TÜRK PEDİATRİ ARŞİVİ
TURKISH ARCHIVES of PEDIATRICS

Turkish Neonatal Society guideline on the transfusion principles in newborns

Türk Neonatoloji Derneği yenidoğanda transfüzyon ilkeleri rehberi

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Cite this article as: Çetinkaya M, Atasay B, Perk Y. Turkish Neonatal Society guideline on the transfusion principles in newborns. Turk Pediatri Ars 2018; 53(Suppl 1): S101-S108.

Abstract

Blood transfusion can be defined as a life-saving procedure in neonates, especially in premature and surgical infants. The indications, threshold hemoglobin, and platelet levels for red cell, platelet, and plasma transfusions in neonates vary among centers and the evidence-based data for possible adverse effects, preterm morbidities, mortality, and neuro-developmental problems associated with transfusions are not clear yet. Herein, we aim to present the transfusion guideline designed to be used in neonatal intensive care units in our country, summarizing clinical findings and threshold levels for red cell, platelet, and plasma transfusions in addition to important practical points of transfusions according to a literature review.

Keywords: Anemia, erythrocyte, guideline, newborn, plasma, platelet, transfusion

Öz

Kan transfüzyonu anemisi olan özellikle prematüre ve cerrahi uygulanacak yenidoğanlarda sıklıkla uygulanan yaşam kurtarıcı bir tedavidir. Yenidoğanda eritrosit, trombosit ve plasma transfüzyon endikasyonları, transfüzyon kararı verdiren eşik hemoglobin, trombosit değerleri merkezlere göre değişmekte olup, transfüzyonların olası yan etkileri ve prematüre morbiditeleri, mortalite ve nörogelişimsel etkileri ile ilgili kanıta dayalı veriler yeterli değildir. Burada, dizin bilgileri değerlendirilerek, eritrosit süspansiyonu, trombosit ve plasma transfüzyonu kararı için klinik bulgulara göre önerilen eşik değerler ve uygulamada dikkat edilecek konuları özetleyen ülkemiz yenidoğan yoğun bakım birimlerinde kullanılmak üzere oluşturulmuş transfüzyon rehberinin sunulması amaçlanmıştır.

Anahtar sözcükler: Anemi, eritrosit, kılavuz, yenidoğan, plazma, trombosit, transfüzyon

Introduction

Transfusions (red blood cell transfusion for symptomatic anemia, exchange transfusion for hemolytic disease of the newborn, and platelet or plasma transfusion for hemorrhage or risk of hemorrhage) are performed frequently in sick newborns including mainly very-low-birth- weight (VLBW) preterm babies. However, threshold hemoglobin and platelet values have not been clearly established for red blood cell and platelet suspension transfusions. Similarly, fresh-frozen plasma (FFP) is being frequently used for non-evidence-based indications.

Here, it was aimed to describe the general properties of red blood cell, platelet, and FFP transfusions, and especially to present recommendations that might form the basis for transfusion decisions.

Red blood cell transfusion principles in newborns

In newborns, a hemoglobin (Hb) or hematocrit (Hct) value 2 SD below the mean value for the postnatal age is defined as anemia. The most common causes of anemia include blood loss, reduced erythrocyte production, and increased erythrocyte destruction. In newborns, shorter lifespan of erythrocytes, higher sensitivity of erythrocytes to oxidative injury, increased dysmorphic erythrocyte ratio, markedly low endogenous erythropoietin (EPO) lev-

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DOI: 10.5152/TurkPediatriArs.2018.01810

els, and limited erythropoiesis capacity cause the development of physiologic anemia (1).

The Hb concentration, which is 16.5 g/dL on average at birth in a newborn baby, increases to 18.4 g/dL in the first 24 hours and decreases to 11.5 g/dL with a physiologic reduction in the subsequent 3-month period. This reduction is more definite in preterm babies. This is caused by suppression of EPO synthesis because of increased blood and tissue oxygen content immediately after delivery. In term babies, the lowest Hb value, which is 9.0-12.0 g/dL, frequently develops in the postnatal 6-12nd weeks. Afterwards, Hb values show an increase up to the age of two years with endogenous EPO secretion due to the perception of hypoxia by tissues and with increased erythropoiesis. In healthy term babies, asymptomatic, physiologic anemia does not generally need treatment (2). Especially in preterm babies born before the 32nd gestational week, the Hb value decreases to 7.0-8.0 g/dL in the postnatal 4-8th weeks due to several factors including phlebotomy losses , low EPO levels, shorter erythrocyte lifespan, increased destruction, infection, inflammation, nutritional deficiencies and chronic disease. This condition, which is termed anemia of prematurity, frequently causes symptoms and requires transfusion (2, 3).

Studies have reported that transfusion is performed in the first two weeks of life in 50% of extremely-low-birthweight (ELBW) babies with a birth weight <1000 g and during hospitalization in the neonatal intensive care unit (NICU) in 90% (1, 4).

Red blood cell transfusion is performed in newborns most frequently in cases of anemia related with surgical procedures, hemorrhagic shock, and anemia of prematurity. However, the prediction that Hb/Hct values in preterm and/or sick newborns could not fully reflect erythrocyte mass in addition to difficulties in assessment of the clinical findings of anemia cause an inability to establish clear-cut threshold Hb values and transfusion-related indications. Therefore, different transfusion protocols are currently being used in many countries and NICUs (5, 6). The main objective of transfusion is to improve tissue oxygenation. Tissue oxygenation is determined by cardiac output, the blood's capacity to carry oxygen and Hb concentration. In recent years, it has been stated that several markers including reticulocyte count, serum lactate level, erythrocyte volume, and serum vascular endothelial growth factor (VEGF) in addition to Hb value and cardiac and respiratory status might be used in determining transfusion requirement in newborns. However, their use in practice is limited (4). With technological advancements, tissue oxygenation can also be determined through measurement of the oxyhemoglobin-deoxyhemoglobin difference using near-infrared spectroscopy (NIRS). In NIRS, oxygenation of different tissues including mainly regional cerebral tissue oxygenation in association with blood flow rates are continuously monitorized. Using NIRS, it has been shown that cerebral oxygenation is disrupted in conditions in which Hb values reduce below 9.7 g/dL and rapidly improve after transfusion (7). However, as there is currently no clear marker showing tissue oxygenation, it is important to know clinical symptoms. Tachycardia, tachypnea, increase in respiratory distress and oxygen need, apnea, bradycardia, reduction in weight gain and activity, pallor, and edema constitute the most frequent clinical findings evaluated in the decision of transfusion.

The lowest Hb value at which tissue oxygenation can be maintained normally has been defined as the critical or threshold Hb value. The decision for transfusion is made according to the clinical and laboratory findings accompanying this value. In practice, the decision for transfusion in NICUs is made with Hb values at which mostly unspecific symptoms related with insufficient tissue oxygenation occur. However, there are no definite and clear data indicating which baby and which Hb level require transfusion. Transfusion performed at lower Hb levels has been defined as limited transfusion, and transfusions performed at higher Hb levels have been defined as liberal transfusion. Clinical results of limited and liberal transfusion were evaluated in two large studies. In the IOWA study, 100 VLBW babies were randomly assigned to limited and liberal transfusion groups with the objective of decreasing transfusion frequency. Although transfusion frequency did not change between the groups, the frequencies of intraparenchymal hemorrhage, periventricular leukomalacia (PVL) and apnea were found to be higher in the limited transfusion group. In the long-term follow-up in which 56 of these babies were included, it was shown that the liberal transfusion group had worse neurocognitive outcomes and smaller brain volume. It was hypothesized that unfavorable neurodevelopmental outcomes developed secondary to the decreased neuroprotective efficiency of EPO as a result of inhibition of EPO secretion in the liberal group (8, 9). In the Premature Infants in Need of Transfusion (PINT) study, in which 451 ELBW babies were included, transfusion was decided according to postnatal age and respiratory state and it was found that the transfusion frequency decreased in the limited transfusion group and there was no difference between the two groups in terms of survival rate and morbidities including retinopathy of prematurity (ROP),

bronchopulmonary dysplasia (BPD), and brain injury, but cognitive retardation was found in the 18-21-month period in babies in the limited group (10). After these studies, a Cochrane meta-analysis polished in 2011 concluded that transfusion frequency decreased, lower Hb levels were obtained, morbidity and mortality rates did not increase at the time of discharge or in the long-term follow-up with limited transfusion policies, but one should not go below the threshold Hb values used in the studies (11). Therefore, randomized studies with larger samples are needed in this area.

Red blood cell transfusion recommendations

In light of this information, although there is no definite Hb value to make a decision for transfusion in term and preterm babies; oxygen requirement, being on a mechanical ventilator, and postnatal age are important factors in this decision. In many guidelines, threshold Hb values for red blood cell transfusion in term and preterm babies have not been specified clearly. However, emergency transfusions should be applied in conditions in which inadequate oxygen distribution accompanying 10-20% blood loss is present or acute blood loss with continuing bleeding is present, or if there is more than 20% blood loss in a term or preterm baby. In conclusion, it is important to control transfusion numbers using guidelines in which threshold Hb values are specified according to criteria including acute or chronic blood loss (Hb reduction rate), gestational week, postnatal age, respiratory and circulatory support, oxygen requirement, clinical findings, and weight gain. The recommendations established by the Turkish Neonatal Society according to the characteristics of the newborn baby, postnatal day, and threshold Hb values are shown in Table 1.

Table 1. The Turkish Neonatal Society's threshold Hb values for transfusion of red blood cell suspension

Postnatal age	Respiratory support, Hb g/dL	Minimal or no respiratory support, Hb g/dL
<1 week	12	10
1-2 weeks	11	9
2-3 weeks	10	8.5
≥4 weeks	9	7

*** At levels below these limits, the decision of transfusion is made by reevaluating the patient in terms of symptoms

Criteria for respiratory support:	Criteria for minimal/absent respiratory support:
For target saturation (90-95%);	For target saturation (90-95%);
- High frequency ventilation	- <2L/min HHFNC
- Conventional mechanical ventilation	- FiO_2 requirement 21-35%
- Non-invasive ventilation	- No oxygen requirement
- >2L/min HHFNC	
- FiO_2 requirement >35%	

***Presence of one of the symptoms in presence of the threshold Hb value above

- Presence of tachycardia or tachypnea for >24 hours (apical heart beat (AHB) >180/min, RR>60/min)
- Two-fold increase in oxygen requirement in the last 48 hours
- A lactate value of ≥2.5 mEq/L or acute metabolic acidosis (pH< 7.20)
- A weight gain of <10 g/kg/day while receiving >120 kcal/kg/day in the last four days
- If major surgery is to be performed in 72 hours

According to the "Guideline for Transfusion of Blood Products Recommendation" published by the Turkish Neonatal Society;

It was recommended that central Hct/Hb should be measured at the time of hospitalization, routine blood sampling should not be performed subsequently unless necessary, the decision for transfusion should be made with consensus at visits unless there is acute blood loss, and transfusion should be considered independent of the threshold value in cases where tissue oxygenation should be urgently corrected in association with clinical symptoms in term or preterm babies. Similarly, it was stated that transfusion should be performed independent of the threshold Hb value in the presence of symptomatic anemia. In patients in whom endogenous EPO is being administered, it was recommended that criteria including reticulocyte count, Hb reduction rate, postnatal age, and O_2 requirement should be considered in addition to the use of the same guideline for transfusion.

It was specified that the Hb/Hct values targeted with red blood cell transfusion should be 12 g/dL and 35%, respectively, and the deeper and more symptomatic anemia is, the more normal Hb values should be targeted. It has been recommended that the threshold Hb value should be 45% in babies with congenital heart disease or those who require extracorporeal membrane oxygenation, 40% in severe cardiopulmonary diseases, and 30% in major surgery.

Recommendations related with erythrocyte suspension to be used in newborns

- Most packed red blood cell suspensions are obtained as a result of the procedure of collection of 450-500 mL whole blood in sterile plastic bags containing citrate-phosphate-dextrose (CPD) as an anticoagulant and separation of erythrocytes from platelet-rich plasma following centrifugation. Subsequently, erythrocytes are placed in sterile bags containing an anticoagulant

and additional solution. With this objective, additional solutions, which frequently contain a mixture of glucose, adenine and mannitol (in some conditions), are used. The half-life is 21 days for packed red blood cell suspensions containing citrate-phosphate-dextrose, five days for those containing citrate-phosphate-dextrose-adenine (CPDA-1), and 42 days for suspensions containing additional solutions. Transfusion of a total of 10 mL/kg CDPA-1-containing red blood cell suspension causes a 9-10% increase in the Htc value of the recipient baby and transfusion of additional solution-containing erythrocyte suspension causes a 7-8% increase. The red blood cell suspension should have a Hct value of 50-60% (12-14).

- Leukocyte-depleted or irradiated red blood cell suspensions are used in neonatal transfusions. The leukocyte depletion procedure is named as "pre-deposit" and it is recommended to be performed after a blood sample is obtained and before storage. Leukocyte depletion aims to prevent cytomegalovirus (CMV) transmission with filtration, febrile reaction, platelet alloimmunization, and immunomodulation. It has been reported that the leukocyte count in the final suspension is reduced by 99.9%, especially with the use of a leukocyte filter (15). Seronegative preterm babies with a birth weight below 1250 g and fetuses who have undergone intrauterine transfusion have an increased risk in terms of transfusion-related CMV infection. Although the use of CMV seronegative blood is the gold standard for prevention of transfusion-related CMV infections, it is thought that leukocyte depletion might be beneficial in communities with a high rate of CMV positivity, including our country (12). In light of these data, leukocyte depletion should be performed following blood sampling in all blood products used in newborns except for granulocytes (16).
- The irradiation procedure is targeted to prevent graft-versus-host disease (GVHD) by decreasing lymphocyte viability in congenital immunodeficiency transfusions, intrauterine transfusion applications, and transfusions from close relatives in preterm infants. Packed Red blood cell suspensions should be transfused after irradiation. The donor lymphocytes are inactivated with irradiation, and the risk of transfusion-related GVHD is decreased. Newborns, and especially preterm babies, are under risk in terms of GVHD and transfusion with irradiated blood is recommended in babies who have suspicious/known congenital immune deficiency and who will undergo intrauterine transfusion or blood exchange. A minimal gamma irradiation dose of 25 Gy is applied in the irradiation of blood products (17, 18). Potassium leakage during storage increases with irradiation and irradiated products have shorter half-lives. The United States Food and Drug Administration (FDA) recommends that irradiated red blood cell suspensions should be consumed in 28 days and non-irradiated ones should be consumed in 42 days. However, transfusion should be applied in 24 hours after irradiation in newborns in whom potassium loading is an issue of concern. It has been reported that the procedure of irradiation does not prevent CMV infection after transfusion (5, 18).
- Erythrocytes may be washed with saline with the objective of cleaning blood components from plasma or from additional solutions or with the objective of decreasing the potassium content. In newborns, washed red blood cell suspensions are used for intrauterine transfusion, for exchange transfusion or if a transfusion of erythrocyte suspension that has waited for longer than 14 days is to be performed at a dose of 20 mL/kg. After the procedure of washing, suspensions that are at room temperature should be used within 4 hours and suspensions that are in a refregirator should be used within 24 hours (5, 18).
- Before transfusion, screening of newborns in terms of blood groups and passive antibodies of maternal origin should be performed. If antibody screening is negative, additional screening in hospital is not needed until the baby is aged 4 months and an ABO and Rh-compatible red blood cell transfusion can be performed. If antibody screening is positive, erythrocyte suspension compatible with maternal antibodies should be given. In all newborns including mainly VLBW preterm babies, transfusion with leukocyte-depleted, irradiated, ABO and Rh-compatible erythrocyte suspension with reduced leukocytes should be performed. Centrifugation should be performed before transfusion with the objective of decreasing the risk of hemolysis by removing plasma containing anti-A and anti-B antibodies before giving O group red blood cell suspension to newborns with A or B blood group.
- Transfusion with red blood cell suspensions obtained from donors who are family members or close relatives is not recommended because of increased complications including transfusion-related GVHD and infection. The mother should not be the donor for her baby because antibodies against erythrocytes, leukocytes, platelets, and HLA antigens are produced by newborn cells in plasma of maternal origin. If maternal erythrocytes are to be used, washing and irradiation should be performed before transfusion.
- In newborns, transfusion should be performed in a pe-

riod of 4 hours without heating at a dose of 10-20 mL/kg using an injector or infusion of blood in bags. Red blood cell suspensions should be prepared as multiple small bags from a single donor in order to decrease exposure to multiple donors as numerous transfusions are performed during hospitalization, especially in preterm babies. These prepared suspensions can be used for up to six weeks if they are stored safely. In recent years, donor exposure, transfusion numbers, and the frequency of reactions have markedly decreased with limited transfusion policies, performance of tests for infection, use of leukocyte filters, irradiation, and application of small-volume (10-20 mL/kg) transfusion in VLBW babies (3, 14, 19).

Issues that should be considered in the application of red blood cell transfusion

- Under normal conditions, an increase of 2-3 g/dL is provided in Hb values as a result of transfusion of a 15-20–mL/kg erythrocyte suspension. Transfusion at a dose of 15-20 mL/kg is frequently sufficient to correct anemia; however, larger amounts of transfusion may be performed to correct hemorrhage. In hemorrhagic shock occurring at the time of delivery, shock fluid (10-20 mL/kg normal saline) and O Rh-negative red blood cell suspension (if the blood is ready) at a dose of 10-20 mL/kg should be given to provide circulation. An O Rh-negative erythrocyte suspension should be transfused at a dose of 15-20 mL/kg in these patients, if marked blood loss is established (>10-20% blood volume) or findings including acidosis, disrupted oxygenation, and heart failure indicating emergency transfusion are present. Therefore, all perinatal centers should provide O Rh-negative red blood cell suspensions, which do not require "cross-match" for emergency situations.
- During transfusion, vital signs should be evaluated at baseline, at the 15th minute, at the 1st hour, and every hour thereafter. Evaluation should be repeated at the end of transfusion and one hour later. Volume loading caused by transfusion should be prevented by subtracting the amount transfused from the total fluid; this is especially important in preterm babies (3, 14, 19).

Complications related with red blood cell transfusion

Currently, transfusion-related risks have been significantly reduced with appropriate donor selection, screening, "cross-match", pathogen inactivation procedures, leukocyte filters, and irradiation procedures. Adverse effects related with leukocytes including immunomodulation, alloimmunization, GVHD, and transfusion-associated lung injury (TRALI), transfusion-related infections, acute volume or electrolyte disorders and transfusion using the wrong blood group constitute the most important risks. Fever, shiver, flushing, urticaria, tachycardia, hypotension, and shock findings should suggest transfusion reaction; transfusion should be discontinued in the event of a reaction, the baby should be stabilized, the event should be recorded, the blood center should be informed and a sample should be sent to laboratory (5, 20). Although it has recently been reported that transfusion-associated necrotizing enterocolitis (TANEC) developing in 48 hours following transfusion may be observed frequently and that mortality is higher in these babies, recent publications related with this issue continue to give contradictory information. It is thought that increased oxygen consumption related with enteral nutrition and nitric oxide-mediated vasodilatation may be responsible from TANEC (5, 19). Similarly, there are reports suggesting that intraventricular hemorrhage (IVH), BPD, and ROP may also be related with transfusion (19). Because of all these risks, restrictive transfusion according to threshold Hb values should be preferred with the objective of preventing poor neurologic outcomes.

Does transfusion have an alternative?

In recent years, measures directed at decreasing the frequency of transfusion in newborns (mainly in VLBW preterm babies) including delaying cord clamping for at least 30 seconds in all term and preterm deliveries, autologous placental transfusion applications, use of EPO or darbopoetin, sending first blood samples from the placenta at admission, reducing the frequency of iatrogenic blood sampling by way of phlebotomy, use of micro methods in studying blood samples, and appropriate nutrition strategies in routine practical use are very important (1, 21, 22).

In view of this information, it is recommended that each unit should have a transfusion protocol prepared according to the postnatal age, clinical findings, need for oxygen with respiratory/circulation support and threshold Hb values according to the Hb reduction rate, and it should be assured that all physicians working in the unit comply with this protocol. Transfusion should be performed with attention paid to the above-mentioned characteristics and application standards in conditions where potential benefit is predicted, with particular consideration to the gain/loss principle in transfusion.

Platelet transfusion principles in newborns

The second blood product that is most commonly used for transfusion in newborns is platelet suspension. Thrombocytopenia is found in approximately 20-35% of

babies who present to the NICU, whereas it is observed in 70% of VLBW babies with a higher rate of accompanying bleeding problems.

A platelet count below 150,000/μL is defined as thrombocytopenia and values below 50,000/μL are defined as severe thrombocytopenia. Thrombocytopenia occurring in the first three days of life is classified as early-onset thrombocytopenia, and thrombocytopenia occurring after the fourth day is classified as late-onset thrombocytopenia. The most common causes of early-onset thrombocytopenia include maternal preeclampsia, pregnancy-induced hypertension or diabetes, intrauterine growth retardation, perinatal infections, perinatal asphyxia, and transplacental transmission of maternal allo- or autoantibodies. Late-onset thrombocytopenia is most commonly caused by postnatal infection and necrotizing enterocolitis (23).

In newborns with severe thrombocytopenia, the most threatening complication is major hemorrhage, mainly intracranial hemorrhages. The frequency of major intraventricular and periventricular hemorrhage is 30% in preterm babies and hemorrhage develops in the first 48 hours in 75% of cases. It is currently thought that the development or progression of IVH can not be prevented by performing transfusion of platelet suspensions in babies with mild or moderate thrombocytopenia because studies have reported that thrombocytopenia is absent before hemorrhage in most babies and thrombocytopenia and coagulopathy develop after hemorrhage.

Recommendations related with platelet suspension to be used in newborns

- Platelet suspensions used in the treatment of thrombocytopenia are in the form of pooled platelet suspensions separated from donors' whole blood and apheresis platelet suspensions, which are obtained from donors by way of cell separation. Apheresis is advantageous in terms of obtaining an adequate platelet count from a donor for transfusion and reducing the frequency of transfusion-related infection/alloimmunization.
- The procedure of leukocyte depletion is important while preparing platelet suspensions and the frequencies of alloimmunization, infection, and febrile reactions are reduced in this way.
- Development of GVHD is prevented with irradiation of platelets.
- The platelet concentrates prepared should be stored at 22°C for five days by shaking in an agitator.
- Transmission of viral disease should be minimized by using CMV seronegative donors for platelet suspensions, similar to erythrocyte suspensions.
- ABO and Rh-compatible platelet suspension with normal donor screening and normal serologic tests is transfused at a dose of 10-20 mL/kg. It should be kept in mind that the required efficiency may not be obtained with platelet transfusion in the presence of ABO incompatibility and acute lethal hemolytic transfusion reaction may develop even in minor incompatibilities (24).

Issues that should be considered in the application of platelet transfusion

- Although the benefit of platelet suspension is indisputable in newborns with active hemorrhage and severe thrombocytopenia, prophylactic platelet transfusion is frequently performed with the objective of preventing major hemorrhages in patients with severe thrombocytopenia. However, a clear benefit of prophylactic platelet transfusion is not known. Therefore, complications of transfusion and hazards of multiple transfusions should be kept in mind. In recent years, platelet mass rather than platelet count has been regarded and this value is targeted to be above 800, 400, and 160, respectively. It has been reported that the frequency of prophylactic platelet transfusion may be reduced using these reference values of platelet mass (21). The threshold platelet values recommended by the Turkish Neonatal Society for transfusion are shown in Table 2.
- Platelets should be ordered from the blood center just before transfusion and transfusion should be initiated as soon as the platelet suspension arrives.
- Vital signs should be monitored before, during, and after transfusion.
- A separate vascular access should be used for platelet transfusion. Transfusion should be initiated with a slow infusion rate and completed in 1 hour by increasing the infusion rate if no reaction occurs. The platelet count should be measured at least twice (one hour and 24 hours after transfusion) to check the efficacy of the transfusion.

Complications associated with platelet transfusion

The most important risks associated with platelet transfusion include infection, alloimmunization, fever, hemolytic and allergic reactions, and transfusion-related lung and intestinal injuries. Complications including transfusion of platelets from a wrong blood group or transfusion without irradiation have been reported frequently. The most common complication is bacterial infection and the risk of bacterial contamination is higher for platelet

Table 2. The Turkish Neonatal Society's threshold platelet values for platelet transfusion

<20,000/μL	All babies
20,000-49,000/μL	<1000 g VLBW baby*
	Sick baby
	Accompanying coagulopathy
	Severe morbidity (grade 3-4 IVH, NEC, sepsis)
	Invasive intervention
	Minor hemorrhage
50,000-100,000/μL	Active/major hemorrhage
	DIC
	Preoperative/postoperative
>100,000/μL	ECMO
	Neurosurgery operations

VLBW: very low birth weight; DIC: disseminated intravascular coagulation; ECMO: extracorporeal membrane oxygenation; IVH: intraventricular hemorrhage; NEC: necrotizing enterocolitis

transfusion compared with red blood cell suspension or FFP because platelet suspensions are kept at room temperature. Platelet suspensions may cause inflammatory injury or increase present inflammation because they contain bioactive factors including platelet-activating factor. An increase in donor exposure occurs with each platelet suspension. It has been shown that transfusion of multiple platelet suspensions is associated with increased mortality (25).

Currently, the majority of platelet transfusions are performed for prophylaxis and the benefits and hazards of this approach are controversial. Therefore, transfusion should be performed according to the specified threshold platelet counts and the patient's clinical status, and one should aim to reduce the frequency of transfusions and prevent potential complications. More studies are needed to use platelet mass rather than platelet count.

Principles and recommendations for transfusion of fresh-frozen plasma in newborns

FFP contains many procoagulant and inhibitor components in the coagulation cascade, acute phase protein, immunoglobulin, and albumin. Although studies have shown that FFP may be mainly beneficial in cases of active hemorrhage and related coagulopathy, it is transfused for prophylaxis with inappropriate indications in more than 60% of newborns (3). Transfusion of FFP has been recommended in cases of hemorrhage accompanying coagulopathy with deficiency of multiple factors including disseminated intravascular coagulation, deficiency of a single coagulation factor or deficiency of vitamin K in recent publications. Use of FFP is not recommended for the prevention of morbidity and mortality in preterm babies, partial exchange transfusion for treatment of polycythemia, for the treatment of sepsis or RDS and for volume replacement in hypotension. In newborns, abnormal coagulation tests alone should not be used as a marker of hemorrhage in the absence of clinical findings. Therefore, FFP transfusion of for correction of coagulation tests in babies who do not have hemorrhage is not an evidence-based approach. In conclusion, FFP should only be used in the presence of hemorrhage and coagulopathy in newborns (26). ABO-compatible FFP or FFP with AB group should be transfused at a dose of 15-20 mL/kg. Depending on the severity of the underlying picture, half of the factors are replaced with a dose of >20 mL/kg and one should watch for volume loading after transfusion. The recommendations of Turkish Neonatal Society for FFP transfusion in newborns are shown in Table 3.

Table 3. The Turkish Neonatal Society's recommendations for administration of fresh-frozen plasma

Dose	10-15 mL/kg, 20 mL/kg in conditions accompanied by severe factor deficiency
Indication	• Bleeding and coagulopathy (e.g., vitamin K deficiency, DIC, congenital deficiencies of coagulation factors),
	• In cases where invasive intervention is to be performed or where the PT and aPTT values are 1.5-fold higher than the normal value by age in a bleeding patient
Conditions where FFP should not be administered	• With the objective of correcting coagulation tests in absence of hemorrhage,
	• Adjuvant treatment in sepsis and RDS,
	• As volume expander in hypotension,
	• With the objective of partial exchange transfusion in polycythemia,
	• In coagulopathy developing during hypothermia in the absence of hemorrhage,
	• With the objective of prophylaxis for preventing IVH.

DIC: disseminated intravascular coagulation; IVH: intraventricular hemorrhage; RDS: respiratory distress syndrome

Conclusion

Transfusions are performed frequently in newborns. Because evidence-based data are insufficient, the decision

for transfusion should be made according to threshold Hb values, clinical symptoms, and tissue oxygenation for erythrocyte suspension, and according to platelet count and/or platelet mass and hemorrhage findings for platelet suspension. The gain/loss balance in terms of the patient and related complications should definitely be kept in mind in transfusion. It is thought that the number of transfusions and indications in NICUs will be limited with the implementation of the Turkish Neonatal Society's Guideline for Recommendations for Transfusion of Blood Products by all clinics in our country.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

Çıkar Çatısması: Yazarlar çıkar çatışması bildirmemişlerdir.

Mali Destek: Yazarlar bu çalışma için mali destek almadıklarını beyan etmişlerdir.

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