Washing of irradiated red blood cells in paediatric cardiopulmonary bypass: is it clinically useful? A retrospective audit


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Abstract

OBJECTIVE: Despite the introduction of smaller cardiopulmonary bypass (CPB) circuits for paediatrics, it is frequently necessary to add irradiated red blood cell concentrate (IRBC) to maintain adequate haemoglobin levels and the oxygen carrying capacity. Irradiation of blood weakens the cell membranes and results in an increase of lactate and potassium concentration. In addition, prolonged shelf time of IRBC may enhance its lactate level. To avoid the adverse effects of increased lactate and potassium concentration during paediatric bypass, prewashing of homologous blood in a cell-saving device was implemented at our institution. A retrospective audit of clinical data was performed to assess the relevance of this method.

METHODS: Preceding the introduction of the blood pre-washing, we investigated 14 units of IRBC for lactate, potassium levels and shelf time. Afterwards, we evaluated the CPB and laboratory data from 69 patients with body weight <10 kg and the lactate levels in the priming of the bypass circuit.

RESULTS: The shelf time of blood units was 7.6 ± 2.7 days (minimum 5, maximum 14 days) with lactate concentration of 12.6 ± 2 mmol/l and potassium concentration of 16.2 ± 4.7 mmol/l. In the priming after pre-washing, the lactate concentration was significantly lower than the standard priming (2.5 ± 0.9 vs 4.5 ± 20 mmol/l, p = 0.002). At the start of bypass, the lactate concentration after pre-washing was still lower (1.5 ± 0.4 vs 1.9 ± 0.9 mmol/l; p = 0.04), but at the end of bypass we detected a significant increase of lactate in the pre-washed group (1.5 ± 0.4 vs 2.2 ± 1.1 mmol/l, p = 0.01). There was no significant difference between the groups at the end of bypass (1.8 ± 0.9 vs 2.2 ± 1.1 mmol/l, p = 0.17). Other clinical and patient data were not significantly different.

CONCLUSIONS: Our retrospective audit shows that pre-washing of IRBCs is not associated with decreased lactate levels at the end of CPB compared with standard use of IRBCs, suggesting that the added value of pre-washing of IRBCs on minimisation of lactate levels during CPB remains doubtful.

Keywords: Paediatric cardiopulmonary bypass • Blood transfusion • Lactate • Patient safety

INTRODUCTION

Despite the recent minimisation of cardiopulmonary bypass (CPB) circuit for neonatal and infant patients, the addition of homologous blood into the priming is required to maintain adequate haemodilution during CPB [1, 2]. The quality of homologous blood strongly depends on preparation and preservation methods as well as on shelf time [3, 4]. To avoid the potential risk of transfusion-related graft versus host diseases in paediatric patients undergoing open-heart surgery, the red blood cells are irradiated (IRBC) [3]. However, the irradiation process weakens the cell membrane of red blood cells and can result in an enhanced concentration of potassium ions (K+) in IRBC units [3]. In addition, RBCs may be stored for up to 14 days before irradiation. A longer shelf time is associated with increased lactate levels in IRBC. Increased concentrations of serum lactate (>4 mmol/l) during CPB are associated with postoperative morbidity and mortality in paediatric patients undergoing complex open-heart surgery [5–7]. Increased K+ concentrations (>5 mmol/l) can cause arrhythmias and cardiac arrest [8]. To prevent high concentration of lactate, potassium and other products of cell degeneration, prewashing of IRBCs in the cell-saving device is advocated [9–11]. In our institution, the priming volume of the CPB circuit for patients with body weight up to 10 kg is approximately 250 ml. Nevertheless, it is necessary to add IRBCs into the priming as well as during CPB to maintain target haematocrit of 0.28 l/l. Although we only sporadically measured increased concentrations of lactate and K+ at the start of CPB, to eliminate any potential risk of the elevated concentrations during CPB we decided, from February 2010, to change our protocol and pre-wash the IRBCs with the cell-saving device that we routinely use in a paediatric cardiac surgery. To assess the relevance of pre-washing of IRBCs concerning lactate levels, we performed a retrospective audit of the collected laboratory data (February 2010–June 2010) and compared these with the laboratory results from the period before the introduction of the pre-washing of...
IRBCs (January 2009-January 2010) into the paediatric cardiac surgery.

MATERIAL AND METHODS

Population

This study is a retrospective audit of CPB and laboratory data collected in 69 consecutive patients with body weight <10 kg, who underwent a cardiac operation in the Erasmus MC, University Hospital of Rotterdam. In 34 patients (group A) operated on from February 2010 to June 2010, the pre-washing of IRBCs was applied in the priming and during CPB. Another cohort of 35 patients (group B) was operated on from January 2009 to January 2010 and received the unwashed IRBCs during the operation. The same surgical, anaesthesia and perfusion team performed all the operations. Collection and audit of the data were performed in compliance with the Hospital Data Protection Policy.

Perfusion technique

The CPB circuit consisted of a Capiox Baby RX-05® oxygenator with hard-shell reservoir, X-coated (Terumo corporation, Tokyo, Japan), a roller pump (Model 55, Stöckert Instrumente, Munich, Germany) and arterial filter (Dideco, Sorin Group, Mirandola, Italy). The tubing internal diameter was in. All tubing was coated with phosphorylcholine (Physio®, Sorin Group, Mirandola, Italy). The tubing internal diameter was in. All tubing was coated with phosphorylcholine (Physio®, Sorin Group, Mirandola, Italy). Priming volume was approximately 250 ml and contained IRBC, fresh-frozen plasma (FFP) and Gelofusine® (B. Braun, Melsungen, Germany). The amount of IRBC in the priming was calculated to achieve a haematocrit of 0.28 l/l during CPB. The prime was always completed with 0.5 g/kg body weight mannitol 200 g/l (Baxter Healthcare, Utrecht, the Netherlands) and 0.5 g/kg body weight human albumin 200 g/l (Sanquin, Amsterdam, the Netherlands). In addition, 4.2 IU heparin/ml priming volume and 2–5 ml NaHCO3 8.4% were given. Non-pulsatile CPB, with mild hypothermia of 28–32 °C, was performed with blood flow rates between 1.8 and 3.2 l/min/m to maintain venous oxygen saturation above 70% and mean arterial pressure between 40 and 60 mmHg. During CPB, α-stat regulation was used. Myocardial protection was achieved with crystalloid cardioplegia. The cardioplegic solution was preferably aspirated into the cell-saving device (Dideco Electa® 55 ml bowl, Mirandola, Italy). Perioperative blood loss was collected and processed by the cell-saving device, together with residual volume of the CPB circuit. In group A, the cell-saving device was used to pre-wash 1 unit of IRBC (275 ml). The parameters used for the washing program were: fill speed and washing speed of 100 ml/min achieved by a centrifugal speed of 5600 rpm. Administration of pre-washed IRBCs, FFP or other fluids during CPB were based upon the system working volumes and the laboratory target values. In accordance with our institutional protocol, no modified ultrafiltration and no antifibrinolytic medication were used. Anticoagulation was monitored through clotting time (activated clotting time, ACT), measured by Hemochron® Jr. (J.T.C Europe, Rodano, Italy). Values of ACT > 440 s were considered adequate for anticoagulation during CPB.

Anaesthesia

Anaesthesia was intravenously (IV) induced with sufentanil 1–2 µg/kg (Janssen-Cilag, Tilburg, the Netherlands), midazolam 0.1–0.2 mg/kg (Roche Consumer Health, Eindhoven, the Netherlands) and pancuronium 0.1–0.15 mg/kg (Organon Technica, Oss, the Netherlands) or propofol 1–2 mg/kg (Zeneca Farma, Riddervodkær, the Netherlands). Maintenance was with IV sufentanil 1 µg/kg/h, IV midazolam 0.1 mg/kg/h or IV propofol 2–6 mg/kg/h titrated to a BIST™ level between 30 and 50 with a BIST™ monitor model A-2000 (Aspect Medical Systems, Natick, MA, USA). Nitrates and inotropes were titrated intravenously for control of systemic and pulmonary arterial blood pressure at the discretion of the attending anaesthetist.

Sample protocol

Blood samples were taken during the operation procedure to measure lactate, potassium, haemoglobin and haematocrit according to our standard protocol: after the induction of anaesthesia before CPB, 5 min after the start of CPB and at the end of CPB; additionally, the CPB priming was sampled. The amount of IRBC in the priming of the CPB circuit and during CPB procedure was noted. Demographic and CPB data: patient's age, weight, height, CPB duration, aorta occlusion duration, lowest CPB temperature and type of cardiac correction, were registered.

Statistical analysis

All continuous data are expressed as a mean ± the standard deviation. The independent sample t-test was used to compare the two groups, and the paired t-test was used to compare results within the groups. A p value ≤ 0.05 was considered statistically significant. A total sample size of 35 patients was capable of detecting a difference of >1 mmol/l in lactate with 74.4% power. The statistical package Statistical Package for Social Sciences (SPSS) 17 for Windows or SPSS 18 for OS-X (SPSS, Chicago, IL, USA) was used for analyses of data.

RESULTS

Retrospective audit

Data from 69 paediatric patients were evaluated in this audit. Patient characteristics and cardiac surgery type are presented in Table 1. Table 2 shows the CPB data and the IRBC transfusion data, together with haematology laboratory results. There were no significant differences between the groups for the total priming volume, concentration of haemoglobin and haematocrit, CPB time and aorta cross-clamp time and lowest temperature. Although the total amount of IRBC was higher for the washed IRBC group, the difference was not significant. Changes of lactate concentration are presented in Table 3. The lactate concentration in the priming of the CPB circuit with unwashed IRBC was significantly lower at 4.5 ± 2mmol/l compared with the lactate concentration in the priming with washed IRBC at 2.5 ± 0.9 mmol/l; p = 0.002. At start of CPB, lactate concentration in the washed IRBC group was 1.5 ± 0.4 mmol/l and in the
within the groups; the result for the washed IRBC group shows a significant increase of lactate concentration; \( p = 0.001 \).

### Quality of IRBC

To assess the quality of the IRBC available in our institution for paediatric patients undergoing cardiac surgery with CPB, 14 consecutive units (275 ml per unit) were evaluated. Each unit contains 90–100 ml saline adenine glucose mannitol (SAGM) solution that results in a product with a haematocrit between 55% and 65%. The units are irradiated with 25 Gy 24 h before use. The mean age of the IRBC units was 7.6 ± 2.7 days, with a minimum of 5 days and a maximum of 14 days. The lactate concentration in the unwashed IRBC units was 12.6 ± 2 mmol/l and the concentration of K+ was 16.2 ± 4.7 mmol/l. The finally concentration in the priming for K+ was 3.6 ± 1.1 mmol/l.

### DISCUSSION

Our retrospective audit shows that pre-washing of IRBC before use in paediatric CPB for patients with body weight <10 kg did not significantly reduce plasma lactate and K+ concentration during CPB. The quality assessment of IRBC used routinely in our institution confirmed the results of the study by Swindell et al. [9] concerning increased concentration of lactate and K+ in the stored allogeneic blood that was irradiated. We measured in our unwashed IRBC a lactate concentration of 12.6 ± 2 mmol/l that is comparable to the results of Swindell et al. [9]: 13.7 ± 1.7 mmol/l. Conversely, our results with regard to K+ concentration were different. We found a mean K+ concentration of 16.2 ± 4.7 mmol/l in unwashed IRBC, whereas Swindell et al. [9] showed concentrations of K+ at 20 mmol/l (above the upper limit of the analyser used in their study). The possible reason we measured a lower K+ concentration was the relatively short shelf time of the IRBC (7.6 ± 2.7 days). In addition, the K+ concentration found in the CPB prime with unwashed IRBC in our study was 3.6 ± 1.1 mmol/l. Our low K+ concentration in the priming could be related to the short storage time of IRBC as well as to the small amount of IRBC added into the prime of the CPB circuit. In group B (unwashed IRBC), only 107 ± 57 ml IRBC was used in a total prime volume of 266 ± 17 ml. Therefore, the relevance of IRBC pre-washing related to the prospect of decreasing K+ concentration in the CPB prime was at the start of our study questionable [12]. Supported by this data, we decided to focus in our...
audit on lactate concentration during CPB. The lactate concentrations in the CPB prime with pre-washed IRBC were significantly lower than in the prime with unwashed IRBC. Nevertheless, plasma lactate concentration measured at the end of CPB was not significantly different between the study groups. The highest levels of lactate concentration were found at the end of CPB, both in the pre-washed group as well as in the unwashed group but they can still be considered as acceptable values during CPB [5–7]. The significant increase of lactate concentration that we found in the pre-washed group can be explained by the larger total amount of IRBC used in this group (however, it was statistically not different between the groups) or can be related to the washing process itself. Washing makes the red-cell membranes more fragile and can result in higher values of lactate. Conversely, the study by De Vroege et al. [10] concluded that deformability and free haemoglobin levels remained unchanged in stored RBCs after washing. There are no publications known to us related to the deterioration of irradiated RBCs during the washing process. The unknown impacts of other CPB-related variables as, for example, cardiotomy suction and the possible variation in quality of IRBC could also influence lactate level during CPB. There is a strong possibility that the amount of IRBC used in the priming of the CPB circuit and during the CPB as well the shelf time of IRBC and the type of medium (SAGM) are of a major influence on the lactate and K⁺ concentrations in the plasma of paediatric cardiac-surgery patients. Our audit does not support further continuation of the procedure of pre-washing IRBC in our institution; in addition the pre-washing process is time consuming and the volume loss occurs always during processing [9]. Consequently, we stopped routine pre-washing of IRBC.

### RECOMMENDATIONS

Based upon results of our audit, we would like to recommend a decision-making protocol for the use of the IRBC pre-washing process in paediatric cardiac surgery:

1. Assess the quality of the IRBC units routinely used in your institution by measuring the concentration of lactate and K⁺ and, if possible, other cell degradation products.
2. Assess in your own clinic the average volume of IRBC used in the priming of your CPB circuit and during CPB.
3. Recalculate the amount of lactate, K⁺ and degradation products related to the IRBC transfusion (absolute amount and the concentration in the priming and during CPB).
4. Estimate if the addition of unwashed IRBC would increase the lactate, K⁺ and other measurable variables above acceptable levels. If not, pre-washing should not be applied in your specific CPB circumstances.
5. Consider washing in relation to the expected duration of the CPB.

### CONCLUSION

Based on the results of this retrospective audit, we can conclude that the clinical relevance of pre-washing of IRBC in our institution, with the present CPB circuit and CPB strategy, has been not convincingly demonstrated. We consider pre-washing of IRBC useful when larger volumes of IRBCs are necessary during the priming and CPB or if only older IRBCs are available.

**Conflict of interest:** none declared.

### REFERENCES