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Reduction of exposure to blood donors in preterm infants submitted to red blood cell transfusions using pediatric satellite packs

Redução da exposição a doadores de sangue em prematuros submetidos a transfusões de hemácias com uso de bolsas de transferência pediátricas

Reducción de la exposición a donantes de sangre en prematuros sometidos a transfusiones de hematíes con uso de bolsas de transferencia pediátrica

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ABSTRACT

Objective: In preterm newborn infants transfused with erythrocytes stored up to 28 days, to compare the reduction of blood donor exposure in two groups of infants classified according to birth weight.

Methods: A prospective study was conducted with preterm infants with birth weight <1000g (Group 1) and 1000–1499g (Group 2), born between April, 2008 and December, 2009. Neonates submitted to exchange transfusions, emergency erythrocyte transfusion, or those who died in the first 24 hours of life were excluded. Transfusions were indicated according to the local guideline using pediatric transfusion satellite bags. Demographic and clinical data, besides number of transfusions and donors were assessed. Logistic regression analysis was performed to determine factors associated with multiple transfusions.

Results: 30 and 48 neonates were included in Groups 1 and 2, respectively. The percentage of newborns with more than one erythrocyte transfusion (90 *versus* 11%), the median number of transfusions (3 *versus* 1) and the median of

blood donors (2 *versus* 1) were higher in Group 1 ($p < 0.001$), compared to Group 2. Among those with multiple transfusions, 14 (82%) and one (50%) presented 50% reduction in the number of blood donors, respectively in Groups 1 and 2. Factors associated with multiple transfusions were: birth weight <1000g (OR 11.91; 95%CI 2.14–66.27) and presence of arterial umbilical catheter (OR 8.59; 95%CI 1.94–38.13), adjusted for confounders.

Conclusions: The efficacy of pediatric satellites bags on blood donor reduction was higher in preterm infants with birth weight <1000g.

Key-words: infant, premature; anemia; erythrocyte transfusion; blood donors.

RESUMO

Objetivo: Em prematuros transfundidos com hemácias preservadas por até 28 dias, comparar a redução de exposição a doadores em dois grupos de pacientes, de acordo com o peso ao nascer.

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Métodos: Estudio prospectivo de prematuros con peso ao nascer <1000g (Grupo 1) e de 1000–1499g (Grupo 2), nascidos entre abril de 2008 e dezembro de 2009. Excluíram-se os recém-nascidos submetidos a exsanguineotransfusão, transfusão de emergência ou óbito antes de 24 horas de vida. As transfusões foram indicadas conforme rotina do serviço, utilizando-se bolsas de transferência pediátricas. Analisaram-se dados demográficos, clínicos e número de transfusões e doadores. Utilizou-se regressão logística para análise de fatores associados às múltiplas transfusões.

Resultados: Incluíram-se 30 prematuros no Grupo 1 e 48 no Grupo 2. A porcentagem de prematuros que receberam mais de uma transfusão de hemácias (90 *versus* 11%), a mediana do número de transfusões (3 *versus* 1) e mediana de doadores (2 *versus* 1) foram maiores no Grupo 1, comparado ao Grupo 2 ($p < 0,001$). Entre aqueles com transfusões múltiplas, 14 (82%) e um (50%) prematuros apresentaram redução de 50% de doadores respectivamente nos Grupos 1 e 2. Os fatores associados a múltiplas transfusões foram peso ao nascer <1000g (OR 11,91; IC95% 2,14–66,27) e presença de cateter arterial umbilical (OR 8,59; IC95% 1,94–38,13), controlados para variáveis de confusão.

Conclusões: A eficácia das bolsas de transferência pediátricas para reduzir a exposição a doadores de sangue foi maior em prematuros com peso ao nascer <1000g.

Palavras-chave: prematuro; anemia; transfusão de eritrócitos; doadores de sangue.

RESUMEN

Objetivo: En prematuros transfundidos con hematíes preservados por hasta 28 días, comparar la reducción de exposición a donantes en dos grupos de pacientes, según el peso al nacer.

Método: Se trata de un estudio prospectivo con prematuros con peso al nacer <1000g (Grupo 1) y de 1000–1499g (Grupo 2), nacidos entre abr/2008 a dic/2009. Se excluyeron recién-nacidos sometidos a exsanguineotransfusión, transfusión de emergencia u óbito antes de 24 horas de vida. Las transfusiones fueron indicadas según la rutina del servicio, utilizando bolsas de transferencia pediátrica. Se analizaron datos demográficos, clínicos y número de transfusiones y donantes. Variables categóricas fueron comparadas por la prueba de chi-cuadrado y numéricas por la prueba *t* o Mann-Whitney. Se utilizó regresión logística para análisis de factores asociados a las múltiples transfusiones.

Resultados: Se incluyeron 30 prematuros en el Grupo 1 y 48 en el Grupo 2. El porcentaje de prematuros que recibió

más de una transfusión de hematíes (89,5 *versus* 10,5%), la mediana del número de transfusiones (3 *versus* 1) y la mediana de donantes (2 *versus* 1) fue mayor en el Grupo 1, comparado al Grupo 2 ($p < 0,001$). Entre aquellos con transfusiones múltiples, 14 (82,4%) y 1 (50,0%) prematuros presentaron reducción de 50% de donantes respectivamente en los Grupos 1 y 2. Los factores asociados a múltiples transfusiones fueron peso al nacer <1000g (OR 11,91; IC95% 2,14–66,27) y presencia de catéter arterial umbilical (8,59; 1,94–38,13), controlados para variables de confusión.

Conclusiones: La eficacia de las bolsas de transferencia pediátricas para reducir la exposición a donantes de sangre fue mayor en prematuros con peso al nacer <1000g.

Palabras clave: Prematuro; anemia; transfusión de eritrocitos; donantes de sangre.

Introduction

Preterm infants, especially those with birth weight less than 1500g, receive numerous red blood cell transfusions, and 65 to 87% of these patients undergo multiple transfusions⁽¹⁾.

The use of restrictive transfusion guideline has reduced the number of transfusions over the years^(1–5). Nevertheless, in Brazil, about 50% of newborns with birth weight less than 1500g receive more than one RBC transfusion during their hospital stay in the Neonatal Unit⁽⁵⁾. In many institutions, such transfusions are performed with RBCs stored for up to 3–7 days. Consequently, each transfusion with the use of traditional bags represents, in general, exposure to a different donor⁽⁶⁾.

Fernandes da Cunha *et al*⁽⁷⁾, employing an aliquot system using a sterile connection device in a prospective randomized study, compared preterm infants who received RBCs stored for up to 3 days with preterm infants who received RBCs stored for up to 28 days. The 26 infants transfused with RBCs preserved for up to 28 days received 114 transfusions and were exposed to 34 blood donors. The 26 neonates who received RBC stored for up to 3 days received 109 transfusions and were exposed to 109 donors. The mean number of transfusions per transfused newborn was similar in both groups (4.4 ± 4.0 *versus* 4.2 ± 3.1 ; $p = 0.904$). However, each neonate transfused with RBC preserved for up to 28 days was exposed, in average, to 1.5 ± 0.8 donors (range: 1 to 4) and, in the traditional group, each neonate was exposed to 4.3 ± 3.4 donors (range: 1 to 13), showing a 70.2% reduction in donor exposure.

Another less costly method and therefore most likely to be adopted in neonatal units is the use of pediatric packs of

packed red blood cell, with four satellite bags, containing RBC from the same donor and reserved for a single newborn. In this method, for each transfusion, one of the small bags from the set is used⁽⁸⁻¹⁰⁾. Hilsenrath *et al*⁽⁸⁾ showed that this method, applied to newborns at risk for transfusion, reduced the median number of donors from 3.6 to 2.0 per patient transfused.

The use of pediatric packs of packed red blood cell would allow reducing exposure to donors, because a single donor could provide up to four transfusions for the same newborn. In this case, even if the patient received four transfusions, he would be exposed only to one donor, with a 75% reduction of donor exposures.

However, in Brazil, there are no studies assessing the efficacy of pediatric packs of packed red blood cell to reduce exposure of very low birth weight preterm infants to blood donors. Thus, the aim of this study was to compare the efficacy of transfusions using pediatric packs with four satellite packs to reduce the exposure to donors in two groups of preterm infants, one with birth weight less than 1000g and another with birth weight between 1000 and 1499g.

Method

This is a prospective cohort of infants with gestational age less than 37 weeks and birth weight less than 1500g, born from April/2008 to December/2009 in a public hospital in the municipality of São Paulo. Neonates who presented any of the following conditions were excluded: death within 24 hours, performance of exchange transfusion for not being able to use the RBC stored for 28 days due to high potassium⁽¹¹⁾ or, need of rapid infusion, because it is recommended that the packed RBC stored for more than 5 days should be infused in at least 4 hours due to the risk of hyperkalemia^(12,13).

The studied newborns were divided into 2 groups according to birth weight: In Group 1, all eligible infants with birth weight lower than 1000g and, in Group 2, those with birth weight from 1000 to 1499g.

The red blood cell transfusions were indicated according to routine guideline⁽⁵⁾ of the neonatal unit and the volume of RBCs prescribed in each transfusion was 15mL/kg of body weight. To reduce the risk of hyperkalemia, each pack of RBC was infused in 4 hours at a speed of 4mL/kg/hour⁽¹⁴⁾.

Preterm infants with indication for transfusion received packed blood cells preserved in CPDA-1 (citrate phosphate dextrose adenine) for up to 28 days, stored in a pediatric packs with four satellite bags, according to the routine of the institution's Blood Center. The red blood cells used in the study were

previously subjected to gamma irradiation at a dose of 25 Gy and filtered with reduction of 99.99% of leukocytes, keeping levels below 5×10^6 leukocytes per unit of blood components⁽¹¹⁾. At each indication of red blood cell transfusion, one of the satellite bags with an approximate volume of 40–50mL was removed, by a closed system, using a tube sealer (dielectric tube sealer for blood bags).

The data collected included medical and obstetric history, conditions of current pregnancy and deliver, demographic and clinical characteristics of the newborn, and transfusion-related information. In relation to demographic and clinical characteristics of the neonates, the following data were recorded: sex, gestational age determined by the best obstetrical estimate or using the New Ballard Score⁽¹⁵⁾, weight to age⁽¹⁶⁾, birth weight, Apgar at 1 and at 5 minutes of life, SNAPPE II (Illness severity score in the first 12 hours of life assessed by the Score for Neonatal Acute Physiology, Perinatal Extension, Version II)⁽¹⁷⁾ and need for resuscitation in the delivery room⁽¹⁸⁾. Data on the clinical outcome in the neonatal unit, procedures performed, and length of stay were also collected.

Categorical variables were compared by the chi-square test and numerical variables by *t* test or Mann-Whitney test. Factors associated with the need for more than one red blood cell transfusion were analyzed by logistic regression. In this analysis, all variables of interest were initially included in the model, with successive elimination of those who lost their statistical significance at each step of the analysis. Statistical analysis was performed with the SPSS17® program, establishing significance at $p < 0.05$. The sample size calculated to detect a difference of one donor between the two groups, considering a standard deviation of 2, 80% power, and an alpha error of 5%, was of 30 patients in each group.

The research protocol was approved by the Research Ethics Committee of the institution, and parents or guardians were asked to sign the informed consent form.

Results

During the study period, 110 patients were preterm infants with very low weight. Among these, 32 (29.1%) met the criteria for exclusion: 23 (20.9%) died before 24 hours of life, 3 (2.7%) required rapid red blood cell infusion in less than 4 hours, and 6 (5.5%) cases of parental refusal. Thus, 78 newborns were included, 30 with birth weight less than 1000g (Group 1) and 48 with birth weight from 1000 to 1499g (Group 2).

Maternal characteristics were similar in Group 1 compared to Group 2: age (28.8 ± 7.5 versus 28.7 ± 7.5 years, $p = 0.929$), number

of previous pregnancies (2.2 ± 1.3 versus 2.6 ± 2.3 , $p=0.355$), number of prenatal care visits (5.4 ± 2.6 versus 6.3 ± 3.4 , $p=0.217$), presence of maternal chronic hypertension (20.0% versus 6.5%, $p=0.075$) and cesarean section (75.9 versus 91.3%, $p=0.066$). The mean birth weight was 775 ± 144 g in Group 1 and 1306 ± 132 g in Group 2. The other demographic and clinical characteristics of newborns in both groups are shown in Table 1.

The percentage of newborns transfused was higher in Group 1 compared to Group 2 (76.7 versus 27.1%, $p<0.001$). In Group 1, among transfused newborns, the median number of transfusions was 3 (range: 1–8) and the median number of blood donors in Group 1 was two (range: 1–4), with a reduction of 33.3% in donor exposure in Group 1, when considering that each transfusion would usually correspond to exposure to one donor. In Group 2, the number of transfusions had a median of two (range: 1–2) per infant transfused and the median number of donors was one (range: 1–2) per infant transfused.

In Group 1, 17 (73.9%) children received more than one transfusion and in Group 2, only 2 (15.4%) among the 13 infants received two transfusions. In Group 1, among neonates who received more than one transfusion, 14 (82.4%) benefited from the use of the protocol and showed a 50% reduction in

exposure to blood donors. In Group 2, only 1 newborn benefited from a reduction of 50% in exposure to donors.

Considering the day of life in which the red blood cell transfusions were performed, it was found that in 9 newborns (30%) in Group 1 and in 1 newborn (2.1%) in Group 2, the expected number of donors according to the expiry date of the RBC pack was lower than the number of donors observed, showing that in these cases not all packs reserved for the patient were used. This happened in a newborn due to hemolytic jaundice by probable presence of antibodies in the donor's blood. In other cases, there was a lack of copper strips for the separation of bags.

To identify which newborns would need to receive more than one transfusion and, thereby, benefit from the donor exposure reduction program, there was initially a comparative analysis between preterm newborns submitted to more than one transfusion and those who received only one or no transfusion (Table 2). Next, we identified the variables available in the first days of life to analyze factors associated with the need for multiple transfusions through logistic regression. In this analysis, the following variables were identified: gestational age <28 weeks; birth

Table 1 - Demographic and clinical characteristics of the studied newborns

	n1	Group 1	n2	Group 2	p-value
Male sex	30	13 (43%)	48	20 (42%)	0.733
Gestational Age (without)	30	26 ± 3	46	31 ± 2	<0.001
1 st minute Apgar	30	6 ± 3	47	7 ± 2	0.016
5 th minute Apgar	30	8 ± 2	47	9 ± 0	0.034
SNAPPE II	30	43 ± 20	46	10 ± 13	<0.001
NB SGA	30	8 (27%)	46	14 (30%)	0.723
PPV in the delivery room	30	17 (57%)	46	24 (52%)	0.701
Htc in the 1 st 12 hours of life	29	44 ± 10	45	52 ± 10	<0.001
RDS	30	28 (93%)	45	8 (18%)	<0.001
PDA	29	22 (76%)	45	12 (27%)	<0.001
Clinical sepsis	29	21 (72%)	45	10 (22%)	<0.001
PIVH	27	20 (74%)	45	16 (36%)	0.002
Thrombocytopenia	29	20 (69%)	45	16 (36%)	0.005
O ₂ at 28 days of life	29	16 (52%)	45	10 (22%)	0.004
ROP	18	9 (50%)	37	7 (19%)	0.017
Mechanical ventilation (days)	29	15 ± 14	45	3 ± 7	<0.001
Blood spoliation (mL/kg)	30	28 ± 15	45	8 ± 5	<0.001
Days of hospitalization	26	65 ± 44	41	44 ± 18	0.032
Death	30	8 (27%)	48	–	<0.001

n1 and n2: number of patients on each group; SNAPPE II: Illness severity score in the first 12 hours assessed by the Score for Neonatal Acute Physiology, Perinatal Extension, Version II; NB SGA: small for gestational age newborn; PPV: positive pressure ventilation; RDS: respiratory distress syndrome; PDA: patent ductus arteriosus; PIVH: peri-intraventricular hemorrhage; ROP: retinopathy of the prematurity; Htc: hematocrit

Table 2 - Characteristics of the infants with more than one transfusion and infants with one or no red blood cell transfusion

	>1 transfusion (n=19)	≤1 transfusion (n=57)	p-value
Gestational age (without)	27±2	30±3	<0.001
Birth weight (g)	817±159	1194±268	<0.001
1 st minute Apgar	6±3	7±2	0.266
5 th minute Apgar	8±2	8±1	0.202
SNAPPE II	42±21	17±20	<0.001
Small for gestational age	3 (16%)	19 (33%)	0.144
Htc 1 st 24 hours of life	44±11	51±10	0.014
PPV bag and mask	12 (63%)	29 (51%)	0.352
PPV tracheal tube	8 (42%)	9 (16%)	0.017
Umbilical artery catheterization	13 (69%)	6 (11%)	<0.001
RDS	18 (95%)	34 (60%)	0.005
Patent ductus arteriosus	16 (84%)	18 (32%)	<0.001
Apnea	16 (84%)	35 (61%)	0.080
Clinical sepsis	16 (84%)	15 (26%)	<0.001
Mechanical ventilation (days)	22±14	3±7	<0.001
O ₂ with 28 days of life	11 (58%)	15 (26%)	0.008
Peri-intraventricular hemorrhage	13 (77%)*	23 (42%)**	<0.001
Retinopathy of prematurity	4 (50%)*	12 (26%)*	0.159
Days of hospitalization	69±48	47±24	0.089
Blood spoliation (mL/kg)	30±16	10±7	<0.001
Death	5 (26%)	3 (5%)	0.008

*n=17, **n=55; &n=8, &n=47. SNAPPE II: Illness severity score in the first 12 hours of life assessed by the Score for Neonatal Acute Physiology, Perinatal Extension, Version II; Htc: hematocrit; PPV: Positive pressure ventilation in the delivery room; RDS: respiratory distress syndrome.

Table 3 - Factors associated with the need for more than one erythrocyte transfusion: univariate logistic regression

	OR	95%CI	p-value
Gestational age <28 weeks	14.93	4.30–51.85	<0.001
Birth weight <1000g	9.72	2.69–35.12	0.001
1 st minute Apgar <7	0.96	0.33–2.79	0.932
5 th minute Apgar <7	1.25	0.22–7.02	0.802
SNAPPE II >30	11.71	3.48–39.45	<0.001
PPV tracheal tube	3.88	1.22–12.32	0.022
Umbilical artery catheterization	21.67	5.71–82.29	<0.001
Htc in the first 24 hours of life <40%	6.49	1.73–24.29	0.005
Respiratory distress syndrome	11.65	1.45–93.59	0.021
Patent ductus arteriosus	16.89	3.50–81.45	<0.001

OR: Odds Ratio; 95%CI: 95% confidence interval; SNAPPE II: Illness severity score in the first 12 hours of life assessed by the Score for Neonatal Acute Physiology, Perinatal Extension, Version II; PPV: Positive pressure ventilation in the delivery room; Htc: hematocrit

weight <1000g, SNAPPE II >30, tracheal intubation in delivery room, presence of umbilical artery catheter, hematocrit in the first 12 hours of life <40%, presence of respiratory distress syndrome, and patent ductus arteriosus (Table 3). These variables were included in the multiple logistic regression model, generating the final model shown in Table 4.

Table 4 - Final model of logistic regression for factors associated with the need for more than one transfusion during hospitalization in the neonatal unit

	OR	95%CI	p-value
Birth Weight <1000g	11.91	2.14–66.27	0.005
Umbilical artery catheterization	8.59	1.94–38.13	0.005

OR: Odds Ratio; 95%CI: 95% confidence interval

Discussion

This is the first study conducted in our location with the objective of assess the efficacy of the pediatric packs of packed red blood cell to reduce blood donor exposure in very low birth weight preterm infants.

The use of pediatric packs showed a 33% reduction of blood donor exposure in preterm infants with birth weight less than 1000g, proving to be more effective in newborns with lower birth weight. Likewise, Van Straaten *et al*⁽¹⁹⁾, in a study using pediatric pack, observed greater reduction of donors in newborns who needed a greater number of blood transfusions.

In this study, 82% of preterm infants who received more than one transfusion showed a reduction of 50% of donors. This result is satisfactory, although it has not reached similar values of those reported by the literature⁽⁸⁾. On the other hand, it is necessary to consider that most existing studies were conducted at a more liberal time regarding the indications of transfusions and, therefore, preterm infants received, in average, a greater number of transfusions than today⁽¹⁾. The effectiveness of pediatric transfer bags depends on the number of transfusions, the time interval between transfusions (considering that the expiration date of the bags is 28 days), and patient's clinical complications⁽¹⁹⁾. In the present study, according to the day of life in which the transfusions occurred, the number of donors observed was greater than the number predicted in 30% of extreme preterm infants, and, one newborn, had a hemolytic reaction after the first transfusion, forcing the change of donor.

On the other hand, the adoption of restrictive criteria for transfusions in our neonatal unit has progressively decreased the number of transfusions in very low birth weight newborns⁽³⁻⁵⁾. This factor may have influenced the lower effectiveness of the protocol to reduce donor exposure presented here. Such analysis can be proven in the group of neonates with birth weights between 1000 and 1499g, in which only two children received more than one transfusion and, hence, the protocol adopted showed low efficacy in reducing the number of donors.

Thus, it is interesting to identify which children have a greater chance of receiving multiple transfusions during hospitalization in the neonatal unit. The identification of these patients would allow the staff to reserve pediatric packs of packed red blood cell for the neonate, improving

cost-effectiveness. In this sense, the multiple logistic regression analysis showed that having a birth weight lower than 1000g increased by 12 times the chance of receiving multiple transfusions, compared with birth weights between 1000 and 1499g. Also, being subjected to umbilical artery catheterization in the first days of life increased by eight times the chance of receiving multiple transfusions. The presence of umbilical arterial catheterization could be related to lower birth weight, especially in those with less than 1000g, and to a greater need for laboratory tests that help to enhance blood spoliation, and thus, increase the need for red blood cell transfusions, similar to what was observed in other studies^(3,5). Therefore, the use of pediatric bags would have greater cost-effectiveness to infants weighing less than 1000g, and especially for those undergoing umbilical artery catheterization. On the other hand, in newborns with 1000-1499g, the use of this protocol seems to bring little benefit due to the fact that most of these children do not need red blood cell transfusions or need only one transfusion at most.

The small sample size included is the main limitation of this study, which does not allow definitive conclusions to be drawn. However, this study suggests, and some authors recommend storing fewer bags for children with higher birth weight in order to obtain the best cost-effective strategy⁽²⁰⁾. An alternative to reduce the number of donors would be the use of a sterile connection device which would allow using a bag for 6 to 8 transfusions, using red blood cells from one single donor for the same newborn. However, its availability is limited in several Brazilian blood centers and it is expensive. This method leads to greater effectiveness in reducing donors than the use of pediatric bags, especially when the number of transfusions per infant is very large and the child's weight is low. Using this system, in a study performed in our neonatal unit⁽⁷⁾, a 70% reduction in donors was observed in infants with birth weight less than 1500g. If this method were used again, it is possible that, its effectiveness would be lower today due to the use of progressively more restrictive transfusion policies, which resulted in the reduction of RBC transfusions^(4,5). That is, either of these two methods of reducing donors, associated to the use of strict criteria for indication of transfusions, can reduce the risks of blood transfusions⁽²¹⁾.

One of the precautions to be taken when transfusing irradiated RBCs refers to the amount of potassium in the bag. Potassium values found by the Fernandes da Cunha *et al*⁽⁷⁾

were of up to 76mEq/L in a pack preserved for 28 days and of 57mEq/L in RBC preserved for up to 3 days. To reduce the risks of hyperkalemia in the newborn, it is recommended a slow infusion in 4 hours and the use of volumes not exceeding 20mL/kg. Despite this risk, the present study did not observe any newborn with hyperkalemia.

Another issue to be discussed refers to the adverse effects of transfusion of old erythrocytes. The storage of red blood cells for prolonged periods can lead to numerous changes, such as: increased potassium in the supernatant due to failure in sodium and potassium pump activity; reduction in the amount of 2-3-diphosphoglycerate (2-3 DPG), which may hinder oxygen release; decreased erythrocyte deformability, making it difficult for erythrocytes to pass through small capillaries; release of free hemoglobin with vasoconstrictor binding capacity; and interaction of free hemoglobin with nitric oxide, increasing vasoconstriction⁽²²⁾. However, current data show no clinical evidence of any of the possible adverse effects of transfusion of RBCs stored for more than 3 days⁽²³⁾. In addition, a randomized, controlled, double blind study conducted with 377 preterm infants with birth weight <1250g in six Canadian tertiary neonatal units⁽²⁴⁾ showed similar clinical outcomes among preterm infants transfused with red cells

preserved for up to 7 days, compared with infants transfused with RBCs stored up to 42 days. In this study⁽²⁴⁾, the main objective was to analyze the incidence of major neonatal morbidities, including necrotizing enterocolitis, retinopathy of prematurity, bronchopulmonary dysplasia, intra-ventricular hemorrhage, and death, evaluated during hospitalization of up to 90 days after randomization. The combined outcome of morbidity was similar in both groups (52.7 *versus* 52.9%), with a relative risk of 1.00 (95%CI 0.82–1.21). When each of the morbidities was analyzed separately, there were no differences between the two groups, and no difference in mortality (16.4 *versus* 16%; OR 0.97; 95%CI 0.61–1.54)⁽²⁴⁾. Thus, this study suggests that strategies to reduce donors in preterm infants using red cells stored for more than 7 days can be used in neonatal units.

The present study showed that the adoption of pediatric packs of packed red blood cell can reduce the exposure of very low birth weight preterm infants to blood donors. It was also found that the lower the newborn's birth weight, the more effective this strategy is, and, therefore, it should be recommended for neonates with birth weight lower than 1000g. However, for preterm infants with birth weight from 1000 to 1499g, the cost-benefit seems to be limited.

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