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ORIGINAL ARTICLE

Effect of Red Blood Cell Storage Duration on Outcome After Paediatric Cardiac Surgery: A Prospective Observational Study

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Background Retrospective reviews have found the use of stored packed red blood cells (PRBCs) in priming to be associated with increased risk of postoperative complications. The purpose of study was to prospectively investigate the influence of duration of storage of PRBCs used in priming the cardiopulmonary bypass (CPB) circuit on the metabolic profile of the patients, and postoperative outcome after paediatric cardiac surgery.

Methods Between January 2015 and December 2015, 198 consecutive children operated for cardiac surgery using CPB and received blood for priming the circuit were included. Patients were divided into two groups based on the duration of storage of the blood, newer PRBCs group who received blood stored for ≤14 days and the older PRBCs group who received blood stored for >14 days.

Results Mean duration of blood storage used for priming in newer PRBCs blood group (n = 103) was 8.4 ± 3.7 days while it was 21.9 ± 4.5 days in older PRBCs group (n = 95). Metabolic parameters of the PRBCs improved to physiological limits in both the groups after initiation of CPB. Postoperative hepatic, pulmonary, haematological complications, sepsis and multi-organ failure were more in the old PRBCs group. However, the difference was not significant. Similarly, there was no significant difference in incidence of prolonged mechanical ventilation, intensive care unit stay and hospital stay and mortality between the two groups.

Conclusions Metabolic parameters of the stored blood become normal after initiation of CPB irrespective of duration of storage. In paediatric patients without significant co-morbidity, undergoing cardiac surgery, transfusion of washed stored blood up to 28 days in CPB priming is safe especially if lesser amount of transfusion is required.

Keywords Cardiopulmonary bypass • Packed red blood cell • Paediatric patients

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Introduction

Packed red blood cells (PRBCs) is often required in the priming of the paediatric cardiopulmonary bypass (CPB) circuit to prevent anaemia during and after the CPB [1]. The volume of PRBCs transfused in the priming may amount to a massive transfusion in neonates and small infants [2]. The storage medium for blood leads to significant alterations in the biochemical and metabolic profile of the PRBCs, which worsens with the increasing duration of storage. These changes, called 'storage lesions', may affect function, viability, and quality of RBCs [3]. The clinical importance of storage lesions has remained controversial and, therefore, there is no consensus regarding cut-off for the fresh or the old PRBCs [4]. Moreover, certain studies found a significant correlation between increasing duration of PRBCs storage and increased rate of morbidity and mortality following transfusion [5–10] while other studies have failed to find any such correlation [11–14]. The probable reasons for these discrepancies are: the retrospective nature of the studies, lack of stringent criteria, heterogeneity of the study designs and patient groups, use of different outcome parameters, and various cut-offs of PRBC age (5–27 days) [9,10,14].

Due to fear of adverse effects of storage, most paediatric cardiac surgery units prefer to use fresh blood for priming of the CPB circuit [15]. Availability of fresh PRBCs is, however, usually limited. Therefore, paediatric surgeons may be compelled to use stored blood to prevent unnecessary delay in surgeries.

We performed this prospective observational study to evaluate the effect of duration of storage of PRBCs used in CPB priming in paediatric cardiac surgery on postoperative morbidity and mortality. We also evaluated for duration of storage of PRBCs on final constitution of prime during and after CPB. We chose 14 days as the cut-off for fresh and stored PRBCs grouping as many previous studies have found a storage duration of more than 14 days to be hazardous [7,10,16].

Material and Methods

The study was approved by our institutional ethics committee and informed and written consent was obtained from the parents of all the patients. Data were collected prospectively in 198 consecutive newborns, infants and small children operated between January 2015 and December 2015 aged between 4 days to 8 years who underwent cardiac surgery using CPB and who required PRBCs transfusion to prime the CPB circuit. The median value of blood storage time was assessed, and patients were attributed to the newer blood group if they received PRBCs in priming that had been stored for $\leq$14 days while patients were attributed to the older blood group if they received PRBCs in priming stored for >14 days.

The primary endpoints of the study were to determine and compare the patients' morbidity and mortality based on the duration of storage of the PRBCs used in priming. For comparison, patients were divided into two groups, newer vs. older blood. The secondary endpoint was to examine the change in metabolic profile of patients during and after CPB based on duration of storage of PRBCs. Postoperative morbidities were determined as per predetermined criteria defined by international paediatric sepsis consensus conference definitions [17]. Morbidities recorded were sepsis, renal failure, hepatic failure, haematological failure, neurological failure and respiratory failure. Multi-organ failure (MOF) was defined as >1 organ failure. Mortality data was recorded for intraoperative death or death during postoperative period within hospital.

Surgical Technique

Anaesthesia was carried out according to our institutional practice. Induction of anaesthesia was achieved with intravenous midazolam, ketamine and opioid anaesthetic (fentanyl) and it was maintained with fentanyl and sevoflurane. Neuromuscular blockade was achieved with repeated dose of vecuronium. All patients were intubated and were mechanically ventilated. Standard monitoring was used, which included a radial or femoral artery catheter for systemic arterial blood pressure monitoring and intermittent blood sampling, a triple lumen right internal jugular or femoral central venous catheter for central venous pressure monitoring, and oesophageal and rectal temperature probes. Cardiac cannulation was performed after intravenous administration of 4 mg/kg of unfractionated heparin and after an activated clotting time of longer than 400 seconds was achieved. Intermittent heparin boluses were administered during CPB to maintain an activated clotting time in this range before and during CPB. Separate venous cannulation of the superior and inferior vena cava or single right atrial cannulation was performed as per the age of patient and surgeons' preference. The arterial cannula was placed into the ascending aorta. All surgeries were performed on mild, moderate or deep hypothermia depending upon the surgery. The CPB circuit included a hollow fibre oxygenator (Quadrox-1 Neonatal HMO, Maquet, Rastatt, Germany) with haemo filter (Hemoconcentrator, Spectra Medical Devices Life Sciences Ltd., Dublin, Ireland).

In all the patients, the CPB circuit was primed with Ringer's lactate solution. The volume of PRBCs added was titrated to reach a haematocrit of 30% once the patient was connected to the circuit and CPB was initiated. The volume of Ringer's lactate equal to PRBCs added to prime was removed from the circuit by ultrafiltration. The total priming volume varied between 300 mL and 800 mL. Therefore, the amount of RBCs used in the priming solution varied according to the patient's baseline haematocrit, weight, and the priming volume used. In all patients, less than a 200 mL of PRBCs was used in priming. Cardiopulmonary bypass flow was targeted at 100 ml/kg to 150 mL/kg and subsequently adjusted according to the patient's temperature.

Data Collection

Demographic data was collected for all the patients included in the study. The collected data include age (days), weight (kilograms), haemoglobin (g/dl), serum creatinine level (mg/dl), liver function test (serum bilirubin level (mg/dl), serum glutamate oxaloacetate transaminase (SGOT) (U/l), serum glutamate pyruvate transaminase (SGPT) (U/l), platelet count (cells/cc), total count (cells/cc). Intraoperatively, a record was made for type of operation, aortic cross clamp and CPB duration (minutes), priming volume (mL), lowest temperature (°C), and lowest haematocrit (%) reached while on CPB.

The duration of storage of PRBCs used in CPB priming was recorded for all the patients. Metabolic data was recorded from the arterial blood analysis. For arterial blood gas analysis, the first sample was drawn from the PRBCs for priming (T0). Then, the calculated amount of PRBCs to achieve the haematocrit of 30% on CPB was added to the priming solution, filtration of equal amount of priming solution was performed and the final priming solution was circulated with low flow of air at room temperature. A second sample was then taken from the CPB priming solution (T1). A third sample was drawn 20 minutes after initiation of CPB (T2). The last blood sample was drawn on arrival to the paediatric intensive care unit (PICU) after the conclusion of the operation (T3).

For metabolic profile, the data recorded were: arterial pH, sodium (mEq/l), potassium (mEq/l), calcium (mEq/l), bicarbonate (mEq/l), and glucose (mg/dl). Postoperatively, a record was made for duration of mechanical ventilation (hours), intensive care unit (ICU) stay (hours), and blood loss (ml). A record was made for postoperative renal, hepatic, pulmonary, neurologic complications, sepsis and mortality.

Statistics

The statistical analysis was performed using SPSS v20.0 (IBM Corp., Armonk, NY, USA). Continuous variables are presented as the mean (SD) and categorical variables as numbers and percentages. To compare the normally distributed data, Student's t test was used. To compare the non-normally distributed data, Mann-Whitney U test was used. Chi square test was used to compare the categorical variables. $p < 0.05$ was considered statistically significant. Covariates included in the multivariate models were body weight, age, aortic cross clamp time, and CPB time, as well as the transfused volume of PRBCs.

Results

Patients were divided into two groups based on the duration of storage of PRBCs used in prime: Newer blood group ($\leq$14 days storage time, n = 103); or Older blood group ($>$ 14 days of storage time, n = 95). Mean duration of storage of the PRBCs used for priming the CPB circuit and subsequent intraoperative transfusions was 8.4 $\pm$ 3.7 days in the newer PRBCs group while it was 21.9 $\pm$ 4.5 days in the older PRBCs group (range: 2 to 28 days). Figure 1 shows the different surgeries performed in both the groups. Table 1 shows the baseline characteristics, preoperative and postoperative haemato-chemical parameters and intraoperative CPB data for patients receiving newer or older blood. There was no statistically significant difference between the new

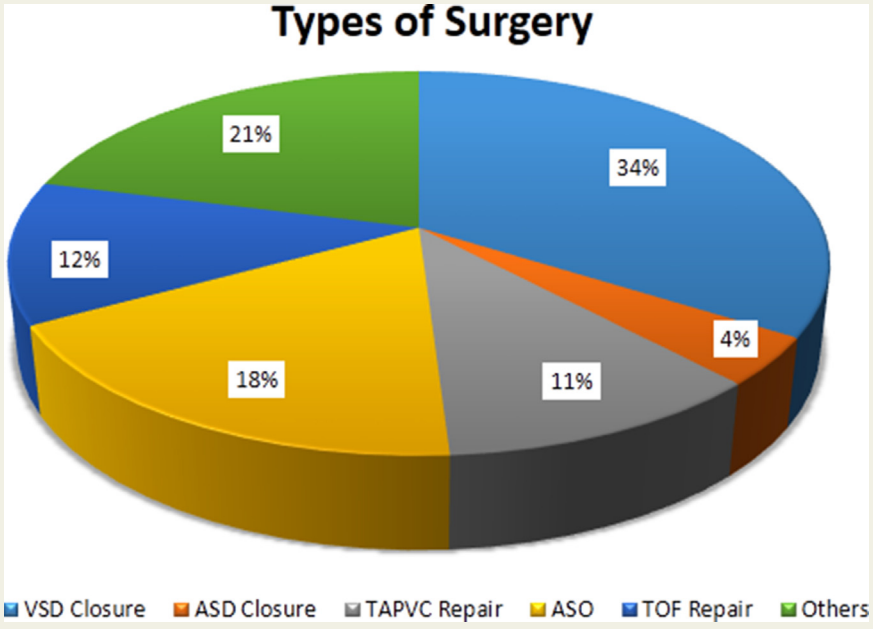

Figure 1 Distribution of different surgical procedures performed.
Abbreviations: ASD, atrial septal defect; VSD, ventricular septal defect; TAPVC, total anomalous pulmonary venous connection; ASO, arterial switch operation; TOF, tetralogy of Fallot.

Table 1 Demographic data, preoperative and postoperative parameters in both the groups.

	Newer PRBCs group (n = 103) Mean ± SD	Older PRBCs group (n = 95) Mean ± SD
Age (days)	437.2 ± 545.4	379.9 ± 471.3
Sex (male)	68	48
Weight (Kg)	6.12 ± 3.1	5.8 ± 3.2
Lowest haematocrit (%)	28.4 ± 3.1	29 ± 3.9
Aortic cross clamp (minutes)	64.5 ± 45.3	52.3 ± 39.3
CPB duration (minutes)	93.3 ± 55.2	82.6 ± 44.9
STAT Score	2 (1-4)	3 (1-5)
Lowest temperature (°C)	31.7 ± 3.4	31.5 ± 2.6
Duration of MVT (hours)	59.4 ± 76.2	80.2 ± 135.9
ICU Stay (days)	8.0 ± 5.8	9.6 ± 11.6
Hospital stay (days)	8.9 ± 6.0	11.1 ± 11.5
Preoperative parameters		
Haemoglobin (g/dl)	11.9 ± 1.5	12.5 ± 2.3
Platelet (numbers/cc)	398125 ± 140831	369895 ± 146217
Creatinine (mg/dl)	0.45 ± 0.22	0.46 ± 0.16
Bilirubin (mg/dl)	1.1 ± 1.8	1.5 ± 1.9
Total count (counts/cc)	13342 ± 4801	11726 ± 3483
SGPT (U/l)	36.8 ± 69	31.7 ± 44.4
SGOT (U/l)	45.6 ± 38.8	63.1 ± 82.0
Postoperative parameters		
Haemoglobin (g/dl)	13.4 ± 2.6	13.2 ± 2.6
Platelet (numbers/cc)	220732 ± 89715	195271 ± 119157
Creatinine (mg/dl)	0.50 ± 0.18	0.47 ± 0.14
Bilirubin (mg/dl)	1.4 ± 1.6	2.2 ± 1.6*
Total count (counts/cc)	15433 ± 5647	13511 ± 4985
SGPT (U/l)	24.5 ± 25.4	25.6 ± 14.1
SGOT (U/l)	125.8 ± 135.0	146.8 ± 83.2

Abbreviations: PRBCs, packed red blood cells; CPB, cardio pulmonary bypass; ICU, intensive care unit; SGOT, serum glutamate oxaloacetate transaminase; SGPT, serum glutamate pyruvate transaminase; STAT Score, The Society of Thoracic Surgeons–European Association for Cardio-Thoracic Surgery Congenital Heart Surgery Mortality Categories (STAT-Mortality Categories).

and old PRBCs groups in terms of age (437.2 ± 545.4 days (median 212 days) vs 379.9 ± 471.3 days (median 184 days, p = 0.58), weight (6.12 ± 3.1 kg vs 5.8 ± 3.247 kg, p = 0.67), STAT Score (The Society of Thoracic Surgeons − European Association for Cardio-Thoracic Surgery Congenital Heart Surgery Mortality Categories (STAT-Mortality Categories)) (median 2 in newer blood group vs 3 in older blood group (p = 0.42)), duration of aortic cross clamp (64.5 ± 45.3 mins vs 52.3 ± 39.3 mins, p = 0.61)), duration of CPB (92.5 ± 58.9 vs. 88.6 ± 45.7 mins, p = 0.71), lowest haematocrit (28.4 ± 3.1 vs. 29 ± 3.9%, p = 0.41), and lowest temperature (31.6 ± 3.4 vs. 31.4 ± 2.6, p = 0.74) on CPB. Similarly, there were no significant differences in the preoperative and postoperative haemato-chemical profile of the patients in two groups except for postoperative bilirubin and serum glutamate pyruvate transaminase (SGPT) which was significantly more in older blood group.

Table 2 shows the metabolic profile of the patients and stored PRBCs in both the groups and changes during and after CPB. Preoperative metabolic profile was comparable in both the groups. In the metabolic profile of the stored blood (T0), the pH of older PRBCs group was significantly lower than newer PRBCs group (6.71 ± 0.1 vs 6.9 ± 0.1 respectively, $p < 0.001$). Further, potassium concentration was significantly more while glucose concentration was significantly lower in older PRBCs group compared to newer PRBCs group (potassium concentration: 11.6 ± 3.7 mEq/l vs 17.8 ± 4.4 meq/l, $p < 0.001$ and glucose concentration: 392.7 ± 114.3 mg/dl vs. 274.9 ± 117.8 mg/dl, $p < 0.001$ respectively). Haematocrit, sodium, calcium levels were comparable in both the groups. Addition of PRBCs to the priming solution resulted in a significant decrease in the haematocrit, potassium, glucose levels in both groups ($p < 0.01$) while there was no significant change in sodium levels. Comparing between the groups, pH was significantly more while potassium was significantly lower in newer blood group. Glucose levels were comparable in both the groups. Twenty (20) minutes after initiation of CPB

Table 2 **Metabolic profile of the patients, stored PRBCs, during and after CPB.**

	Newer PRBCs group (n = 103)	Older PRBCs group (n = 95)	P value
Preoperative data (Mean ± SD)			
pH	7.46 ± 0.11	7.43 ± 0.09	0.11
HCT (%)	37.7 ± 4.3	39.375 ± 8.9	0.24
K^+ (meq/L)	3.36 ± 0.5	3.33 ± 0.6	0.76
Na^+ (meq/L)	140.8 ± 5.0	141.7 ± 6.2	0.43
Ca^+ (meq/L)	1.0 ± 0.3	1.1 ± 0.3	0.12
Glucose (mg/dl)	103.2 ± 47.1	99.1 ± 41.1	0.64
Packed red blood cell (T0) (Mean ± SD)			
pH	6.90 ± 0.1	6.71 ± 0.1	<0.001
HCT (%)	49.2 ± 5.6	51.4 ± 7.7	0.09
K^+ (meq/L)	11.6 ± 3.7	17.8 ± 4.4	<0.001
Na^+ (meq/L)	154.6 ± 12.8	149.3 ± 16.1	0.25
Ca^+ (meq/L)	0.23 ± 0.2	0.21 ± 0.1	0.65
Glucose (mg/dl)	392.7 ± 114.2	274.9 ± 117.8	<0.001
Prime (T1) (Mean ± SD)			
pH	7.1 ± 0.1	7.0 ± 0.2	<0.001
HCT (%)	27.5 ± 5.4	28.1 ± 5.2	0.09
K^+ (meq/L)	7.4 ± 1.7	10.9 ± 2.3	<0.001
Na^+ (meq/L)	154.9 ± 9.7	147.3 ± 6.7	<0.001
Ca^+ (meq/L)	0.8 ± 0.2	0.9 ± 0.2	0.10
Glucose (mg/dl)	90.6 ± 22.9	81.5 ± 27.5	0.07
On CPB (T2) (Mean ± SD)			
pH	7.46 ± 0.1	7.43 ± 0.1	0.14
HCT (%)	30.7 ± 3.6	31.2 ± 3.3	0.48
K^+ (meq/L)	4.1 ± 0.8	4.4 ± 1.0	0.16
Na^+ (meq/L)	143.1 ± 7.3	144.0 ± 5.6	0.46
Ca^+ (meq/L)	1.2 ± 0.3	1.2 ± 0.2	0.85
Glucose (mg/dl)	193.9 ± 67.4	199.6 ± 78.4	0.69
End Off CPB (T3) (Mean ± SD)			
pH	7.44 ± 0.1	7.43 ± 0.1	0.44
HCT (%)	36.7 ± 5.2	36.3 ± 5.0	0.66
K^+ (meq/L)	3.6 ± 0.8	3.7 ± 0.9	0.28
Na^+ (meq/L)	144.3 ± 3.8	144.7 ± 5.5	0.63
Ca^+ (meq/L)	1.2 ± 0.3	1.3 ± 0.3	0.39
Glucose (mg/dl)	213.7 ± 67.5	208.6 ± 55.21	0.68

Abbreviations: PRBCs, packed red blood cells; HCT, haematocrit; K^+, potassium, Na^+, sodium; Ca^+, calcium; CPB, cardiopulmonary bypass.

(T1), metabolic profile improved to normal physiological limits and remained normal after weaning off CPB (T2) except glucose levels. Glucose levels were significantly more than physiological limits in both the groups at both time points (T2 and T3). At both time points, metabolic profile was comparable in both the groups.

In the newer PRBCs group, mean amount of intraoperative PRBCs transfusion was 123 ± 11 ml while total amount of PRBCs transfusion was 192 ± 88 ml. Similarly, in the older PRBCs group, mean amount of intraoperative PRBCs transfusion was 128 ± 14 ml while total transfusion was 206 ± 94 ml. Therefore, mean amount of intraoperative PRBCs transfusion in newer PRBCs group was 26 ml/kg while total transfusion was 40 ml/kg. The same transfusion in old PRBCs group was 29 ml/kg and 45 ml/kg, respectively. There was no significant difference in intraoperative and postoperative transfusion in both the groups. A total of 26% patients in the newer PRBCs group and 44% of patients in the old PRBCs group developed at least one complication (Figure 2). The most common complication in the newer PRBCs group was pulmonary (9%) while in the old PRBCs group it was hepatic (18%). In the older PRBCs group, a total of 15% patients developed MOF compared to 8% in newer PRBCs group. Similarly, 13% of patients in the older PRBCs group required prolonged mechanical ventilation compared to 12% of patients in the newer PRBCs group. Incidence of all postoperative complications including MOF was more in the old PRBCs group. The only exception was neurological

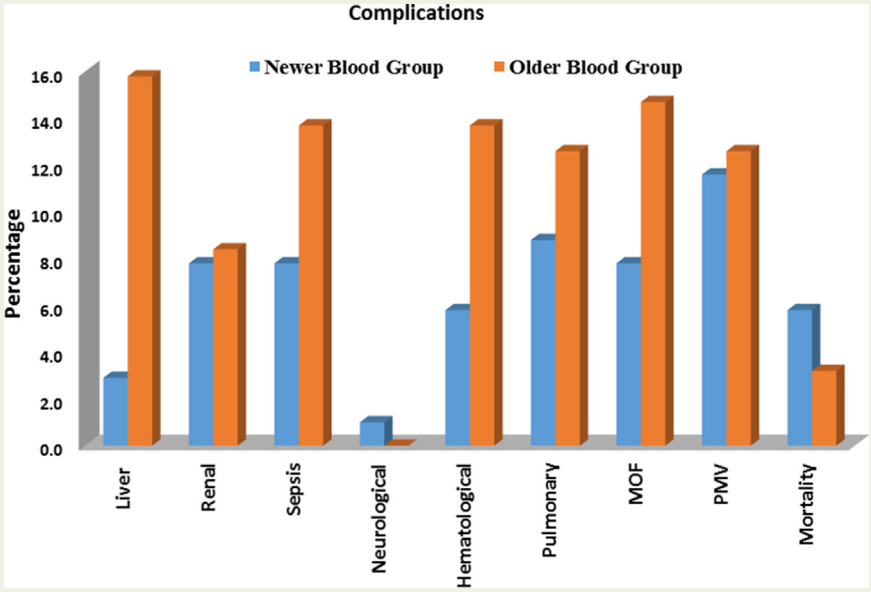

Figure 2 Postoperative complications and mortality in both the groups.
Abbreviations: MOF, multi organ failure; PMV, prolonged mechanical ventilation.

complication which was more in the newer PRBCs group. However, none of the complications reached the statistically significant level on univariate analysis except liver dysfunction. Liver dysfunction was significantly more common in the old PRBCs group. However, after correcting for other confounding factors like age, weight, aortic cross clamp time, CPB time, and volume of PRBCs transfused, none of the complications was found to be significantly associated with duration of storage.

As with postoperative complications, duration of mechanical ventilation, and duration of ICU and hospital stay were more in the old PRBCs group (Table 1). However, none of these parameters reached the statistically significant level. There were no intraoperative deaths. A total of six patients in the newer PRBCs group and three patients in the old PRBCs group died in the postoperative period (Figure 2). The difference was not statistically significant.

Discussion

Since the first report by Koch et al. [7] on the association between the transfusion of old stored PRBCs and poor outcome after coronary artery bypass grafting, many studies found similar associations in patients undergoing paediatric cardiac surgery. Studies have also reported that use of old stored PRBCs in the priming of the CPB circuit increases the risk of postoperative complications in paediatric patients. Ranucci et al. [1], in their retrospective review, found that the intraoperative transfusion of PRBCs that had been stored for >4 days was associated with a significantly increased risk of postoperative pulmonary complications in paediatric patients operated for cardiac surgery with blood prime of the CPB circuit. Similarly, Redlin et al. [4] in their retrospective study, found a significantly increased risk of postoperative blood transfusion, prolonged mechanical ventilation and increase in C reactive protein in patients receiving older PRBCs. Our results are inconsistent with these studies. In our study, we did not find any association between the duration of PRBCs storage and the risk of postoperative complications, prolonged mechanical ventilation or postoperative transfusion. Also, the amount of postoperative transfusion, duration of mechanical ventilation, ICU stay and hospital stay were comparable in both the groups. Our results are in agreement with recent randomised control trials. A randomised control trial by Steiner et al. [18] in patients undergoing complex cardiac surgery, by Fergusson et al. in very low birth weight infants [19], and by Lacroix et al. [20] in critically ill adults failed to show any morbidity or survival advantage with transfusion of fresh PRBCs compared to old stored PRBCs. In our study, we also did not find any morbidity or survival advantage with transfusion of newer blood.

The deleterious effects of stored blood are presumed to be due to its metabolic and biochemical changes, depletion of 2,3-diphosphoglycerate, a greater built-up of inflammatory mediators in the supernatant volume and immunomodulatory effect of transfused blood [21,22]. Metabolic changes such as hyperkalaemia, citrate toxicity, lactic acidosis and hypothermia may lead to depression of left ventricular function, while haemolysis with the generation of free haemoglobin interacts with nitric oxide (NO) that leads to endothelial dysfunction ultimately contributing to intravascular thrombosis and vasoconstriction. Free iron may increase the risk of infections [23]. However, apart from the duration of storage of PRBCs and the preexisting condition of the recipient i.e. trauma, cardiac or ICU patients, the deleterious effects of the transfused PRBCs predominantly

depends upon the volume of PRBCs transfused. A study by Weinberg et al. [10] in 1,647 trauma patients, found that, in patients who received one or two units of PRBCs, crude in-hospital mortality was similar between the patients transfused with <14 days or >14 days stored blood (mortality 14.0% vs. 13.5% respectively, $p = 0.80$). Similarly, a recent retrospective review by Manlhiot et al. [24] in 1,225 paediatric patients operated for cardiac surgery on CPB found that PRBCs stored for >14 days was a not a significant risk factor for postoperative bleeding, renal insufficiency, duration of hospital stay and mortality only if the amount of postoperative transfusion was <150 ml/kg.

Both these studies may explain the reason for the variable associations reported by several retrospective and prospective studies between duration of storage of PRBCs and postoperative outcome. Most of these studies have not compared the amount of PRBCs transfusion and postoperative complications [5–14]. The probable reason for the absence of association between the postoperative complications and duration of storage of PRBCs in our study was the small amount of PRBCs transfusion. In our study, the mean amount of transfusion in new PRBCs group and old PRBCs group was 40 ml/kg and 45 ml/kg, respectively.

Apart from the effect on postoperative outcome, another major concern with the use of old stored PRBCs in the prime is massive and rapid transfusion of substantial metabolic load including potassium that may result in haemodynamic instability [25,26]. Studies have recommended washing the PRBCs in a cell saver before addition to the prime [27] or ultrafiltration of priming fluid before initiation of CPB to reduce the adverse effects of stored PRBCs [28]. In our study, we used ultrafiltration of PRBCs prior to initiation of CPB to decrease the metabolic load of the stored PRBCs. We found that ultrafiltration of the prime, reduced the overall metabolic load of PRBCs; still the final prime in old PRBCs group had a significantly low pH and high potassium compared to new PRBCs group. However, this metabolic load did not have any harmful effect as shown by comparable duration of mechanical ventilation ($p = 0.8$) and ICU stay ($p = 0.82$) between the two groups. Our results also showed that storage duration of PRBCs used for priming had a minimal effect, if any, on metabolic changes immediately after the onset of CPB, during the entire course of CPB and early after weaning regardless of the volume of priming solutions used.

As expected, we found a significant increase in postoperative bilirubin and SGPT in the old PRBCs group due to more haemolysis of the old stored PRBCs. However, both these did not have any significant impact on postoperative outcome.

Limitations

There are three limitations of our study. First, we have used blood stored up to 28 days. So we cannot predict the outcome with use of PRBCs stored for 29 to 42 days duration. Second, although not statistically significant, most of postoperative complications were frequent in the old PRBCs group. As the amount of PRBC transfused in our series was only 40 ml/kg, we cannot generalise the outcome to patient requiring >150 ml/kg PRBCs transfusion. Third, the total number of patients included in our series was small and without associated significant co-morbidities. The significance of our results may change with an increase in the number of patients and in high risk patients. Therefore, we recommend randomised controlled trials including a larger number of patients, patients with associated preoperative co-morbidities and patients requiring a larger volume of PRBCs transfusion.

Conclusion

Metabolic parameters of the stored PRBCs become normal after initiation of CPB irrespective of duration of storage of PRBCs. Transfusion of PRBCs stored for >14 days in CPB priming during paediatric cardiac surgery does not lead to adverse outcomes. Based on our findings, we conclude that blood stored up to 28 days can be safely used in CPB prime in paediatric patients where a lesser amount of total transfusion is expected.

References

[1] Ranucci M, Carlucci C, Isgrò G, Boncilli A, De Benedetti D, Torre TDL, et al. Duration of red blood cell storage and outcomes in pediatric cardiac surgery: an association found for pump prime blood. Crit Care 2009;13:1–12.
[2] Leal-Noval SR, Rincón-Ferrari MD, García-Curiel A, Herruzo-Avilés A, Camacho-Laraña P, Garnacho-Montero J, et al. Transfusion of blood components and postoperative infection in patients undergoing cardiac surgery. Chest 2001;119:1461–8.
[3] Van de Watering L. Red cell storage and prognosis. Vox Sang 2011;100:36–45.
[4] Redlin M, Habazettl H, Schoenfeld H, Kukucka M, Boettcher W, Kuppe H, et al. Red Blood cell storage duration is associated with various clinical outcomes in pediatric cardiac surgery. Transfus Med Hemother 2014;41:146–51.
[5] Zallen G, Offner PJ, Moore EE, Blackwell J, Ciesla DJ, Gabriel J, et al. Age of transfused blood is an independent risk factor for post-injury multiple organ failure. Am J Surg 1999;178:570–2.
[6] Offner PJ, Moore EE, Biffl WL, Johnson JL, Silliman CC. Increased rate of infection associated with transfusion of old blood after severe injury. Arch Surg 2002;137:711–6.
[7] Koch CG, Li L, Sessler DI, Figueroa P, Hoeltge GA, Mihaljevic T, et al. Duration of red-cell storage and complications after cardiac surgery. N Engl J Med 2008;358:1229–39.
[8] Leal-Noval SR, Munoz-Gomez M, Arellano-Orden V, Marin-Caballos A, Amaya-Villar R, Marin A, et al. Impact of age of transfused blood on cerebral oxygenation in male patients with severe traumatic brain injury. Crit Care Med 2008;36:1290–6.
[9] Spinella PC, Carroll CL, Staff I, Gross R, Mc Quay J, Keibel L, et al. Duration of red blood cell storage is associated with increased incidence of deep vein thrombosis and in hospital mortality in patients with traumatic injuries. Crit Care 2009;13:R151.
[10] Weinberg JA, McGwin Jr G, Vandromme MJ, Marques MB, Melton SM, Reiff DA, et al. Duration of red cell storage influences mortality after trauma. J Trauma 2010;69:1427–31.
[11] Leal-Noval SR, Jara-Lopez I, Garcia-Garmendia JL, Marin-Niebla A, Herruzo-Aviles A, Camacho-Larana P, et al. Influence of erythrocyte concentrate storage time on postsurgical morbidity in cardiac surgery patients. Anesthesiology 2003;98:815–22.
[12] Van-de-Watering L, Lorinser J, Versteegh M, Westendord R, Brand A. Effects of storage time of red blood cell transfusions on the prognosis of coronary artery bypass graft patients. Transfusion 2006;46:1712–8.

[13] Kneyber MC, Gazendam RP, Markhorst DG, Plotz FB. Length of storage of red blood cells does not affect outcome in critically ill children. Intensive Care Med 2009;35:179–80.
[14] Yap CH, Lau L, Krishnaswamy M, Gaskell M, Yii M. Age of transfused red cells and early outcomes after cardiac surgery. Ann Thorac Surg 2008;86:554–9.
[15] Keidan I, Amir G, Mandel M, Mishali D. The metabolic effects of fresh versus old stored blood in the priming of cardiopulmonary bypass solution for pediatric patients. J Thorac Cardiovasc Surg 2004;127:949–52.
[16] Jin Min J, Bae JY, Kim TK, Hong DM, Hwang HY, Kim KB, et al. Association between red blood cell storage duration and clinical outcome in patients undergoing off-pump coronary artery bypass surgery: a retrospective study. BMC Anesthesiology 2014;14:95.
[17] Wheeler DS, Jeffries HE, Zimmerman JJ, Wong HR, Carcillo JA. Sepsis in the pediatric cardiac intensive care unit. World J Pediatr Congenit Heart Surg 2016;201(2):393–9.
[18] Steiner ME, Ness PM, Triulzi DJ, Sloan SR, Delaney M, Granger S, et al. Effects of red-cell storage duration on patients undergoing cardiac surgery. N Engl J Med 2015;372:1419–29.
[19] Fergusson DA, Hébert P, Hogan DL, LeBel L, Rouvinez-Bouali N, Smyth JA, et al. Effect of fresh red blood cell transfusions on clinical outcomes in premature, very low-birth-weight infants: the ARIPI randomized trial. JAMA 2012;308:1443–51.
[20] Lacroix J, Hébert PC, Fergusson DA, Tinmouth A, Cook DJ, Marshall JC, et al. Age of transfused blood in critically ill adults. N Engl J Med 2015;372:1410–8.
[21] Tinmouth A, Fergusson D, Yee IC, Hebert PC. Clinical consequences of red cell storage in the critically ill. Transfusion 2006;46:2014–27.
[22] D'Alessandro A, Liumbruno G, Grazzini G, Lolla Z. Red blood cell storage: the story so far. Blood Transfus 2010;8:82–8.
[23] Zimring JC. Fresh versus old blood: are there differences and do they matter ASH Education Book, 1. 2013;p. 651–5.
[24] Manlhiot C, McCrindle BW, Menjak IB, Yoon H, Holtby HM, Brandão LR, et al. Longer blood storage is associated with suboptimal outcomes in high-risk pediatric cardiac surgery. Ann Thorac Surg 2012;93:1563–70.
[25] Brown KA, Bissonnette B, McIntyre B. Hyperkalaemia during rapid blood transfusion and hypovolaemic cardiac arrest in children. Can J Anaesth 1990;37:747–54.
[26] Hall TL, Barnes A, Miller JR, Bethencourt DM, Nestor L. Neonatal mortality following transfusion of red cells with high plasma potassium levels. Transfusion 1993;33:606–9.
[27] Swindell CG, Barker TA, McGuirk SP, Jones TJ, Barron DJ, Brawn WJ, et al. washing of irradiated red blood cells prevents hyperkalaemia during cardiopulmonary bypass in neonates and infants undergoing surgery for complex congenital heart disease. Eur J Cardiothorac Surg 2007;31:659–64.
[28] Shimpo H, Shimamoto A, Sawamura Y, Fujinaga K, Kanemitsu S, Onoda K, et al. Ultrafiltration of the priming blood before cardiopulmonary bypass attenuates inflammatory response and improves postoperative clinical course in pediatric patients. Shock 2001;16(Suppl 1):51–4.