

Storage red blood cell (RBC) transfusion (prime) for extracorporeal circulation circuit in pediatric cardiac surgery: postoperative impact on biochemical changes

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Abstract

Background: In neonates, approximately 20% of red blood cell (RBC) and most of the plasma products are used for surgical procedures. The major reason for transfusion in cardiac surgery is because the extracorporeal circulation circuit (ECC) needs to be primed with blood. Biochemical changes take place when RBCs are kept for a phase of time and are together termed the storage lesion.

Objective: To clarify the incidence and nature of postoperative liver function, sepsis, and renal function associated with storage RBC prime for cardiopulmonary bypass circuit in new born, infants, and small children.


Materials and Methods: A total of 50 consecutive patients who underwent ECC between January 2014 and September 2015 and required blood prime were included in this study. Patients who required RBC were divided into two groups based on patients age and storage RBC age. Arterial blood sample and storage RBCs bag samples were collected in vivo for the assessment for postoperative biochemical parameters determinations.

Result: Postoperative white blood cell for >7-day storage RBCs prime in >365 days age patients is 16982.5 ± 4808.45 . Postoperative serum glutamic pyruvic transaminase (SGPT) for >7-day storage RBCs prime in >365 days age patients mean (\pm SD) was 23.5 ± 7.56 . Postoperative serum glutamic oxaloacetic transaminase (SGOT) for >7-day storage RBCs prime in >365 days age patients was 139.88 ± 70.32 . Postoperative serum bilirubin for >7-day storage RBCs prime in >365 days age patients was 2.13 ± 0.99 . Postoperative urea for >7-day storage RBCs prime in >365 days age patients was 25.88 ± 6.73 . Postoperative serum creatinine for >7-day storage RBCs prime in >365 days age patients was 0 ± 0 .

Conclusion: The age of storage RBCs and age of patient results in increased postoperative patients' white blood counts, SGPT, SGOT, serum creatinine, and blood urea.

KEY WORDS: Storage RBCs, extracorporeal circuit, white blood counts, SGPT, SGOT, serum creatinine, blood urea

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Introduction

The cardiopulmonary bypass (CPB) circuits available presently still need a large priming volume, and it may be greater than the total blood volume of neonates and patient and institutional practices. Presently, banked packed red blood cells (PRBCs) preserved in storage media are assigned for preparing the CPB circuit in infants and children to maintain the temperature-appropriate hematocrit levels, to prevent

the hemodilution, and adequate tissue oxygen delivery. However, use of PRBCs is related to important metabolic disparities and their complications.^[1,2]

Approximately, six to eight of 1,000 newborns show a congenital heart malformation, often requiring surgery. Extracorporeal membrane oxygenation (ECMO) provides life support to patients with respiratory and/or cardiac failure. After cardiac surgery, ECMO is indicated in 0.5%–3.5% of infants.^[3] Currently, 1%–2% of critically ill newborns are treated by ECMO. The most frequent indications for ECMO in newborns are meconium aspiration syndrome and congenital diaphragmatic hernia, together accounting for more than 50% of ECMO procedures. The metabolic effect of transfusion RBCs (prime) is an area of significant concern, which required substantial attention for extracorporeal circulation circuit prime^[4] for pediatric patients. The retrospective trial shows difference between all possible outcomes, including contributing perioperative factors for transfused older RBCs and fresher RBCs, with age of patients. The effect of prime storage RBCs remains a highly controversial issue. In a study by Koch, functional and structural changes of stored RBCs begin after 2–3 weeks of storages.^[4,5] In storage RBCs, substantial changes will take place. These changes result in the formation of cellular and chemical entities that may alter recipient biology, for newborns, infants, and small children require the use of intraoperative homologous RBCs transfusion for cardiopulmonary bypass. Homologous transfusion has more of an impact on the physiology of pediatric patients than an adult physiology. According to the study by Koch *et al.*,^[6] the age of RBC storage and complications after cardiac surgery^[7] and effect of blood transfusion on long-term survival after cardiac operation was independently associated with increased mortality and morbidity in adult cardiac surgery. This study is the result of risk and complication of storage blood transfusion^[8,9] for newborns, infants, and small children. The storage RBCs priming may cause changes in metabolic profile of the patients and lead to differences in postoperative complication rates.^[6–10]

We, at our institute, prospectively evaluated the effect of length of storage of RBCs on the biochemical factor in children undergoing corrective cardiac surgery. Specific attention was given to serum glutamic pyruvic transaminase (SGPT), serum glutamic oxaloacetic transaminase (SGOT), serum creatinine (s.creatinine), and blood urea.

Materials and Methods

In this study, we enrolled 50 consecutive newborns, infants, and small children, who underwent extracorporeal circulation circuit with various age of storage RBCs that are used for priming. The protocol was approved by the ethical clearance committee of our institute. Patients who required RBC were divided into two groups based on patients age and storage RBC.

Surgery and Parameters Tested

Anesthesia was induced with inj. fentanyl (40–100 µg/kg) and inj. vecuronium (0.1–0.15 mg/kg). All patients underwent

extracorporeal circulation with moderate hypothermia ($32 \pm 5^\circ\text{C}$), roller pump, and membrane oxygenator. The perfusion flow was kept over 2.4 L/min during normothermia and 1.8 L/min during hypothermia in all patients. The mean arterial pressure was kept between 35 and 40 mm Hg with inj. phenylephrine and inj. sodium nitroprusside. Arterial blood gas was monitored every half an hour or on any occasion when necessary. The priming solution contained 300–400 mL of Ringer's lactate solution, heparin 5000 U/l, and 100–150 mL of packed red cells. Systemic heparin was given through the internal jugular line by an anesthesiologist before cannulation.

Parameters Tested

Preoperative

Blood samples were collected within 2 to 3 days before operation by vein puncture. Full blood count, urea, s.creatinine and electrolytes, SGPT, SGOT, and total bilirubin (tb) were tested. In all patients, serological viral studies were performed to rule out infection with Hepatitis B (HBsAg) and HIV virus.

Perioperative

In every operation, the routine clinical monitors including lead electrocardiogram, the radial arterial line, the pulse oximeter, nasopharyngeal temperature, urine output, central venous pressure line, operating time, CPB time, aortic cross-clamp time, PRBC volume during CPB, mechanical ventilation time, and intensive care unit (ICU) stay time (days) were recorded.

Postoperative

We obtained blood sample daily through the central venous line or vein puncture on the first, second, and third postoperative days and analyzed for concentrations of hemoglobin, SGPT, SGOT, tb, total white cell count, urea, and s.creatinine.

Statistical Analysis

Statistical analysis was carried out using SPSS software, version 10.0 (SPSS Inc., USA). Data were presented as mean \pm SE of the mean. The χ^2 -test and Student's *t*-test were used to compare categorical variables. Stepwise logistic regression was employed for multivariate analysis. Values of *P* less than 0.05 were considered significant.

Result

Arterial blood sample and storage RBCs bag samples were collected in vivo for assessment for postoperative biochemical parameters determinations. A total of 29 (58%) male and 21 (42%) female subjects were included. Their age ranged from 2 to 1,700 days (mean 479.48 ± 488.08).

The perioperative of infection rate is shown in Table 1. For sepsis, white blood cell (WBC) counts concentrations of postoperative patients were analyzed. Postoperative WBC for ≤ 7 -day storage RBCs prime in < 365 days age patients mean (\pm SD) was $16,834.67 \pm 6,334.74$, and postoperative WBC for > 7 -day storage RBCs prime in > 365 days age patients mean (\pm SD) was $16,982.5 \pm 4,808.45$.

Table 1: Perioperative of infection rate

| Variable | Age-wise distribution (days) | ≤7 days RBCs (n = 25) | | | >7 days RBCs (n = 25) | | |
|----------|------------------------------|-----------------------|----------------------|-------|-----------------------|----------------------|--------|
| | | Pre | Post | P | Pre | Post | P |
| WBC | ≤365 | 13,035.8 ± 3,534.34 | 16,834.67 ± 6,334.74 | 0.052 | 12,109.65 ± 3,725.03 | 14,572.88 ± 4,087.14 | 0.075 |
| | >365 | 13,270.9 ± 3,388.6 | 18,118 ± 5,010.21 | 0.02 | 11,254.63 ± 2,439.64 | 16,982.5 ± 4,808.45 | 0.0095 |

WBC, white blood cell.

Table 2: Perioperative liver function

| Variable | Age-wise distribution (days) | ≤7 days RBCs (n = 25) | | | >7 days RBCs (n = 25) | | |
|-----------|------------------------------|-----------------------|---------------|---------|-----------------------|----------------|---------|
| | | Pre | Post | P | Pre | Post | P |
| Bilirubin | ≤365 | 1.07 ± 1.71 | 1.6 ± 1.72 | 0.405 | 2 ± 2.83 | 2.47 ± 2.12 | 0.5875 |
| | >365 | 0.4 ± 0.7 | 1 ± 0.67 | 0.659 | 0.5 ± 0.53 | 2.13 ± 0.99 | 0.0002 |
| SGPT | ≤365 | 20.73 ± 5.85 | 17.87 ± 4.93 | 0.159 | 22.82 ± 16.14 | 25.82 ± 10.25 | 0.5223 |
| | >365 | 16.5 ± 3.72 | 19.3 ± 5.17 | 0.181 | 20.75 ± 6.54 | 23.5 ± 7.56 | 0.4495 |
| SGOT | ≤365 | 40.87 ± 12.59 | 99.73 ± 42.98 | <0.0001 | 47.47 ± 26 | 138.94 ± 60.01 | <0.0001 |
| | >365 | 33.2 ± 6.23 | 101.6 ± 31.08 | <0.0001 | 43.13 ± 19.01 | 139.88 ± 70.32 | 0.0021 |

SGPT, serum glutamic pyruvic transaminase; SGOT; serum glutamic oxaloacetic transaminase.

Table 3: Perioperative renal function

| Variable | Age-wise distribution | ≤7 days RBCs (n = 25) | | | >7 days RBCs (n = 25) | | |
|----------|-----------------------|-----------------------|-------------|-------|-----------------------|--------------|--------|
| | | Pre | Post | P | Pre | Post | P |
| Urea | ≤365 | 24.07 ± 7.65 | 30.53 ± 9.2 | 0.046 | 23.94 ± 15.76 | 26.35 ± 6.3 | 0.5623 |
| | >365 | 20.5 ± 7.95 | 29 ± 8.72 | 0.035 | 17.75 ± 5.73 | 25.88 ± 6.73 | 0.0209 |
| S.cr | ≤365 | 0.13 ± 0.35 | 0.2 ± 0.41 | 0.619 | 0.12 ± 0.33 | 0.29 ± 0.47 | 0.2312 |
| | >365 | 0 ± 0 | 0.4 ± 0.52 | 0 | 0 ± 0 | 0 ± 0 | 0 |

S.cr, serum creatinine.

The perioperative liver functions are shown in Table 2. For impaired liver function, SGPT, SGOT, and serum bilirubin were analyzed. Postoperative SGPT for ≤7-day storage RBCs prime in <365 days age patients mean (± SD) was 17.87 (± 4.93). Postoperative SGPT for >7-day storage RBCs prime in >365 days age patients mean (± SD) was 23.5 ± (7.56). Postoperative SGOT for ≤7-day storage RBCs prime in <365 days age patients mean (± SD) was 99.73 (± 42.98). Postoperative SGOT for >7-day storage RBCs prime in >365 days age patients was 139.88 (± 70.32). Postoperative serum bilirubin for ≤7-day storage RBCs prime in <365 days age patients was 1.6 (± 1.72). Postoperative serum bilirubin for >7-day storage RBCs prime in >365 days age patients was 2.13 (± 0.99).

The perioperative renal functions are shown in Table 3. For renal function, postoperative s. creatinine and blood urea were analyzed. Postoperative s.creatinine for ≤7-day storage RBCs prime in <365 days age patients mean (± SD) was 0.2 (± 0.41). Postoperative s.creatinine for >7-day storage RBCs prime in >365 days age patients mean (± SD) was 0 (± 0). Postoperative urea for ≤7-day storage RBCs prime in <365 days age patients mean (± SD) was 30.53 (± 9.2). Postoperative urea for >7-day storage RBCs prime in >365 days age

patients mean (± SD) was 25.88 (± 6.73). Analysis of possible risk factors of RBCs transfusion postoperative is shown in Table 4.

Discussion

This prospective study showed that postoperative total WBC count and transient liver damage could occur after extracorporeal circulation in pediatric cardiac surgery. Intraoperative transfusion of RBC that had been stored for more than 7 days was associated with a significantly increased risk of postoperative complications in newborns, infants, and children aged 5 years or less undergoing cardiac surgery when blood was used to prime the CPB circuit. It is notable that, in our study, pulmonary complications were observed significantly, more in patients receiving >7-day RBCs. In pediatric patients, one or two units of RBCs can be considered a massive transfusion. We also observed that systemic infection occurred at a nonsignificant higher rate in pediatric patients receiving >7-day RBCs. The bioactive substances released by leukocytes may be responsible for this effect. The rate of ARF was observed to be higher in the patients receiving >7-day RBCs.

Table 4: Analysis of possible risk factors of RBCs transfusion postoperative

| | Age distribution | ≤7 days RBCs | | >7 days RBCs | | P |
|--------------------|------------------|--------------|---------------|--------------|----------------|--------|
| | | n | | n | | |
| CPB duration (min) | ≤365 | 15 | 69.33 ± 34.07 | 17 | 83.53 ± 36.93 | 0.2091 |
| | >365 | 10 | 58.9 ± 25.44 | 8 | 85.38 ± 20.16 | 0.029 |
| Cross-clamp (min) | ≤365 | 15 | 45.07 ± 27.9 | 17 | 52.47 ± 28.93 | 0.4636 |
| | >365 | 9 | 37.67 ± 22.82 | 7 | 58.57 ± 19.36 | 0.0731 |
| Lowest temperature | ≤365 | 15 | 32.07 ± 2.69 | 17 | 32 ± 2.26 | 0.9368 |
| | >365 | 10 | 33.5 ± 2.46 | 8 | 32.38 ± 2.62 | 0.3479 |
| Lowest HCT % | ≤365 | 15 | 26.87 ± 3.11 | 17 | 28.82 ± 4.14 | 0.1468 |
| | >365 | 10 | 28.1 ± 3.51 | 8 | 28 ± 4.24 | NS |
| Postop. MVT (h) | ≤365 | 15 | 58.4 ± 48.11 | 17 | 53.76 ± 71.9 | 0.834 |
| | >365 | 10 | 20.8 ± 10.28 | 8 | 22.38 ± 11.11 | 0.7585 |
| Postop. blood loss | ≤365 | 15 | 13.33 ± 29.68 | 17 | 20.59 ± 30.92 | 0.5046 |
| | >365 | 10 | 75 ± 95.01 | 8 | 96.25 ± 272.24 | 0.82 |
| Preop. HCT | ≤365 | 15 | 36.73 ± 4.46 | 17 | 38.18 ± 6.87 | 0.491 |
| | >365 | 10 | 38.1 ± 5.07 | 8 | 37.88 ± 4.05 | 0.9218 |
| On CPB HCT | ≤365 | 15 | 30.73 ± 3.67 | 17 | 31.12 ± 3.16 | NS |
| | >365 | 10 | 30.1 ± 4.68 | 8 | 31.25 ± 2.19 | NS |
| Off CPB HCT | ≤365 | 15 | 37.53 ± 4.12 | 17 | 36.88 ± 4.61 | NS |
| | >365 | 10 | 35.9 ± 6.57 | 8 | 34.25 ± 2.31 | NS |
| Postop. RBCs | ≤365 | 15 | 52.33 ± 66.54 | 17 | 74.29 ± 102.86 | 0.4856 |
| | >365 | 10 | 78.6 ± 135.95 | 8 | 100 ± 106.37 | 0.7205 |
| ICU stay | ≤365 | 15 | 8.2 ± 8.06 | 17 | 8.47 ± 6.83 | 0.919 |
| | >365 | 10 | 4.7 ± 2 | 8 | 4 ± 2.33 | 0.5024 |

CPB, cardiopulmonary bypass; HCT, hematocrit; RBCs, red blood cells.
NS, nonsignificant.

It has been well-known that early jaundice and transient liver damage could occur after extracorporeal circulation surgery.^[11,12] This study showed that the overall incidence of the postoperative systemic infection was 88% (22/25). The RBCs storage time for pediatric patients is significantly associated with postoperative morbidity outcome.

The overall incidence of the postoperative hyperbilirubinemia (>7 days) was 36 % (9/25), and abnormal SGOT was 88% (22/25), similar to the literature report.^[13] This result shows that postoperative hyperbilirubinemia occurs more frequently in patients who received >7-day RBCs. The early transient postoperative hyperbilirubinemia occurs after modern extracorporeal circulation. It is mainly caused by an increase in both conjugated and unconjugated bilirubin concentration and associated with a higher mortality.^[14] The tb concentration is important. Our patients who developed postoperative jaundice had received significantly more blood transfusions, which would certainly cause an increased bilirubin load to the liver.^[15] The postoperative hyperbilirubinemia is a multifunctional process, which is caused by both the impaired liver function of bilirubin transport and increased production of bilirubin because of hemolysis. CPB can lead to a severe and complicated change of pathophysiology of the liver. Operation

stress, reperfusion injury, endotoxemia, and inflammatory reaction may contribute to the liver injury.^[16-18]

The main limitation of this study is the relatively small study population. However, studies addressing outcomes after cardiac operations in pediatric patients aged ≤5 years cannot include as many patients population as studies focused on adult patients, because the overall population size is smaller. The population size of this study was large enough to explore biochemical changes and morbidity, but not mortality. The fact that even with a limited number of patients and events we could identify significant associations between morbidity outcome variables and RBC storage time is probably owing to the large impact that one or two units of stored RBCs may have in patients with a small body surface area. Even one or two units of RBCs can be considered a massive transfusion in very small pediatric patients.

Conclusion

We conclude that two factors—age of storage RBCs and age of patient—result in increased postoperative patients WBC counts, SGPT, SGOT, s.creatinine, and blood urea.

The storage time of RBCs used for priming the CPB circuit during cardiac operations is associated with increased major biochemical changes and primarily affects pulmonary and renal function. There is a significant association between the storage time of RBCs and the risk of experiencing a serious postoperative complication. This risk increases with increasing storage time even within the group of patients receiving newer (less than 5-day-old) blood. Therefore, the use of the freshest possible blood is suggested for priming the CPB circuit. We could not identify the same association between RBC storage time and bad outcomes in patients being transfused but not receiving blood prime.

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