Neonatal RBC Transfusions – Comparison of Two Patterns

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Key Words

Neonatal RBC transfusion · Blood donor exposure · Transfusion rate

Summary

Background: Red blood cell (RBC) transfusions performed over 5 years in a neonatal ward were retrospectively analyzed. Despite the fact that ‘fresh’ RBC small-volume transfusions given to preterm infants are called ‘traditional’ or even ‘historic’, this method of treatment is still used in all neonatal wards in Poland. **Patients and Methods:** A total of 846 RBC units were transfused to 216 patients, including 26 term and 190 preterm neonates. The transfusion rate and donor exposure rate were calculated. The same parameters were calculated for hypothetical use of blood satellite packs for transfusions in the analyzed patients and compared with the original data. **Results:** Application of a limited donor program could diminish the donor exposure rate more than twofold, from 3.5 to 1.63, in the very-low-birth-weight infants group and reduce the maximum number of donors from 11 to 3, at the same transfusion rate of 5.35. **Conclusion:** Introduction of strict RBC transfusion guidelines and a limited-donor blood program would improve transfusion therapy.

Schlüsselwörter

Neonatale RBC-Transfusionen · Exposition von Blutspendern · Transfusionsrate

Zusammenfassung

Einleitung: Transfusionen von Erythrozyten (red blood cells; RBC), die über einen Zeitraum von 5 Jahren auf einer neonatologischen Station durchgeführt worden sind, wurden retrospektiv analysiert. Ungeachtet der Tatsache, dass Transfusionen kleiner Mengen «frischer» Erythrozyten bei früh geborenen Kindern als «traditionell» oder sogar «historisch» gelten, ist diese Behandlungsmethode auf allen Neugeborenenstationen in Polen üblich. **Patienten und Methoden:** Die Gesamtsumme von 846 RBC-Einheiten wurde 216 Patienten, von denen 26 termingerechte und 190 frühgeborene Säuglinge waren, transfundiert. Das Verhältnis zwischen durchgeführten Transfusionen und der Anzahl der Expositionen von Spendern (donor exposure rate) wurde berechnet. Dieselben Parameter wurden für hypothetische Transfusionen von Satellitblutpackungen bei den untersuchten Patienten berechnet und mit den Originaldaten verglichen. **Ergebnisse:** Die Anwendung eines Programms, das eine begrenzte Anzahl an Spendern vorsieht, könnte die «donor exposure rate» um das Zweifache verringern. In der Gruppe der Kinder mit sehr geringem Geburtsgewicht reduziert sie sich von 3,5 auf 1,63, und die maximale Anzahl an Spendern verringert sich von 11 auf 3, bei einer Transfusionsrate von 5,35. **Schlussfolgerung:** Die Einführung von strengeren Richtlinien bei der Transfusion von Erythrozyten und einem Programm mit einer begrenzten Anzahl von Blutspendern würde die Transfusionstherapie verbessern.

Introduction

The treatment of newborns, particularly those of very low birth weight (VLBW), is very complex. The introduction of new techniques and methods has increased survival. This success has yielded new challenges, with neonatal blood component therapy being one of them.

Anemia of prematurity is a common complication in this age group, due to iatrogenic blood loss, postnatal suppression of hematopoiesis because of a lack of erythropoietin, and defective nutrition. It can be aggravated by commonly occurring infections in immunocompromised premature newborns [1]. Thus, most VLBW infants require multiple small-volume blood transfusions [2]. This often lifesaving procedure has some probability of complications. The complications, such as infections (hepatitis, cytomegalovirus, HIV, bacterial) [3], graft versus host disease (GvHD), and metabolic disorders, are the same in every age group. Their probability increases with the number of transfusions and donors, that is, with the transfusion rate (TR) and donor exposure rate (DER) [4]. The latter parameter depends on the pattern of transfusion. The traditional use of fresh blood (<7 days of storage) has been replaced in many neonatal centers by repeated use of dedicated units of stored red blood cells (RBC; <42 days of storage) for each infant. One of the costs of diminished DER is a worsened metabolic profile of RBC after extended storage [5–7]. The aim of this study was to compare the red blood cell (RBC) transfusions in a neonatal ward over the last 5 years with the hypothetical use of blood satellite packs. The use of such packs has not been implemented in our ward because of local regulations. An idea for improving the pattern of neonatal RBC transfusion is presented below [8]. It combines the benefits of fresh and dedicated blood units. We suggest the use of multiple, small-volume donations from one donor for one infant, instead of repeated use of a dedicated unit (i.e., a dedicated blood donor instead of a dedicated blood unit). This would be of obvious benefit from a medical point of view, but difficult to realize because of organizational and financial restrictions.

Materials and Methods

RBC transfusions performed in a 5-year period (2000–2004) in the Neonatal Ward of the Department of Obstetrics and Perinatology, Pomeranian Medical University, Szczecin, Poland, were retrospectively analyzed. Blood was issued according to national guidelines [9], adapted from [10]. Recommendations for use include the following: a hematocrit (Hct) of less than 40% in infants on assisted ventilation or with severe cardiopulmonary disease; a Hct of less than 30% in infants with tachypnea, tachycardia, diminished activity, episodes of apnea and poor weight gain; and/or phlebotomy losses accounting for 5–10% of the infant's total blood volume.

TR (average number of transfusions per infant) and DER (average number of donors to whom an infant is exposed) were calculated [4, 11]. The same parameters were calculated for hypothetical use of blood satellite

packs for transfusions in the analyzed patients and compared with the original data.

In recent years, a considerable decrease in the proportion of RBC recipients among all newborns has been observed. To explain this phenomenon, we compared Hct values (one of the most important parameters indicating the need for transfusion) before the first transfusion in successive years. All statistical data (mean, standard deviation (SD), median, percentile, Fisher's test, Student's t-test) were calculated where appropriate using Microsoft Excel software. The differences were considered significant when $p < 0.05$.

Subjects Studied

A total of 846 RBC units were transfused to 216 patients, including 26 term and 190 preterm neonates. No patient received erythropoietin treatment. All RBC units were irradiated with a dose of 25 Gy. Preterm newborns were divided into 2 groups according to body weight: VLBW or group I, weighing less than 1,500 g, and low birth weight (LBW) or group II, weighing at least 1,500 g but less than 2,500 g. Hypothetically and arbitrarily, satellite packs were prepared for 8 and 4 transfusions for each recipient in group I and II, respectively. If a patient had received transfusions in 2 successive years, he or she was attributed to the latest one.

Results

Demographic and laboratory characteristics are presented in table 1. The number of all newborns, RBC recipients, and transfusions, the number and percentage of preterm neonates, and the proportion of RBC recipients to all newborns in successive years are presented in table 2. Of 5,316 newborn infants including 597 preterm ones, 216 received 846 RBC units. Despite there being a comparable percentage of preterm neonates, one can observe a considerable decrease in both the number of RBC recipients and the proportion of RBC recipients among all newborns in successive years.

Hct is one indication for RBC transfusion, among others. A continuous drop in mean pretransfusion Hct values in successive years was observed, from 0.37 ± 0.05 in 2000 to 0.33 ± 0.03 in 2004. Statistically significant differences were proved for Hct means between 2000 and the other years and 2001 and the final 2 years.

26 term newborns received 35 units from 26 donors. There were no more than 2 transfusions per newborn, and these were always from a single donor. TR was 1.35 and DER was 1.0 in the term newborn infants group. In group I (VLBW), 123 infants received 658 units of RBC from 430 donors. The TR was 5.35 and DER was 3.50. In group II (LBW), 67 infants received 153 units of RBC from 102 donors. TR and DER were 2.28 and 1.52, respectively. The hypothetical use of blood satellite packs is analyzed below. For obvious reasons, only preterm newborns are considered. All term newborn recipients received up to 2 RBC units from the donor.

Let's presume that each preterm infant received type-specific RBC from a dedicated unit equipped with 7 (for 8 transfusions) or 3 satellite bags (for 4 transfusions) for groups I and II, respectively, and that there were no unexpected, additional transfusions. If we had used 8-pack units in group I, 123 new-

Table 1. Demographic and laboratory characteristics of the study groups

	Group I, <1,500 g	Group II, ≥1,500 g	Mature newborns	All
Number of RBC recipients	123	67	26	216
Male (%)	72 (58.5)	40 (59.7)	10 (38.5)	122 (56.5)
Female (%)	51 (41.5)	27 (40.3)	16 (61.5)	94 (43.5)
Caesarean section (%)	97 (78.9)	47 (70.1)	3 (11.5)	147 (68.1)
Natural labour (%)	26 (21.1)	20 (29.9)	23 (88.5)	69 (31.9)
Apgar score < 5 in 1st min (%)	59 (48)	14 (20.9)	2 (7.7)	75 (34.7)
Apgar score < 5 in 5th min (%)	28 (22.8)	5 (7.5)	0 (0)	33 (15.3)
Gestational age, weeks	28.1 ± 2.6	32.4 ± 2.4	39.2 ± 2.3	30.8 ± 4.5
Birth weight, g	1,005 ± 278	1,794 ± 270	3,247 ± 442	1,519 ± 790
Hgb, mmol/l	9.37 ± 1.51	10.22 ± 2.56	8.63 ± 1.36	9.54 ± 1.94
Hct	0.44 ± 0.07	0.53 ± 0.5	0.42 ± 0.07	0.46 ± 0.28

Table 2. The number of all newborns, preterm newborns, the percentage and proportion of preterm newborns and RBC recipients, and the number of RBC recipients and transfusions, in successive years

Year	Number of all newborns	Number of preterm newborns	Percentage preterm newborns	Proportion of RBC recipients / all newborns	Number of RBC recipients	Number of RBC transfusions
2000	1,199	168	14	0.050	60	215
2001	1,057	125	11.8	0.049	52	197
2002	989	93	9.4	0.038	38	165
2003	950	85	8.9	0.038	36	153
2004	1,121	126	11.2	0.027	30	116
Total	5,316	597			216	846

Table 3. Comparison of the number of RBC units and donors as well as TR and DER of preterm groups I and II, with real transfusions and hypothetical use of multi-packs

	Group I, <1,500 g (n = 123)		Group II, ≥1,500 g (n = 67)	
	real	hypothetical 8-packs	real	hypothetical 4-packs
Number of RBC units	658	658	153	153
Number of donors	430	200	102	76
TR	5.35	5.35	2.28	2.28
DER	3.50	1.63	1.52	1.13

born infants would have received 658 units of RBC from 200 donors, and TR and DER would have been 5.35 and 1.63, respectively. If we had used 4-pack units in group II, 67 newborn infants would have received 153 units of RBC from 76 donors, and TR and DER would have been 2.28 and 1.13, respectively. Comparisons of the above data are presented in table 3 and figure 1. Figure 1 presents the minimum, maximum, median, and 25th and 75th percentiles for the number of donors as well as DER values for preterm newborn groups I and II with real transfusions and with hypothetical use of multi-pack RBC units.

Discussion

Despite the fact that ‘fresh’ RBC small-volume transfusions given to preterm infants are called ‘traditional’ [6] or even

‘historic’ [12], this method of treatment is still used in all neonatal wards in Poland. In Western countries, this method has been supplanted by repeated use of a dedicated unit of stored RBC for each infant [11, 13, 14]. Apart from the common possible side effects of each transfusion, there are 4 objections to the latter method: i) the rise in plasma potassium, ii) the drop in RBC 2,3 diphosphoglycerate, iii) the possible toxicity of additives present in solutions used for extended storage, and iv) the decrease in pH. Several theoretical and practical studies have demonstrated that using RBC stored up to 42 days is safe. It has been proven that possible changes in biochemical or toxic factors are of no clinical significance provided that transfusion volumes are small [5–7]. Thus, this rationale does not apply to large-volume transfusions, such as exchange transfusion or transfusion in extensive surgery. Acceptability in clinical practice does not mean that there is no effect. Without doubt, ‘fresh’ blood has a better biochemical

Fig. 1. Comparison of transfusion-related data. The shaded boxes denote original data, the open boxes denote data with the use of hypothetical, multi-pack, dedicated donors. The outline of the boxes denotes the 75th and 25th percentiles, the left arrows the medians, the right arrows the DER, and the outer crossbars the maximum and minimum numbers of donors. There is no box on the rightmost bar because the 75th and 25th percentiles are equal.

profile than that which is stored. Nevertheless, multiple use of fresh blood in preterm infants is inevitably connected with exposure of the baby to a high number of donors. Furthermore, the probability of transfusion-associated diseases as well as alloantibody production is proportional to donor exposure. Fatal consequences have prompted a change in the transfusion pattern to one using stored RBC in order to limit exposure to donors. Several detailed transfusion guidelines for neonates recommend dedicated, single-donor programs to limit the exposure rate [14–16].

The hypothetical introduction of such a program in our ward would benefit only preterm infants, and the highest benefit would be observed in VLBW infants weighing less than 1,500 g. Application of the program could diminish DER more than twofold, from 3.5 to 1.63, in this group and reduce the maximum number of donors from 11 to 3, at the same TR of 5.35. A drop in DER from 1.52 to 1.13 and in the maximum number of donors from 7 to 3 would benefit LBW infants weighing

less than 2,500 g. The procedure is proven to be cost-effective [17]. These findings are in our opinion strong enough to encourage acceptance of this new transfusion pattern in neonatal clinical practice by local authorities.

We would like to present the idea mentioned earlier [8] which combines the benefits of both transfusion patterns. We suggest that small-volume donations from one donor be dedicated to one preterm infant (i.e., the use of a dedicated donor instead of a dedicated unit). In this scheme, dedicated blood is ‘stored’ in a living organism (the donor), is always fresh, and is issued on demand. There is no wastage of blood, in contrast to both previous methods. Irradiation would not shorten the storage period as it does in the conventional methods [16]. There would be no need to predict the number of donations. The method would require making an exception to the 8-week donor deferral period, but the collection of small amounts of blood at shorter intervals does not seem to affect the donors’ health. Parents, from a psychological point of view, are the

best candidates for being multiple, dedicated donors. There are inconsistent recommendations concerning biological parents as direct donors. Although some evidence suggests that unrelated donor blood is safer than parents' blood [18], another study [19] recommends direct parental donations provided the RBC are irradiated to avoid transfusion-associated GvHD, and maternal plasma antibodies are removed to avoid hemolysis or immune cytopenia in a newborn infant. From a medical point of view, the best candidate donor for the described method is an unrelated, experienced donor. We are interested in starting a campaign to persuade donors to participate in this program. The cost-effectiveness of the procedure is yet to be determined. It seems reasonable not to repeat diagnostic tests for transfusion-transmitted diseases before each transfusion, provided that the time since the last transfusion is shorter than the period of the seronegative window (11–45 days) [20]. Examination of the donor by a physician before each donation is essential.

Despite the knowledge gained from research and practice in prescribing RBC transfusion, there are still controversies and a lack of unique indications in neonatal transfusion therapy [1, 7, 15]. In our ward, RBC transfusion guidelines allow for some physician discretion on site. A decrease in the number of transfusions in successive years can be observed, which is consistent with other publications [2, 21]. Further improvement in this field can be achieved by diminishing iatrogenic blood losses using in-line blood gas and chemistry monitors [22]. Hct, one of the most important factors in transfusion decision making, has consistently dropped in successive years in our study. In summary, 4 courses of action in neonatal wards such as ours should be possible and desired: i) introduction of strict RBC transfusion guidelines; ii) introduction, with the acceptance of local authorities, of a limited-donor blood program; iii) persuading donors to donate multiple small-volume donations for one infant; and iv) introduction of in-line blood gas and chemistry monitors for VLBW infants.

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