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ANALYSIS OF TRANSFUSION OF PACKED RED BLOOD CELLS IN NEONATES IN NEONATAL INTENSIVE CARE UNIT

Dr. Salve Sharma[1], Dr. Kartik Samyal[2], Dr. Mitali Sharma[3*], Dr. Vijay Sawhney[4], Dr. Ambika Sambyal[5]

[1]Senior Resident, Department of Transfusion Medicine, GMC Jammu, India.
[2]Senior Resident, Department of Pediatrics, GMC Jammu, India.
[3*]Assistant Professor, Department of Transfusion Medicine, GMC Jammu, India.
[4]Associate Professor, Department of Transfusion Medicine, GMC Jammu, India.
[5]MS Opthalmology, GMC Jammu, India.

***Corresponding Author:** Dr. Mitali Sharma
*Assistant Professor, Department of Transfusion Medicine, GMC Jammu, India.
Mail id: mitali89sharma@gmail.com

Abstract:
Background: The small blood volume and immature organ systems in the neonate necessitate special approaches in neonatal transfusion practice. Blood components in the form of packed red cells are mainstay of treatment in neonatal intensive care units. Due to increasing demand of transfusion therapy in neonatal age group, it is of prime importance to ensure the quality, accurate dose and well-defined indication of the component transfused.
Aim: To analyze the transfusion practices of neonates in neonatal intensive care unit.
Materials and methods: The study was conducted in the department of IHBT, GMC Jammu done over a period of 1 year. This is prospective observational study comprising of 76 neonates who were admitted in neonatal intensive care unit and received transfusion therapy in the form of packed cells.
Results: Out of 76 neonates, 45 (59.21%) neonates were females and 31 (40.79%) neonates were males. 62 (81.58%) were preterm and 14 (18.42%) were term neonates. 5 neonates (6.58%) were extremely low birth weight, 11 (14.47%) were Very low birth weight, 46 (60.53%) were low birth weight and 14 (18.42%) were normal birth weight. Small volume transfusions were given mainly comprising of 18 (25.71%) who received volume less than 15 ml, 40 (57.14%) received 16-25 ml and 12 (17.14%) were transfused with volume more than 25 ml of PRBC. Shock was found to be the major indication for transfusion in 30 neonates (39.47%) followed by anemia (25%), bleeding (18.42%), sepsis (11.84%) and hypoxic ischemic encephalopathy (1.32%). 31 neonates (41.33%) received single transfusion and 44 neonates (58.67%) received multiple transfusion. Donor exposure is calculated based on the feasibility of multiple aliquots from single donor unit of PRBC. 72.6% neonates were exposed to 1 donor, 21.92% neonates were being exposed to 2 donors and 5.48% neonates were exposed to 3 donors.
Conclusion: Packed red cells are the major component transfused to preterm neonates being admitted in neonatal intensive care unit. Aliquoting from a single donor unit is an important step in the direction of providing safe and effective blood component therapy to neonates.

Keywords: Neonates, Packed red cells, neonatal intensive care unit, transfusion therapy.

Introduction:

Packed Red cells are frequently transfused and comprise critical therapies for infants and neonates especially preterm neonates in neonatal intensive care units.[1] The majority of RBC transfusions to neonates are given to maintain hematocrit or blood hemoglobin concentration at a satisfactory level to optimize oxygenation. During their stay in neonatal intensive care unit, majority of the extremely low-birth-weight (ELBW) infants of less than 28 weeks receive at least one red blood cell transfusion and many end up receiving multiple transfusions.[2]

Neonatal transfusion practices differ from adult transfusions keeping in considerations their small blood volume and immature organ systems. The blood volume in a full term new born is approximately 85 ml/kg, while that in a preterm newborn is about 100 ml/kg. Blood volume in an adult is about 70 ml/kg. The difference in physiological parameters, hematological parameters and immature organ systems necessitates special approaches in neonatal transfusion practices.[4]

During the first weeks of life, all infants experience a decline in circulating RBC mass (hematocrit or blood hemoglobin concentration). This decline results both from physiological factors and, in sick premature infants, from phlebotomy blood losses. [3]

The premature or critically ill neonates are often given packed red blood cells component transfusion for a variety of reasons in neonatal intensive care units which thereby improve oxygen support and cardio respiratory status.

Repeated small-volume 'top-up' red cell transfusions are commonly carried out in preterm babies, mainly to replace losses from repeated blood testing exacerbated by reduced red cell production (Anemia of prematurity). Physiological causes for the anaemia of prematurity include [4]

(1)Diminished erythropoietin secretion.

(2)Decrease in survival of fetal red cells.

(3)Increasing blood volume due to rapid growth.

This is usually self-limited and well-tolerated; however in certain situations like blood loss due to repeated phlebotomy, sepsis and severe anemia, intervention may be required in the form of transfusion of blood and blood components.

Volume of Packed Red Cells which were used for transfusion were administered according to the following formula-

(Cloherty and Stark's Manual of Neonatal Care, 8th edition)

$$\boldsymbol{Volume\ of\ Transfusion} = \frac{\boldsymbol{Weight\ (in\ Kg) \times (Blood\ Volume/Kg) \times (Hct\ Desired - Hct\ Observed)}}{\boldsymbol{Hct\ of\ Blood\ to\ be\ given}}$$

- Hct of the packed RBCs was assessed with the help of cell analyser.
- Dose is 15-20 mL/kg; larger volumes may need to be divided in more than one aliquots.
- Blood volume in full-term neonates- 85 mL/kg.
- Blood volume in pre-term neonates-100mL/kg.

- Blood Components and Dosing of Small Blood Volumes in Neonatal and Pediatric patients- **(AABB Technical Manual, 19th Edition).**

Component	***Dose***	***Expected Increment***
Red blood cells	**10-15 mL/kg**	**Hb increase: 2-3g/dL**

Age of red cells transfused belonged to <5 days to 7 days old and stored in CPDA-1 were used to avoid high levels of potassium and to maximize red cell survival.

Due to increasing demand of transfusion therapy in neonatal age group, it is of prime importance to ensure the quality, accurate dose and well defined indication of the component transfused. This

prospective study gives an insight about the transfusion practices in neonates in neonatal intensive care unit in our centre.

AIM:

- To study the indications for transfusion in neonates.
- Assessment of Aliquoting for small volume transfusions from single donor unit blood and blood components in neonates.

METHODOLOGY:

The present study was conducted over a period of one year in the Department of Immunohematology and Blood Transfusion, SMGS Hospital, Government Medical College Jammu in collaboration with the Department of Pediatrics, Jammu, which is a tertiary care hospital.
The study was undertaken after the approval of Institutional Ethical Committee, Government Medical College, Jammu.

STUDY DESIGN: Prospective, Observational study.

STUDY POPULATION: Newborns admitted to neonatal intensive care unit (NICU) who required transfusion therapy were included in the study after taking into consideration the inclusion and exclusion criteria as described below-

INCLUSION CRITERIA-

- Gestational age at birth ≥28 completed weeks.
- Neonate who receives at least one blood component transfusion during the stay in NICU.

EXCLUSION CRITERIA-

- Major congenital abnormality.
- Newborns submitted to exchange transfusion protocols.
- Neonates with Hemoglobinopathies.

Neonates who were admitted in Neonatal intensive Care unit were included during the study period. The clinical history, blood product details, laboratory parameters and clinical parameters were evaluated. Parameters observed are as under:
Birth weight, Gestational Age of the neonate, Gender, blood group of the neonate, blood group of mother and father (if available), hemoglobin, hematocrit, clinical diagnosis, total days of NICU stay. The requisition of the blood components was assessed for product details i.e. type of the blood product, volume of the product, age of the unit and blood group. In addition, pre-transfusion hemoglobin or hematocrit and total number of donor exposures was noted. The indications for transfusion were assessed from the clinical diagnosis as per the protocol followed in neonatal intensive care unit.
Whole blood was collected from the healthy donor as per the guidelines for Blood Donor Selection and Donor referral, 2017. The whole blood is then subjected to component preparation and the packed red cells are said to be leucoreduced. The packed red cells are NAT for HIV, HBsAg and HCV. Syphillis and malarial parasite is tested via Rapid tests. The blood unit negative for these transmitted transfusion infections is available to be transfused.

Pre-transfusion testing-

It was done in the Department of Immunohematology and Blood Transfusion Medicine according to **AABB Technical Manual, 19th edition.**

- Blood group - ABO (forward group) and Rh typing was done.

- Mother's blood group and Father's blood group (if possible) was done.
- Screening was done for unexpected red cell antibodies using either plasma or serum from the mother.
- Crossmatch-compatibility testing and repeat ABO and D typing were not to be conducted as long as all of the following criteria were met:
- The antibody screening result is negative
- Transfused RBCs are group O, ABO identical, or ABO compatible and
- Transfused cells are either D negative or the same D type as the patient.
- Before non-group O RBCs to be issued, the neonate's plasma or serum is to be tested to detect passively acquired maternal anti-A or anti-B in anti-globulin phase.
- If antibody is present, ABO-compatible RBCs is to be transfused until the acquired antibody is no longer detected.
- If an unexpected non-ABO alloantibody is detected in the neonate's or mother's specimen, the neonate is transfused with RBCs units lacking the corresponding antigen or units that are compatible by antiglobulin crossmatch with maternal serum.

Aliquoting for small-volume transfusion- Small aliquots of blood component to be transfused were made out of a blood unit of 450 ml or 350 ml blood collection bag. These aliquots were made as per the requisition received for particular blood group and blood volume to be transfused.
Sterile bag to bag connecting device of Terumo Penpol was used for making small volume units in transfer bags for keeping closed system. The parent blood unit is then reserved for that particular neonate for further transfusion up to 7 days from the day of collection. Multiple aliquots were drawn from the single donor unit for small top-up transfusion to the neonate. This enabled the neonate to limit donor exposure, prevents circulatory overload and potentially decrease donor related risks.

Results:
In our study, 76 neonates were included who were admitted in neonatal intensive care unit. Neonates who were more than 28 weeks of gestation were analyzed for their transfusion requirements. In our study, 45(59.21%) neonates were males and 31(40.79%) neonates were females. 62 (81.58%) neonates were preterm neonates and 14 (18.42%) were term neonates. Among preterm neonates, 32 (42.11%) were early preterm which is less than 34 weeks of gestation and 30 (39.47%) were late preterm that is between 34 and 37 weeks of gestation. The mean gestational age in our study was found to be 33.73 ± 3.40 In present study, neonates were also classified on the basis of birth weight, 5 neonates (6.58%) were extremely low birth weight (less than 1000 g), 11 neonates (14.47%) were very low birth weight (less than 1500 g), 46 neonates (60.53%) were low birth weight neonates (less than 2500 g) and 14 neonates (18.42%) were normal birth weight neonates (between 2500-4000g). Mean birth weight was found to be 2000±594.9 gms.
Out of total small volume transfusions, 138 units (59.74%) of packed red cells were transfused. In our study, the most frequently transfused neonates were between 34 to 37 weeks of gestation followed by less than 34 weeks of gestation and those neonates who had birth weight less than 2500 g followed by those between 2500 g to 4000 g.
In present study, Shock was found to be the major indication for transfusion of PRBC in 30 neonates (39.47%) followed by anemia in 19 neonates (25%), bleeding in 14 neonates (18.42%), sepsis was found in 10 neonates (11.84%) and 2 neonates (1.32%) were transfused for hypoxic ischemic encephalopathy. In our study prematurity and shock was the major indication for transfusion in neonatal intensive care units followed by anemia, bleeding and sepsis (Fig 1).

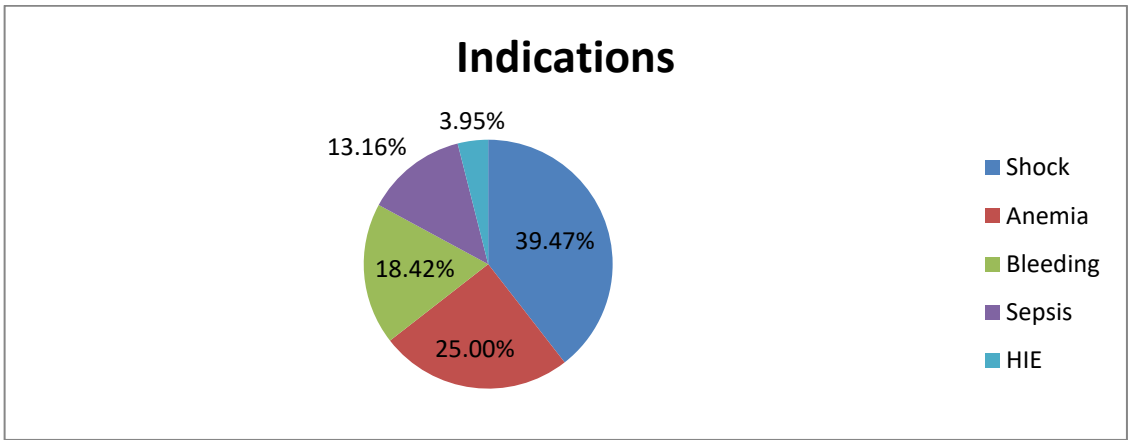

Fig 1: Indications for small volume transfusions in neonates.

Neonates were transfused as small Top up transfusion. Dosage is calculated as 10-20 ml/kg. In our study, 20 neonates (25.68%) received PRBC volume less than 15 ml, 45 neonates (59.46%) received 16-25 ml and 11 neonates (14.47%) were transfused with volume more than 25 ml. The mean volume of PRBC transfused was found to be 20.93 ± 5.77 (Fig 2).

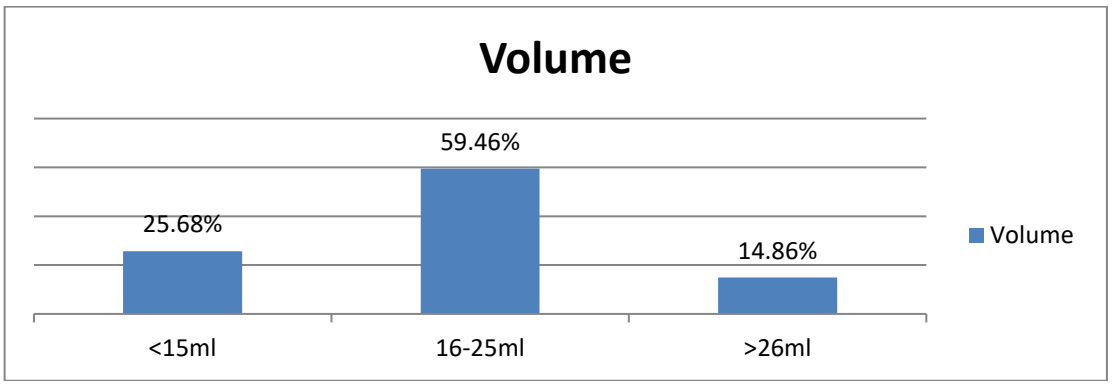

Fig 2: Small volume transfusions in Neonates.

In our study, 58.67 % of neonates received more than one PRBC transfusion. In present study, mean number of transfusion per neonate came out to be 1.93±1.2.
In our study, 27 packed red cells (19.57%) were less than 2 days old, 96 (69.57%) were between 2-5 days old and 15(10.86%) packed red cells were more than 5 days old. The mean age of packed red cells was found to be 3.77±1.40 days (Fig 3).

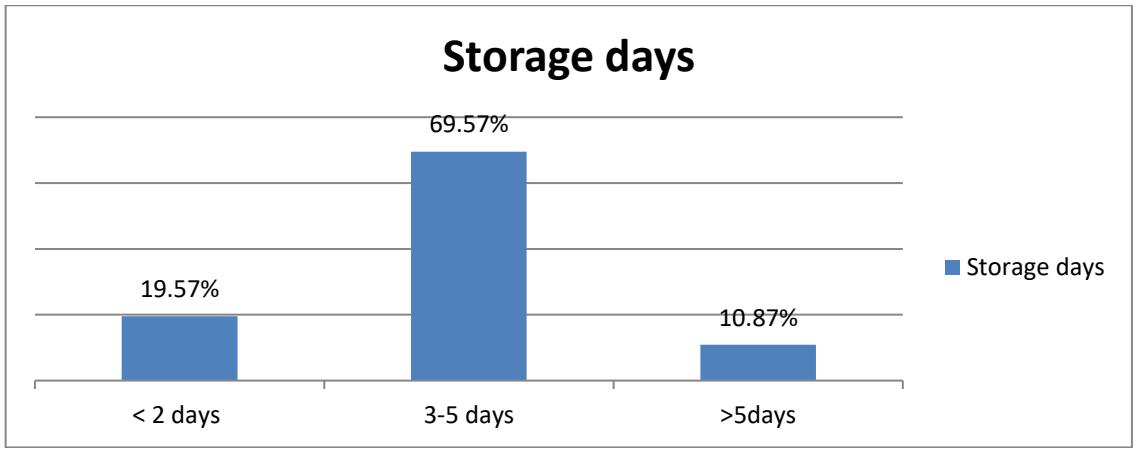

Fig 3: Number of small volume PRBC transfused as per day of storage

In present study, donor exposure was calculated based on the feasibility of multiple aliquots from single donor unit of PRBC. 53 (69.74%) neonates were exposed to 1 donor, 16 (21.05%)) neonates were being exposed to 2 donors and 7(9.21%)) neonates were exposed to 3 donors. The mean donor exposure came out to be 1.52 ±0.67 (Table 1).

Table 1: Total number of donor exposure to the neonate receiving PRBC transfusion.

DONOR EXPOSURE	Frequency	(%)
1	53	69.74
2	16	21.05
3	7	9.21
MEAN DONOR EXPOSURE	1.52 ±0.67	100

Donor exposure is calculated based on the feasibility of multiple aliquots from single donor unit of PRBC. 53 neonates (69.74%) were exposed to 1 donor, 16 neonates (21.05%) neonates were being exposed to 2 donors and 7 neonates (9.21%) neonates were exposed to 3 donors. The mean donor exposure was found to be 1.52 ±0.67 (Table 2).

Table 2: Distribution of neonates receiving single or multiple PRBC transfusion.

PRBC RECEIVED	NO. OF NEONATES	PERCENTAGE
SINGLE	31	40.79
MULTIPLE	45	59.21
MEAN NO. OF TRANSFUSION PER NEW BORN	1.96 ± 1.08	100

Discussion:

The most commonly used blood components in neonates are red blood cells. Red cell transfusion could be exchange transfusion for hyperbilirubinemia, or top-up transfusion for correction of anaemia. Red cell transfusions are given to maintain the haematocrit (Hct) at a level judged best for the clinical condition of the infant. [5] Several guidelines have been published over the last two decades for red blood cell transfusion in neonates. [6,7,8] Most of the recommendations are based on clinical experience rather than on evidence.

Blood component transfusions of red blood cells (RBCs), platelets and fresh frozen plasma (FFP) are commonly administered to preterm infants, but the evidence base for these transfusions, particularly for platelets, has thus far been limited.[9] Since 2019, three large randomised controlled trials (RCTs) were published. The Effects of Transfusion Thresholds on Neurocognitive Outcomes of Extremely Low-Birth-Weight Infants (ETTNO) and Transfusion of Prematures (TOP) trials reported no difference between the effects of liberal versus restrictive RBC thresholds on death or neurocognitive deficit at 2 years' corrected age. [10-12]

The mean gestational age in our study was found to be 33.73 ± 3.40 weeks. **Giridharan J *et al.*, (2013) [13]** conducted a study and found that the majority of neonates admitted in NICU who received transfusion therapy were Late Preterm (64%). In a similar study conducted by **Dogra *et al.*, (2018) [4]** on 61 neonates belonging to the age group of 27-41 weeks of gestation, it was observed that the mean age was 32.4 ± 3.4 weeks.

Mean birth weight was found to be 2000±594.9 gms. A study done by **Dogra *et al.*, (2018) [4]** the study group of neonates had mean birth weight of 1374±390.9 g.

In our study, the most frequently transfused neonates were between 34 to 37 weeks of gestation followed by less than 34 weeks of gestation and those neonates who had birth weight less than 2500

g followed by those between 2500 g to 4000 g. As per study done by **Conti *et al.*, (2013)** [14] the most heavily transfused neonates were between 24 and 29 weeks of gestation and less than 1000g. **Dogra *et al.*, (2018)**[4] showed that the most frequently transfused neonates were between 31 and 35 weeks of gestation closely followed by those between 27 and 30 weeks of gestation and those less than 1500g closely followed by those weighing 700-1000g.

The mean volume of PRBC transfused was found to be 20.93 ± 5.77. A study conducted by **Arlettaz *et al.*, (2020)** [15] surveyed neonatal services and found that (23%) neonatal units transfuse as per 10 ml/kg, another six (23%) transfuse 15 ml/kg and five (19%) transfuse 20 ml/kg. A prospective study by **Dogra *et al.*, (2018)**[4] found out that the mean volume of red cell was 39.6 ± 57.55ml.

In present study, mean pre transfusion Hemoglobin was found to be 9.82 ± 2.17gm/dl. Mean pre transfusion hematocrit came out to be 30.22 ± 6.98%. These mean values were found almost similar in the study by **Portugal *et al*., (2014)** [16] where mean hemoglobin and hematocrit values were 9.0±1.4 and 27.4 ± 4.3 respectively. **Dogra *et al*., (2018),** [4] in their study shown that the mean pre transfusion hematocrit was 25.3±4.4%.

In our study prematurity and shock was the major indication for transfusion in neonatal intensive care units followed by anemia, bleeding and sepsis.

A study by **Hume *et al.*, (1997)** [17] stated that the anemia of prematurity, not related to phlebotomy losses, was the most commonly stated reason for administering a small-volume RBC transfusion.

In our study, 58.67 % of neonates received more than one PRBC transfusion. In present study, mean number of transfusion per neonate came out to be 1.93±1.2. The study by **Portugal *et al.*, (2014)** [16] reported that over half of neonates received more than one transfusion. **Dogra *et al.*, (2018)**[4] reported that 20% neonates received multiple PRBC transfusion. A study by **Santos *et al.*, (2010)** [18] which was a multicenter prospective cohort of preterm infants of birth weight of less than 1500g found out that 55.9% received at least one RBC transfusion.

In present study, donor exposure was calculated based on the feasibility of multiple aliquots from single donor unit of PRBC. The mean donor exposure came out to be 1.52 ±0.67. The study conducted by **Dogra *et al.***, (2018) [4] found that the total donor exposure of 20 neonates was 1.2.

LIMITATIONS

- The study had a small sample size and various confounding factors.
- The study design didn't have any neonatal follow up protocol as a result of which we failed to obtain the long-term adverse effects of neonatal RBC transfusions.

CONCLUSION:

This study concludes that packed red cells are the major component transfused to preterm neonates being admitted in neonatal intensive care unit. Aliquoting from a single donor unit is an important step in the direction of providing safe and effective blood component therapy to neonates. Thus, the results from this study give additional insight on transfusion practices of neonates admitted in neonatal intensive care units.

Conflict of interest: Nil

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