CONTINUING MEDICAL EDUCATION

The usage of blood components in obstetrics

**Dalia Adukauskienė[1], Audronė Veikutienė[2], Agnė Adukauskaitė[3],
Vincentas Veikutis[4], Kęstutis Rimaitis[5]**
*[1]Department of Intensive Care, Kaunas University of Medicine,
[2]Department of Cardiac, Thoracic, and Vascular Surgery, Kaunas University of Medicine,
[3]Kaunas University of Medicine, [4]Institute for Biomedical Research, Kaunas University of Medicine,
[5]Department of Anesthesiology, Kaunas University of Medicine, Lithuania*

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Summary. *Major obstetric hemorrhage remains the leading cause of maternal morbidity and mortality worldwide. Even though blood transfusion may be a life-saving procedure, an inappropriate usage of blood products in obstetric emergencies especially in cases of massive bleeding is associated with increased morbidity and risk of death. Thorough knowledge of the etiology, pathophysiology, and optimal therapeutic options of major obstetric hemorrhage may help to avoid lethal outcomes. There are evidence-based data about some risks related with transfusion of blood components: acute or delayed hemolytic, febrile, allergic reactions, transfusion-related acute lung injury, negative immunomodulative effect, transmission of infectious diseases, dissemination of cancer. This is why the indications for allogeneic blood transfusion are restricted, and new safer methods are being discovered to decrease the requirement for it. Red cell alloimmunization may develop in pregnancy; therefore, all pregnant women should pass screening for irregular antibodies. Antierythrocytic irregular antibodies may occur due to previous pregnancies or allogeneic red blood cell transfusions, and it is important for blood cross-matching in the future. Under certain circumstances, such as complicated maternal history, severe coagulation abnormalities, severe anemia, the preparation of cross-matched blood is necessary. There is evidence of very significant variation in the use of blood products (red cells, platelets, fresh frozen plasma, or cryoprecipitate) among clinicians in various medical institutions, and sometimes indications for transfusion are not correctly motivated. The transfusion of each single blood product must be performed only in case of evaluation of expected effect. The need for blood products and for their combination is necessary to estimate for each patient individually in case of obstetric emergencies either.*

Indications for transfusion of blood components in obstetrics are presented in order to improve the skills of doctors and to optimize therapeutic options in obstetric emergencies.

Introduction

The transfusion of the blood components in emergencies in obstetrics can increase the morbidity and mortality, if not done rationally (1).

It is recommended to act moderately concerning blood component transfusions: to avoid their usage as possible and to use safer methods instead, even though the analyzing techniques of the donor (allogeneic) blood improve and the risks of blood-born infectious diseases decrease. However, there is a probability to transmit some new or still unidentified infectious agents (parvoviruses, agents of Creutzfeldt-Jakob disease, etc.) during the transfusion (2). However, allogeneic blood transfusion accounts for noninfectious mortality too. Moreover, the main causes of allogeneic blood transfusion-related deaths in the United States are transfusion-related acute lung injury and hemolytic transfusion reactions (3). Besides, there is more and more evidence that immunomodulation, induced by allogenic blood transfusion, may cause postoperative infections, prompt multiple organ dysfunction syndrome and increase mortality

Correspondence to D. Adukauskienė, Department of Intensive Care, Kaunas University of Medicine, Eivenių 2, 50028 Kaunas, Lithuania. E-mail: daliaadu@gmail.com

Adresas susirašinėti: D. Adukauskienė, KMU Intensyviosios terapijos klinika, Eivenių 2, 50028 Kaunas
El. paštas: daliaadu@gmail.com

(4). Probably the highest risk is to transfuse a blood component, which is not cross-matched (5). The blood samples for cross-matching should be taken recently, because during pregnancy the patient might become alloimmunisated at any time (this usually happens during the last trimester of the pregnancy) (1, 6).

The risk-benefit ratio of blood component transfusion was analyzed in few randomized controlled trials, which showed that a liberal tactics of red cell transfusion in perioperative period and emergencies is not superior; furthermore, it increases the risk of death in some patients' groups (6, 7). That is why some alternative methods of transfusing blood components are becoming more popular nowadays in perioperative period, so it is important in obstetric emergencies as well: the use of autologous blood, pharmacological means (antihemorrhagics, recombinant erythropoietin, iron supplementation), blood substitutes, etc. (8–10).

The principles of blood components transfusion in obstetrics

Pretransfusion compatibility testing, called "group and screen," determines the ABO and Rh(D) group and performs a red cell antibody screening. Therefore, this testing should be done for a pregnant woman during her first visit to a doctor and at the 28th week of gestation (1, 12). Another type of blood testing is cross-matching. It is performed to determine the compatibility of the donated blood with its intended recipient.

Cross-matching of blood should be requested under the following circumstances:
1. major antepartum, intrapartum, postpartum hemorrhage;
2. placenta previa;
3. severe pre-eclampsia or eclampsia;
4. significant coagulation disorders;
5. anemia (when Hb <10 g/dL) prior to cesarean section;
6. before an operation, when there are some significant obstetric abnormalities (uterine fibroids, previous classical cesarean section, previous placenta accreta) (13).

Conditions, when cross-matching is not necessary:
1. elective or emergency cesarean section;
2. manual removal of placenta without postpartum hemorrhage;
3. elective surgery because of missed abortion;
4. anemia (Hb <10 g/dL) prior to anticipated vaginal delivery (13, 14).

Principles to observe are as follows:
1. Obstetric units should always have group O Rh D-negative, Kell-negative blood available for emergency cases;
2. However, in emergency circumstances, uncross-matched group-specific blood is preferred to group 0 Rh D-negative blood;
3. In the absence of acute blood loss, antenatal and postnatal patients should only be transfused, when reduction of hemoglobin is associated with evident symptoms of anemia;
4. When there are coagulation disorders, a hematologist's advise is recommended concerning the blood transfusion (13).

Blood components used for transfusion in women of reproductive age must be Kell-negative in order to avoid alloimmunization and subsequent hemolytic disease of the newborn (unless it is known that a woman is Kell-positive) (1).

If anti-K antibodies are found during pregnancy, they most likely have appeared due to previous transfusion (unlikely to anti-c antigen), so this should be kept in mind concerning future red cell transfusions.

If a pregnant woman is cytomegalovirus (CMV) seronegative, the corresponding (CMV seronegative) red cell and platelet products should be used. In case the CMV status is unknown, it is recommended to use CMV-seronegative or leukodepleted blood components (since it is thought that using leukocyte filters significantly reduces the risk of transmitting CMV). However, in emergency circumstances, the transfusion should not be delayed if there are no CMV-seronegative blood components available.

When should red cells be transfused?

Since there are no universally defined criteria, indicating the red cell transfusion, various hospitals do it differently. What is more, the need for transfusion is often not motivated enough (2, 15, 16). The guidelines for use of blood components, provided in scientific literature, are not always proven by scientific evidence or conclusions of randomized controlled trials; furthermore, they are often based just on best clinical experience (2, 15–17).

While defining indications for red cell transfusion, one cannot base it only on the values of hemoglobin (Hb) and hematocrit (Ht). Firstly, one have to evaluate patient's age, main disease and comorbidities, expected surgical procedures, coagulation abnormalities, the amount of blood expected to be lost because of

bleeding, clinical and physiological parameters, showing an overall condition of a patient, and tolerance to an expected tissue hypoxemia due to anemia. What is more, one must take into consideration body temperature, heart function, heart rate, arterial blood pressure, renal function, venous blood oxygen saturation, and blood oxygen partial pressure.

The main indication for red cell transfusion is to keep adequate oxygen-carrying capacity of blood and to avoid or reduce tissue hypoxia.

The red cell transfusion should not be done only to increase the Hb level (except the cases of severe symptoms of anemia and the need to ameliorate the oxygen-carrying capacity).

The oxygen delivery and consumption ratio in tissues shows the adequacy of tissue oxygenation. The delivery of oxygen depends on its blood levels and cardiac output. In case of anemia, the delivery of oxygen is ameliorated by physiological adaptability mechanisms: the hemoglobin affinity for oxygen decreases, oxygen-hemoglobin dissociation curve shifts to right, oxygen release from red cells increases, peripheral vascular resistance and blood viscosity decrease; furthermore, the cardiac output increases due to increased heart rate, stroke volume, and contractility (4). The body's ability to compensate anemia is reduced by ischemic heart disease, heart failure, pulmonary and peripheral vascular diseases, drugs, which reduce cardiac output (e.g. beta blockers) (2, 18).

The consumption of oxygen depends on these factors: physical activity, body temperature, sympathetic and metabolic activity, heart rate, and the effect of certain drugs (e.g. anesthetics) (2, 18, 19).

Young and healthy women without hypovolemia can tolerate acute anemia quite well – the delivery of oxygen remains adequate, and there are no severe symptoms of anemia even though Hb concentration decreases to 7 g/dL (1, 2, 9, 20).

When treating major hemorrhage, firstly, the volume of lost blood should be estimated and only then the red cells transfused. The goal of maintaining adequate tissue perfusion is normovolemia; therefore, one of the main principals treating acute bleeding is to restore circulating blood volume by fluids, but not by red cell transfusion (2, 4, 9, 18, 21).

Ht should not be considered as the only laboratory marker when estimating bleeding level, because this marker can be influenced by the initial infusion therapy. So namely monitoring of the Ht value would reveal the reduction of it, indicating the progress of bleeding.

Evaluation of blood lactate level is a very sensitive early indicator in the evaluation of bleeding severity. Lactates (product of anaerobic glycolysis) indirectly show the oxygen deficiency, tissue hypoperfusion, and severity of hemorrhagic shock. If lactate concentration decreases (≤2 mmol/L) in 24 h, the prognosis of a patient is better. Base deficit (estimated by analysis of arterial blood gases) is also an indirect indicator of tissue acidosis due to reduction of perfusion (17, 22, 23).

Hypothermia is associated with acidosis, hypotension, and coagulopathy. Hypothermia impairs platelet aggregation and activity of coagulation factors, suppresses body's enzyme systems, so in bleeding all means to maintain normothermia should be used in purpose to reduce heat loss: electric mattress pads, warm covering of a patient, warming of infusion fluids till body's temperature is restored (9, 15).

Indications for red cell transfusion due to the blood loss level:
- Loss of <15% of circulating blood volume (CBV) (up to 750 mL) – no need to transfuse red cells, unless anemia or severe heart or pulmonary diseases were diagnosed before hemorrhage;
- Loss of 15–30% of CBV (around 750–1500 mL) – crystalloids and synthetic colloids should be given; usually there is no need for red cell transfusion, unless anemia or severe heart or pulmonary disease is diagnosed and the bleeding continues;
- Loss of 30–40% of CBV (around 1500–2000 mL) – hypovolemia by crystalloids and synthetic colloids must be corrected urgently, and red cell transfusion is usually indicated;
- Loss of >40% of CBV (>2000 mL) – urgent correction of hypovolemia, including red cell transfusion, must be performed (2, 4, 9, 23).

Indications for red cell transfusion according to Hb level:
- Hb >10 g/dL, patient's condition is stable – no indication for red cell transfusion;
- Hb <6 g/dL, transfusion almost always indicated;
- Hb 6–10 g/dL, indication for transfusion is based individually for every patient and should be motivated (1, 2, 4, 9, 24).

When Hb level is ≤7 g/dL and anemia is asymptomatic, transfusion is needed if massive bleeding is expected during surgery or the patient belongs to a high anesthetic risk group (4).

One unit of donor erythrocytes (around 250 mL)

for a 70-kg patient increases Hb for about 0.5–1 g/dL (if bleeding does not continue). Therapeutic effect and clinical symptoms of anemia should be evaluated after every single transfused red cell unit (25).

When should platelets be used:
- In prophylaxis of hemorrhage:
  – platelet count of $<10\times10^9$/L,
  – coagulation disorders, petechiae, ecchymoses, thrombocytopenia of $10–20\times10^9$/L,
- Prior to surgical or invasive procedures, with platelet count of $<50\times10^9$/L;
- In case of microvascular bleeding without thrombocytopenia, when impairment of platelet function is confirmed by laboratory tests. Platelets are transfused if this impairment cannot be treated by other ways (e.g. in case of congenital platelet disorders);
- Performing epidural anesthesia or analgesia, with platelet count of $<100\times10^9$/L.

In case of normal vaginal delivery, thrombocytopenia of $<50\times10^9$/L is safe without need for prophylactic platelet transfusion (9, 20, 24, 25).

Platelets should not be transfused (except the cases of life-threatening hemorrhage) under these circumstances:– autoimmune thrombocytopenia,– thrombotic thrombocytopenic purpura,– heparin-induced thrombocytopenia,– posttransfusion purpura (26).

A usual dose of platelets is 1 unit/10 kg or 1 therapeutic dose (consisting of 4–6 units), or 1 pack of apheresed platelets.

After platelet transfusion, the therapeutic effect is evaluated in 10–60 minutes, 18 and 24 hours. Clinical studies have showed that the best time to evaluate the effectiveness of platelet transfusion is after 1 hour (27–29). One unit of platelet concentrate has on average $5.5–7.5\times10^9$ of platelets, and if there is no bleeding, it increases platelet count for $5–7.5\times10^9$ for a 70 kg patient (9, 25). One unit of apheresed platelets has approximately $3.5–4\times10^{11}$ platelets and increases recipient's platelet count for $30–40\times10^9$/L (25).

When should fresh frozen plasma be used:
- Coagulopathy and bleeding of different origin;
- Bleeding in case of disseminated intravascular coagulation (DIC);
- Thrombotic thrombocytopenic purpura;
- Congenital or acquired deficiency of different coagulation factors, when there is no possibility to get a certain factor's (e.g. V or XI) concentrate;
- Deficiency of specific plasma proteins (e.g. antithrombin III).

Fresh frozen plasma (FFP) is transfused, if in case of hemorrhage, the prothrombin time or activated partial thromboplastin time is prolonged for ≥1.5 times (1, 25).

If there is no hemorrhage, FFP should not be used for correction of hypovolemia or normalizing coagulation indexes (25).

A recommended initial dose of FFP is 10–15 mL/kg (at an average 3–4 units for a 70-kg adult patient); however, some repeated doses might be needed later on after evaluation of therapeutic effect on bleeding (9, 30).

When cryoprecipitate should be used:
- Hemorrhage due to hypofibrinogenemia or dysfibrinogenemia;
- DIC syndrome;
- Von Willebrand's disease (when factor VIII concentrate is not available);
- Hemorrhage due to factor XIII deficiency.

Treating hypofibrinogenemia and transfusing cryoprecipitate of 1–2 units/10 kg increases plasma fibrinogen concentration for approximately 500 mg/L (25).

Fibrinogen count in plasma of ≥1 g/L is sufficient to maintain hemostasis (9, 24, 25, 30).

Massive hemorrhage
Blood loss is considered massive, if:
- All blood volume is lost within a 24-hour period (normal blood volume in the adult is approximately 7% of ideal body weight);
- Or 50% blood volume loss within 3 hours;
- Or a rate of loss of 150 mL/min (1).

During massive blood loss, firstly, hypovolemia should be managed by crystalloids and colloids infusions as well as tissue hypoxia avoided by donor erythrocytes. This leads to increased coagulopathy risk due to dilution of coagulation factors (21). FFP should be added, in case of massive hemorrhage, when prothrombin time or activated partial thromboplastin time is prolonged for ≥1.5 times (31). If then fibrinogen plasma level is lower than 1 g/L, it is recommended to use cryoprecipitate as well. It should be borne in mind that during hemorrhage, monitoring of Hb, Ht and blood coagulation tests must be done regularly (1, 9, 24). Both, FFP and cryoprecipitate should be given according to clinical view and coagulation test results.

In massive blood loss, when platelet count is $<50\times10^9$/L, it is also recommended to use donor platelets, and platelet count should be maintained at

$\geq50\times10^9$/L (1, 29, 32, 33). Nevertheless, platelet count should be $\geq75\times10^9$/L in cases of an increase in fibrin degradation products, DIC syndrome, or fibrinolysis (30–32).

DIC syndrome in obstetrics is induced not only by massive hemorrhage, but also is often predisposed by amniotic fluid embolism, placental abruption, pre-eclampsia, and activated coagulation due to tissue trauma (1, 31). During DIC syndrome, coagulation factors are used up, so their levels in blood drop, especially of fibrinogen, factor V, VIII, and XIII (31). DIC syndrome should be suspected if prothrombin time, activated partial thromboplastin time are prolonged, thrombocytopenia, low fibrinogen concentration, bleeding in sites of tissue trauma, venipunctures, where intravenous catheters are indwelled. In case of a high risk of DIC syndrome and if coagulation test results are late as well as bleeding is difficult to stop by other means, FFP transfusion should be performed even if there are no test results available yet (30).

The strategy to minimize the use of donor blood

In some cases, when there is a high risk of major hemorrhage (e.g. placenta previa), pre-autologous blood may be deposited. Yet, it is not needed in normal pregnancy (1, 9).

Intraoperative cell salvage (IOCS) and reinfusion is recommended, when blood loss is anticipated to be >1500 mL (1). Blood from the surgical field is collected, mixed with anticoagulants, filtered through a special filter, and pumped into a reservoir, where it is centrifuged. After separating red cells from plasma, they are being washed with physiological solution. Such autologous red cells are then suspended in isotonic solution and reinfused to the patient. Plasma, platelets, leukocytes, free Hb, and remnants of damaged cells are collected to a special bag, which is afterward thrown off (10, 34, 35). Life span of reinfused red cells is the same as the patient's red cells, what is more, morphology and osmolar resistance do not change. It is evident that the quality of transfused autologous red cells is better than the quality of allogeneic red cells. However, the use of IOCS in obstetrics is risky (particularly the risk of amniotic fluid embolism), and therefore, it has been limited due to probable contamination by amniotic fluid, fetal blood cells, and immunization (especially anti-D formation for Rh D-negative women) (36, 37). The use of this method is more indicative to those women who refuse donor blood transfusion, since it reduces demand for donor blood in case of massive intraoperative bleeding. Nonetheless, the use of cell salvage in obstetrics is considered controversial, and clinical experience is insufficient (38).

Pharmacological strategy

In obstetrics, recombinant factor VIIa (rFVIIa) should be used only for life-threatening bleeding (39–41). Furthermore, there is no evidence of beneficial prophylactic use of rFVIIa in order to reduce bleeding during the cesarean section. Since the frequency of thromboembolic complications after usage of rFVIIa for patients without hemophilia is not estimated, effectiveness and safety of usage of rFIIIa in obstetrical bleeding are not fully defined (42–44).

Conclusions

In obstetrics, when there is a massive blood loss and circulating blood volume must be restored, firstly, crystalloids and colloids should be infused, but not donor red cells. Indications for red cell transfusion are estimated according not only to the values of Hb and Ht, but to clinical and physiological parameters reflecting the general condition of a patient as well. However, when Hb level is <60 g/L, red cell transfusion is usually required. The main indication for red cell transfusion is the need to restore red cell count in order to improve the ability of blood to transport oxygen and to prevent tissue and organ hypoxia. In case of acute bleeding, platelet count should be maintained at $\geq50\times10^9$/L. Fresh frozen plasma is used for correction of hypovolemia and normalization of coagulation only in case of hemorrhage. Hypofibrinogenemia is corrected by cryoprecipitate, when plasma fibrinogen count is <1 g/L.

In case of massive bleeding or DIC syndrome in obstetrics, coagulation test results and thrombocytopenia level are estimated and a combination of donor platelets, fresh frozen plasma, and cryoprecipitate is given, while rFVIIa is used for life-threatening, unmanageable bleeding.

Intraoperative cell salvage is recommended when massive hemorrhage is anticipated (placenta previa or placenta accreta), when cross-matched donor blood is unavailable in cases of rare blood type or alloantibodies present due to immunization, also when a patient refuses transfusion of donor blood components.

Kraujo komponentų vartojimas akušerijoje

Dalia Adukauskienė[1], Audronė Veikutienė[2], Agnė Adukauskaitė[3],
Vincentas Veikutis[4], Kęstutis Rimaitis[5]
[1]Kauno medicinos universiteto Intensyviosios terapijos klinika,
[2]Kauno medicinos universiteto Širdies, krūtinės ir kraujagyslių chirurgijos klinika,
[3]Kauno medicinos universitetas, [4]Kauno medicinos universiteto Biomedicininių tyrimų institutas,
[5]Kauno medicinos universiteto Anesteziologijos klinika

Raktažodžiai: nėščiųjų ir gimdyvių kritinės būklės, kraujavimas, kraujo komponentų perpylimas.

Santrauka. Gausus nėščiųjų ir gimdyvių kraujavimas visame pasaulyje išlieka pagrindine gimdyvių sergamumo ir mirštamumo priežastimi. Kraujo komponentų perpylimas kai kuriais atvejais gali tapti gyvybę gelbstinčia procedūra, tačiau kritinės būklės akušerijoje, ypač prasidėjus gausiam kraujavimui, didina sergamumą ir mirties riziką, jei kraujo komponentų skiriama netinkamai. Todėl išsamios žinios apie gausaus nėščiųjų ir gimdyvių kraujavimo etiologiją, patologinę fiziologiją ir optimalią gydymo taktiką padeda išvengti blogos baigties. Nustatyta, kad kraujo komponentų perpylimas susijęs su nepageidaujamais reiškiniais recipientei: ūminės ar uždelstos hemolizinės, hiperterminės, alerginės reakcijos, ūminis plaučių pažeidimas, neigiamas imunomoduliacinis poveikis, įvairių infekcinių ligų pernešimas, piktybinių navikų išplitimo rizika. Tai skatina siaurinti indikacijas alogeninio kraujo vartojimui. Sukuriami nauji metodai, mažinantys alogeninio kraujo poreikį. Nėštumo metu gali pasireikšti aloimunizacija, todėl kiekvienai nėščiajai būtina nustatyti priešeritrocitinius antikūnus, kurie gali būti susiformavę dėl ankstesnių nėštumų ar buvusių donorinių eritrocitų perpylimų, o tai labai svarbu parenkant eritrocitus pacientei ateityje. Prieš numatomą gimdymą tapataus kraujo komponentų atsargos ruošiamos esant nepalankiai akušerinei anamnezei, kraujo krešėjimo sutrikimams, sunkiai anemijai. Įvairiose gydymo įstaigose gydytojų taktika, skiriant donorinius kraujo komponentus (eritrocitus, trombocitus, šviežiai šaldytą plazmą arba krioprecipitatą), nevienoda, o indikacijos jų perpylimui neretai būna nepakankamai pagrįstos. Kiekvienas kraujo komponentas turėtų būti skiriamas įvertinus, kokio gydomojo poveikio tikimasi jo perpylus. Akušerijoje kritinės situacijos metu kraujo komponentų ir jų derinių poreikis kiekvienai pacientei turėtų būti įvertintas individualiai. Kraujo komponentų vartojimo indikacijos akušerijoje pateikiamos siekiant tobulinti gydytojų žinias ir optimizuoti gydymo taktiką kritinių akušerinių būklių metu.

References

1. Royal College of Obstetricians and Gynaecologist. Blood transfusion in obstetrics. Green-top guideline No. 47. London: RCOG; 2007.
2. Murphy MF, Wallington TB, Kelsey P, Boulton F, Bruce M, Cohen H, et al., and British Committee for Standards in Haematology Blood Transfusion Task Force. Guidelines for the clinical use of red cell transfusions. Br J Haematol 2001; 113:24-31.
3. Vamvakas EC, Blajchman MA. Transfusion-related mortality: the ongoing risks of allogeneic blood transfusion and the available strategies for their prevention. Blood 2009;113(15): 3406-17.
4. Guidelines for transfusion of red blood cells-adults. 2nd ed. New York; 2004. p. 1-5. Available from: URL: http:/www.wadsworth.org/labcert/blood_tissue
5. Serious Hazards of Transfusion Steering Group. Serious Hazards of Transfusion (SHOT) Annual Report 2004. London: Royal College of Pathologists; 2004.
6. Chapman JF, Elliott C, Knowles SM, Milkins CE, Poole GD; Working Party of the British Committee for Standards in Haematology Blood Transfusion Task Force. Guidelines for compatibility procedures in blood transfusion laboratories. Transfus Med 2004;14:59-73.
7. Hebert PC, Wells G, Blajchman MA, Marshall J, Martin C, Pagliarello G, et al. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. N Eng J Med 1999;340:409-17.
8. Vincent JL, Baron JF, Reinhart K, Gattinoni L, Thijs L, Webb A, et al. Anemia and blood transfusion in critically ill patients. JAMA 2002;288:1499-507.
9. Fuller AJ, Bucklin B. Blood component therapy in obstetrics. Obstet Gynecol Clin N Am 2007;34(3):443-58.
10. Veikutienė A, Širvinskas E, Adukauskienė D. Autologinio kraujo perpylimas. (Transfusion of autologous blood.) Medicina (Kaunas) 2008;44(6):482-8.
11. Sirvinskas E, Sneider E, Svagzdiene M, Vaskelyte J, Raliene L, Marchertiene I, et al. Hypertonic hydroxyethyl starch solution for hypovolaemia correction following heart surgery. Perfusion 2007;22:121-7.
12. British Committee for Standards in Haematology Blood Transfusion Task Force, Gooch A, Parker J, Wray J, Qureshi H. Guideline for blood grouping and antibody testing in pregnancy. Transfus Med 2007;17(4):252-62.
13. Better use of blood in Northern Ireland: guidelines for blood transfusion practice. 2001. p. 35-7. Available from: URL: http://www.crestni.org.uk/publications/blood_transfusion.pdf

14. Practice guidelines for obstetric anesthesia: an updated report by the American Society of Anesthesiologists task force on Obstetric Anesthesia. Anesthesiology 2007;106(4):1-21.

15. Napolitano LM. Perioperative anemia. Surg Clin N Am 2005;85:1215-27.

16. Hutton B, Fergusson D, Tinmouth A, McIntyre L, Kmetic A, Hebert PC. Transfusion rates vary significantly amongst Canadian medical centres. Can J Anaesth 2005;52(6):581-90.

17. Spahn DR, Cerny V, Coats TJ, Duranteau J, Fernandez-Mondejar E, Gordini G, et al. Management of bleeding following major trauma: a European guideline. Crit Care 2007; 11:R17.

18. Madjdpour C, Spahn DR. Allogeneic red blood cell transfusion: physiology of oxygen transport. Best Pract Res Clin Anaesthesiol 2007;21(2):163-71.

19. Weiskopf RB, Feiner J, Hopf H, Viele MK, Watson JJ, Lieberman J, et al. Heart rate increases linearly in response to acute isovolemic anemia. Transfusion 2003;43:235-40.

20. Mercier FJ, Van de Velde M. Major obstetric hemorrhage. Anesthesiology Clin 2008;26:53-66.

21. Adukauskienė D, Mažeikienė S, Veikutienė A, Rimaitis K. Želatinos infuziniai tirpalai. (Infusion solutions of gelatin derivates.) Medicina (Kaunas) 2009;45(1):77-84.

22. Jansen AJ, van Rhenen DJ, Steegers EA, Duvekot JJ. Postpartum hemorrhage and transfusion of blood and blood components. Obstet Gynecol Surv 2005;60:663-71.

23. Santoso JT, Saunders BA, Grosshart K. Massive blood loss and transfusion in obstetrics and gynecology. Obstet Gynecol Surv 2005;60(12):827-37.

24. Practice guidelines for perioperative blood transfusion and adjuvant therapies. An updated report by the American Society of Anesthesiologists task force on perioperative blood transfusion and adjuvant therapies. Anesthesiology 2006; 105:198-208.

25. Practice guidelines for blood transfusion. 2nd ed. Geneva; 2007. p. 8-41. Available from: URL: http://www.redcross.org/services/biomed/profess/pgbtscreen.pdf

26. Guidelines for the use of platelet transfusions. British Committee for Standards in Haematology Blood Transfusion Task Force. Br J Haematol 2003;122:10-23.

27. Adukauskienė D, Kinderytė A, Veikutienė A. Indikacijos trombocitų transfuzijai. (Indications for platelet transfusion.) Medicina (Kaunas) 2008;44(11):905-9.

28. Sensebe L, Giraudeau B, Bardiaux L, Deconinck E, Schmidt A, Bidet ML, et al. The efficiency of transfusing high doses of platelets in hematologic patients with thrombocytopenia: results of a prospective, randomized, open, blinded end point (PROBE) study. Blood 2005;105(2):862-4.

29. Goffinet F, Mercier FJ, Teyssier V, Pierre F, Dreyfus M, Mignon A, et al. Postpartum haemorrhage: recommendation for clinical practice by the CNGOF (December 2004). Gynecol Obstet Fertil 2005;33:268-74.

30. Stainsby D, MacLennan S, Thomas D, Issac J, Hamilton PJ; British Committee for Standards in Haematology. Guidelines on the management of massive blood loss. Br J Haematol 2006;135:634-41.

31. Hardy JE, De Moerloose P, Samama M. Massive transfusion and coagulopathy: pathophysiology and implications for clinical management. Can J Anaesth 2004;51:293-310.

32. Kobayashi T, Terao T, Maki M, Ikenoue T. Diagnosis and management of acute obstetrical DIC. Semin Thromb Hemost 2001;27:161-7.

33. Slichter SJ. Relationship between platelet count and bleeding risk in thrombocytopenic patients. Transfus Med Rev 2004;18:153-67.

34. Carless PA, Henry DA, Moxey AJ, O'Connell DL, Brown T, Fergusson DA. Cell salvage for minimising perioperative allogeneic blood transfusion. Cochrane Database Syst Rev 2006;4:CD001888.

35. Waters JH. Indications and contraindications of cell salvage. Transfusion 2004;44(Suppl 12):S40-4.

36. Waters JH, Biscotti MD, Potter PS, Philipson E. Amniotic fluid removal during cell salvaged in the caesarean section patient. Anesthesiology 2000;92:1531-6.

37. Clark V. Facilities for blood salvage (cell saver technique) must be available in every obstetric theatre. Int J Obstet Anesth 2005;14(1):50-2.

38. Catling S. Blood conservation techniques in obstetrics: a UK perspective. Int J Obstet Anesth 2007;16:241-9.

39. Vincent JL, Rossaint R, Riou B, Ozier Y, Zideman D, Spahn DR. Recommendations on the use of recombinant activated factor VII as an adjunctive treatment for massive bleeding – a European perspective. Crit Care 2006;10:R120.

40. Karalapillai D, Popham P. Recombinant factor VIIa in massive postpartum haemorrhage. Int J Obstet Anesth 2007;16:29-34.

41. Ahonen J, Joleka R. Recombinant factor VIIa for life-threatening post partum haemorrhage. Br J Anaesth 2005;94:592-5.

42. Spahn D, Tucci M, Makris M. Is recombinant FVIIa the magic bullet in the treatment of major bleeding. Br J Anaesth 2005;94:553-5.

43. Boehlen F, Morales MA, Fontana P, Ricou B, Irion O, de Moerloose P. Prolonged treatment of massive postpartum haemorrhage with recombinant factor VIIa: case report and review of the literature. BJOG 2004;111:284-7.

44. O'Connell KA, Wood JJ, Wise RP, Lozier JN, Braun MM. Thromboembolic adverse events after use of recombinant human coagulation factor VIIa. JAMA 2006;295(3):293-8.