JECT. 2001;33:223–226
The Journal of The American Society of Extra-Corporeal Technology

Balanced Ultrafiltration, Modified Ultrafiltration, and Balanced Ultrafiltration with Modified Ultrafiltration in Pediatric Cardiopulmonary Bypass

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Presented at AmSECT's 39th International Conference in Miami Beach, Florida on March 22–25, 2001

Abstract: This study evaluates the effect of balanced ultrafiltration, modified ultrafiltration, and balanced ultrafiltration with modified ultrafiltration on inflammatory mediators in children's open-heart surgery. Eighty children with congenital heart disease were randomly divided into four groups: control group (C group); balanced ultrafiltration group (BUF group); modified ultrafiltration group (MUF group); and balanced ultrafiltration with modified ultrafiltration group (B+M group). Clinical data of these groups were similar. Tumor necrosis factor (TNF), interleukin-8(IL-8), and E-selectin were measured at the beginning of cardiopulmonary bypass (CPB), 30 min later, at the cessation of CPB, at the cessation of MUF (MUF group and B+M group), and 2 hours postoperatively. During CPB, the concentrations of TNF, IL-8, and E-selectin increased significantly in C and MUF groups and did not change significantly in BUF and B+M groups. In the period of MUF, TNF and IL-8 increased; whereas, E-selectin did not change. The study shows that ultrafiltration can filter out the inflammatory mediators, but only BUF can decrease the concentrations of them. Moreover, MUF only can concentrate blood. Combining both techniques has both effects, but the effect of BUF was offset by MUF. **Keywords:** ultrafiltration, cardiopulmonary bypass, inflammatory mediator. *JECT. 2001;33:223–226*

Cardiopulmonary bypass (CPB) has been implicated as a major cause of edema and inflammatory reaction, which leads to morbidity and mortality after open-heart surgery. It has been suggested that the use of ultrafiltration can filter out excessive water and low molecular weight inflammatory mediators (1, 2). Several different methods of ultrafiltration have been documented (3, 4). Balanced ultrafiltration (BUF) was used to ultrafiltrate patients during the whole CPB time. In our previous study, we found the concentrations of some inflammatory mediators; for example, tumor necrosis factor (TNF), did not decrease during modified ultrafiltration (MUF) (5). The objective of this study was to evaluate the effect of BUF, modified ultrafiltration (MUF), and BUF with MUF(B+M) on inflammatory mediators in pediatric open-heart surgery.

MATERIALS AND METHODS

The study protocol was approved in advance by the ethical committee of Shanghai Children's Medical Center. Eighty children with congenital heart disease were randomly divided into four groups: a control group (C group), a BUF group, a MUF group, and a group with both techniques (B+M group), 20 patients in each group. Patient characteristics including age, weight, bypass time, aortic cross clamp time, and diagnosis are shown in Table 1.

CPB Techniques

A roller pump system (Sarns 8000; Sarns Inc./3M Health Care; Ann Arbor, MI) and a membrane oxygenator (Minimax Plus; Medtronic Inc., Anaheim, CA) were used in all cases. Lactated Ringer's solution was used as the basic priming solution, and packed red blood cells, fresh frozen plasma, and 20% albumin were used to maintain the hemotocrit at approximately 25% and colloid pressure about 12 mmHg. The total priming volume was 600–650 mL.

Anticoagulation was achieved with an initial bolus of 2 mg/kg heparin injected into the right atrium before cannulation. Another 15–20 mg was added to the priming solution. Moderate hypothermia (25–28°C) was used in all patients. The pump flow rate was adjusted depending on body temperature. Alpha-stat blood gas management was used and sodium bicarbonate was administered when necessary. According to the blood concentration of calcium,

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Received March 25, 2001; accepted October 11, 2001.

Table 1. Patient characteristics.

	C Group	BUF Group	MUF Group	B+M Group
Age (years)	2.10 ± 1.10	2.42 ± 1.08	2.23 ± 1.52	2.15 ± 1.27
Weight (kg)	11.02 ± 1.95	11.05 ± 1.72	10.78 ± 2.22	9.70 ± 2.23
Bypass time (min)	62.4 ± 23.2	58.5 ± 22.2	67.3 ± 20.5	68.9 ± 22.0
Aortic clamp time (min)	34.3 ± 14.4	42.6 ± 21.7	40.8 ± 16.1	42.5 ± 14.2
Diagnosis				
VSD	13	14	13	14
TOF	7	6	7	6

the calcium was used at 5–10 min after the heart began rebeating. Myocardial preservation was achieved using crystalloid St Thomas's solution in a dose of 15 mL/kg initially with a subsequent half-dose every 20 min.

Ultrafiltration Techniques

An ultrafiltrator (Minntech Hemoconcentrator 0.3m^2; Minntech, USA) was placed with the inlet connected to the arterial line and the outlet to the venous line in BUF, MUF, and B+M groups. An additional roller pump was used to control the ultrafiltration flow rate. Negative pressure of 50–100 mmHg was applied to the filtrate port during the time of BUF or MUF.

BUF

After the time of aortic clamping, BUF begins with a flow rate of 8–10 mL/kg/min and stops at the same time of CPB stopping. During the period of BUF, lactate Ringer's solution whose volume is in congruity with that of ultrafiltrate is added in the venous reservoir.

MUF

The ultrafiltrator was kept isolated during bypass by clamping the inlet line. After the patient was weaned from bypass and became hemodynamically stable, the inlet of the ultrafiltrator was released, and ultrafiltration was commenced with a flow rate of 10–30 mL/kg/min. The venous reservoir was kept primed by Ringer's lactate solution. MUF time was 10–12 min.

Variables Recorded

Blood samples were taken at the following points in time: the beginning of CPB(5 min after CPB started), 30 min later, at the cessation of CPB, at the cessation of MUF (MUF group and B+M group), and 2 h postoperatively. TNF, IL-8 and E-selectin were measured.

Statistical Methods

Data were analyzed with analysis of variance (ANOVA) to compare results of groups and a paired Student's-*t* test was used to compare data within each group. All results are expressed as means ± standard error. Statistical significance was defined as $p < .05$.

RESULTS

All patients survived the surgery and were discharged in good condition. No complications directly attributable to the ultrafiltration were observed.

The volumes of ultrafiltrate were 815.0 ± 300.9mL (550–1200 mL) in BUF group and 394.4 ± 81.4 mL (280–500 mL) in MUF group. In B+M group, 996.5 ± 513.7 mL (530–1500 mL) and 361.7 ±121.6 mL (250–500 mL) ultrafiltrate were removed by BUF and MUF, respectively. In the MUF group, the hematocrits increased from 24.1 ± 2.9% to 33.7 ± 1.7% compared to 23.7 ± 2.7% to 34.3 ± 2.1% in the B+M group.

TNF

There was no significant difference in four groups preoperatively. During CPB, TNF concentration increased significantly ($p < .05$) in C and MUF group and did not change significantly in the other two groups. Then, during MUF, the concentration increased slightly in the MUF and B+M group ($0.1 > p > .05$).

IL-8

Though the concentrations of IL-8 increased significantly in C and MUF groups during CPB, there were no significant differences in four groups at the cessation of CPB. During MUF, they increased significantly in MUF and B+M group. IL-8 concentration was significantly higher in MUF group than that in B+M group ($p < .05$). 2 h postoperative, the concentrations show no differences in four groups.

E-Selectin

During CPB, the concentrations of E-selectin also increased in C and MUF groups ($p < .05$), and they decreased slightly in BUF and B+M groups ($0.05 < p < .1$). During MUF, they did not change significantly. At 2 h after operation, the concentrations of all three substances did not significantly differ in all groups (Table 2).

Clinical Observations

There were no significant differences in chest drainage or urine output among four groups for the first 24 h postoperatively. The days spent on ventilator and the duration

Table 2. Concentration of TNF, IL-8, E-selectin.

		CPB Begin	30 min Later	Bypass Stop	MUF Stop	2 hours Postop
TN F (ng/mL)	C group	10.46 ± 2.94	10.96 ± 3.59	13.63 ± 4.17**		10.62 ± 3.34
	BUF group	11.43 ± 2.97	11.96 ± 3.72	12.27 ± 3.82		10.36 ± 3.29
	MUF group	10.77 ± 3.44	11.85 ± 2.90	13.47 ± 3.92**	14.59 ± 5.31**	11.85 ± 3.87
	B+M group	11.53 ± 4.14	11.15 ± 3.47	11.64 ± 3.53	12.28 ± 3.57	11.61 ± 2.90
IL-8 (ng/mL)	C group	4.02 ± 1.21	3.97 ± 1.01	4.56 ± 1.22**		3.73 ± 0.92
	BUF group	4.24 ± 1.02	4.20 ± 1.14	4.38 ± 1.15		3.95 ± 1.05
MUF group		3.82 ± 0.79	4.03 ± 1.07	4.74 ± 1.02*	6.91 ± 1.96**	4.08 ± 1.08
	B+M group	4.12 ± 1.15	4.12 ± 0.93	4.32 ± 0.78	5.14 ± 1.14	4.31 ± 1.73
E-sel ectin (p g/mL)	C group	25.21 ± 6.59	27.09 ± 8.88	29.79 ± 8.47**		25.12 ± 7.11
	BUF roup	26.12 ± 4.70	28.20 ± 5.96	25.20 ± 4.02		25.68 ± 5.62
	MUF group	24.77 ± 6.53	26.28 ± 5.10	30.66 ± 6.79**	29.16 ± 7.18**	23.90 ± 5.82
	B+M group	25.88 ± 6.34	25.30 ± 5.81	22.12 ± 5.75	24.23 ± 4.49	26.27 ± 5.76

*$p < .05$ between groups.
**$p < .05$ compare to the CPB begin in same group.

of stay in the intensive care unit did not significantly differ either.

DISCUSSION

Because of hypothermia, the exposure of blood on large areas of synthetic material surfaces and so on, cardiopulmonary bypass is a powerful agonist for the production and release of inflammatory mediators. Now ultrafiltration is used to ameliorate inflammatory reaction.

Ultrafiltration, as an old technique, was used before 1953 when Gibbon did the first CPB operation. However, it was also regarded as a new one, because MUF method was set up by Naik in 1991 (6). This method is a technique that mainly ultrafiltrated the patient after separated from bypass to reverse hemodilution occurring during cardiac operations. In pediatric CPB, MUF has been shown to reduce total body water, increase arterial pressure, increase cardiac index, and decrease pulmonary vascular resistance. Moreover, some studies have demonstrated that some inflammatory mediators can be removed by ultrafiltration (7, 8). Thereafter, ultrafiltration came of age, and many ultrfiltration methods were developed; for example, dilutional ultrafiltration (9), balanced ultrafiltration (3), venous–venous modified ultrafiltration (4), and so on.

This study and our early study (5) demonstrated that ultrafiltration can remove some inflammatory mediators, for example: E-selectin and endothelin. Especially during CPB, the BUF technique can decrease the concentrations of them by filtering out the water and adding "fresh" water into reservoir. Some studies showed MUF can remove some inflammatory mediators (2, 9), but in our early study, we found the concentrations of TNF, IL-8, and ET did not decrease (5). The concentration of TNF even increased during MUF. In this study, this phenomenon also occurred. According to the results of BUF, we can imagine that MUF can also remove some mediators, but because it only removes some water without adding "fresh" water, which can dilute the inflammatory mediators, MUF can only filter them out in isoconcentration and cannot decrease the concentrations of them. However, in this study, the concentration of IL-8 increased significantly during MUF, but it did not change markedly in the earlier study. We were surprised at this phenomenon. We compared these two studies and found two differences between them. First, the flow rate of MUF in this study is higher. This technique has been used in our hospital for more than 5 years. It was found that during MUF time, the hemodynamics improved, so we tried to increase the flow rate to shorten the time. At the beginning of MUF, the flow rate of 10mL/kg/min was used and added slowly to 20–30 mL/kg/min when hemodynamics became stable. Thus, blood was concentrated to the same level as previous study but the time, about 5 min, was saved. Second, the negative pressure was lower. With the higher flow, lower pressure was needed. 50–100 mmHg was added to ultrafiltrator; whereas, 150 mmHg was added in the earlier study. It was inferred that IL-8 may combine with protein and the higher negative pressure is helpful to decompose them, so more IL-8 can be filtered out than in the earlier study. During MUF, the concentration of IL-8 increased more in the MUF group than in the B+M group may result from the new synthetic surface of ultrfiltrator contacting with the blood. In this study, we also found the control group had lower values for all mediators at 2 h postoperatively. It is interesting and requires further study.

Clinical benefits, such as reduction of duration of mechanical ventilator by using hemofiltration reported by Journois (10) and the postoperative bleeding reduction observed by Naik (1), were not observed in this study. This may be attributed to the fact that the malformation of the patients included was not severe.

This study showed that the inflammatory mediators did not decrease during MUF. The patients with MUF were also uneventful in ICU. Hennein (4) also reported the patients with conventional ultrafiltration or venovenous

MUF had rapid clearance of IL-10, an anti-inflammatory cytokine. All of them suggest the inflammatory reaction can be ameliorated by ultrafiltration. The mechanism of it may be connected not only with the concentrations of known inflammatory mediators but some unknown substances or other causes. In addition, this study also shows different inflammatory mediators have different sieving coefficients, so TNF and IL-8 increase during MUF; whereas, E-selectin does not.

This study showed that BUF can decrease the concentrations of inflammatory mediators, MUF can concentrate the blood efficiently, and using both of them may have combining effects, but the effect of BUF was offset by MUF.

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