CLINICAL ASSESSMENT IN NEONATAL TRANSFUSION GUIDELINES

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Abstract

Background Packed Red Blood Cell (PRBC) transfusions are often administered to patients in the neonatal intensive care unit.

Aims The purpose of this study was to determine whether current blood transfusion clinical practice guidelines are as useful as clinical judgement in identifying patients in need of a PRBC transfusion.

Methods The study is a post-transfusion survey on premature newborns less than 32 weeks old that received a PRBC transfusion. These patients were divided into three groups, based on the criteria used for transfusion: (a) clinical practice guidelines; (b) clinical judgement/symptoms of need for PRBC transfusion; or (c) both. These three groups were further subdivided based on clinical response to transfusion. Demographic data and clinical variables were compared among the groups. 35 preterm infants who received transfusions were identified. Thirteen patients (37%) were transfused based on guidelines, 4 (11%) based on clinical judgement, and 18 (52%) based on both.

Results Neonates transfused based on guidelines alone were more likely to have received the transfusion in the first week of life, had a lower pre-transfusion hematocrit, were less symptomatic and had a higher likelihood of requiring mechanical ventilation. Neonates transfused based on clinical judgement were more likely to be on non-invasive ventilatory support and were more symptomatic. Neonates who improved after a transfusion had a lower pre-transfusion hematocrit (p=0.03), were more symptomatic (p=0.01) and were more likely to be on non-invasive ventilatory support (p=0.02) when compared to the group without clinical improvement. The group without improvement had an increase in oxygen requirement (+3.8±2.4) after the transfusion (p=0.0004).

Conclusion Guidelines on when to transfuse stable growing premature newborns with PRBC should be reevaluated to include more clinical judgement and perhaps be more restrictive for critically ill neonates.

Key words: preterm newborn, blood transfusion, guidelines, anemia of prematurity

Introduction

Newborns, especially premature infants from neonatal intensive care units (NICU) are among the most likely to be transfused of all hospitalized patients[1]. During the first 2 weeks of life, when blood losses are frequent, approximately 50% of Extremely Low Birth-Weight (ELBW) infants (<1000g) receive their first transfusion[2]. By the end of hospitalization over 80% of ELBW infants receive at least one transfusion[3,4]. Although the number of transfusions received by premature infants remains significant, it has dropped in the last 20 years mainly because of more restrictive transfusion guidelines[5,6].

The main objective of this study was to try and determine if the current NICU Packed Red Blood Cell (PRBC) transfusion guidelines are better than the clinical perception of symptoms in determining the need for transfusion. The secondary aim of this study was to find which symptom of anemia was most frequently associated with ordering a PRBC transfusion.

The hypothesis of the study is that infants that received PRBC transfusions based solely on guidelines did not have a significant clinical improvement and that the association of clinical perception is more predictive of the need for packed red blood cell transfusion.

Materials and methods

The study took place in 2010 (January – December) at the IOMC-"Polizu" Maternity neonatal intensive care unit (NICU). All preterm infants under 32 weeks old that received PRBC transfusions during this period were included. The guidelines used for PRBC transfusion were based on disease severity, as illustrated in Table I. We retrospectively analyzed transfusion criteria with the help of a questionnaire. Using the answer to Question 1: "Which is the indication for transfusion?" newborns were split into 3 groups: (a) newborns transfused based on the guidelines; (b) newborns transfused based on clinical perception and symptoms; and (c) newborns transfused based on both (guidelines and clinical perception). Patients were further subdivided into two subgroups, based on clinical improvement after the PRBC transfusion. The questionnaire also included other questions: "Was the transfusion beneficial for the newborn?", "Did you use other therapeutic measures?", "Which intervention was most beneficial to the patient".

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Clinical improvement was defined as a 10% decline of at least one of the following parameters: (i) fraction of inspired oxygen (FiO2), (ii) heart rate in the case of tachycardia (>160 beats/min), or (iii) episodes of apnea, bradycardia, or desaturation (ABD). These parameters were chosen because of their frequent association with the anemia of prematurity.

Table I. Packed red blood cell transfusions guideline in the NICU.

Transfusion recommendations		**The volume of packed red blood cells transfused**
Hypovolemic shock due to acute blood loss		Determined by the physician
Hct≤38%:/Hb≤12	MV with MAP> 8 and FiO2 > 40% HFV with MAP>14	10-15 ml/kg 2-4 hours
Hct≤35%:/Hb≤10 **Hct≤30%:/Hb≤9**	Average MV MAP≤8 and FiO2<40% HFV with MAP<14 Minimal ventilatory support NCPAP 4-5 and FiO2≤35%	10-15 ml/kg 2-4 hours
Hct≤25%:/Hb≤8	Without MV FiO2 21-40% and one of the following: - Tachycardia HR>180 or - Tachypnea RR>60 ≥ 24 or - Doubling of oxygen requirement - Weight gain <10 g/kg/day for 4 days if ≥120 cal/kg/day - Apnea/bradycardia (>9/12 hours or 2/24 hours that require BM ventilation - Lactate ≥2,5 mEq/l or metabolic acidosis pH<7,2 - Preoperative	15-20 ml/kg 2-4 hours 10 ml/kg x 2
Hct≤21%:/Hb≤6	Asymptomatic and with an absolute reticulocyte count <100.000/µl (2%)	20 ml/kg 2-4 hours or 10 ml/kg x 2

Hct=hematocrit, Hb=hemoglobin, MV=mechanical ventilation, MAP=mean airway pressure

Results

During the study period, 120 preterm infants under 32 weeks were admitted to the NICU, 35 of them receiving at least one PRBC transfusion; these 35 infants received a total of 129 transfusions. Thirteen patients (37.1%) received transfusions based solely on the guidelines, 4 (11.4%) patients were transfused based on the clinical perception of symptoms and 18 (51.4%) patients received transfusions based on both criteria (guidelines and clinical perception). There were no significant differences concerning gestational age and current weight among the 3 groups. The guideline-based group received more transfusions during the first 7 days of life compared to the other groups (p=0.006). These infants also required more intensive ventilatory support (p=0.019) and had a lower mean pre-transfusion hematocrit (p=0.002). Mean hematocrit did not differ significantly among the 3 groups during the first week of life (p=0.8). In the subsequent weeks of life the "transfusion trigger" hematocrit was significantly lower in the guideline-based transfusion group (p<0.05). Infants that were transfused based on the clinical perception of anemia symptoms or by using a combination of guidelines and symptoms had more episodes of tachycardia and ABD (p=0.001) when compared with the group that received transfusions according to the guidelines (Table II).

Table II. Comparison of clinical parameters among the three transfusion groups.

	Transfusion guideline	**Symptoms**	**Symptoms and guideline**	**P value**
Hematocrit pre-transfusion 1 (first 7 days)	32,6 ±2,5	29,2 6,8	30,6±5,6	0.8
Hematocrit pre-transfusion 2 (days 8-14)	28,6±7,3	30,4±3,8	33±2.6	0.002
Hematocrit pre-transfusion 3 (days15-28)	24.3±4.2	29.6±3.5	27.5±4.	0.02
Hematocrit pre-transfusion 4 (>28days)	22±3.9	22.8±4.9	27 (1 caz)	0.001
Mean FiO2 before transfusion (%)	37,6±21,7	47,5±24	25,5±6,3	0.025
Change of the FiO2 after transfusion(%)	- 10	- 5,8	- 2.5	NS
Number of infants with tachycardia	1 (7,7%)	6 (33%)	4 (100%)	0.002
Number of infants with ABD	3 (23%)	8 (44%)	4 (100%)	0.001
Number of infants with clinical improvement	11 (84%)	10 (55,6%)	2 (50%)	NS

Without taking into account the reasons for the transfusions, the 35 infants were subdivided into 2 subgroups based on the presence or absence of clinical improvement (Table III). There were no statistically significant differences concerning clinical improvement among the 3 groups, although we did observe a favorable trend for clinical improvement in the group that received transfusions based only on the guidelines. Preterm infants with clinical improvement after transfusion had a ~ 13% reduction in O2 requirement compared to a ~ 4% increase in O2 requirement in the group without clinical improvement (p=0.004). Most patients in the group that saw clinical improvement were treated with non-invasive ventilation (nCPAP) or oxygen therapy without mechanical ventilation (p=0.002). Patients with clinical improvement after transfusion also had a lower mean hematocrit (p=0.03, more episodes of ABD (p=0.002) and tachycardia (p=0.013) before the transfusions, compared to those that did not improve.

Table III. Comparison of clinical parameters between groups with and without clinical improvement after transfusion.

	Clinical improvement	Without clinical improvement	P value
Number of infants	22 (62,9%0	13 (37,1%)	
Pre-transfusion hematocrit (%)	28.9±6.5	33.2±2.6	0.03
Post-transfusion hematocrit (%)	36±3.9	34.3±3.4	0.01
FiO2 (%), pre-transfusion	41.3±24.7	40.9±19.9	0.2
Change of FiO2(%)	28.5±9.9	44.7±22.3	0.004
IPPV	6	14	0.03
NCPAP	2	1	0.6
MAP > 8 FiO2 >40%	2	5	0.8
MAP 6-8 FiO2 <40%	3	3	0.7
MAP 4-5 FiO2 <35%	6	2	0.02
Number of tachycardic patients	6 (34,2%)	0	0.02
Number of patients with ABD	7 (31.8)	0	0.01
Other interventions	14 (63.6%)	10 (76.9%)	0.6

Most (78%) patients in both of the groups also received other interventions, such as antibiotic therapy, increased ventilatory support, increased FiO2, aminophylline, inhaled bronchodilator therapy, and diuretics, simultaneously with red blood cell transfusion.

In the subgroup of patients that had clinical improvement and received multiple interventions, the clinical impression was that transfusions contributed to improvement in 72% of cases. In cases without clinical improvement after transfusion, other interventions in particular increased ventilatory support (54%) seemed to have benefited the patient.

Discussion

In our study, 35 of the 120 preterm infants (<32 weeks gestational age) that were admitted to the NICU received a total number of 129 PRBC transfusions for a variety of reasons. When deciding on an early transfusion, it is important to keep in mind that despite the progress made in transfusion practice, complications still exist[7,8]. Transfusion guidelines for neonates are still unclear and there is much controversy surrounding the optimal timingoftransfusions[9,10]. The hematocrit is generally kept at higher than physiologic values for ill neonates, although there is no clear evidence of benefit in doing so. Hematocrit alone is a poor indicator of tissue oxygenation[10,11]. There is no single, optimal biochemical marker or sign that can be used to ascertain the need for transfusion[12,13]. Without a reliable marker to guide optimal transfusion timing, clinical judgement seems to be the most important tool used by the medical staff when determining the need for a transfusion.

In our study, there were no statistically significant differences in clinical improvement among the three groups of infants; there was a positive trend in the group that received transfusion based on the guidelines. However, we believe it is important to include clinical signs and clinical judgment in the practice of red blood cell transfusion.

Many aspects of our transfusion guidelines should be reviewed. For example, according to the guidelines, all infants with "severe cardio-pulmonary disease" (HFV, FiO2> 40% NO, MAP> 8 cm H2O) with a hematocrit <40%, or infants with "moderate cardio-respiratory disease" (MAP 6 -8 cm, FiO2> 35%) with a hematocrit ≤ 35% should receive transfusions[14].

As shown in our study, 37% of infants in the group that did not show clinical improvement were ventilated with MAP>8cmH2OandFiO2>40% versus 14% in the group that showed clinical improvement (p=0.02), indicating little to no benefit after transfusion[15].

It is possible that the volume of transfused blood was detrimental to the infant due to lung overloading with a subsequent increase in oxygen requirement. This is a problem in the first week of life when preterm newborns are in the early stages of respiratory distress, due to surfactant deficiency. The guidelines for this subgroup (preterm critically ill in the first week of life) should be reviewed to assess the potential risks generated by volume overload, as they might outweigh the benefits of increased oxygen-carrying capacity.

More patients from the group with clinical improvement required minimal ventilatory support (MAP 4-5 cm H2O, FiO2<35%) compared to the group without clinical improvement (37% vs. 14%, p=0.002). Based on the current guidelines, these patients should not be transfused until the hematocrit drops below 30%, and in some cases<24%[14,16].

In our current guidelines tachycardia is used as a criterion only for stable growing newborns. However, we found that patients that were tachycardic before being transfused were 6 times more likely to achieve clinical improvement. We recommend that tachycardia be included in the guidelines for all categories. Most patients with clinical improvement required multiple therapeutic interventions and blood was the primary factor of improvement in 72% of the cases.

Conclusions

Based on our study, we recommend that PRBC transfusion guidelines currently used to assess ventilatory-dependent critically ill premature newborns should be used cautiously, in accordance with the complex physiology of neonatal respiratory pathology.

For stable growing infants, transfusion guidelines should be re-assessed to include more clinical judgement.

For all newborns, red blood cell transfusion guidelines should be revised to include more clinical parameters, with emphasis on the use of tachycardia as a "need to transfuse" trigger.

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