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### Scientific comment

## Comment on: Transfusion practices in a neonatal intensive care unit in a Brazilian town<sup>☆</sup>



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The overall use of allogeneic red blood cell (RBC) transfusions in the neonatal practice remains relatively high and still varies widely among centers.<sup>1</sup> Moreover, transfusion decisions are often based on low quality scientific evidence alongside, often exaggerated anxiety toward any symptom suggestive of anemia.

In this issue of the *Revista Brasileira de Hematologia e Hemoterapia*, Portugal et al.<sup>2</sup> analyzed the transfusion practices in five neonatal intensive care units (NICUs) in Juiz de Fora, MG, Brazil. The analysis of transfusion rates and factors associated with RBC transfusions in neonates is essential to monitor transfusion compliance guidelines. The transfusion rates reflect transfusion practices and also the local quality of neonatal care because RBC transfusions are associated with most cases of neonatal morbidity, and are mostly due to phlebotomy blood losses.<sup>3</sup> Thus, a neonatal unit with a low transfusion rate probably adopts strict controls against blood spoliation, restrictive guidelines for RBC transfusions, control of causes of morbidity such as sepsis, intraventricular hemorrhage and restricts, as far as possible, the use of mechanical ventilation<sup>3</sup> in compliance with good clinical practices.

The study of Portugal et al.<sup>2</sup> is a retrospective investigation that included neonates admitted to NICUs who received at least one packed RBC transfusion, regardless of their gestational age or birth weight. Data related to the 12-month study period were collected by chart reviews and RBC transfusions were classified as liberal or restrictive according to the criteria of the 2011 Cochrane database for systematic reviews.<sup>4</sup>

This study of 949 patients admitted to NICUs included 133 neonates. Of these, 20.9% received at least one packed RBC transfusion; 50 neonates received one (37.6%) and 83 (62.4%) received more than one RBC transfusion. The number of transfusions was similar for neonates transfused according to the liberal and restrictive transfusion guidelines [1.6 ( $\pm 1.6$ ) vs. 1.1 ( $\pm 1.5$ )]. The most common clinical complications at the time of transfusion were sepsis and prematurity, as observed in most other studies. The final model of logistic regression analysis of independent variables (pre-transfusion hemoglobin and hematocrit values, mean number of transfusions per newborn, and liberal and restrictive groups) showed that intraventricular hemorrhage [ODDS ratio (OR): 2.04; 95% confidence interval (95% CI): 1.05–3.95;  $p$ -value=0.033] and death (OR: 2.57; 95% CI: 1.30–5.09;  $p$ -value=0.007) were associated with the restrictive guidelines.<sup>2</sup> This result may be due to the choice of variables for the logistic regression model.

One study that analyzed the use of restrictive guidelines compared to liberal guidelines showed that the use of restrictive criteria after controlling for birth weight, phlebotomy blood loss, mechanical ventilation and intraventricular hemorrhage reduces the number of transfusions.<sup>3</sup>

Most published studies related to transfusion practices in neonatal units included very low and/or extremely low birth weight preterm infants. However, Portugal et al.<sup>2</sup> studied neonates regardless of their gestational age and birth weight, which is also very interesting. However, this approach makes data analysis more difficult because the restrictiveness

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<sup>☆</sup> See paper by Portugal et al. on pages 245–9.

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of transfusion guidelines described by Robin and Kirpalani,<sup>4</sup> which were adopted in this study, were designed for very low birth weight preterm infants and not for those born at full term. The inclusion of full term neonates may explain some controversial results found by these authors.<sup>2</sup> It is possible that the restrictive character of transfusion guidelines is not the same for neonates of different gestational ages and birth weight. Moreover, the retrospective design, the low number of transfused neonates included in the study and the absence of non-transfused patients could also have contributed to the results of this research.<sup>2</sup>

In this context, Robin and Kirpalani<sup>4</sup> showed that there was no evidence that using a lower hemoglobin transfusion threshold had a negative effect on mortality, major morbidities or on survival without major morbidity in very low birth weight infants. Also, a recently published meta-analysis of randomized controlled trials including very low birth weight preterm infants showed that restrictive RBC transfusion guidelines resulted in statistically significant lower mean numbers of transfusions and there was no evidence of effect on ultrasonographically diagnosed brain injury, retinopathy of the prematurity, bronchopulmonary dysplasia, necrotizing enterocolitis or death.<sup>5</sup>

Christensen et al.<sup>6</sup> showed that after a transfusion compliance program was established in their neonatal unit, the transfusion rate dropped from 58% to 25% over a 9-year period and, in parallel, the severe intraventricular hemorrhage rate also declined, from 17% to 8%. They also found that intraventricular hemorrhage occurred in 27% of those who received RBC transfusions during the first week compared to less than 2% of those who did not receive early transfusions ( $p$ -value <0.001), opposite to the results found by Portugal et al.<sup>2</sup> and Bell et al.<sup>7</sup>

In regard to the outcome of death during hospitalization in the neonatal unit, dos Santos et al.<sup>8</sup> found that, after adjusting for confounders, the relative risk of death during hospital stay was 50% higher in infants who received at least one RBC transfusion in the first 28 days of life compared with infants who did not receive a transfusion. Moreover, the risk of death after 28 days of life was 90% higher in infants who received more than two RBC transfusions during their hospital stay, compared with infants who received one or two transfusions.

Therefore, on analyzing the aforementioned studies, there seems to be some advantage of using restrictive guidelines for RBC transfusions in very low birth weight preterm infants; however, there is no scientific evidence of definite guidelines for RBC transfusions,<sup>4,5</sup> for both preterm and full term

neonates. Therefore, the challenge lies in identifying the patients who are at risk of complications from severe anemia with hypoxemia/ischemia and transfusing them without exposing neonates to unwarranted risks of inappropriate transfusions. Moreover, neonatologists should realize that better transfusion practices rely not only on choosing the transfusion guidelines, but also on how to avoid risk factors for transfusions in neonates, mostly by strict control of phlebotomy blood losses for laboratory tests.

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## Conflicts of interest

The author declares no conflicts of interest.

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