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Impacts of different hemofiltration methods on the prognosis of patients with sepsis.

Jilu Ye*, Xuehua Pu, Xiaofeng Chen

Department of Critical Care Medicine, Jiangsu Taizhou People's Hospital, Taizhou, Jiangsu Province, PR China

Abstract

The aim of this study was to explore the therapeutic effects of Continuous High-Volume Hemofiltration (CHVHF) in treating sepsis combined with Multiple Organ Dysfunction Syndrome (MODS). A total of 100 patients with sepsis induced by various causes in combination with MODS (S-MODS) and who were treated in the Department of Critical Care Medicine of our hospital from March 2013 to December 2015 were selected and randomly divided into group A (n=53, for CHVHF) or group B (n=47, for common volume hemofiltration, CVHF). The post-treatment changes of observation indexes were then compared and analysed. Patients in group A exhibited an improvement in body temperature and heart rate (P<0.01), while their Color Index (CI), Mean Artery Pressure (MAP), Systemic Vascular Resistance Index (SVRI), and Stroke Volume Index (SVI) all tended to be stable (P<0.01). Meanwhile, their MODS scores and APACHEII scores decreased significantly (P<0.01), and their Procalcitonin (PCT) and Arterial Blood Lactate level (ABL) improved after treatment. Therefore, CHVHF can stabilize the vital signs and hemodynamics of S-MODS patients as well as improve their tissue perfusion and restore organ functions.

Keywords: Sepsis, Continuous hemofiltration, Multiple organ dysfunction syndrome.

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Introduction

In addition to the lethal nature of sepsis, some patients with severe sepsis can develop Multiple Organ Dysfunction Syndrome (MODS) despite timely treatments that reduce inflammation or resolve the underlying lesion. In this way, sepsis has become a major public health problem [1] as well as one of the major causes of death in critically ill patients. Indeed, if septic shock occurs, the mortality can be as high as 50% [2]. According to statistics from the US Centers for Disease Control and Prevention (CDC), 75 million people suffer from sepsis each year. Among these individuals, approximately 9% develop severe sepsis and 3% develop septic shock, which is also the main cause of death in Intensive Care Units (ICU) [3,4]. Researchers have focused on developing a treatment paradigm that improves the overall recovery of patients experiencing sepsis. Among the systematic treatment regimens currently being developed for sepsis, hemofiltration has become one controversial focus. Recent studies have shown that High-Volume Hemofiltration (HVHF) can clear *in vivo* harmful substances for patients with sepsis, thereby improving the prognosis of sepsis. HVHF is a widely used Continuous Venovenous Hemofiltration (CVVH)-based blood filtration technology. Recently, Continuous High Volume Hemofiltration (CHVHF) has been developed [5], which has improved the clearance of solutes with large and medium molecular weights. Studies have shown that CHVHF can effectively improve the prognosis of patients with sepsis and, when performed as early as possible, can achieve better results [6]. Currently, many pre-clinical studies [7-10] and early clinical trials [11-13] have shown great promise; however, the results of multi-center clinical studies are disappointing [14,15]. Moreover, it is still not clear yet whether CHVHF can effectively control the conditions of post-sepsis MODS. This study applied CHVHF and CVHF separately to treat S-MODS patients to compare and analyse the efficacy of these two treatment regimens in resolving sepsis in patients.

Information and Intervention

Clinical data

A total of 100 S-MODS patients treated in the Department of Critical Care Medicine of our hospital from March 2013 to December 2015 were selected and randomly divided into group A (n=53, for CHVHF) or group B (n=47, for CVHF). There was no statistical difference in the sex, age, and inflammation type between the two groups (χ^2=0.023, P=0.879; t=0.818, P=0.416; χ^2=0.756, P=0.505, Table 1). All patients were diagnosed according to the "International treatment guidelines of 2008 SSC severe sepsis and septic shock" [16], while the "Marshall Table of multiple organ dysfunction syndrome in 1995 (MODS table)" [17] was used to score organ dysfunction. All patients belonged to the low-output and high-resistance type as well as scored more than 5 points on the MODS table. Patients were excluded if they were pregnant, had chronic renal

failure, were<18 years of age, or receiving immunosuppressive therapy.

This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Taizhou People's Hospital. Written informed consent was obtained from all participants.

Research methods

All patients were catheterized in the internal jugular vein or the femoral vein to establish the vascular approach. Either a heparin-free method was used to maintain an Activated Partial Thromboplastin Time (APTT) of 40-60 s, or low molecular weight heparin or common heparin was used to achieve anticoagulation [18]. The two groups underwent CHVHF simultaneously, with the treatment in group A persisting for 24-30 h each with a substitution amount of 50-60 ml/(kg•h) and a blood flow amount as 200-250 ml/min. Treatment in group B was identical, except that the substitution amount in group B was only 30 ml/(kg•h).

Evaluation

The changes in body Temperature (T), Heart Rate (HR), MODS score, and APACHEII score of the two groups at different time periods before and after CHVHF were recorded and analysed. Changes in Procalcitonin (PCT) level, Arterial Blood Lactate level (ABL), and hepatonephric function were evaluated in arterial and venous blood samples, which were obtained before and after CHVHF. The Cardiac Index (CI), invasive arterial pressure (MAP), Systemic Vascular Resistance Index (SVRI), Stroke Volume Index (SVI), and Central Venous Pressure (CVP) of the two groups were monitored before and after CHVHF.

Statistical methods

SPSS13.0 was used to analyse data. Measurement data were analysed using the chi-squared test, while count data were analysed using an independent sample t test. Intergroup comparisons were performed using the F test (univariate analysis of variance), with P<0.05 being assumed to indicate a statistically significant difference.

Results

Disease outcomes

Among the 53 S-MODS patients in group A, 40 patients were cured and discharged, 4 patients stopped undergoing treatment for various reasons, and 9 patients died, with the mortality rate being 17.1%. Meanwhile, among the 47 S-MODS patients in group A, 35 patients were cured and discharged, 5 patients stopped undergoing treatment for various reasons, and 9 patients died, with the mortality rate being 19.1%. These was no statistically significant difference in the overall mortality between the two groups (χ^2=0.650, P=0.885) (Table 2).

The post-treatment T and HR in the two groups were both significantly reduced, with the pre- and post-treatment MODS scores and APACHEII scores exhibiting statistically significant differences (t=7.059, P<0.01; t=12.014, P<0.01; t=4.639, P<0.01; t=10.306, P<0.01; respectively). Due to the reduction in indexes, such as T, HR, MODS score, and APACHEII score, it can be concluded that the patient's vital signs were stabilizing. The post-treatment T, HR, MODS score, and APACHEII score in group A were more significantly reduced than in group B (t=6.867, P<0.01; t=4.300, P<0.01; t=1.697, P=0.043; t=4.367, P<0.01; respectively) (Table 3).

Hemodynamic changes before and after treatment

All patients exhibited significant improvements after undergoing CHVHF for 48 h and 72 h, with their CI, MAP, SVRI, and SVI, gradually stabilizing as well as exhibiting a statistically significant difference before and after treatment (F=30.026, P<0.01; F=87.950, P<0.01; F=367.944, P <0.01; F=217.257, P<0.01; respectively). The patients in group A exhibited a more notable increase in CI, MAP, and SVI after treatment than did group B. Similarly, group A exhibited a more notable decrease in CAP and SVRI after treatment than did group B (t=-2.764, P=0.004; t=-4.731, P<0.01; t=5.273, P <0.01; t=-5.839, P<0.01; respectively) (Tables 4 and 5).

Changes in hepatonephric function before and after treatment

The PCT and ABL values of the patients in group A were significantly increased when compared to normal values before treatment, but gradually decreased to within normal ranges after treatment. The patients exhibited hepatonephric dysfunction before treatment, which gradually became normal after treatment. Furthermore, the differences in PCT and ABL before CHVHF and at 24 h, 48 h, and 72 h after CHVHF were statistically significant (F=21.210, P<0.01; F=76.410, P<0.01; F=86.060, P<0.01; F=199.800, P<0.01; F=120.900, P<0.01; F=162.100, P<0.01; respectively) (Table 6).

Table 1. Comparison of general information between the two groups.

Item	A (n=53)	B (n=47)	t/χ^2	P
Men (n)	29	25	0.023	0.879
Age (years)	45.03 ± 5.33	44.20 ± 4.75	0.818	0.416

Severe pneumonia (n)	11	9	0.756	0.505
Acute purulent inflammation (n)	9	9		
Severe pancreatitis (n)	8	7		
Severe multiple injuries (n)	10	9		
Postoperative abdominal infection (n)	8	7		
Digestive perforation combined with abdominal infection (n)	7	6		

Table 2. *Disease outcomes and mortalities in the two groups.*

Group	n	Cured	Giving-up treatment	Death	Mortality (%)
A	53	40	4	9	17.1
B	47	34	5	8	19.1

χ^2	-	0.65
0.885		
P	-	

Table 3. *Changes of vital signs in the two groups before and after treatment.*

Group	n	T				HR				MODS score				APACHEII score			
		Before	After	t	P	Before	After	t	P	Before	After	t	P	Before	After	t	P
A	53	38.6 ± 0.8	37.2 ± 1.0	7.059	<0.01	121.7 ± 14.5	90.0 ± 12.6	12.014	<0.01	7.9 ± 3.3	5.3 ± 2.4	4.639	<0.01	17.1 ± 3.3	9.2 ± 4.5	10.306	<0.01
B	47	38.7 ± 0.8	38.4 ± 0.7	2.055	0.042	120.9 ± 14.2	101.1 ± 13.2	7.435	<0.01	7.9 ± 3.3	6.2 ± 2.9	2.817	0.04	17.1 ± 3.4	12.9 ± 3.9	5.91	<0.01
t	-	0.624	6.867	-		-0.278	4.3	-		0.002	1.697	-		0.003	4.367	-	
P	-	0.534	<0.01			0.782	<0.01			1	0.043			1	<0.01		

Table 4. *Hemodynamic changes before and after treatment.*

Group	n	CI					MAP				
		Before	48 h later	72 h later	F	P	Before	48 h later	72 h later	F	P
A	53	2.0 ± 1.0	3.9 ± 1.9	4.5 ± 2.1	30.026	<0.001	77.0 ± 5.3	86.5 ± 6.8	92.4 ± 5.9	87.95	<0.001
B	47	2.5 ± 1.0	3.3 ± 1.4	3.5 ± 1.4	8.025	<0.001	76.8 ± 5.1	81.1 ± 4.4	86.1 ± 7.4	20.54	<0.001
t	-	0.499	-1.778	-2.764	-		-0.192	-4.648	-4.731	-	
P	-	0.619	0.038	0.004			0.848	<0.001	<0.001		

Table 5. *Hemodynamic changes before and after treatment.*

Group	n	SVRI					SVI				
		Before	48 h later	72 h later	F	P	Before	48 h later	72 h later	F	P
A	53	2768 ± 213	1985 ± 163	1850 ± 185	367.944	<0.001	33.0 ± 6.8	55.0 ± 6.1	57.2 ± 6.9	217.257	<0.001
B	47	2766 ± 211	2299 ± 194	2043 ± 180	165.413	<0.001	32.5 ± 6.0	44.0 ± 6.1	48.5 ± 8.0	69.964	<0.001
t	-	-0.0047	8.793	5.273	-		-0.388	-9	-5.839	-	
P	-	0.963	<0.001	<0.001			0.699	<0.001	<0.001		

Table 6. *Changes of PCT, ABL, and hepatonephric function in group A.*

Item	Before CHVHF	24 h after CHVHF	48 h after CHVHF	72 h after CHVHF	F	P

PCT (μg/L)	7 ± 3	5 ± 3	3 ± 2	2 ± 1	21.21	<0.01
ABL (mmol/L)	6.8 ± 2.7	3.4 ± 2.1	2.7 ± 1.7	1.7 ± 0.9	76.41	<0.01
ALT (U/L)	123.4 ± 41.5	68.2 ± 24.1	51.4 ± 21.6	45.2 ± 18.7	86.06	<0.01
TBIL (μmol/L)	35.1 ± 8.1	19.3 ± 4.5	16.3 ± 4.0	11.3 ± 3.2	199.8	<0.01
BUN (mmol/L)	25.4 ± 6.1	14.2 ± 4.4	12.3 ± 4.3	9.0 ± 3.7	120.9	<0.01
Scr (μmol/L)	173.9 ± 31.5	117.9 ± 27.2	89.2 ± 30.3	67.3 ± 11.5	162.1	<0.01

Discussion

While sepsis is common, with approximately 18 million cases of sepsis annually, it is an emergent threat [19]. In the ICU, approximately 41% of critically ill patients develop sepsis, with sepsis being the main cause of death among critically ill patients in ICU. The rate of death in sepsis-caused secondary MODS has been reported to range from 32% to 61%. MODS normally occur in late sepsis and are caused by interactions between a large number of inflammatory mediators and pro-inflammatory substances that are released following ischemia-reperfusion, infection, or other factors. This represents a "waterfall effect" that reflects the activation of an inflammatory cascade [20]. Immune imbalance is the main cause of S-MODS. Therefore, in order to fundamentally reduce the mortality of sepsis, imbalances in the immune system must be corrected. Continuous hemofiltration can help reduce the rate of mortality in sepsis as it can correct the abnormally increased level of blood vasoactive substances *via* its filtration, adsorption, and diffusion activities [21]. HVHF is an important method of Continuous Renal Replacement Therapy (CRRT), and the use of HVHF can decrease mortality and improve prognosis because it enables a reduction in the severity of paralysis of the immune system, thereby reducing the risk of secondary infection. CRRT can effectively correct the acid-base and electrolyte imbalance in patients with sepsis, and comprehensively reduce the concentration peaks of a variety of inflammatory mediators *in vivo*. Therefore, early CRRT can reduce the impact of inflammatory mediators on hemodynamics and endothelial cells as well as downregulate the overall inflammatory response in a temporally appropriate manner [22,23]. In sepsis, anaerobic metabolism results in a high level and low clearance rate of ABL. HVHF can effectively address this severe lactic acidosis [24]. Furthermore, it can also improve inflammation-damaged organ function, particularly hepatonephric function, and greatly improve oxygenation in patients with ARDS [25,26].

In a comparison with CVHF, we found that CHVHF can significantly reduce the body temperature and heart rate of patients with S-MODS as well as reduce their MODS and APACHEII scores. Furthermore, these differences were statistically significant, which is consistent with many other Chinese studies, thereby indicating that CHVHF can help stabilize the vital signs of S-MODS patients [27].

This study demonstrated that CHVHF can significantly improve SVI, CI, and MVP in S-MODS patients as well as reduce ABL and central venous pressure. Furthermore, CHVHF can interfere with the synthesis of such cardiovascular composites, such as endothelin and myocardial depressant factor [28], which indicates that CHVHF can improve the hemodynamics of and tissue perfusion in S-MODS patients. It further demonstrates that this therapy has an important role in recovering organ functions in S-MODS patients [29,30]. PCT is a highly specific serological index for the diagnosis of sepsis, and the results of this study demonstrated that PCT gradually decreased to normal after CHVHF, thereby demonstrating the significant role of CHVHF as a potential therapy for sepsis.

In summary, CHVHF can stabilize the vital signs of patients with S-MODS as well as improve their hemodynamics, tissue perfusion, and organ functions. Therefore, CHVHF can be considered a promising therapy for S-MODS.

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Conflict of Interest

All authors have no conflict of interest regarding this paper.

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***Correspondence to**

Jilu Ye

Department of Critical Care Medicine

Jiangsu Taizhou People's Hospital

PR China