Intraoperative cell salvage in infants undergoing elective cardiac surgery: a prospective trial


Department of Cardiothoracic Surgery and Department of Anaesthesiology, Erasmus MC, University Medical Center Rotterdam, Dr. Molewaterplein 40, 3015 GD Rotterdam, The Netherlands

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Abstract

Background: For a long time intraoperative cell salvage was considered not to be applicable in paediatric patients due to technical limitations. Recently, new autotransfusion devices with small volume centrifugal bowls and dedicated paediatric systems allow efficient blood salvage in small children. The purpose of this prospective non-randomised study was to determine the impact of intraoperative cell salvage on postoperative allogeneic blood products transfusion in infant patients undergoing cardiac surgery with cardiopulmonary bypass.

Methods: Two consecutive cohorts (122 patients) were studied. The first cohort underwent procedures between January 2004 and July 2005 with only blood salvage from the residual volume. The second cohort consisted of patients operated on from August 2005 to December 2006, with additional use of intraoperative cell salvage. The following variables were analysed: peri- and postoperative blood loss, transfusion of homologous blood products and cell salvage product, haematological and coagulation data, measured before, during and after the operation.

Results: Additional intraoperative cell salvage significantly enhanced the amount of cell saving product available for transfusion (183 ± 56 ml vs 152 ± 57 ml, p = 0.003) and significantly more patients in this group received the cell saving product postoperatively. Consequently, allogeneic blood transfusion was significantly reduced in volume as well as in frequency. We did not observe any adverse effects of intraoperative cell salvage.

Conclusion: Intraoperative cell salvage, employed as an adjuvant technique to the residual volume salvage in infants undergoing first time cardiac surgery with cardiopulmonary bypass, was a safe and effective method to reduce postoperative allogeneic blood transfusion. Considering current cell salvage related expense and the cost reduction achieved by diminished allogeneic transfusion, intraoperative cell salvage in infants demonstrated no economic benefit.

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1. Introduction

Intraoperative cell salvage (ICS) has been developed and adopted in different fields of surgery as a blood conservation technique to reduce allogeneic transfusion requirements related to excessive blood loss. This technique recovers blood lost in the operative field, purifies it and returns the obtained red blood cells (RBCs) concentrate to the patient. Although there are no doubts about the safety and efficacy of this technique in adult patients undergoing cardiac operation with or without cardiopulmonary bypass (CPB) [1–3], recent studies questioned the positive impact of ICS on allogeneic transfusion need in other fields of adult surgery [4,5].

The effectiveness and safety of ICS in small children is not well documented. For a long time ICS was considered not to be applicable in paediatric patients due to the technical limitations to wash and haemoconcentrate small volumes of salvage blood (<300 ml). More recently, new autotransfusion devices allow efficient blood salvage in small children by introducing small volume centrifugal bowls and dedicated paediatric systems.

In infants undergoing cardiac surgery with CPB, transfusion of allogeneic blood products is almost unavoidable, to counteract extreme haemodilution and to compensate for perioperative blood loss [6–9]. Therefore, salvage of red blood cells from the CPB circuit after the procedure is adopted as a practical blood conservation measure to minimise allogeneic transfusion needs. In our institution this technique is routinely used in children as well as in adult patients [10,11].

The purpose of this prospective non-randomised study was to determine the impact of ICS, as additional blood conservation technique, on allogeneic blood products transfusion in infant patients undergoing elective cardiac surgery. To assess safety and haematological consequences of
ICS perioperative blood loss, haematological and coagulation data were also evaluated.

2. Material and methods

2.1. Population

Between January 2004 and December 2006, 135 consecutive infant patients with a body weight of less than 10 kg underwent an elective, first time cardiac operation with CPB in our institution. All patients were eligible to take part in this prospective observational study. The study was conducted according to the institutional standards and parental informed consent was obtained for all patients. After completion of the study, the institutional review board confirmed procedural compliance retrospectively and a formal approval was waived (MEC 2007-306).

Exclusion criteria were preoperatively known clotting disorders and procedures that required deep hypothermic circulatory arrest (DHCA).

Two consecutive cohorts were studied. The first cohort (control group) underwent procedures with blood salvage from the residual volume of CPB circuit, between January 2004 and July 2005. At that point, in additional to the residual volume salvage, ICS was introduced and used in all infant patients operated on thenceforth. The second cohort (ICS group) consisted of patients operated on from August 2005 to December 2006. The same surgical team performed all the operations.

2.2. Anaesthesia, anticoagulation, cardiopulmonary bypass and cell salvage

Before induction of anaesthesia, all patients were monitored with a five-lead, two-channel electrocardiogram, non-invasive blood pressure measurement, and pulse oximetry. After the insertion of a peripheral venous line, general anaesthesia was induced with midazolam 0.2 mg/kg, sufentanil 2 mcg/kg and pancuronium 0.15 mg/kg. Patients were nasotracheally intubated and pressure controlled ventilated (PCV) using a Siemens 900C ventilator. Anaesthesia was maintained with midazolam 0.1 mg/kg/h and sufentanil 1 mcg/kg/h. Invasive monitoring via a femoral arterial line and an internal jugular central venous catheter was performed, and a Foley bladder catheter and rectal temperature probe were inserted. Before going on CPB all patients received 30 mg/kg iv methylprednisolone, 30 mg/kg iv magnesium sulphate, 1 mg/kg iv furosemide, 40 mg/kg iv cefazoline and 1 mg/kg iv ranitidine.

Anticoagulation was established with an initial bolus 300 IU/kg BW of porcine heparin and additional heparin was administrated to maintain activated clotting time higher than 480 s during the whole procedure. Initial protamine neutralisation was performed and if necessary additional protamine was given.

The CPB circuit consisted of a Capiox Baby Rx hollow-fibre oxygenator with hard-shell reservoir (Terumo, Tokyo, Japan), a roller pump with 1/4 in. silicone tubing (Raumedic REHAU, Muri, Switzerland), a D736-40 Micron (Dideco, Mirandola, Italy) arterial filter and PVC 1/4 in. arterial and venous tubing. The CPB systems were not coated. In accordance with our infant CPB protocol no modified ultrafiltration and no antifibrinolytic medication was used.

CPB prime contained homologous red blood cells concentrate, fresh-frozen plasma (FFP) and Gelofusine (B. Braun, Melsungen, Germany). The amount of RBCs added to the priming was calculated to achieve a haematocrit (Hct) of 28% during CPB. The prime was completed with 0.5 g/kg mannitol, 0.5 g/kg human albumin 20% solution, 4.2 IU heparin/ml priming volume and 2—5 ml NaHCO3 8.4%.

Nonpulsatile CPB, with mild hypothermia of 28—32 °C, was performed with blood flow rates between 1.8 and 3.2 l/min/m2 to maintain venous oxygen saturation above 70% and mean arterial pressure between 40 and 60 mmHg. During CPB a-stat regulation was used. Myocardial protection was achieved with crystalloid cardioplegia.

Administration of RBCs, FFP, crystalloids or colloids during CPB was based upon the system working volumes, target values for haematocrit (not lower than 28% for acyanotic as well as cyanotic patients) and colloid osmotic pressure (not lower than 15 mmHg).

After CPB, residual volume of the circuit was in all cases processed by HaemoLite 2 plus (Haemonetics, Bothwell, UK) cell saving device with a centrifugal bowl of 100 ml. In the ICS group all blood loss from skin incision to commencement of CPB and then after administration of protamine to skin closure was also salvaged. The HaemoLite 2 plus utilised an automatic protocol with centrifuge speed of 8000 rpm, pump speed of 300 ml/min by filling, washing and transfusing, and pump speed of 150 ml/min by concentrating. Washing volume was 500 ml. All those parameters were not manually interrupted during the study. Only completely filled bowls were automatically processed (in the last cycle the ‘concentrate’ option was used to fill the bowl completely) and accepted for transfusion. In all cases the entire salvage volume was processed. The harvested cell saving (CS) product had a haematocrit of 60%.

2.3. Laboratory tests, blood loss and blood products transfusion

The haematocrit and platelet (Plt) count were measured 1 day before the operation, at the start and end of the operation, during the CPB at the 5 min on bypass and at the end. During the postoperative period, measurements were performed at 6 and 24 h. Fibrinogen (Fib) concentration, prothrombin time (expressed as international normalised ratio, PT ratio) and activated partial thromboplastin time (expressed as APTT ratio to a normalised control value) were measured at the start and end of the operation and at 6 and 24 h postoperatively.

Blood loss was recorded at the end of the operation and at 6 and 24 h postoperatively.

In the operation room (OR) blood loss represented the sum of blood loss calculated from swabs, discarded suction volumes (control group) or collected volumes (ICS group) and the chest drain output. In the intensive care unit (ICU), the volume of chest tube drainage was counted as blood loss. Post CPB and postoperatively the decision to transfuse RBCs, CS product, FFP or platelet concentrate was based upon the
patient's clinical status and laboratory tests. Acyanotic as well as cyanotic patients were transfused to maintain a level of Hct above 30%. The CS product, if available, was always considered first line blood replacement therapy. Institutional transfusion policy allowed transfusion of this product only up to 6 h and overdue remnants of the CS product were always discarded. Transfusion of FFP was administrated in case of enhanced blood loss and prolonged PT values (PT ratio >1.5). Platelet concentrate was administrated if the Plt count at the end of CPB was less than 100 × 10^9/L.

The volume of blood products transfused in the OR, including blood products added to the circuit prime and during the CPB, and administrated at the ICU was recorded.

2.4. Data analysis

Continuous data are presented as a mean ± standard deviation (SD); categorical data are presented as proportions. All data were assessed for normality of distribution and equality of variance. Continuous independent data were compared with unpaired t test and one-way analysis of variance ANOVA (in case of normally distributed data) or Mann–Whitney test (in case of non-normally distributed data). Repeated measures of continuous variables were compared using repeated measures ANOVA. Categorical data were compared with the chi-square test. Pearson's correlation test quantified the relation between two variables where appropriate. A p value less than 0.05 was considered statistically significant. All statistical analyses were performed using SPSS 13.0 statistical software (SPSS, Chicago, IL). In order to detect a 50% reduction in postoperative RBCs transfusion with a power of 80% and an alpha value of 0.05, 60 patients in each group were required.

3. Results

3.1. Population and CPB data

One hundred and twenty-two patients completed the study. Twelve patients who underwent DHCA were excluded as well as one patient with delayed sternum closure (1 day after operation). There were no patients with preoperative clotting disorders and no re-thoracotomies were required during the study period. All patients survived. Patient's gender, age, body weight, body surface area, CPB time, aorta cross-clamp time, time at the ICU and cardiac anomaly are presented in Table 1.

In the control group 38% of patients was diagnosed with cyanotic type of congenital heart disease versus 42% in the ICS group (p = 0.76).

3.2. Laboratory tests result and blood loss

In the control group, mean Hct values measured the day before operation and before start of the CPB were lower than the ICS group, but results showed no significance (Fig. 1). Otherwise, the Hct values were not significantly different between the groups. There was no evidence for preoperative secondary erythrocytosis related to cyanotic type of heart disease (Table 2). The Plt count was not significantly different between the groups at the times of measurements (Fig. 2), as well as the mean values of PT ratio, APTT ratio and Fib concentration (Table 3). After 6 h postoperatively the mean values of Fib concentration were within the normal range, APTT and PT values were normalised at 24 h.

There were no significant differences in terms of a total blood loss (Table 4) at any indicated time.

3.3. Blood salvage and blood products transfusion

Results of blood salvage and CS product transfusion are presented in Fig. 3. The mean amount of CS product, generated from residual volume of CPB circuit and intraoperative blood loss, in the ICS group was significantly more than in the control group (183 ± 56 ml vs 152 ± 57 ml, p = 0.003). The mean volume of shed blood collected in the autotransfusion device was 66 ± 25 ml, with an estimated mean Hct of 30%. Only in 10 out of 59 patients in the ICS group (16.9%) was the autotransfusion device triggered to open.

3.4. Outcomes

The mean volume of blood products transfused in the OR, including blood products added to the circuit prime and during the CPB, and administrated at the ICU was recorded.
group, did the collected shed blood have adequate quantity and quality to produce a full bowl at the end of the CPB without additional salvage of the CPB residual volume.

In the OR after the cessation of CPB, there was no significant difference in the amount of transfused CS product or allogeneic RBCs between the two groups and there was no significant difference in the frequency of transfusion (Tables 4 and 5). On the other hand, during the first 6 h postoperatively 79% of patients in the ICS group received CS product versus 46% ($p < 0.0001$) in the control group. The mean volume transfused was not significantly different between the groups (ICS group: $52 \pm 45$ ml vs control group: $43 \pm 50$ ml, $p = 0.32$). Frequency of allogeneic RBCs transfusion in the ICU during the first 6 h was significantly lower in the ICS group than in the control group (27% vs 59%, $p < 0.0001$) as well as the mean volume transfused ($14 \pm 15$ ml vs $37 \pm 35$ ml, $p = 0.008$).

In relation to the FFP and Plt concentrate transfusion, no significant differences between the groups were observed considering volume and transfusion frequency at any time of measurements.

4. Comment

This prospective observational study investigated the effects of ICS on allogeneic blood transfusion in infants, who underwent an elective first time cardiac operation with CPB. Our results demonstrated that ICS significantly enhanced the amount of CS product available for transfusion. In the postoperative period, significantly more patients in the ICS group received CS product, therefore the frequency of allogeneic RBCs transfusion was significantly reduced as well as the mean transfused volume. We did not observe in the ICS group any adverse effects of CS product transfusion in terms of increased postoperative bleeding, derangement of clotting pathway or enhanced transfusion of platelets concentrate and FFP.

Prospective studies addressing the effects of intraoperative cell salvage in adult cardiac surgery have been performed since the late seventies. Results proved that intraoperative and postoperative cell salvage was effective, safe and that autotransfusion of washed cells was not associated with clinically significant derangement of clotting profiles [2,11], although mechenochemical activation of platelets and leucocytes was found in the salvage blood [12]. Initially, cell salvage of the residual CPB volume was successfully introduced in our institution in adult cardiac surgery. Later on intraoperative cell salvage was subsequently combined with it as a routine blood conservation measure [13]. Availability of the new autotransfusion system, which processes small volumes of blood (100 ml bowl), gave us the opportunity to adapt this technique also in small children undergoing cardiac surgery. Primarily, we investigated the impact of the cell salvage from the residual volume of CPB circuit and the results showed a significant reduction of allogeneic RBCs transfusion in the postoperative period [14]. Although, recent studies in infants undergoing surgical correction of craniosynostosis or acetabuloplasty found intraoperative cell salvage effective in limiting allogeneic blood transfusion [15], it is obvious that ICS is not equally useful for all types of surgery. Its effectiveness strongly

![Fig. 2. Platelets count in pre-, per- and postoperative period. CPB: cardio-pulmonary bypass; ICS: intraoperative cell salvage; OR: operation room.](image-url)
depends on the ability to collect shed blood from the operating field, the haematocrit of collected blood as well as the transfusion trigger.

In this study, in infants with a body weight less than 10 kg who underwent cardiac surgery with CPB, intraoperative blood loss collected in the autotransfusion device was, in 83% of the cases, not sufficient to fill completely the bowl of 100 ml, without additional salvage from the residual volume of the CPB circuit. We did not accept partially filled bowls for further processing to avoid an unpredictable and too low haematocrit [16]. Because of that, the CS product was not available earlier for transfusion until the salvage of CPB haematocrit[16]. Because of this, the CS product was not available earlier for transfusion until the salvage of CPB haematocrit. We did not accept partially filled bowls for further processing to avoid an unpredictable and too low haematocrit [16]. Because of that, the CS product was not available earlier for transfusion until the salvage of CPB haematocrit[16].

Fig. 3. Use of the cell saving product. CS: cell saving product; ICS: intraoperative cell salvage; ICU: intensive care unit; OR: operation room.

4.1. Study design and limitations

The study compared two cohorts of patients that underwent operations in different periods, nevertheless there were no differences in perioperative management, CPB and population data as well as the ratio between cyanotic and acyanotic patients in each group. Consequently, significantly more allogeneic RBCs were used in the prime of the CPB circuit and a second unit of allogeneic blood was required for transfusion after the cessation of CPB. This occurred in 48% of patients in the control group versus 23% in compared to as much as 59% of patients in the control group. Patients in the ICS group received on average 14 ± 15 ml of allogeneic RBCs and patients in the control group; 37 ± 35 ml. After 6 h allogeneic RBCs were routinely administrated in both groups, because the CS product acceptance for transfusion elapsed after this time. The study of Hishon et al. and Amand et al. [17,18] demonstrated minimal chemical deterioration and limited microbiologic contamination in blood salvaged from the CPB circuit and stored at room temperature for an 18 h period. Therefore, prolongation of the acceptable transfusion period for CS product could be beneficial with regard to a further reduction of allogeneic blood requirements. Use of the ICS had no consequence for the FFP and platelet concentrate transfusion as well as for the coagulation pathways and Fib concentration changes in the perioperative period. Additionally, our study results revealed that allogeneic blood was in many cases transfused in the ICU even though there was sufficient amount of CS product available (Fig. 3). This phenomenon was considered to be a major study limitation.
ICS group \((p = 0.04)\). Both groups showed a significant correlation (control group \(r = 0.86\), ICS group \(r = 0.78\), both \(p = 0.05\)) between transfusion of a second unit allogeneic RBCs in the OR and use of allogeneic blood during the first six postoperative hours. These findings support the hypothesis that, against the protocol, homologous blood transfusion was continued in the ICU if the previous exposure to the specific unit of blood took place in the OR. Consequently, postoperative use of the CS product was limited (Fig. 3). After reconsideration of those findings, the study data on allogeneic RBCs transfusion during the first six postoperative hours were recalculated. To correct for this bias, patients who utilised the whole volume of the first unit allogeneic RBCs before the end of the CPB were excluded from the recalculation. Even so, frequency of allogeneic RBCs transfusion in the ICS group was significantly lower than in the control group (23% vs 41%, \(p = 0.03\)), but difference in the average transfused volume did not show significance (12 ± 11 ml vs 23 ± 32 ml, \(p = 0.11\)).

We also performed a financial cost–benefit analysis based upon the reduction of allogeneic RBCs transfused in the ICS group compared to the control group. Introduction of the ICS reduced transfusion of allogeneic RBCs by 18 units (total cost of €3348), but required an investment of €4725 (€75 per patient to collect shed blood). If the primary bias was removed from the study the reduction of allogeneic transfusion was only three units (total cost €560) but required an investment of €2655. Therefore, the cost made to collect shed blood was higher than the financial savings associated with the reduction of allogeneic blood transfusion.

4.2. Conclusions

Autologous transfusion is considered to be worthy as a prevention of transfusion-transmitted diseases, transfusion reactions and immune-related problems; although a unit of CS product costs slightly more than a unit of allogeneic blood. The ICS, used as an adjuvant technique to the cell salvage from the CPB residual volume, in infants undergoing first time cardiac surgery proved to be safe and effective to produce more CS product available for transfusion. The ICS was also effective in reducing postoperative allogeneic blood transfusion in terms of frequency as well as volume. Therefore, ICS was validated to be a useful blood conservation measure in infant cardiac surgery. Prolongation of the acceptable transfusion time for the CS product, strict realisation of the postoperative transfusion protocol (CS product as the first line transfusion therapy) and adjustment of the transfusion trigger would be beneficial for the effectiveness of ICS. Under those conditions, ICS potentially could be an economic benefit.

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