

Original Article

Effects of HVHF therapy on serum inflammatory factors, pulmonary function, and hemodynamic indexes of patients with sepsis complicated by acute respiratory distress syndrome

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Received June 9, 2018; Accepted September 11, 2018; Epub May 15, 2019; Published May 30, 2019

Abstract: Objective: The goal of this study was to observe the effects of continuous high-volume hemofiltration (HVHF) therapy on serum inflammatory factors, pulmonary function, and hemodynamic indexes of patients with sepsis complicated by acute respiratory distress syndrome (ARDS). Methods: A total of 82 patients with sepsis complicated by ARDS were equally divided into the HVHF group and the control group. Patients in the control group were given anti-infection treatment and primary affection while patients in the HVHF group received continuous HVHF treatment additionally based on treatment in the control group. At three days after treatment, the levels of tumor necrosis factor- α (TNF- α), interleukin-6 (IL-6), and procalcitonin (PCT) in the serum of patients in the two groups were detected. At the same time, arterial partial pressure of oxygen (PaO₂), arterial partial pressure of carbon dioxide (PaCO₂) and the ratio of fraction of inspired oxygen (FiO₂) to PaO₂ between the two groups were compared, and heart rate (HR), mean arterial pressure (MAP), pulmonary artery wedge pressure (PAWP) and cardiac index (CI) were monitored. Results: The detection results at three days after treatment showed that the levels of TNF- α , IL-6, and PCT in serum of patients in the control and HVHF groups were (25.68 \pm 8.86 vs. 15.55 \pm 3.98) ng.L⁻¹, (89.68 \pm 31.44 vs. 65.32 \pm 45.01) ng.L⁻¹ and (7.77 \pm 1.01 vs. 5.04 \pm 0.89) ng.L⁻¹, respectively, demonstrating that inflammatory factors in both groups declined and changes in the HVHF group were more obvious than those in the control group (P <0.05). Moreover, the hemodynamic indexes and pulmonary function in the two groups were improved to some extent. However, the levels in the HVHF group were more remarkably increased compared to those in the control group, in which PaO₂, FiO₂/PO₂, PAWP and CI were significantly different (P <0.05). In addition, clinical monitoring indexes [white blood cell count and Acute Physiology and Chronic Health Evaluation II (APACHE II)] in the HVHF group were more significantly improved than those in the control group, and the mortality rate acquired in follow-up investigation was lower than that in the control group. Conclusion: Therefore, continuous HVHF treatment is very helpful in the protection of main organ functions and for recovery of pulmonary function. It can enhance survival rate as it can strengthen the scavenging capacity of inflammatory factors in the blood circulation, and has efficacy in improving hemodynamics and tissue oxygenation, as well as maintaining a steady internal environment. Therefore, continuous HVHF therapy can provide an effective reference value for clinical practice and applications.

Keywords: HVHF, acute respiratory distress syndrome, inflammatory factors, pulmonary function, hemodynamics

Introduction

Sepsis is a common serious infection disease in the Intensive Care Unit (ICU). Its rapid progression often leads to systemic inflammatory response syndrome (SIRS), with secondary onset of multiple organ dysfunction syndrome (MODS), among which ARDS is the most common complication. Inflammatory mediators are

closely related to the progression of ARDS. Tumor necrosis factor- α (TNF- α) and interleukin-6 (IL-6) in macrophages and airway epithelial cells are usually activated in the early stage of sepsis so that more inflammatory factors and reactive oxygen species can be released to damage lung tissues [1]. At present, combination therapy of anti-infection and mechanical ventilation is the commonly used clinical treat-

HVHF in patients with ARDS

Table 1. Comparison of general data between patients

Group	Gender		Age (years old)	APACHE II	MAP (mmHg)
	Male	Female			
Control group (n=41)	27	14	40.32±4.08	18.12±4.01	60.6±10.3
HVHF group (n=41)	25	16	39.03±5.11	18.38±3.68	61.3±9.9

ment of ARDS, but control of the disease is still not quite promising. Recently, the hemofiltration technique has been used as an adjuvant therapy for treatment of systemic infectious disease for many years [2, 3], and it has gradually become an important method to rescue severe patients in ICU instead of being simply used for the treatment of acute kidney injury since it has the function of scavenging inflammatory mediators and indirectly reducing the end-organ damage by septic shock [4, 5]. In this study, continuous HVHF was applied in treating patients with sepsis complicated by ARDS, and the inflammatory factors, pulmonary function and hemodynamic indexes before and after treatment were observed, so as to provide important guidance for clinical treatment.

Data and methods

Research objects and grouping

A total of 82 patients diagnosed with sepsis complicated by ARDS who admitted to the ICU from May 2017 to October 2017 were selected as the research objects. Sepsis was diagnosed according to the diagnostic criteria established in the consensus conference by American College of Chest Physicians/Society of Critical Care Medicine (ACCP/SCCM) in 2001, and ARDS was diagnosed according to the diagnostic criteria made by the Respiratory Society of Chinese Medical Association (CMA). Exclusion criteria: patients with severe primary cardiopulmonary disease, malignant tumor or other immune diseases, and those who could not undergo blood purification treatment. All patients signed the informed consent, and the study was approved by the Ethics Committee. The general clinical data of the two groups were comparable ($P>0.05$).

Research methods

The selected 82 patients with sepsis complicated by ARDS were randomly divided into the HVHF group and the control group. Patients in

both groups received anti-infection and primary affection treatment, pulmonary edema control, protection of gastrointestinal function, and nutrition support, as well as

mechanical ventilation. At the same time, patients in the HVHF group were treated with continuous renal replacement therapy (CRRT) via a hemodialysis machine (Baxter Corp., USA) for three days, and changes in the indexes before and after treatment were compared.

Observation indexes

Biotek microplate reader (BD Corp., USA) was applied to detect the expression of TNF- α , IL-6, and procalcitonin (PCT). Arterial partial pressure of oxygen (PaO_2), arterial partial pressure of carbon dioxide (PaCO_2) and the ratio of fraction of inspired oxygen (FiO_2) to PaO_2 were compared between the two groups using the GEM premier 3000 blood-gas analyzer (USA). PULSION hemodynamic detector (German) was employed to detect the hemodynamic indexes, including heart rate (HR), mean arterial pressure (MAP), pulmonary artery wedge pressure (PAWP) and cardiac index (CI). The changes in clinical indexes were detected, including white blood cell count and Acute Physiology and Chronic Health Evaluation II (APACHE II). The mortality rates of patients in the two groups were acquired in follow-up investigation and compared.

Statistical methods

International Business Machine (IBM) Statistical Product and Service Solutions (SPSS) 19.0 software was employed for data analysis. Measurement data are presented as ($\bar{x} \pm s$), t test was used for the intra-group comparison, and analysis of variance was applied for the multiple-group comparison. Correlation analysis was conducted using Pearson's correlation analysis. $P<0.05$ suggested that the difference was statistically significant.

Results

Comparisons of general conditions between two groups (age, gender, disease severity, etc.)

There were no statistically significant differences in age, gender, APACHE II and MAP between

HVHF in patients with ARDS

Table 2. Comparison of TNF- α , IL-6, and PCT levels in serum between the two groups

Group	Phase	PCT (ng.L ⁻¹)	IL-6 (ng.L ⁻¹)	TNF- α (ng.L ⁻¹)
Control group (n=41)	Before treatment	13.88 \pm 2.21	122.06 \pm 66.59	40.23 \pm 21.22
	After treatment	7.77 \pm 1.01*	89.68 \pm 31.44*	25.68 \pm 8.86*
HVHF group (n=41)	Before treatment	13.68 \pm 1.98	128.29 \pm 68.77	42.56 \pm 24.45
	After treatment	5.04 \pm 0.89*.#	65.32 \pm 45.01*.#	15.55 \pm 3.98*.#

Note: Compared with the same group before treatment, * P <0.05. Compared with control group, # P <0.05.

Table 3. Comparison of pulmonary function indexes between two groups

Group	Phase	PaO ₂ (mmHg)	PaCO ₂ (mmHg)	FiO ₂ /PO ₂
Control group (n=41)	Before treatment	49.87 \pm 16.82	40.56 \pm 1.35	103.35 \pm 23.25
	After treatment	63.25 \pm 7.77	36.56 \pm 2.12	130.36 \pm 13.65*
HVHF group (n=41)	Before treatment	48.25 \pm 17.12	41.56 \pm 1.81	105.35 \pm 20.21
	After treatment	100.01 \pm 6.69*.#	33.21 \pm 1.98*	200.12 \pm 10.32*.#

Note: Compared with the same group before treatment, * P <0.05. Compared with the control group, # P <0.05.

Table 4. Comparison of hemodynamic indexes between the two groups

Group	Phase	MAP (mmHg)	PAWP (mmHg)	CI (L/min \times m ²)	SVRI (kPa \times s)
Control group (n=41)	Before treatment	59.6 \pm 10.3	3.3 \pm 1.0	2.4 \pm 0.8	88.5 \pm 10.2
	After treatment	78.4 \pm 9.7	6.6 \pm 0.9*	3.2 \pm 0.9	120.1 \pm 9.6*
HVHF group (n=41)	Before treatment	60.1 \pm 9.9	3.4 \pm 0.8	2.5 \pm 1.0	89.8 \pm 10.5
	After treatment	77.5 \pm 10.4*.#	6.8 \pm 1.1*	4.0 \pm 1.1*.#	130.7 \pm 7.9*

Note: Compared with the same group before treatment, * P <0.05. Compared with the control group, # P <0.05.

the two groups of patients, and the data were comparable (**Table 1**).

Comparison of TNF- α , IL-6, and PCT levels in serum between the two groups

The levels of TNF- α , IL-6, and PCT in serum of patients in the control and HVHF groups at 3 days after treatment were (25.68 \pm 8.86 vs. 15.55 \pm 3.98) ng.L⁻¹, (89.68 \pm 31.44 vs. 65.32 \pm 45.01) ng.L⁻¹ and (7.77 \pm 1.01 vs. 5.04 \pm 0.89) ng.L⁻¹, respectively. The levels in both groups declined, and changes in HVHF group were more obvious (P <0.05), indicating that HVHF is more effective than conventional therapy in scavenging patients' inflammatory mediators and inhibiting inflammation reaction (**Table 2**).

Comparison of pulmonary function indexes between the two groups

After treatment, FiO₂/PO₂ and PaO₂ in the control and HVHF groups were both increased while PaCO₂ was decreased, and changes in HVHF group were more remarkable (P <0.05), suggesting that HVHF can improve hypoxemia

and is conducive to the recovery of pulmonary function (**Table 3**).

Effects of hemodynamic indexes in the two groups

The hemodynamic indexes (HR, MAP, PAWP and CI) in both groups at 3 days after treatment were improved to some extent compared with those before treatment. There was a greater growth in the levels in HVHF group than those in control group, and the differences in PAWP and CI were statistically significant (P <0.05), indicating that HVHF can keep hemodynamics in a relative smooth and steady state to some extent (**Table 4**).

Changes in white blood cell count and APACHE II at 3 days after treatment

White blood cell counts in both groups were overtly decreased at 3 days after treatment compared with those before treatment, and APACHE II in both groups was improved as well. Changes in the HVHF group were more significant, and the differences were statistically sig-

Table 5. Comparison of clinical indexes in serum between the two groups

Group	Phase	White blood cell count ($\times 10^9/L$)	APACHE II
Control group (n=41)	Before treatment	16.98 \pm 2.15	18.12 \pm 4.01
	After treatment	12.29 \pm 0.82*	11.79 \pm 1.09*
HVHF group (n=41)	Before treatment	16.58 \pm 2.21	18.38 \pm 3.68
	After treatment	10.09 \pm 0.77* [#]	9.43 \pm 1.28** [#]

Note: Compared with the same group before treatment, * $P < 0.05$, ** $P < 0.01$. Compared with the control group, [#] $P < 0.05$.

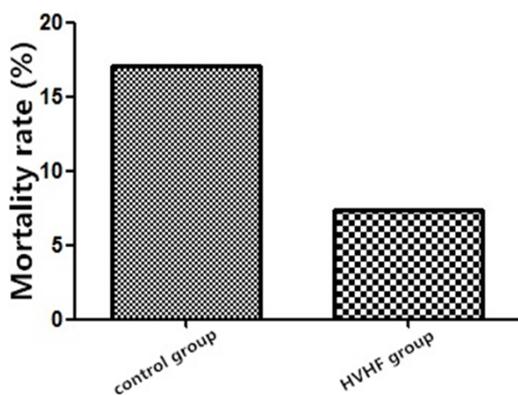


Figure 1. Comparison of the mortality rate between control group and HVHF group (%).

nificant ($P < 0.05$), manifesting that HVHF can improve the clinical symptoms efficiently (Table 5).

Comparison of the mortality rate between the two groups of patients through the follow-up investigation

In the follow-up investigation for the two groups of patients after hospital discharge, the deaths in the control and HVHF groups were 7 cases (17.1%) and 3 cases (7.32%), respectively, suggesting that the prognosis of patients in the HVHF group is superior to that in the control group ($P < 0.05$) (Figure 1).

Discussion

As to the ARDS caused by sepsis, the diffuse inflammatory pulmonary edema of lung tissues leads to hypoxemia and damage of pulmonary function, which endangers lives greatly. It is vital to scavenge inflammatory mediators in blood circulation and inhibit inflammatory reaction in the clinical treatment of ARDS. In the network of cell inflammatory factors, the in-

flammatory mediator releases TNF- α first, whose combination with receptors will activate the downstream signal pathway and stimulates secretions of cell inflammatory factors such as interleukin-1 β (IL-1 β) and IL-6. At the same time, it will inhibit the production of anti-inflammatory factors and lead to inflammatory cascades [6]. IL-6 can lead to

the continued presence of inflammatory by inducing and activating various immune cells. In the early stage of sepsis, the PCT in serum is detected to be increased and it will quickly increase to the peak as the disease progresses [8].

Since the use of continuous blood purification as the treatment of sepsis complicated by multiple organ failure by Barzilay et al. [9], the therapy of continuous blood purification has been rapidly developed in the field of critical diseases like sepsis. Researchers have revealed that continuous HVHF can improve hemodynamics and oxygen supply of tissues, thus enhancing the survival rate of patients [10, 11]. The therapy in which the replacement capacity of fluid is more than 50 mL/(kg/h) is defined as HVHF by Honore et al. [13]. The large-aperture filter and filtration membrane used in present clinical practice can only intercept 30~50 kD substance and can be used for the non-selective removal of IL-1, IL-6, IL-8, IL-10, and TNF- α . According to a study, nonselective removal is more efficient than single interception targeting one ingredient [12]. Using the membrane with a mean replacement capacity of 31 mL.kg⁻¹.h⁻¹ and high interception capacity (≤ 100 KD), the inflammatory mediators in plasma can be removed partly, and the immunoreaction can be regulated so as to improve the clinical symptoms of ARDS efficiently [14-16].

The research results manifested that at three days after treatment, the levels of TNF- α , IL-6, and PCT in the serum of patients in the control group and the HVHF group were (25.68 \pm 8.86 vs. 15.55 \pm 3.98) ng.L⁻¹, (89.68 \pm 31.44 vs. 65.32 \pm 45.01) ng.L⁻¹ and (7.77 \pm 1.01 vs. 5.04 \pm 0.89) ng.L⁻¹, respectively, demonstrating that inflammatory factors in both groups decline, and changes in HVHF are more obvious. More-

over, the hemodynamic indexes (HR, MAP, PAWP and CI) in both groups were improved to some extent. There was a greater growth in the levels in HVHF group than those in control group, and the differences in PAWP and CI were statistically significant ($P < 0.05$), indicating that HVHF can keep hemodynamics in a relative smooth and steady state to some extent. The results demonstrated that HVHF was more effective than conventional therapy. On the one hand, it can eliminate inflammatory mediators and alleviate the injury of alveolar epithelial cells and pulmonary edema, and on the other hand, it can improve the prognosis of patients with ARDS by improving oxygen supply of tissues and the internal environment of acidosis [17-20]. In addition, comparisons between the results at 3 days after treatment and those before treatment indicate that the clinical monitoring indexes (white blood cell count and APACHE II) in the HVHF group were more significantly improved than those in the control group. In follow-up investigation for the two groups of patients after hospital discharge, the deaths in the control and HVHF groups were 7 cases (17.1%) and 3 cases (7.32%), respectively, suggesting that the prognosis of patients in HVHF group is superior to that in control group ($P < 0.05$). In conclusion, therapy of continuous HVHF is conducive to the protection of main organ functions and the recovery of pulmonary function so as to increase the patient's survival rate as it can enhance the scavenging capacity of inflammatory factors in blood circulation and has evident superiority in improving hemodynamics and tissue oxygenation, as well as maintaining a steady internal environment. Therefore, continuous HVHF therapy can provide effective reference value for clinical practice and applications.

Disclosure of conflict of interest

None.

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