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Transfusion practices in a neonatal intensive care unit in a city in Brazil

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ABSTRACT

Objective: Newborn infants are the most heavily transfused population inside intensive care units. The hemoglobin level used to indicate the need of transfusions is not well established. The aim of this study was to evaluate transfusional practices in newborns in the neonatal intensive care units of one specific city.

Methods: Red blood cell transfusion practices of all transfused newborns in all five of the neonatal intensive care units of the city were analyzed. Data are reported as descriptive statistics, including numbers and percentages and means and standard deviation. Univariate analysis, followed by stepwise logistic regression was performed in respect to transfusional data and outcomes.

Results: A total of 949 patients were admitted to the intensive care units during the 12-month study period with 20.9% receiving at least one transfusion, most (62.4%) of whom received more than one transfusion. The mean number of transfusions per infant was 2.7 ± 2.16; in the liberal transfusion group the mean number was 1.59 ± 1.63 and in the restrictive group it was 1.08 ± 1.51. The mean hemoglobin and hematocrit levels were 9.0 g/dL (± 1.4 g/dL) and 27.4% (± 4.3%), respectively. The most common indications for blood transfusions were sepsis and prematurity.

Conclusion: This study shows that the characteristics and the transfusion practices for newborns admitted in the neonatal intensive care units of Juiz de Fora are similar to recent pubications. There was no significant reduction in the number of transfusions per child in the restrictive group compared to the liberal group. Restrictive transfusions are an independent risk factor for peri-intraventricular hemorrhages and death.

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Introduction

According to data for 2011 of the Brazilian National Health Service (SUS), very low birth weight newborns represent 32.0% of all childhood mortality. Cross-sectional studies show that they are the most transfused age group in tertiary care facilities. Forty-five to 85% of premature newborns in a neonatal intensive care unit (NICU) receive at least one blood transfusion during hospital stay, making them the population group that is most at risk to transfusion-related adverse effects and complications.[1–6]

The fast growth of the newborn infant, the erythropoietin and iron deficiency inherent to this age group, the low erythropoiesis, the shorter life span of fetal hemoglobin, the oxidative hemolysis that occurs due to sepsis and, especially, iatrogenic loss due to frequent blood sampling are the main factors contributing to the need to transfuse.[2,7]

Despite being a widely used practice, there is still a lack of scientific evidence in regards to the decision of when to transfuse RBCs. Each day more evidence appears about the association of RBC transfusions with morbidity and mortality in the newborn infant, such as changes in cellular immune response, especially T-cell mediated response, necrotizing enterocolitis, retinopathy of the premature infant, bronchopulmonary dysplasia, intraventricular hemorrhage and even death.[7–16]

The number of papers addressing this issue is increasing with an attempt to compare liberal and restrictive transfusion practices, in order to reduce the frequency of transfusions and, consequently, the occurrence of adverse effects.[7,17–19] For this, authors are trying to find clinical variables that may be correlated to the need of RBC transfusions in the neonatal population, as well as risk factors and adverse effects associated with transfusion procedures.[5–7]

Thus, the aim of this study was to gain knowledge on transfusional practices in the NICUs of the city of Juiz de Fora by evaluating the clinical and transfusional characteristics related to this procedure.

Methods

Study design

A cross-sectional study was performed between January 1st and July 31st 2011 and January 1st and July 31st 2012. All medical records of newborn infants that received RBC transfusions in all five NICUs of the city were reviewed.

The study was submitted to and approved by the Ethics Committee of the Universidade Federal de Juiz de Fora (# 337/2011).

All studied NICUs are referral centers for high-risk pregnancy. Two only provide care for National Healthcare Service patients, two only accept private health insurance patients and the other provides care for both systems. The five units have a total of 70 beds.

The following data were gathered from patient's medical records by filling in a questionnaire designed for this study: number of births in each center, maternal, neonatal,

Table 1 – Cut-off levels for hemoglobin (g/dL) in the absence of respiratory support.	
Post-gestational age	Level (g/dL)
1st week	10.0
2nd week	8.5
3rd week	7.5

clinical and demographic characteristics of each case, number of newborn infants that received at least one in-hospital RBC transfusion, number of RBC transfusions that were performed on Days 1–14, Days 15–28 and after Day 28 of hospital stay until hospital discharge, volume of blood transfused, volume of blood drawn for laboratory tests, hemoglobin and hematocrit levels before transfusion and the indication that led to the need of transfusion.

Patient population

All newborn infants that were admitted to one of the five NICUs and that received at least one RBC transfusion were included in this study. However, infants with the following conditions were excluded: death within the first 24 h. after birth, newborns submitted to an exchange transfusion protocol, hemolytic disease of any etiology and major congenital anomalies.

Data collection

Statistical analysis was performed using data derived from the research protocol, with the aim of identifying clinical conditions related to RBC transfusions within the target population. Demographic and clinical variables were reported as descriptive statistics. Continuous variables were described by means and standard deviation and categorical variables as numbers and percentages, as appropriate.

Cut-off hemoglobin levels, believed to be safe for transfusions, were established to evaluate transfusional practices based on the 2011 Cochrane Database for Systematic Reviews (Table 1).[18] Infants receiving transfusions when their hemoglobin was above the cut-off level were allocated to the liberal group and those receiving transfusions when their hemoglobin was below the cut-off level were allocated to the restrictive group. The mean numbers of transfusions per newborn in each group were calculated.

Univariate analysis was then performed comparing the liberal and restrictive groups in respect to transfusion variables (mean hemoglobin level, mean hematocrit level, mean number of transfusions per infant) and relevant neonatal outcomes (mechanical ventilation, intra-ventricular hemorrhage, bronchopulmonary dysplasia, necrotizing enterocolitis, retinopathy of the premature and death). Correlations were identified using the chi-square test for categorical variables and t-test for continuous variables. Statistically relevant variables were submitted to a stepwise logistic regression model to show which transfusional variables are independently related to these outcomes.

Data analysis was performed using the Statistical Package for Social Sciences computer software (version 15.0) for

Table 2 – Clinical data of the newborn infants.

	Number of records	Mean ± SD	Range
Ultrasound gestational age (weeks)	126	30.29 ± 3.9	23–30
Birth weight (g)	133	1424.5 ± 677.7	386–3620
1st minute Apgar	128	5.91 ± 2.3	0–9
5th minute Apgar	125	7.92 ± 1.6	1–10
Mechanical ventilation (days)	125	12.79 ± 15.7	0–91
Oxygen (days)	131	24.56 ± 21.7	0–91
Total parenteral nutrition (days)	132	8.73 ± 7.9	0–39
Umbilical catheter (days)	133	2.65 ± 2.7	0–11
Weight gain at 28 days (g)	125	163.12 ± 192.5	2755–635
Weight at hospital discharge (g)	132	1778.17 ± 1291.4	0–8600
Hospital stay (days)	133	48.1 ± 42	1–366

Data were missing from some patient records.

Windows (SPSS, Inc., Chicago, IL). Differences were considered significant when p-values were less than 0.05.

Results

During the study period, 949 newborn infants were admitted into the five NICUs of the city. Of these, 200 received RBC transfusions. Fifty-four newborn infants were excluded from the study: one because of hemolytic disease, five were submitted to exchange transfusion, five were syndromic patients (3 Down Syndromes and 2 Edwards Syndrome), 42 had major congenital anomalies (4 severe congenital heart defects, 29 congenital gastro-intestinal abnormalities, 4 myelomeningoceles and 5 others), and one was considered an outlier (169 days of hospital stay, 21 RBC transfusions, birth weight 500 grams and 24 weeks gestational age). The medical records of 13 patients were not found or incomplete, which represents a loss to study of 9.0%. Therefore, 133 met the inclusion criteria and were analyzed in this study. The mean gestational age was 30.3 weeks (range: 23–40 weeks) and the mean birth weight was 1424.5 ± 677.7 g (range: 386–3620 g).

Analysis of the maternal characteristics showed that the deliveries of 87 (65.4%) newborn infants were by cesarean section, seven (5.2%) mothers had diabetes, 31 (23.3%) has hypertension, 55 (41.3%) received antenatal corticosteroids and 15 (11.2%) had a histo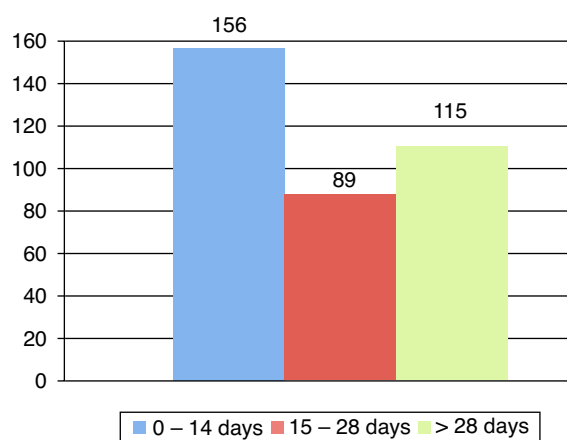ry of premature (over 18 h) rupture of the membrane. Ninety-four infants (74.4%) were born in the National Healthcare System. Seventy-four were male (55.6%) and 56 were female (42.1%). Three Medical Records did not report the gender of the newborn infant.

The clinical characteristics and complications of the newborn infants are shown in Tables 2 and 3.

The incidence of transfusions over the studied period was 20.9%. Fifty (37.6%) newborn infants received one transfusion and 83 (62.4%) newborn infants received more than one. Figure 1 shows the distribution of the number of transfusions in the first 14 days of life, 14–28 days and after 28 days until hospital discharge. The mean number of transfusions per newborn during the period was 2.71 (±2.162) and the mean volume transfused was 20 mL/kg. The mean hemoglobin and hematocrit levels were 9.0 g/dL (±1.4 g/dL) and 27.4% (±4.3%), respectively. The mean number of transfusions per newborn in the liberal group was 1.59 (±1.63) and in the restrictive group it was 1.08 (±1.51).

After the final logistic regression model using the transfusion variables (pre-transfusion hemoglobin and hematocrit levels, mean number of transfusions per newborn in the liberal

Figure 1 – Number of transfusions stratified by age.

Table 3 – Complications of the newborn infants.

	Number of records	Frequency (%)
Resuscitation in delivery room	87	68.5
Mechanical ventilation	112	84.2
Umbilical catheter	83	63.4
Bronchopulmonary dysplasia	52	40.9
Patent ductus arteriosus	56	52.3
Use of vasopressors	75	56.8
Intra-ventricular hemorrhage	59	49.2
Degree I/II	30	27
Degree III/IV	21	18.9
Retinopathy of the premature	44	57.9
Necrotizing enterocolitis	25	19.1
Sepsis		
Early onset	128	96.3
Late onset	104	78.2
Total parenteral nutrition	105	78.9
Death	34	25.6

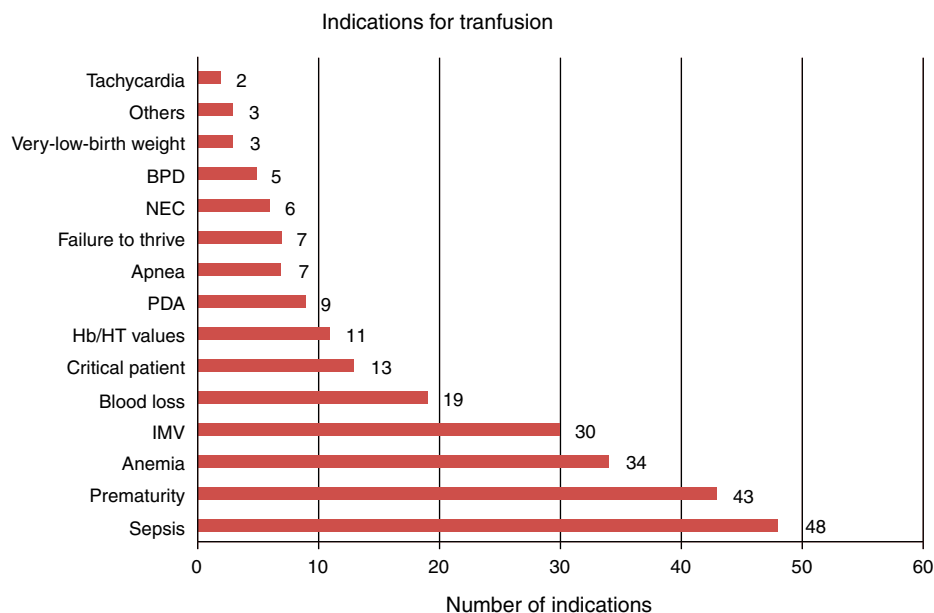Data were missing from some patient records.

Figure 2 – Indications of red blood cell transfusions most commonly reported by the physicians.
BDP: bronchopulmonary dysplasia; NEC: necrotizing enterocolitis; PDA: patent ductus arteriosus; Hb: hemoglobin;
HT: hematocrit; IMV: invasive mechanical ventilation.

and restrictive groups), the only characteristic that proved to be an independent risk for any of the outcomes was restrictive transfusions. This is a risk factor for the following outcomes: intra-ventricular hemorrhage (ODDs ratio: 2.04; 95% confidence interval: 1.05–3.95; *p*-value = 0.033) and death (ODDs ratio: 2.57; 95% confidence interval: 1.30–5.09; *p*-value = 0.007).

Figure 2 shows the most reported indications of the need of red blood cell transfusions as prescribed by the physicians. The most frequent causes were sepsis, prematurity and anemia.

Discussion

Transfusional therapy is a common procedure in the NICU. However, transfusional data in NICUs are not well known. On considering recent publications describing the many transfusion complications, the importance of a better understanding the risk factors becomes more apparent.

The choice of clinical and demographic data reported in this study was based on the main factors described as risk factors in the target population in the literature.[3,6]

The maternal and neonatal data that characterize the population of this study are similar to data found in literature.[3–6,20–23] Differences found could be explained by the fact that most papers only include very low birth weight newborns.[3–6,20–23] The incidence of transfusions found in this study is much lower than what was found in previous reports (55.9% in Santos et al.[6]; 85.0% in Fabres et al.[3]), probably due to this same reason.

Over half of the infants received more than one transfusion during their hospital stay similar to what was reported by dos Santos et al.[6] However, it was lower than the results of her most recent publication.[7] The distribution of the transfusions

in this study stratified by age group was similar when compared to these works[6,7]; the highest incidence of transfusions was in the first 14 days of life followed by after 28 days of age, probably due to late complications, especially in the extremely premature newborn infant group.[5,6]

This study found a lower mean number of transfusions per newborn than what is reported in literature,[4,6,20–23] with the exception of the report by Freitas and Fanceschini.[5] In the liberal group of two clinical trials[20,22] the mean number of transfusions per infant was more than twice the mean number found in the current study.

The fact that there were no significant differences between the number of transfusions in the liberal group and the number of transfusions in the restrictive group shows that the decision to transfuse using restrictive criteria does not reduce the number of transfusions per infant.

It is worth noting that the level used to categorize patients between liberal and restrictive transfusional regimens was the cut-off considered safe for newborn infants not on ventilation support as reported by Robin and Haresh.[18] Thus, very low cut-off levels were used which could explain the results found by logistic regression, in which the restrictive group was found to be a risk factor for intra-ventricular hemorrhage and death. Only one other report, by Bell et al.,[22] found a higher incidence of degree IV intra-ventricular hemorrhages for a restrictive group. There are no other studies reporting a higher incidence of death when using restrictive transfusional regimens.[4,6,20,22,23] It must also be remembered that this is a retrospective report and that there was no control group of non-transfused newborn infants. The creation of a cut-off level was an effort to get around this issue, so that it could be used as a statistical tool that would allow a comparison between two transfusional regimens.

When analyzing the most commonly reported indications of RBC transfusions by physicians, the most frequent reason was sepsis, closely followed by 'prematurity'. Late-onset sepsis is the condition that is most associated with a need to transfuse.[5,6] However, it is the authors' impression that the term sepsis in this study is much more related to the severe condition of these newborns than to the classic meaning of sepsis itself, which would classify this indication as 'the critical condition of the patient' instead of 'sepsis' per se. Kasat, Hendricks, Muñoz and Mally[24] described the most common indications for transfusion reported by physicians and nurses: desaturation episodes, tachycardia – which was the least common indication in the current study, bradycardia, pallor, apnea and sepsis.

The present study has its own limitations, as it was a retrospective study, which made it impossible to evaluate, for instance, episodes of apnea. Even so, the results give extra knowledge on the transfusional profile of newborn infants admitted in NICUs.

Conclusion

The characteristics of the transfused newborn infants in the NICUs of this study do not diverge from the literature in respect to current transfusional practices. The variability found in this practice also shows the difficulty in deciding when to transfuse during the clinical practice of the neonatologist.

There was no statistical difference in the number of transfusions per infant between the restrictive and liberal groups. The restrictive group was associated with higher risk for intraventricular hemorrhages and death.

Conflict of interest

The authors declare no conflicts of interest.

REFERENCES

1. Strauss RG. Transfusion therapy in neonates. Am J Dis Child. 1991;145:904–11.
2. Luban NL. Management of anemia in the newborn. Early Hum Dev. 2008;84:493–8.
3. Fabres J, Wehrli G, Marques MB, Philips V, Dimmitt RA, Westfall AO, et al. Estimating blood needs for very-low-birth-weight infants. Transfusion (Paris). 2006;46:1915–20.
4. Venancio JP, Santos AM, Guinsberg R, Peres CA, Shinzato AR, Lora MI. Strict guideline reduces the need for RBC transfusions in premature infants. J Trop Pediatr. 2007;53:78–82.
5. Freitas BA, Franceschini SC. Fatores associados à transfusão de concentrado de hemácias em prematuros de uma unidade de terapia intensiva. Rev Bras Ter Intensiva. 2012;24:224–9.
6. Santos AM, Guinsburg R, Procianoy RS, Sadeck LS, Netto AA, Rugolo LM, et al. Variability on red blood cell transfusion practices among Brazilian neonatal intensive care units. Transfusion (Paris). 2010;50:150–9.
7. Santos AM, Guinsburg R, Procianoy RS, Sadeck LS, Netto AA, Rugolo LM, et al. Red blood cell transfusions are independently associated with intra-hospital mortality in very low birth weight preterm infants. J Pediatr. 2012;159:371–460.
8. Chambers LA, Eder AF. Noninfectious complications of blood transfusion. Arch Pathol Lab Med. 2007;131:708–18.
9. Wang-Rodriguez J, Fry E, Fiebig E, Lee TH, Busch M, Mannino F. Immune response to blood transfusion in very low birthweight infants. Transfusion (Paris). 2000;40:25–34.
10. Josephson CD, Wesolowski A, Bao G, Sola-Visner MC, Dudell G, Castillejo MI, et al. Do red cell transfusions increase the risk of necrotizing enterocolitis in premature infants? J Pediatr. 2010;157, 972-8e1–3.
11. Bak SY, Lee S, Park JH, Park KH, Jeon JH. Analysis of the association between necrotizing enterocolitis and transfusion of red blood cell in very low birth weight preterm infants. Korean J Pediatr. 2013;56:112–5.
12. Dani C, Reali MF, Bertini G, Martelli E, Pezzati M, Rubaltelli FF. The role of blood transfusions and iron intake on retinopathy of prematurity. Early Hum Dev. 2001;62:57–63.
13. Hirano K, Morinobu T, Kim H, Hiroi M, Ban R, Ogawa S, et al. Blood transfusion increases radical promoting non-transferrin bound iron in preterm infants. Arch Dis Child Fetal Neonatal. 2001;84:F188–93.
14. Baer VL, Lambert DK, Henry E, Snow GL, Christensen RD. Red blood cell transfusion of preterm neonates with a Grade 1 intraventricular hemorrhage is associated with extension to a Grade 3 or 4 hemorrhage. Transfusion (Paris). 2011;51:1933–9.
15. Marik PE, Corwin HL. Efficacy of red blood cell transfusion in the critically ill: a systematic review of the literature. Crit Care Med. 2008;36:2667–74.
16. Kneyber MC, Hersi MI, Twiski JW, Markhorst DG, Plotz FB. Red blood cell transfusion in critically ill children is independently associated with increased mortality. Intensive Care Med. 2007;33:1414–22.
17. Crowley M, Kirpalani H. A rational approach to red blood cell transfusion in the neonatal ICU. Curr Opin Pediatr. 2010;22:151–7.
18. Robin W, Haresh K. Low versus high haemoglobin concentration threshold for blood transfusion for preventing morbidity and mortality in very low birth weight infants. Cochrane Database of Syst Rev. 2011:CD000512.
19. Venkatesh V, Khan R, Curley A, Hopewell S, Doree C, Stanworth S. The safety and efficacy of red cell transfusions in neonates: a systematic review of randomized controlled trials. Br J Haematol. 2012;158:370–85.
20. Kirpalani H, Whyte RK, Andersen C, Asztalos EV, Heddle N, Blajchman MA, et al. The premature infants in need of transfusion (PINT) study: a randomized, controlled trial of a restrictive (low) versus liberal (high) transfusion threshold for extremely low birth weight infants. J Pediatr. 2006;149:301–7.
21. Sucena LP, Furlan MF. Incidência da utilização de leite materno ordenhado em uma Unidade de Terapia Intensiva neonatal e caracterização dos recém nascidos. Arq Ciênc Saúde. 2008;15:829.
22. Bell EF, Strauss RG, Widness JA, Mahoney LT, Mock DM, Seward VJ, et al. Randomized trial of liberal versus restrictive guidelines for red blood cell transfusion in preterm infants. Pediatrics. 2005;115:1685–91.
23. Chen HL, Tseng HI, Lu CC, Yang SN, Fan HC, Yang RC. Effect of blood transfusions on the outcome of very low body weight preterm infants under two different transfusion criteria. Pediatr Neonatol. 2009;50:110–6.
24. Kasat K, Hendricks-Munõz KD, Mally PV. Neonatal red blood cell transfusions: searching for better guidelines. Blood Transfus. 2011;9:86–94.