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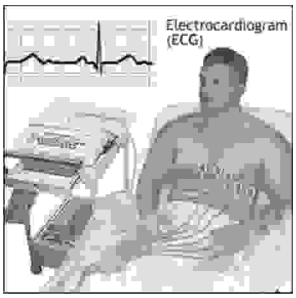
MODIFIED ULTRAFILTRATION IN ADULT CARDIAC SURGERY IS IT REALLY BENEFICIAL?

A POSPECTIVE RANDOMIZED CLINICAL TRIAL



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ABSTRACT ... safdar06@yahoo.com. **Background:** Cardiopulmonary bypass initiates systemic inflammatory response syndrome (SIRS) causing deleterious effects on various body systems with increased morbidity. Modified ultrafiltration (MUF) is a technique that removes excess water and inflammatory mediators from the circulation in the post-bypass period resulting in reduced bleeding, less blood transfusion requirements and overall reduced morbidity. **Materials and Methods:** 96 patients were randomly selected and divided into two groups. In Group I called MUF group (n=50), modified ultrafiltration was carried out for 15 min in the post bypass period. Group II called NON-MUFgroup (n=46), MUF was not carried out. Clinical assessment was based on ASA class. Mean cardiopulmonary bypass and aortic cross clamp times were 95.42 &56.94 min and 77.98 & 43.64 min in the MUF & NON-MUF groups respectively. Variables were expressed as mean and percentage. In the MUF group , there was increase in Hb by more than 2g/dl in 32 patients (64%) whereas in the NON-MUF group, this increase was only in 12 patients (20%). Mean postoperative chest drainage was far less (422 ml) in MUF group as compared to NON-MUF group (842.50 ml).Transfusion (449.12ml Vs 996.58 ml) and postoperative ventilatory requirements(40% Vs 47.8%) were also less in MUF group than NON-MUF group. Inotropic support was nearly comparable in both the groups but overall morbidity (Low cardiac output state, sepsis, reopening) was less in the MUF group (18%) as compared to NON-MUF group (30%). Mean ICU stay was also less in MUF group (mean 51.52 hrs) than in NON-MUF group (mean 55.43 hrs). One patient in each group died. **Conclusion:** Modified Ultrafiltration is associated with improved hemoglobin, less postoperative bleeding, reopening and transfusion requirements with overall reduced morbidity and ICU stay. However, the need for inotropes were not significantly different in the two groups.

Key words: Extracorporeal circulation, Modified ultrafiltration, inflammatory mediators.

INTRODUCTION

Extracorporeal circulation is notorious to initiate systemic inflammatory response syndrome (SIRS) with wide spread effects on various systems of body[1,2]. Major

physiological disturbances are caused by exposure of blood to synthetic surfaces, hemodilution, cellular breakdown, release of cytokines, temperature variations and non-pulsatile flow[3,4]. The heart, lungs, kidneys and coagulation system are primarily affected, however in some cases neurological and gastrointestinal disturbances are also seen[5].

Modified ultrafiltration (MUF) ensures removal of excess water and inflammatory mediators/debris at the end of cardiopulmonary bypass resulting in improved hemoglobin, reduced postoperative bleeding, transfusion requirements and overall reduced morbidity and mortality[6].

The fact that MUF attenuates the effects of post-perfusion syndrome has been studied well in infants and children but there is a limited experience in adult population.

A prospective randomized clinical study was conducted in our hospital - Armed Forces Institute of Cardiology/National Institute of Heart Diseases (AFIC/NIHD), a 300 bedded tertiary care cardiac institute to find out the impact of MUF on post-bypass hemoglobin, postoperative bleeding, reopening, blood/blood products transfusion requirements, need for inotropic support, duration of postoperative ventilation, ICU stay and over all morbidity.

Technical Considerations

After successful separation from cardio pulmonary bypass (CPB), venous cannula was left in right atrium, it was then cut and connected with a blood filled tubing from haemofilter called "modified ultrafiltration line" (MUF line). Arterial blood was allowed to drain from aortic cannula, it passed through the haemofilter where fluid was filtered out (suction applied at this level to maintain filtration volume of 90-110 ml/min) and this filtrated, concentrated blood was returned to the right atrium via MUF line, so a reverse of CPB circulation was adopted.

PATIENTS AND METHODS

After approval from the hospital research and ethical committee, this prospective randomized study was carried out. A total of 96 patients were randomly selected (Feb. 2006-April 2006) and divided into two groups.

Table-I. Demographic and operative date

MUF Group (n = 50)	**NON-MUF Group (n = 46)**
Age 15-70 year (mean 50.7 years) SD ± 14.7	Age 14-69 year (mean 48.7 years) SD ± 11.29
Male = 34	Male = 39
Female = 16	Female= 07
Mean CPB Time 95.42 min SD ± 27.05	Mean CPB Time 77.98 min SD ± 21.90
Mean Aorta X Clamp Time 56.94 min SD ± 14.28	Mean Aorta X Clamp Time 73.67 min SD ± 16.67
Operative Procedures	**Operative Procedures**
Coronary artery bypass graft 39 (including 8 emergency cases)	Coronary artery bypass graft 36 (including 3 emergency cases)
Mitral valve replacement 07 (incl. 01 re-do case)	Mitral valve replacement 06
Mitral & Aortic valve replacement 01	Aortic valve replacement 03
Aortic Valve Replacement 01	Coronary Artery Bypass 01
Atrial septal defect closure 02	Graft + Aortic Valve Replacement

In Group I called "MUF group" (50 patients), modified ultrafiltration was carried out after separation for CPB. Group II called "NON-MUF group" (46 patients), modified ultrafiltration was not carried out, however; continuous ultrafiltration was done in both the groups during CPB yielding 1.2–1.6 L filtrate. Patients less than 14 years of age and those with haemodynamic instability at the conclusion of CPB were excluded from the study. Risk stratification was based on ASA (American society of anaesthesiologists) Class.

Demographic details, operative procedures and ASA status are in table 1 & 2.

Table-II. ASA class

ASA Class	MUF (n=50)	%age	Non MUF (n=46)	%age
Class I	36	72%	31	67.4%
Class II	06	12%	14	304%
Class III	08	16%	1	2.2%
Total	50	100%	46	100%

Perfusion Methods

Cardiopulmonary bypass circuit was primed with Ringer's lactate (20 - 25 ml/kg), mannitol 20% (02 ml/kg), systemic heparinization 300 iu/kg body weight and methyl prednisolone (20 mg/kg). Non-pulsatile flow of 70–80 ml /kg body weight (2.4L/m^2 BSA) was used in all patients. Myocardial protection was achieved with blood cardioplegia (St. Thomas Solution 10ml added in 500 ml of autologous blood) and repeated with half dose of cardioplegic solution every 15–20 min. Systemic Hypothermia (32 C^0 core temperature) was maintained during surgical procedure. Activated clotting time (ACT) was estimated before administering heparin and kept > 480 seconds during CPB.

At the conclusion of cardiopulmonary bypass with stable haemodynamic and respiratory parameters, MUF was started. Drainage of blood was facilitated from aortic cannula, it then passed through haemofilter where filtrate got separated and then this concentrated blood was returned back to the right atrium via MUF line. Filtration rate of 90–110 ml/min was maintained for 15 min post bypass and overall 1.3–1.6 L filtrate was removed.

Monitoring during the procedure included ECG, non-invasive & invasive intra-arterial blood pressure, central venous pressure (CVP), oxygen saturation (SPO_2), arterial blood gases, serum electrolytes (Na^+, K^+, Ca^{++}), core & peripheral body temperature and urine output. Hemoglobin (Hb) and hemotocrit (Hct) during CPB and after the conclusion of MUF were estimated. Hb less than 9 gram/dl was an indication of packed red blood cell (PRBC) transfusion.

Patients in the MUF group were given half the calculated dose of protamine sulphate (3mg/kg body wt.) after the completion of MUF followed by activated clotting time (ACT) estimation. In the NON–MUF group, full dose of protamine (6mg/kg body wt.) was given. Mean cardiopulmonary bypass & aortic cross clamp times were 95.42 (SD±27.05) and 56.94 min (SD±14.28) in the MUF group and 77.98 min (SD±20.90) & 43.67 min (SD±16.67) in the NON-MUF groups respectively.

Patients with increased postoperative chest drainage, prolonged CPB time were given PRBC, fresh frozen plasma (FFP) and platelets concentrates on required basis.

Parameters studied include post-bypass & post-MUF Hb, chest drainage, quantity (in ml) of packed red blood cells (PRBC), fresh frozen plazma (FFP), & platelets transfused, reopening (due to excessive bleeding/cardiac tamponade), inotropic support required and duration of ventilation for more than 6 hours, mean ICU stay and overall morbidity. Results are shown in table III

Overall morbidity (cardiac temponade, low cardiac output state, respiratory failure, myocardial infarction, sepsis) was 18% in MUF group (9 patients) as compared to NON-MUF group 30.4% (14 patients).

It is important to note that much of the benefits of MUF were seen as improved Hb, less postoperative bleeding, transfusion requirements of PRBC, FFP & Platelets, need

for reopening and ICU stay, thus contributing to overall decreased morbidity.

However, need for inotropes and ventilatory support were not much different amongst the two groups.

Complications noticed during modified ultrafiltration were hypotension, hypothermia, atrial arrhythmias. Metabolic acidosis was noticed in ICU in 8 patients, all responded well to volume replacement therapy.

Table-III.

MUF Group (n=50)	**NON MUF Group (n=46)**
Mean post bypass Hb = 9.48g	Mean post bypass Hb = 8.45 g (range 6-10.6g/dl)
Mean Post MUF Hb = 10.69 (range Hb 7.4-13.3 g/dl)	Increase in Hb>2g/dl 12 patients (20%)
Increased in Hb>2g/dl in 32 pts (64%)	Mean chest drainage 8422.50 ml (range 350-1650 ml)
Mean chest drainage = 422 ml (range 100-1400 ml)	**TRANSFUSION REQUIREMENTS**
TRANSFUSION REQUIREMENTS (MEAN)	PRBC (36 units) 996.58 ml FFP (21 units) 504 ml Platelets 3 patients 294.29 ml
PRBC (34 units) 449.12 ml FFP (15 units) 360.40 ml Platelets(11 units) 161.82 ml)	Reopening 3 patients (6.52%)
Reopening 1 patient (02%)	Inotropes 19 patients (41.3%)
Inotropes 21 patients (42%)	Ventilation >6 hrs 22 patients (47.8%)
Ventilation > 6hrs 20 patients (40%)	Mean ICU stay = 55.43 hrs
Mean ICU stay= 51.52 hrs (Myocardial infarction = 3) (Low cardiac output & sepsis = 3) Respiratory failure = 2 Cardiac Temponade = 1	Morbidity =14 patients (30.4%) (Myocardial infarction = 2) Low cardiac output & sepsis = 6 Respiratory failure = 3 Cardiac temponade =3

DISCUSSION

It is well known that extracorporeal circulation induces systemic inflammatory response syndrome (SIRS) with release of inflammatory mediators in the body causing fluid overload, hemodilution, coagulation disturbances, tissue edema and decreased end organ perfusion, all contributing to increased morbidity[7]. Much of the benefits of MUF has been claimed in children in controlling the SIRS and only limited experience exists in adult population[8]. only two trials on selected patients for CABG surgery exist with unconvincing data[9]. Recently, cardiac surgery has grown up to include more high risk patients with advanced age & comorbidities, emergency procedures, complicated surgeries including re-operations requiring prolonged CPB times[10].

Our randomized trial was carried out to see whether the MUF has any beneficial effects in improving hemoglobin, reducing CPB related bleeding complications & transfusion requirements, reopening, inotropic support, duration of ventilatory requirements, ICU stay and to overall lowering the morbidity.

Of all the variables studied, the impact of MUF was greatly seen in improving Hb (>2g/dl in 64% cases of MUF group as compared to 26% cases of NON-MUF group). There was strikingly reduced postoperative chest drainage in MUF group as compared to NON-MUF group

(422.20ml versus 842.50ml respectively). Requirements of PRBC, FFP & platelets was far less in MUF than in Non-MUF group. It is interesting to note that in the MUF group there were more high risk patients (ASA Class III & Emergency cases, increased CPB & aorta cross clamp time) as compared to Non-MUF group. In MUF group 08 patients (16%) were from ASA Class III whereas in Non-MUF group only 01 patient (2.2%) was from ASA Class III.

08 patients in the MUF group were operated upon for CABG in emergency due to acute severe myocardial ischemia and all of them were on heparin and tirofiban preoperatively and none of them was reopened for excessive bleeding whereas only 03 patients in the NON-MUF group were operated for emergency CABG and 01 of them was reopened for cardiac tamponade due to excessive bleeding. With MUF crystalloid overload is reduced and dilutional coagulopathy becomes less marked. It is well documented that dilutional coagulopathy is of more clinical significance in paediatric population as compared to adults where platelets dysfunction and abnormal fibrinolysis play a more significant role[11].

Previous two studies of CABG patients could not determine the role of MUF in controlling bleeding and in one of these studies even aprotinin (kinin inactivator) was also used[12]. whereas none of our patients received aprotinin.

It is documented that MUF improves global left ventricular function in children with congenital heart disease but in our study, the need for inotropic support was nearly equal (rather slightly more in MUF group) in MUF and NON-MUF groups (42% and 41.30% respectively), probably other factors like myocardial stunning, cardiopulmonary bypass and aorta cross clamp time (causing ischemia), complexity of cardiac disease and surgical procedure, all may have more pronounced role in deciding the initiation of inotropic support rather than the effects of modified ultrafiltration alone[13].

Much of the benefits of ultrafiltration on pulmonary functions has been claimed in children but duration of ventilation and time to extubate them in ICU remains controversial in determining the evidence of pulmonary complications[14].

However, there is an evidence that less intrapulmonary shunting occurs in patients who undergo ultrafiltration[15]. In our study, less postoperative ventilatory support (less than 6 hours) was required in MUF group (40%) as compared to NON-MUF group (47.8), although this difference was not marked, yet it was observed in ICU that patients who had undergone MUF maintained better oxygenation in the postoperative period and this is supported by the randomized controlled study of Battista Luciani and associates[16,17]. Mean ICU stay was also less in MUF Group. Despite all the benefits of MUF in reducing the morbidity, it is difficult to define the exact factors determining the in-hospital morbidity, however overall morbidity (bleeding, reopening, postoperative MI, low cardiac output syndrome, respiratory failure & sepsis) was less in MUF group (18%) as compared to NON-MUF group (23%). Mortality figure was nearly comparable as three patients in each group died 6% and 6.5% respectively, this is in consistence with most of the adult and paediatric series[16].

Some other advantages of MUF are removal of air or debris from the ascending aorta while the blood is being drained during ultrafiltration, less protamine requirement to neutralize residual effects of heparin as most of it is removed during filtration (we used half the calculated dose of protamine in MUF group followed by ACT estimation), thus obviating some of its ill effects.

Complications noted during MUF were hypotension,hypothermia and metabolic acidosis, all responded well to volume infusion and gradual rewarming, atrial arrhythmias (may be due to hypokalemia or aright atrial manipulation during procedure) were self limiting and did not result in hemodynamic compromise.

Limitations

As the complications and morbidity associated with CPB are vast, it is difficult to study multiple interdependent and independent parameters in one study for which probably

larger trials are required. Secondly, we do not have the facilities to measure the levels of inflammatory mediators or to determine platelets function directly.

CONCLUSION

Modified ultrafiltration removes fluid overload and inflammatory mediators associated with CPB thus contributing to less bleeding, blood transfusion requirements or re-explorations and results in overall reduced morbidity. It is cost effective with no threatening complications and hands over a relatively dried up, less oozy and better oxygenated patient to ICU.

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