The metabolic effects of fresh versus old stored blood in the priming of cardiopulmonary bypass solution for pediatric patients

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Objectives: Pediatric cardiopulmonary bypass involves the creation of a large obligatory priming reservoir. Packed red blood cells are an essential part of the cardiopulmonary bypass priming solution in children. The storage media in packed red blood cells might cause significant acid-base, glucose, and electrolyte imbalances, which have been associated with severe complications. The purpose of the present study was to evaluate the metabolic effects of fresh (≤ 5 days) versus old (> 5 days) stored packed red blood cells added to the priming solutions of pediatric patients undergoing cardiac surgery.

Methods: Blood samples were drawn from cardiopulmonary bypass priming of 30 consecutive pediatric patients undergoing cardiac surgery. Patients were divided into 2 groups. Fresh (≤ 5 days old) stored packed red blood cells were added to the priming solution in group 1, and old (> 5 days old) stored packed red blood cells were added to the priming solution in group 2. In each group blood samples were drawn from the packed red blood cells on arrival to the operating room and from the priming solution immediately after packed red blood cells were added and after 20 minutes of prime circulation. Samples were also collected at the beginning of cardiopulmonary bypass and after 30 minutes. The last sample was collected on arrival to the pediatric intensive care unit. The levels of potassium, glucose, and lactate and the acid-base balance were analyzed in each sample.

Results: There was a linear increase in potassium levels in packed red blood cell samples with increasing packed red blood cell age, ranging from 5.4 to 18.4 mEq/L. Significant differences in the concentrations of potassium, glucose, and lactate and the acid-base balance were found when comparing old and fresh packed red blood cells in samples taken during the packed red blood cell and early prime time. Those differences resolved after 20 minutes of reconstitution of the priming solution. The age of the packed red blood cells had no effect on the samples taken during bypass and those taken in the pediatric intensive care unit.

Conclusion: The significantly higher concentration of potassium and lactate and lower pH in old stored packed red blood cells has a minimal effect on the final constitution of priming solution before and during cardiopulmonary bypass in children undergoing corrective cardiac surgery.

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Current cardiopulmonary bypass (CPB) and extracorporeal membrane oxygenation (ECMO) circuit design requires a large priming volume compared with the blood volume of neonates and infants. The main constituents of priming solutions used are crystalloids, colloids, and banked blood. The proportions of each depend on the size of the patient and institutional practice. Packed red blood cells (PRBCs) preserved in extended-storage media are the standard product dispensed by most blood banks for priming the pediatric CPB (PCPB) or ECMO reservoir in infants and children. Although PRBCs are essential in maintaining temperature-appropriate hematocrit levels and adequate oxygen delivery in small children, they are associated with significant metabolic imbalances, which have been associated with severe complications.¹⁻⁴ When blood is stored, many alterations occur in its constituents, in particular an increase in potassium levels. Cases of mortality during rapid transfusion of stored PRBCs in neonates^{1,3} or immediately after institution of ECMO in a neonate⁵ have been reported.

Many institutional protocols advocate limiting the use of PRBCs in priming solution for the CPB or ECMO circuit to relatively fresh stored PRBCs to avoid such complications. The supply of fresh PRBCs is limited and might create delays. We prospectively evaluated the effect of length of storage of PRBCs on the final constitution of the priming solution before and after CPB in children undergoing corrective cardiac surgery. Specific attention was given to potassium, lactate, and glucose levels and the acid-base balance.

Materials and Methods

Blood samples were drawn from CPB priming solutions of 30 consecutive pediatric patients undergoing cardiac surgery. Fresh PRBCs were preferred, and patients would only receive old PRBCs if no fresh blood was available. Priming solution consisted of Plasmalyte, albumin, and fresh (≤ 5 days) stored PRBCs in 18 patients and Plasmalyte, albumin, and old (> 5 days old) stored PRBCs in 12 patients. Blood samples were first drawn from PRBCs (stored at 4°C in citrate-phosphate-dextrose-adenine 1 [CPDA-1] preservative solution) immediately after irradiation with 2500 rad and transportation into the pediatric cardiac operating room. This unit of PRBCs was then added to the CPB priming solution. In all patients, we used the VPCML plus oxygenator and tubing (Cobe Cardiovascular) fitted for patient weights of 4 to 30 kg. The CPB priming solution was created according to our institutional protocol, which includes adding 1 unit of PRBCs (280 ± 50 mL) to 450 mL of Plasmalyte, 20 mL of albumin 25%, and medications (methylprednisolone, mannitol, cefazolin, heparin, and bicarbonate). Once the unit of PRBCs was added to the priming solution, a second sample was taken from the CPB priming solution. Circulation of the priming solution with low flow of air at room temperature was started, and a third sample was taken after 20 minutes. Another set of blood samples was drawn when

the patients were first connected to the CPB pump and after 30 minutes. The last blood sample was drawn on arrival to the pediatric intensive care unit (PICU) after the conclusion of the operation. Comparisons between corresponding variables at different times in each group were carried out by using the Student *t* test. Correlation between potassium levels and age of the PRBCs was determined by using the Pearson correlation test for parametric variables.

Results

Thirty infants and children undergoing corrective cardiac surgery were included in the study. In 18 patients the PCPB circuit was primed with fresh stored CPDA-1 PRBCs and in 12 patients with old stored CPDA-1 PRBCs. No statistical difference between the groups was detected in terms of age (1.2 ± 1.8 vs 0.9 ± 2 years, $P = .23$; age range, 3 days-5 years), weight (10.5 ± 5.8 vs 8.5 ± 6.5 kg, $P = .2$; weight range, 4-20 kg), and duration of CPB (102 ± 58 vs 115 ± 75 minutes, $P = .47$). The mean storage time in the fresh stored PRBC group was 2.7 ± 1 days (median, 3 days) and was significantly shorter compared with the storage time of the old stored PRBC group (11 ± 7.2 days; median, 8 days; $P = .005$). There was a significantly lower concentration of potassium in fresh PRBCs compared with that seen in PRBCs stored for 5 days or more (9.2 ± 2 vs 15 ± 6.8 mEq/L, $P < .02$). A positive correlation was found between the age of the PRBCs and their potassium concentrations ($r = 0.4$, $P = .035$, Figure 1). Adding those PRBCs to the priming solution caused a significant increase in the potassium level at priming time 0 (4.9 ± 0.7 vs 5.9 ± 0.6 mEq/L, $P = .003$) but diminished at priming time 20 (4.5 ± 0.7 vs 4.8 ± 0.8 mEq/L, $P = .15$), once CPB had begun (3.39 ± 0.45 vs 3.69 ± 0.38 mEq/L, $P = .06$), and on arrival to the PICU (3.4 ± 0.84 vs 3.8 ± 0.36 mEq/L, $P = .17$). Glucose levels were significantly lower in old PRBCs (153 ± 133 vs 300 ± 75 mg/dL, $P = .01$); the trend continued during early priming (28 ± 14 vs 77 ± 19 mg/dL, $P < .01$) but resolved after 20 minutes of priming (65 ± 30 vs 82 ± 16 mg/dL, $P = .2$). No difference in blood glucose levels was detected in samples taken at the beginning of CPB and on arrival to the PICU. A similar improvement in acid-base balance was noted once priming solution circulation continued for 20 minutes (Table 1).

Discussion

The effect of priming CPB circuits with either fresh or old stored PRBCs has not been previously studied. Fresh PRBCs are presumably more balanced metabolically than stored PRBCs, they contain less potassium, and they have higher concentrations of glucose, lower concentrations of lactate, and higher pH.⁶

Our results clearly demonstrate that although fresh PRBCs are more metabolically balanced than stored

Figure 1. Correlation between days of PRBC storage and potassium levels.

TABLE 1. Potassium, lactate, glucose, and acid-base balance during the various stages (all values presented as mean ± SD)

	PRBC <5 d old					PRBC ≥5 d old				
	PRBC	Prime 0	Prime 20	CPB	PICU	PRBC	Prime 0	Prime 20	CPB	PICU
Potassium (mEq/L)	9.2 ± 2	4.9 ± 0.7	4.5 ± 0.7	3.39 ± 0.45	3.4 ± 0.84	15 ± 6.8†	5.9 ± 0.6*	4.8 ± 0.8	3.69 ± 0.38	3.8 ± 0.36
Lactate (mg/dL)	100.8 ± 26	29 ± 12	31 ± 10	31 ± 17	43 ± 50	88 ± 32	65 ± 7*	33 ± 21	33 ± 18	48 ± 28
Glucose (mg/dL)	300 ± 75	77 ± 19	82 ± 16	124 ± 25	132 ± 13	153 ± 133†	28 ± 14*	65 ± 30	120 ± 20	162 ± 45
pH	7.1 ± 0.2	7.45 ± 0.18	7.45 ± 0.1	7.44 ± 0.15	7.36 ± 0.1	6.75 ± 0.2*	7.29 ± 0.12*	7.42 ± 0.2	7.42 ± 0.1	7.38 ± 0.1
Bicarbonate (mEq/L)	22 ± 4	23.9 ± 7	24 ± 5	24 ± 6	22 ± 8	18 ± 5†	17.5 ± 2*	23 ± 2	25 ± 3	21 ± 5
CO ₂ (mm Hg)	113 ± 30	37 ± 20	35 ± 8	32 ± 4	37 ± 4	155 ± 40†	44 ± 16	37 ± 16	35 ± 8	34 ± 4

Comparisons between corresponding values at different times in each group were carried out with the Student *t* test.

**P* ≤ .01.

†*P* < .05.

PRBCs, there is no significant difference in the composition of the solution after 20 minutes of prime circulation. Furthermore, we found no statistical difference in the analysis of blood samples during CPB and in the PICU after the operation, regardless of the different priming solutions used. One of the major concerns with prolonged storage is excess potassium in the red cell supernatant, which could cause cardiac problems. The problem of posttransfusion induction of clinically significant hyperkalemia might be exacerbated by irradiation of PRBC concentrate to prevent graft-versus-host disease,⁷ but this effect seems to be minimized once the PRBCs are irradiated after storage, as in our study. At a

storage temperature of 4°C, the red cell sodium-potassium pump is essentially nonfunctional, and intracellular and extracellular levels gradually equilibrate. In addition, the hemolysis that occurs during the storage period results in increased potassium levels in the supernatant. However, because the total volume of plasma in red cell concentrates is low (70 mL), the total potassium burden is small.⁸ The addition of PRBCs to a relatively large balanced solution decreases significantly the potential adverse effects associated with the relatively larger load of potassium and lactate. The pH of CPDA-1 is acidotic (5.5). When this solution is added to a unit of freshly drawn blood, the pH of the blood

immediately decreases to approximately 7.0 to 7.1.⁹ As a result of accumulation of lactic and pyruvic acids by metabolism and glycolysis, the pH of PRBCs continues to decrease. A large portion of the acidosis can be accounted for by the high partial pressure of carbon dioxide. However, once priming solution circulates with adequate ventilation, acid-base imbalance caused by the increase in the levels of carbon dioxide resolves within minutes of the circulation. In this study we did not investigate the effects of old stored blood on oxygen affinity and delivery, the rate of hemolysis, or the level of cytokines and vasoactive mediators because these determinations were beyond the scope of the study.

In conclusion, our findings show that as far as potassium levels and acid-base balance are concerned, PCPB priming can be safely performed with stored PRBCs if the priming solution is circulated for 20 minutes before the initiation of CPB.

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