytes needs to be done, and for platelet transfusions to apply typical platelet concentrations in accordance with the antibodies present.This would reduce the risk of antibodies emerging, reduce the cost of transfusion testing and care for transfusion reactions.
Keywords: Transfusion, Myelodysplastic Syndrome, Antibodies

PP 045

CLINICIANS USAGE OF BLOOD – COMPARATIVE STUDY

Nikoloska I, Apostolovska R, Useini S, MakarovskaBojadjieva T, Velkova E,Trajkova J, Ristovska E,Neceva V
National Institute for Transfusion Medicine, Skopje, RNMacedonia

Introduction. The rational use of blood is an imperative. New methods in surgery make some changes in the usage of blood.
Aim.The aim of this study is to compare the clinical usage of blood in Clinical center -Majka Tereza Skopje in the period of 2006-2013 and 2020-2021.
Material and methods. We analyzed pre-transfusion testing data for this retrospective study as well as the data from the blood distribution department.
Results. In 2006, 20 756 X-M (cross match) were made from which 11748 (56,6%) were used for surgical patients: 20% for Abdominal Surgery(AS); 19,5% for Orthopedic (O), 13% for Gynecology and obstetrician (GO), 12% for Urology (U), 11,5% for Intensive Care Unite(ICU), 10% for ThoracoVascular Surgery(TVS), 6,5%for Traumatology (T), 6% for Neurosurgery (NS), 1% for Pediatric Surgery(PdS) and 0,5% for Plastic Surgery (PS).
In 2013, 20 835 X-M were made from which 11 218 (53,8%) were used for surgical patients from which 10% for AS, 10,5% for O, 18% for GO, 12% for U, 16% for ICU, 7,5% for TVS, 13,5% for T, 8,5% for NS, 3% for PdS, 1% for PS. In 2020, 19769 X-M were made from which 9659 (53,6%) were used for surgical patients from which 8,3% for AS; 10,1% for O, 20,4% for GO; 11,3% for U, 16,6% for ICU, 6,5% for TVS, 8,8% for T, 6,0% for NS, 2,6% for PdS, 2,1% for PS and for Cardio Surgery (CS) 6,8%. The results for 2021 are similar to 2021 except for CS (13,4%).
Conclusion: From the results we can conclude that percentage of issued blood units for AS, O, U, ICU and T surgery is decreased (less invasive surgical methods were introduced), while for U, TVS and GO is increased. For the rest of the surgery departments, the usage of blood is similar for the analyzed period. The demand for blood in cardio surgery has increased due to the introduction of heart transplantation 2021.

Key words: blood, interaction,surgery

PP 045

PP 046

EVALUATION OF BLOOD USAGE IN THE SPECIAL HOSPITAL FOR GINEKOLOGY AND OBSTETRITION

Trajkova J, Nikoloska I, Ristovska E, Makarovska Bojadjieva T, Grubovik Rastvorcheva R
Institute for transfusion medicine, Skopje, RN Macedonia

Introduction: SpecialHospital,,Mother Teresa,, in Skopje is gynecological-obstetricians hospital were childbirths and surgery is performed. Immunohaematology investigations (pretransfusion testing and antibody screening) and blood products delivery is performed by the transfusion medicine department in the hospital.
Aim: The aim of this study is to show the range of blood tests which were performed and to evaluate blood usagein the period of three years (2019-2021).
Material and method: We analyzeddata from our information system for telemedicine through which validation of immunohaematology tests is performed and also from the donor/patient information system. All testing were performed manually using gel cards (Bio-Rad) which were interpretated and validated through the Banjo-reader.
Results.In 2019, 2020 and 2021, 1509 blood group typing(BGT) and 288 Indirect Antiglobulin Tests (IAT), 1929 BGT and 262 IAT and 1476 BGT and 226 IAT in2021 were performed respectively. In 2019, 2020 and 2021, 778, 807 and 603 blood groups (BG) and direct antiglobulin tests (DAT) for new borne were performed, respectively. In 2019, 240 cross-matched red blood cells (RBC), 67 fresh frozen plasma (FFP) units, 5 cryoprecipitate (CPR) doses and 2 platelet units (PU) were issued. In 2020, 278 cross-matched RBC,104 FFP, 12 CRP and 5 PU were issued. In2021, 379 cross-matched RBC and 213 FFP were issued. More than 60% of all of the blood components were intended for pregnant women to deal with postpartum bleeding complications.
Conclusion. According to the results, the usage of RBC and FFP is increased (0,5 % to 0, 8% from all used blood units), although the volume of immunohaematology pretransfusion testing did not show significant changes. Rational use of blood is an imperative and clinicians should reconsider the indications for blood transfusion.
Key word: blood,ginekology,interreactions

PP 046

PP 047

THE ASSOCIATION BETWEEN ABO BLOOD GROUP AND SARS-COV-2 INFECTION

Tashkovska M,[1]Georgievski K,[1]MakarovskaBojadjieva T,[2]Ristovska E,[2] Todorovski B[2], Aceska E[2], Neziri V[2]
[1]City General Hospital 8th September, Skopje, North Macedonia
[2] Institute of Transfusion Medicine, Faculty of Medicine, Ss. Cyril and Methodius University in Skopje, Republic of North Macedonia

Introduction: The association between ABO blood group and certain diseases is already known, so the pandemic caused by SARS-CoV-2 raised the question of whether a blood group can affect the susceptibility to infection. A number of studies have shown that individuals with blood type A are at greater risk, while those with blood type O are at lower risk of infection.
Aim: To investigate whether there is an association between ABO blood group and SARS-CoV-2 infection.
Material and method: In this retrospective case-control study, we evaluated 182 patients with confirmed COVID-19, hospitalized in the City General Hospital 8-th September from June to August, 2020. ABO blood group was determined by two methods, blood group plate test and microcolumn gel card test (BioRad). The distribution of ABO blood groups was analyzed in 2255 blood donors as a control group. A comparison of ABO blood group representation was made in patients with COVID-19 in relation to blood donors. Statistical analyzes were performed by p-value determination.
Results: The gender distribution of patients with COVID-19 was 109 (60%) men and 73 (40%) women, while among blood donors, 1849 (82%) were men, and 406 (18%) were women. The distribution of ABO blood groups in patients is 26.4%, 48.4%, 14.3%, 11.0%, while in blood donors it is 32.6%, 41.1%, 18.5% and 7.8% for O, A, B and AB respectively. These results show a significantly higher frequency of blood group A in patients with SARS-CoV-2 compared to the control group (p=0.05), and a lower frequency of blood group O, which is not statistically significant (p=0.08).
Conclusion: The obtained results indicate that individuals with A blood group are more susceptible to SARS-CoV-2 infection, while individuals with O blood group do not have a significantly lower risk of SARS-CoV-2 infection compared to other blood groups.
Keywords: ABO blood group, COVID-19, SARS-CoV-2

PP 047

PP 048

POTROŠNJA KRVI KOD HOSPITALIZOVANIH PACIJENTA USLED COVID-19 INFEKCIJE

Bakić Oršit D, Rajković D, Zdelar Stojanović Lj, Crvenkov T, Petrović B, Nikolić Lj.
Univerzitetski klinički centar Srbije, Beograd, Srbija

Uvod. Covid-19 je infektivna bolest izazvana virusom SARS-CoV-2,koja je zbog brzog širenja infekcije u celom svetu, proglašena je pandemija, u martu 2020. Pokazalo se da lečenje kovid infekcije zahteva multidisciplinarni pristup zbog različitih komorbiditeta pacijenata. Iako je COVID-19 infektivno obolenje, u izvesnim slučajevima u sklopu različitih terapija u lečenju infekcije potrebna je i transfuzija krvi i krvnih komponenata.
Cilj. Cilj ovog rada je da prikaže potrošnju krvi i krvnih komponenata kod pacijenata sa COVID-19 infekcijom.
Materijal i metode. Retrospektivnom analizom analizirana je potrošnja krvnih komponenti kod pacijenata hospitalizovanih u Kovid bolnici Batajnica u periodu od 01.01.-30.06.2022. U ovom period ukupno je bilo zbrinuto 4720 pacijenata starosne dobi od 30 do 90 godina.
Rezultati. Prema analiziranim podacima, u periodu od 6 meseci, od ukupno 4720 pacijenata 486 (10.3%) pacijenata je zahtevalo transfuziju krvnih komponenti. Njih 437 je dobilo 1224 jedinice eritrocita od toga 35 jedinica cele krvi. Pacijenti su transfundovani sa 1 do 5 jedinica krvi/eritrocita. Prosečno je primenjeno 3 (2.8) jedinice krvi po transfundovanom pacijentu što iznosi 0.26 jedinica po hospitalizovanom pacijentu. Kod 142 pacijenta ukupno je primenjeno 578 jedinica zamrznute sveže plazme (ZSP) što je prosečno 4 jedinice ZSP po transfundovanom pacijentu i 0.12 jedinica po hospitalizovanom pacijentu. Krioprecipitat je primenjen kod 29 pacijenata, ukupna količina je 376 jedinica što je 13 jedinica po transfundovanom pacijentu. Koncentratima trombocita je transfundovano 138 pacijenata sa 1578 jedinica koncentrata, prosečno 11.4 jedinice trombocita po transfundovanom pacijentu. Prosečna potrošnja po hospitalizovanom pacijentu je 0.33 jedinice trombocita.
Zaključak. Prema broju utrošenih jedinica krvnih komponenti rezultati našeg istraživanja ukazuju da je u ovom periodu epidemije bilo potrebno obezbediti eritrocite za ¼ (0.26) hospitalizovanih pacijenata, trombocite za 1/3 (0.33), a ZSP za svakog desetog (0.12) pacijenta.
Podaci ovog istraživanja mogu biti doprinos i smernica za planiranje i obezbeđivanje dovoljnih količina krvi i krvnih komponenti u okviru sličnih epidemija.
Ključne reči: Transfuzija, Epidemija, COVID

PP 048

BLOOD CONSUMPTION FOR HOSPITALIZED PATIENTS WITH COVID-19 INFECTION

Bakić Oršit D, Rajković D, Zdelar Stojanović Lj, Crvenkov T, Petrović B, Nikolić Lj.
Serbian University Clinical Centre, Belgrade, Serbia

Introduction. Covid-19 is an infectious disease caused by SARS-CoV-2 which was proclaimed a pandemic in March 2000 due to its fast spreading. Healing of Covid infection requires a multidisciplinary approach due to different patients' comorbidity. Although COVID-19 is an infectious disease, under some circumstances, as part of various therapies, transfusion of blood and blood components is also needed.
Goal. The goal of this paper is to give information about blood and blood component consumption for patients with COVID-19 infection.
Materials and Methods: Retrospective analysis of blood components used for COVID-19 patients in the Batajnica hospital in the period from 1st January 2002 to 30th June. During this period 4720 patients aged from 30 to 90 years were hospitalized in the Batajnica hospital.
Results: According to analyzed data, during six months, 486 (10.3%) patients out of 4720 needed blood component transfusions. Four hundred thirty seven (437) patients received 1224 erythrocyte units and 35 units of whole blood. Patients get 1 to 5 units of blood/erythrocytes. On average there were 3 (2.8) unit of blood per transfused patient, which is 0.26 units per hospitalized patient. Exactly 142 patients received 578 units of frozen fresh plasma (FFP) which is 4 units of FFP per transfused patient and 0.12 % per hospitalized patient. Also, 379 units of Cryoprecipitates are used for 29 patients, which is 13 units per transfused patient. 138 patients received 1578 units of thrombocyte concentrate which is an average of 11.4 per patient transfused patient and an average of 0.33 units per hospitalized patient.
Conclusion: Results of research analyses show that during the analyzed period erythrocytes were needed for ¼ (0.26) of patients, thrombocytes for 1/3 (0.33), and FFP for each tenth patient (0.12) patients. Results of this research may be contributions and guidelines for planning and providing sufficient blood and blood component in case of similar epidemic periods.
Keywords: Transfusion, Epidemy, COVID

PP 049

CLINICAL USE OF FRESH FROZEN PLASMA WITH INAPPROPRIATE BLOOD GROUP – CASE REPORT

B.Panev[1], V.Dejanova[2], M.Shorova[1], N.Jovanova[1], M.Ibraimi[2], R.Grubovik-Rastvorcev[2], E.Petkovic[2]
[1]*Regional Center for transfusion medicine Shtip*
[2]*Institute for transfusion medicine Skopje 2*

Background: Fresh frozen plasma corrects coagulopathy by replacing or supplying plasma proteins in patients who are deficient or have defective plasma proteins. A standard dose of 10 to 20 mL/kg (4 to 6 units in adults) will increase factor levels by approximately 20%. FFP is contraindicated when coagulopathy can be more effectively corrected with specific therapy and when blood volume can be adequately replaced by other volume expanders.The term Chemovigilance means "vigilance", i.e. monitoring all side effects of blood transfusion and their transmission from the donor to the recipient. The objectives of Hospital commissions is to define blood transfusion policies adapted to local clinical activities,to regularly evaluate the practice of transfusion of blood and blood products.
Objective: The significance of chemovigilance in clinical practice and the role of the Hospital Commission.
Material and methods: Report of non-compliance for issued blood product, by the Institute for Transfusion Medicine - Skopje, i.e. issued SSP with an inappropriate blood group to a patient located at the Clinic for Orthopedic Diseases.
Case report: A 79-year-old female patient, hospitalized at the Clinic for Orthopedic Diseases due to a hip fracture. On 20.10.2021, the Clinic for Orthopedic Diseases sent a request for 2 units (A+) of fresh frozen plasma. On the same day, ITM - Skopje issued 2 units of SSP with blood group O +, at the clinic for orthopedic diseases an application was made for one unit of SSP with barcode 1081301 (out of the two required), and the unapplied SSP with barcode 1081520 was returned to ITM with all the documentation. After the SSP component was returned to ITM - Skopje, a correction was made with a new requirement and 2 new units of SSP with the appropriate blood group (A +) were issued. A consultation was made with the Department of Immunohaematology and it was requested to send a blood sample from the patient for screening of anti-erythrocyte antibodies and possible post-transfusion hemolytic reaction.
Results: From the above screening is done: Patient's blood group, Rhfactor, Phenotyping, Indirect antiglobulin test and Direct antiglobulin test. Screening results for anti-erythrocyte antibodies and the possibility of a post-transfusion hemolytic reaction are negative.
Conclusion: A human error was confirmed by the Hospital Commission when issuing and applying the blood component SSP. In order to avoid unwanted events, greater vigilance and vigilance of ITM employees is recommended when dispensing the blood component by checking the data (generals of the patient, blood group) and checking the data from the label of the blood component (blood group, bar code) . Greater vigilance of the nurse when receiving the supplied blood component and a mandatory check of the patient's identity and blood group, especially immediately before its application. Audit systems (control) for the clinical use of components strengthen the efficiency and safety of transfusion practice.

Keywords: chemovigilance, post-transfusion hemolytic reaction.

PP 049

PP 050

NACIONALNI DAVALAC- OD ZAHTEVA ZA PRETRAŽIVANJE REGISTRA DO PRIKUPLJANJA MATIČNIH ĆELIJA HEMATOPOEZE

Blagojević G., Lako-Šoškić B., Jovanović B., Kačaki N., Miladinović Ž, Andrić Z.
Institut za transfuziju krvi Srbije

Uvod: Baza Registra davalaca matičnih ćelija hematopoeze (MĆH) Srbije se pretražuje na osnovu zahteva za pretraživanje, nacionalnih i internacionalnih transplantacionih centara (TC). Nakon potvrđene HLA tipizacije davaoca, TC pokreću proceduru za prikupljanje jedinica MĆH.
Cilj: Prikazati broj prikupljenih jedinica MĆH u odnosu na broj poslatih zahteva za pretraživanje i potvrdu tipizacije od nacionalnog davaoca.
Materijal i metode: Retrospektivnom analizom su obuhvaćeni zahtevi za pretraživanje, dobijanje uzoraka za potvrdnu HLA tipizaciju i prikupljanje MĆH u periodu od 01.01.2009. do 01.09.2022. Kao izvor podataka korišćeni su formulari za pretraživanje Registra, slanje uzoraka za potvrdnu HLA tipizaciju i prikupljanje MĆH i protokoli za pretraživanje. Potvrdna HLA tipizacija je rađena u nadležnoj laboratoriji TC-a. Ukoliko je zahtev upućen od strane inostranog TC-a, uzorak periferne krvi uzet na K2-EDTA za potvrdnu HLA tipizaciju se dostavljao inostranom centru. Za bolesnike koji su lečeni u Srbiji, potvrdna HLA tipizacija je rađena na Odeljenju za tipizaciju tkiva Instituta za transfuziju krvi Srbije. Ukoliko je potvrđena HLA tipizacija, davalac je ostajao rezervisan za datog bolesnika, a TC je pokretao proceduru za dobijanje MĆH.
Rezultati: Za 226 inostranih bolesnika je dostavljen zahtev za pretraživanje Registra MĆH Srbije.Uzorak za potvrdnu HLA tipizaciju je tražen od 21 nacionalnog davoca, od toga je 10 dalo uzorak. Nakon potvrđene HLA tipizacije, 5 davalaca je rezervisano za inostrane bolesnike, a dva su donirala MĆH. Od jednog su prikupljeni i limfociti za donorsku infuziju limfocita. Za 410 bolesnika koji su lečeni u Srbiji je dostavljen zahtev za pretraživanje. Uzorak za potvrdnu HLA tipizaciju je tražen od 33, od toga je 15 davalaca dalo uzorak. Nakon potvrđene HLA tipizacije, 10 davalaca je rezervisano za bolesnike, koji su lečeni u Srbiji a 4 su donirala MĆH. Zaključak: Od ukupnog broja poslatih zahteva za pretraživanje Registra, 1% je finalizovan prikupljanjem jedinica MĆH.
Ključne reči: nacionalni davalac, matične ćelije hematopoeze, HLA tipizacija

PP 050

NATIONAL DONOR - FROM PRELIMINARY SEARCH REQUESTS TO THE COLLECTION OF STEM CELLS

Blagojević G., Lako-Šoškić B., Jovanović B., Kačaki N., Miladinović Ž, Andrić Z.
Blood Transfusion Institute of Serbia

Introduction: Searching of Serbian Bone Marrow Donor Registry (SBMDR) database is based on requests from national and international Transplant Centres (TC). After the confirmed HLA typing of the donor, TC starts the procedure for stem cells (SC) collection.
The aim: Represent the number of collected SC in relation to the number of received search requests and requests for confirmatory typing of the national donor.
Material and methods: The retrospective analysis included requests for searching, obtaining samples for confirmatory HLA typing and collecting SC in the period from 01.01.2009 to 01.09.2022. As a data sources, various documents were used, such as Preliminary Search Forms, Requests for Confirmatory Typing (CT) and SC Collections, and Searching Protocols. CT was done in a competent laboratory at TC. For international requests, blood samples taken on K2-EDTA for CT were delivered to the international TC. For patients who were treated in Serbia, CT was done at Tissue Typing Department in Blood Transfusion Institute of Serbia. If the HLA typing was confirmed, the donor remained reserved for the given patient, and the TC started the procedure for obtaining SC. Results: The search requests SBMDR were submitted for 226 international patients. Blood samples for CT were requested from 21 national donors, of which 10 provided blood samples. After CT were confirmed, 5 donors had been reserved for international patients, and 2 of them donated stem cells. Lymphocytes were collected from one donor for donor lymphocyte infusion.
The search requests were sent for 410 patients who were treated in Serbia. CT Requests were asked from 33 donors, and 15 of them provided blood samples. After HLA Typing Results were confirmed, 10 donors had been reserved for patients, and 4 of them donated SC. Conclusion: Approximately 1% of the total number of searching requests were finalized by collecting SC.
Keywords: National Donor, Hematopoietic Stem Cells, HLA Typing

PP 051

THE IMPORTANCE OF PRETRANSPLANT SCREENING FOR HLA ANTIBODIES OF HEART TRANSPLANT RECIPIENTS

Dukić T., Dmitrović J., Lako Šoškić B., Korać N., Andrić Z.
Blood Transfusion Institute of Serbia, Tissue Typing Department

Introduction: The presence of donor specific antibodies (DSA) increases the risk of poor outcome after heart transplants, including development of antibody-mediated rejection (AMR), graft failure, cardiac allograft vasculopathy and mortality. Pretransplant screening is performed to all patients for heart transplantation in Tissue Typing Copmaprtment in the Institute for blood Transfusion of Serbia.
The aim: Aim of this study was to present the results of HLA antibody screening of patients preparing for heart transplantation in Serbia from 2018. to 2021.
Material and methods: Total of 305 sera samples of heart transplant candidates were tested by complement dependent cytotoxicity (CDC) test and Luminex based assays. Patients sera were tested as native, diluted and DTT treated to determine IgG, IgM antibodies and prozone effect. CDC was performed using both commercial plates (One lambda, West Hills, California) and homemade panel of lymphocytes. Luminex method was performed using LIFECODES LifeScreen Deluxe kit and LIFECODES LSA Class I and Class II (Immucor, Stamford, CT, USA). Results were analyzed by Software Match-IT version 1.3.
Results: Out of the total number of tested, 39 (12,8%) had positive screening results. Out of positive results, three sera (0,98%) were positive only by CDC method, which showed the presence of IgM antibodies. With both methods, with PRA range of 5-65% and MFI(Mean Fluorescence Intensity) > 8000 were positive 6/39 (1.96%). Only by Luminex method with MFI < 6000, were positive 30/39. Out of total number of Luminex positive patients, 15 showed positivity for class I, 19 for class II, and 2 patients were positive for both classes. DSA IgG HLA antibodies detected by CDC are considered as a contraindication for transplantation whereas DSA detected only by Luminex method pose a relative risk depending on MFI value.
Conclusion:Pretransplant testing of HLA antibodies in heart transplant candidates sera gives the opportunity to better assess the risk for transplantation and to make the right choice when potential donor appears.
Key words: Anti-HLA antibodies, Heart transplantation, Luminex method

PP 051

PP 052

EFFECT OF MELATONIN ON KIDNEYS IN RATS WITH ENDOTOXIN-INDUCED SEPSIS

Sokolović D[1], Stanojković Z[1], Lazarević M[2]
Blood Transfusion Institute Niš
Clinic for Cardiovascular and Transplant Surgery,
University Clinical Centre of Niš

Introduction: Sepsis is a syndrome that leads to dysfunction of various organs. An animal model that mimics sepsis uses lipopolysaccharide (LPS), an endotoxin recognized as the most potent bacterial mediator of sepsis. Melatonin is a hormone produced in the pineal gland. Melatonin plays an important role in the aging process, stimulation of immune functions and prevention of kidney failure. These effects of melatonin are associated with the removal of various toxic reactants based on oxygen and nitrogen and reducing the intensity of oxidative stress.
Objective: The objective of this study was to determine the effect of melatonin on kidney tissue in rats with endotoxin-induced sepsis.
Material and methods: This study aimed to evaluate the potential of melatonin in the prevention of LPS-induced kidney damage in Wistar rats by determining serum and tissue biochemical markers reflecting kidney function (urea and creatinine levels), as well as a panel of biomarkers related to oxidative stress (Xanthine oxidase - XO enzyme activity, as well as thiobarbituric acid reactive substances - TBARS and protein carbonyl content - PCC level).
Results: Pre-treatment with melatonin prevented LPS-induced increase in kidney serum markers (urea and creatinine levels), as well as decrease in antioxidant capacity of kidney tissue.
Conclusion: In rats with LPS-induced sepsis, melatonin was shown to play a significant role in alleviating oxidative stress in the kidney tissue. This research was funded by the Scientific funding agency of the Republic of Serbia (Grant No. 7750154, Acronym NPATPETTMPCB).
Key words: Melatonin, Sepsis, Oxidative stress

PP 052

PP 053

DONOR THROMBOCYTAPHERESIS IN THE INSTITUTE FOR TRANSFUSION MEDICINE OF THE REPUBLIKA SRPSKA

Ćejić V,Radojković-Sredić D,Cimeša-Čeko S,Guzijan G, Topić-Popržen A, Pavlović S,Udovičić N.
The Institute for Transfusion Medicine of the Republika Srpska, Banja Luka

INTRODUCTION: With the procedure of donor thrombocytapheresis, a healthy person donates blood through an automatic blood cell separator, which is programmed to separate and collect the desired number of platelets while simultaneously returning all other blood components.
OBJECTIVE: The objective is to present data on collected apheresis platelets at the Institute for Transfusion Medicine of the Republika Srpska in the period from February 2021 to August 2022.
MATERIALS AND METHODS: Separation of apheresis platelets was performed on the TRIMA ACCEL 7 automatic blood cell separator, using sets (LRS, Platelet/Plasma) for single use and collection of leukoreduced platelets.
RESULTS: In the analysed period, 108 donor thrombocytapheresis were performed from 46 voluntary donors, in which the platelet concentrates obtained had a yield of 3-4.5x 1011. The apheresis procedure was performed once in 20 (43.48%) donors, more than once in 26 (56.52%) donors, during the legally prescribed period of every 15 days. Out of the total number of performed apheresis, during 94 (87.03%) procedures two units of platelets were separated, and in 14 (12.9%) one unit. The average age of the donors was 36 years, the average haematocrit value before the procedure was 44.02%, after the procedure it was 42.68%, average hemoglobin value was 150.81 g/L, platelets before the procedure 239.15x109/L, after the procedure 190 ,74x109/L, processed volume was 2522.4 ml, used AC 273.12 ml. The procedure lasted for 43 minutes in average, with an average of 392.3 ml separated of the final product with leukocytes below 1x106. We pathogenically inactivated 9 (8.33%) platelet concentrates collected in nutrient solution (SSP+) with a volume of over 300ml on the INT100 INTERCEPT Illuminator.
CONCLUSION: Platelet concentrates obtained by the procedure of donor thrombocytapheresis meet all quality requirements in accordance with the latest recommendations from the Council of Europe. Considering the great clinical importance of apheresis platelets, our plan is to increase the number of apheresis procedures and expand our existing register of voluntary platelet donors.
Key words: thrombocytapheresis, voluntary donor, separator

PP 053

DONORSKE TROMBOCITAFEREZE U ZAVODU ZA TRANSFUZIJSKU MEDICINU REPUBLIKE SRPSKE

Ćejić V, Radojković-Sredić D, Cimeša-Čeko S, Guzijan G, Topić-Popržen A, Pavlović S,Udovičić N.
Zavod za Transfuzijsku Medicinu Republike Srpske, Banja Luka

UVOD: Postupkom donorske trombocitafereze, zdrava osoba daje krv pomoću automatskog aparata–separatora krvnih ćelija, koji je programiran da izdvoji i prikupi željeni broj trombocita uz istovremeno vraćanje svih ostalih sastojaka krvi.
CILJ: Prikazati podatke o prikupljenim afereznim trombocitima u Zavodu za transfuzijsku medicinu Republike Srpske u periodu od februara 2021. godine do avgusta 2022.godine.
MATERIJAL I METODE: Izdvajanja afereznih trombocita su rađena na automatskom separatoru krvnih ćelija TRIMA ACCEL 7 pri čemu su korišćeni setovi (LRS, Platelet/Plasma) za jednokratnu upotrebu i prikupljanje leukoredukovanih trombocita.
REZULTATI: U navedenom periodu urađeno je 108 donorskih trombocitafereza od 46 dobrovoljnih davalaca, kod kojih su dobijeni koncentrati trombocita imali prinos od 3-4,5x 1011. Aferezna procedura je urađena jedanput kod 20 (43,48%) davalaca, više puta kod 26 (56,52%) davalaca u zakonski propisanom periodu na svakih 15 dana. Od ukupnog broja urađenih afereza, tokom 94 (87,03%) procedure su izdvojene dvije jedinice, a kod 14 (12,9%) jedna jedinica trombocita. Prosječna starost davalaca je bila 36 godina, prosječan hematokrit prije procedure je bio 44,02%, nakon procedure je iznosio 42,68%, prosječan hemoglobin 150,81 g/L, trombociti prije izvođenja procedure 239,15x109/L, nakon procedure 190,74x109/L, procesuirani volumen 2522,4 ml, utrošeni AC 273,12 ml. Procedura je trajala prosječno 43 min uz izdvojeno prosječno 392,3 ml konačnog proizvoda sa leukocitima ispod u hranjivom rastvoru (SSP+) sa volumenom preko 300ml na aparatu INT100 INTERCEPT Illuminator.
ZAKLJUČAK: Dobijeni koncentrati trombocita postupkom donorske trombocitafereze ispunjavaju sve zahtjeve kvaliteta u skladu sa najnovijim preporukama Savjeta Evrope. S obirom na veliki klinički značaj afereznih trombocita u planu nam je da povećamo broj afereznih procedura i proširimo naš već postojeći registar dobrovoljnih davalaca trombocita.
Ključne riječi: trombocitafereza, dobrovoljni davalac, separator.

PP 054

PREGNANCY-RELATED THROMBOSIS-CASE REPORT

Todorovski B,Grubovic Rastvorceva R, Petkovikj E, Dejanova Ilijevska V, Makarovska Bojadzieva T, Velkova E, Todorovska E,Useini S, Ristovska E, Petkovska A.
Institute for Transfusion Medicine of the Republic of Macedonia-Skopje

Introduction: Women are at increased risk of thromboembolism during pregnancy and the postpartum period.
Objective: Of this case report is to present a pregnant patient with thrombotic complications during her pregnancy.
Materials and methods: The haemostatic parameters, and complete blood count were measured at the laboratory in the Department for haemostatic and thrombotic disorders at the Institute for Transfusion Medicine of Republic North Macedonia-Skopje. Doppler ultrasound was performed in a private hospital.
Case report and results: Our case study is a young pregnant woman, with a medical history of varicose veins. This was her first regular pregnancy, and she had no history of thrombotic complications in the past. During the first trimester, she received iron supplementation and hormone therapy.Medical compressive stockings were also prescribed for the varicose vein in her right leg. In 30thgestational week, she noticed redness, swelling and pain in her right leg. The haemostatic parameters showed hypercoagulability and 4-fold increased D-dimer levels.Ultrasound doppler imaging was performed and it showed a thrombotic formation in the right great saphenous vein. After that she received therapeutic anticoagulation with low molecular weight heparin (LMWH) (1mg/kg s.c. twice daily), that lasted until planned vaginal delievery (discountinued 24 hours before delivery). Anti-Xa assay showed optimal therapeutic range (0.8 IU/mL). After the delivery, and during the lactaton period anticoagulation with prophylactic dose of LMWH continued (enoxaparin 40 mg/daily). Later, oral anticoagulation(warfarin) followed in the next few months, until another doppler ultrasound showed complete recanalization and resolution of the thrombotic process.
Conclusion: During pregnancy and delivery, risk of thromboembolic complications is increased, due to multiple factors. Prevention in pregnant and postpartum women is crucial, and anticoagulation with heparin should be managed, which is the drug of choice. Treatment of thrombosis should be continued for at least six weeks after birth.
Keywords: Pregnancy, Thrombosis, Heparin.

PP 054

PP 055

THROMBOPHILIC MUTATIONS IN WOMEN WITH IN VITRO FERTILIZATION FAILURE

Petkovikj E, Grubovic R, Hristova A, Petkovska V, Neceva V, Useini S.
Institute for Transfusion medicine Skopje of Republic of North Macedonia

Background: In vitro fertilization (IVF) failure is multifactorial condition and hereditary thrombophilia as hypercoagulable state has been mentioned as one of them. There are limited data on the association between thrombophilia with IVF failure in Macedonian population.
The aim of the study was to analyse the representation of thrombophilic mutations in Macedonian women with IVF failure and healthy controls.
Methods: In this case-control study we evaluated 70 women, divided in two groups. The case group included 34 women with history of women with three or more failed IVF cycles. The control group included 36 women, age matched, who gave birth to at least one healthy baby without obstetric complications. All women included in the study have signed the informed consent approved by the Ethical Committee of the Medical faculty in Skopje. Presence of gene mutations for prothrombin G20210A, factor V Leiden G1691A (FVL) and methylentetrahydrofolate reductase C677T (MTHFR) was examined in both groups.
Results: Prothrombin G20210A heterozygous was found in 5.9% of the case group vs. 5.5% in the control group; FVL heterozygous was found in 20.6% of the case group vs. 2.8% in the control group with a significant statistical difference (p=0.0194); MTHFR homozygous was found in 20.6% of the case group vs. 5.5% in the control group. Combined thrombophilic mutations were present in 17.6% in the case group and 5.6% in the control group.
Conclusion: Hereditary thrombophilia is more prevalent in women with IVF failure than the control group. The presence of at least one thrombophilic mutation especially FVL heterozygous and MTHFR homozygous may have significant role in IVF failure.
Keywords: thrombophilia, factor V Leiden, MTHFR, prothrombin.

PP 055

PP 056

MEASURING ERYTHROCYTE DEFORMABILITY AND HETEROGENEITY USING EKTACYTOMETRY COUPLED TO FLOW CYTOMETRY

Drvenica I[1], Trivanović D[1], Radmilović M[2], Vučetić D[3,4], Krmpot A[2], Ilić V [1]
Institute for Medical Research, National Institute of Republic of Serbia, University of Belgrade, Belgrade, Serbia
Institute for Physics, Belgrade, National Institute of Republic of Serbia, University of Belgrade, Belgrade, Serbia
Institute for Transfusiology and Haemobiology, Military Medical Academy, Belgrade, Serbia
Faculty of Medicine, Military Medical Academy, University of Defence, Belgrade, Serbia

Introduction: Decreased deformability of erythrocytes is a characteristic of several disorders (sickle cell anaemia, Plasmodium infection, and iron deficiency, etc.),and is conveniently measured by ektacytometry. However, ektacytometry measures deformability of entire erythrocyte populations and does not provide information on altered deformability of individual erythrocytes or affected subpopulations, induced by constant oxidative stress, physical stress,metabolic depletion, and loss of ion gradients during their 120 days life span. We present an approach based on ektacytometry coupled to flow cytometry analysis to monitor the deformability of subpopulations of erythrocytes.
Materials and Methods:We have examined the effects of in vitro changes of osmotic gradient (from 155 mM to 93 mM phosphate buffer) and treatment by oxidative agent (0.5 mM and 0.75 mM terc-bytilhydroperoxide (TBPH)) on deformability and shape of human erythrocyte isolated from healthy male donors, using RheoScan D 300 (RheoMeditech. Inc., Korea) and BD FACSCalibur flow cytometer (Becton Dickinson, USA).
Results:Ektacytometry revealed a decrease in erythrocytes deformability by changes in osmolality or treatment with TBPHper se. The erythrocytes underwent both treatments could not be analysed due to their lysis by applied shear stress in the ektacytometer. However, the samples of an equal population of normal erythrocytes and erythrocytes rigidified by 0.5 mM TBPH (slight rigidization) showed elongation indices in the physiological range, i.e., the effect of the treatments was annulled. The same result was obtained by flow cytometry. On the other hand, altered population of oxidized cells by 0.5 mM TBPH was detected in hypoosmotic 93 mM buffer, based on their forward scatter (FSC), and side scatter (SSC) parameters.
Conclusion: To detect subtle changes in the erythrocyte's subpopulations mechanobiology alternative techniques are needed. They should provide the measurement of deformability in pathological conditions, and in healthy people exposed to physical or/and environmental stress, but also in stored erythrocytes.
Key words: Erythrocyte rigidity; Oxidative stress; Osmotic fragility.
Acknowledgement: This study was funded by Science Fund of Republic of Serbia through HEMMAGINERO project (HEMOGLOBIN-BASED SPECTROSCOPY AND NONLINEAR IMAGING OF ERYTHROCYTES AND THEIR MEMBRANES AS EMERGING DIAGNOSTIC TOOL, No 6066079)

PP 056

PP 057

ODREĐIVANJE D-DIMERA U KLINIČKOJ PRAKSI

Šurbevski M[1], Šurbevska Boneva B[2], Taškovska M[1], Stojčeva D[1]
[1] JZU GOB „8. Septembar"; Skoplje
[2] JZU Institut za plućne bolesti i tuberkulozu Skoplje

Uvod: D-dimeri (D-d) su proizvodi razgradnje fibrina (FDP), sa molekulskom težinom od oko 180 kDa. Poluvreme raspadanja D-d je oko 8 sati, a eliminacija se odvija preko bubrega i retikulo-endotelnog sistema (RES).
Cilj rada: Određivanje koncentracije D-d kod ambulantnih pacijenata sa različitim kliničkim simptomima.
Materijal i metode: Analizirali smo koncentraciju D-d kod slučajno odabranih pacijenata (146 žena i 179 muškaraca). Pol i starost pacijenata su takođe randomizirani.
Određivanje D-d u krvi obavljeno je u našoj laboratoriji na aparatu BCS XP System, manual version 1,3, 2008/9. Kao kontrolnu grupu koristili smo krv od 47 dobrovoljnih davalaca krvi. U kontrolnoj grupi, 43 ispitanika nije imalo povišene vrednosti D-d iznad praga od (550 mg/L FEU). Kod 4 od njih vrednosti su bile iznad granične vrednosti, a najviši nivo je 1,13 mg/L FEU .
Rezultati: Od ukupno 325 pregledanih uzoraka, kod 146 pacijenata dokazali smo povećanu koncentraciju D-d u krvi (vrednosti veće od 1000 mg/L FEU). Od toga, nivo D-d od 1,0 do 5,0 mg/L FEU je dokazan kod 107, a D-d iznad 5,0 mg/L FEU kod 39 pregledanih pacijenata.
Koncentraciju D-d bila je povećana kod pacijenata sa različitim dijagnozama i kliničkom slikom: kongestivna srčana insuficijencija (8), hronična opstruktivna plućna bolest i upala pluća (22), cerebralni infarkt ili krvarenje (18), abdominalna oboljenja i karlični bol (45) maligne bolesti (9), prelom kuka (5), angina pektoris i srčana insuficijencija (18), hirurške intervencije i druga oboljenja (21).
Pronašli smo veoma visoku vrednost D-d (preko 5,0 mg/L FEU) kod 39 pacijenata. Veći broj njih sa sumnjom na akutni inflamatorni proces, povredu ili malignu bolest.
Zaključak: Povećana vrednost D-d u krvi može se dokazati kod sistemskih oboljenja vezivnog tkiva, infekcija, reumatskih oboljenja, postojanja hematoma, velikih hirurških intervencija, malignih oboljenja. Povećana koncentracija D-d nije specifičan parametar za određeno kliničko stanje ili dijagnozu.
Ključne reči: D-dimeri, dijagnoza, koncentracija

PP 057

DETERMINATION OF D-DIMER IN CLINICAL PRACTICE

Shurbevski M[1], Shurbevska Boneva B[2], Tashkovska M[1], Stojcheva D[1]
[1] PHI GOB "8th of September"; Skopje
[2] PHI Institute for Lung Diseases and Tuberculosis Skopje

Introduction: D-dimers (D-d) are fibrin degradation products (FDP), with a molecular weight of about 180 kDa. Half-life for decomposition of D-d is about 8 hours, and the elimination takes place through the kidneys and the reticulo-endothelial system (RES).
Objective: To determine D-d concentrations in patients with different clinical symptoms.
Material and methods: We analyzed the level of D-d in randomly selected patients (146 women and 179 men). The gender and age of the patients were also randomized. We determined the D-d in blood, in our laboratory, using BCS XP System device manual version 1.3, 2008/9. As a control group, we used blood from 47 voluntary blood donors. In the control group, 43 subjects did not have elevated D-d values above the threshold (550 mg/L FEU). In 4 of them, the values were above the Cut-off, and the highest level is 1.13 mg/L FEU.
Results: From the total 325 examined samples, we detected increased level of D-d in blood (values higher than 1000 mg/L FEU) in 146 patients. Of these, 107 had D-d level of 1.0 to 5.0 mg/L FEU , and 39 had D-d above 5.0 mg/L FEU.
We detected increased concentration of D-d in patients with different diagnoses and clinical picture: congestive heart failure (8), chronic obstructive pulmonary disease and pneumonia (22), cerebral infarction or bleeding (18), abdominal diseases and pelvic pain (45) malignant diseases (9), hip fracture (5), angina pectoris and heart failure (18), surgical interventions and other illnesses (21). 39 patients had very high D-d value (over 5.0 mg/L FEU). Most of them were suspect of acute inflammatory process, injury, or malignant disease.
Conclusion: Increased value of D-d in the blood can be detected in systemic diseases of the connective tissue, infections, rheumatic diseases, existence of hematoma, major surgical interventions, malignant diseases. The increased concentration of D-d is not a specific parameter for a particular clinical condition or diagnosis.
Key words: D-dimers, diagnosis, concentration

PP 058

PREVALENCA MTHFR C677T POLIMORFIZMA KOD PACIJENATA UPUĆENIH NA TESTIRANJE U ZAVOD ZA TRANSFUZIJSKU MEDICINU FBIH: PERIOD JANUAR 2021-MART 2022

Sićanica S., Ahmetović-Karić G., Ćatović-Baralija E., Ljuca A., Mehić K.
Zavod za transfuzijsku medicinu FBiH, Sarajevo, BiH

Ključne riječi: MTHFR, C677T, prevalenca

Uvod:
Metilentetrahidrofolat reduktaza (MTHFR) je ključni enzim u metabolizmu folata i homocisteina (Hcy), koji katalizira demetilaciju 5,10-metilentetrahidrofolat u 5-metilentetrahidrofolat. Gen za MTHFR se nalazi na 1.hromozomu (lokus 1p36.3). Sadrži 11 egzona i 10 introna. Najčešći polimorfizam, koji može dovesti do smanjene aktivnosti enzima, je zamjena citozina (C) timinom (T) na položaju 677 u egzonu 4, što rezultira zamjenom aminokiseline alanina u valin.
Polimorfizam u genu za MTHFR, C677T, je čest u populacijama, a prevalencija se razlikuje zavisno o etničkom porijeklu i geografskom položaju populacije. Česta je u evropskoj populaciji, gdje učestalost homozigota za alel T iznosi 10-12%, dok je vrlo rijetko zastupljena u Afroamerikanaca (1-2%).

Materijal i Metode:
Istraživanje je provedeno u Zavoda za transfuzijsku medicinu FBiH, u periodu januar 2021 - mart 2022. godine. Obrađeno je 217 pacijenata. Uzorci su uzeti iz periferne krvi u epruvete sa EDTA. Za izolaciju DNK korišten je komercijalni kit FASSST DNA Releaser (Clonit). Genotipizacija mutacije MTHFR C677T je rađena na Cepheid Real-Time PCR. Korišten je komercijalni kit Duplica Real Time MTHFR C677T kit (Clonit).

Rezultati:
Starosna dob pacijenata kretala se od 2 do 74. Medijan dobi za skupinu iznosio je 35. U ispitivanom uzorku od 217 pacijenata utvrđeno je: 91 (33,58%) CC genotip, 95 (35,1%) CT genotip i 31 (11,44%) TT genotip. Utvrđeno je da je 126 (58%) ispitanika nosioc polimorfizma MTHFR C677T. Distribucija C alela u ispitivanoj grupi je iznosila 277 (63,82%), a T alela 157 (36,18%). Ispitivana populacija se nalazi u Hardy-Weinberg ravnoteži (p=0,44).

Diskusija i zaključak:
Više od 45% svjetske populacije su nosioci MTHFR C677T polimorfizama. Frekvenca homozigotnih nosioca u Evropskoj populaciji iznosi 5-15%. Podaci studije o MTHFR C677T polimorfizmu kod zdrave Bosansko-Hercegovače populacije (Amela K. at all) pokazuje da je jedan od oblika MTHFR 677 mutacije zastupljen kod 55,55% ispitivane grupe, što je u skladu sa rezultatima ovog istraživanja.

PP 058

PREVALENCE OF MTHFR C677T POLYMORPHISM IN PATIENTS WHO WERE TESTED IN THE INSTITUTE FOR BLOOD TRANSFUSION MEDICINE FBIH: PERIOD JANUARY 2021-MARCH 2022

Sićanica S., Ahmetović-Karić G., Ćatović-Baralija E., Ljuca A., Mehić K.
Institute for Blood Transfusion Medicine of FBiH, Sarajevo, BiH

Keywords: MTHFR, C677T, prevalence

Introduction: Methylenetetrahydrofolate reductase (MTHFR) is a key enzyme of folate and homocystein metabolisms that catalyzes demetilation of 5,10-methylenetetrahydrofolate to 5-methylenetetrahydrofolate. The MTHFR gene is located on chromosome 1 (locus 1p36.3). It contains 11 exons and 10 introns. The most common polymorphism, which can lead to reduced enzyme activity, is the substitution of cytosine (C) with thymine (T) at position 677 in exon 4, which leads to the substitution of the amino acid alanine for valine.
The polymorphism in the MTHFR gene, C677T, is common in populations and the prevalence varies depending on the ethnic groups and geographic distribution of the population. It is common in the European population, where the frequency of homozygotes for the T allele is 10-12% and on the other side it is very rare in African Americans (1-2%).

Material and Methods: The research was conducted in the Institute for Blood Transfusion Medicine of FBiH, in the period January 2021 - March 2022. A total of 217 patients were treated. Samples were taken from peripheral blood in tubes with EDTA. The commercial kit FASSST DNA Releaser (Clonit) was used for DNA isolation. Genotyping of the MTHFR C677T mutation by the real-time PCR method was performed on the Cepheid Real-Time PCR with the commercial kit Duplica Real Time MTHFR C677T kit (Clonit).
Results: The age of the patients ranged from 2 to 74. The median age for the group was 35. In the examined sample of 217 patients we finde: 91 (33.58%) CC genotype, 95 (35.1%) CT genotype and 31 (11.44%) TT genotype. It was determined that 126 (58%) subjects were carriers of the MTHFR C677T polymorphism. The distribution of the C allele in the examined group was 277 (63.82%), and the T allele 157 (36.18%). The studied population is in Hardy-Weinberg equilibrium (p=0.44).
Discussion and conclusion: More than 45% of the world's population are carriers of MTHFR C677T polymorphisms. The frequency of homozygous carriers in the European population ranges between 5-15%. Data from the study published on the MTHFR C677T polymorphism in the healthy population of Bosnia and Herzegovina (Amela K. at all) shows that one form of the MTHFR 677 mutation is present in 55.55% of the examined group, which is in accordance with the results of this study.

PP 059

INDICATIONS FOR SCREENING HEMOSTASIS AND D-DIMER TEST IN PREGNANCY

Tashkovska M[1] Georgievski K[1,] Shurbevski M[1], Rajcevski R[1], Makarovska Bojadjieva T[1],Velkova E[2],Ristovska E[2],Petkovik E[2], Dejanova Ilijevska V,2 Todorovski B[2], Aceska E[2] , Ismaili Lj[2]
[1] *City General Hospital 8th September, Skopje, North Macedonia*
[2] *Institute of Transfusion Medicine, Faculty of Medicine, Ss. Cyril and Methodius University in Skopje, Republic of North Macedonia*

Introduction. Normal pregnancy is associated with alterations of the hemostatic system toward a hypercoagulable state which indicate increased thrombin activity and altered fibrinolysis throughout pregnancy. Because of this the usefulness of screening hemostasis and D-dimer testing in pregnant women even with gestation age adapted reference ranges is questionable.
Aim. To analyze indications for ordering screening hemostasis, D-dimer test and thromboprophylaxis in pregnancy.
Material and method. Platelet count, screening hemostasis PT, aPTT, TT and D-dimer test were performed in 101 pregnant women using blood counter Medonic and coagulometer BCS XP System-Siemens respectively. According to the indications for ordering coagulation testing pregnant women were divided in four groups.
Results. The first group included 10 (9.9%) women with history of thrombotic or hemorrhagic disorder, from which 3 women were with varicose veins and 7 with previously diagnosed hemorrhagic disorder. The second group included 41 (40.6%) women with history of recurrent abortions. The third group included 14 (13.9%) women with pregnancy complications from which 6 with placental abnormalities, 2 with uterine myoma, 3 with cerclage, 3 with decreased amniotic fluid. The fourth group included 36 (35.6%) women without history of thrombo-hemorrhagic disorder, obstetric or pregnancy complications.
Results were interpreted according to the referent values: Platelet count (150-450 x 109/L), PT (10-14s), aPTT (28-38s), TT (16-24s) and D-dimer (<500 ng/mL). In total, the mean PT, aPTT, TT, D-dimer and platelet count were 10.6s, 27.2s,16.1s, 409.9 (148-1960) ng/mL and 238 x 109/L in the first trimester, 10.5s, 25.2s, 15.9s, 1191.6 (148-2960) ng/mL and 244 x 109/L in the second trimester and 10.3s, 25.0s, 15.9s, 1670 (762-3817) ng/mL and 243 x 109/L in the third trimester. There was no significant difference in the coagulation test results according to the patient groups. In 60 (59.4%) of the pregnant women, low molecular weight heparin was prescribed.
Conclusion. According to our results indications for coagulation testing and thromboprophylaxis in pregnant women are still unclear which leads to unnecessary laboratory testing and misuse of heparin in pregnancy.
Key words: pregnancy, D-dimer test, thromboprophylaxis

PP 059

PP 060

PROCENA EFEKTIVNOSTI PRIMENE VKA KOD BOLESNIKA U TOKU 2019.GODINE (PRE PANDEMIJE COVID-19) U POREĐENJU SA 2021. (U TOKU PANDEMIJE COVID-19)

Saračević M[1], Basarić D[1], Maslać A[1], Miković D[1] Kovač M[1,2]
[1] Institut za transfuziju krvi Srbije, Odeljenje za ispitivanje poremećaja hemostaze, Beograd
[2] Medicinski Fakultet Univezitet u Beogradu , Srbija, Beograd

Uvod: Oralna antikoagulantna terapija antagonistima vitamina K se primenjuje u prevenciji i lečenju venskog tromboembolizma, u prevenciji moždanog udara kod bolesnika sa non-valvularnom fibrilacijom i bolesnika sa ugrađenim veštačkim srčanim zaliscima. Važno redovno praćenje bolesnika i održavanje kvaliteta terapije. Kvalitet terapije se prati preko TTR (Time in Therapeutic Range) koji je za kardiološke dijagnoze > 70%, a za venske tromboze i embolije > 65%. U svakom slučaju je najpoželjniji TTR > 65%.
Cilj: Praćenje pacijenata na oralnoj antikoagulantoj terapiji i određivanje TTR pre i u toku pandemije COVID-19.
Materijal i metode: U praćenje je uključeno 108 bolesnika sa dijagnozama: aritmija absoluta (18 bolesnika), duboka venska tromboza i plućna embolija (30 bolesnika), aortni veštački srčani zalistak (35 bolesnika) i mitralni veštački srčani zalistak (25 bolesnika) koji su praćeni u toku 2019. (pre pandemije) i 2021. (u vreme pandemije) godine. Podaci o bolesnicima su dobijeni iz registra bolesnika na antikoagulantnoj terapiji Instituta za transfuziju krvi Srbije.
Rezultati: U oba perioda je kod 9 od 18 bolesnika sa aritmijom absolutom (50%), kod 15 od 35 bolesnika sa aortnim zaliskom (43%) i kod 5 od 25 bolesnika sa mitralnim zaliskom (20%) utvrđeni TTR je bio veći od 70%, a kod 17 od 30 bolesnika sa trombozom (57%) je TTR bio veći od 65%. Poželjni TTR > 65% je kod pacijenata sa aritmijom absolutom imalo njih 14 (77%) pre pandemije, a 9 (50%) u toku pandemije, sa aortnim zaliskom 17 (49%) pre, a 16 (45%) u toku pandemije, sa mitralnim zaliskom 8 (32%) pre, a 6 (24%) u toku pandemije.
Zaključak: Za referentne TTR vrednosti prema dijagnozi nije bilo značajnije razlike pre i u toku pandemije, ali je za poželjni TTR > 65% postojala značajna razlika pre i u toku pandemije kod pacijenata sa artimijom absolutom. S obzitrom da su TTR niži od referentne vrednosti, neophodna je edukacija bolesnika da bi se postigao bolji kvalitet primene VKA, odnosno ukoliko nije moguće poboljšanje TTR savetuje se prevođenje na nove oralne antikoagulanse.
Ključne reči: Antikoagulantna terapija, TTR, procena

PP 060

ASSESSMENT OF THE EFFECTIVENESS OF THERAPY WITH VKA IN PATIENTS DURING 2019 (BEFORE THE PANDEMIC COVID-19) AND COMPARED TO 2021 (DURING THE PANDEMIC COVID-19)

Saracevic M., Basaric D[1], Maslac A[1], Mikovic D[1], Kovac M[1,2]
[1] National Blood Transfusion Institute of Serbia, Haemostasis Department, Belgrade
2 Faculty of Medicine, University of Belgrade, Serbia, Belgrade

Introduction: Oral anticoagulant therapy with vitamin K antagonists is used in the prevention and treatment of venous thromboembolism, in the prevention of stroke in patients with non-valvular fibrillation and patients with artificial heart valves. It is important to regularly monitor the patient and maintain the quality of therapy. The quality of therapy is monitored through TTR (Time in Therapeutic Range), which is > 70% for cardiologic diagnoses, and > 65% for venous thrombosis and embolism. In any case, the TTR that benefts them most is > 65%.
Objective: Follow-up of patients on oral anticoagulant therapy and determination of TTR before and during the COVID-19 pandemic.
Material and methods: The follow up included 108 patients with the following diagnoses: arrhythmia absoluta (18 patients), deep vein thrombosis and pulmonary embolism (30 patients), aortic artificial heart valve (35 patients) and mitral artificial heart valve (25 patients) which were monitored during 2019 (before the pandemic) and 2021 (during the pandemic). Data on patients were obtained from the register of patients on anticoagulant therapy of the National Blood Transfusion Institute of Serbia.
Results: In both periods, in 9 of 18 patients (50%) with arrhythmia absoluta, in 15 of 35 patients (43%) with aortic valve and in 5 of 25 patients (20%) with mitral valve the determined TTR was higher than 70% and in 17 out of 30 patients (57%) with thrombosis the TTR was higher than 65%. The desired TTR > 65% had 14 (77%) patients with arrhythmia absoluta before the pandemic and 9 (50%) during the pandemic, with aortic valve 17 (49%) before and 16 (45%) during the pandemic, with mitral valve 8 (32%) before, and 6 (24%) during the pandemic.
Conclusion: There was no significant difference before and during the pandemic for the reference TTR values according to the diagnosis, but for the desirable TTR > 65% there was a significant difference before and during the pandemic in patients with arrhythmia absoluta. Given that the TTRs are lower than the reference value, patient education is necessary to achieve a better quality of VKA administration and if it is not possible to improve the TTR, it is recommended to switch to new oral anticoagulants.
Key words: Anticoagulant therapy, TTR, assessment

PP 061

THE MONITORING OF ASPIRIN AND CLOPIDOGREL THERAPY BY TWO MODELS OF AGGREGOMETERS CHRONO-LOG MODEL700 AND INNOVANCE PFA-200 AND COMPARATION OF RESULTS

Neceva V, Todorovska E, Dejanova V, Apostolovska R, Nikoloska I
Institute of Transfusion Medicine, Faculty of Medicine, Ss. Cyril and Methodius University in Skopje, Republic of North Macedonia

Background: Agreggomethry is the method for assessment of Platelet function, identification patients at risk for thrombosis or bleeding, determination of proper therapeutic doses and detection of resistance to certain drugs.
Aim. The monitoring of Aspirin and Clopidogrel therapy by Chrono Log 700 (Col/ADP) and by Innovance PFA 200 (Col/Epi, Col/ADP).
Material and Methods: Two hundred seventy nine 279 patients on aspirin therapy, 250 patients on clopidogrel and 250 patients without therapy as a control were investigated. Reference valueson for ADP are (69-88 %) and for Collagen are (70-94 %) on Chrono Log 700. Reference values on PFA 200 are 82-150 s for Col/Epi and 62-100 s for Col/ADP. Responders to aspirin therapy had (closure time) CT > 150 s, and to clopidogrel CT >106 s. At overdosed patients CT >300s.
Results: A total of 279 patients on Aspirin had decreased Col Aggregation on Chrono Log 700 (36.51 %+19) and prolonged Col/Epi CT 264 s on PFA 200. Among them 128 patients (46 %) were over dosed. Colagen Aggregation on Chrono Log was 700 (24 % + 12.3) and prolonged CT >300 s on PFA 200.
Patients on Clopidogrel, had decreased ADP induced aggregation on Chrono Log (29.01 %+13) and prolonged P2Y CT (230 s) on PFA 200. Out of 250 patients 49 (20 %) were overdosed. The tests show hypoaggregation on both analysers: ADP was (19 % +15.3) and P2Y CT>300 s.
Control group of patients had normal aggregation tests on both analysers. Col/Epi CT was 115+24 s and Col/ADP CT was 84+12 s measured on PFA 200. ADP and on Chrono Log 700 was 69.01%+13 and Col induced aggregation 66.51 %+19.
Conclusion: Two methods are simple to use and, sensitive to antiplatelet therapy. The obtained results with two investigated methods correlate with each other even in overdosed patients.

PP 061

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THE CHALLENGES OF REORGANIZATION, RATIONALIZATION AND INFORMATIZATION OF TRANSFUSION SERVICE IN CROATIA – EXPERIENCES OF THE UNIVERSITY HOSPITAL OSIJEK; CLINICAL INSTITUTE FOR TRANSFUSION MEDICINE

Dalibor Ratić
Clinical Institute for Transfusion Medicine,University Hospital Osijek

Abstract

The safety of transfusion treatment is the basic task of consolidating the transfusion service with clearly defined goals such as uniform safety and quality of blood products throughout the Republic of Croatia, sufficient supply and self-sufficiency of safe and high-quality blood products and services, work economy, standardization of transfusion treatment, and connection to the national IT program. The main problem with the transfusion service in Croatia was the excessive number of centers for transfusion medicine where blood products are prepared, so equipment, financial resources, and experts were used irrationally. Adoption of the basic network of transfusion activity for blood and blood products rationalized and reorganized the transfusion activity. In less than two and a half years, the University Hospital Osijek Clinical Institute for Transfusion Medicine took over the tasks of collecting, testing, storing, and distributing blood products for seven health institutions in four counties prescribed by the legal acts of the Republic of Croatia, and in a relatively short period of time, it was the first in the Republic of Croatia to successfully complete the planned reorganization of the service.

Keywords*:* transfusion, reorganization, rationalization.

Sažetak

Sigurnost transfuzijskog liječenja je osnovna zadaća okrupnjavanja transfuzijske službe uz jasno definirane ciljeve kao što su ujednačena sigurnost i kvaliteta krvnih pripravaka u cijeloj RH, dostatna opskrba i samodostatnost sigurnim i kvalitetnim krvnim pripravcima i uslugama, ekonomičnost rada, standardizacija transfuzijskog liječenja, te povezivanje u nacionalni informatički program. Glavni je problem transfuzijske službe u Hrvatskoj bio u prevelikom broju centara za transfuzijsku medicinu u kojima se pripremaju krvni pripravci pa su se oprema, financijska sredstva i stručnjaci neracionalno upotrebljavali. Donošenjem Osnovne mreže transfuzijske djelatnosti za krv i krvne pripravke učinjena je racionalizacija i reorganizacija transfuzijske djelatnosti. U nepune dvije i pol godine Klinički je zavod za transfuzijsku medicinu preuzeo poslove prikupljanja, testiranja, čuvanja i distribucije krvnih pripravaka za sedam zdravstvenih ustanova u četiri županije propisanim zakonskim aktima RH, te je u relativno kratkom roku prvi u RH uspješno završio planiranu reorganizaciju službe.

Ključne riječi: transfuzija, reorganizacija, racionalizacija

Background

Transfusion medicine covers a wide range of activities: voluntary blood donation (collection, production, testing, storage, and distribution of blood products) and clinical transfusion medicine with molecular diagnostics. It is one of the few medical specializations that unites science, technology, medicine, public health, and society in general. The development and progress of transfusion medicine partly support the progress of modern medicine. In the societies of developed countries, almost every form of work is carried out by means of an organization of some kind. Unlike concepts such as family or community, which are defined by their membership, culture, affinity, or location, an organization is defined by its purpose. Reorganization (rearrangement, restructuring) is a set of measures and organizational efforts whose goal is to change the organizational structure and organizational processes in order to improve methods and results, and it is motivated by certain shortcomings and weaknesses of the existing structure.

The main problem with the transfusion service in Croatia was the excessive number of centers for transfusion medicine where blood products are prepared, therefore, equipment, finance, and experts were used irrationally. At the same time, small centers could not meet the high-quality assurance and quality control standards of blood products.

Aim

The safety of transfusion treatment was the basic task of consolidating the transfusion service with clearly defined goals such asuniform safety and quality of blood products throughout the Republic of Croatia, sufficient supply and self-sufficiency of safe and high-quality blood products and services, work economy, standardization of transfusion treatment, and connection to the national IT program.

Discussion

The economic and professional management of a complex transfusion service is based on the adoption of new technologies (computerization, automation, robotics), consolidation of transfusion units, management, quality assurance and control, hemovigilance, materiovigilance, and work in accordance with good organizational practice and regulations of European directives.

A major step forward in the reorganization of the transfusion service was made by the establishment of the legal basis (one law and three ordinances), and the path toward changes was defined and started. The preconditions for the reorganization of the transfusion service were the realization of financial support, computerization of the transfusion service, increase in blood prices, and reorganization of work in the transfusion services. The IT connection of the transfusion services with the "e-Delphyn" program produced by "Hemasoft" from Spain began with the purchase of the program in 2007.

Computerization enables the workforce to shift from repetitive tasks to creative ones, and the tasks of sorting, searching and data processing are taken over by the machine. A very important form of computerization is the improvement of communication, which enables information to be immediately available to all interested parties, regardless of physical distance. With the adoption of the Basic Network of Transfusion Services for blood and blood products, the transfusion service was rationalized, and from the existing 32 transfusion units the following blood establishments were established: Croatian Institute of Transfusion Medicine, three regional transfusion centers (Rijeka, Split and Osijek) and two sub-regional centers (Varaždin and Dubrovnik). All other transfusion units were reorganized exclusively for clinical transfusion activity.

According to the instructions of the Ministry of Health of the Republic of Croatia and according to the requirements of the profession, the University Hospital Osijek Clinical Institute for Transfusion Medicine started the reorganization of the transfusion service in 2011, with numerous challenges ahead of us. First of all, there was the interpretation and possibility of applying legal acts, ensuring a sufficient number of educated staff, computerization of the service at the national level with staff education, employee motivation, implementation and quality assurance of the system, reorganization of the existing organizational structure, and purchase of equipment. Such major changes required detailed planning and a certain period of time.

In less than two and a half years from August 1st, 2011. when we took over blood establishment activities from the General Hospitals in Našice, on June 1, 2012,Vinkovci, on December1, 2012, Virovitica, on December 10,2012,Vukovar, on January1, 2014,SlavonskiBrod and Nova Gradiška. With the implementation of the IT system "e-Delphyn" on May 2, 2013, we successfully completed the reorganization of the transfusion service prescribed in the legal acts of the Republic of Croatia. In the mentioned period, University Hospital Osijek, Clinical Institute of Transfusion Medicine took over the collection, testing, storage, and distribution of blood products for seven health institutions in four counties (Osječko – baranjska, Vukovarsko – srijemska, Brodsko – posavskaiVirovitičko – podravska counties).

In that period, not everything was always easy, challenges followed one after another, there were ups and downs, and higher and lower motivation, but we had a clear goal in front of us, which certainly would not have been possible without the great enthusiasm and commitment of all employees. Fear and resistance to change are well known in organizational psychology as normal reactions to something new and unknown. The formula for avoiding employee resistance is not simple and is not applicable in the short term. In the psychological literature, rationalization is called the "sour grapes - sweet lemon" reaction. Thedefensemechanism is used when we portray insignificant successes as great or praise what we were forced to choose (sweet lemon) and when we speak of an unattainable goal with disparagement (sour grapes).

Conclusion

The time factor, enthusiasm, as well as a clear inspiring vision of a better future are predictors of the success of implementing any change in the organization, but the biggest incentive for team efficiency is good communication with all participants in the organizational change.

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UP 68

RAD INSTITUTA ZA TRANSFUZIJU KRVI SRBIJE U VREME PANDEMIJE COVID – 19

Stamatović T.
Institut za transfuziju krvi Srbije (ITKS)

Mere ograničavanja kretanja, karantin i samoizolacija su uvedeni na teritoriji Republike Srbije u cilju sprečavanja širenja transmisije COVID-19 infekcije u vreme vnredne situacije 2020g godine. Međutim, ove mere su se jako odrazile na odziv dobrovoljnih davalaca krvi kako u Sali ITKS, tako i na terenu i na redovno snabdevanje zdravstvenih ustanova jedinicama krvi i komponentama krvi.
Osnovni zadatak Instituta tokom pandemije je bio da se obezbede dovoljne količine krvi/komponenata krvi, a da se pri tom održe sigurnost dobrovoljnih davalaca krvi i zaposlenih u Institutu.
Uz saradnju i podršku CK Srbije i CK Beograda, organizovane su dodatne akcije u lokalnoj zajednici, posebno na teritoriji grada Beograda, sa molbom lokalnim samoupravama da ovu aktivnost ne tretiraju kao okupljanje ljudi, već kao preduslov lečenja obolelih kojima je krv neophodna. Pored uobičajenog izbora davalaca krvi, pojačan je nadzor, davaocima krvi se preporučuje da ne dolaze u Institut ukoliko imaju neke od simptoma kovida ili ako su bili u kontaktu sa zaraženima. Način rada se menjao u skladu sa preporukama Kriznog štaba a prilikom organizacije akcija dobrovoljnog davanja krvi se poštuju preventivne mere radi sprečavanja prenosa virusa, u skladu sa propisima i donetim merama, (uvođenje i poštovanje higijensko-epidemioloških mera, nošenje zaštitne opreme za zaposlene i davaoce krvi, dezinfekcija prostorija i površina, dezinfekcija kombija i autobusa, postavljanje dezobarijera, merenje temperature, održavanje distance).
Problem sa kojim smo se suočili je i smanjen broj zdravstvenih radnika zaposlenih u Institutu, delom zbog zdravstvenih problema zaposlenih prouzrokovanih virusom, delom zbog potreba bolnica u kovid sistemu, koje su preuzimale određen broj lekara i laboratorijskih/medicinskih tehničara Instituta kao ispomoć u radu.
I pored svih problema sa kojima smo se susretali za vreme trajanja pandemije, Institut za transfuziju krvi Srbije je uspeo da obezbedi dovoljne količine sigurne krvi za nesmetano funkcionisanje zdravstvenog sistem, a istovremeno održi sigurnost i zaštitu dobrovoljnih davalaca krvi kao i zaposlenih.
Ključne reči: davalaštvo krvi, Covid, kvalitet.

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THE WORK OF THE BLOOD TRANSFUSION INSTITUTE OF SERBIA DURING THE COVID-19 PANDEMIC

Stamatović T.
Blood Transfusion Institute of Serbia (BTIS)

Movement restriction measures, quarantine and self-isolation were introduced on the territory of the Republic of Serbia in order to prevent the spread of the transmission of the COVID-19 infection during the emergency situation in 2020. However, these measures had a strong impact on the response of voluntary blood donors both in the BTIS Hall and in the field and on the regular supply of blood units and blood components to health institutions.
The main task of the BTIS during the pandemic was to provide sufficient amounts of blood/blood components, keeping the safety of voluntary blood donors and employees of the Institute at the same time.
With the cooperation and support of the Red Cross of Serbia and the Red Cross of Belgrade, additional actions were organized in the local community, especially in the territory of the city of Belgrade. In addition to the usual selection of blood donors, monitoring has been increased, blood donors are recommended not to come to the Institute if they have any of the symptoms of Covid or if they have been in contact with infected people. The working hours were adopted in accordance with the recommendations of the Crisis Board. During the organization of voluntary blood donation actions, preventive measures are observed to prevent the transmission of the virus, in accordance with the regulations and adopted measures.
Another problem we faced was the reduced number of health workers employed at the Institute, partly due to the health problems of employees caused by the virus, partly due to the needs of hospitals in the Covid system, which took over a certain number of doctors and laboratory/medical technicians of the Institute as work aids.
Despite all the problems we encountered during the pandemic, the BTIS managed to provide sufficient quantities of safe blood for the unhindered functioning of the health system and at the the same time keeping the safety and protection of voluntary blood donors as well as employees.
Key words: blood donation, Covid, quality

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PRIKAZ BROJA DARIVATELJA KRVI U PERIODU 2019 – 2021 U ODNOSU NA PANDEMIJU COVID 19 I GDJE SMO DANAS

Stojčić O , Sesar.M, Knežević J.
Transfuzijski centar, Sveučilišna Klinička bolnica Mostar

UVOD: Dobrovoljni darivatelj krvi je prema definiciji koju je odredila Međunarodna udruga transfuziologa, Međunarodni Crveni križ, Svjetska zdravstvena organizacija i Europsko vijeće, a prihvaćena je u svim zemljama svijeta, osoba koja daruje krv, plazmu ili stanične dijelove krvi po svojoj slobodnoj volji i ne prima za to nikakvu nadoknadu.
CILJ: Prikazati broj darivatelja u periodu od 2019 - 2021 s naglaskom smanjena odnosno povećanja broja darivatelja tijekom pandemije .
MATERIJAL I METODE: Podatci su prikupljeni retrospektivno uvidom u registre dobrovoljnih darivatelja krvi i bolnički informatički sustav (BIS). Podatci su statistički obrađeni u programu Microsoft Excel – u, prikazani su grafički i u tablicama.
REZULTAT: Analizom podataka u periodu 2019 – 2021 uvidio se pad broja darivatelja tijekom pandemije i zatvaranja i preporuka o smanjenim kontaktima i okupljanjima većeg broja ljudi na jednom mjestu. U 2019 god prije početka pandemije broj upisanih darivatelja krvi je 11275 i broj održanih akcija darivanja krvi 168, u 2020 godini u vrijeme pandemije broj darivatelja pada za 14 % upisanih 9737 i115 akcija darivanja krvi manje za 31% u odnosu na 2019 god. i radi se u promijenjenim uvjetima. U 2021 godini upisanih 11344 gdje vidimo porast za 1% u odnosu na 2019 god i porast za 25 % u donosu na 2020 godinu.
ZAKLJUČAK: Pandemija COVID 19 promjenila je organizaciju zdravstvenog sustava, način pružanja zdravstvenih usluga samim tim i organizaciju darivanja krvi. Za pružanje kvalitetne usluge važno nam je očuvanje temeljnih vrednota zdravstvene skrbi. Kreativnost i inovativnost koje su zdravstveni djelatnici pokazali treba da bude strategija za razvoj prakse utemeljene na dokazima.
KLJUČNE RIJEČI : davalaštvo, pandemija, krv

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DESCRIPTION OF THE WORK OF THE DONOR TESTING DEPARTMENT DURING THE PANDEMIC COVID 19 - OUR RESULTS

Žujović S[1], Jovičić M[2], Dukić Novaković M[1]
[1]Blood Transfusion Institute of Serbia, Belgrade
[2]CHC "Dr Dragisa Mišović" Belgrade

Introduction: During the Covid 19 pandemic, the Donor Testing Department performed its activities in accordance with all current professional recommendations.
Aim: Presentation of the work results of the Donor Testing Department in the Blood Transfusion Institute of Serbia during the Covid 19 pandemic in 2021.
Methods: Voluntary donor samples testing is fully automated. Immunohaematological tests are performed using the microtiter plate method on Qwalys and Neo Iris devices, while serological tests of transfusion transmissible disease (TTD) are performed using the ELISA and CMIA methods on Architect, Alinity, Liaison and Evolis devices. Molecular testing of TTD for all blood donor samples collected in the Republic of Serbia are performed on Cobas 6800 devices.
Results: 69 614 blood donor samples, apheresis thombocytes and convalescent Covid plasma were tested at the Department for Immunohaematological Testing of and the Department for TTD by serological technique for HBsAg, HCV, HIV and Syphilis during 2021.
190 774 samples were tested at the Department for TTD by molecular technique for HBV, HCV and HIV markers during 2021.
In addition to mandatory tests, 236 confirmatory tests for TTD markers were performed. 299 blood donors were typed in order to expand the register of typed blood donors.
The Donor Testing Department participated in external interlaboratory comparison programs (EDQM, EQAS, Randox) and achieved maximum performance in all areas. In addition to all work tasks, employees of the department during 2021. were engaged as an professional help to health institutions that were in the Covid system.
Conclusion: The achieved level of number and quality of analyses and services of the Donor Testing Department is adequate to the demands and expectations of users, regardless of the increased demands during the pandemic.
Key words: blood donor, testing, sample, quality, pandemic

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DISTRIBUCIJA KRVI I KOMPONENATA KRVI U PERIODU 2021–2022. GODINE

A. Stojiljković, O. Obradović, M. Luković, B. Petrović, S. Mijović, J. Anđelić, D. Stojić
Institut za transfuziju krvi Srbije

Uvod: U skladu sa Zakonom o transfuzijskoj medicini distribucija komponenata krvi bolničkim bankama krvi u centralnom regionu se od oktobra 2020. godine obavlja sa Odeljenja za pripremu komponenata krvi. Proces potpunog preuzimanja u centralnom regionu završen je u martu 2022. godine.
Cilj rada: Prikaz i analiza raspodele jedinica krvi i komponenata krvi koje su distribuirane bolničkim bankama tokom 2021. i 2022. godine.
Materijal i metode: Retrospektivna analiza podataka koji se odnose na distribuciju krvi i komponenata krvi, preuzetih iz Informacionog sistema Instituta za transfuziju krvi Srbije.

Rezultati: U 2021. godini krv i komponente krvi su distribuirane za 14 bolničkih banaka, a u 2022. godini za 18 banaka krvi. U 2021. godini distribuirano je 26 589 jedinica eritrocita, 12 496 jedinica sveže zamrznute plazme, 3 676 jedinica krioprecipitata i komponente trombocita – 6 407 koncentrata, 222 pulova i 5 jedinica afereznih trombocita. U periodu 01.01–01.09.2022. distribuirano je 37 788 jedinica eritrocita, 19 199 jedinica sveže zamrznute plazme, 13 924 jedinica krioprecipitata i komponente trombocita – 13 620 koncentrata, 947 pulova i 1 750 jedinica afereznih trombocita. Tokom prvih devet meseci 2022. godine izdato je 42% jedinica eritrocita više u odnosu na celu 2021. godinu pre svega jer se od 15. marta vrši i distribucija ka bolničkoj banci Univerzitetskog kliničkog centra Srbije.

Zaključak: Odeljenje za pripremu komponenata krvi Instituta za transfuziju krvi Srbije uspešno je preuzelo sve poslove distribucije krvi i komponenata krvi bolničkim bankama centralnog regiona. Postojanje informacionog sistema koji bi povezao sve bolničke banke omogućio bi bolje upravljanje zalihama rezervi krvi i njihovo adekvatnije raspoređivanje ka bolničkim bankama krvi, a sve s ciljem boljeg zbrinjavanja pacijenata.

Ključne reči: distribucija, banke krvi, informacioni sistem

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DISTRIBUTION OF BLOOD AND BLOOD COMPONENTS IN THE PERIOD 2021–2022.

A. Stojiljković, O. Obradović, M. Luković, B. Petrović, S. Mijović, J. Anđelić, D. Stojić
Blood Transfusion Institute of Serbia

Introduction: In accordance with the Law of Transfusion Medicine, the distribution of blood components to hospital blood banks in the central region of Serbia is carried out from October 2020 by the Department for the preparation of blood components. The process of complete takeover in the central region was completed in March 2022.
Aim: Presentation and analysis of the distribution of blood units and blood components that were distributed to hospital banks during 2021 and 2022.
Material and methods: Retrospective analysis of data related to the distribution of blood and blood components, taken from the Information System of the Blood Transfusion Institute of Serbia.
Results: In 2021, blood and blood components were distributed to 14 hospital banks, and in 2022 to 18 blood banks. In 2021, 26,589 units of red cells, 12,496 units of fresh frozen plasma, 3,676 units of cryoprecipitate and platelet components - 6,407 concentrates, 222 pools and 5 units of apheresis platelets were distributed. In the period 01.01 till 01.09.2022. 37,788 units of red cells, 19,199 units of fresh frozen plasma, 13,924 units of cryoprecipitate and platelet components - 13,620 concentrates, 947 pools and 1,750 units of apheresis platelets were distributed. During the first nine months of 2022, 42% more red cell units were issued compared to the whole of 2021, primarily because the distribution to the hospital bank of the University Clinical Center of Serbia has been taking place since March 15.
Conclusion: The Department for the preparation of blood components of the Blood Transfusion Institute of Serbia has successfully taken over all the tasks of distributing blood and blood components to hospital banks in the central region. The existence of an information system that would connect all hospital banks would enable better management of blood reserves and their more adequate allocation to hospital blood banks, all with the aim of better patient care.

Key words: distribution, blood banks, information system

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PRIKAZ SLUČAJA:MOLEKULARNO ODREĐIVANJE RHD GENA KOD SEROLOŠKI RhD-NEGATIVNOG DARIVAOCA KRVI

Musić E., Vilić-Hasanović V.
Zavod za transfuzijsku medicinu FBiH, Sarajevo, Bosna i Hercegovina

UVOD: Serološko određivanje RhD antigena hemaglutinacijskim tehnikama, uključujući i indirektni antiglobulinski test (IAT), zbog varijabilne senzitivnosti reagenasa nekada nije dovoljno u detektovanju vrlo slabih RhD varijanti (slabi D i parcijalni D). Obzirom da je RhD visoko imunogen, transfuzije eritrocitnih krvnih pripravaka koji sadrže te RhD varijante mogu izazvati aloimunizaciju kod RhD negativnih pacijenata. Shodno tome, neki transfuzijski centri pretežno zapadnih zemalja, su implementirali molekularno testiranje svih serološki RhD negativnih darivaoca krvi na prisutnost RHD sekvenci. Prema nekim smjernicama, primarno je potrebno odrediti RHD genotip PCR-SSP (polymerase chain reaction-sequence specific primers) metodom svim davaocima koji u svom Rh fenotipu pokazuju ekspresiju C ili E antigena uz odsustvo D antigena.
CILJ RADA: Detekcija RHD varijanti kod serološki RhD-negativnih darivatelja krvi u svrhu sprečavanja aloimunizacija RhD negativnih pacijenata.
MATERIJAL I METODE: Serološke: Imunohematološke metode određivanja RhD antigena u mikrogel karticama, mikrotitarskim pločama te IAT. Molekularno: Fluogene metoda-PCR-SSP (polymerase chain reaction-sequence specific primers) metoda bazirana na detekciji fluorescencije iz fluorohroma.
REZULTATI: U sklopu rutinskog testiranja metodom hemaglutinacije u mikrotitarskoj ploči (Bio-Rad), dobrovoljnom darivaocu krvi je prilikom prvog darivanja određena krvna grupa, rezultat A RhD-negativan, test u IAT-u bez aglutinacija, Rh fenotip Ccee. Prilikom narednog darivanja testirano je metodom hemaglutinacije u mikrogel kartici (Bio-Rad), rezultat A RhD negativno. PCR-SSP metodom na komercijalnim RBC-Fluogene kit-ovima (inno-train) utvrđena D weak varijanta tip 11.
ZAKLJUČAK: Molekularno određivanje krvnogrupnih gena darivaoca krvi u situacijama, koje nisu ili ne mogu biti serološki razriješene donosi brojne benefite. Međutim, postavlja se pitanje da li je već sada potrebno serijsko testiranje serološki RhD-negativnih darivaoca molekularnim tehnikama, čime bi se pratili dolazeće standarde, koji su utemeljeni na naučnim dokazima s ciljem preveniranja neželjenih transfuzijskih događaja.
KLJUČNE RIJEČI: DNA, RhD antigen, molekularna dijagnostika.

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CASE REPORT: MOLECULAR DETERMINATION OF THE RHD GENE IN A SEROLOGICALLY RhD-NEGATIVE BLOOD DONOR

Music E., Vilić-Hasanović V.
Institute for Transfusion Medicine FBiH, Sarajevo, Bosnia and Herzegovina

INTRODUCTION: Serological determination of RhD antigen by hemagglutination techniques, including the indirect antiglobulin test (IAT), due to the variable sensitivity of reagents, is sometimes not sufficient in detecting weak RhD variants (weak D and partial D). Since RhD is highly immunogenic, transfusions of erythrocyte blood products containing these RhD variants can cause alloimmunization in RhD-negative patients. Consequently, some transfusion centers, predominantly in Western countries, have implemented molecular testing of all serologically RhD-negative blood donors for the presence of RHD sequences. According to some guidelines, it is primarily necessary to determine the RHD genotype by PCR-SSP (polymerase chain reaction-sequence specific primers) method for all donors whoes Rh phenotype show the expression of C or E antigen with the absence of D antigen.
OBJECTIVE: Detection of RHD variants in serologically RhD-negative blood donors in order to prevent alloimmunization of RhD-negative patients.
MATERIALS AND METHODS: Serological: Immunohaematological methods of determining RhD antigen in microgel cards, microtiter plates and IAT. Molecular: Fluogene method-PCR-SSP (polymerase chain reaction-sequence specific primers) method based on the detection of fluorescence from fluorochromes.
RESULTS: As part of routine testing with the hemagglutination method in a microtiter plate (BioRad), a blood group was determined for a voluntary blood donor during the first donation, result A RhD-negative, IAT test without agglutination, Rh phenotype Ccee. The next donation was tested by the hemagglutination method in a microgel card (BioRad), and the result was RhD negative. D weak variant type 11 was determined by PCR-SSP method on commercial RBC-Fluogene kits (inno-train).
CONCLUSION: Molecular determination of blood group genes of blood donors in situations that are not or can not be resolved serologically brings numerous benefits. However, the question arises as to whether serial testing of serologically RhD-negative donors with molecular techniques is already necessary in order to follow the upcoming standards, which are based on scientific evidence with the aim of preventing unwanted transfusion events.
KEY WORDS: DNA, RhD antigen, molecular diagnostics.

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SISTEM KONTROLE KVALITETA U ZAVODU ZA TRANSFUZIJU KRVI NIŠ

Srdjan Spasić
Zavod za transfuziju krvi Niš

Sistem kontrole kvaliteta predstavlja niz procedura, resursa i organizacionu politiku rukovodstva radi dostizanja kvaliteta. Kontrola kvaliteta u transfuziji ima za cilj da obezbedi dovoljnu količinu krvi , krvnih produkata, plazme i proizvoda od plazme visokog kvaliteta sa minimalnim rizicima po davaoce i pacijente.
Sistem kontrole kvaliteta obuhvata: upravljanje kvalitetom i promenama, organizaciju kadrovima, prostorije uključujući i mesta za prikupljanje na terenu, opremu i materijale, dokumentaciju, prikupljanje krvi, pripremu komponenata, skladištenje i distribuciju, praćenje kvaliteta, testiranje krvi, ugovaranje, odstupanja, žalbe, neželjene reakcije,povlačenje jedinica, korektivne i preventivne mere, interne provere, eksterne provere i mere za poboljšanje.
Nivoi transfuzioloških laboratorija na nivou davaoca:
Trijaža davaoca
- odredjivanje vrednosti hemoglobina na terenu i u salipre davanja krvi
- provera kr. gr. na pločici
- odredjivanje vene za venepunkciju
- prateća dokumentacija
Testiranje davaoca
- Kontrola kr. gr. u laboratoriji, skrining antitela kod svih davaoca i Rh fenotip kod negativnih davaoca.
- Markeri transfuzijom prenosivih infekcija HIV, HCV, TPH i HBS
- NAT testiranje istih
- Prateća dokumentacija , kompjuterska radna lista, rezultati i dnevna evidencija korišćenih reagenasa.
Obrada krvi i priprema komponenata
- Obučenost osoblja
- Pravilno podmeravanje i centrifugiranje
- Rad na automatskim ekstratorima
- Sterilna konekcija
- Etiketiranje proizvoda
- Skladištenje i čuvanje produkata
Distribucija
- Prijem uzoraka i trebovanja
- Unos podataka u IS
- Provera kr. gr. i probe kontabilnosti
- Vodjenje pisane dokumentacije
Laboratorija za kontrolu kvaliteta
- Pravljenje godišnjeg plana za kontrolu kvaliteta
- Odabir komponenata za kontrolu kvaliteta
- Merenje količine
- Pravilno uzorkovanje
- Ispitivanje hemolize
- Hematološka kontrola
- Bakteriološka kontrola
Kljucne reci: kvalitet, organizacija, transfuzija

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TRANSFUZIOLOŠKO ZBRINJAVANJE PACIJENATA SA COVID-19 INFEKCIJOM

Maslovarić M, Antić A.
Zavod za transuziju krvi Niš

Uvod. COVID-19 pandemija predstavlja poseban izazov za transfuzijsku službu, imajući u vidu da se potrebe za transfuzijom krvnih produkata za lečenje pacijenata sa SARS-CoV-2 infekcijom mogu povećati u uslovima limitiranih rezervi krvi i smanjenog broja dobrovoljnih davaoca. Iako postoji sve veći broj podataka o trombotičnim posledicama ove infekcije, malo je informacija o potrebama za transfuziološkim zbrinjavanjem ovih pacijenata, a što je neophodno za adekvatno upravljanje zalihama krvi tokom pandemije. U ovom radu smo retrospektivno analizirali podatke o primenjenim krvnim produktima za lečenje pacijenata obolelih od SARS-CoV-2 infekcije, koji su tokom 2021. godine lečeni na Klinici za infektivne bolesti i Centru za anesteziju i reanimaciju Kliničkog centra u Nišu, kao i COVID bolnici u Kruševcu.
Rezultati. Pacijenti oboleli od SARS-CoV-2 lečeni u Centru za anesteziju i reanimaciju primili su 3.070 jedinica eritrocita, 1.681 jedinicu zamrznute sveže plazme, 2.451 dozu trombocita, 810 doza krioprecipitata i 79 jedinica rekonvalescentne kovid plazme. Pacijenti lečeni na infektivnoj klinici primili su 138 jedinica eritrocita, 147 jedinica zamrznute sveže plazme, 147 doza trombocita i 55 jedinica rekonvalescentne plazme, dok je kovid bolnici u Kruševcu izdato 20 jedinica eritocita, 18 jedinica plazme i 56 doza trombocita.
Zaključak. Ispitivanje je pokazalo da COVID-19 pacijenti imaju nisku potrošnju krvnih produkata. Buduće studije treba usmeriti u pravcu razjašnjenja mehanizama koji utiču na primenu transfuzija kod hospitalizovanih pacijenata sa SARS-CoV-2 infekcijom.

Ključne reči: COVID-19, transfuzija, krvne komponente

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TRANSFUSION CARE OF PATIENTS WITH COVID-19 INFECTION

Maslovarić M, Antić A.
Blood transfusion institute Niš

Introduction. The COVID-19 pandemic represents a special challenge for the transfusion service, bearing in mind that the need for transfusion of blood products for the treatment of patients with SARS-CoV-2 infection may increase in conditions of limited blood reserves and a reduced number of voluntary donors. Although there is an increasing amount of data on the thrombotic consequences of this infection, there is little information on the need for transfusion care of these patients, which is necessary for adequate management of blood supplies during the pandemic. In this paper, we retrospectively analyzed the data on the blood products used for the treatment of patients suffering from SARS-CoV-2 infection, who were treated during 2021 at the Clinic for Infectious Diseases and the Center for Anesthesia and Reanimation of the Clinical Center in Niš, as well as the COVID Hospital in Kruševac.
Results. Patients with from SARS-CoV-2 treated in the Center for Anesthesia and Reanimation received 3,070 units of erythrocytes, 1,681 units of frozen fresh plasma, 2,451 doses of platelets, 810 doses of cryoprecipitate and 79 units of convalescent covid plasma. Patients treated at the Clinic for Infectious Diseases received 138 units of erythrocytes, 147 units of frozen fresh plasma, 147 doses of platelets and 55 units of convalescent plasma, while in the Covid hospital in Kruševac received 20 units of erythrocytes, 18 units of plasma and 56 doses of platelets.
Conclusion. The study showed that COVID-19 patients have a low consumption of blood products. Future studies should be directed towards elucidating the mechanisms that influence the use of transfusions in hospitalized patients with SARS-CoV-2 infection.

Key words: COVID-19, transfusion, blood components

UP 75

IZAZOVI U FORMIRANJU ODELJENJA KLINIČKE TRANSFUZIJE U UNIVERZITETSKOM KLINIČKOM CENTRU SRBIJE

Tomić D, Životić B, Mijović L.

Uvod
U skladu sa zakonom o transfuzijskoj medicini 15.marta 2022. formirana je nova organizaciona jedinica u Univerzitetskom kliničkom centru Srbije. Odeljenje za kliničku transfuziju i hemovigilancu UKCS nastalo je odvajanjem dva odeljenja Instituta za transfuziju krvi Srbije, od kojih su formirana dva odseka Odsek za pretransfuziona ispitivanja i internu distribuciju krvi i Odsek za terapijske aferezne procedure. Odeljenje za kliničku transfuziju i hemovigilancu UKCS je prvo odeljenje koje se odvojilo od matične ustanove ITKS sa ulogom da za sada obavlja poslove banke krvi prvenstveno za Urgentni centar, Kliničkog centra Srbije.
Cilj
Prikazati proces formiranja Odeljenja probleme i organizacione poteškoće, otežano snabdevanje reagensima, nedostatak opreme i načine na koje smo ih prevazilazili.
Metode
Analiza organizacionih postupaka, komunikacija sa drugim odeljenjima, Pravnom službom, službom za javne nabavke kao i drugih postupaka koje smo sproveli da bi smo omogućili dalji rad Odeljenja.
Rezultati
Odeljenje je po formiranju uspelo da nastavi rad zadržavši potreban kvalitet rada. Na Odeljenju je promenjena sistematizacija, opisi poslova zaposlenih. Oprema i mobiliraj su na osnovu ugovora o korišćenju na određeno vreme ustupljeni od strane ITKS. Odeljenje je uključeno u redovan sistem snabdevanja reagensima preko Centralne apoteke UKCS. Kadar je zanovljen po raspisanom konkursu što je omogućilo rasterećenje zaposlenih, zbog odlaska značajnog broja tehničara i lekara u ITKS. Povećan je rad na aparatima za imunoserološka testiranja, te povećana bezbednost rada. Odeljenje je nastavilo rad uspesno prevazilazeći nestašice krvi sa kojima se susrećemo.
Zaskljućak
Transformacija Odeljenja u skladu sa zakonom sprovedena je relativno uspešno. Smatramo da bi postupak bio adekvatniji da je transformacija sprovedena blagovremeno u periodu koji je zakonski predviđen. Predstoje nam i budući postupci kojima bi smo okogućili i zadovoljenje potrebnih standarda Odeljenja kao i njegovu akreditaciju. Smatramo da je ovo jedan od prvih koraka koji je načinjen u cilju implementacije Zakona o transfuzijskoj medicini.

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CHALLENGES IN THE FORMATION OF THE CLINICAL TRANSFUSION DEPARTMENT IN THE UNIVERSITY CLINICAL CENTER OF SERBIA

Tomić D, Životić B, Mijović L.

Introduction In accordance with the law on transfusion medicine on March 15, 2022, a new organizational unit was formed in the University Clinical Center of Serbia (UCCS). The Department for Clinical Transfusion and Hemovigilance UCCS was created by the separation of two departments of the Institute for BloodTransfusion of Serbia (IBTS), from which two departments were formed, the Department for pre-transfusion testings and internal distribution of blood and the Department for therapeutic apheresis procedures. The Department of Clinical Transfusion and Hemovigilance UCCS is the first department that separated from IBTS with the role of performing blood bank primarily for the Emergency Center of UCCS.
Objective To show the process of forming the Department, problems and organizational difficulties, difficult supply of reagents, lack of equipment and the ways in which we overcame the difficulties .
Methods Analysis of organizational procedures, communication with other departments, the Legal Service, the public procurement service, as well as other procedures that we implemented to enable the further work of the Department.
Results After its formation, the department was able to continue its work while maintaining the required quality
of work. Systematization and job descriptions of employees have been changed in the Department.The equipment and furniture were provided by IBTS on the basis of a contract on use for a certain period of time. The department is included in the regular supply system of reagents through the UCCS Central Pharmacy. The staff was renewed according to the announced competition, which made it possible to relieve the employees, due to the departure of a significant number of technicians and doctors to IBTS. Work on machines for immunoserological testing has increased, and work safety has increased. The department has continued to work successfully overcoming the blood shortages we are facing.
Conclusion Transformation of the Department in accordance with the law was carried out relatively successfully. We believe that the procedure would have been more adequate if the transformation had been carried out in a
timely manner within the period provided by law. We also have future procedures ahead of us, which would ensure that the required standards of the Department are met, as well as its accreditation. We believe that this is one of the first steps taken in order to implement the Law on Transfusion Medicine.

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TESTIRANJE DOBROVOLJNIH DAVAOCA KRVI NA PRISUSTVO HEPATITIS C VIRUSNE INFEKCIJE

Spasić M.
Zavod za transfuziju krvi Niš

Uvod:Hepatitis C virus može dovesti do ciroze jetre ili pojave hepatocelularnog karcinoma.U cilju sprečavanja prenosa hepatitisa C putem transfuzije krvi skrining na prisustvo anti HCV antitela kod dobrovoljnih davaoca krvi obavezan je od 1994 godine u Zavodu za transfuziju krvi Niš a molekularno testiranje je mandatorno u našoj zemlji od 2019 godine.
Cilj:Analiza rezultata testiranja na prisustvo hepatitisa C kod dobrovoljnih davalaca krvi iz Jugoistočne Srbije u periodu 2020-2021.
Materijali i metode:Uzorci krvi dobrovoljnih davaoca uzeti u epruvetama sa antikoagulansom (EDTA) serološki su testirani korišćenjem hemiluminiscentnih testova (Alinity s anti HCV- Abbott,Advia Centaur aHCV-Siemens) ili ELISA testova (Monolisa Ag/At Ultra V2- Biorad),kao i NAT metodom(Cobas MPX). Ponovo reaktivni uzorci na prisustvo anti HCV antitela su po algoritmu testirani potvrdnim testom Inno-Lia HCV Score – Fujirebio.
Rezultati:Na prisustvo anti HCV antitela testirano je ukupno 73716 uzoraka,45 uzorka su ponovo reaktivni na prisustvo anti HCV antitela (12 uzoraka davaoca koji su prvi put dali krv).Kod 10 dobrovoljnih davaoca krvi je potvrđeno prisustvo anti HCV antitela, 3 je bilo neodređeno i 32 negativno nakon potvrdnog testiranja.Pet uzorka davaoca koji su prvi put dali krv je serološki i molekularno bilo reaktivno na markere HCV infekcije.
Zaključak:Prevalenca i incidenca hepatitisa C kod dobrovoljnih davaoca krvi sa područja Jugoistočne Srbije je niska.Uvođenje obaveznog NAT testiranja dobrovoljnih davaoca krvi na prisustvo hepatitisa C značajno je povećalo bezbednost transfuzije krvnih produkata.

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TESTING OF VOLUNTEER BLOOD DONORS FOR THE PRESENCE OF HEPATITIS C VIRUS INFECTION

Spasić M.
Blood Transfusion Institute Niš

Introduction: Hepatitis C virus can lead to cirrhosis of the liver or the appearance of hepatocellular carcinoma. In order to prevent the transmission of hepatitis C through blood transfusion, screening for the presence of anti HCV antibodies in voluntary blood donors has been mandatory since 1994 at the Blood Transfusion Institute Niš, and molecular testing has been introduced as mandatory in our country since 2019.
Objective: Analysis of the results of testing for the presence of hepatitis C in voluntary blood donors from Southeast Serbia in the period 2020-2021.
Materials and methods: Blood samples of voluntary donors were taken in test tubes with anticoagulant (EDTA) and serologically tested using chemiluminescent tests (Alinity s anti HCV-Abbott, Advia Centaur aHCV-Siemens) or ELISA tests (Monolisa Ag/At Ultra V2- Biorad), as well as the NAT method (Cobas MPX). Double reactive samples for anti HCV antibodies were tested according to the algorithm with the
confirmatory test Inno-Lia HCV Score - Fujirebio.
Results: A total of 73716 samples were tested for the presence of anti HCV antibodies, 45 samples were double reactive for the presence of anti HCV antibodies (12 samples from the first-time donors). The
presence of anti HCV antibodies was confirmed in 10 voluntary blood donors, 3 were indefinite and 32 negative after the confirmatory testing. Five samples of donors who gave blood for the first time were serologically and molecularly reactive to markers of HCV infection.
Conclusion: The prevalence and incidence of hepatitis C among voluntary blood donors from Southeastern Serbia is low. The introduction of mandatory NAT testing of voluntary blood donors for the presence of hepatitis C significantly increased the safety of transfusion of blood products.

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MONITORING I EVALUACIJA VREMENA IZDAVANJA REZULTATA NA ODELJENJU ZA TIPIZACIJU TKIVA

Stanković S., Dukić T., Dmitrović J., Jovanović B., Miladinović Ž., Andrić Z.
Odeljenje za tipizaciju tkiva, Institut za transfuziju krvi Srbije, Beograd, Srbija

Uvod: Odeljenje za tipizaciju tkiva kao akreditovana laboratorija od strane Evropske federacije za imunogenetiku (EFI), mora da ispunjava propisane standarde, koji se vremenom revidiraju i dopunjavaju. Jedan od zahteva EFI standarda je praćenje i evaluacija vremena izdavanja rezultata analiza. Cilj rada je da se prikažu rezultati uvođenja monitoringa i evaluacije vremena izdavanja rezultata laboratorijskih ispitivanja. Materijal i metode: Ovim radom obuhvaćeni su rezultati za 14 programa laboratorijskih ispitivanja. Vreme izdavanja rezultata definisano je uputstvom (SOP 096-38 Izdavanje rezultata ispitivanja) na osnovu koga se obavlja praćenje usklađenosti datuma izdavanja rezultata sa definisanim vremenom i beleže se odstupanja u odgovarajuće formulare. Evaluacija je rađena na 6 meseci tokom godinu dana. Prihvatljiv nivo odstupanja je do 5% za svaku grupu rezultata. Rezultati: Ukupno je analizirano 2727 rezultata, od toga 1155 u prvih, a 1572 u drugih 6 meseci. Sa prihvatljivim odstupanjem vremena izdavanja rezultata je bilo 1021 rezultat u prvih 6 meseci, dok je za 4 programa ispitivanja pokazano odstupanje do 40% (14/116; 43/153; 17/46; 12/32), a za dva odstupanje do 75% (31/48; 15/21). Evaluacijom monitoringa ustanovljeno je da je potrebno primeniti korektivne mere u smislu izmene vremenskog opsega izdavanja rezultata u skladu sa realnim kapacitetom laboratorije, potrebama dodatnog testiranja i zahtevima kliničara. U drugih 6 meseci svi rezultati su izdati u okviru korigovanog vremenskog intervala. Zaključak: Uvođenjem praćenja vremena izdavanja rezultata na Odeljenju za tipizaciju tkiva, omogućeno je uočavanje problema u radu laboratorije, sprovođenje korektivnih mera i unapređenje kvaliteta rada u skladu sa standardima.

Ključne reči: kvalitet, monitoring rezultata, evaluacija

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MONITORING AND EVALUATION OF RESULT ISSUE TIME AT THE TISSUE TYPING DEPARTMENT

Stankovic S., Dukic T., Dmitrovic J., Jovanovic B., Miladinovic Z., Andrić Z.
Tissue Typing Department, Blood Transfusion Institute of Serbia

Introduction: The Tissue Typing Department is an accredited laboratory by the European Federation for Immunogenetics (EFI). The standards, which are revised by the responsible authority, must be followed. Monitoring and evaluation of the required time frame for the issuing of the results of analysis is one of them.The aim is to present the results of the introduction of monitoring and evaluation of the required time frame for the preforming results of laboratory tests. Material and methods: The results of 14 laboratory test programs are covered by this study. The required time frame for performing results is defined by Standard Operating Procedures (SOP 096-38-Issuance of the test results). It was monitored whether there were deviations in the time needed for the issuance of the results defined by standards. Any deviation from the defined standards was recorded through certain forms.
The evaluation was done two times a year. The acceptable level of deviation is up to 5% for each group of results. Results: A total of 2727 results were analyzed, of which 1155 in the first half of the year and 1572 in the second. Regarding the results for the first half of the year, in the acceptable time frame, there were 1021 results. For 4 test programs (14/116; 43/153;17/46; and 12/32), the deviation from the defined time frame was up to 40% and for two (31/48; and 15/21) it was 75%. As a result of monitoring, corrective measures were obtained regarding the time frame for issuing test results. The time frame was determined according to the capacity of the laboratory, additional testing and the requirements from the clinics. Regarding the results for the second part of the year, all results were performed within the newly defined time frame. Conclusion: The implementation of monitoring for the time frame for issuing results in the Tissue Typing Department, allows us to identify problems in laboratory work, implement corrective measures, and improve the quality of work in accordance with standards.

Keywords: quality, results monitoring, evaluation

UP 78

DIREKTNI ANTIGLOBULINSKI TEST NA URGENTNOM CENTRU

Đorđević I, Lukić V
Urgentni centar, odeljenje za Kliničku transfuziju i hemovigilancu, Univerzitetski klinički centar Srbije

Uvod
Moderna transfuzija započinje otkrivanjem postojanja krvnih grupa i njihovog značaja za lečenje bolesnika, kao i imunoglobulina i komponenata komplementnog sistema. Uvođenjem Kombsovog testa započeto je rutinsko testiranje pristustva antitela u serumu kao i globulina vezanih za eritrocitne antigene. Do uvođenja monoklonskih antitela u redovnu transfuziološku praksu direktan antiglobulinski test (DAT) je bio od značaja za pored ostalog i za sigurnije određivanje RhD statusa bolesnika.
Cilj
Cilj rada je bio da pokaže koliko je u ispitivanom periodu urađeno DAT prilikom određivanja krvnih grupa i tokom postupka unakrsnih testova kod bolesnika i koliki je značaj ovog testa u redovnoj kliničkoj praksi.
Metoda
Sprovedeno je retrospektivno ispitivanje u periodu od pet meseci tokom 2022 godine na odeljenju za Kliničku transfuziju i hemovigilancu Urgentnog centra, Univerzitetskog kliničkog centra Srbije (UC). DAT je rađen metodom u epruveti, metodom u gel mikroepruveti i metodom imunoadrsorpcije na Immucore aparatu. Ispitivanje je obuhvatalo bolesnike koji su lečeni na svim odeljenjima Univerzitetskog kliničkog centra Srbije. Podaci su dobijeni iz informacionog sistema koji se koristi za hemovigilancu na UCu.
Rezultati
Tokom ispitivanog perioda urađeno je 12374 DAT i to metodom u epruveti 11773 i 6501 metodom imunoapsorpcije i to: tokom određivanja krvnih grupa metodom u epruveti 4431 i metodom imunoadsorpcije 5862. Tokom unakrsnih testova metodom u epruveti je urađeno 7342 DAT i metodom u gel mikroepruveti 639. Pozitivan DAT tokom određivanja krvne grupe je otkriven kod 88 uzoraka i to 5 metodom u epruveti i 83 metodom imunoadsorpcije i 36 metodom imunoadrsorpcije tokom unakrsnih testova. Tokom ispitivanog perioda indetifikovano je 29 antieritrocitnih antitela pri čemu nije bilo biohemijskih potvrđenih znakova hemolize eritrocita.
Zaključak
Sa obzirom na rutinsku primenu monoklonskih antitela i mogućnosti poluatumatskog i automatskog testiranja krvnih grupa i unakrsnih testova, kao i na osnovu dobijenih rezultata neophodno je dodatno razmotriti svrsishodnost rutinske upotrebe DAT tokom ovih postupaka.

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DIRECT ANTIGLOBULIN TEST AT THE EMERGENCY CENTER

Đorđević I, Lukić V.
Emergency Center, Department of Clinical Transfusion and Hemovigilance, University Clinical Center of Serbia

Introduction
Modern transfusion begins with the discovery of the existence of blood groups and their importance for the treatment of patients, as well as immunoglobulins and components of the complement system. With the introduction of the Coombs test has began the routine testing of the presence of antibodies in serum as well as globulins bound to erythrocyte antigens. Until the introduction of monoclonal antibodies into regular transfusion practice, the direct antiglobulin test (DAT) was important for, among other things, more reliable determination of the patient's RhD status.
Objective
The objective of this work was to show how much DAT was performed in the examined period in determination of blood groups and in the procedure of cross-testing in patients and the importance of this test is in regular clinical practice.
Material and methods
A retrospective study was conducted over a period of five months during 2022 at Department of Clinical Transfusion and Hemovigilance in the Emergency Center, University Clinical Center of Serbia (UCS). DAT was performed using the test tube method, the gel microtube method, and the immunoadsorption method on the Immucore apparatus. The study included patients who were treated in all departments of UCS. The data was obtained from the information system used for hemovigilance at UCS.
Results
During the examined period, 12374 DAT were performed using the test tube method 11773 and 6501 using the immunoabsorption method, namely: during the determination of blood groups using the test tube method 4431 and the immunoadsorption method 5862. During the cross-match testings, 7342 DAT were performed using the test tube method and
639 using the gel microtube method. Positive DAT during blood group determination was detected in 88 samples, 5 by the test tube method and 83 by the immunoadsorption method and 36 during cross-match testings. During the investigated period 29 anti-erythrocyte antibodies were identified, while there were no confirmed biochemical signs of erythrocyte hemolysis.
Conclusion
Considering the routine use of monoclonal antibodies and the possibility of semi-automatic and automatic testing of blood groups and cross-match testings, as well as based on the results obtained, it is necessary additionally to consider the expediency of routine use of DAT during these procedures.

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ANALIZA TREBOVANJA KOMPONENTI ERITROCITA- NAMENA I NJIHOVO IZDAVANJE

Radović M, Radović I, Jovanović Srzentić S

Uvod: Odeljenje za pretransfuziona ispitivanja, distribuciju krvi i produkata od krvi i hemovigilancu Instituta za transfuziju krvi Srbije od 15.03.2022. pruža usluge bolničke banke krvi (BBK) za zdravstvene ustanove koje nemaju sopstvenu BBK. Njihov spektar delatnosti je veoma širok i obuhvata internističko i hirurško zbrinjavanje pacijenata od neonatalnog perioda do bolesnika u terminalnim fazama bolesti.
Cilj: Prikaz i analiza strukture pristiglih trebovanja za komponente eritrocita (Er) i izdavanja komponenti po njima.
Metod: Izvršena je analiza podataka iz trebovanja pristiglih u periodu 01.05.2022.-31.08.2022. i iz informacionog sistema Odeljenja.
Rezultati: U posmatranom periodu primljeno je 3278 trebovanja iz 14 državnih i 27 privatnih zdravstvenih ustanova. Od ukupnog broja 3086(94,2%) se odnosilo na trebovanje komponenti Er. Trebovano je 1-6 jedinica Er sa medijanom 2. Na zbrinjavanje akutnog krvarenja odnosilo se 125(4,1%) trebovanja. U terapijske svrhe Er su trebovani 1071(34,7%) puta. Radi planirane intervencije ili porođaja Er su trebovani 1864(60,4%) puta. Bez oznake namene je bilo 26(0,8%) trebovanja. Kod akutnog krvarenja u 11(8,8%) slučajeva spremljeni Er nisu podignuti. Najmanje otkazanih trebovanja ima u terapijske svrhe 37(3,5%). Kod planiranih intervencija Er nisu izdavani po 1580(84,8%) trebovanja.
U 1352 slučaja kada je izvršeno izdavnje, podignute su 1-4 jedinice Er sa medijanom 1.
Zaključak: S obzirom na širok spektar delatnosti zdravstvenih ustanova koje pokrivamo neophodno je sagledavanje njihovih individualnih karakteristika kako bismo bili u stanju da zadovoljimo potrebe njihovih pacijenata. Rutinska primena type and screen pristupa doprinosi efikasnijem funkcionoisanju BBK.
Ključne reči: komonenta eritrocita, trebovanje za krv, bolnička banka krvi

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ANALYSIS OF BLOOD ORDER FORMS- INTENDED USE AND ISSUING OF RED BLOOD CELL UNITS

Radovic M, Radovic I, Jovanovic Srzentic S
Blood Transfusion Institute of Serbia, Belgrade, Serbia

Introduction: Department of pretransfusion testing, distribution of blood and blood products and haemovigilance of Blood Transfusion Institute of Serbia, from March 15th 2022 delivers services of hospital blood bank (HBB) to health institutions who do not have their own HBB. Their spectrum of services is quite broad covering internal medicine and surgical branches for patients of all ages from neonatal period to terminally ill patients.
Objective: To analyse and display structure of received blood order forms for red blood cell (RBC) components and component issuing.
Method: Analysis of blood order forms received between May 1st - August 31st 2022 and data extracted from the information system of the Department.
Results: In a given period a total of 3278 blood order forms from 14 public and 27 private health institutions were received. Of that number 3086(94.2%) were for RBC components. Number of ordered RBC components was 1-6 with a median of 2. For therapy of acute bleeding 125(4.1%) orders were received. For therapy of non-bleeding patients RBC components were ordered 1071(34.7%) times. In 1864(60.4%) of cases order was made for elective surgical intervention or delivery. For 26(0.8%) blood order forms there was no information on intended usage. RBC components prepared for correction of acute bleeding were not requested for issuing in 11(8.8%) cases. The smallest rate of cancelled orders is for non-bleeding patients 37(3.5%). Regarding elective surgery and delivery RBC units were not requested for issuing for 1580(84.8%) of order forms.
In 1352 cases when RBC units were issued, the number of units ranged 1-4, with a median of 1.
Conclusion: Regarding a broad spectrum of medical services in health institutions for whom we conduct HBB services, it is necessary to analyse their individual characteristics in order to meet their patients' needs. Routine employment of type and screen procedure will make HBB operations more effective.
Key Words: red blood cell unit, blood order form, hospital blood bank

UP 80

IZBOR KOMPATIBILNE KRVI ZA PACIJENTE U NEONATALNOM DOBU

Savić A, Radović I, Jovanović Srzentić S
Institut za transfuziju krvi Srbije, Beograd, Srbija

Uvod: U neonatalnom periodu karakteristična je slabija ekspresija odnosno potpuno odsustvo pojedinih antigena (Ag) ugljenohidratne građe (A, B, Lea, Leb, I) kao i moguće prisustvo antieritrocitnih antitela (At) poreklom iz cirkulacije majke. Osim što je za transfuziju potrebno izabrati sa njima kompatibilne Er, bitno je i proceniti njihov potencijal da izazovu hemoliznu bolest novorođenčeta.
Cilj: Prikaz i analiza rezultata imunohematološkog testiranja neonatusa u Institutu za transfuziju krvi Srbije (ITKS) u periodu 15.03.2022-31.08.2022.
Metod: Izvršena je retrospektivna analiza podataka prikupljenih iz informacionog sistema i protokola Odeljenja za pretransfuziona ispitivanja, distribuciju krvi i produkata od krvi i hemovigilancu ITKS. Određivanje krvne grupe (KG) i direktnog antiglobulinskog testa (DAT) rađeno je metodom u gelu na DiaClon ABO/Rh for Newborns DVI+ BioRad Laboratories, Inc. karticama. Skrining At rutinski se radi uz KG metodom u IAT-u u gelu na Coombs Anti-IgG karticama uz korišćenje komercijalnih ID-DiaCell I-II-III i ID-DiaCell ABO eritrocita (Er) istog proizvođača. Identifikacije At su rađene istim metodom sa komercijalnim ID-DiaPanel Er.
Rezultati: U ispitivano periodu određivanje KG i skrining antieritrocitnih antitela urađen je za 448 neonatoloških pacijenata.
Kod 31 (10,4%) neonatusa non-O KG utvrđeno je postojanje prirodnih izohemaglutinina IgG klase transportovanih iz cirkulacije majke. Anti-A je dokazano kod 22 (71,0%), a anti-B kod 9 (29,0%) neonatusa. U 4 (12,9%) slučaja DAT je bio pozitivan. U jednom slučaju anti-A je dokazano samo u eluatu sa DAT-pozitivnih Er.
Antieritrocitna At usmerena na druge klinički značajne krvnogrupne Ag su detektovana kod 5 (1,1%) neonatusa. Dokazane specifičnosti bile su: po 2 (40,0%) slučaja anti-c i anti-D i jedan slučaj (20%) anti-K At. Oba deteta sa anti-c At imala su Rh fenotip CcDee. Deca sa anti-D i anti-K At bila su antigen-negativna.
Zaključak: Skrining klinički značajnih i ABO At klase IgG neophodan je klinički dijagnostički parametar. Standardizacija testiranja na nacionalnom nivou je neophodna za osiguravanje kvaliteta.
Ključne reči: imunohematološko testiranje, neonatus, antieritrocitna antitela

UP 80

SELECTION OF COMPATIBLE BLOOD FOR TRANSFUSION TO NEONATES

Savic A, Radovic I, Jovanovic Srzentic S
Blood Transfusion Institute of Serbia, Belgrade, Serbia

Introduction: Neonatal period is characterized by weaker expression or complete lack of certain carbohydrate antigens (Ag) eg. A, B, Lea, Leb, I and possibility of detection of antierythrocyte antibodies (Ab) of maternal origin. These Abs are important for selection of compatible blood. Also their potential to cause hemolytic disease of newborn must be assessed.
Objectives: To display and analyze immunohaematological test results of neonates at Blood Transfusion Institute of Serbia (BTIS), from March 1st 2022 to August 31th 2022.
Method: Retrospective analysis of data obtained from the information system and protocols of BTIS Department of pretransfusion testing, distribution of blood and blood products and haemovigilance was preformed. ABO/RhD typing and direct antiglobulin testing (DAT) was done in gel on DiaClon ABO/Rh for Newborns DVI+ BioRad Laboratories, Inc. cards. Ab screening was performed in IAT in gel on Coombs Anti-IgG cards with commercial red blood cells (RBC) ID-DiaCell I-II-III and ID-DiaCell ABO form the same manufacturer. Ab identification was carried out by the same method with commercial ID-DiaPanel RBCs.
Results: In a given period type and screen procedure was performed for 448 neonates.
In 31(10.4%) of non-O neonates existence of natural isohemagglutinins of IgG class, actively transported from maternal circulation was established. Anti-A was present in 22(71.0%) and anti-B in 9(29%) neonates. In 4(12.9%) of these cases DAT was positive. In one case anti-A was only identified from eluat of DAT-positive RBCs.
Abs to other clinically important Ags were detected in 5(1.1%) neonates. Their specificities were: anti-c and anti-D, in 2(40.0%) cases each and anti-K in one (20.0%) case. Neonates with anti-c had CcDee Rh-phenotype. Neonates with anti-D and anti-K Abs were negative for corresponding Ags.
Conclusion: Screening of clinically important and ABO Ab of IgG class is necessary clinical diagnostic parameter. Standardization of testing on national level is important for quality assurance.
Key words: immunohaematological testing, neonates, antierithrocite antibodies

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KARAKTERISTIKE HEMOLIZNE BOLESTI FETUSA I NOVOROĐENČETA UZROKOVANE anti-c ANTITELOM – PRIKAZ SLUČAJA

Al Mamoori A. M., Radović I., Jovanović Srzentić S.
Institut za transfuziju krvi Srbije, Beograd, Srbija

Uvod: U hemoliznoj bolesti fetusa i neonatusa (HBFN) anemija nastaje usled ekstravaskularne hemolize eritrocita (Er) uzrokovane majčinim antieritrocitnim antitelima (At) IgG klase. Aktivni transport At u cirkulaciju fetusa započinje oko 16. nedelje gestacije i dostiže maksimum pred porođaj. Po rođenju, usled nezrelosti jetre neonatusa dolazi do naglog porasta indirektnog bilirubina koji može prouzrokovati trajna neurološka oštećenja. U našoj sredini teški oblici HBFN najčešće su uzrokovani anti-D At. Podjednako tešku kliničku sliku može imati i HBFN uzrokovana anti-K i anti-c At.
Prikaz slučaja: Prilikom rutinskog određivanja krvne grupe A RhD-pozitivnog novorođenčeta starog jedan dan uočen pozitivan polispecifični direktni antiglobulinski test (DAT) jačine 3+, pozitivan skrining u indirektnom antiglobulinskom testu (IAT-u) i pozitivna reakcija sa A1 ER u IAT-u. Zbog nedovoljne količine plazme u uzorku izvedena kisela elucija At sa Er korišćenjem DiaCidel BioRad Laboratories, Inc. kita. U eluatu dokazano anti-c At IgG klase. Monoklonskim serumima sa At IgM klase određen Rh fenotip: CcDee. Uspostavljen kontakt sa neonatologom i obavešten je o nalazu. Primljeno novo trebovanje za 2 jedinice krvi za eksangvino transfuziju. Identifikacija At iz novog uzorka potvrdila je nalaz iz eluata. Pripremljene dve jedinice kompatibilnih O RhD-pozitivnih Er fenotipa CCDee u AB plazmi koje su uspešno primenjene.
Zaključak: Ovde je prezentovan težak slučaj HBFN uzrokovan ne tako čestim At. Zbog neadekvatnog imunohematološkog praćenja u trudnoći propuštena je prilika da se dijagnoza postavi prenatalno. Metodom elucije prevaziđen je problem male količine inicijalnog uzorka i omogućen pravovremeni izbor jedinica Er čija je kompatibilnost potvrđena testiranjem sa novim uzorkom.
Ključne reči: antieritrocitna antitela, elucija, hemolizna bolest fetusa i neonatusa

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CHARACTERISTICS OF HEMOLYTIC DISEASE OF FETUS AND NEWBORN CAUSED BY anti-c ANTIBODY- CASE REPORT

Al Mamoori A. M, Radovic I, Jovanovic Srzentic S
Blood Transfusion Institute of Serbia, Belgrade, Serbia

Intorduction: Extravascular hemolysis of erythrocytes (Er) mediated by maternal IgG class antibodies (Ab) is a causative agent of anemia in hemolytic disease of fetus and newborn (HDFN). Active transport of Abs into a fetal circulation begins at 16th week of gestation and reaches its' maximum just before birth. After birth, due to not fully developed hepatic function of newborn, steep increase in unconjugated bilirubin may cause permanent neurological damage. In our population severe cases of HDFN are predominantly caused by anti-D Ab. Equally dramatic clinical presentation of HDFN may result from the presence of anti-K and anti-c Ab.
Cause presentation: During routine type and screen procedure of a group A RhD-positive, one day old newborn positive polyspecific direct antiglobulin test (DAT) 3+ in strength, positive Ab screen in indirect antiglobulin test (IAT) and positive reaction with A1 ER in IAT were observed. Amount of plasma in the sample was insufficient for Ab identification so acid elution of Abs from neonatal ERs was performed using DiaCidel BioRad Laboratories, Inc. kit. Anti-c Ab of IgG class was identified in eluat. Rh phenotype was determined using IgM containing monoclonal antisera as CcDee. Neonatologist was immediately contacted and informed of findings. Two units of blood for exchange transfusion were requested by the neonatologist. Ab identification from a new sample confirmed finding from the elute. Two units of compatible O RhD-positive ER Rh phenotype CCDee in AB plasma were prepared and successfully administered.
Conclusion: We presented severe case of HDFN caused by not so prevalent Ab. Due to absence of immunohaematological testing in pregnancy chance for prenatal diagnosis of condition was omitted. Problem of small amount of the initial sample was solved by elution method which enabled timely selection of units of ER whose compatibility was confirmed by testing with new sample.
Key words: antierythrocite antibodies, elution, hemolytic disease of fetus and newborn

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VIŠEINSTITUCIONALNA SARADNJA U TRANSFUZIOLOŠKOM ZBRINJAVANJU SENZIBILISANOG POLITRANSFUNDOVANOG PEDIJATRIJSKOG BOLESNIKA

Katić M[1], Stanojević Z[1], Kuzmanović M[1,2], Šerbić O[1,2], Radonjić Z[1], Andrić B[1], Popović M[3], Dukić Novaković M[3], Jovičić M[3], Radović I[3], Jovanović Srzentić S[3], Antić A[4], Vučetić D[5], Gojkov D[5], Popović Dmitrović J[5], Ivanović Stojčević D[5], Stamatović Janićijević N[5], Živković M[5]

[1] Institut za zdravstvenu zaštitu majke i deteta Srbije "Dr Vukan Čupić " IZZMID
[2] Medicinski fakulet Univerziteta u Beogradu
[3] Institut za transfuziju krvi Srbije ITKS
[4] Zavod za transfuziju krvi Niš ZTK NIŠ,
[5] Institut za transfuziologiju i hemobiologiju VMA Beograd (ITHB VMA)

Uvod Imunizacija na eritrocitne antigene nije retka pojava kod politransfundovanih hematoonkoloških bolesnika. Ako postoji više aloantitela nastaje problem obezbeđivanja kompatibilnih jedinica eritrocita (ER).

Cilj rada Prikazati značaj saradnje više transfuzijskih ustanova radi obezbeđivanja dovoljnih količina fenotipiziranih eritrocita za zbrinjavanje višestruko senzibilisanog deteta.

Materijal i metode Za imunohematološko testiranje korišćene su gel kartice i metoda u tečnoj fazi, tehnika je bila manuelna i automatizovani imunohematološki analizator.

Rezultati Bolesnica R.J (12 god), leči se u IZZMID od 2018, krvna grupa B RhD(+) Dg. Neoplazma malignum cerebri, Anaemia aplastica. U uzorku plazme bolesnice identifikovana su antitela: anti-E, anti-Jkb, anti-Leb i anti-Kpa. Do marta 2022. ukupno je primila 122 jedinice fenotipiziranih ER. Iz ITKS izdata je 101 jedinica (B RhD+/-66 i O RhD+/-35), od toga resuspendovanih ER osiromašenih leukocitima i trombocitima 29, a filtrovanih ER 72 jedinice. Urađeno je 233 interreakcije, 457 fenotipizacija. Od 2018. postoji registar tipiziranih davalaca njih 8, koji se pozivaju po potrebi bolesnice. Od 2020. u zbrinjavanje bolesnice uključio se ITHBVMA, izdao je 15 jedinica ER (ORhD+/-10,B RhD+/-5), od toga 13 jedinica filtrovanih ER, 2 jedinice resuspendovanih ER. Za pronalaženje prvih 6 kompatibilnih jedinica fenotipizirano je 245 jedinica ER. Od juna 2021. pozivaju se davaoci po zahtevu (dvojica) i izdano je još 9 jedinica ER. U 2020. Er za R.J. obezbeđuje i ZTK Niš, ukupno 7 jedinica (6 B RhD poz/1ORhD-) od koji je jedna jedinica ER filtrirana. U ZTK Niš fenotipizirano 105 jedinica ER. Bolesnici je pripremljeno 75 jedinica BRhD+/2RhD- i 22 O RhD+/25RhD- ER.

Zaključak: Za bolesnicu je tipizirano 807 jedinica ER. Od primljenih jedinica ER 37% bilo je krvne grupe O a 20% RhD negativnih. Za obezbeđivanje kompatibilnih jedinica ER neophodno je angažovanje više transfuzijskih institucija. Formiranje registara davalaca koji daju ciljano krv nakon zahteva kliničkog lekara omogućilo je znatno brže zbrinjavanje.

Ključne reči: imunizacija, fenotipizacija, eritrociti

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MULTI-INSTITUTIONAL COOPERATION IN THE TRANSFUSION CARE OF A SENSITIZED POLYTRANSFUSED PEDIATRIC PATIENT

Katić M[1], Stanojević Z[1], Kuzmanović M[1,2], Šerbić O[1,2], Radonjić Z[1], Andrić B[1], Popović M[3], Dukić Novaković M[3], Jovičić M[3], Radović I[3], Jovanović Srzentić S[3], Antić A[4], Vučetić D[5], Gojkov D[5], Popović Dmitrović J[5], Ivanović Stojčević D[5], Stamatović Janićijević N[5], Živković M[5]

[1] Mother and Child Health Care Institute of Serbia "Dr. Vukan Čupić"
[2] Faculty of Medicine, University of Belgrade
[3] Blood Transfusion Institute of Serbia
[4] Blood Transfusion Institute Niš
[5] Institute for Transfusion and Hemobiology Military Medical Academy Belgrade (ITHBMMA)

Introduction Immunization against red blood cell antigens (RBCs) is not a rare occurrence in polytransfused hemato-oncology patients. If there are multiple alloantibodies, the problem of providing compatible RBCs units arises.

The aim is to show the importance of the cooperation of several transfusion institutions in order to ensure sufficient quantities of phenotyped RBC for the multiple sensitized child.

Material and methods For immunohaematological testing, gel cards/ liquid phase methods were used. The techniques were manual/automated immunohaematological analyzer.

Results Patient R.J (12 yr), treated since 2018, B RhD(+) Dg. Neoplasma malignum cerebri, Anaemia aplastica. Antibodies were identified: anti-E, anti-Jkb, anti- Leb and anti-Kpa. She received a total of 122 units of phenotyped RBCs until March 2022. From BTIS 101 RBCs units (B RhD+/-66 and O RhD+/-35) were issued, of which 29 were resuspended RBCs, and 72 were filtered RBCs. There were 233 interactions, and 457 phenotyping performed. The register of typed donors (8), was established in 2018. Since 2020 ITHBMMA has been involved in the care of the patient, issuing 15 units of RBCs (ORhD+/-10, B RhD+/-5), of which 13 units of filtered RBCs, 2 units of resuspended RBCs. The 245 RBCs units were phenotyped to find the first 6 compatible units. From June 2021; two donors invited by request, and 9 units more of RBCs have been issued. In 2020; RBCs were also provided by BTI Niš, a total of 7 units (6 B RhD pos/1ORhD-), of which one was filtered RBC. In BTI Niš, 105 RBCs units were phenotyped. The 75 units of BRhD+/2RhD- and 22 O RhD+/24RhD- RBCs were prepared for the patient.

Conclusion: The total of 807 RBC units were phenotyped. The RBC units applied 37% were blood type O, 20% RhD -. In order to provide compatible RBCs units, it is necessary to engage several transfusion institutions. Forming registers of donors who give blood after the request of a clinical physician has enabled significantly faster treatment.

Key words: immunization, phenotyping, erythrocytes

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IZOLACIJA DNK KAO INTEGRALNI DEO MOLEKULARNE TIPIZACIJE ERITROCITNIH I TROMBOCITNIH ANTIGENA

Pelemiš V[1], Radović I[1], Vlatković A[1], Jovanović Srzentić S[1], Nikola Kačaki[2]
Institut za transfuziju krvi Srbije (ITKS)
Odeljenje za imunohematologiju1, Odeljenje za tipizaciju tkiva2

Uvod: Molekularna imunohematološka ispitivanja postala su sastavni deo imunohematološke prakse. Izolacija DNK ključni je korak u laboratorijskim postupcima potrebnim za izvođenje daljih molekularnih testiranja. Postoji nekoliko metoda izolovanja DNK, ali se u našoj laboratoriji ekstrakcija DNK vrši manuelnom metodom iz cele krvi.

Cilj: Prikazati postupke prikupljanja, skladištenja i manuelne ekstrakcije nukleinskih kiselina koji mogu potencijalno uticati na uspeh izolacije DNK, kao i molekularnu tipizaciju eritrocitnih i trombocitnih antigena na aparatu FluoVista.

Materijal i metode: Uzorak cele krvi mora da bude pravilno obeležen, a uzima se na odgovarajućem antikoagulansu (EDTA, finalno 10% v/v). U periodu od uzimanja do prijema, uzorak mora biti čuvan na konstantnoj temperaturi po propisima proizvođača. Za potrebu izolacije genomske DNK koristimo komercijalni kit QIAamp DNA Blood mini kit, QIAGEN, Germany. Za proveru uspešnosti samog postupka ekstrakcije nukleinske kiseline neophodno je odrediti koncentraciju i čistoću DNK. Sam postupak testiranja i interpretacije rezultata vrši se na aparatu FluoVista, metodom Fluogene PCR-SSP, sa fluorescentnim očitavanjem rezultata.

Rezultati: Na Odeljenju za imunohematološka ispitivanja ITKS od početka 2021. uspešno se radi izolacija DNK, što se potvrđuje odgovarajućim vrednostima koncentracije i čistoće na aparatu NanoDrop. Koncentracije su se kretale od 25,0 do 50,2 ng/µl, a čistoća od 1,77 do 1,84, što je zadovoljavalo uslove za rad metodom FluoGene. U periodu od 2020. do 2022. ispitana su 22 uzorka, RhD-negativnih osoba, koje su u fenotipu imale C i ili E antigen, kao i 20 osoba sa serološki slabim D antigenom. D weak tip 1 i tip 3 dokazani su u po 10 slučajeva. Genotipizacija HPA antigena u cilju dijagnostike FNAIT urađena je u 10 slučajeva, a inkompatibilnost u HPA antigenima oca i majke dokazana je u 8 slučajeva.

Zaključak: Primena savremenih metoda značajno doprinosi unapređenju rada u imunohematološkim laboratorijama, uz strogo poštovanje svih test procedura.

Ključne reči: krvne grupe, genotipizacija, izolacija DNK

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ISOLATION OF DNA AS AN INTEGRAL PART OF OF RED CELL AND PLATELET ANTIGENS GENOTYPING

Pelemiš V[1], Radović I[1], Vlatković A[1], Jovanović Srzentić S[1], Nikola Kačaki[2]
[1]Blood Transfusion Institute of Serbia (BTIS)
[2]Department for Immunohaematology1, Department for HLA typing

Introduction: Molecular immunohaematological tests have become an integral part of immunohaematological practice. Isolation of DNA is a key step. There are several methods of DNA isolation, but in our laboratory DNA extraction is done manually from whole blood.

Objective: To describe procedures for collection, storage and manual extraction of nucleic acids that can potentially affect the success of DNA isolation, as well as molecular typing of red cell and platelet antigens on the FluoVista device.

Material and methods: Properly labelled blood sample is taken on a suitable anticoagulant (EDTA, final 10% v/v). For the isolation of genomic DNA, we use the commercial kit QIAamp DNA Blood mini kit, QIAGEN, Germany. The actual procedure of testing and interpretation of the results is performed on the FluoVista device, using the Fluogene PCR-SSP method, with fluorescent reading of the results.

Results: DNA isolation has been successfully performed at the Department of immunohaematology BTIS since the beginning of 2021, which is confirmed by the appropriate concentration and purity values on the NanoDrop device. Concentrations ranged from 25.0 to 50.2 ng/µl, and purity from 1.77 to 1.84, which satisfied the conditions for working with the FluoGene method. In the period from 2020 to 2022, 22 samples of RhD-negative persons, whose phenotype had C and or E antigen, as well as 20 persons with serologically weak D antigen, were examined. D weak type 1 and type 3 were proven in 10 cases each. HPA antigen genotyping in order to diagnose FNAIT was performed in 10 cases, and incompatibility in HPA antigens of father and mother was proven in 8 cases.

Conclusion: The application of sophisticated methods significantly contributes to the improvement of work in immunohaematological laboratories, with strict observance of all test procedures.

Key words: blood groups, genotyping, DNA isolation

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REZULTATI TRANSFUZIOLOŠKIH ISPITIVANJA PRIMENOM APARATA IH-500-DVOGODIŠNJE ISKUSTVO-

Pešić Stevanović I, Ljubenov M, Milošević S, Bojčetić Panovski B, Ristić S.
Ginekološko-akušerska klinika „Narodni front", Beograd, Srbija

UVOD: Stupanjem na snagu Zakona o transfuzijskoj medicini i podzakonskih pravilnika predviđena je automatizacija u ovlašćenim transfuzijskim ustanovama i bolničkim bankama krvi u Republici Srbiji. Primena automatskih analizatora u transfuzioloških ispitivanjima poboljšava kvalitet, efikasnost i organizaciju rada.
CILJ RADA: Prikazati dvogodišnje rezultate rada i transfuzioloških ispitivanja uvođenjem aparata IH -500.
METOD RADA: Retrospektivnom metodom izvršena je analiza rada aparata IH-500 kao i pisanih i informacionih zapisa o rezultatima transfuzioloških ispitivanja korišćenjem gel tehnike u periodu od 01. 01. 2018. - 31. 12. 2019. godine.
REZULTATI: U Odeljenju bolničke banke krvi Ginekološko-akušerske klinike „Narodni front" gel aglutinaciona tehnika ispitivanja uvedena je 2004. godine a aparat IH-500 jula 2017. godine. Zdravstveni informacioni sistem uveden je 2016. godine a informacioni sistem Delphyn 2017. godine. U periodu od 01. 01. 2018. - 31. 12. 2019. godine na aparatu IH-500 urađeno je ukupno 48079 testova: krvnih grupa novorođenčadi 10908, krvnih grupa pacijentkinja hospitalizovanih u Klinici 5857, Rhesus fenotipova 798, direktnih Coombs-ovih testova 12922, indirektnih Coombs-ovih testova 13878, identifikacija antieritrocitnih antitela 285 i interreakcija 3431. Takođe u istom vremenskom periodu urađeno je 280 testova kontrole kvaliteta.
ZAKLJUČAK: Primena automatskog aparata za transuziološka testiranja IH-500 u našem Odeljenju sa bolničkom bankom krvi omogućila je izvođenje svih transfuzioloških ispitivanja saglasno Zakonu i važećim pravilnicima u Republici Srbiji. Ovim je značajno poboljšan kvalitet rada, povećana efikasnost u radu, omogućena visoka specifičnost i standardizacija a pacijentima bezbednija primena produkata od krvi.
Superiornost automatizacije ogleda se i u uniformnosti, smanjenju vremena izvođenja testova i troškova angažovanja pomoćnog osoblja, a s druge strane obezbeđuje sigurnost, senzitivnost i bezbednost u sistemu identifikacije pacijenata kojima je neophodno lečenje primenom produkata od krvi.
Ključne reči: IH-500, gel aglutinaciona tehnika

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RESULTS OF TRANSFUSION TESTS USING THE IH-500 TWO YEARS OF EXPERIENCE

Pešić Stevanović I, Ljubenov M, Milošević S, Ristić S, Bojčetić Panovski B
Clinic of gynecology and obstetrics „Narodni front", Beograd

Introduction:In the Legislative process with the entry into force of the Law on Transfusion Medicine and some other regulations, automation is foreseen in authorized transfusion institutions and hospital Blood banks in the Republic of Serbia. The use of automatic analyzers in transfusion tests improves the quality, efficiency and work organization.
Objectives: Presentation of two-year results and transfusion tests after the introduction of the IH-500 instrument.
Methods: In retrospective study, analyzing of the operation of the IH-500 instrument as well as written and informational records on the results of transfusion tests was undertaken using the gel technique in the period from January 1st, 2018 to December 31, 2019.
Results: In the department of the hospital Blood Bank in the Clinic of Gynecology and Obstetrics "Narodni front", the gel agglutination test technique was introduced in 2004, and the IH-500 instrument was introduced in July 2017. The health information system was introduced in 2016 and Delphyn Data System in 2017. In the period from January 1, 2018 to December 31, 2019, a total of 48,079 tests were performed on the IH-500 instrument: blood groups of newborns 10,908, blood groups of female patients hospitalized in the clinic 5,857, Rhesus phenotypes 798, direct Coombs tests 12922, indirect Coombs tests 13878, identification of anti-erythrocyte antibodies 285 and interactions 3431. Also in the same period of time, 280 quality control tests were performed.
Conclusion:The application of the IH-500 automatic instrument for transfusion testing in our department with the hospital Blood Bank ensured the performance of all transfusion tests in accordance with the Law and relevant regulations in the Republic of Serbia. That significantly improved the quality of work, increased work efficiency, enabled high specificity and standardization and safer application of blood products.
The superiority of automation may also be reflected in the uniformity, reduction in the time of performing tests and the cost of hiring support staff, on the other hand, it ensures safety, sensitivity and security in the system of identifying patients who need treatment with the use of blood products.
Keywords: IH-500, gel agglutination technique

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INVESTIGATION OF THE RATIONALITY OF REGULAR USE OF DIRECT ANTIGLOBULIN TEST AT THE DEPARTMENT FOR CLINICAL TRANSFUSION AND CHEMOVIGILANCE OF THE EMERGENCY CENTER OF THE UNIVERSITY CLINICAL CENTER OF SERBIA

Đorđević N, Lukić V.
Emergency room, University clinical center of Serbia

Introduction: Until the introduction of the Coombs test, it was only possible to detect erythrocyte agglutination and perform cross-match tests at room temperature due to the pentameric structure of the IgM antibody. With the discovery of the importance of the antihuman globulin test (AHG) in the detection of globulins, immunoglobulins of the IgG class as well as complement components, indirect and direct antiglobulin tests (IAT and DAT) were introduced into the regular work of transfusion services. Today, during blood grouping and cross-match testing procedures, monoclonal antibodies for DAT are widely used, as well as various methods.
Objective: The objective of the work was to show how much money was spent in the examined period for performing DAT tests depending on the method .
Material and method: A retrospective study was conducted in the period from March to August 2022 at the Department of Clinical Transfusion and Hemovigilance of the Emergency room (ER) of the University Clinical Center of Serbia (UCCS). DAT was performed using the tube method, the gel method in a microtube, and the semi-automated solid medium method on the Immucore apparatus. The study included patients who were treated in all departments of the UCCS. Data were obtained from the information system used for hemovigilance at ER.
Results: During the examined period, 12374 DAT were performed, including 10293 tests during determination of blood groups and 2081 during cross-match tests. During the determination of blood groups, DAT was performed using the test tube method in 4431 samples and 5862 samples for method in a solid medium. During the cross-match tests, 7342 DAT were performed using the test tube method and 639 using the gel microtube method. Based on the available data on the prices of AHG reagents, test tubes, gel microtubes and solid medium testing, the total cost for DAT testing was 3,000,000 dinars for the examined period.
Conclusion: By introducing the standard application of monoclonal antibodies and the possibility of semi-automatic and automatic testing of blood groups and cross-match testing, as well as based on the obtained data on the cost of routine DAT testing, it is necessary to additionally consider the expediency of routine use of DAT during these procedures with the idea of redirecting funds for further improvement of laboratory work .
Key words:
Direct antiglobulin test, antihuman globulin test

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TEHNIČARSKE POSTER PREZENTACIJE
TECHNICIAN POSTER PRESENTATIONS

HOTEL CROWNE PLAZA
Beograd, Srbija / Belgrade, Serbia
9-12. novembar 2022. / November 9th-12th 2022

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DIJAGNOSTIKA SOLUBILNOG ANTIGENA-A NAKON ABO INKOMPATIBILNE ALOGENE TRANSPLANTACIJE MATIČNIH ĆELIJA HEMATOPOEZE METODOM ADSORPCIJE-ELUCIJE

Vitorović V[1], Pavlović O[1], Katić M[1], Andrić B[1], Šerbić O[1,2], Radonjić Z[1], Vujić D[2,1], Zečević Z[2,1], Simić M[1], Gobeljić B[1]
[1] Institut za zdravstvenu zaštitu majke i deteta Srbije „Dr Vukan Čupić", Beograd
[2] Medicinski fakultet Univerziteta u Beogradu, Beograd

Uvod: Redovno praćenje promena krvne grupe nakon ABO inkompatibilne alogene transplantacije matičnih ćelija hematopoeze i ispravno serološko tumačenje rezultata važan su deo posttransplantacione kontrole pacijenata i ishoda transplantacije. U nekim slučajevima, antigen početne krvne grupe primaoca i dalje se sintetiše u nehematopoetskim organima primaoca, izlučuje se i adsorbuje na eritrocitima stvorenih od donorskih matičnih ćelija hematopoeze (MĆH).
Cilj: Prikaz imunohematološke dijagnostike solubilnog antigena-A kod pacijenta nakon minor ABO inkompatibilne transplantacije matičnih ćelija hematopeze.
Materijal i metode: Primenjena je metoda adsorpcije-elucije upotrebom tečne faze (epruveta), gel metode (kartica) i manuelne/automatizovane tehnike (IH-500).
Rezultati: Naša bolesnica I.Š. je 8-godišnja devojčica AB RhD - negativne krvne grupe. sa akutnom limfoblastnom leukemijom transplantirana MĆH iz kostne srži od HLA- podudarnog srodnog donora B RhD+ krvne grupe. Šest meseci nakon transplantacije, registrovano je prisustvo perzistentnog antigena-A, uprkos 100% himerizmu. Izvršili smo metodu adsorpcije-elucije da bismo potvrdili da je ovaj antigen solubilan. Korišćeni su eritrociti ORhD - negativni ccddee zdravog donora koji su pomešani sa plazmom pacijenta i ostavljeni preko noći na + 4ºC. Nakon pranja eritrocita fiziološkim rastvorom, eritrociti su podeljeni u dve epruvete. U prvu epruvetu (A) dodat je monoklonski serum anti-A, u epruvetu (B) anti-B. Epruvete su ostavliene preko noći na + 4ºC radi adsorpcije antitela od strane antigena na eritrocitima. Višak antitela uklonjen je ispiranjem fiziološkim rastvorom. Za eluciju antitela sa antigena na eritrocitima dodato je 1200 µL fiziološkog rastvora, a zatim su ćelije inkubirane na 52ºC 10 minuta i centrifugirane. Eluatima su dodavani A1, A2, B i O eritrociti. Eluat A pokazao je aglutinaciju jačine 3+ sa A1 eritrocitima i aglutinaciju 2+ sa A2 eritrocitima.
Zaključak: Metoda adsorpcije-elucije je jeftina i jednostavna metoda kojom se može potvrditi solubilni antigen. Važno je izvršiti detaljne analize određivanja krvne grupe nakon ABO inkompatibilne alogene transplantacije MĆH, posebno ako se planira transfuzija eritrocita bolesniku.
Ključne reči: solubilni antigen, adsorbcija-elucija, transplantacija

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IDENTIFICATION OF SOLUBLE ANTIGEN –A- AFTER ABO INCOMPATIBLE ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION BY THE ADSORBTION-ELUTION STUDY

Vitorović V[1], Pavlović O[1], Katić M[1], Andrić B[1], Šerbić O[1,2], Radonjić Z[1], Vujić D[2,1], Zečević Z[2,1], Simić M[1], Gobeljić B[1]
[1] Mother and Child Health Care Institute of Serbia „Dr Vukan Čupić", Belgrade
[2] University of Belgrade, Faculty of Medicine, Belgrade

Introduction: Regular monitoring of blood group changes after ABO incompatible (ABOi) allogeneic hematopoietic stem cell transplantation (HSCT) and correct serologic interpretation of results are an important part of monitoring these patients and transplantation outcomes. In some cases, the antigen of the recipient's original blood type persistently synthesized in the recipient's non-hematopoietic organs has been secreted and adsorbed on the surface of donor-derived red blood cells (RBCs).
Aim: To show the immunohaematological study for proof of soluble antigen A in patient after minor ABOi HSCT.
Material and methods: We performed adsorbtion-elution study using (tube) and gel (card) method and manuel/automated technique (IH 500).
Results: Our patient Š.I. was 8-year-old girl, AB RhD -, with acute lymphoblastic leukemia, transplanted with a bone marrow from HLA-matched related donor blood group BRhD+. The presence of persistent antigen A was registered six months after HSCT, despite 100% chimerism. We performed an adsorbtion-elution study to confirm that this antigen is soluble. A healthy donor's ORhD -, ccddee RBCs were mixed with patient's plasma and stored overnight at + 4°C. After being washed with saline, we devided RBCs fraction in two tubes, added monoclonal anti A antibody in the first tube (A), and anti B in second tube (B) and stored overnight at + 4°C for the adsorption of antibodies by antigens on RBCs. Excess antibodies were removed by washing with saline. For the elution of antibodies from antigens on RBCs, 1200 µL of saline was added and then cells were incubated at +52°C for 10 minutes and centrifuged. The eluate was reacted with A1, A2, B and O RBCs. Results of eluat agglutination showed strength 3+ with A1 RBCs and 2+ with A2 RBCs.
Conclusion: The adsorbtion-elution study is cheap and simple method that can be used to confirm soluble antigen. It is important to perform detailed examination to determine the precise blood type after ABOi HSCT, especially when transfusion of RBCs is planned.
Key words: soluble antigen, adsorbtion-elution, transplantation

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DOBROVOLJNO DARIVANJE KRVI NA PODRUČJU REGIJE PRIJEDOR, PERIOD 2011-2021. GODINE

Radinović B, Tatić Sevimli D
Zavod za transfuzijsku medicine Republike Srpske, Prijedor, BiH

Uvod: Zavod za transfuzijsku medicinu Republike Srpske sastoji se od deset transfuzioloških službi, među kojima je i transfuzija Prijedor. Njen osnovni zadatak je obezbijediti dovoljne količine krvi pacijentima s prijedorske regije.
Cilj: Prikazati dobrovoljno darivanje na području prijedorske regije u desetogodišnjem periodu, te uporediti statistiku obrađenih davanja u službi u odnosu na terensko darivanje krvi, kao i prikazati razloge zbog kojih davaoci nisu mogli darivati krv.
Materijal i metode: Analiziran je desetogodišnji izvještaj informacionog sistema prijedorske transfuzije, koji je dio integrisanog sistema Zavoda, te protokoli rada službe u periodu od 2011. do 2021. godine.
Rezultati: U periodu od 2011-2021. godine, ukupno je pregledano 31.922 davalaca. Krv je na području prijedorske regije dalo 28.904 (90,5%) davalaca, od čega je 24.624 (85%) davalaca krv darivalo u službi, dok je 4.280 (15%) na terenu. U navedenom izvještaju, 3.018(9,5%) davalaca iz nekog razloga nisu mogli darivati krv. Od tog broja u službi 2617 davalaca (86,7%), na terenu 401 (13,3%). Najviše je vraćeno na ljekarskom pregledu 1860 (62%), u službi 1663 (89,4%), na terenu 197 (10,6%). Zbog niske vrijednosti hemoglobina, 864 (28,8 %) davalaca nisu darivali krv, u službi 697 (80,6%), na terenu 167 (19,3%). Zbog ostalih razloga krv nije dalo 294 (9,81%) davalaca, u službi 257 (87,4%), na terenu 37 (12,6%).
Zaključak: Godina iz navedenog perioda, u kojoj je uzeto najviše doza, jeste 2018.u kojoj je krv darovalo 3.192 davalaca, dok je godina sa najmanjim brojem davanja bila 2020-a, sa 2.200 uzetih doza krvi. Zahvaljujući modernizaciji rada, promociji dobrovoljnog davalaštva, te sve boljoj saradnji sa mnogim aktivima DDK, na području regije Prijedor, darivanje krvi je bilo u konstantnom porastu, dok se evidentan pad desio zbog pandemije korona virusa kao uostalom i u cijelom svijetu u toku 2020.godine. Relaksacijom kovid mjera, uvedenih zbog pandemije korona virusom, ponovo je došlo do porasta broja uzetih doza krvi.
Ključne riječi: Davaoc, transfuzija, Prijedor

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SPROVOĐENJE EKSTERNIH MEĐULABORATORIJSKIH KONTROLA NA ODSEKU ZA TESTIRANJE MARKERA TRANSFUZIJOM PRENOSIVIH BOLESTI MOLEKULARNOM TEHNIKOM U INSTITUTU ZA TRANSFUZIJU KRVI SRBIJE

Simonović D., Antonijević I., Milosavljević S., Stefanović S., Veličković J., Vuković N., Vušković A., Kovačević M., Dukić M.
Institut za transfuziju krvi Srbije, Beograd

UVOD: Eksterne međulaboratorijske kontrole , Proficiency testing (PT) su važan faktor sigurnosti kvaliteta rada laboratorije. Molekularno testiranje markera transfuzijom prenosivih bolesti u Institutu za transfuziju krvi Srbije se obavlja od 2019. godine za sve uzorke dobrovoljnih davalaca krvi i komponenata krvi prikupljenih na teritoriji Republike Srbije.
CILJ: Prikaz rezultata uspešnosti rada Odseka za testiranje markera transfuzijom prenosivih bolesti molekularnom tehnikom u programima eksternih kontrola kvaliteta rada - European Directorate for the Quality of Medicines & HealthCare (EDQM) i Quality Control for Molecular Diagnostics (QCMD) u perodu 2020-2022. godine.
METODE: Ispitivanje i analiza nepoznatih uzoraka sprovodi se istim metodama i tehnikama koje laboratorija koristi u rutinskom radu. Ispitivanje prisustva HBV, HCV, HIV molekularnom metodom (NAT) u uzorcima eksternih kontrola obavljeno je na aparatima Roche Cobas 6800. Testiranje je sprovodeno pojedinačnim postavljanjem uzoraka-individualno testiranje (ID).
REZULTATI: Od 2020. do 2022.godine sprovedene su tri studije u okviru EDQM programa. U svakom programu testirano je po 5 uzoraka na oba aparata , pri čemu su dobijeni identični rezultati na oba aparata. Od 2021. godine laboratorija se uključila u QCMD program. Kontrole su sprovedene u 2021. i 2022. godini. Paneli za testiranje su sadržavali po 8 uzoraka. U oba programa eksternih kontrola kvaliteta rada, u svim do sada izvedenim studijama uspešnost rada laboratorije je bila 100%.
ZAKLJUČAK: Učešće u PT šemama omogućava poređenje vlastitih rezultata sa rezultatima iz drugih laboratoratorija, te redovnu, objektivnu i nezavisnu procenu kvaliteta rutinskog rada. Zadovoljavajući rezultati kontrola kvaliteta rada potvrđuju preciznost i tačnost rada laboratorije, što doprinosi bezbednosti i kvalitetu krvi i krvnih komponenata.

Ključne reči: Eksterne međulaboratorijske kontrole, NAT, kvalitet rada

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EXTERNAL INTERLABORATORY CONTROLS ON THE DEPARTMENT FOR TESTING TRANSFUSION TRANSMISSIBLE DISEASE MARKERS BY MOLECULAR TECHNIQUE AT THE NATIONAL BLOOD TRANSFUSION INSTITUTE OF SERBIA

Simonović D., Antonijević I., Milosavljević S., Stefanović S., Veličković J., Vuković N., Vušković A., Kovačević M., Dukić M.
National Blood Transfusion Institute of Serbia, Belgrade

INTRODUCTION: External inter-laboratory controls, Proficiency testing (PT) are an important factor in the quality assurance of laboratory work. Molecular testing of transfusion-transmissible disease markers at the National Blood Transfusion Institute of Serbia has been performed since 2019. for all samples of voluntary blood donors and blood components collected on the territory of the Republic of Serbia.
OBJECTIVE: Presentation of the work results on the Department for testing transfusion transmissible disease markers by Molecular Technique in the programs of external quality control - European Directorate for the Quality of Medicines & HealthCare (EDQM) and Quality Control for Molecular Diagnostics (QCMD) in the period 2020-2022.
METHODS: Examination and analysis of unknown samples is carried out using the same methods and techniques that the laboratory uses in routine work. Examination of the presence of HBV, HCV, HIV by the molecular method (NAT) in the samples of external controls was performed on Roche Cobas 6800 devices. The testing was carried out by placing individual samples - individual testing (ID).
RESULTS: From 2020 to 2022, three studies were conducted within the EDQM program. In each program, 5 samples were tested on both devices, and identical results were obtained on both devices. From 2021, the laboratory joined to the QCMD program. Controls were carried out in 2021 and 2022. The each test panel contained 8 samples. In both programs of external quality control, in all studies performed so far, the success of the laboratory work was 100%.
CONCLUSION: Participation in PT schemes enables comparison of own results with results from other laboratories, as well as regular, objective and independent assessment of the quality of routine work. Satisfactory results of work quality controls confirm the precision and accuracy of laboratory work, which contributes to the safety and quality of blood and blood components.
Keywords: External interlaboratory controls, NAT, quality of work

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TERAPIJSKA IZMENA PLAZME – KBC ZEMUN DEO SAVREMENOG MULTIDISCIPLINARNOG PRISTUPA BOLESNIKU

Pantelić J, Lučić R, Mišković N, Gojković I
Služba za transfuziju krvi KBC Zemun, Beograd,Srbija

UVOD: Prema poslednjim preporukama međunarodnog udruženja za afereze (ASFA 2019) evidentirano je 84 bolesti i 157 indikacija za primenu afereza. Terapijska izmena plazme (TIP) je aferezna procedura koja je prihvaćena kao prvi izbor lečenja kod nefroloških, neuroloških i hematoloških bolesnika.
CILJ: Retrospektivna analiza primene TIP-a u lečenju bolesnika u KBC Zemun u periodu od 01.04.2018 - 01.08.2022. godine.
MATERIJAL I METODE: Sve procedure TIP su izvedene na automatskom uređaju za afereze Spectra Optia (Terumo BTC). Korišćeni podaci o bolesnicima i procedurama dobijeni su iz istorija bolesti, afereznog protokola i protokola izdatih krvnih komponenti.
REZULTATI: U periodu od 01.04.2018. do 01.08.2022. urađeno je ukupno 145 procedura TIP-a kod 35 bolesnika, od kojih su 19 (54,28%) bili muškog, a 16 (45,85%) ženskog pola. Najčešće indikacije za primenu TIP su bile Guillain-Barreov sindrom (13) i Sclerosis multiplex (8). Kod 5 bolesnika TIP je bio prvi terapijski izbor (I kategorija po ASFA klasifikaciji) primenjen zbog vitalne ugroženosti, od kojih su 3 imala trombotičnu trombocitopenijsku purpuru, a dva Myasteniu gravis. Ostale indikacije su pripadale II kategoriji. Od ukupnog broja bolesnika najčešće se radio protokol od 3-5 izmena na drugi dan,dok su se kod bolesnika sa TTP-om izmene radile svakodnevno najviše 18 zaredom. Za supstituciju je kod 75% bolesnika korišćen 5% albumin, dok je kod pacijenata sa TTP-om upotrebljena kriosupernatantna i sveže zamrznuta plazma. Svi pacijenti su imali vaskularni pristup preko dvoluminalnog centralnog venskog katetera.
ZAKLJUČAK: U našoj ustanovi dominiraju neurološke dijagnoze kao glavna indikacija za terapijsku izmenu plazme. Povoljan efekat TIP-a se zasniva na blagovremenoj primeni, na volumenu otklonjene plazme tokom celog procesa i timskom radu lekara i tehničara.

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PRIMENA KRVNIH KOMPONENTI KOD COVID-19 BOLESNIKA U JEDINICAMA INTEZIVNOG LEČENJA KBC ZEMUN

Perković Mauzer T, Ranđelović I, Dinetović D, Kulić A.
Služba za transfuziju krvi KBC Zemun, Beograd, Srbija

UVOD: Prema poslednjim podacima 5% bolesnika sa teškim oblikom COVID-19 zahtevaju prijem u jedinice intezivnog lečenja (JIL). Pacijenti primljeni u JIL, generalno imaju povećanu potrebu za transfuzionim lečenjem krvnim komponentama. Kao jedan od centara za lečenje COVID-19 bolesnika KBC Zemun je u četiri JIL-a zbrinjavao najteže COVID-19 bolesnike koji su zahtevali respiratornu potporu mehaničkom ventilacijom.
CILJ: Analizirati primenu krvnih komponenti kod kritično obolelih COVID-19 bolesnika koji su lečeni u JIL KBC Zemun u periodu od 15.03.2020. do 15.03.2021. godine
MATERIJAL I METODE: Podaci o pacijentima (pol, starost) dobijeni su iz elektronskih istorija bolesti, a podaci vezani za primenjene krvne komponente iz protokola izdatih krvnih komponenti.
REZULTATI: U JIL KBC Zemun u periodu od 15.03.2020 do 15.03.2021. lečeno je ukupno 278 bolesnika, od toga 190 muškaraca (68,34%) i 88 žena (31,65%). Najviše obolelih je bilo starije životne dobi od 65 do 85 godina. U toj grupi bilo je 68,42% muškaraca (130), dok je u ženskoj grupi bolesnika ova starosna grupa imala 87,5% (77). Kod 129 bolesnika (46,4%) indikovana je transfuzija krvnim komponentama (85 muškaraca i 44 žena). Glavne indikacije transfuzionog zbrinjavanja kritično obolelih COVID-19 bolesnika su bili pridruženi komorbiditeti koji su doprinosili multisistemskoj disfunkciji organa, koagulopatija uključujući DIK ili krvarenje. Za transfuziono lečenje primenjeno je 963 jedinice SZP, 552 krioprecipitata i 291 koncentrat trombocita. Transfundovani bolesnici iz JIL-a su u proseku primili 5 jedinica koncentrata eritrocita (ukupno primenjeno 748 jedinica) i po sedam jedinica SZP. Potrošnja krvnih komponenti kod ostalih hospitalizovanih bolesnika (8025) je bila značajno manja i indikovane su hematološkim i onkološkim bolesnicima zbog anemije i trombocitopenije. Izdato je 1797 resuspendovanih i filtriranih eritrocita , 922 jedinice SZP, 203 krioprecipitata i 308 koncentrata trombocita.
ZAKLJUČAK: Iako protokol lečenja SARS-CoV2 infekcije ne zahteva suportivnu terapiju krvnim komponentama, gotovo polovina COVID-19 bolesnika u JIL-u je imalo potrebu za transfuzionim lečenjem.

PP 066

PP 067

BLOOD DONATION PRACTICES AND DETERMINANT FACTORS AMONG NURSING STUDENTS

Borisova T., Popov R., Terzieva K., Stoyanchova T.
Transfusion Hematology Center, Military Medical Academy, Sofia, Bulgaria

Introduction:
From social perspective, blood donation is seen as a well-established practice all over the world, with blood donors being an integral part of every healthcare institution. The difficulties associated with finding and recruiting blood donors are faced by the majority of countries around the world. Nursing students, being future healthcare professionals, can participate in recruiting and encouraging blood donors, as well as help counter the deficit of blood and blood products.
Objectives:
Finding the determinant factors influencing the blood donation practice among nursing students.
Methods and materials:
A study has been conducted, using a direct, individual, anonymous questionnaire between 136 third- and fourth-year nursing students from the Medical University of Sofia during the second semester of the 2021/2022 academic year. [100% females, mean age – 26.9 years, with the majority of the participants - 103 (75.5%) being in the 21–25-year range.]
Results:
Only 26.4% of the respondents have ever donated blood. The majority, represented with 71.3%, have identified “fear of needles” as being the primary deterrent for donating blood. “Fear of blood and injury” is the second most common factor, as listed by 44.8% of the participants, while “incomplete knowledge” is the main deterrent for 39.7% of those surveyed. [Note*- The combined percentage exceeds 100% due to the multiple-choice answers]. Opinions and attitudes towards blood donation appear to be positive, as 96.3% of the respondents have expressed their intention of donating blood in the future. Almost all of the participants (91.9%) would donate blood for a friend or relative in need, while one person would donate if financially compensated.
Conclusions:
Although the presence of positive attitudes and intentions regarding blood donation is evident, the practice itself among nursing students is low. A need for developing and implementing donation campaigns, which are to be specifically aimed at medical universities, is emerging, in order to raise motivation and recruit donors among this group.
Key words:
Determinant factors, students, blood donation

PP 067

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CURRENT HEPATITIS B CHALLENGES IN TRANSFUSION MEDICINE – THE GAME IS NOT OVER

Ramune Sepetiene MD, PhD
Area Medical Director at Abbott Transfusion Medicine
Abbott Laboratories

Keywords: Hepatitis B diagnostics, laboratory assays for HBV, antiHBcor for blood donors

The lecture includes an overview of Hepatitis B challenges in Transfusion Medicine and is intended for all laboratory staff and transfusion related specialists.

HBV is still responsible for more than 250 million chronic infections worldwide. Lack of therapeutic strategies due to the highly specific virus DNA structure challenges the ability to exterminate this blood born infection.

Known variability of HBV genotypes and subtypes within different geographic location must be considered when determining a testing solution. This lecture will follow the historical background to current laboratory practice from early Serology to current NAT assays and discuss practical examples and insights. A short introduction will be included with specific HBV characteristics and host reaction highlighting the variability of immune response supporting the laboratory findings and current testing approach.

The pathogenesis of Hepatitis B is resulting in the need for different testing strategies used. Variability in HBV prevalence rate supports different testing algorithms to be used in routine practice. A discussion of good laboratory practice models for early HBV detection as related to blood centers will be provided to enhance capabilities of HBV detection by combining different assays and laboratory methods.

Sponsor symposium lecture Mak System / Sponzorsko predavanje Mak System

DIGITAL TRANSFORMATION OF TRANSFUSION SERVICES AND CELL & GENE THERAPIES

Giulio Bognolo MD
Chief Product and Chief Medical Officer

Three key factors are becoming more and more relevant in Transfusion medicine, Cell and Gene therapy. Leveraging data to create novel insights and predictions, novel approaches to transfusion practices and personalised care, and usability expectations and demand from digital solutions. This symposium is the opportunity to bring together the leading clinicians and one of the global leading digital supplier to share journeys, hear about strategies and new developments, and explore opportunities together.

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AGREGACIJA TROMBOCITA– OD DIJAGNOZE DISFUNKCIJE TROMBOCITA DO PRAĆENJA ANTITROMBOCITNE TERAPIJE / PLATELET AGGREGATION – FROM DIAGNOSING PLATELET DYSFUNCTION TO MONITORING ANTIPLATELET THERAPY

Sanja Lalić Ćosić

Svetlosna agregometrija (LTA – engl. Light transmission aggregometry) je široko primenjivana metoda za dijagnozu disfunkcije trombocita, uključujući trombasteniju i von Willebrand-ovu bolest. Smatra se „zlatnim standardom“ i preporučuje se od strane Komiteta za nauku i standardizaciju Međunarodnog društva za trombozu i hemostazu (SSC/ISTH – engl. Scientific and Standardization Committee of the International Society of Thrombosis and Haemostasis). Dok su u prošlosti ova ispitivanja izvođena na poluautomatskim analizatorima, 2015. godine prvi put je uveden automatizovani funkcionalni test agregacije trombocita na automatizovanim analizatorima koagulacije krvi Sysmex CS serije. Primena ovog testa značajno je doprinela standardizaciji same procedure ispitivanja i na taj način redukovala kompleksnost njenog izvođenja, kao i potencijalne izvore greške svojstvene za primenu poluautomatskih analizatora, pružajući mogućnost da samo izvođenje testiranja postane manje intenzivno i zahtevno.

Pored primene u dijagnostifikovanju disfunkcije trombocita, LTA se danas koristi i za praćenje farmakološkog odgovora pacijenata na kombinovanu antitrombocitnu terapiju. Kao jedan od najintenzivnije ispitivanih tretmana, dvojna antitrombocitna terapija (DATT) se u kliničkoj praksi često propisuje kao metoda primene antiagregacionih lekova, a antagonisti P2Y12 receptora (klopidogrel) zajedno sa COX-1 inhibitorom (acetilsalicilna kiselina – aspirin) su zbog svoje dokazane efikasnosti najčešće primenjivani antitrombocitni lekovi. Međutim, genetska varijabilnost CYP2C19 smanjuje aktivnost enzima i uzrokuje rezistenciju na klopidogrel, te uslovljava povećan rizik od kardiovaskularnih događaja. Stoga je određivanje rezistencije na lekove kritično za rukovođenje u donošenju odluka u antitrombotičkoj terapiji.

Sponsor symposium lecture Alura / Sponzorsko predavanje Alura

VISKO-ELASTO TROMBOELASTOGRAFIJA

Nebojša Savić
Univerzitetski klinički centar Srbije, Beograd, Srbija

Uvod: Poremećaji perioperativne koagulacije krvi predstavljaju dinamičan i složeni izazov u modernoj hirurgiji, pogotovo kod hirurških intervencija skopčanih sa velikim i masivnim krvarenjem. Neophodnost dobijanja brzih, jasnih i nedvosmislenih odgovora na ispoljeno sistemsko mikrocirkulatorno krvarenje, zahteva primenu odgovarajućih perioperativnih modernih dijagnostičkih metoda i testova. Primena pre, tokom i posle operativnih zahvata antikoagulantnih, antitrombocitnih i antifibrinoliznih lekova, zahteva jasan terapijski odgovor na vrstu i stepen izmenjene koagulacije krvi. Kod određenih operacija i procedura upotreba vantelesnog krvotoka dodatno negativno utiče na koagulaciju krvi. Primena visko-elasto tromboelastografije (Clot Pro) sa odabirom različitih testova za evaluacije koagulacije iz uzorka cele krvi, predstavlja metodu izbora za dobijanje brzih i jasnih odgovora o poremećajima koagulacije i primenu odgovarajuće ciljane hemostazne terapije.

Cilj, materijal i metod: Clot Pro je metoda brzog, jasnog i nedvosmislenog definisanja vrste i stepena jednostavnih i složenih poremećaja koagulacije iz uzorka cele krvi bolesnika („point of care"). Odabirom različitih testova, gde su reagensi integrisani unutar plastičnih nastavaka za pipetiranje, omogućava njihovo direktno mešanje sa celom krvi , što pojednostavljuje i povećava brzinu pipetiranja. U plastičnoj komori cela krv sa reagensima preko oscilirajućeg uronjenog klipa registruje proces koagulacije krvi. Verifikacija trodimenzionalnog događaja dinamične koagulacije krvi registruje se kao dvodimenzionalna slika na monitoru aparata. Tumačenjem i upoređivanjem parametara koagulacionog procesa različitih testova: CT (cloting time), CFT (clot formation time), angle alfa, A5, A10, A20, A30 (clot amplitude/time) i MCF (maximum clot firmnes), ML% (maximum lisis), LT (lisis time), odslikava se vrsta i stepen poremećaja koagulacije, a to određuje primenu odgovarajuće ciljane hemostazne terapije.

Kombinovanjem različitih pojedinačnih testova Clot Pro, primereno dinamici i obimu krvarenja, perioperativnoj primeni antikoagulatnih lekova (uključujući i direktne antikoagulante), antitrombocitnih lekova i antifibrinolitika, omogućava nam istovremeno kombinovanje 9 različitih testova (EX-test, FIB-test, AP-test, IN-test, HI-test, RVV-test, ECA-test, TPA-test, NA-test) na 6 radnih kanala aparata. Ciljano testiranje koagulacije krvi u realnom vremenu definiše ciljanu hemostaznu terapiju.

Rezultati: vrsta i stepen jednostavnih i složenih poremećaja perioperativne koagulacije krvi brzo, jasno i nedvosmisleno definiše Clot Pro u realnom vremenu. Deficit funkcionalnog fibrinogena, deficit trombocita i/ili poremećaj funkcije trombocita, pojedinačni ili globalni deficit plazmatskih faktora koagulacije, efekat heparina velike ili male molekulske mase, predoziranje protaminom, hiperfibrinoliza, efekat klasičnih i direktnih antikoagulantnih lekova, efekat antifibrinoliznih lekova, ali i hiperkoagulabilnost krvi efikasno dijagnostikuje Clot Pro.

Zaključak: sveukupno praćenje perioperativne koagulacije krvi obavezuje na rutinsku upotrebu Clot Pro, gde uz edukovano medicinsko osoblje i dobar organizacioni koncept, optimizuje vođenje ciljane perioperativne hemostaze.

Ključne reči: visko-elasto tromboelastrografija, poremećaji hemostaze, ciljana terapija

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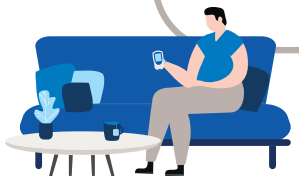

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* Oral Anticoagulants; ** Walk Away Reagent Management (W.A.R.M)

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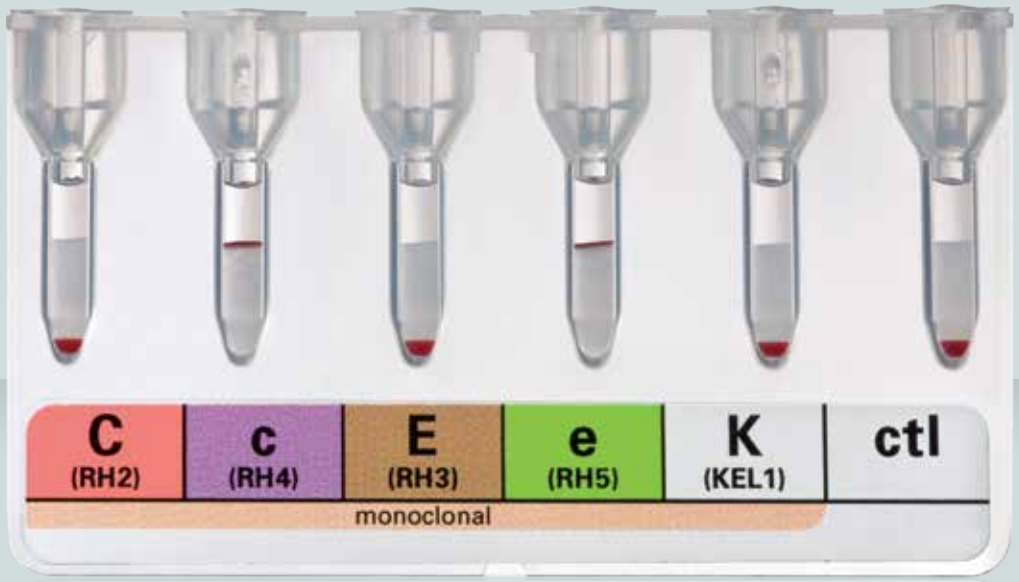

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