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DONORS PLATELET TRANSFUSIONTOB

ABSTRACT

The article summarizes recent data on the safety and efficacy of preparation and transfusion of donor platelets. There are discussed the features of a) the recruitment and selection of donors; b) the advantages and disadvantages of different methods of platelet concentrates production; c) platelet concentrates inventory management; d) immunological and infectious safety of platelet concentrates; e) deal with undesired constituents remaining in platelet concentrates. There are made the practical recommendations for better choice of platelet concentrate for patient safety. In conclusion, it is noted that in Russia should be normalized timing for: buffy-coat isolation and pooling, platelet concentrate leukodepletion, as well as a gradual transition to 100% transfusion of pathogen-reduced platelet concentrates.

Keywords: blood, donor, platelets, apheresis, pooling, transfusion, pathogen inactivation, immunization, safety

INTRODUCTION

In recent years a successful improvement in infectious and immune safety of allogeneic blood components has been observed. The implementation of quality systems in blood transfusion organisations, technical support and government regulations provided a comprehensive level of safety and efficacy in blood components [1-6]. Along with this, as a result of globalisation and evolution of microorganisms, new threats of infections arise [7-13]. Also, the blood component recipient spectre is changing as well: more patients with oncohematology are required to have frequent blood transfusions for a longer period of time. This increases the compound risk of allogeneic impact [14-20].

Whilst executing platelet transfusion certain safety procedures should be followed::

- sufficient amount of platelet concentrate (PC/CP) must be stored;
- timely delivery of appropriate PC must be in place for the patients;
- blood transfusion infections screening;
- decrease of immunological risks;
- blood transfusion goal achievement;
- unnecessary transfusion rejections;
- monitoring and testing of side effects [21-36].

There two principal methods of donor platelet production:

1) apheresis from another donor
2) extraction from the whole donor blood

The latter can be of two types:

1) platelet enriched plasma
2) extract of the platelet concentrate from the pool of leuko platelet layers (LPL) [37-40].

In theory, it is fair to assume the patients who receive the pool of platelet from 4-6 donations face lower risk of infection and allogeneic impact than the recipients of platelet concentrate apheresis of a single donor. However, the 15-year experience of European Hematological Control does not support but even proves the contrary of results [41].

Hence there is an interest to generalise recent data about the safety and efficacy of platelet production and transfusion.

Engagement and selection of blood donors

Ther requirements for donors of whole blood and apheresis are relatively similar. The latter requires certain concentration of platelets and a solid vein access.

When separating the whole blood from erythrocytes and plasma the platelets are:

- a side product;
- imply zero costs;
- being LPL discard.

Therefore, the cost to produce Platelet Concentrate from the whole blood is lower than deriving it from machine apheresis [42-43].

Though it is another topic of discussion to assess the risk of contamination when conducting the pooling of LPL. Theoretically the risk can be higher on one hand. On the other hand it might be lower due to the neutralisation of bacteria with phagocytes and plasma opsonins (antibodies, complement). According to many national norms and standards the minimum time required for conducting leukodepletion is 2 hours and maximum is 24. Further to this, the amount of bacteria in contamination of apheresis can be higher due to a large volume of collected transfusion environment. This also demands thorough disinfection of a donor's skin [44-46].

Apheresis:

- prolonged;
- is usually conducted in a small group of carefully selected donors;
- can not be performed in transporting conditions;
- carries the risk of citrate intoxication and demineralisation of bones [47].

Production of platelet concentrates: advantages and disadvantages

The quality and safety of platelet concentrates, regardless of their initial source - whole blood or apheresis, might depend on various factors such as the types of containers (configuration and plastic, separator type, method of blood extraction) types of leukofilters, types and usage of scaling (additional) solute, technology and usage of pathogens inactivity, usage of X-Ray or Gamma-Ray, and finally, expiration dates). The combination of these factors are summarised in the table below.

Whilst comparing these products it is crucial to not only compare the "pooled" against "apheresis" platelets concentrates, but also take into account all the factors. In addition, it is also important to consider the before and after

The process of platelet concentrate production from whole blood and apheresis method

Donation

Whole blood	**Apheresis**
LPL	Apheresis Platelet Concentrate
Preparation	
Container	Container
Scale-stirring	Machine
Temperature (before transportation)	Filter
Transportation (time, temperature)	
Recycle	
Store before initiation	
Leukodepleation	
Centrifuge	
Extraction	
Pooling (manual, machine)	
Scaling Solute	
Pathogens Inactivation	
X-Ray	
Store/Stirring	
Delivery	
More than 5 million variations	More than 10 thousand variations

Figure 1. LPL pooling: wash of primary containers with scaled solutions

side effects experienced by donors.

A revolutionary progress in quality of platelet concentrate from the pool of LPL was made after the machine implementation of automatic separation of blood from components and hemacontainers “up-down” (pic. 1, 2). The advantages of such systems are:

- fast and precise production of any necessary blood components;
- no manual work (with the Macropress Smart REVO system cannula breaking in tubes of hemacontainers is automatic without human involvement) (pic. 2-5);
- the maximum amount of platelets produced (in Irkutsk, approximately 1×1011 of cells from a single donor);
- minimum loss of hemoglobin and plasma [48, 49].

Management of platelet concentrate stock

Managing the stock of platelet concentrate is a challenge due to the fact that the maximum period of storage is 5 days as per the regulations in Russia. The delivery of platelet concentrates is highly affected by the long weekend days as well as by inappropriate epidemiological conditions which result in delays of patient’s treatment. Further to this the Chikungunya and Dengue fever waves are also well known for influencing the delivery time. In Russia, the period of delivery time may increase due to the unique 18-hour delay of of the blood diagnostics initiation [50].

On the other side, exceeding amount of platelet preparation may lead to its obsolete and significant cost.

Both situations lead to serious ethical problems. The depreciation of platelets is hardly acceptable for volunteering. The obsolete platelet concentrates may be used for preparation of Lysate, the universal growth factor for cultural laboratories. Nevertheless, only a few clinics have opportunities to utilise depreciated platelet concentrates [51].

The platelet stock management has to consider the biological specificities of each product such as phenotypes ABO and Rh, HLA and/or HPA, as well as cytomegalovirus-negative status (although the characteristics of the latter is non-crucial after the leukodepletion and pathogen inactivation) Creoconcentration and long storage of platelets is complicated and leads to a large loss of cells. The alternative methods of long storage such as lyophilisation - changing the pressure and atmosphere are yet to be developed.

Safety of platelet concentrate: main goals

There are two main goals of concentrate platelet safety:

1) to minimise the risk of blood transfusion infection;

2) to minimise the risk of alloimmune impact;

Leukodepletion or in other words leukoreduction is an important process

Figure2. Centrifugeof LPL pool

Figure 3. Machine separation on Platelet Concentrates from the LPL pool: canule breakage

that links the two problems stated above.

Leukodepletion (leukoreduction)

Leukodepletion is a decrease or reduction of leukocytes by 3 log10 and in Russia the platelet concentrate dose contains no more than 1 × 106 of cells (1 million leukocytes).

There are built-in filters in the modern machine apheresis systems that eliminate leukocytes. The Platelet Concentrate produced from the LPL pool is filtered at the early stages, 18-24 hours after the blood collection. The implementation of universal (from 100% doses) leukodelpletion led to a rapid decrease in transferring innercell viruses such as cytomegalovirus, T-lymphotropic human virus and the Epstein–Barr virus. For the recipients of numerous transfusions Platelet Concentrate leukodepletion is a key element of HLA-alloimmunisation prevention [52].

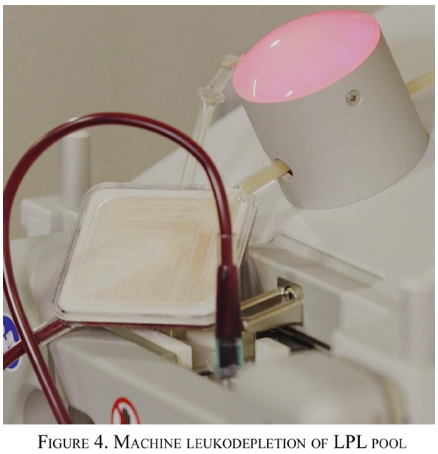
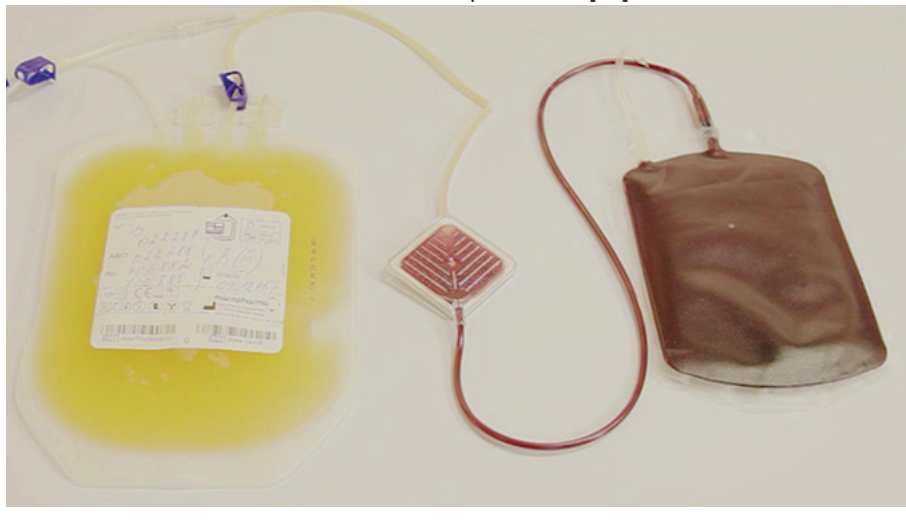


Figure 4. Machine leukodepletion of LPL pool



Immunomodulation and immunomodulation danger

The majority of immunomodulating effects of transfusion are related to the leukocytes content in the blood components. Therefore the leukodepletion reduces the transfusion-related immunomodulation (TRIM) the effects of which are mostly harmful.

Leukodepleted concentrated platelets are effective to prevent Non-Hemolytic Reactions (NHR) and alloimmunisation. It is universally acknowledged that leukodepletion decreases the proinflammatory effects of donated leukocytes - the excesses of inducible synthase of oxide nitrogen, cytokines, chemokines, which are the main indicators of high fever and ague (typical for NHR).

The anti-inflammatory effects of early leukodepletion are more advanced as opposed to bedside leukodepletion effects, as leukocytes begin to disintegrate and released proinflammatory factors of Platelet Concentrate within 24 hours after blood preparation. For that reason, the early leukodepletion also decreases alloimmunisation as it prevents the transfusion of dissoluble antigens of donated leukocytes.

In half of the registered NHR cases Platelet Concentrates is the source of it even though it is only 10% of transfused blood components [53]. It also considered that platelets are the source of majority of inflammatory mediators. However, the proinflammatory factors, released by leukocytes, and activating the proinflammatory factors of platelets, should not be excluded either.

The mechanisms of transfused alloimmunisation are not fully investigated, and perhaps there many more factors to discover. Nevertheless, some progress in the field of Platelet Concentrates transfusion was achieved. It is proved that excessive B-lymphocytes play key role in anti-presenting cells [54].

Infections safety of Platelet Concentrate

The general safety regulation of blood components are applicable to platelet concentrates respectively.

The donor selection is one the crucial safety stages in blood transfusion. Recently, there are more reasons and criteria appearing against donation. Even though such reasons and criteria are implemented for safety purposes, it is not sufficiently enough to prove their justification [55-60].

Bacterial contamination: detection

The risk of bacterial contamination of Platelet Concentrate is high due the fact that the storage temperature of 22 ± 2 °C facilitates the growth of almost all types of bacteria. In Russia such casess were not registered, whilst in France in 2013, the clinical hemotransmitted bacterial infection was developed amongst 3,4 and 0,87 of recipients per 1000 apheresis and pooled transfusions of Platelet Concentrates. Despite the efforts to eliminate infections, their frequency remains stable, approximately 2,3 per 1000 transfusions in 2012 and 2013. In the last five years the apheresis of platelet transfusion leads to five times more bacterial infections than the transfusion of pooled platelets [61].

In Russia it is not obliged to test platelets for bacteria even though some oragnisations practice various globally acknowledged methods such as BactAlert (Biomerieux, France) and BACTEC (Becton-Dickinson, USA).

The search for bacteria might be compulsory in case of production release or quality control. There are certain problems of cultural bacteria detection systems such as the delay of delivery by 24 or 48 hours and the significant amount of false positive and false negative results [62]. In Europe the platelets expiration date can be extended to 5-7 days if the bacteria detection and pathogens inactivation process implemented.

The tests to detect bacteria in Platelet Concentreates with the use of varios types of ligands just before delivery and transfusion do exist and are also developing. These are BacTx ™ (Immunetics, USA) and amongst polyclonal antibodies PGD-Test (Verax, USA). The effects of these test are yet to be proved.

From the practical point of patient's safety another alternative to bacteria detection is pathogens inactivation.

Viruses in blood transfusion

As opposed to plasma, the quarantine of Platelet Concentrates is almost impossible. In comparison to erythrocytes, Platelet Concentrates apheresis is prepared from regular donors who practice frequent donations within 2-week interval. With this kind of donation the risk of "period window" - inception of virus infection non-detectable by laboratory diagnostics, increases. The increase of interval between donations (no less than 2 months for whole blood) reduces the risk of donation during "period window" of virus infection.

Following this, the virus safety of Platelet Concentrates engages:

- pooling of LPL produced from whole blood;
- plasma in Platelet Concentrates is replaced by scaled solution;
- pathogens inactivation.

Pathogens inactivation in Platelet Concentrates

There are two methods to process Platelet Concentrates to achieve pathogens inactivation:

- amotosal-HCl and UVA-A – Intercept (Cerus, USA),
- riboflavin and UVA-B - Mirasol (Terumo BCT, USA).

There is one more method that is under development and considers only UVA-C and stirring without chemical additives. - Teraflex (Macopharma, France). In Russia the Intercept method is implemented since 2003.

There are three significant advantages of pathogens inactivation.

First of all, these methods eliminate the growth of bacteria which makes them competitive enough with bacteria screening. Quite often screening provides false negative results when the bacteria amount is low which is typical for non-symptom donors with the low level of bacteria. There is no single case of bacterial infections registered by hemocontrol in France and Switzerland, as well as in the series of Intercept-processed Platelet Concentrate studies [63].

Secondly, in spite of existing pathogen inactivation methods that do not inactivate spores, they are relevant to vermins and fungus such as malaria, toxoplasma, leishmania and etc.

Finally, the pathogens inactivation reduces the level of hemotransmissive virus infections. If the high concentration of bacteria is in the blood infected by sepsis then viremia might be high in the blood non-symptom donors. The Intercept method helped to provide the clinics with safe platelets during the virus epidemy in Reunion in 2006 (Chikungunya virus) and in French Caribbean in 2006 (Dengue virus). Further to this, the Intercept method is used to process the plasma of Ebola convalescents which is later used to cure the patients. There is no risk of other virus infections such as HIV (typical for Africa) and the antibodies against Ebola are remaining [64].

It is also interesting to observe the experiment of pooling of 2 LPL, pathogens inactivation with Intercept and separation of 2 curing doses of Platelet Concentrates [65].

Non-desirable components remained in Platelet Concentrates: the strategy of preventions, culture and elimination

The transfusion of Platelet Concentrates may lead to:

- NHR (more often that other blood components);
- acute lung damage related to

transfusion (TRALI);

- allergic reactions;
- bacterial infections.

These side effects can be completely or at least prevented with special precaution methods.

Non-desirable components remained in Platelet Concentrates can be divided into two categories:

- antibodies, mainly anti-HLA, as a result of donor alloimmunisation;
- biological substances with anti-inflammatory effect.

The anti-HLA antibodies in plasma may be a consequence of previous blood transfusion and more often pregnancies.

There are three suggested strategies for prevention:

- anti-HLA antibodies screening,
- restriction of female donation,
- use of additive solutions.

The additive solutions reduce the amount of plasma in 65-80% of Platelet Concentrates. The content of various additional solutions differs and evolves. This explains its differences in platelet activation and clinical effectiveness. The morphology assessment, life duration, functional activity, metabolism and aggregated capability of platelets demonstrated that extended storage of platelets in additive solution SSP+ mainly allows to sustain its metabolic in vitro cells characteristics rather than storing it in autologous plasma [66-69].

The expiration date of Platelet Concentrates and its clinical effectiveness as well as the growth of proinflammatory effect is actively discussed in the field. The excessive of proinflammatory cytokines and other biological substances increases after 3 days of storage [70].

Each action toward Platelet Concentrates may theoretically lead to activation or apoptosis of cells. The impact of plastics, centrifuge, filters, gas, solutions and temperature changes may create stress that further leads to damages. Perhaps different platelets react to differently to other various signals. It also possible the production of biological substances determined by the donor specificities, and the reaction to biological substance injection determined by recipient's specificities.

The individual reaction of platelets is the advantage of pooled Platelet Concentrates. The adverse reaction and a breakdown of donor's stored platelets will lead to a functional deficiency of 100% of apheresis Platelet Concentrate cells, but 15-25% of pooled Platelet Concentrates.

Prevention of posttransfusion "transplant against master" disease

Some patients are needed to be irradiated with Platelet Concentartes to prevent the posttransfusion disease called "transplant against master" (PT-DTAM). The main method of inactivation of the remaining lymphocytes against the disease is either X-Ray or gamma-irradiation.

This practice is insufficient to inactivate the infectious pathogens, and it is enough to slightly damage membranes of platelets and increase its activation and apoptosis.

The damaging effect might be prevented if the prevention methods of disease are fully assessed:

- new methods of leukodepletion that are capable to reduce the amount of leukocytes in a dose to less than 105;
- pathogens inactivation methods aimed at damaging of nucleic acids but not damaging platelets. It is observed that the effectiveness of Intercept against the disease (PT-DTAM) is higher than the X-Ray irradiation. And it is confirmed not only by the certifications, but also by implementing the appropriate regulations in the norms of blood transfusion organisation of various countries (Kuwait, Saudi Arabia). On the 14th of January 2016 the American Association of Blood Banks recommended to replace the gamma-irradiation of Platelet Concentrates procedure by its Intercept method [71].

Prevention of alloimmunisation

Numerous platelet transfusions may lead to a development of alloimmunisation and a decrease in future effectiveness of transfusions. The match sampling of Platelet Concentrates with the recipient's serum is not regulated by the Russian norms. The selection of HPA antigens is also not available. The leukoreduction significantly lowers the foundation of anti-HLA antibodies among patients who receive myeloablative chemotherapy. In addition, there is no data about the effectiveness of leukoreduction for the purpose of alloimmunisation prevention among immune competitive patients. Ultraviolet which is included in all methods of pathogens inactivation of Platelet Concentrates lowers the speed of development and the rate of alloimmunisation, and also the duration of anti-HLA of antibodies [72]. The mechanisms of this effect is yet to be studied. If such pathogens inactivation behaviour confirms, then it will become more valuable.

The best choice of Platelet Concentrates for patients' safety

At first sight it is always possible to check whether there any erythrocyte adulterants in the Platelet Concentrates as it should not be red. It is also easy to determine the absence of aggregates - when pressure is applied to the lowest level of Platelet Concentrate the cell spine must be even (the effect of "snowstorm").

Unlike erythrocytes the Platelet Concentrates transfusion is not limited by the absolute immunological barriers and usually does not require a cross sampling (except the well-known alloimmunisation). The release of Platelet Concentrates is conducted on first-in/first-out basis. In different countries there are various practices of ABO-matching of Platelet Concentrates

Typical methods of safety increase and Platelet Concentrates effectiveness:

- ABO-identity;
- Transportation terms control;
- objective assessment (container solidity, cell spine);
- HLA or HPA match in the event of refractoriness and neonatal alloimmune thrombocytopenia;
- the effect of aligned platelet growth monitoring (EGP).

Practical recommendations

The pooled Platelet Concentrates from LPL must be prioritised when possible. The appropriately selected apheresis of Platelet Concentrates should be transfused to alloimmune patients. The use of additive solutions should be in place.

The HLA antibodies injection prevention policy must also be facilitated (male plasma, donor screening). The pathogen inactivated Platelet Concentrates must be used for transfusion purposes.

ABO-identity should be accomplished. The donors with low titre of anti-A, B must be selected in the events of platelet transfusion of O type to other blood type recipients with a compulsory replacement of plasma by the additive solution.

Bear in mind that the effectiveness of Platelet Concentrate diminished after 3 and more days of storage.

CONCLUSION

The methods of Platelet Concentrate safety and transfusion effectiveness are rapidly evolving. Nevertheless, the effective systems of hemacontrol contains 25-30% of transfusion reactions related to Platelet Concentrates transfusion. This means that further advancement is this field is required.

In Russia the dates should be regulated: the release of LPL, pooling of LPL, leukodepletion of Platelet Concentrates as well as moderate shift to a 100% of pathogens inactive Platelet Concentrate transfusion.

The intense search of the best platelet production and implication protocols is conducted globally. Even the quantity of dose differs throughout the world: 2×1011

of cells in Europe, 3×1011 of cells in the USA. Hence the results of the research are not always the same. It is also important to take into account the growing difference between the established practice and new developing methods of Platelet Concentrates preparation, processing, storage and implication.

By no doubt the key goal is the curing effectiveness of transfusions and patient safety. On the other hand, the economical aspects as well as the efficient allocation of donor resources and ethical issues in donor-related work are also quite crucial.

Re-evalution of prevention activities and implication of platelets for curing purposes as well as the parameters which should be selected for the effectiveness and transfusion quality, lead to some new perspectives.

REFERENCES

1. Gubanova M.N. Kopchenko T.G. Zhiburt E.B. Selection of the platelet concentrates production from whole blood. Vestnik of blood service Russia, 9, 2009. - pp. 20-22.
2. Gubanova M.N. Madazaev. S.R. Zhiburt, E.B. Infections distribution and frequency amongst donors in Russia. Questions of virology, 60(6), 2015. - pp. 29-31.
3. Zhiburt E.B. Prevention of post-transfusion hepatitis. Saint Petersburg: Terra Medica, 1998. – P.52.
4. Zhiburt E.B. Golubeva A.V. The TT Virus. The Journal of Microbiology, Epidemiology and Immunobilogy, 3, 2001. – pp. 117-220.
5. Zhiburt E.B. Transfusiology. Saint Petersburg: Piter, 2002.
6. Zhiburt E.B. Gubanova M.N. Shestakov Y.A. Maksimov V.A. New hemotransmissed infections and their prevention. Transfusiology, 7(4), 2006. - pp. 56-67.
7. Zhiburt E.B. Fedorov N.A. Reizman P.V. NAT screening of virus infections amongst donors increasing blood safety. Clinical diagnostics, 12, 2006. - pp. 22-23.
8. Zhiburt E.B. Gubanova M.N. Distant and proximate. Tropical infections in the blood services in Russia. Transfusiology, 9(1), 2008. - pp. 20-24.
9. Zhiburt E.B. Gubanova M.N. Maksimov V.A. Hemastransmissed virus of Eastern Nile. Epidemiology and Infectious diseases, 3, 2007. - pp. 28-32.
10. Zhiburt E.B. Transfusion dictionary. M., RAEN, 2012.
11. Zhiburt E.B. GMP of blood service organization. M: ID KDU, University Book, 2016.
12. Zhiburt E.B. Benchmark of blood preparation and transfusion. RAEN, M., 2009.
13. Zhiburt E.B. Madzayev S.R. Preparation and transfusion of platelets. RAEN, M., 2013.
14. Zhiburt E.B. Vergopulo A.A. Gubanova N.A. Kopchenko T.G. Blood and platelet donor effectiveness in Russian Federation subjects. Glav.Vrach, 2, 2009. - pp. 23-29.
15. Zhiburt E.B. Karavaev A.V. Vaisman D.A. Madzaev S.R. Special features of national risk assessment of infectious blood transfusion. Vestnik Roszdravnadzor, 1, 2013. - pp. 75-77.
16. Zhiburt E.B. Madzaev S.R. Mazgumova R.Z. Methodical questions in infections screening among donors. Vestnik of blood service Russia, 1, 2013. - pp. 30-32.
17. Zarubin M.V. Zaznobov M.E. Kurnosov N.B. [et al.], Platelet storage managing in regional blood service. Kazan Medical Journal, 96(3), 2015. - pp. 407-413.
18. Zarubin M.V. Kupcevich P.S. Smirnova, O.Y. [et al.]. Centralization of blood service in Irkutsk region. Siberian Medical Journal, 7, 2014. - pp. 97-101.
19. Kodenev A.T. Vashchenko G.A. Kapustov V.I. Zhiburt Y.B. Mastering of concentrate platelet production. Vestnik of blood service Russia, 2, 2010. - pp. 22-25.
20. Lyauzheva F.M. Tlenkopachev R.S. Zhiburt Y.B. Donor culling with infections markers in Kabardino-Balakar Republic. Transfusiology, 15(4), 2014. - pp. 40-46.
21. Protopopova E.B. Filina N.G. Kuzmin, N.S., [et al.]. The quality of regular platelet donations. Vestnik of blood service Russia, 2, 2015. - pp. 35-38.
22. Protopopova E.B. Mochkin N.E. Madzaev S.R. [et al.]. Platelets transfusion in transplantation of autologous stem cells. Vestnik of National Medical Surgery Center of Pirogova N.I, 10(2), 2015. - pp. 84-85.
23. Protopopova E.B. Mochkin N.E. Sultanbaev U.S., [et al.]. Thrombocytopenia after transplantation of autologous stem cells. Kazan Medical Journal, 96(3), 2015. - pp. 428-431.
24. Skorikova S.V. Buritkabaev Z.K. Savchuk T.N. Zhiburt E.B. Distribution of HIV, Heptitis C virus, Hepatitis B infections of donors in Astana. Questions of virology, 60(1), 2015. - pp. 34-36.
25. Tankayeva H.S. Makhachev B.M. Zhiburt E.B. The Evolutions of blood service in child clinics. Vestnik of blood service, 2, 2015. - pp. 43-46.
26. Fedorov N.A. Eylov A.A. Suhanov Y.S. Zhiburt E.B. NAT blood and other material testing for pathogens and mutation. Moscow: Poligraphservice. -2003.
27. Filina N.G. About the quality of platelet concentrates. Transfusiology, 12(4), 2011. -pp. 32-37
28. Filina N.G. Kolotvina T.B. Titova S.A. Zhiburt E.B. Provisional screening of donors with alanine transaminase activity has lost the economic effectiveness. Transfusiology, 12(3), 2011. - pp. 61-64.
29. Shevchenko Y.L. Zhiburt E.B. Secure blood transfusion. - Saint Petersburg: Piter, 2000.
30. AABB authorizes use of the INTERCEPT blood system for platelets to reduce the risk of transfusion-associated graft versus host disease [Online]. Available from: http://www.businesswire.com/news/home/20160114005342/en/ [Accessed 30/01/2016].
31. Cerelli E., Nocera M., Di Bartolomeo E. et al. Effect of adhesive properties of buffy coat on the quality of blood components produced with Top & Top and Top & Bottom bags. Blood Transfus. 2015; 13(2):265-73.
32. Garraud O., Cognasse F., Tissot J.D. et al. Improving platelet transfusion safety: biomedical and technical considerations. Blood Transfus. 2015; 16:1-14.
33. Jackman R.P., Deng X., Bolgiano D. et al. Leukoreduction and ultraviolet treatment reduce both the magnitude and the duration of the HLA antibody response. Transfusion. 2014; 54(3):672-80.
34. Lafeuillade B., Eb F., Ounnoughene N. et al. Residual risk and retrospective analysis of transfusion-transmitted bacterial infection reported by the French National Hemovigilance Network from 2000 to 2008. Transfusion 2015; 55(3): 636-46.
35. Petrik J., Lozano M., Seed C. R. et al. Hepatitis E, Vox Sang, 110(1), 2016. pp. 93-103.
36. Pietersz R.N., Reesink H.W., Panzer S. et al. Prophylactic platelet transfusions. Vox Sang, 103(2), 2012. - pp. 159-176.
37. Roth W.K., Busch M.P., Schuller A. International survey on NAT testing of blood donations: expanding implementation and yield from 1999 to 2009. Vox Sang, 102(1), 2012. - pp. 82-90.
38. Sandgren P., Diedrich B. Pathogen inactivation of double-dose buffy-coat platelet concentrates photochemically treated with amotosalen and UVA light: preservation of in vitro function. Vox Sang. 2015; 108(4):340-9.
39. Seghatchian J. Multilayer-strategy to enhance optimal safety of the blood supply: The role of pathogen inactivation

for optimizing recipient safety and helping health care cost containment: Moderator views. Transfus Apher Sci. 2015; 52(2):233-6.

40. van Griensven J., Edwards T., de Lamballerie X. et al. Evaluation of Convalescent Plasma for Ebola Virus Disease in Guinea. N Engl J Med. 2016 7; 374(1):33-42.

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OBESITY AS A METABOLIC FACTOR OF THE RISK OF CARDIOVASCULAR DISEASES

ABSTRACT

Obesity is currently one of the serious problems of modern society and medicine. The article gives an overview of obesity as one of the main metabolic risk factors for cardiovascular diseases. The reasons of the development of obesity and pathogenetic mechanisms of complications development from the side of the cardiovascular system are considered against its background, as well as the risk to human health in the presence of visceral obesity. We present data on child obesity as a metabolic base of cardiovascular diseases at which a prolonged accumulation of adipose tissue leads to the most serious disorders of human organs and systems, primarily cardiovascular one.

Keywords: obesity, overweight, cardiovascular diseases, epicardial fat.

According to the WHO, overweight and obesity are determined as «abnormal or excessive fat accumulation that presents a risk to health'' [5]. Obesity plays a role in the development of a number of cardiovascular risk factors (FR). The researchers defined pathogenetic basis of the negative effect of obesity on the structural and functional activity of heart and blood vessels. An obese person has a greater risk of developing cardiovascular disease (CVD), which in turn can lead to severe heart diseases [24].

Many factors can cause obesity, including genetic (more than 50 candidate genes). But most people do not have monogenic inheritance of obesity. There are many studies being held to find candidate genes that can affect obesity and overweight. Currently, the role of mutations in the PPAR genes (peroxisome proliferator-activated receptors), fatty acid-binding protein 2, (FABP2), ADRB2 and ADRB3 (G-protein adrenergic receptors) is under study. The latter are considered as an interesting finding in nutrigenetics, confirming the hypothesis of «economical genotype». In people with a body overweight and with a mutation of the ADRB3 gene, daily energy consumption, altered lipolysis and increased abdominal obesity decrease are noted [6]. Despite the revealed interrelationships of gene mutations with overweight, the question of direct role of genetic factors in the development of obesity remains controversial. One cannot ignore environmental factors, such as lifestyle, diet, physical activity, stressful situations and bad habits. To date, according to the WHO, the main reasons of obesity are an excessive supply of nutrients with food and a low level of physical activity, which does not allow consuming the amount of energy coming from food [5, 8, 9].

Clinically obesity can be an independent disease (exogenous-constitutional obesity) or a syndrome that develops at various diseases, such as hypothyroidism, hypercorticism, polycystic ovary syndrome, Cushing's syndrome, etc. (in the latter case, excess weight can be eliminated after curing or compensation of the main disease). In this case, it must be remembered that obesity itself leads to disruption of the sexual glands, the hypothalamo-pituitary system and the adrenal glands. For example, the establishment of a diagnosis of neuroendocrine form of the hypothalamic syndrome is inappropriate, since the formation of hypothalamic stigmas such as cyanotic striae, pigmentation in places of friction, the formation of acanthosis of obese, unclean skin and functional disorders of the hypothalamic-pituitary system is not the cause, but the result and manifestation of obesity, and the degree of their severity correlates with the duration and severity of obesity [20].

Excess body weight contributes to increased levels of total cholesterol and low-density lipoprotein (LDL) and very low density (VLDL) in plasma. It has been established that the production of cholesterol (Ch) in people with obesity increases by an average of 20 mg per