To cite this article: Bozdogan D, Sirlak M, Eyileten Z, Uysalel A. Effects of modified ultrafiltration on postoperative hepatic and renal function of pediatric patients with congenital cyanotic/non-cyanotic heart defect who underwent open heart surgery: Retrospective study. Turk J Clin Lab 2020; 5: 378-386.

Original Article

Effects of modified ultrafiltration on postoperative hepatic and renal function of pediatric patients with congenital cyanotic/non-cyanotic heart defect who underwent open heart surgery: Retrospective study

Açık kalp cerrahisi uygulanan siyanoti/non-siyanotik konjenital kalp hastalıklarında modifiye ultrafiltrasyonun postoperatif karaciğer ve böbrek fonksiyonları üzerine etkisi: Retrsopektif çalışma

Deniz BOZDOGAN*[1], Mustafa SIRLAK[2], Zeynep EYILETEN[2], Adnan UYSALEL[2]

[1]Bakircay University, School of Medicine, Cigli Training and Research Hospital, Departmant of Cardiovascular Surgery, Izmir/TURKEY
[2]Ankara University, School of Medicine, Department of Cardiovascular Surgery, Ankara/TURKEY

Abstract

Aim: Increased total body water and capillary permeabilty in pediatric cardiopulmonary bypass can cause organ disfunction. Modified ulltrafiltration is developed to decrease total body water and attenuate organ disfunction. The purpose of this study, is to investigate retrospective effects of modified ultrafiltration on postoperative hepatic and renal functions of pediatric patients with congenital cyanotic/noncyanotic heart defect who underwent open heart surgery.

Material and methods: In this study, we assessed 93 children who underwent pediatric cardiac surgery with cardiopulmonary bypass from January 2009 to August 2011.Patients were divided into two groups. Group 1 (n=62) patients, to whom modified ultrafiltration was performed, compared with 31control patients (group 2). Patients who had redo cardiac surgery, preoperative organ disfunction, autoimmune disease, genetic disorders, shunt and emergency operations were excluded. Pre and postoperative biochemical parameters, postoperative urinary output, chest tube drenaige, diüretic usage, blood and blood product transfusion, dialysis requirement and mortality were compared.

Results: Age, weight, body surface area, congenital defect type and number, preoperative and intraoperative blood samples measurement, cross clamp time, cardiopulmonary bypass time were similar between 2 groups (p>0,05). The percant increase in creatinine level was statistically significant between the two groups, when these changes were re-evaluated according to the body surface area by univariate analysis(p<0,05). Percent increase in total plasma protein level was also statistically significant between the groups (p<0,05) (6,5% in group 1 and -5,5% in group 2). Percent increase in plasma albumin level was -18,2% in group 1, and -13,4% in group 2. When these changes were re-evaluated according to the body surface area by univariate analysis, a significant statistical difference was detected. (p<0,05). While two patients required dialysis in group 1, dialysis was performed in 4 patients in group 2. There was no statistical difference between the groups in terms of dialysis needed(p<0,05). There was no difference between the groups in terms of mortality (p>0,05)

Conclusion: Hemodynamic, pulmonary, hematologic and immunologic effects of modified ultrafiltration are well known. Although our study group was not big enough to get a conclusion, we believe that modified ultrafiltration can be an effective method in preservation of renal and hepatic function of the patients who underwent total reconstructive congenital heart surgery.

Keywords: modified ultrafiltration; cardiopulmonary bypass; pediatric open heart surgery

Corresponding author*: Deniz Bozdoğan, Bakircay University, School of Medicine, Cigli Training and Research Hospital, Departmant of Cardiovascular Surgery, Izmir/TURKEY
E-mail: denbozdogan@gmail.com
ORCID: 0000-0002-0572-2008
Recevied: 04/05/2020 accepted: 15/08/2020
Doi: 10.18663/tjcl.834290

Volume 11 Number 5 p: 378-386

Öz

Amaç: Pediatrik kardiyopulmoner baypas total vücut sıvında ve damar geçirgenliğinde artmaya neden olur. Dokular aralarına sızan bu sıvı organ fonksiyonlarında bozulmalara neden olmaktadır. Modifiye ultrafiltrasyon çocuklarda kardiyopulmoner baypasa bağlı oluşan toplam vücut sıvı artışının neden olduğu organ fonksiyon bozukluklarını önlemek amacıyla geliştirilmiştir. Bu çalışmada amacımız konjenital kalp hastalığı nedeni ile kardiyopulmoner baypas kullanılarak opere edilen siyanotik ve siyanotik olmayan çocuklarda MUF kullanımının karaciğer ve böbrek fonksiyonları üzerine etkisiniaraştırmaktı.

Gereç ve Yöntemler: Ocak 2009 ile ağustos 2011 yılları arasında Ankara Üniversitesi Tıp Fakültesi Kalp ve damar cerrahisi kliniğinde opere edilen modifiye ultrafiltrasyon kullanılan (grup 1) n:63, kullanılmayan (grup 2) n:31 toplam 93 hasta çalışmaya dahil edildi. Daha önceden bilinen operasyon ve organ fonksiyon bozukluğu olan, acil şartlarda operasyona alınan, sistemik ve otoimmün hastalığı olan ve kompleks kardiyak anomali nedeni ile parsiyel düzeltme yapılan hastalar çalışmaya dahil edilmedi. Organ fonksiyonlarının değerlendirilmesi amacıyla operasyon öncesinde ve sonrasında kan örnekleri alındı. Hastalar operasyon sonrası ilk 8 ve 24.saat idrar miktarı, drenaj miktarı, diüretik kullanımı, inotrop kullanımı, kan ve kan ürünü kullanımı, diyaliz ihtiyacı ve mortalite açısından retrospektif olarak incelendi.

Bulgular: Preoperatif verileri ve operasyon verileri açısından gruplar benzerdi. Grup 1 için kreatinin düzeyinin operasyon sonrasında yüzde değişim oranı %56,5, grup 2 için %25,8 olarak hesaplandı. Vücut yüzey alanına göre univaryant analizde anlamlı olarak bulundu. (p:0,031<0,05) Total protein değerlerinin operasyon sonrası değişim yüzdesi (-)%6,5, grup 2 için (-)%5,5 olarak hesaplandı. Bu sonuçlar istatistiksel olarak anlamlı bulundu. (p:0,04<0,05) Albümin düzeylerindeki yüzde değişim oranı açısından grup1 (-)%18,2, grup 2 için (-)%13,4 olarak hesaplandı. Bu değişimler vücut yüzey alanına göre yeniden univaryant analiz ile değerlendirildiğinde anlamlı istatsitiksel fark saptandı (p=0,05). Grup 1 için dializ ihtiyacı olan hasta sayısı 2, Grup 2 için 4 hasta olarak bulundu. Bu sonuç istatistiksel olarak anlamlı bulundu (p=0,05). Mortalite grup1 için 4 hasta, grup 2 için 1 hasta olarak bulundu. Mortalite açısından gruplar arasında anlamlı istatistiksel fark hesaplanmadı (p>0,05).

Sonuç: Pediatrik açık kalp cerrahisinde modifiye ultrafiltrasyonun kullanımının böbrek yetmezliği gelişimini azalttığı ve karaciğer fonksiyonlarını koruduğunu düşünmekteyiz.

Anahtar kelimeler: modifiye ultrafiltrasyon; kardiyopulmoner baypas; pediatrik açık kalp cerrahisi

Introduction

In cardiopulmonary bypass, the body's defense cells and proteins are activated as a result of contact of blood with non-epithelial surfaces. This condition, called systemic inflammatory response syndrome (SIRS), is one of the mechanisms responsible for the undesirable effects of CPB.[1]

After the surface contact, the complement system is activated. Inflammatory mediators join the circulation. These mediators affect vascular endothelial permeability, heart function, intestinal fluid amount, coagulation system and end organ functions.[2]

Unlike adult patients, pediatric patients undergoing open heart surgery via cardiopulmonary bypass are more susceptible to both excessive body fluid increase due to high prime volume and systemic inflammatory response, because of incomplete maturation of organs and tissues. Various ultrafitration strategies developed to reduce cytokines and fluid load have also been used for pediatric patients.[3] Zero balanced modified ultrafiltration(MUF) is one of these strategies. It has been claimed that modified Ultrafiltration, developed to reduce excess fluid in the body, helps to remove inflammatory cytokines from the circulation and reduces the effects of some mediators by filtering them.[4]

Like many other organs, impaired liver function is common after CPB. High transaminases, hyperbilirubinemia, decrease in coagulation factors, prolongation of coagulation parameters and increase in bleeding can be detected. Total body protein may be reduced, making it difficult to retain body fluid in the intravascular space. it can also cause hepatorenal syndrome. Depending on the inability to remove toxic agents, toxic ileus may develop as well as central nervous system changes. even hepatic coma may develop.[5] Due to all these factors, mortality and morbidity increase.[6] As claimed in some studies, liver functions can be preserved and the incidence of hyperbilirubinemia can decrease with the use of MUF.[7] MUF can also assure a significant difference in the amount of chest tube drainage and in the development of hepatic coma and hepatorenal syndrome.[8]

Hemoconcentration provided by modified ultrafiltration has

positive effects on the clotting system. In a study conducted by Chew et al.[9], It was found that the use of blood and blood product and chest tube drainage significantly decreased in patients undergoing MUF compared to the CUF and control group. In the same study, fibrinogen, factor VII (FVII) levels were increased, while platelet count, factor IX (FIX) and factor X (FX) levels did not change.

MUF targets a higher hematocrit (Hct) value than before CPB. In this way, it provides hemoconcentration of blood and increases in total body protein and albumin levels.[10] Children underdeveloped kidney function can be preserved. Studies have been claimed to prevent impaired kidney function even if it does not improve kidney function significantly.

Material and Methods

This study was carried out in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the Ankara University Faculty of Medicine, Ankara, Turkey.

In this study, between January 2009 and August 2011 at Ankara University Faculty of Medicine Cardiovascular Surgery Cebeci Heart Center, the data of patients with cyanotic and non-cyanotic heart disease and operated under cardiopulmonary bypass were collected. In order to investigate the effect of using zero-balanced MUF on kidney and liver functions, Patients were divided into two groups. 62 patients who were operated after routine use of the technique in the first group (group 1) and 31 patients who were operated before the routine use in the second group (group 2) were included. The data of 93 patients were collected and analyzed retrospectively. Patients with a body weight between 3 and 30 kg and without any previous known systemic autoimmune, genetic, kidney and liver diseases, who were not used total circulatory arrest technique, who were not performed emergency / urgent surgery, who did not have heart failure and who did not have shunt surgery were included in the study.

All patients were hospitalized one week before the operation and evaluated by the pediatric cardiology specialist and pediatric infection diseases specialist. Dental diseases were consulted in terms of focal infection focus. 1 day before the operation, all rutine blood sample tests were reevaluated.

Cardiopulmonary bypass was established in all patients by aortobicaval cannulation with median sternotomy. Mild to moderate (28-32^{o}C) hypothermia was achieved during cardiopulmonary bypass. After cardiopulmonary bypass was terminated, the previously integrated MUF cycle has been activated and filtration was performed. Care was taken to maintain stable hemodynamics during the procedure. The hematocrit value was increased to 35% -40% levels. After the MUF process, decanulation was done. The bleeding control was completed and the sternum was closed with steel wires and transferred to the cardiovascular surgery intensive care unit. All surgical procedures were performed by the same surgical team.

Blood samples were collected from all patients in the early postoperative period (immediately after the operation and 8 hours after the operation) and at the 24th hour.

In our study, BUN, creatinine, total protein and albumin values were collected from the blood samples that were collected in the preoperative, postoperative 8th and 24th hour to evaluate kidney function. In addition, the total amount of fluid delivered to the patient, total urinary output and chest tube drainage, as well as the need for furosemide, duration of hospitalization and intensive care unit stay and the amount of blood and blood products were recorded. The need for hemodialysis and / or peritoneal dialysis was also noted.

Evaluation of liver function was made by preoperative, postoperative early (8th hour) and postoperative 24th hours value of AST, ALT, GGT, ALP, LDH, TOTAL PROTEIN, ALBUMIN, TOTAL / DIRECT BILIRUBIN, INR, APTT values. In addition, the amount of chest tube drainage and blood and blood product usages were also collected during intensive care follow-ups.

Statistical Analysis

SPSS 17.0 package program was used for statistical analysis of the data. Categorical measurements were summarized as numbers and percentages, and continuous measurements as mean and standard deviation (median and minimum - maximum where necessary). Chi-square test statistics were used to compare categorical measurements between groups. In the comparison of continuous measurements between groups, T test (Student T Test) was used in independent groups, and Mann Whitney U test was used if assumptions were not provided. Spearman Correlation test statistics were used to compare continuous variables between groups. Due to limited sample size, intensive care unit's datas were recalculated according to body mass index by univariate analysis. Statistical significance level was taken as 0.05 in all test.

Results

In our study, the number of patients is an important limiting factor. In some critical data, a mathematical difference was detected, but no statistical significance was found. Also there is not enough data to be used to evaluate the systemic inflammatory response, In addition, the fact that the deterioration in the basic biochemical parameters showing end organ damage is mathematically less.

The diagnosis and operation data of the patients are presented in Table 1 below.

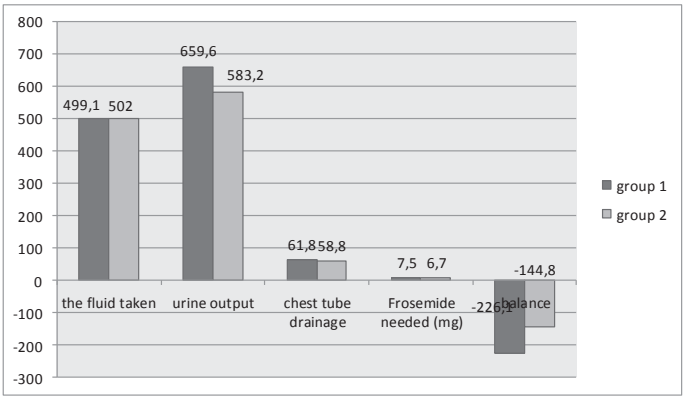
Volume 11 Number 5 p: 378-386

Table 1. Patient Diagnoses and Operations by Groups				
Diagnosis	Operation	Group:1	Group:2	Total
ASD	ASD closure	10	11	21
ASD, PDA	ASD closure, PDA ligation	1	0	1
VSD	VSD closure	20	6	26
VSD, PDA	VSD closure, PDA ligation	1	1	2
VSD, PS	VSD closure, with transanüler patch	1	0	1
ASD,VSD	ASD clusure, VSD closure	3	3	6
AVSD	Closure with Modified single patch technique	8	6	14
AVSD, PDA	Closure with Modified single patch technique, PDA ligation	1	1	2
TOF	Total correction	12	2	14
SUBAORTIC MEMBRAN	Closure with Modified single patch technique	4	1	5
COR TRİATRİATUM	Membran excision	1	0	1
Total		62	31	93
ASD, atrial septal defect; VSD, ventriculer septal defect; PDA, patent ductus arteriosus; PS, pulmonery stenosis; AVSD, atrioventriculer septal defect; TOF, Tetralogy of Fallot				

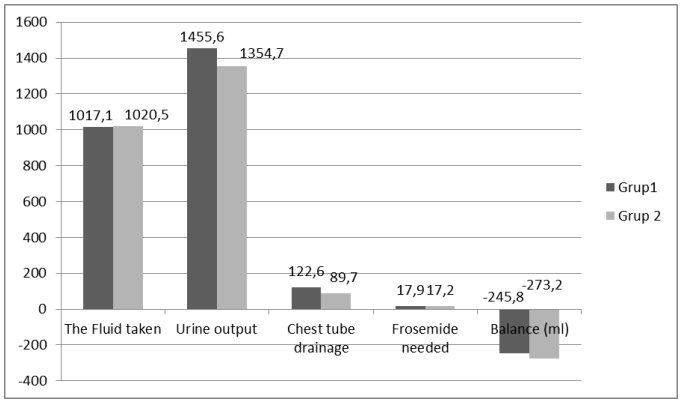
The demographic data and preoperative blood sample results of the study groups are presented in Table 2 below. There was no statistical difference between the groups(p> 0.05).

There was no statistically significant difference between the study groups in terms of intraoperative data. (p> 0.05) (Table 3)

İntensive care unit datas were collected and presented in graph 1 for first 8 hours and graph 2 for first 24 hours.



Graphic 1. First 8 hours of ICU data



Graphic 2. First 24 hours ICU data

Table 2. Demographic data			
Gender(M/F)	Group:1 (n:62)	Group:2 (n:31)	P value
	28/34(%45-55)	19/12(%62,1-37,9)	0,552
	(mean)	(mean)	
Age (ay)	49,5	38,5	0,420
Weight (kg)	14,5	12,4	0,425
Body surface area (kg/m^2)	0,59	0,54	0,554
BLOOD SAMPLES			
BUN (mg/dl)	11,4	11,0	0,546
CRE (mg/dl)	0,59	0,8	0,193
SODIUM	138,4	139,7	0,783
POTASSIUM	4,01	4,2	0,806
TOTAL BODY PROTEIN (g/dl)	6,62	6,8	0,195
ALBUMIN (g//dl)	5,73	4,6	0,078
TOTAL BILIRUBIN (mg/dl)	0,61	0,6	0,352
DIRECT BILIRUBIN (mg/dl)	0,14	0,2	0,816
ALT (U/L)	21,5	31,1	0,708
AST (U/L)	46,3	40,2	0,841
GGT (U/L)	14,7	22,9	0,535
LDH (U/L)	372,8	441,6	0,443
ALP (U/L)	158,6	194,4	0,204
BLEEDING PROFILE			
APTT (second)	31,9	31,7	0,473
INR	1,13	1,09	0,232
INFLAMMATORY MEDIATOR CRP (mg/L)	2,2	3,0	0,725
BSA, Body surface area; BUN, blood ürine nitrogen; CRE, creatinin; ALT, alanin aminotransferase; AST, aspartat aminotransferase; GGT, gama glutamyl transferase; LDH, lactat dehydrogenase; ALP, alcaline phosphatase; APTT, actived prothrombin time; CRP, C- reactive protein.			

The groups were compared in terms of ICU data and it is presented in Table-4 and Table-5 below. Percent changes between postoperative values were evaluated. Due to the limited number of samples, intensive care data were recalculated by univariate analysis according to body mass index (p(BSA)).

Table 3. Intraoperative Data

Intraoperative data	Group:1	Group:2	P value
CPB time (min)	117,0	99,1	0,131
Cross Clamping time (min)	74,9	66,4	0,129
Hemoglobulin (g/dl)			
Before CPB	9,5	9,7	0,543
During CPB	7,8	7,8	0,485
After CPB	8,0	7,9	0,623
Hematocrit (%)			
Before CPB	28,5	36,6	0,106
During CPB	23,4	32,7	0,134
After CPB	23,9	23,9	0,615

CPB: Cardiopulmonary bypass,

The use of fresh frozen plasma was found 219.1 ± 147.5ml for group 1. Group 2 was 167.7 ± 111.0ml. There was no statistically significant difference between the groups in the values examined with the Mann Whitney U test (P> 0.05)(Table 4). However, univariate analysis was performed to calculate the use of fresh frozen plasma proportioned to the patient's BSA. Fresh frozen plasma use was higher in group 1 and it was statistically significant (p: 0.011<0.05) (Table 4).

Dialysis requirement was 2 patients for group 1. 4 patients were found for group2. There was a statistically significant difference between the groups (p: 0.058). In group 2, the number of patients in need of dialysis was higher (p = 0.05) (Table 4).

The percent change of creatinine was calculated as 56.5% for group 1. Group 2 was 25.8%. There was no difference in statistical tests using Mann Whitney U and chi-square test. (p> 0.05) But there was a significant difference in univariate analysis acording to BSA. It was observed that the recalculated percent change of creatine was higher in Group 1. (p: 0.031<0.05) (Table 5).

The percent change of total protein level was calculated as -6.5% in group 1, -5.5% in group 2. There was statistically significant difference was found between the groups. (p<0.05).(Table 5).

Percent change of plasma albumin level after operation was found to be -18.2% in group 1. This change rate for Group 2 was calculated as -13.4%. There was no statistically significant difference between the groups. (P> 0.05). However, according to BSA, a statistically significant difference was found in recalculated percentage change rate in univariate analysis. (p = 0.05) It was observed that the decrease in Group 1 was higher (Table 5).

Table 4. ICU Data

ICU data	Group:1	Group:2	p value	p (BSA) (univariate analysis)
Lenght of stay in ICU (hour)	63,0	56,5	0,971	
Fluid taken (ml)				
8 hours	499,1	502,0	0,789	
24hours	1017,2	1020,5	0,987	
Chest Tube Drainage (ml)				
8 hours	61,8	58,8	0,335	
24hours	122,6	89,7	0,453	
Urine Output (ml)				
8 hours	659,6	583,2	0,393	
24hours	1455,6	1354,6	0,854	
Frosemide needed (mg)				
8 hours	7,4	6,7	0,849	
24 hours	17,9	17,2	0,363	
Balance (ml)				
8 hours	-226,1	-144,9	0,189	
24hours	-245,8	-273,2	0,883	
Inotropic drug				
Dopamine	41	20	0,877	
Dobutamine	22	8	0,347	
Adrenalin	18	8	0,744	
Noradrenalin	2	0	0,551	
Milrinon	19	14	0,168	
NTG	5	2	1,000	
Blood product usage(ml)				
Packed RBC	218,3	208,9	0,740	-0,940
FFF	219,1	167,7	0,123	0,011*
PLATELET CONCENTRATE	97,6	96,7	0,584	0,873
Dialysis neened	2	4	0,058*	
Exitus	4	1	0,662	

RBC, red boold cell; FFF, fresh Frozen Plasma; .

Table 5. Postoperative blood samples' results

Percentage change (%)	Group:1	Group:2	P (percentage change)	P (BSA) (univariate analysis)
BUN	80,6	79,6	0,496	
KRE	56,5	25,8	0,138	0,031*
SODIUM	11,5	13,7	0,328	
POTASIUM	23,3	27,0	0,643	
TOTAL PROTEIN	-6,5	-5,5*	0,040*	0,416
ALBUMIN	-18,2	-13,4	0,194	0,056*
TOTAL BILIRUBINE	179,7	119,0	0,313	0,105
DIREKT BILIRUBINE	110,5	182,1	0,792	0,304
ALT	25,0	22,6	0,058	0,282
AST	190,0	315,0	0,149	0,103
GGT	45,3	47,7	0,694	
LDH	126,6	180,8	0,600	
ALP	-42,1	-57,1	0,098	
APTT	-4,7	-1,6	0,555	
INR	26,8	8,3	0,458	
CRP	277,8	185,8	0,224	

Volume 11 Number 5 p: 378-386

Discussion

It is a technique that has been demonstrated by various studies that modified ultrafiltration has positive effects on heart and lung function, coagulation and inflammatory system. It has been found to reduce end organ damage. For this reason, many centers perform pediatric cardiac surgery have added MUF to their operation techniques and use them widely. Although the incidence of complications of CPB decreases in pediatric patients after the use of MUF becomes widespread, it still appears as an important and serious problem.

Today, the use of CPB is absolutely necessary in the corrective surgery of complex congenital heart diseases. Besides its advantages such as providing an immobile and bloodless working area, complications that can be seen due to the development of systemic inflammatory response syndrome (SIRS), coagulation system disorders, multiple organ failure are its major disadvantages.[2]

In children, hypothermia, hemodilution, and prolonged CPB increase the amount of fluid that escapes the interstitial space. As a result, total body fluid rises by 11-18%. Modified ultrafiltration reduces this amount of fluid by up to 4%.[11]

It has been determined that with the modified ultrafiltration, inflammatory mediators of a size that can pass through the pores of the filter can be removed from the blood, thereby reducing the systemic inflammatory response.[12] Due to the randomized and non-randomized results regarding this issue, there have been many controversial publications. Hiramatsu et al. Showed that ET-1 levels decreased in patients undergoing MUF.[13] Wang et al. argue that IL-8 and ET-1 levels decrease and TNF-α level does not change.[14] Pearl et al. Found that MUF did not change the TXB2 and LTB4 levels after KPB.[15] Chew et al. Showed that there is no change in TNF-α, IL1-beta, IL-ra, C3d and C4d levels.[9] In our study, there was no data regarding the inflammatory cytokine values and no evaluation could be made. However, there was no significant decrease in the MUF group in terms of CRP values ($p > 0.05$).

Kidney functions are not fully developed in children under 3 years old and under 10 kg, Glomerular filtration rate is low, bicarbonate re-absorption is insufficient, and urinary concentration is very low. Kidneys' ability to remove the increased acid and liquid load is low .[16]

Excessive use of blood products poses an additional burden on the kidneys in the postoperative period. In contrast, increasing the amount of hematocrit and oxygen in blood helps to maintain renal cortex functions. Activation of the renin angiotensin system and Vasospasm are reduced. Oxygen delivery to tissues increases and the workload of the kidneys decreases.[17]

In our study, it was observed that the creatinine value increased statistically significant in group 1 patients in contrast to expectations in blood samples made to evaluate the change in kidney function ($p < 0.05$). This adverse effect can be explained by high hemoconcentration and relative hypovolemia. A statistically significant decrease in the need for postoperative dialysis in group 1 indicates that although creatinine is elevated, kidney function is preserved ($p < 0.05$). Likewise, the difference in the amount of fluid given to the patients within 8 and 24 hours and the improvement of creatinine values afterwards supports hypovolemia.

In our study, no statistically significant difference was found in terms of BUN, urine output, balance, and furosemide use. In the group without modified ultrafiltration, the amount of urine was higher in the first 24 hours. Osmotic pressure of the blood decreases as some of the fluid escaping to the interstitial space is taken back during the operation by the modified ultrafiltration. Accordingly, the first 8 and 24 hours urine output may decrease in patients undergoing modified ultrafiltration. On the contrary, the increase in urine output seen at the end of the first 24 hours in patients without ultrafiltration may be related to the transfer of fluid that escapes to the interstitial space during the CPB to the intravascular area during intensive care follow-ups. There is no difference between groups in the first 8 hours in terms of furosemide use. however, more furosemides were used in the group with MUF in 24 hours. this may be associated with both decreased fluid in the intravascular area and forced diuresis.

There was no statistically significant difference between the study groups in terms of the need for dialysis ($p > 0.05$). The need for dialysis was numerically higher in group patients without ultrafiltration. This result may indicate that some of the inflammatory cytokines and excess fluid collected in the interstitial area are removed and kidney function is preserved in patients with MUF. This result also supports that the rise in KRE may be due to relative hypovolemia rather than renal damage.

Increased total body fluid-induced liver congestion in children can lad to a reduction of liver-induced clotting factors (fibrinogen, prothrombin, Factor V, VII, IX, and X) and toxic radicals released after ischemia reperfusion injury.[18] The decrease in the synthesis of plasma proteins, which have important functions, may increase liver damage by causing excess fluid to escape into the tissue

spaces[2] Consequently, bleeding disorder and chest tube drainage may increase.[3] Also development of hepatorenal syndrome, low cardiac output, ileus, ascites can be seen. Although the frequency of these complications decreases after the use of modified ultrafiltration has become widespread, it is still an important and serious problem.[10]

In our study, there was no statistically significant difference between the patient groups in terms of liver transaminase levels, but there was more increase in the group without MUF. This result supports the view that liver function and end organ damage are reduced in patients who underwent MUF stated in the study by Elliot et al.[19]

When plasma protein changes were examined, it was seen that total plasma protein levels decreased more in the MUF group. The decrease in the total protein values in the MUF group independent of the albumin may be due to the filtration of the immunoglobulins. In addition, although there is no statistically significant difference between the groups in terms of FFF use in the postoperative period, the increased presence of the MUF can be explained by the loss of immunoglobulin.

When evaluated in terms of chest tube drainage, the first 8 hours in the MUF group was lower. This finding Naik et al. matches the results of his work. The meaningless statistical analysis can be explained by the fact that the patient groups do not contain a sufficient number of patients.

Edema in the heart is reduced by modified ultrafiltration. In 1993, Elliot et al. In 1998, Rivera et al.[20] showed that MUF decreased heart size, increased systemic vascular resistance, increased systolic blood pressure, decresed heart rate, so increased cardiac index and decreased inotropic support needs.[21,22] In contrast, Mauerman et al. Showed that MUF was not effective on the development of atrial fibrillation in adult patients.[23] Naik et al. Measured his heart rate, blood pressure, right and left atrial pressures, pulmonary artery pressure, and cardiac output before and after MUF, there was no change in left atrial pressure, decrease in heart rate, increase in systolic pressure and cardiac index without change in systemic vascular resistance.[24] It has been determined. In the same study, it was reported that heart sizes decreased significantly after MUF. Hodges et al. confirmed the increase in cardiac index and systolic pressure after MUF.[25] In this study, it was determined that there was no effect of decreasing plasma fentanyl level after MUF on arterial pressure change. Davies et al. determined that the increase in systolic arterial pressure was due to the improvement in intrinsic left ventricular systolic functions. Post-diastolic width and post-diastole pressure decrease after modified ultrafiltration have been associated with an increase in left ventricular compliance due to reduced myocardial edema.[20] No data to confirm these findings were found in our study. it was seen that the need for inotropic support decreased significantly in patients undergoing MUF, but no statistical difference was found due to insufficient number of patients (Table 4). It is seen that the use of Milrinon is higher in group 2.

Hemoconcentration provided by modified ultrafiltration has positive effects on the coagulation system. In the study conducted by Chew et al., It was found that the use of blood and blood products and chest tube drainage decreased compared to the CUF and control group in patients with MUF. In the same study, it was stated that modified ultrafiltration also influences the coagulation factors.[26] fibrinogen, factor VII (FVII) level increased, platelet, factor IX (FIX) and factor X (FX) levels were shown to be unchanged.[27]

Coagulopathy is a well-defined problem after cardiopulmonary bypass. Ootaki et al. Reported an increase in Hct, platelet, total plasma protein and albumin values in patients with MUF. Fibrinogen, prothrombin, and FVII levels were higher, but showed no change in FIX and FX.[28] In our study, no significant difference was found in terms of hematocrit and platelet counts. Total plasma proteins were lower in group 1. The decrease in total protein without decreasing albumin can be explained by loss of globulin due to filtration ($p<0.05$). Adequate data for statistical analysis could not be obtained regarding fibrinogen and coagulation factors.

Hemostasis mechanism changes after cardiopulmonary bypass is the most important factor responsible for post-operative blood loss and blood product use. In studies conducted by Naik, Bando, Gurbuz and Draaisma, they were found that the use of blood and chest tube drainage decreased significantly in patients with MUF.[29] In our study, no mathematical and statistical difference was found between the groups in terms of blood use. This has been linked to insufficient number of patients included in the study.

Conclusion

Since our study was planned as a retrospective study, the data that could ensure the effectiveness of MUF could not be reached sufficiently. therefore MUF appears to be effective in maintaining kidney and liver function, although there is insufficient data available. İn to the future, more randomized controlled prospective studies are needed.

Volume 11 Number 5 p: 378-386

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest

References

1. Naik SK, Knight A, Elliott M. A prospective randomized study of a modified technique of ultrafiltration during pediatric open-heart surgery. Circulation 1991; 84: 422-31.
2. Krispinsky LT, Stark RJ, Parra DA et al. Endothelial-dependent vasomotor dysfunction in infants after cardiopulmonary bypass. Pediatr Crit Care Med 2020; 21: 42-9
3. Ziyaeifard M, Alizadehasl A, Aghdaii N et al. The effect of combined conventional and modified ultrafiltration on mechanical ventilation and hemodynamic changes in congenital heart surgery. J Res Med Sci. 2016; 21: 133.
4. Milovanovic V, Bisenic D, Mimic B et al. Reevaluating the Importance of Modified Ultrafiltration in Contemporary Pediatric Cardiac Surgery. J Clin Med 2018; 7:498.
5. Zakkar M, Guida G, Angelini GD. Modified ultrafiltration in adult patients undergoing cardiac surgery. Interact Cardiovasc Thorac Surg 2015; 20: 415-21.
6. Raja SG, Yousufuddin S, Rasool F, Nubi A, Danton M, Pollock J. Impact of modified ultrafiltration on morbidity after pediatric cardiac surgery. Asian Cardiovasc Thorac Ann 2006; 14: 341-50.
7. Williams GD, Ramamoorthy C, Chu L, et al. Modified and conventional ultrafiltration during pediatric cardiac surgery: Clinical outcomes compared. J Thorac Cardiovasc Surg 2006; 132: 1291-8.
8. Shann KG, Giacomuzzi CR, Harness L et al. Complications relating to perfusion and extracorporeal circulation associated with the treatment of patients with congenital cardiac disease: consensus definitions from the Multi-Societal Database Committee for Pediatric and Congenital Heart Disease. Cardiol Young. 2008; 18: 206-14.
9. Chew MS, Brix-Christensen V, Ravn HB et al. Effect of modified ultrafiltration on the inflammatory response in paediatric open-heart surgery: A prospective, randomized study. Perfusion 2002; 17: 327-33.
10. Timpa JG, O'Meara LC, Goldberg KG et al. Implementation of a multidisciplinary bleeding and transfusion protocol significantly decreases perioperative blood product utilization and improves some bleeding outcomes. J Extra Corpor Technol 2016; 48: 11-8.
11. Gaynor JW. Use of Modified Ultrafiltration After Repair of Congenital Heart Defects. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu 1998; 1: 81-90.
12. Lang SM, Syed MA, Dziura J et al. The effect of modified ultrafiltration on angiopoietins in pediatric cardiothoracic operations. Ann Thorac Surg 2014; 98: 1699-704.
13. Hiramatsu T, Imai Y, Kurosawa H et al. Effects of dilutional and modified ultrafiltration in plasma endothelin-1 and pulmonary vascular resistance after the Fontan procedure. Ann Thorac Surg 2002; 73: 861-5.
14. Wang W, Huang HM, Zhu DM, Chen H, Su ZK, Ding WX. Modified ultrafiltration in paediatric cardiopulmonary bypass. Perfusion 1998; 13: 304-10.
15. Pearl JM, Manning PB, McNamara JL, Saucier MM, Thomas DW. Effect of modified ultrafiltration on plasma thromboxane B2, leukotriene B4, and endothelin-1 in infants undergoing cardiopulmonary bypass. Annals of Thoracic Surgery 1999; 68: 1369-75.
16. Yuan SM. Acute kidney injury after pediatric cardiac surgery. Pediatr Neonatol 2019; 60: 3-11.
17. Li J, Hoschtitzky A, Allen ML, Elliott MJ, Redington AN. An analysis of oxygen consumption and oxygen delivery in euthermic infants after cardiopulmonary bypass with modified ultrafiltration. Ann Thorac Surg 2004; 78: 1389-96.
18. Wang MJ, Chiu IS, Hsu CM et al. Efficacy of ultrafiltration in removing inflammatory mediators during pediatric cardiac operations. Ann Thorac Surg 1996; 61: 651-6.
19. Elliott MJ. Ultrafiltration and modified ultrafiltration in pediatric open heart operations. Ann Thorac Surg 1993; 56: 1518-22.
20. Davies MJ, Nguyen K, Gaynor JW et al. Modified ultrafiltration improves left ventricular systolic function in infants after cardiopulmonary bypass. J Thorac Cardiovasc Surg 1998; 115: 361-9.

21. Türköz A, Tunçay E, Balci ŞT et al. The effect of modified ultrafiltration duration on pulmonary functions and hemodynamics in newborns and infants following arterial switch operation. Pediatr Crit Care Med 2014; 15: 600-7.
22. Ziyaeifard M, Alizadehasl A, Massoumi G. Modified ultrafiltration during cardiopulmonary bypass and postoperative course of pediatric cardiac surgery. Res Cardiovasc Med 2014; 3: 17830.
23. Mauermann WJ, Nuttall GA, Cook DJ, Hanson AC, Schroeder DR, Oliver WC. Hemofiltration during cardiopulmonary bypass does not decrease the incidence of atrial fibrillation after cardiac surgery. Anesth Analg 2010; 110: 329-34.
24. Ricci Z, Polito A, Netto R et al. Assessment of modified ultrafiltration hemodynamic impact by pressure recording analytical method during pediatric cardiac surgery. Pediatr Crit Care Med 2013; 14: 390-5.
25. Hodges UM, Berg S, Naik SK, Bower S, Lloyd-Thomas A, Elliot M. Filtration of fentanyl is not the cause of the elevation of arterial blood pressure associated with post-bypass ultrafiltration in children. J Cardiothorac Vasc Anesth 1994; 8: 653-7.
26. Kuratani N, Bunsangjaroen P, Srimueang T, Masaki E, Suzuki T, Katogi T. Modified versus conventional ultrafiltration in pediatric cardiac surgery: A meta-analysis of randomized controlled trials comparing clinical outcome parameters. J Thorac Cardiovasc Surg 2011; 142: 861-7.
27. ournois D, Israel-Biet D, Pouard P et al. High-volume, zero-balanced hemofiltration to reduce delayed inflammatory response to cardiopulmonary bypass in children. Anesthesiology 1996; 85: 965-76.
28. Ootaki Y, Yamaguchi M, Oshima Y, Yoshimura N, Oka S. Effects of modified ultrafiltration on coagulation factors in pediatric cardiac surgery. Surg Today 2002; 32: 203-6.
29. Andreasson S, Göthberg S, Berggren H, Bengtsson A, Eriksson E, Risberg B. Hemofiltration modifies complement activation after extracorporeal circulation in infants. Ann Thorac Surg 1993; 56: 1515-7.