The Effect of Different Doses of Daytime CRRT on Immune Function in Patients with Severe Pneumonia Complicated and Acute Kidney Injury

Wenlu Ma, Xiaomei Miao, Chao Ruan, Fangfang Xia, Dan Tao, Bing Li

Nephrology Department, Traditional Chinese Medicine Northern Hospital, Baotou City, Inner Mongolia Autonomous Region, 014030, China

Introduction. To analyze the effect of different doses of daytime CRRT on immune function in patients with severe pneumonia complicated with acute kidney injury.
Method. A study was conducted on patients with severe pneumonia complicated with acute kidney injury in our hospital. Randomly divided into three groups and given different treatment plans. Observe the therapeutic effects of three groups.
Result. Comparison before and after treatment showed significant improvements in immune function, renal function, intestinal mucosal function, and clinical scores (APACHE II and SOFA) in all three groups of patients (P<0.05). The high-dose group outperformed the low-dose group in terms of CD4+, CD8+, CD4+/CD8+, BUN, Scr, Cysc, D-Lac, DAO, BT, as well as APACHE II and SOFA scores, with the medium dose group outperforming the low-dose group (P<0.05).
Conclusion. In the treatment of patients with severe pneumonia complicated with acute kidney injury, different doses of daytime CRRT can effectively improve the patient's immune function, renal function, and gastrointestinal mucosal function, alleviate the condition, and promote patient recovery. However, compared with low and medium doses, high-dose daytime CRRT has a more significant effect on improving immune function and renal function, and has a more obvious protective effect on intestinal mucosal barrier function, showing a significant dose effect, providing important reference for clinical treatment.
Keywords. Different Dosages, Daytime CRRT, Severe Pneumonia, Acute Kidney Injury, Immunity, Renal Function, Intestinal Mucosal Function, Clinical Scoring

INTRODUCTION

Severe pneumonia and acute kidney injury are common clinical critical illnesses that seriously affect the patient's physiological functions. When the two occur together, their complexity and severity increase significantly [1-2]. Severe pneumonia is a lung infection caused by various pathogens, characterized by rapidly developing lung inflammation, often accompanied by systemic inflammatory response syndrome, and in severe cases can lead to acute respiratory distress syndrome and multiple organ dysfunction syndrome [3]. Acute kidney injury refers to a clinical syndrome in which kidney function declines rapidly, resulting in the inability to effectively remove metabolic waste and maintain electrolyte balance [4]. The systemic inflammatory response caused by severe pneumonia can lead to changes in renal hemodynamics and damage the renal tubules, thereby inducing or aggravating acute kidney injury. After acute kidney injury occurs, the accumulation of metabolic waste and fluid load can in

turn aggravate lung infection, forming a vicious cycle [5]. CRRT is a blood purification treatment for critically ill patients. It helps maintain hemodynamic stability and internal environment balance by continuously and slowly removing metabolic waste and excess water from the body. CRRT also affects the immune function of patients while treating acute kidney injury. Studies have shown that CRRT can remove inflammatory mediators and reduce inflammatory response, but its specific mechanism of immune function is not completely clear, and different doses of CRRT may have different effects on immune function [6]. Based on this, the purpose of this study was to investigate the effects of different doses of daytime CRRT on immune function in patients with severe pneumonia complicated with acute kidney injury, to compare the changes of immune function indexes before and after different doses of CRRT treatment, and to evaluate the relationship between CRRT dose and immune function, so as to provide theoretical basis for individualized treatment of CRRT in clinical practice and improve the prognosis of patients.

1. MATERIALS AND METHODS

1.1 Clinical Information

A total of 60 patients with severe pneumonia and acute kidney injury enrolled to our hospital from January 2021 to December 2023 were studied. Inclusion criteria [7-8]: ① diagnosed with severe pneumonia. ② met the RIFLE, AKIN or KDIGO criteria. ③ CRRT treatment. ④ signed informed consent. Exclusion criteria: ① chronic kidney disease or previous history of chronic dialysis. ② severe heart disease, such as unstable angina, recent myocardial infarction or severe heart failure. ③ active bleeding or coagulation dysfunction. ④ severe liver disease. ⑤ pregnant or lactating women. ⑥ irreversible brain damage or coma. ⑦ other serious complications. The patients were randomly divided into low-dose group [(20 ml/(kg·h)], medium-dose group [(40 ml/(kg·h)], and high-dose group [(60 ml/(kg·h)]. The male-to-female ratio in the low-dose group was 10:10, the age was 18-70 years old, and the course of disease was 1-9 days. the male-to-female ratio in the medium-dose group was 11:9, the age was 20-69 years old, and the course of disease was 1-8 days. the male-to-female ratio in the high-dose group was 9:11, the age was 19-71 years old, and the course of disease was 1-10 days. The general data of the three groups were compared (P>0.05).

1.2 Methods

All patients received daytime CRRT treatment, established vascular access, and selected CRRT mode according to the patient's condition, such as CVVH, CVVHDF or CVVHD. The blood flow was 160-250 ml/min, the loading dose of low molecular weight heparin was 15-25 IU/kg, and the subsequent intravenous maintenance dose was 5~10 IU/(kg•h). 4% trisodium citrate was infused before the filter to make the serum citrate concentration in the filter reach 4~6 mmol/L, and calcium chloride or calcium gluconate solution was supplemented after the filter. Low-dose group [(20ml/(kg·h)], medium-dose group [(40ml/(kg·h)], high-dose group [(60ml/(kg·h).

Treatment was 12h per day and continued for 7d.

1.3 Observation Indicators

（1）Immune function: BD FACSCanto II was used to measure the levels of CD4+, CD8+ and CD4+/CD8+ in blood samples.

（2）Renal function: BUN, Scr and Cysc levels in blood samples were measured using a fully automatic biochemical analyzer.

（3）Gastrointestinal mucosal function: ELISA was used to measure the levels of D-Lac, DAO and BT in blood samples.

（4）Clinical scores [9-10]: APACHE II score and SOFA score were used respectively. APACHE II score involves physiological score, age score and chronic health status score. The highest score is 71 points. The higher the score, the more serious the patient's condition. SOFA score involves the respiratory system, blood system, liver, circulatory system, nervous system and renal system. The highest score is 24 points. The higher the score, the worse the prognosis.

1.4 Statistic Analysis

SPSS27.0 software was used for processing. The count data were tested by χ^2 test, expressed as n (%). The measurement data were tested by t test, expressed as ($\overline{x} \pm s$). The difference of P<0.05 was statistically significant.

2 RESULTS

2.1 Comparison of Immune Function among Three Groups

After treatment, the CD4+, CD8+ and CD4+/CD8+ in the high-dose group were higher than those in the medium-dose group and the low-dose group, and the medium-dose group was higher than the low-dose group, P<0.05, see Table 1.

Table 1 Comparison of Immune Function among Three Groups($\overline{x} \pm s$)

Group	Cases	CD4+		CD8+		CD4+/CD8+	
		Before	After	Before	After	Before	After
Low-Dose	20	23.82±4.59	26.85±2.56	22.09±4.53	19.70±2.58	1.11±0.31	1.51±0.11
Medium-Dose	20	24.01±5.34	31.01±3.26	21.82±3.31	17.01±2.21	1.09±0.53	1.88±0.22
High-Dose	20	24.05±5.41	36.05±4.52	21.98±5.22	14.05±2.32	1.10±0.41	2.15±0.32
F		0.011	33.861	0.019	28.314	0.011	38.040
P		0.989	0.001	0.981	0.001	0.989	0.001

2.2 Comparison of Kidney Function among Three Groups

After treatment, BUN, Scr and Cysc in the high-dose group were lower than those in the medium-dose group and the low-dose group. The medium-dose group

was lower than the low-dose group, $P<0.05$, see Table 2.

Table 2 Comparison of Kidney Function among Three Groups ($\bar{x} \pm s$)

Groups	Cases	BUN(mmol/L)		Scr(μmol/L)		Cysc(mg/L)	
		Before	After	Before	After	Before	After
Low-Dose	20	11.08±4.31	9.49±1.03	151.88±15.52	132.31±8.12	1.78±0.31	1.43±0.12
Medium-Dose	20	11.10±4.41	7.28±1.12	152.01±16.92	112.78±7.11	1.80±0.41	0.88±0.07
High-Dose	20	11.15±4.06	5.22±1.23	152.05±17.42	95.75±5.10	1.72±0.23	0.51±0.05
F		0.001	71.450	0.001	140.749	0.331	586.849
P		0.999	0.001	0.999	0.001	0.720	0.001

2.3 Comparison of Intestinal Mucosal Function among Three Groups

After treatment, D-Lac, DAO and BT in the high-dose group were lower than those in the medium-dose group and the low-dose group, and the medium-dose group was lower than the low-dose group, $P<0.05$, see Table 3.

Table 3 Comparison of Intestinal Mucosal Function among Three Groups ($\bar{x} \pm s$)

Groups	Cases	D-Lac(mmol/L)		DAO(U/L)		BT(U/L)	
		Before	After	Before	After	Before	After
Low-Dose	20	39.82±4.59	20.85±3.56	13.09±3.53	8.70±2.58	12.11±2.31	9.51±1.51
Medium-Dose	20	40.01±4.34	19.01±3.26	12.82±3.31	7.01±2.21	12.09±2.53	7.08±1.02
High-Dose	20	39.95±4.41	15.05±2.52	12.98±3.22	4.05±1.32	12.10±2.41	3.15±0.72
F		0.010	17.770	0.033	25.030	0.001	161.075
P		0.991	0.001	0.968	0.001	0.999	0.001

2.4 Comparison of Clinical Scores Among Three Groups

After treatment, the APACHE Ⅱ score and SOFA score in the high-dose group were lower than those in the medium-dose group and the low-dose group, and the medium-dose group was lower than the low-dose group, $P<0.05$, see Table 4.

Table 4 Comparison of Clinical Scores Among Three Groups ($\bar{x} \pm s$, Points)

Groups	Cases	APACHEII		SOFA	
		Before	After	Before	After
Low-Dose	20	25.52±3.59	18.85±2.56	18.79±2.53	10.70±1.58
Medium-Dose	20	25.46±3.34	15.01±2.26	19.02±2.31	7.61±1.21
High-Dose	20	25.49±3.36	13.02±2.23	18.81±2.36	4.29±1.03

F	0.001	31.785	0.056	122.836
P	0.999	0.001	0.945	0.001

3 DISCUSSION

3.1 High-Dose CRRT Can More Effectively Improve Immune Function

Both severe pneumonia and acute kidney injury are closely related to the patient's immune function [11-12]. In severe pneumonia, the body's immune response is activated, but excessive immune response can lead to immune damage. For example, viruses can bind to specific receptors on host cells and directly infect kidney cells, leading to kidney cell dysfunction or death, reducing the kidney's ability to remove metabolic waste from the body, and affecting the kidney's role in maintaining the homeostasis of the immune system, causing local and systemic immune response damage, and reducing the body's ability to eliminate pathogens. Acute kidney injury can further affect the body's immune status due to the accumulation of uremic toxins and dysfunction of renal immune cells [13]. At the same time, severe pneumonia combined with acute kidney injury can cause systemic inflammatory response syndrome, leading to the release of a large number of proinflammatory factors, affecting the activation, proliferation and differentiation of T cells, resulting in a decrease in the number of CD4+ T cells and impaired function. It can also affect the cytotoxicity of CD8+ T cells and reduce the ability to eliminate pathogens and tumor cells. Therefore, it is necessary to actively improve the patient's immune status and improve the treatment effect. CRRT helps improve immune function. CRRT can continuously and slowly remove metabolic waste and excess water from the body and correct electrolyte disorders, avoid the impact of rapid changes on hemodynamics, and reduce the pressure on the heart and circulatory system caused by rapid changes in osmotic pressure and blood volume. It is essential for maintaining the normal function of immune cells because immune cells need a stable internal environment to perform their functions. CRRT can also maintain electrolyte balance, which is essential for the signal transduction and cell activity of immune cells. For example, calcium ions play a key role in T cell activation and cytokine release, which helps maintain the integrity and function of the immune system. At the same time, CRRT can efficiently remove inflammatory mediators from the body. In severe pneumonia and AKI, inflammatory mediators are often overproduced, leading to excessive inflammatory responses, inhibiting or interfering with normal immune functions. For example, excessive cytokines such as TNF-α and IL-6 will inhibit the proliferation and function of T cells, while CRRT can effectively remove inflammatory mediators and reduce the negative impact on immune cells, thereby helping to restore normal immune responses. CRRT can regulate fluid balance, help improve microcirculation, and increase tissue perfusion. Improved microcirculation is crucial for the immune system because immune cells need a good blood supply to reach sites of infection or inflammation. Good microcirculation not only provides immune cells with necessary nutrients and oxygen, but also helps remove metabolic waste, providing ideal

conditions for immune response. In critical illness, abnormal accumulation of immune cells can lead to a decrease in the number of immune cells in the peripheral blood, affecting the immune response. CRRT helps redistribute immune cells by clearing inflammatory mediators in the body and improving microcirculation, enabling them to

reach the site of infection more effectively. It also reduces tissue edema and improves tissue perfusion, promoting the infiltration of immune cells in damaged tissues and enhancing local immune responses, thereby helping to restore normal immune cell distribution and improving the immune system's ability to eliminate pathogens [14]. In this study, after treatment, the CD4+, CD8+, and CD4+/CD8+ in the high-dose group were higher than those in the medium-dose group and the low-dose group, and the medium-dose group was higher than the low-dose group, $P<0.05$. This shows that high-dose CRRT is more effective in promoting the recovery of immune cells and the reconstruction of immune function. The reason is that high-dose can more effectively clear inflammatory mediators in the body and reduce the inhibitory effect of inflammatory response on immune cell function. High-dose CRRT provides more sufficient nutrition and oxygen for immune cells, promoting the effective activation and migration of immune cells. At the same time, high-dose CRRT is more effective in maintaining the stability of the internal environment, helping to regulate the distribution of immune cells in the body, reducing abnormal accumulation, and enabling immune cells to participate in immune responses more effectively.

3.2High-Dose CRRT Can More Effectively Improve Renal Function

In this study, after treatment, BUN, Scr and Cysc in the high-dose group were lower than those in the medium-dose group and the low-dose group, and the medium-dose group was lower than the low-dose group, $P<0.05$. This shows that high-dose CRRT has more obvious advantages in clearing metabolic waste from the body and improving renal function. The reason is that high-dose CRRT has a stronger clearance ability and can more effectively clear metabolic waste and toxins from the blood. At the same time, high-dose CRRT can more stably maintain the patient's blood volume and blood pressure without causing hemodynamic fluctuations, providing better perfusion conditions for the kidneys. In addition, high-dose treatment can more effectively improve microcirculation, reduce systemic inflammatory response, optimize the internal environment, and promote the recovery of renal function.

3.3High-dose CRRT Can More Effectively Improve Intestinal Mucosal Function

In this study, after treatment, D-Lac, DAO and BT in the high-dose group were lower than those in the medium-dose group and the low-dose group, and the medium-dose group was lower than the low-dose group, $P<0.05$. This suggests that high-dose CRRT is more effective in reducing intestinal inflammation and protecting the intestinal mucosal barrier. The reason is that high-dose CRRT has a stronger ability to clear inflammatory mediators and endotoxins, reducing the damage of inflammation to the intestinal mucosa. At the same time, high-dose CRRT can

maintain the integrity of the intestinal mucosa by improving intestinal blood flow and reducing intestinal edema, and the immunomodulatory effect of high-dose CRRT can have a positive effect on intestinal inflammation.

3.4High-dose CRRT Can More Effectively Control the Disease and Improve Prognosis

In this study, after treatment, the APACHE Ⅱ score and SOFA score of the high-dose group were lower than those of the medium-dose group and the low-dose group, and the medium-dose group was lower than the low-dose group, $P < 0.05$. This indicates that the score of the high-dose group decreased the most, which is related to the fact that high-dose CRRT improves the patient's condition in many aspects.

In summary, in the treatment of patients with severe pneumonia and acute kidney injury, different doses of daytime CRRT can effectively improve the patient's immune function, renal function and gastrointestinal mucosal function, relieve the condition and promote the patient's recovery. However, compared with low-dose and medium-dose, high-dose daytime CRRT has more significant effects on improving immune function and renal function, and has a more obvious protective effect on intestinal mucosal barrier function, showing an obvious dose effect, which provides an important reference for clinical treatment.

REFERENCES

[1] Ge Shunzhou, Liu Hongjing, Wang Haibo. Effects of different continuous renal replacement therapy (CRRT) doses on ICU patients with septic shock[J]. Systems Medicine, 2023, 8(21): 83-86.

[2] Xu Jiaxin, Du Wenhui, Wang Qingjun, Zhao Hongyan. Effects of different doses of CRRT in patients with severe pneumonia and acute kidney injury and their impact on APACHE Ⅱ score[J]. Clinical Medical Research and Practice, 2023, 8(21): 37-40.

[3] Chen Zhifang . Effect of different doses of CRRT replacement fluid on the prognosis of children with acute kidney injury secondary to severe pneumonia[J]. Contemporary Nurses (Second Half Monthly), 2023, 30(04): 69-72.

[4] Kuang Xiaoqing. Effects of different therapeutic doses of CRRT on intestinal mucosal barrier function and immune function in patients with severe sepsis and acute kidney injury[J]. Chinese and Foreign Medical Research, 2022, 20(36): 50-53.

[5] Peng Wenqing, Xu Yuewen, Tang Liangxia, Shao Weiwei, Hu Xuesong, Zhang Lili, Wu Yong. Observation on the effect of different filtration doses of continuous renal replacement therapy in the treatment of critically ill patients with acute kidney injury[J]. Journal of Clinical Military Medicine, 2021, 49(12): 1359-1361+1364.

[6] Deng Zhenfeng. Effects of different treatment doses of CRRT on the clearance of inflammatory mediators in patients with acute renal failure combined with heart failure and respiratory failure[J]. Primary Medicine Forum, 2021, 25(14): 1966-1967.

[7] Chu Xinxu . Changes of different doses of VitC during continuous renal replacement therapy in patients with sepsis-induced AKI[D]. Bengbu Medical College, 2021.

acute kidney injury in rabbits caused by different doses of non-ionic monomeric iodine contrast agents using intravoxel incoherent motion and diffusion tensor imaging [D]. China Medical University, 2021.

[9] Peng Xiaohong, Xi Jianhong, Zhang Li. Analysis of the effect of different doses of continuous renal replacement therapy on severe pneumonia combined with sepsis[J]. Chinese Journal of Medical Frontiers (Electronic Edition), 2020, 12(07): 129-133.
[10] Bai Zhun, Liu Xuli, Zeng Weizhong, Peng Suna, Wu Shuanghua. Effects of different doses of CRRT on immune function, intestinal mucosal barrier function and prognosis in patients with severe sepsis[J]. Hebei Medicine, 2020, 42(12): 1856-1859.

[11] Xu Dong. Effect of CRRT treatment dose on inflammatory response and prognosis in patients with sepsis[J]. Chinese and Foreign Medical Research, 2019, 17(35): 161-163.
[12] Liu Jintao. Effects of different CRRT treatment doses on clinical efficacy, stress response and cellular immune function in patients with septic shock[J]. World Composite Medicine, 2019, 5(04): 124-126.
[1 3] Xie Yuan, Liu Zimeng, Zheng Fenshuang, Xu Zongming. Different doses of continuous renal replacement therapy for the treatment of severe pneumonia combined with acute kidney injury[J]. Journal of Practical Medicine, 2018, 34(21): 3598-3602.
[1 4] Wang Lei. Effects of different CRRT treatment doses on clinical efficacy, stress response and cellular immune function in patients with septic shock[J]. Shandong Medicine, 2018, 58(18): 85-87.

Corresponding Author:
Wenlu Ma
Nephrology Department, Traditional Chinese Medicine Northern Hospital, Baotou City, Inner Mongolia Autonomous Region, 014030, China
E-mail: bfyysnk@163.com