Dedicated donor unit transfusions reduces donor exposure in pediatric surgery patients

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Abstract:

BACKGROUND: Many strategies have been explored to reduce multiple donor exposures in neonates such as use of restrictive transfusion protocols, limiting iatrogenic blood loss, use of recombinant erythropoietin and single donor programs.

METHOD: In our study we assessed the feasibility of dedicating single donor units with reserving all the components from the same donor for the specified neonates/infants undergoing surgery and estimating reduction of donor exposure. Fifty neonates undergoing surgery were included in the prospective study group and the transfusion details were compared with 50 retrospective cases with same inclusion criteria.

RESULTS: An intra-operative blood loss of >13 ml/Kg was significantly associated with transfusion (P<0.05) which was most frequently administered in the intra-operative period. Donor exposure rate of overall transfusion was 1.15 in the study group as compared to 4.03 in the retrospective control group. In study group Donor Exposure Rate (DER): Transfusion Rate (TR) ratio was 1:1.5 and Transfusion per Donor Unit (TPDU) of 1.5, means that one donor unit contributed to 1.5 transfusions in each patient and contributed to 50% reduction in donor exposure in each patient as compared to retrospective control group.

CONCLUSION: Our study showed that by practicing dedicated donor unit transfusion policy, for neonates undergoing surgery we could significantly reduce the donor exposure.

Keywords:
Dedicated donor units, donor exposure, intraoperative blood loss neonatal transfusion

Introduction

Transfusion therapy is often required in neonates and infants for various reasons. During the first few weeks of neonatal life, there is a physiological decrease in red cells. In healthy term infants, the nadir blood hemoglobin generally does not fall below 9 g/dl at 10–12-week old,[1] this decline is well tolerated by term infants. In preterm infants, the decline occurs earlier and it is more pronounced. Confounding factors such as phlebotomy[2,3] for blood testing in sick neonates and the underlying clinical condition like sepsis necessitate red cell transfusion support. In addition, transfusion support is necessary in pediatric surgical procedures. Apart from red cells, the patients may also require platelet and fresh frozen plasma (FFP) transfusion. Most of the red cell transfusions are required as top-up transfusions which are small volume (10–15 ml/kg), hence optimal practice in such situations is to provide aliquots from the primary blood bag as pediatric units.[4] Neonates and infants undergoing surgery may require multiple top-up transfusions of red cells and also platelet and plasma support. Hence, multiple transfusions lead to multiple donor exposure (DE). This is of greater concern

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in neonatal life since these patients are more likely to develop adverse effects of transfusion like the transfusion transmitted infections (TTIs) and immunomodulation.

Many strategies have been explored to reduce multiple DEs in neonates and infants; use of restrictive transfusion protocols, limiting iatrogenic blood loss, use of recombinant erythropoietin, and single donor programs. There is paucity of studies in literature on dedicated donor (DD) unit program. There are no published studies from India on the subject, and none of the studies reported in world literature used all three linked components. In the present study, we assessed the feasibility of dedicating single donor units with all three blood components (red cells, platelets, and FFP) from the same unit for the specified neonates/infants undergoing surgery and estimating the blood utilization, wastage, and reduction in DE.

**Materials and Methods**

This was a prospective observational study on the neonates and infants who underwent surgery with transfusion support using DD units (DD). The data obtained was compared with the retrospective data of the transfusion practice followed in patients of pediatric surgery matched for inclusion criteria.

A total of fifty patients were included in the prospective study group. The study population included preterm, term neonates, and infants, who were expected to receive multiple blood transfusions as a result of the surgical intervention or multiple phlebotomies for laboratory testing in neonatal surgical intensive care unit. The study was ethically approved by the institutional committee.

**Inclusion criteria**
- Any neonate or infant (<3 months) planned for surgery
- No history of the previous transfusion at the time of entry in the study.

**Exclusion criteria**
- Patients undergoing emergency surgery (as emergency surgery would not have given enough time for all three components to be dedicated from the same donor).

All the subjects enrolled in the study, after fulfilling the inclusion criteria, were assigned an ABO Rh (D)-matched donor unit and all the three components (packed red blood cells, PRBCs FFP, and platelet concentrates) from the donation were reserved for that particular patient. The department issued a special Identification number (ID. No.) to all the patients enrolled for the DD units. This DD unit number became the reference number for future communications between the treating clinician and the transfusion medicine (TM) department staff.

**Preparation of pediatric component bags (dedicated donor units)**

Freshly prepared (on the day of collection) PRBCs were selected for preparing pediatric bags. The PRBC unit (280–300 ml) was connected to two sterile transfer bags using a sterile connecting device (Fresenius NPBI Transfusion Technology, Hamburg, Germany). An equal volume of PRBC was divided into the three bags (primary bag and two attached transfer bags). After division, all three pediatric bags were labeled according to their primary bags and the same DDU ID No. was given to them. Then, these bags were separated and kept reserved for the neonate for whom they were prepared. Similarly, before freezing freshly separated plasma (200–220 ml) was connected to one sterile transfer bag using a sterile connecting device. An equal volume of plasma was divided into the two bags (primary bag and one attached transfer bag). After division both the pediatric bags were labeled according to their primary bags and with labels of DD unit ID No. and were separated and frozen at −80°C and reserved for the neonate for whom they were prepared. The volume of PC varied from 50 to 70 ml when prepared from 450 ml whole blood, so these were preserved as such. Fifty whole blood units, each was separated into PRBCs, FFPs, and PCs. Three aliquots of PRBC, 2 aliquots of FFP, and one unit PC was prepared from each whole blood unit, thus, a total of 300 component aliquots were available during the study.

**Transfusion possibilities on the dedicated donor units**

The utilization of the DD units for the purpose of transfusion had four possibilities:

**a.** If the patient was discharged before the shelf life of the components, then all the components were taken up in the normal inventory of blood and blood components, these were issued to other neonates/infants

**b.** If the patient has utilized all/one of the components of the DD units and was expected to undergo more transfusions then, a new DD unit was dedicated to him/her, according to the need, after discussion with the treating clinician

**c.** If the patient stayed admitted for more than the shelf life of the blood component, then the present DD units were taken up in normal inventory, and a new component was dedicated to him/her after discussion with the treating clinician depending on the need to transfuse

**d.** All the components were taken up in normal inventory in case of emergency and issued for urgent demands.
DD units assigned to a neonate or infant were kept reserved for them till the shelf life of the respective blood components PRBC for 35 days (at 4°C), FFP for 1 year (at or below −30°C), and PC for 5 days (at 22°C). They were issued to the patient as and when required.

**Control group**
Control group was retrospective and comprised previously admitted neonates fulfilling the inclusion criteria. Record of 50 such neonates was studied for transfusion details. These patients had been admitted to the pediatric surgery department during the previous 1 year. Aliquots of PRBC and FFP were issued to them but not from one DD.

**Parameters evaluated**
a. Transfusion details: For each patient, the following information was recorded; details of transfusion of RBC unit, PCs, and FFPs, the number of donor units required to fulfill the transfusion requirements of each patient and the number of components from the DD units which were not transfused to the intended recipients.
b. Clinical details: Note was made of any transfusion-related adverse event, pre- and post-transfusion hemoglobin, hematocrit, serum potassium levels and if available platelet counts. The length of hospital stay was also recorded.

c. Transfusion rate (TR) = Number of Transfusions per neonate and was calculated by Number of Transfusion/Number of Neonates

d. DE rate (DER): DER represents the total number of DEs per patient, and this was calculated by following formula:

\[
DER = \frac{\text{Number of DEs}}{\text{Number of patients transfused}}
\]

e. Transfusion per Donor Unit (TPDU): Number of transfusions from single donor unit = Number of transfusion/Number of donors required.

Statistical analysis of the transfusion details of prospective as well as retrospective patient data was done; reduction in rate of DER was assessed and compared between the study and control group.

**Results**

The demographic details of both the patient groups (Group 1: Study group—prospective group; Group 2: Control group—retrospective group) and type of surgery they underwent [Table 1] were comparable (P > 0.05).

Table 2 shows the transfusion of each component and DE in two groups. In “Group 1,” 28 patients had 58 transfusion events as compared to 28 patients with 160 transfusion events in “Group 2.” Out of 58 transfusion events in “Group 1,” 50 were from DD units, and 8 were from non-DD units making total DE as 35. As there were no DD units in “Group 2” DE for 160 transfusion events was 160.

Number of patients receiving single unit PRBC transfusions was comparable between two groups [Table 3] but number of patient receiving two units of PRBC transfusions was significantly higher in Group 2 (P = 0.006). Number of patients receiving double unit platelets and plasma transfusion was also significantly higher in Group 2 with P = 0.0001 for platelet transfusion and 0.012 for FFP transfusion.
The intraoperative surgical blood loss (ml/kg) for each patient in both groups was assessed and its association with blood transfusion was seen. In both groups patients who received transfusion had mean blood loss more than 13 ml/kg. Mean blood loss in patients who received transfusion in Group 1 was 13.13 ± 3.68 ml/kg and Group 2 was 13.56 ± 7.63 ml/kg. Patients who did not receive transfusion had mean blood loss of 4.36 ± 4.12 ml/kg and 4.82 ± 3.33 ml/kg in Group 1 and 2, respectively.

Each platelet transfusion event is associated with the DE. In Group 1, only first transfusion of platelet was from the DD unit, whereas in Group 2, all the transfusion events were from different donors. The most common indication for platelet transfusion was thrombocytopenia due to sepsis.

Most common indication for plasma transfusion was to correct the coagulation profile of the patients postsurgery. DDU of plasma was kept in two aliquots, but all 13 patients were transfused with only one aliquot in Group 1. The total number of transfusions in the retrospective group had a higher number of plasma transfusion as compared to Group 1 due to the change in policy to restrictive transfusion of plasma in postoperative period and replacing it with albumin at the time of the study. Hence for comparing DERs in two groups, FFP transfusions were not considered [Table 4]. A total of 58 transfusions were monitored in the study group, and none of them reported any adverse event relating to transfusion. Improvement in posttransfusion hemoglobin (12.2 ± 3.1 to 14.01 ± 2.99 g/dL) and hematocrit (36.6 ± 7.2 to 42.89 ± 7.7%) was observed (P = 0.001). Platelet count also improved significantly from pretransfusion value of 3.82 ± 1.6 × 10^3 to 8.84 ± 2.79 × 10^3/dl (P < 0.001).

DER considering only PRBC and platelet transfusion for Group 1 was 1.15 which is significantly lower than DER of 4.03 in Group 2 [Table 4]. This decrease in DER in Group 1 was due to transfusion of linked units to these patients and decrease in overall transfusions.

TPDU which is number of transfusion from single donor unit (Number of transfusion/Number of donors required) was 1.5 in the study group as compared to 1 in control group. This means that one donor unit contributed to 1.5 transfusions in each patient in the study group.

Utilization of dedicated donor units

Details of utilization of the aliquoted blood units are depicted in Table 5. Fifty of these linked components were transfused to the study Group 1 and rest of the components were released for other neonates admitted to the hospital at that time except for 9 PCs which were discarded as these were outdated (18% of total platelets dedicated and 3% of total components aliquot dedicated).

| Parameter | Group 1 | Group 2 | P |
|-----------|---------|---------|---|
| A: PRBC transfusion and donor exposure | | | |
| No. of patients with PRBC transfusion | 22 | 19 | 0.067 |
| Single unit transfusion | 22 | 12 | 0.006 |
| Two unit transfusion | 0 | 7 | |
| B: Platelet transfusion and donor exposure | | | |
| No. of patients with platelet transfusion | 13 | 19 | 0.198 |
| Single unit transfusion | 10 | 0 | 0.0001 |
| More than two unit transfusion | 3 | 19 | |
| C: FFP transfusion and donor exposure | | | |
| No. of patients with FFP transfusion | 13 | 17 | 0.383 |
| Single unit transfusion | 13 | 4 | 0.012 |
| More than two unit transfusion | 0 | 13 | |

| Parameter | A | B | C |
|-----------|---|---|---|
| No. of Patients | PRBC transfusion | PC transfusion | Total* |
| Group 1 | 22 | 13 | 26 |
| Group 2 | 27 | 18 | 45 |
| Donor Exposure | 22 | 8* | 30* |
| DER | 1.0 | 0.61 | 1.15 |

*Donor exposure is 8 in case of total 18 platelet transfusions for 13 patients, as 10 were from DDU where donor exposure is already included with PRBC donors and rest 8 transfusions were from non DDU units. *Total is not just the addition of parameter for PRBC and PC as some of the patients received more than one component and in group 1 patients received linked units also

| Dedicated donor units |
|-----------------------|
| Type of Blood Components | Prepared | Used by study group | Released for other neonates | Not used/wasted |
| RBCs | 150 | 27 | 123 | Nil |
| PC | 50 | 10 | 31 | 9 |
| FFP | 100 | 13 | 87 | Nil |
| Total | 300 | 50 | 241 | 9 |
Discussion

Limited donor program has been a matter of interest\textsuperscript{[11]} for the pediatrician as well as TM specialists for a long time. The main driving forces for these programs were the primarily appropriate use of blood in patients of pediatric age group. With time other concern with multiple DE such as risk of TTI and immunomodulation also gained importance.\textsuperscript{[9]} TTI is a serious concern associated with transfusion especially in developing countries like India which still rely on serological testing for TTI screening. This makes limiting DE in our setting more relevant. Many studies focused on different groups of pediatric patients and used a variety of protocols to minimize the DE through transfusion as shown in Table 6.

Our study demonstrates that patients undergoing pediatric surgery usually require multiple transfusions of different blood components. Issuing linked blood components from DD unit reduced the DER in the study group (1.15) as compared to control group (4.03) where each blood component was from a different blood donor. In a similar study by Wood et al.,\textsuperscript{[10]} on preterm infants showed that DER fell to 2.0 in DD unit group as compared to 4.9 in the retrospective control group. DD unit group was called “BBB” scheme (banked baby blood)\textsuperscript{[9]} in this study, and this study only considered red cell transfusions. Another study by Strauss et al.,\textsuperscript{[11]} on pediatric surgery patients assessed whether single donor would be able to satisfy the RBC needs of patients which were ineligible to undergo autologous transfusion concluded that need of most RBC transfusions of elective pediatric surgery patient can be fulfilled from single donor which otherwise would have been exposed to multiple donors.

An important concern is that if these pediatric units are not utilized by the patients for whom they are dedicated, and these units are not timely diverted to general inventory and made available for other patients, this can lead to increased wastage of these units. In our study, only 50 out of 300 (16.6\%) dedicated pediatric units were utilized by the study group, and rest of the units were diverted to other patients. In a study by Wang-Rodrig et al.,\textsuperscript{[12]} it was observed that there is up to 60\% wastage of these pediatric units if these units are not shared with other infants. To minimize blood wastage without compromising the goal of limiting DE, they suggested that each infant’s transfusion requirements should be investigated. The infants predicted to have high transfusion requirements should receive blood from a unit dedicated to their individual use and other infants should be assigned to receive blood from a unit that could be shared among as many as four similar infants. In our study, the intraoperative surgical blood loss was predictive for transfusion as patients in both groups who received transfusions had mean blood loss more than 13 ml/kg, and these patients should be a candidate for DD units, and patients with lower blood loss can be assigned to use blood components from shared units.

Table 6: Comparison of various studies on dedicated donor unit program and related donor exposure in neonates

| Author Year; Country | Study | Type of Patients | Study groups | N | Transfusion Rate | Donor Exposure rate | Transfusion per Donor Unit |
|----------------------|-------|-----------------|--------------|---|-----------------|----------------------|--------------------------|
| Wood A et al.,\textsuperscript{[11]} 1995; UK | Dedicated PRBC unit protocol was compared with retrospective data for practice of issuing pedipack from new donor for each transfusion. | Neonatal admitted in NICU | Retrospective | 43 | 5.6 | 4.9 | Data |
| | | | Prospective | 29 | 5.3 | 2 | Not Available |
| Wang-Rodriguez, J et al.,\textsuperscript{[12]} 1996; USA | Decision making model was designed based on predicted transfusion requirements for the newborns to either issue: Dedicated unit (dedicate one unit) Shared unit: (one unit for four newborns) | Premature Infants | Dedicated units | 24 | 4.6±2.4 | 1.5±0.7 | 3.5±1.7 |
| | | | Shared units | 23 | 2.6±1.6 | 1.3±0.5 | 4.1±1.9 |
| Ibojie J et al.,\textsuperscript{[13]} 2003 UK | Two time points reviewed, before and after, following the introduction of a paedipack system: Retrospective period; 1996-1997 Prospective period; 1999-2000 | Neonates admitted to neonatal units (NNU) | Retrospective | 79 | 2.3 | 2.3 | 1 |
| | | | Prospective | 78 | 7.5 | 2.4 | 3.2 |
| Our Study | Dedicating Donor Unit (all the components from a donation reserved for one patient) transfusion Compared with retrospective data from practice of issuing pedipack from new donor for each transfusion. | Newborns for Paediatric Surgery | Retrospective | 50 | 4.03 | 4.03 | 1 |
| | | | Prospective | 50 | 1.73 | 1.15 | 1.5 |

Transfusion Rate (TR) = Number of transfusion per neonate = Number of transfusion/Number of neonates transfused
Donor Exposure Rate, (DER) = Total number of donor exposures per patient = Number of donor exposures/Number of patients transfused
Transfusion per Donor Unit (TPDU) = Number of transfusion from single donor unit = Number of transfusion/Number of donors required
A study by Ibojie et al. showed that DER:TR ratio is a better demonstrator of reduction of DE than DER alone. The author reviewed 2 time points, before and after the introduction of pedipack system in the UK. The analysis concluded that a high TPDU correlates with a reduction in DER:TR ratio hence achieving greater benefits. In our study, DER:TR ratio was 1:1.5 in DDU group as compared to 1:1 in retrospective control group and TPDU was 1.5, this means that one donor unit contributed to 1.5 transfusions in each patient and DDU programme contributed to 50% reduction in DE in each patient as compared to retrospective control group.

In this study, volume of each aliquot of PRBC was 80–100 ml, but most of the patients were transfused with a volume range of 30–50 ml of PRBC and mean transfusion volume from each PRBC aliquot was 49.5 ± 11.3 ml, therefore, making more aliquot of 50–60 ml each would result in further reduction of wastage of blood.

Significantly higher numbers of patients were transfused two units of PRBC in Group 2 as compared to Group 1 (none). These were thoracic[2] Genito-Urinary[1] and Gastrointestinal[4] surgery patients in Group 2 who received dual transfusions. The detailed analysis of type and indication of surgery was not done as a part of our analysis hence conclusively it cannot be commented on the reason of significantly higher number of dual transfusions in Group 2.

Major reason of multiple DEs in our study was platelet transfusions. As these have short shelf life and no aliquots were prepared, many patients who required platelets in postoperative period or who required more than one platelet transfusion lead to transfusion from some other donor leading to multiple DEs (resulting in 8 transfusions from non-DDU units in Group 1, Table 2). Use of restrictive transfusion policy is the only way of reducing this DE. In the present study, an additional benefit observed was practice of the restrictive transfusion policy due to effective interaction between the TM and pediatric surgery doctors.

Limitations of study

- The control group taken in the study was retrospective patients. Prospective control group was not chosen because this would have posed ethical issues as DD unit is a better practice and knowingly the neonates would have been deprived of this.
- A marked decrease was observed in platelet and FFP transfusions in DD unit group as compared to retrospective control group. This bias was likely due to close communication between the TM resident and clinical resident and frequent ward rounds by the TM resident. Furthermore, chief of the clinical unit was involved during decision of transfusion in DD unit group leading to more restrictive transfusion policy in the DD unit group as compared to control group.
- FFP transfusions were markedly decreased in DD unit group as practice changed from FFP transfusion to albumin solution transfusions. Before the study period, there was limited availability of albumin solution during transfusions in control group. To avoid influence of this policy on comparison between two groups, FFP transfusions were excluded at the time of calculating the DER in two groups.

Conclusion

Intraoperative transfusion is the most common indication to transfuse RBC in surgical patients (neonates), and an intraoperative blood loss of more than >13 ml/kg is significantly associated with transfusion. DER of overall transfusion was 1.15 (excluding FFP transfusions) in the study group as compared to 4.03 in the retrospective control group. In study group DER:TR ratio was 1:1.5 and TPDU of 1.5, means that one donor unit contributed to 1.5 transfusions in each patient and contributed to 50% reduction in DE in each patient as compared to retrospective control group.

Close communication and regular ward rounds of TM specialist to the clinical wards is an important part of making this program a success. Our study showed that by practicing DD unit policy for neonates undergoing surgery, we could significantly reduce the DE. We also minimized blood wastage by releasing nonutilized pediatric units to neonates/infants requiring top-up transfusion for various other surgical and/or medical conditions. Close interaction between the two departments helped to practice a restrictive transfusion policy.

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Conflicts of interest

There are no conflicts of interest.

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