EFFECTS OF MODIFIED ULTRAFILTRATION ON BLOOD PRODUCTS REQUIREMENT IN CHILDREN UNDERGOING OPEN HEART SURGERY

Muhammad Tariq, Yasmin Musaddiq, Shahab Naqvi, William M. Novick, Mazhar Qayyum, Iftikhar Ahmed, Kamal Saleem

Armed Forces Institute of Cardiology Rawalpindi

ABSTRACT

Objective: To find out the effects of modified ultrafiltration on blood products requirement for transfusion in congenital heart disease children after open heart surgery.

Design: This was a quasi-experimental study between two clinical groups. Patients were assigned to both groups by using convenient sampling; to do Modified Ultrafiltration or not was surgeon's preference who was unaware whether the patient is participating in any study or not.

Place and Duration of Study: The study was carried out at Armed Forces Institute of Cardiology/National Institute of Heart Diseases (AFIC/NIHD) Rawalpindi between August, 2005 and September, 2006.

Patients and Methods: Total 200 patients were included in this study and were divided equally into two groups; study group (MUF) and control group (non MUF) keeping hundred patients in each group.

Results: Significantly increased level of hemoglobin after MUF (9.7±1.4 gm/dl before MUF versus 13.6±1.6 gm/dl after MUF, p<0.001) and significantly decreased volume of blood products required for transfusion in study group (24.1±24.5 ml/kg versus control: 43.81±42.4 ml/kg, p<0.001). Significantly increased hemoglobin level was observed during first three days of ICU stay (12.6±1.8 g/dl versus control: 11.6±2.1 g/dl, p=0.001on first postoperative day , 11.3±1.8 g/dl versus control: 10.8±1.9 g/dl, p=0.039 on second postoperative day and 11.3±1.5 g/dl versus control: 10.5±1.8 g/dl, p=0.022 on third postoperative day).

Conclusion: From this study we concluded that use of MUF is well tolerated in all the patients and due to removal of extra water from patients circulation after separation from CPB resulted in hemodynamic benefits, significantly less use of blood products and better postoperative hemoglobin and hematocrit management.

Keywords: Blood products, open heart surgery, congenital heart diseases

INTRODUCTION

Approximately one percent of all the children borne alive have congenital heart disease and in Pakistan it is estimated that there are more than 30000 children born yearly with congenital heart defects that will require surgery to correct [1]. Kalimuddin (2003) reported that 8 to 10 percent of all the newborns in the country had some sorts of congenital heart disease and 50 percent of these die without treatment [2]. Despite the surgical ability to correct complex defects in such small babies, limitations in outcome are sometime encountered related to the systems necessary for surgical repair. In particular, exposure to cardiopulmonary bypasses (CPB). During CPB the heart and lungs of patient are bypassed and their function is performed by heart-lung machine.

In order to remove air from CPB circuit, it is primed with crystalloid solutions. During bypass these solutions are mixed in the patient's vascular system resulting in hemodilution. The decrease in patient's hematocrit level, platelets and clotting factors due to hemodilution causes increased postoperative bleeding, more need of blood products for transfusion. The mixing of

Correspondence: Dr Muhammad Tariq, Dept of Perfusion, Aneasthediology & Cardiac Surgery, AFIC/ NIHD Rawalpindi

Email: tariqrao_afic@yahoo.com

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crystalloid solutions with circulating blood of patient also causes decrease of colloid osmotic pressure. As a result, fluid moves into the extra vascular tissues producing edema and an elevation in total body water after CPB in children [3]. Wernovsky and colleagues (1995) reported an average positive fluid balance of 664 ml, equivalent to a 30 percent weight gain in neonates and infants undergoing arterial switch surgery [4]. Ultrafiltration (UF) is a technique used for removal of extra water from circulation during CPB. There are different UF techniques which are performed during CPB like conventional ultrafiltration (CUF), dilutional ultrafiltration and zero-balanced ultrafiltration (Z-BUF). The modified ultrafiltration (MUF) technique has been added to these filtration techniques with the advantage of filtering the patient's extra cellular volume, resulting in greater hemoconcentration after separation from CPB. It is more effective in concentrating the patient's blood. The main objective of this study was to investigate the effects of modified ultrafiltration on blood products requirement for transfusion and postoperative management of hemoglobin and hematocrit values.

PATIENTS AND METHODS

This was a quasi-experimental study carried out at Armed Forces Institute of Cardiology and National Institute of Heart Diseases (AFIC/NIHD). All consecutive patients less than twelve years of age referred for cardiac surgical procedures between August, 2005 and September, 2006, were included in this study. Patients with a preoperative mechanical ventilator support, ongoing corticosteroid therapy, recurrent infection, re-operation, emergency operation with age more than twelve years and those undergoing went open heart surgery with deep hypothermic circulatory arrest were excluded from this study. Total 200 patients were included and they were divided into two equal groups, study group (MUF group) and control group (nonMUF group), with 100 patients in each group. The study group comprised of patients in whom modified ultrafiltration was performed after separation from CPB where as control group comprised of patients in which modified ultrafiltration was not performed.

All the patients were operated under general anesthesia with our standard anesthesia protocols for pediatric patients. All patients were premedicated with chloryl hydrate, promethazine and paracetamol. Opioid based anesthesia with either morphine or fentanyl infusion was used with muscle relaxants and endotracheal intubation. KION SIEMENS pediatric anesthesia ventilator with facility for end tidal carbon dioxide and anesthetic concentration monitoring was used. Subsequently intra arterial and central venous pressure lines were placed. At induction base line arterial blood gases and activated clotting time were recorded. Throughout CPB fentanyl infusion/midazolam or morphine boluses were used to maintain anesthesia.. Anticoagulation was achieved with initial bolus of 3 mg/kg (300 IU/kg) heparin injected through central venous line before cannulation.. The cardiopulmonary bypass system was composed of a Stokert Compact Heart-Lung machine (Stokert Instrument GMBH, Munich) and micro porous polypropylene membrane oxygenators. Our standard perfusion protocols were used in all patients with aortic and bicaval venous cannulation and during bypass flow rates were maintained at 2.4 liters per square meter of body surface area per minute except for transient periods. Warm blood cardioplegia was used in all the cases. Mean arterial pressure was kept at 40 to 60 mmHg during CPB. Polystan hemofilters (Maquet

Cardipulmonary AG, Hirrlingen, Germany) BC 20 Plus and BC 60 Plus were used to perform ultrafiltration techniques. Modified ultrafiltration was performed in all the patients included in the study group and our target was to achieve the desired hematocrit or to transfuse the entire left over fluid of CPB circuit to the patient. In order to achieve the desired hematocrit level, we used the formula: $\frac{a-b}{b} \times c =$ Filtrate volume, where a = final hematocrit desired, b = final hematocrit on bypass, c = patient's estimated blood volume. Blood was removed from aortic cannula, passed through the hemofilter, and the concentrated blood was returned to the right atrium. After completion of MUF protamine was administered at a dose of 3 mg/kg body weight to bring activated clotting time (ACT) to normal values (107±13 seconds).

Blood samples were taken before operation, 10 minutes after on bypass, before coming off bypass, at the end of MUF, on 1st 2nd and 3rd postoperative days.

Statistical Analysis

Data had been analyzed using SPSS version 11.0 Continuous variables are expressed as mean + standard deviation of the mean. Independent samples student t test was applied for the comparison between the two groups. Discrete variables were summarized as number (percent) of patients and were compared by Chi square test either Fisher's exact test or Pearson's x2 test as required. Paired t test was done to compare the values of hemoglobin and hematocrit in study group before and after MUF. A p-value 0.05 or less was considered statistically significant.

RESULTS

Two hundred patients were included in the study 100 in each group. Both the groups were comparable and well matched technically and clinically for patients' demographics including age, sex, height, weight, body surface area, type of surgical procedure performed, preoperative hemoglobin and hematocrit values, perioperative ultratefiltrate volume removed during CPB, aorta cross clamp time and CPB (Table 1,2). Significantly increased level of hemoglobin (9.7±1.4 gm/dl before MUF versus 13.6±1.6 gm/dl after MUF, p<0.001) hematocrit (29.8±4.3 percent before MUF versus 40.9±4.9 percent after MUF, p<0.001) was observed after modified ultrafiltration in patients of study group (Fig. 1).

Total amount of packed red blood cells equired for transfusion in operating room and during ICU stay were 24±20.3 ml/kg in nonMUF group and 15.6±12.4 ml/kg in MUF group. A significantly increased (p = 0.000) volume of packed red blood cells was required for transfusion in the non MUF group as compared to that of MUF group (Fig.2). Total amount of fresh frozen plasma required for transfusion in operating room (OR) and during intensive care unit (ICU) stay were 14.6 ± 22.4 ml/kg in non modified ultrafiltration group and 6.8 ± 11.6 ml/kg in modified ultrafiltration group. Patients in modified ultrafiltration group received significantly less (p= 0.002) volume of fresh frozen plasma as compared to the non MUF group (Fig.2). Similarly total volume of platelets required for transfusion in operating room and during ICU stay were 5.2±11.5 ml/kg in non MUF group and 1.7±4.6 ml/kg in MUF group. Patients in modified ultrafiltration group received significantly less (p =0.006) platelets as compare to the patients of non modified ultrafiltration group (Fig.2).

The hemoglobin levels for non MUF and MUF group were 11.6±2.1 g/dl versus 12.6±1.8 g/dl at postoperative day1, 10.8±1.9 g/dl versus 11.3±1.8 g/dl at postoperative day2, 10.5±1.8 g/dl versus 11.3±1.5 g/dl at postoperative day3, respectively. There were significantly higher hemoglobin levels were observed in the MUF group as compared to that of non MUF group during ICU stay (Fig 3).

Similarly hematocrit percentage for non MUF and MUF group were 35.5±6.9 versus 39.2±6.6 at postoperative day1 ($p<0.001$), 33±6.3 versus 35.1±5.9 at postoperative day2, 31.5±5.3 versus 33.6±4.6 at postoperative day3, respectively. There were significantly higher hematocrit percentage were observed in the MUF group as compared to the non MUF group during first three days of ICU stay (Fig.4).

DISCUSSION

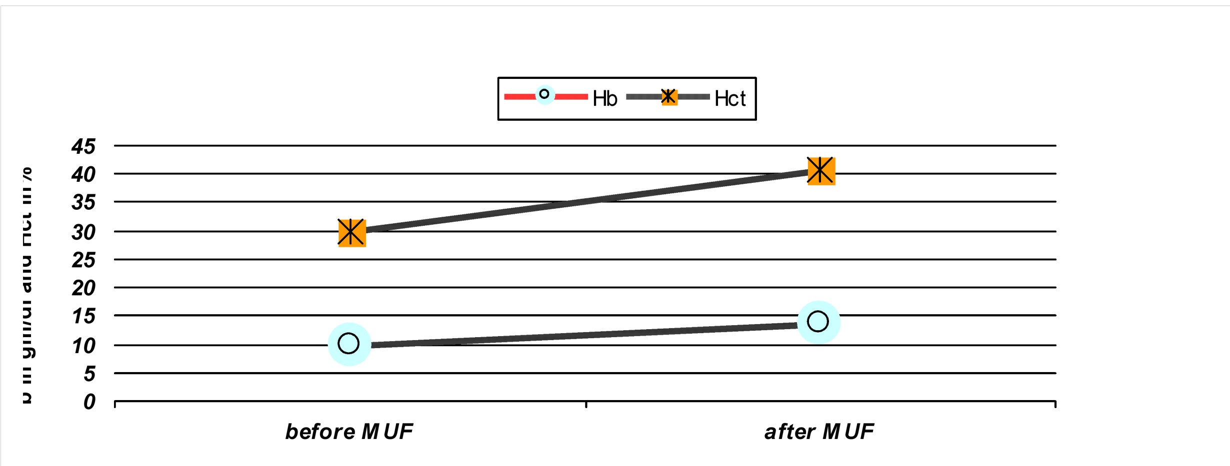
Most of the previous studies which reported benefits of MUF are usually in comparison with patients not receiving any ultrafiltration and patients receiving MUF [5-10]. In our study, only difference among the groups was use of MUF technique, while pre-bypass, zero-balance and conventional ultrafiltration techniques were performed in patients of both the groups.

The mean volume of blood products (RCC, FFP and Platelets) required for transfusion were significantly lower in patients of study group as compared to the patients of control group in which modified ultrafiltration was not used. Significant decrease in postoperative requirement of blood products for transfusion in study group was due to use of MUF which reversed hemodilution by removing extra water from

Table 1: Characteristics of Patients Included in non Modified Ultrafiltration (Non MUF) and Modified Ultrafiltration (MUF) Groups

Characteristics	Non MUF (N=100)	MUF (N=100)	P-value
Age (months)	78.4±45.4	76.1±40.4	0.703^{NS}
Height (cms)	110.4±27.7	106.2±21.3	0.235^{NS}
Weight (kg)	18.9±11.1	16.8±7	0.108^{NS}
BSA (m^2)	0.8±0.3	0.7±.2	0.246^{NS}
CPB Time (min)	91.4±44	92±52.4	0.929^{NS}
Ao X Time (min)	51.4±26.6	45.1±23.6	0.076^{NS}
Pre-op Hb (g/dl)	13.3±3	12.8±3	0.215^{NS}
Pre-op Hct (%)	40.5±9.6	38.4±9.2	0.121^{NS}
Hb durin CPB	8.8±1.6	9.1±1.8	0.251^{NS}
Hct during CPB	27.1±5.3	28.1±5.7	0.171^{NS}
Hb end of CPB	9.4±1.6	9.7±1.3	0.172^{NS}
Hct end of CPB	28.9±5	29.8±4.3	0.181^{NS}
Male/Female (ratio)	70/30	64/36	0.451^{NS}
UF volume (ml/kg)	44.5±15.6	47.4±15.8 9.7±1.4	0.196^{NS}

Continuous variables are expressed as mean ± standard deviation while discrete variables are expressed as ratios. **CPB,** Cardiopulmonary bypass; **BSA,** Body surface area; **Ao X,** Aorta cross clamp; **Pre-op,** Preoperative; **UF,** Ultrafiltrate



patient's circulation and resulted in significant increase in hemoglobin and hematocrit values. In contrast to our findings Thompson et al. (2001) found no difference between CUF and MUF with respect to efficacy of hemoconcentration (i.e. Pre CPB vs. post CPB hematocrit) and requirements for postoperative blood products [11]. In their study in both the groups ultrafiltration was terminated after a predetermined volume of fluid was removed according to the formula. Volume to be removed = priming solution + additional fluid during CPB – CUF fluid – urine output. We think, because of this study design, it was not surprising that they found no significant difference between both the groups. In our study design our target was to achieve the desired hematocrit or to transfuse the entire left over fluid of CPB circuit to the patient.

Therefore it is important to consider the method used 40.9±4.9dified ultrafiltration while evaluating the outcomes of different studies. We think the method of achieving desired hematocrit level or by transfusing all the left over bl13.5±1.6 CPB circuit back to patient in concentrated form rather than removing predetermined volume, are more effective.

Our study confirms the results of previous studies [12-15] and revealed the superiority of MUF over patients not received MUF for the maintenance of desired hemoglobin and hematocrit levels after separation from CPB. Regarding effectiveness of modified ultrafiltration, we observed that use of MUF technique exclusively concentrates the circulating blood which is why hemoglobin and hematocrit showed a highly significant increase in a short period of time in children undergoing cardiac surgery with CPB. The volume of the residual blood in the CPB circuit decreases to zero within 5-10 minutes after MUF is initiated.

Table-2: Di performed modified ult

Procedures
ASD
AVSD
Glen's
MVR
T.C
PAPVR
VSD

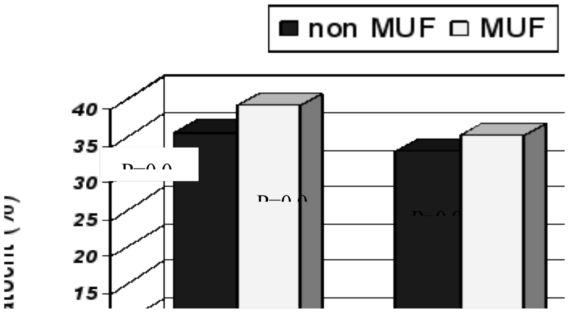


Fig. 4: Hematocrit Values during First Three Postoperative Days.

Data are expressed as numbers and percentages. **ASD,** Atrial septal defect; **AVSD, A**trio-ventricular septal defect; **MVR,** Mitral valve replacement; **T.C,** Total correction; **PAPVR,** Partial anomalous of pulmonary venous return; **VSD,** Ventricular septal defect; **NS N**on significant Partial anomalous of pulmonary venous return; **VSD,** Ventricular septal defect; **NS N**on significant

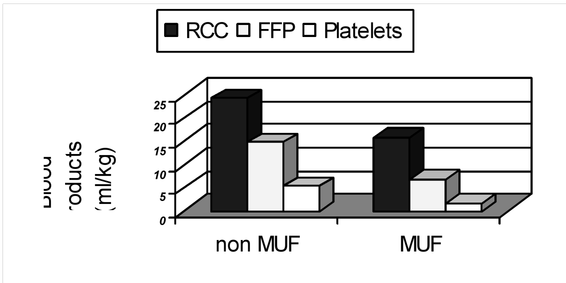


Fig. 2: Packed Red Blood Cells, Fresh Frozen Plasma and Platelets Required For Transfusion

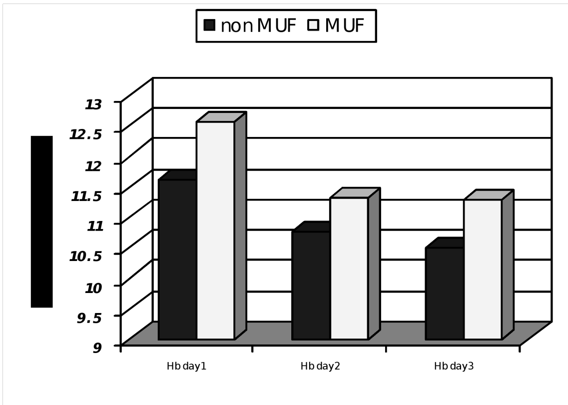


Fig. 3: Hemoglobin Concentration during First

Historically, open heart surgery has been associated with a high usage of blood transfusion. The high transfusion rates associated with cardiac surgery have been well characterized and are likely due to the coagulopathy, platelet dysfunction, and red cell hemolysis that occur as a result of the cardiopulmonary bypass circuit [16-19]. In current era, with the great concern over infectious spread of viral agents and potential immuno-suppressive effects, the avoidance of donor blood is an important goal. As modified ultrafiltration leads to an increase in hemoglobin and hematocrit levels after separation from CPB, it reduces the need for blood and blood products requirements for transfusion by both removing the excess water from patient's circulatory system and returning approximately all CPB circuit blood to the patient in a concentrated form. Many patients or their families do not wish to receive any more than the absolute minimum of donor blood. The use of MUF allows this situation to exist. Our data argue very strong in favor of the use of MUF in hemodilutional and moderate hypothermic CPB in pediatric cardiac surgery.

CONCLUSION

We observed from our present work that use of MUF is well tolerated in all the patients and resulted in significant increase in hemoglobin and hematocrit level and significantly less blood products required for transfusion. We submit that the use of modified ultrafiltration is an additional incremental strategy that may contribute to further improvements in outcome

LIMITATIONS

The technique of ultrafiltration makes a total blinding to the operating room team is impossible. Further more it was a large scale study comprises of 200 patients and it was difficult for us to randomize the patients.

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