Evaluation of Erythrocyte Suspension Usage in Neonates

Yenidoğanlarda Eritrosit Süspansiyonu Kullanımının Değerlendirilmesi

Emel ÖMERCİOĞLU[1], Ayşegül ZENCİROĞLU[2]

[1]Department of Pediatrics, Division of Developmental Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey
[2]Department of Neonatology, University of Health Sciences of Turkey, Dr Sami Ulus Maternity and Children Research and Training Hospital, Ankara, Turkey

ABSTRACT

Objective: Erythrocyte suspension (ES) transfusion is frequently used in neonatal intensive care units (NICU). We evaluated the use of ES in hospitalized patients in the NICU of our hospital in terms of transfusion rate, indication, laboratory control, complications, and adherence to the guidelines.

Material and Methods: Patients who were hospitalized at the University of Health Sciences of Turkey, Dr Sami Ulus Maternity and Children Research and Training Hospital, NICU, in 2016, and who received ES were included in this descriptive study.The demographic and clinical characteristics of the patients, the quantity of ES used, and the laboratory tests of the first three transfusions were recorded.The compliance of ES usage indications with the transfusion guidelines published in the Nelson Pediatric Textbook and the Turkish Neonatology (TND) Society Blood Products Transfusion Guidelines was assessed.

Results: One hundred and ninety one of the 1538 admitted patients in the NICU received a total of 633 ES, for a 12.4% ES usage rate. Following an evaluation of the first three transfusions, it was determined that there was 66% compliance with the TND Blood Products Transfusion Guide and 64% compliance with the Nelson Pediatric Textbook transfusion protocol. It was significant that the frequency of retinopathy of prematurity (p=0.015) and intracranial hemorrhage (p=0.001) was high in premature infants who received more than one ES.

Conclusion: Although transfusion is life-saving in crucial circumstances, there may be a cause-effect relationship between the detected morbidity and complications. Each newborn should be carefully evaluated individually and within the framework of the guidelines before having to decide on an erythrocyte transfusion.

Key Words: Complication, Erythrocyte transfusion, Indication, Newborn

ÖZ

Amaç: Yenidoğan yoğun bakım ünitelerinde (YYBÜ) eritrosit süspansiyonu (ES) transfüzyonu sıklıkla kullanılmaktadır. Çalışmamızda hastanemiz YYBÜ'de yatan hastalarda ES kullanımı; transfüzyon sıklığı, endikasyon, laboratuvar kontrolü, komplikasyonlar ve rehberlere uygunluk açısından değerlendirildi.

Gereç ve Yöntemler: Tanımlayıcı nitelikte olan bu çalışmaya Sağlık Bilimleri Üniversitesi, Ankara Dr. Sami Ulus Kadın Doğum, Çocuk Sağlığı ve Hastalıkları SUAM YYBÜ'nde 2016 yılında yatarak izlenen ve yatışı sırasında ES alan hastalar dâhil edildi. Hastaların demografik ve klinik özellikleri, kullanılan ES sayısı ve ilk üç transfüzyona ait laboratuvar testleri

0000-0001-9551-9996 : ÖMERCİOĞLU E
0000-0002-3488-4962 : ZENCİROĞLU A

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Correspondence Address / Yazışma Adresi:
Emel ÖMERCİOĞLU
Department of Pediatrics, Division of
Developmental Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey
E-posta: emelomercioglu@gmail.com

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kaydedildi. ES kullanım endikasyonlarının Nelson Pediatric Textbook transfüzyon önerileri ve Türk Neonatoloji (TND) Derneği Kan Ürünleri Transfüzyon Rehberi'ne uygunluğu değerlendirildi.

Bulgular: Çalışma süresince YYBÜ'ne yatan 1538 hastadan 191'ine toplam 633 ES transfüzyonu verilmişti, ES kullanım oranı % 12.4'tü. İlk üç transfüzyon incelemesinde TND Kan Ürünleri Transfüzyon Rehberine %66 oranında, Nelson Pediatric Textbook (2016) transfüzyon protokolüne göre ise %64 oranında uygunluk olduğu belirlendi. Birden fazla ES alan prematüre bebeklerde prematüre retinopatisi (p=0.015), intrakranial kanama (p=0.001) sıklığının yüksek olması anlamlıydı.

Sonuç: Transfüzyon uygulaması ciddi ihtiyaç durumunda hayat kurtarıcı olmakla birlikte saptanan morbidite ve komplikasyonlar ile arasında neden sonuç ilişkisi olabilir. Eritrosit süspansiyonu transfüzyonu kararı öncesi her yenidoğan bebeğin bireysel olarak ve rehberler çerçevesinde dikkatle değerlendirilmesi gerekmektedir.

Anahtar Sözcükler: Komplikasyon, Eritrosit transfüzyonu, Endikasyon, Yenidoğan

INTRODUCTION

Neonatal anemia is a frequent issue in neonatal intensive care units (NICUs). In order to improve the oxygen carrying capacity and maintain the functions of vital organs in anemic newborns, erythrocyte suspension (ES) transfusion is a life-saving procedure. Furthermore, long-term anemia has the potential to impact the brain development of both preterm and term infants, as well as other aspects of a pre-existing chronic disease (1). Although data on transfusion practices in late preterm and term newborns is limited, studies have found that 50% of extremely low birth weight (ELBW) infants with a birth weight of 1000 g were transfused within the first two weeks of life and 90% were transfused during their stay in the NICU (2, 3).

In addition to the critical benefits of ES transfusion, it has been linked to a number of complications, including an increased risk of infection, various immunological responses, and particularly in premature infants, necrotizing enterocolitis (NEC), bronchopulmonary dysplasia (BPD), retinopathy of prematurity (ROP), intracranial hemorrhage (ICH), and long-term neurodevelopmental issues (3-6). Along with these risks, Hb values that require transfusions in newborns, challenges evaluating clinical anemia findings, and the hypothesis that current Hb/Hct values in premature and/or ill newborns may not accurately reflect erythrocyte mass may lead to uncertainties in indications for transfusion (2, 7). According to ETTNO (Effects of Transfusion Thresholds on Neurocognitive Outcomes of Extremely Low-Birth-Weight Infants) and TOPS (Transfusion of Premature), two comprehensive studies investigating transfusion threshold values and complication relationships in very low birth weight premature infants, higher transfusion thresholds do not decrease the risk of death or neurodevelopmental retardation. The use of restrictive transfusion approaches (Hb 7–9 g/dl in stable, growing premature infants and 9–11 g/dl in critically ill neonates) has been recommended primarily (8-10).

There is currently no global agreement on this issue, despite criteria such as the severity of anemia, the necessity for respiratory support, clinical symptoms, and laboratory values being similar in different national or international guidelines for neonatal transfusion. Numerous studies have found that implementing and adhering to guidelines is associated with a decrease in the number of transfusions and transfusion complications (11, 12). In our study, the use of ES in patients hospitalized in the NICU of our hospital was examined within the framework of indication, laboratory control, and complications, and its suitability was evaluated according to two guidelines, one of which is national and one of which is international.

MATERIALS and METHODS

This descriptive study was carried out at the University of Health Sciences of Turkey, Dr. Sami Ulus Maternity and Children's Research and Training Hospital, SUAM Neonatal Intensive Care Unit (NICU). The research was approved by the Health Sciences University, Ankara, Pediatrics, Hematology, and Oncology, SUAM Clinical Research Ethics Committee (2018-044). All newborn patients hospitalized in 2016 had their files reviewed retrospectively, and 191 patients who received ES were included in the study. Data on the cases' prenatal, natal, and postnatal histories [maternal age, pregnancy history, chronic disease, gestational week, birth weight, mode of delivery -normal spontaneous vaginal delivery (NSVY) or cesarean section (C/S)-, need for positive pressure ventilation (PBV)/ resuscitation at birth, APGAR scores, genders , laboratory findings -prothrombin time (PT), activated prothrombin time (aPTT), Hb, Hct, platelet count-, accompanying clinical manifestations -ICH, infection, RDS, ROP, congenital anomaly, patent ductus arteriosus (PDA), cyanotic/ severe congenital heart disease, metabolic disease, perinatal asphyxia, indirect hyperbilirubinemia (IHB)-, total hospital stay, transfusion history (number of ES and other transfusions, prior to and following ES, a laboratory control, indication and complication record), and outcome (discharge and death)] were obtained from electronic file records. Labaratuary tests completed no more than 72 hours before and after ES application were evaluated for Hb and Hct values before and after transfusion. The accompanying RDS, ROP, perinatal asphyxia, and apnea conditions were defined using the pertinent sections of the Turkish Neonatology Society's diagnosis and treatment recommendations (13).

The indications (clinical and laboratory findings) listed in the Nelson Pediatric Textbook transfusion protocol and the TND Blood Products Transfusion Guide were considered

for assessments of the use of ES (14, 15). In accordance with these protocols, it was assessed whether the patients received transfusions. Patients were classified as "appropriate transfusion" if they met all laboratory and clinical requirements and "inappropriate transfusion" if they did not meet both requirements. Compliance with any criteria clinically or in the laboratory was determined as "partially appropriate transfusion." For patients who received multiple transfusions, the first three transfusions were taken into account when determining eligibility.

Statistical analyses were performed using the IBM SPSS for Windows Version 22.0 package program. The numerical variables were summarized as mean, standard deviation, median (minimum-maximum), and interquartile range (IQR) values. Numbers and percentages were used to display categorical variables. The Mann-Whitney U test and, when there were more than two groups, the Friedman test were used to determine whether there were differences between the two groups in terms of numerical variables. The Spearman and Pearson correlation coefficients were used to investigate the relationship between various variables. Significance level was accepted as p <0.050. For the purpose of controlling risk factors, odds ratios (OR) and confidence intervals were computed.

RESULTS

ES transfusions were administered to 191 of 1538 patients (997 term and 541 preterm) hospitalized in the NICU during the one-year study period, with an ES use rate of 12.42%. Among these newborns, 69 (36.13%) were preterm and 122 (63.87%) were term (Table I). Infants who were born preterm used ES at a rate of 12.38%, whereas term infants used it at a rate of 12.23%. It was determined that patients received ES at a dose of 10–15 ml/kg.

Patients were admitted for various reasons, such as: 69 (36.13%) have cyanotic or severe cardiopulmonary heart disease, 47 (24.60%) have prematurity, 17 (8.90%) have hypoxic ischemic encephalopathy (HIE), 13 (6.80%) have sepsis, 9 (4.71%) have NEC, 9 (4.71%) have IHB, and 7 (3.70%) have gastrointestinal system anomalies (duodenal atresia, omphalocele, gastroschisis, intestinal obstruction, etc.). 6 (3.14%) have metabolic diseases, 5 (2.62%) have pneumonia, three (1.60%) have acute renal failures, three (1.60%) have anemias, one (0.52%) has a syndromic infant, one (0.52%) has a hypotonic infant, and one (0.52%) has had the umbilical catheter removed by angiography. A summary of the clinical conditions that the patients experienced prior to or following the ES is shown in Table II.

It was determined that a total of 633 ES were given to the 191 patients included in the study, and the number of transfusions/number of transfused patients ratio was found to be 3.31 (±3.33). This rate was 3.22 (±2.12) for preterms and 3.40 (±3.13) for term; and there was no difference between preterm and term newborns (p>0.050). There were identified 121 patients (63.40%) who received ES more than once. ES administered more than once in 62.72% preterm infants and 63.13% of term infants (p>0.050) (Table III). In 2016, 102 of the 541 preterm

Table I: Demographic data and general characteristics of patients.

Variable	n (%) / Median (lower-upper quarter)
Gender (Male/Female)	100 (52.40) / 91(47.60)
Mode of delivery (NSVD*/C/S)	71 (37.17) / 117(61.25)
Term/Preterm	122 (63.87) / 69 (36.13)
Gestational week (n=191)	37 (30-38)
Preterm	29 (27-31)
Term	38 (37-39)
Birth weight (gr)	2450 (1475-3000)
Extremely low birth weight (<1000 gr)	21 (11)
Very low birth weight (1500 gr)	47 (24.60)
Low birth weight (<2500 gr)	92 (48.17)
Normal birth weight (2500-4000 gr)	91 (47.64)
PPV† need at birth (yes/no/unknown)	48 (25.13) / 48 (25.13) / 95 (49.74)
Maternal age	26 (18-34)
Maternal chronic disease (yes/no/unknown)	22 (11.51) / 118 (61.78) / 51 (26.70)

***NSVD:** *Normal spontaneous vaginal delivery* †**PPV:** *Positive pressure ventilation*

Table II: Clinical characteristics of patients

Clinic / Medication*	n (%) / Ortalama (± SD)
RDS	45 (23.56)
ROP	28 (14.65)
Infection/sepsis	161 (84.29)
ICH	55 (28.79)
NEC	27 (14.13)
Perinatal asphyxia	26 (13.61)
Congenital anomaly	133 (69.63)
Cyanotic/severe congenital heart disease	69 (36.12)
PDA	120 (62.82)
Metabolic disease	11 (5.76)
IHB	56 (29.31)
Respiratory support	163 (85.34)
Apnea	34 (17.80)
Caffeine therapy	50 (26.17)
Thrombocytopenia	109 (57.06)
Coagulopathy	106 (55.49)
APGAR score (1. minute)	6.04 (±2.46)
APGAR score (5. minute)	7.75 (±1.82)
Discharge/Exitus	139 (72.80) / 52 (27.20)

** The same patient could have multiple characteristics*

Table III: ES use rates among patients

	Total (n=191) (mean±SD/%)	Term (n=122) (mean±SD/%)	Preterm (n=67) (mean±SD/%)	p
Number of transfusions/number of transfused patients	3.31 (±3.33)	3.40 (±3.13)	3.22 (±2.12)	>0.050
Multiple ES use	63.40	63.13	62.72	>0.050

**p<0.005 is significant*

Table IV: Pre- and post-transfusion Hb/Hct values for the patients

Hb (g/dl)/Hct (mean ± SD)	1. ES transfusion	p	2. ES transfusion	p	3. ES transfusion	p
Pre tx Hb	9.66 ± 1.97		9.41 ± 1.70		9.41 ± 1.49	
Post tx Hb	12.90 ± 2.08	0.000	12.90 ± 2.20	0.000	12.38 ± 1.92	0.000
Hb increase rate	%34		%37		%31	
Pret tx Hct	29.85 ± 6.32		28.79 ± 5.28		28.69 ± 4.40	
Post tx Hct	38.87 ± 6.61	0.000	38.91 ± 6.80	0.000	37.47 ± 5.76	0.000
Hct increase rate	%30		%35		%31	

**p<0.005 is significant*

infants admitted to our hospital had VLBW, 47 of whom were transfused at least once, and the ES transfusion rate was 46%. Twenty of the remaining 439 infants had received at least one transfusion, with a 4.50% ES transfusion rate. In comparison to other preterm infants, preterms with VLBW had a significantly higher rate of ES use (p<0.010).

Prior to transfusion, the laboratory control rate for the Hb and Hct parameters was 100%; however, after transfusion, the rates were 87%–87% and 90%, respectively, and the difference was not statistically significant (p>0.050). Hb increase rates were determined to be 34%, 37%, and 31%, respectively, with Hct increase rates being 30%, 35%, and 31%, respectively, before and after transfusions. All increases were statistically significant (p<0.050) (Table IV). In patients with cyanotic or severe cardiopulmonary heart disease, the mean number of transfusions was 4.12±3.72, compared to 2.83±2.91 in the remaining 122 patients, and this high number of transfusions was significant (p<0.050). Mean pre-transfusion Hb (10.41± 1.16 p =0.000) and Hct (32.14±3.56; p = 0.000) values and post-transfusion Hb (13.50±1.58) (p = 0.021) and Hct (40.73 ±4.85; p = 0.032) mean values were significantly higher in patients with cyanotic or severe cardiopulmonary heart disease.

All three initial ES transfusions were evaluated, and it was found that 250 (66%) of the total 378 transfusions were given with indications of "appropriate" or "partially appropriate" in accordance with the TND Blood Products Transfusion Guide, whereas 128 (34%) were given with an indication of "inappropriate." According to the Nelson Pediatric Textbook transfusion protocol, it was found that 243 (64%) of 378 ES transfusions were administered with "appropriate" or "partially appropriate" indications and 135 (36%) with "inappropriate" indications. Preterm and term infants were compared for use in indications appropriate and inappropriate for the guidelines (as per the recommendations of the TND and the Nelson Pediatric Textbook, respectively) (p= 0.176–0.555 for TX1, TX2, and TX3, and p = 0.566-0.320 for TX3), and no significant distinction was identified in the compliance rates of the two groups.

Regarding all transfusions, 98.40% of the patients had no complications. Two (1.04%) of the 191 patients who received the first ES transfusion had circulatory overload, and one (0.52%) had hypoglycemia; circulatory overload was detected in one (0.84%) of 118 patients who received the second ES transfusion; and circulatory overload was detected in two (2.90%) of 69 patients who received the third ES transfusion. Of the 191 patients evaluated for the study, 139 (72.80%) were discharged, and 52 (27.20%) died during their follow-up (Table II). In 2016, 89.65% (52/58) of patients who died in the NICU received ES at least once. Term infants had a 2.89-fold higher mortality risk than preterm infants (OR:2.89, %95 confidence interval;1.34-6.23) (Supplementary material 1). A comparison of those who used ES once or more revealed that 42 (80.80%) of those who passed away and 79 (56.83%) of those who were discharged used it more than once. It was significant that ES was used frequently in patients who passed away (p=0.002<0.050). Patients who received ES more than once had a 3.19-fold higher mortality risk than those who only received it once (OR:3.19, %95 confidence interval;1.48-6.87) (Supplementary material 1). There was no significant difference between babies who were discharged and those who died in terms of compliance with the guidelines for transfusions (p<0.050).

In preterms who required one or more ES transfusions, it was examined whether there were differences in the rates of premature comorbidities. There was no difference between preterms who received one or more ES transfusions in terms of RDS (p = 0.765), surfactant use (p = 0.523), necrotizing enterocolitis (NEC), or mortality rate (p = 0.055). Premature neonates who received more than one ES, however, had a significantly higher frequency of ROP (p = 0.015) and ICH (p = 0.001).

DISCUSSION

In the cohort study by Patterson et al. (16), they reported information for 16.20% of the transfused newborns in the NICUS Data Collection, while in the study by Portugal et al. (17), of the newborns who were admitted to the NICU, 20.90% received at least one transfusion, and the mean number of transfusions was 2.70±2.16. Another study that examined the 6-year transfusion data of premature infants <32 weeks found that 44% of them received at least one ES, with a mean of 2.30±1.60 transfusions (4). In a study that was conducted in Turkey and examined both term and preterm infants, ES use was 12.60% and the average number of transfusions was 4, whereas another study looking at preterm infants discovered that ES transfusion was used at a rate of 50% (18, 19). The rate of ES use and the number of transfusions/number of transfused patients in our study were comparable to or lower than those reported in the literature. Additionally, the literature supports our findings, which indicated that VLBW newborns had an ES transfusion rate of 46%, which was higher than that of other preterm babies (3, 6, 20). The risk of comorbid diseases like ICH, NEC, sepsis, and RDS, the rise in the survival of preterm infants with low gestational ages, the significant iatrogenic blood loss brought on by phlebotomy, and the lack of adequate evidence-based criteria for transfusion indications may all play a part in this circumstance (20, 21).

According to the Turkish Neonatalogy Association's recommendations, a transfusion of 10–20 ml/kg of ES should increase hemoglobin by 2-3 g/dL and Hct by 7–10%. Furthermore, the targeted Hb/Hct levels following an ES transfusion should be 12 g/dL and 35% (14). Following ES transfusion, the study's increase rates and targeted Hb and Hct levels were all within optimal ranges (14). In an Indian study of newborns born <1500 g and/or <32 weeks the mean pre- and post-transfusion Hb% was 8.1±1.9 g/dl and 10.4±1.8 g/dl, respectively. The mean Hb% improvement was 2.3±2.1 g/dL (22). Pre- and post-transfusion values and rates of increase were comparable to our study in a related study in which transfusion-related file records in the tertiary NICU were examined (23). In response to concerns about longer-term neurodevelopmental outcomes, the TOPS and ETTNO trials paved the way for a wider acceptance of restrictive ES transfusion strategies (e.g., Hb 7-9 g/dl in stable, growing preemies and Hb 9-11 g/dl in critically ill neonates or those needing respiratory support) (8-10). The neonatology clinic at our hospital provides tertiary intensive care services as well as being a center for congenital heart disease and therapeutic hypothermia. It is believed that our unit, which cares for critically ill newborns, is more in line with restrictive transfusion policies given the threshold values and literature-recommended guidelines for ES use.

Mazine et al. (24) conducted a prospective, multicenter study in which the transfusion intakes of 175 patients under the age of 18 (47 of whom were newborns) with cyanotic or acyanotic heart disease were examined in the pediatric intensive care unit. Comparable to our study, it has been reported that the pre-transfusion Hb values of patients with cyanotic heart disease are 11.8±2.1 g/dL, significantly higher and statistically significant than those of patients with acyanotic heart disease (24). The primary goals of transfusions in this high-risk population are to increase the blood's capacity for transport as well as provide tissue oxygenation. The mean post-transfusion Hct values in this study were 40.70±4.85% in the group with cyanotic heart disease, which was significantly higher than the group without cyanotic heart disease. The target Hct value for newborns with cyanotic or severe cardiopulmonary heart disease is recommended at 40%–45% in the TND Blood Products Transfusion Guide (14) In light of the literature on this subject, more research is required to determine the thresholds, risks, and advantages of ES transfusions in children with cyanotic or congenital heart disease (25).

Even though there is no definite Hb value to make a decision for transfusion in preterm and term babies, oxygen requirement, being on a mechanical ventilator, and postnatal age are significant considerations in this decision. The threshold Hb values for ES transfusion in term and preterm newborns have not always been specified with clarity in many guidelines. Newborn transfusions are also given current information as part of the Technical Assistance Project for Improving the Blood Transfusion Management System in Turkey, which is being carried out in our nation (26). Given all of this information, it is obvious that each intensive care unit should adopt and adhere to its own set of transfusion guidelines when deciding whether or not to transfuse ES to patients. In this study, in about two-thirds of cases, transfusion indications were in compliance with the guidelines. In a comprehensive study that covered all NICUs in Switzerland, it was found that 46% of the facilities adopted transfusion practices in accordance with the guidelines, but these guidelines were also very distinct between clinics, and there was no consensus among them (7). In a study with neonatal clinicians in Australia and New Zealand, overall 35% participants and 25% participants working in level 3 neonatal units reported that their local institutions did not have a guideline on blood transfusion for infants with anemia of prematurity. Participants from the tertiary neonatal units were more likely to report that their local institution had a guideline compared with participants from levels 1 or 2 neonatal units (27). In the United States, there was a 65% rate of compliance with the guidelines prior to the organization of electronic programs to increase clinicians' awareness of transfusion, which was comparable to our study (28). In the study by D'Amato et al. (4), it was noted that after six years, the ES transfusion rate had decreased to 31% from 44% when the guidelines were strictly followed. Nevertheless, studies show that adhering to the recommendations decreases the need for transfusions, the risk of mortality, and complications such as ICH and NEC, which are believed to be linked to transfusion (4, 11). It is critical to strictly follow the guidelines in order to reduce heterogeneity

and prevent transfusion risks in clinical practice. Due to the retrospective nature of our study, it was hypothesized that there might be a dearth of clinical data records and that the compliance rates could be lower than they actually are. The low complication rate in our study could also be attributed to adequate information entry into the electronic file system. The very low rate of transfusion-related complications was linked in a study conducted in the tertiary NICU to the lack of long-term follow-up and the examination of file records alone (23).

The higher mortality rate of term infants in this study may be due to common diseases like HIE, congenital heart disease, and metabolic disease, despite the fact that preterm infants are generally thought to have serious health problems. Clinicians may have a tendency to use ES more frequently in newborns who have a clinically high mortality risk, which could clarify the association between the use of multiple ES and mortality rates and risks in this study. It has been demonstrated that there is a correlation between the number of transfusions and the risk of mortality in certain studies examining the transfusion practices of premature newborns (4, 6, 29).

The frequency of ES transfusion and its prematurity-related complications are currently the subject of studies (3, 29). In this study, preterms who received ES transfusions more than once were more likely to experience ROP and ICH. According to a thorough literature review and meta-analysis, ES transfusion is an independent risk factor for ROP in preterm infants (5). Multiple ES transfusions were found to increase the risk of ROP and NEC in a study conducted by Ghirardello et al. (6). The frequency of ES transfusion and the risk of ICH were found to be correlated in a different study examining the transfusion practices of premature infants (4). There have also been studies that claim there is no link between the number of transfusions and prematurity complications (22, 29). Although ES transfusion is not the only cause due to the multifactorial nature of the morbidities commonly encountered in premature babies, given the proven risks of transfusion, this vulnerable group should be handled very selectively before transfusion.

One of the strengths of this study is that the transfusion indication evaluation is thorough, not only in terms of adherence to the guidelines but also by contrasting preterm and term, discharged and exitus, and patient groups that received one or more transfusions. The fact that our unit is a tertiary NICU and admits a variety of patients from the nearby provinces and regions also helps to reduce any potential biases in the patient selection process for our study. One of the limitations of this study was the exclusion of ES transfusions after the third transfusion and the scanning of newborn hospital records only within a year. This retrospective study had additional limitations, such as the inability to assess long-term complications and deficiencies in the observation and recording of symptoms in the documents.

As a result, it was found in this study that ES transfusions carried out in our neonatal clinic were in high compliance with both our national guideline and the recommendations in the Nelson Pediatric Textbook, as well as occurring at rates comparable to studies in the literature. For almost all transfusions, the increases in laboratory values prior to and following the transfusion were within the ranges deemed suitable by the TND Blood Products Transfusion Guidelines. The relationship between the frequency of ROP and ICH and the number of transfusions given to preterm infants was remarkable. Preventing unnecessary transfusions, particularly in premature infants, may reduce morbidity. It is critical to carefully assess each newborn baby individually and within the criteria of the guidelines in order to reduce ES transfusions that can be regarded as tissue transplants; this will be a more rational approach.

REFERENCES

1. Zerra PE, Josephson CD. Transfusion in neonatal patients: review of evidence-based guidelines. Clin Lab Med 2021;41:15-34.
2. Çetinkaya M, Atasay B, Perk Y. Türk Neonatoloji Derneği yenidoğanda transfüzyon ilkeleri rehberi. Türk Pediatri Arşivi 2018;53:101-8.
3. Villeneuve A, Arsenault V, Lacroix J, Tucci M. Neonatal red blood cell transfusion. Vox Sang 2021;116:366-78.
4. D'Amato G, Faienza MF, Palladino V, Bianchi FP, Natale MP, Christensen RD, et al. Red blood cell transfusions and potentially related morbidities in neonates under 32 weeks' gestation. Blood Transfus 2021;19:113-19.
5. Zhu Z, Hua X, Yu Y, Zhu P, Hong K, Ke Y. Effect of red blood cell transfusion on the development of retinopathy of prematurity: A systematic review and meta-analysis. PLoS One 2020;15:e0234266.
6. Ghirardello S, Dusi E, Cortinovis I, Villa S, Fumagalli M, Agosti M, et al. Effects of red blood cell transfusions on the risk of developing complications or death: an observational study of a cohort of very low birth weight infants. Am J Perinatol 2017;34:88-95.
7. Arlettaz Mieth R, Gosztonyi L, Hegemann I, Bassler D, Rüegger C. Neonatal red blood cell transfusion practices in Switzerland: national survey and review of international recommendations. Swiss Med Wkly 2020;150:w20178.
8. Kirpalani H, Bell EF, Hintz SR, Tan S, Schmidt B, Chaudhary AS, et al. Higher or lower hemoglobin transfusion thresholds for preterm infants. N Engl J Med 2020;383:2639-51.
9. Franz AR, Engel C, Bassler D, Rüdiger M, Thome UH, Maier RF, et al. Effects of liberal vs restrictive transfusion thresholds on survival and neurocognitive outcomes in extremely low-birth-weight infants: the ETTNO randomized clinical trial. JAMA 2020;324:560-70.
10. Gammon RR, Al-Mozain N, Auron M, Bocquet C, Clem S, Gupta GK, et al. Transfusion therapy of neonatal and paediatric patients: They are not just little adults. Transfus Med 2022;32:448-59.
11. Boix H, Sánchez-Redondo MD, Cernada M, Fernández MGE, González-Pacheco N, Martín A, et al. Recommendations for transfusion of blood products in neonatology. AnPediatr (Engl Ed) 2022;97:60. e1-. e8.
12. Cibulskis CC, Maheshwari A, Rao R, Mathur AM. Anemia of prematurity: how low is too low? J Perinatol 2021;41:1244-57.

13. Turkish Neonatology Association: Home, Diagnosis and Treatment Guidelines. Accessed: 25 Şubat 2023. Available from: https://www.neonatology.org.tr/neonatoloji/tani-ve-tedavi-rehberleri/
14. Perk Y, Atasay B, Çetinkaya M. Türk Neonatoloji Derneği Kan Ürünleri Transfüzyon Rehberi-2016. Available from: 25 Şubat 2023.
15. Maheshwari A, Carlo WA. Blood Disorders. In: Kliegman RM, Stanton BF, St. Geme III JW, Schor NF, Behrman RE (eds). Nelson Textbook of Pediatrics. 20nd ed. Philadelphia, ABD: Elsevier 2016:880-89.
16. Patterson JA, Bowen JR, Francis S, Ford JB. Comparison of neonatal red cell transfusion reporting in neonatal intensive care units with blood product issue data: a validation study. BMC Pediatr 2018;18:86.
17. Portugal CAA, Paiva APd, Freire ÉS, Chaoubah A, Duarte MC, Hallack Neto AE. Transfusion practices in a neonatal intensive care unit in a city in Brazil. Rev Bras Hematol Hemoter 2014;36:245-49.
18. Turhan A. Evaluation of Blood Transfusion Applications in Newborn Intensive Care Unit; Single Center Experience. The Journal of Current Pediatrics 2019;17:85-95.
19. Arman D, Nursu K. Evaluation of Risk Factors Associated with Red Blood Cell Transfusion in Preterm Infants. Medical Bulletin of Zeynep Kamil 51:9-13.
20. Saito-Benz M, Flanagan P, Berry MJ. Management of anaemia in pre-term infants. Br J Haematol 2020;188:354-66.
21. Meyer MP, O'Connor KL, Meyer JH. Thresholds for blood transfusion in extremely preterm infants: A review of the latest evidence from two large clinical trials. Front Pediatr 2022;10:957585.
22. Priya RS, Krishnamoorthy R, Panicker VK, Ninan B. Transfusion support in preterm neonates< 1500 g and/or< 32 weeks in a tertiary care center: A descriptive study. Asian J Transfus Sci 2018;12:34-41.
23. Dogra K, Kaur G, Basu S, Chawla D. Red cell transfusion practices in neonatal intensive care unit: an experience from tertiary care centre. Indian J Hematol Blood Transfus 2018;34:671-76.
24. Mazine A, Rached-D'Astous S, Ducruet T, Lacroix J, Poirier N, Pediatric Acute Lung Injury, et al. Blood transfusions after pediatric cardiac operations: a North American multicenter prospective study. Ann Thorac Surg 2015;100:671-7.
25. Cholette JM, Willems A, Valentine S, Bateman S, Schwartz SM. Recommendations on red blood cell transfusion in infants and children with acquired and congenital heart disease from the Pediatric Critical Care Transfusion and Anemia Expertise Initiative. Pediatr Crit Care Med 2018;19:S137.
26. Taslak Ulusal Hasta Kan Yönetimi Rehberleri. 26 Şubat 2023. Available from: https://hastakanyonetimi.saglik.gov.tr/Content/ListIndex/?id=28/
27. Saito-Benz M, Sandle ME, Jackson PB, Berry MJ. Blood transfusion for anaemia of prematurity: Current practice in Australia and New Zealand. J Paediatr Child Health 2019;55:433-40.
28. Keir A, Grace E, Stanworth S. Closing the evidence to practice gap in neonatal transfusion medicine. Semin Fetal Neonatal Med 2021;26:101197.
29. Crawford TM, Andersen CC, Hodyl NA, Robertson SA, Stark MJ. The contribution of red blood cell transfusion to neonatal morbidity and mortality. J Paediatr Child Health 2019;55:387-92.

Supplementary material 1: Investigation of mortality risk in newborns and use of multiple ES in different groups

Variables	p	OR	95 % CI
Mortality risk (term/preterm)	0.003	2.89	1.34-6.23
Use of multiple ES (discharge/exitus)	0.002	3.19	1.48-6.87

***OR:** Odds ratios, †**CI:** Confidence intervals*