

Cryoprecipitate and Platelet Administration during Modified Ultrafiltration in Children Less than 10 kg Undergoing Cardiac Surgery

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Abstract: The timing of blood product administration after cardiopulmonary bypass (CPB) may influence the amount of postoperative transfusion and chest tube output. We performed a retrospective study of a novel technique of administering blood products during modified ultrafiltration (MUF) in congenital cardiac surgery. A Control Group (CG; $n = 55$) received cryoprecipitate and platelets after modified ultrafiltration. The Treatment Group (TG; $n = 59$) received cryoprecipitate and platelets during MUF. Volumes of blood products transfused in the operating room, initial coagulation parameters in the cardiac intensive care unit, and first 24-hour chest tube output were recorded. Age (116 ± 198 versus 84 ± 91 days), weight (4.6 ± 1.8 versus 4.5 ± 1.4 kg), duration of bypass (121 ± 50 versus 139 ± 57 minutes), and Aristotle scoring (9.3 ± 2.7 versus 9.1 ± 3.1) were not significantly different when comparing the control and treatment groups, respectively. Intraoperative packed red blood cells (74.4 ± 34.8 versus 79.3 ± 58.0 mL/kg, $p = .710$), fresh-frozen plasma (58.3 ± 27.1 versus 59.1 ± 27.2 mL/kg, $p =$

$.849$), cryoprecipitate (7.3 ± 5.1 versus 8.6 ± 5.9 mL/kg, $p = .109$), and platelet (19.0 ± 14.6 versus 23.7 ± 20.8 mL/kg, $p = .176$) administration were the same in the control and treatment groups, respectively. However, fibrinogen levels on arrival in the coronary intensive care unit were significantly higher (305 ± 80 versus 255 ± 40 mg/dL, $p < .001$) in the CG compared with the TG. Twenty-four-hour chest tube output was not significantly different but the CG (17.76 ± 9.34 mL/kg/24 hours) was trending lower than the TG (19.52 ± 10.94 mL/kg/24 hours, $p = .357$). In an attempt to minimize CPB-associated bleeding and transfusions, we changed our practice by adjusting the timing of blood product administration after patient separation from CPB. The goals of the change in practice were not measurably different in terms of shorter intraoperative times, fewer blood transfusions, or less chest tube output at our institution. **Keywords:** congenital heart disease, modified ultrafiltration, cryoprecipitate, platelets, cardiopulmonary bypass. JECT. 2013;45:107–111

Over the past decade, there have been many advances in the management of bleeding in children undergoing heart surgery. These advances have included changes in surgery, anesthesiology, and cardiopulmonary bypass (CPB). Surgeons routinely use hemostatic agents instilled directly at the site of bleeding in the form of gels and sponges (1). Anesthesiologists are using newer drugs such as factor VIIa (2) and older drugs such as aminocaproic acid, which have resurfaced after the recall of aprotinin (1). Anesthesiologists are monitoring the clotting process

with thromboelastography, which is more dynamic than traditional clotting tests such as prothrombin time (3). Cardiopulmonary bypass circuits have become smaller and more biocompatible leading to decreased contact activation of the inflammatory response and potentially mitigating CPB's effects on hemostasis. Perfusionists routinely use various forms of ultrafiltration in an attempt to hemoconcentrate red blood cells and clotting factors during (conventional ultrafiltration) and immediately after (modified ultrafiltration [MUF]) CPB. We recently introduced a change in our blood product transfusion practice in an attempt to decrease volume shifts during the MUF process and promote earlier hemostasis. Instead of administering all of the blood products intravenously after CPB and MUF, we changed to administering blood products during MUF, directly into the MUF circuit. This article describes a retrospective study of this change in practice.

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MATERIALS AND METHODS

This is a retrospective study of patients before and after our change in blood product transfusion practice. Approval was obtained from the Children's Hospital Colorado, Organizational Research Risk & Quality Improvement Review Panel (1209-5). All patients weighing less than 10 kg who underwent surgical repair of congenital heart disease on CPB from April 2011 to April 2012 were included in the study. Patients were allocated into one of two cohorts. The first patient cohort or Control Group (CG) were those patients who underwent traditional MUF without concomitant transfusion of platelets and cryoprecipitate. The second cohort of patients was the Treatment Group (TG) who received platelets and cryoprecipitate during MUF. Additional blood products were administered after MUF in both groups as necessary.

Protocols for CPB in both cohorts were identical. There were no changes in clinical practice other than the timing of the blood product administration. There were no changes in personnel during the study period as well. The FX05 (Terumo Cardiovascular, Ann Arbor, MI) or VKMO 11,000 (Maquet Cardiovascular, Wayne, NJ) oxygenators constructed with integrated arterial line filters were used in both groups. Cardiopulmonary bypass circuits consisted of SMAR_xT (Sorin Group, Arvada, CO) coated tubing with 3/16-inch arterial, 1/4-inch venous lines, and 1/4-inch pump head tubing. A hemoconcentrator (DHF) .2 (Sorin Group) was used in every case. The cardioplegia circuit consisted of 1:4 tubing and a Vanguard blood cardioplegia device (Sorin Group). The same circuits were run on either a SystemOne (Terumo Cardiovascular) or S5 (Sorin Group) heart–lung machine. Both heart–lung machines have mast-mounted pumps and there was no difference between the two in regard to circuit setup and prime volumes. The CPB prime consisted of Plasmalyte A (Baxter Healthcare Corporation, Deerfield, IL), packed red blood cells (PRBCs), and fresh-frozen plasma (FFP). Heparin, sodium bicarbonate, mannitol, calcium chloride, and aminocaproic acid were added to the prime based on patient body weight. No aprotinin (Bayer AG, Pittsburgh, PA) was used in either group of patients. The PRBCs and FFP underwent ultrafiltration with 1000 mL of Plasmalyte A injection before bypass.

On CPB, the hematocrit was maintained above 30%, flow rates were 125–200 mL/kg/min, and the mean arterial blood pressure was kept above 40 mmHg. For patients cooled to a rectal temperature of 28°C or below, pH stat blood gas management was used. Oxygenators were ventilated with 100% FiO₂ for patients cooled below 22°C. The CDI[®] 500 (Terumo Cardiovascular) blood gas monitor was used on every case and calibrated with the i-STAT[®] System (Abbott Point of Care, East Windsor, NJ) point-of-care analyzer at the start of CPB. Blood gases and

activated clotting times using the i-STAT[®] System were evaluated at least every 60 minutes during CPB. Activated clotting times were maintained greater than 480 seconds. Arterial, venous, and cardioplegia blood temperatures were monitored with temperatures not exceeding 37°C. Vacuum-assisted venous drainage was used with a maximum reservoir pressure of –50 mmHg. Hypothermic del Nido cardioplegia (4) was given initially at 30 mL/kg and subsequent doses of 15 mL/kg at 60- to 90-minute intervals. A Continuous Autotransfusion System (Fresenius Kabi, Bad Homburg, Germany) was standard on all cases.

Arterial–venous MUF (Figure 1) was performed on the CG immediately after bypass. Modified ultrafiltration flow rates ranged from 10 to 30 mL/kg/min and the technique was terminated when all residual venous reservoir and oxygenator volume had been transfused and displaced by crystalloid. Treatment group MUF was performed in a similar fashion as the CG with the addition of cryoprecipitate and platelets to the MUF circuit after the residual volume had been transfused. In the TG, calcium chloride (10–30 mg/kg) was administered by perfusion into the MUF circuit when the central venous pressure increased with an associated decrease in MAP. The need for calcium chloride appears to be directly proportional to the speed and quantity of MUF-administered blood products.

Patient height, weight, age, reoperation, CPB time, deep hypothermic circulatory arrest occurrence, and Aristotle scoring were recorded. Total time in the operating room and time from the end of CPB to leaving the operating room were documented. Hematocrit measurements recorded included: following arterial line placement, induction of CPB, CPB nadir, pre-CPB wean, and post-MUF. Fibrinogen, hematocrit, international normalized ratio, and platelet count are drawn as a standard of care on arrival in our cardiac intensive care unit. Assessment of initial 24-hour blood loss was expressed in mL/kg of chest tube drainage. Measurement of blood product transfusions in the first 24-hour period after surgery included PRBCs, FFP, platelets, and cryoprecipitate.

Study data were recorded using an Excel (Microsoft, Redmond, WA) spreadsheet on a secured departmental server. All data are reported as mean ± standard deviation. A Student's *t* test was performed for normally distributed data and rank sum statistical analysis was performed for nonnormally distributed data. Results were deemed statistically significant at a *p* value ≤ .05.

RESULTS

From April 2011 to April 2012, 114 patients weighing less than 10 kg underwent surgical repair for congenital heart disease on CPB. Patient demographics are listed in

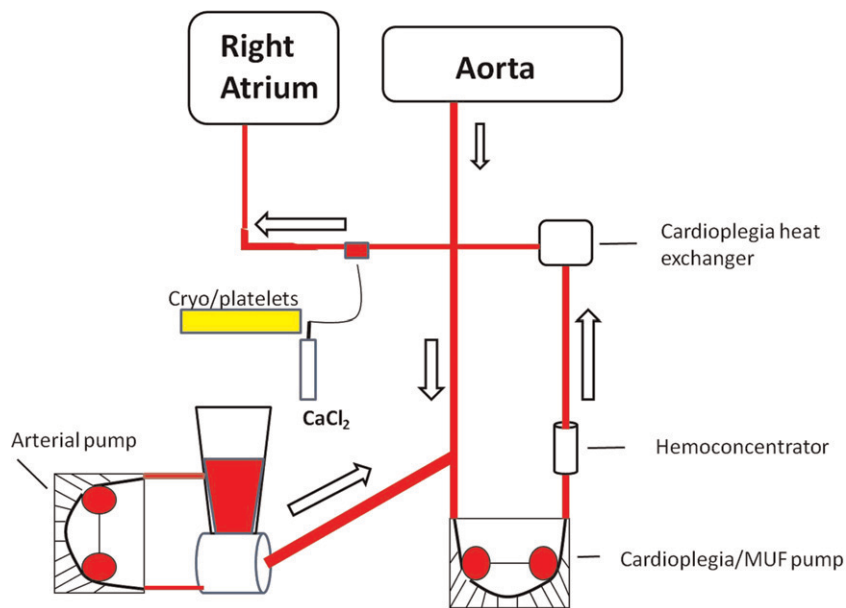


Figure 1. Modified ultrafiltration circuit. The blood products are administered in the circuit beyond the cardioplegia heat exchanger.

Table 1. The baseline, last hematocrit on CPB, and post-MUF hematocrit were not significantly different between the control and treatment groups (Figure 2). The transfused volumes of intraoperative PRBCs, FFP, cryoprecipitate, and platelets were not significantly different between the control and treatment groups (Table 2). Modified ultrafiltration time increased from 8.7 minutes in the CG to 11.5 minutes in the TG. After MUF, cell saver volume given to the anesthesia team was significantly greater in the treatment group. (113.6 ± 49.9 mL versus 141.4 ± 45.4 mL, $p = .0028$). Time from the end of CPB to the patient leaving the operating room was not significantly different in the control versus treatment groups, respectively (96 ± 33 minutes versus 86 ± 25 minutes).

Postoperative coagulation parameters drawn on arrival in the cardiac intensive care unit are displayed in Table 3. Twelve of 55 (22%) patients in the CG received postoperative blood product transfusion compared with 18 of 59 (30%) of patients in the TG. Twenty-four-hour chest

tube output was not significantly different between the control and treatment groups, respectively (17.76 ± 9.34 versus 19.52 ± 10.94 mL/kg/24 hours, $p = .357$). No adverse events such as visible clots or obstructed bypass components were observed in either group.

DISCUSSION

There are several centers currently transfusing blood products to pediatric heart surgical patients during MUF. However, to the best of our knowledge, no published reports exist in the current literature pertaining to this clinical practice. The methodology described of administering the products distal to the cardioplegia heat exchanger results in the cryoprecipitate and platelets being exposed to the least amount of foreign surface area within the circuit. Obtaining the cryoprecipitate and platelets before beginning MUF was sometimes challenging. On several

Table 1. Patient demographics.

| | Control Group | Treatment Group | <i>p</i> Value | |
|-------------------|----------------------------------|--------------------------------------|----------------|----|
| Number | 55 | 59 | | |
| Dates | April 11, 2011, to March 1, 2012 | November 21, 2011, to April 12, 2012 | | |
| Age | 116 ± 198 days | 84 ± 91 days old | .2766 | NS |
| Weight | 4.6 ± 1.8 kg | 4.5 ± 1.4 kg | .6884 | NS |
| Redo rate | 27.5% | 12.0% | | |
| CPB | 121 ± 50 minutes | 139 ± 57 minutes | .0806 | NS |
| DHCA | 18 cases | 19 cases | | |
| Aristotle scoring | 9.3 ± 2.7 | 9.059 ± 3.1 Z score = -1.787 | .074 | NS |

Control Group (CG) is platelets and cryoprecipitate administered after MUF. Treatment Group (TG) is platelets and cryoprecipitate administered into the MUF circuit.

CPB, cardiopulmonary bypass; DHCA, deep hypothermic circulatory arrest; NS, nonsignificant.

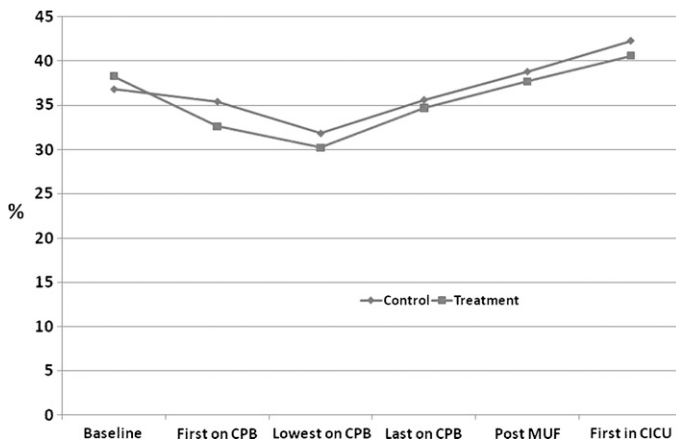


Figure 2. Intraoperative mean hematocrit. Control Group (CG) is platelets and cryoprecipitate administered after MUF. Treatment Group (TG) is platelets and cryoprecipitate administered into the MUF circuit. CPB, cardiopulmonary bypass; MUF, modified ultrafiltration; CICU, cardiac intensive care unit.

occasions, the cryoprecipitate and platelets arrived in the operating room after the CPB circuit contents were already transfused into the patient. Therefore, these patients received the products after MUF and thus fell into the CG. An unforeseen challenge in applying this technique was the need for extra calcium chloride administration by perfusion during the transfusion of products to maintain hemodynamic stability throughout the MUF procedure. Calcium administration would normally be performed by anesthesiology during product infusion after separation from CPB, like in the CG. One observation apparent in the TG was an increase in duration of MUF time by 2.8 minutes. The extra time was needed to administer the additional blood products slowly while maintaining patient hemodynamic stability.

One rationale for our change in practice was to decrease the amount of blood products a patient would need by promoting earlier hemostasis with the administration of blood products during MUF. Small children undergoing cardiac surgery generally bleed significant quantities of blood products (>25 mL/kg blood products/24 hours) (5–7). It was anticipated that this retrospective study

Table 2. Intraoperative transfusions.

| | Control Group | Treatment Group | <i>p</i> Value | |
|---------------------|-------------------|-------------------|----------------|----|
| Red blood cells | 74.4 ± 34.8 mL/kg | 79.3 ± 58.0 mL/kg | .710 | NS |
| Fresh=frozen plasma | 58.3 ± 27.1 mL/kg | 59.1 ± 27.2 mL/kg | .849 | NS |
| Cryoprecipitate | 7.3 ± 5.1 mL/kg | 8.6 ± 5.9 mL/kg | .109 | NS |
| Platelets | 19.0 ± 14.6 mL/kg | 23.7 ± 20.8 mL/kg | .176 | NS |

Control Group (CG) is platelets and cryoprecipitate administered after MUF. Treatment Group (TG) is platelets and cryoprecipitate administered into the MUF circuit.
NS, nonsignificant; MUF, modified ultrafiltration.

Table 3. Cardiac intensive care unit coagulation parameters.

| | Control Group | Treatment Group | <i>p</i> Value | |
|---------------------------------|---------------|-----------------|----------------|-------|
| Hematocrit (%) | 42.3 ± 5.5 | 40.6 ± 5.2 | .0904 | NS |
| Fibrinogen (mg/dL) | 305 ± 80.0 | 255 ± 40.2 | .0002* | <.001 |
| INR | 1.21 ± .11 | 1.28 ± .14 | .0072* | <.05 |
| Platelets (10 ³ /uL) | 233 ± 79.6 | 216 ± 70.6 | .6215 | NS |

*Control Group (CG) is platelets and cryoprecipitate administered after MUF. Treatment Group (TG) is platelets and cryoprecipitate administered into the MUF circuit.

INR, international normalized ratio; NS, nonsignificant; MUF, modified ultrafiltration.

would reveal a reduction in product transfusion in the operating room. No statistical significance was reached when intraoperative transfusions data between the CG and TG were compared. However, the trend toward greater transfusion in the TG of all four blood products was concerning. Since the analysis in this report, we have adjusted the TG methodology. On average, 29.5 mL of cryoprecipitate and 76.9 mL of platelets were being administered during MUF in the TG. Currently, perfusion administers all of the cryoprecipitate and only 50% of the platelets. Anesthesia now administers the rest of the platelets after protamine and surgical hemostasis. Further analysis of this technique modification is currently underway.

Another rationale for our change in practice was to achieve greater hemodynamic stability both during and after MUF. Typically after separation from CPB, there are significant changes in hemodynamic variables including preload, myocardial contractility, and systemic vascular resistance. The anesthesia team responds to these changes in hemodynamics with volume administration in the form of blood products and adjusting vasoactive drug requirements. Hemodynamic changes were not measured specifically in this study but the clinical impression was one of greater hemodynamic stability immediately after MUF in the TG.

Point-of-care testing of platelet function and clot strength in the operating room have not been found to be predictive of the risk of postsurgical bleeding (6). Therefore, our current standard of care is to order two random donor equivalent of platelets and 10 mL/kg of cryoprecipitate for children weighing less than 10 kg (7). In the postoperative intensive care unit, blood product administration may continue sometimes for up to 12–24 hours before coagulation normalizes. In the cardiac intensive care unit, international normalized ratio and fibrinogen were found to be statistically significantly better in the CG but these differences were not clinically significant. The reason for this difference we can only speculate on but may relate to possible adherence of proteins to the MUF circuit or some other cause. However, reassuringly chest tube output

was not significantly greater in the TG and well within the range of other studies (5–7).

Although the benefits of MUF have been well documented (8–11), there is still a need for further research with this technique. Many changes have occurred in CPB practice since the first publications on MUF. Vacuum-assisted drainage (12) and integrated arterial line filters (13) have assisted in the reduction in average prime volumes previously of 750 mL to current reports of 325 mL (14). Additionally, minimal acceptable hematocrit before deep hypothermic circulatory arrest and termination of CPB have increased to 24.9% and 29.0%, respectively, from lower values in the past (14). Figure 2 reflects our minimal hematocrit protocol (>30%), which is much higher than older MUF studies with minimal hematocrit requirements (>20%) (15). All these factors may blunt the effects of present-day MUF and warrant critical re-evaluation of this technique.

The administration of large quantities of blood products is associated with increased postoperative complications, which may manifest as multiorgan dysfunction. This is especially true for lung and kidney injury, which may result in longer ventilation times and renal insufficiency in the postoperative period (16). Additionally, exposure to multiple blood donor units is known to cause the development of antibodies in many of these patients undergoing multiple surgeries palliated for severe congenital heart disease, which may prevent some of these patients not being candidates for subsequent orthotopic heart transplantation (17).

CONCLUSION

In an attempt to minimize CPB-associated bleeding and achieve greater hemodynamic stability, we changed our practice pattern by adjusting the timing of blood product administration after patient separation from CPB. The goals of the change in practice were not measurably different in terms of shorter intraoperative times, fewer blood transfusions, or less chest tube output at our institution. The authors view this retrospective review as the first step in proceeding with a prospective randomized study because the possible clinical impression of greater hemodynamic stability associated with this transfusion technique necessitates further investigation.

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