Effects of Nafamostat Mesilate and Systemic Unfractionated Heparin Anticoagulation on Coagulation, Renal Function, and 28-day Survival Status in Critically Ill AKI CRRT Patients

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Keywords. Acute kidney injury; Continuous renal replacement therapy; Nafamostat Mesilate; Heparin; Coagulation function; Renal function; existence

Introduction. To investigate the effect of continuous renal replacement therapy (CRRT) in patients with severe acute kidney injury (AKI) by using Nafamostat Mesilate (NM).
Methods. Eighty patients with AKI who underwent CRRT from March 2022 to January 2022 were divided into control group (n = 40, treated with unfractionated heparin) and Observation group (n = 40, treated with NM). The duration of the first filter use, the number of filters used 72 hours after treatment, coagulation and renal functions, adverse reactions, bleeding events, length of stay in intensive care unit (ICU) and survival status at 28 days were compared between the two groups.
Results. The observation group used the first filter for a longer period of time than the control group, and after 72 hours of treatment, the number of filters used was less than that of the control group ($P < .05$); Compared with before treatment, the levels of fibrinogen (FIB) and platelet count (PLT) in the observation group and control group decreased after 48 hours of treatment, while the levels of activated partial thromboplastin time (APTT), prothrombin time (PT), thrombin time (TT), and international normalized ratio (INR) increased. However, the levels of FIB and PLT in the former group were higher, while the levels of APTT, PT, TT, and INR were lower ($P < .05$); Compared with before treatment, the levels of creatinine (Scr), urea nitrogen (BUN), and serum cystatin C (CysC) in the observation group and control group decreased after 48 hours of treatment, and the former was even lower ($P < .05$); the incidence of bleeding events in the observation group was lower than that in the control group, the length of stay in ICU was shorter than that in the control group, and finally the 28-day survival rate was higher than that in the control group ($P < .05$). The adverse reactions of the two groups were similar ($P > .05$).
Conclusions. NM can improve the coagulation function and renal function in patients with severe AKI undergoing CRRT, prolong the duration of the filter use, reduce the number of filters used, shorten the length of ICU stay, reduce the incidence of bleeding events, and improve the prognosis.

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Original Paper

INTRODUCTION

Acute Kidney Injury (AKI) is defined as a clinical syndrome marked by a rapid deterioration of kidney function within a short timeframe, typically resulting from factors such as medications, infection, and urinary tract obstruction, among others.[1,2] AKI is linked to a high mortality rate; however, early recognition and timely effective management can maximize renal function recovery and improve prognosis.[3,4] Continuous Renal Replacement Therapy (CRRT) is a method, which is employed for blood purification by mimicking the filtration principle of the renal glomerulus. Compared to traditional hemodialysis, CRRT can stabilize the patient's hemodynamics, CRRT can correct acid-base imbalance and regulate body temperature while stabilizing patient hemodynamics.[5,6] Additionally, CRRT offers advantages such as high biocompatibility, high solute clearance rate, and minimal side effects, achieving high satisfaction in patient treatment.[7] However, during CRRT, patients are at increased risk of extracorporeal circuit (ECC) clotting, which may compromise treatment continuity. To prevent this, appropriate anticoagulation therapy is necessary.[8] Systemic unfractionated heparin is a commonly used anticoagulant in clinical practice. The anticoagulant effects of unfractionated heparin include anticoagulation, antiplatelet aggregation, and microcirculation improvement. However, heparin anticoagulation also has drawbacks, such as affecting the immune system and increasing the risk of bleeding, making it unsuitable for patients with AKI who have a high bleeding risk or multiple organ dysfunction. Nafamostat mesilate (NM), a protease inhibitor, has a short half-life and exerts a good anticoagulant effect by inhibiting the activity of various enzymes involved in the coagulation process, such as pancreatic proteases, thrombin, and fibrinolytic enzymes.[9] While NM has been widely reported for use worldwide, clinical experience with NM in China remains limited.[10] Hence, this study aims to examine the effectiveness of NM compared to systemic unfractionated heparin anticoagulation on coagulation, renal function, and 28-day survival status in critically ill patients with AKI who undergo CRRT, with the goal of further elucidating the application evidence of NM in critically ill AKI patients treated with CRRT.

MATERIALS AND METHODS

General Information

This study has been approved by the Hospital Ethics Committee (No. 2022000132) From March 2022 to January 2024, the observation group comprised 40 patients with acute kidney injury (AKI) who underwent continuous renal replacement therapy (CRRT) and were administered Nafamostat Mesilate for anticoagulation. During the same period, the control group consisted of an equivalent number of 40 AKI patients treated with CRRT but received systemic anticoagulation with unfractionated heparin. The two groups were compared in terms of sex, primary disease type, etc. to ensure good balance ($P > .05$). (Table 1)

Inclusion and Exclusion Criteria

The inclusion Criteria were: (1) meet the diagnostic criteria for AKI: Serum creatinine increases by 0.3 mg/dL or 25.6 μmol/L within 48 hours;[11] (2) meet the indications for CRRT treatment; (3) have signed informed consent. The exclusion Criteria were: (1) concurrent history of chronic kidney disease or persistent hypotension; (2) coexisting coagulation abnormalities; (3) active bleeding tendency; (4) use of antiplatelet or anticoagulant drugs in the month prior to enrollment; (5) newly diagnosed thrombotic diseases within the six months prior to enrollment; (6) concurrent acute bacterial endocarditis; (7) death within 24 hours of hospital admission; (8) inability to cooperate with the study due to psychiatric disorders.

Methods

Both groups underwent CRRT treatment. To ensure effective establishment of temporary vascular access, a double-lumen central venous catheter (model: 12F 16 cm) was placed via the femoral or internal jugular vein. The CRRT was performed by using a Japanese Asahi Kasei hemofiltration machine (model: ACH-10) with matching tubing sets. The blood filter used was of AFP-10S type (membrane area: 1.5 m^2), and the replacement fluid was sodium Lactated Ringer's solution (Shanghai Xinfan Biotechnology Co. Ltd. SFDA approval number: H13022134, 500 mL). The settings were as follows: pre-dilution replacement rate set at 35 mL/kg/h, blood flow rate set at 150-180 mL/min, Pre-dilution replacement solution volume set at 3000 mL/h, and replacement fluid temperature

Table 1. Comparison of General Information Across Both Groups

Indicators	Observation group (n = 40)	Control group (n = 40)	Statistic value	*P*
Sex[n (%)]				
Male	26 (65.00)	28 (70.00)	$\chi^2 = 0.228$	.633
Female	14 (35.00)	12 (30.00)		
Primary disease type [n (%)]				
Renal artery thrombosis	19 (47.50)	21 (52.50)	$\chi^2 = 0.540$	.910
Hepatorenal syndrome	8 (20.00)	6 (15.00)		
Hypoxemia	7 (17.50)	6 (15.00)		
Sepsis	6 (15.00)	7 (17.50)		
Age ($\bar{x} \pm s$, year)	58.48 ± 4.17	59.28 ± 4.66	t = 0.809	.421
BMI ($\bar{x} \pm s$, kg/m^2)	24.51 ± 1.02	24.39 ± 1.17	t = 0.489	.626
WBC ($\bar{x} \pm s$, ×109/L)	16.89 ± 3.15	17.12 ± 3.01	t = 0.334	.739
HGB ($\bar{x} \pm s$, g/L)	91.46 ± 5.22	92.34 ± 6.23	t = 0.685	.496
MAP ($\bar{x} \pm s$, mmHg)	63.58 ± 6.46	62.85 ± 5.97	t = 0.525	.601
Serum potassium (K) ($\bar{x} \pm s$, mmol/L)	4.11 ± 0.52	3.93 ± 0.48	t = 1.609	.112
Serum sodium (Na) ($\bar{x} \pm s$, mmol/L)	135.68 ± 10.41	134.98 ± 9.55	t = 0.313	.755
Serum calcium (Ca) ($\bar{x} \pm s$, mmol/L)	1.03 ± 0.11	1.05 ± 0.14	t = 0.710	.480
APACHEII score ($\bar{x} \pm s$, points)	18.45 ± 3.18	17.58 ± 2.89	t = 1.281	.204
SOFA score ($\bar{x} \pm s$, points)	9.15 ± 1.23	8.80 ± 1.45	t = 1.164	.248
Baseline Comorbidity [n (%)]				
hypertension	12 (30.00)	10 (25.00)	$\chi^2 = 0.527$	.913
diabetes mellitus	10 (25.00)	11 (27.50)		
hyperlipemia	11 (27.50)	10 (25.00)		
coronary disease	7 (17.50)	9 (22.50)		

set at 36.5~37.5℃, and ultrafiltration rate is 3%. Prior to treatment, the circuit and filter were pre-loaded with 5000 U of heparin + 1000 mL of normal saline, followed by a rinse with 1000 mL of normal saline. During CRRT treatment, the filter was rinsed with 200 mL of normal saline every 2 hours. Throughout the treatment process, close monitoring of patient consciousness, respiration, blood pressure, heart rate, urine output, etc., was performed. Instrument parameters and blood flow were adjusted based on fluctuations in the patient's blood pressure and cardiac function. Safety restraints were implemented for patients exhibiting agitation.

Control Group(40 cases with AKI)

The control group comprised 40 patients of AKI in which systemic unfractionated heparin anticoagulation therapy was administered during the CRRT treatment. Systemic unfractionated heparin anticoagulation treatment was administered by using heparin sodium injection (2 mL: 12,500 U, SFDA approval number: H32020612, Jiangsu Wanbang Biopharmaceuticals) diluted with normal saline and administered intravenously. The total dose was 12,500 U, with an initial dose of 10-20 U/kg, and the maintenance dose was adjusted to 3~15 U/kg/h based on the specific condition of the patient.

Observation Group (40 cases with AKI)

The observation group comprised 40 patients of AKI in which Nafamostat Mesilate (NM) anticoagulant therapy was administered during the CRRT treatment. NM (Jiangsu Durui Pharmaceutical Co., Ltd., SFDA approval number: H20203509, 50 mg) was administered before the start of extracorporeal circulation. The initial dose was 0.4mg/kg, and the maintenance dose during extracorporeal circulation was 0.4 mg/kg/h.

Observation Indicators

(1) Observation and recording of the time of first filter usage in both groups: This refers to the time from the initiation of filter use to either the scheduled replacement time, or termination of CRRT due to various reasons such as patient bleeding, filter clotting, change in anticoagulation method, etc. The number of filters used after 72 hours of treatment in both groups will also be

recorded. (2) Coagulation function indicators: Five mL of fasting venous blood was collected from patients, pre-treatment and 48 hours post-treatment initiation. After routine anticoagulation centrifugation, coagulation function indicators including fibrinogen (FIB), prothrombin time (PT), activated partial thromboplastin time (APTT), thrombin time (TT) were measured by using the GW-3000 fully automatic coagulation analyzer produced by Shandong Accurdx Biological Technology Co., Ltd. Platelet count (PLT) were measured by using the URIT-3060 fully automatic blood cell analyzer produced by Shanghai Huanxi Medical Equipment Co., Ltd. International normalized ratio (INR) was calculated by using the tissue thromboplastin reagent kit (manufacturer: Dade-Behring, USA, international sensitivity index ISI: 1.08). (3) Renal function indicators: Fasting venous blood samples were collected from both groups prior to treatment initiation and 48 hours after treatment commencement. After centrifugation, serum creatinine (SCr), blood urea nitrogen (BUN), and serum cystatin C (CysC) levels were measured by using the fully automatic biochemical analyzer (manufacturer: Nanjing Beiden Medical Co., Ltd., model: YolitCA-801B). (4) Bleeding events: Incidence of skin and mucous membrane bleeding, gastrointestinal bleeding, puncture site bleeding, etc., were recorded in both groups. (5) Adverse reactions: Incidence of diarrhea, hyperkalemia, nausea/vomiting, hypocalcemia in both groups were recorded. (6) Comparison of the length of stay and 28-day survival rate between the two groups.

Statistical analysis

Statistical analysis was conducted by using Statistic Package for Social Science (SPSS) 23.0 software. All measurement data were Normality test. Measurement data conforming to normal distribution were described by means ± standard deviation ($\bar{x} \pm s$) , within-group comparisons were performed with paired-sample t-test, with corrected t-test (t'-test) when variance was uneven, and measures of partial-normal distribution were described with median (m) and interquartile range (QR), using Mann-whitney U test. For count data described using percentages (%), chi-square test or corrected chi-square test was employed for comparison, with $P < .05$ indicating statistically significant differences.

RESULTS

Comparison of First Filter Use Time and Number of Filters Used After 72 Hours of Treatment Across Both Groups

The observation group exhibited a longer duration of first filter usage as compared to the control group, and the number of filters used after 72 hours of treatment was lower than that in the control group ($P < .05$) (Table 2 and Figure 1).

Comparison of Coagulation Function Related Indicators Before and After 48 Hours of Treatment in Both Groups

Compared to baseline, both groups exhibited a decrease in FIB and PLT counts, and an increase in APTT, PT, TT, and INR after 48 hours of treatment. However, the observation group had higher FIB and PLT counts, and lower APTT, PT, TT levels,

Table 2. Comparison of First Filter Use Time and Number of Filters Used After 72 Hours of Treatment Across Both Groups ($\bar{x} \pm s$)

Groups	First filter use time (h)	Number of filters used after 72h of treatment (pcs)
Observation group (n = 40)	5.25 ± 0.41	1.92 ± 0.67
Control group (n = 40)	4.37 ± 0.25	2.46 ± 0.49
t	11.590	4.115
P	< .001	< .001

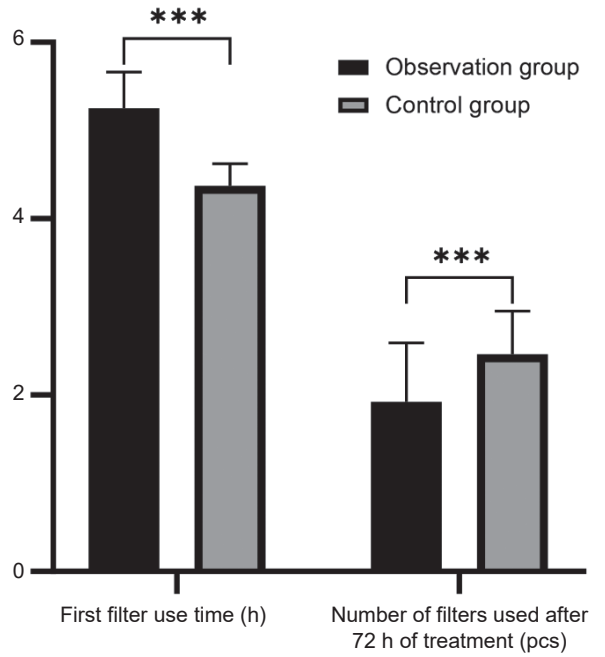

Figure 1. Comparison of First Filter Use Time and Number of Filters Used After 72 Hours of Treatment Across Both Groups (***$P < .001$)

and INR values compared to the control group ($P < .05$) (Table 3 and Figure 2).

Comparison of Renal Function Related Indicators Pre- and 48 Hours Post Treatment in Both Groups

Compared to baseline, both groups exhibited a decrease in SCr, BUN, and CysC levels after 48 hours of treatment. However, the observation group had lower levels of these indicators compared to the control group ($P < .05$) (Table 4 and Figure 3).

Comparison of Occurrence of Bleeding Events Across Both Groups

The incidence of bleeding events was lower in the observation group as compared to the control group ($P < .05$) (Table 5).

Table 3. Comparison of Coagulation Function Related Indicators Before and After 48 Hours of Treatment in Both Groups ($\bar{x} \pm s$)

Groups	APTT (s)		FIB (g/L)		PT (s)	
	Pre-treatment	48h post treatment	Pre-treatment	48h post treatment	Pre-treatment	48h post treatment
Observation group (n = 40)	39.87 ± 3.15	48.89 ± 4.36[a]	3.98 ± 0.51	2.74 ± 0.42[a]	12.34 ± 1.85	18.33 ± 1.59[a]
Control group (n = 40)	40.28 ± 3.72	63.47 ± 5.21[a]	3.81 ± 0.45	2.05 ± 0.59[a]	13.06 ± 1.77	21.78 ± 2.06[a]
t	0.532	13.573	0.719	6.026	1.779	8.385
P	.596	< .001	.474	< .001	.079	< .001
Groups	**TT (s)**		**PLT (×10^9/L)**		**INR**	
	Pre-treatment	**48h post treatment**	**Pre-treatment**	**48h post treatment**	**Pre-treatment**	**48h post treatment**
Observation group (n = 40)	19.21 ± 2.08	22.84 ± 2.89[a]	251.73 ± 22.16	181.33 ± 11.85[a]	1.95 ± 0.11	2.91 ± 0.39[a]
Control group (n = 40)	18.85 ± 2.13	26.77 ± 3.16[a]	249.21 ± 21.38	162.58 ± 16.37[a]	1.98 ± 0.12	3.62 ± 0.45[a]
t	0.765	5.804	0.517	5.868	1.166	7.541
P	.447	< .001	.606	< .001	.247	< .001

Note: Comparing with the pre-treatment within the same group, [a]$P < .05$.

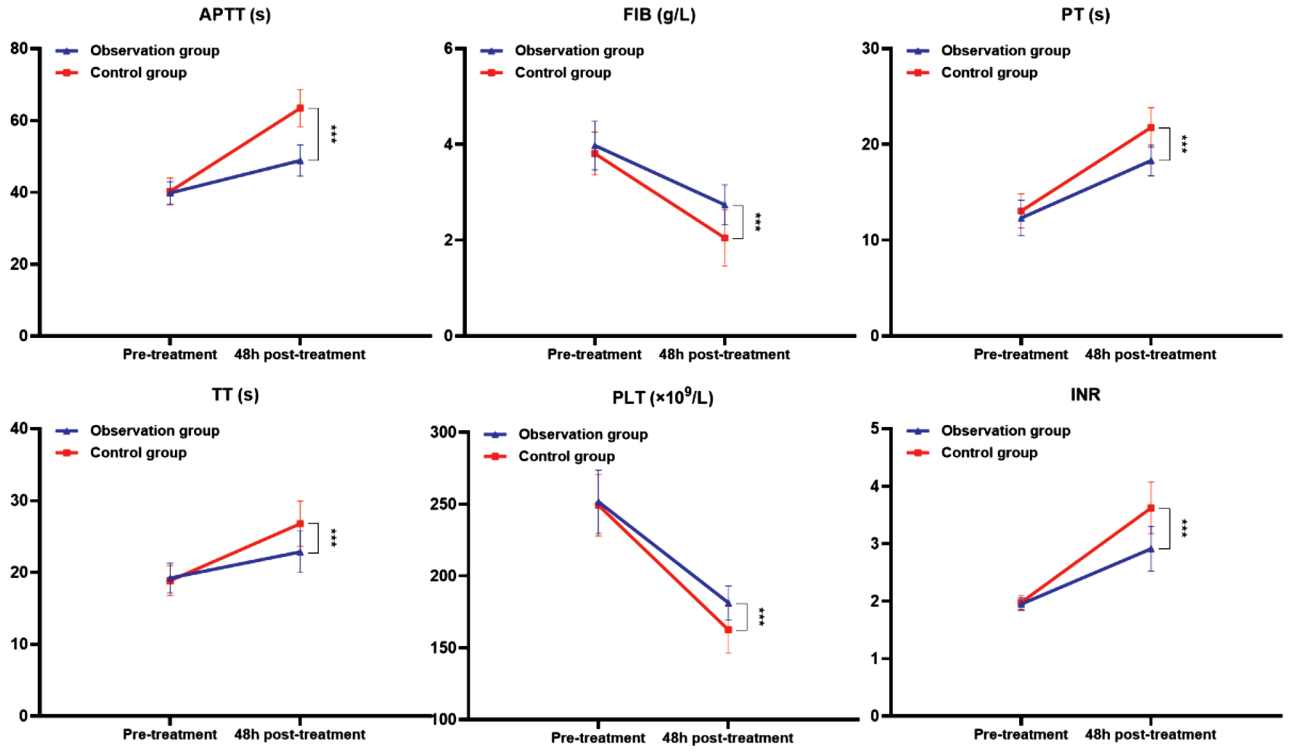

Figure 2. Comparison of Coagulation Function Related Indicators Before and After 48 Hours of Treatment in Both Groups ($^{***}P < .001$)

Table 4. Comparison of Renal Function Related Indicators Pre- and 48 Hours Post Treatment in Both Groups ($\bar{x} \pm s$)

Groups	Scr (μmol/L)		BUN (mmol/L)		CysC (mg/L)	
	Pre-treatment	48 h post treatment	Pre-treatment	48 h post treatment	Pre-treatment	48 h post treatment
Observation group (n = 40)	378.51 ± 39.12	109.86 ± 15.33[b]	20.26 ± 3.47	10.81 ± 2.14[b]	2.26 ± 0.38	1.09 ± 0.13[b]
Control group (n = 40)	375.84 ± 38.45	127.76 ± 19.82[b]	21.45 ± 3.88	14.86 ± 2.72[b]	2.33 ± 0.41	1.38 ± 0.26[b]
t	0.308	5.695	1.446	7.401	0.792	6.310
P	.759	< .001	.152	< .001	.431	< .001

Note: Comparing with the pre-treatment within the same group, [b]*P* < .05.

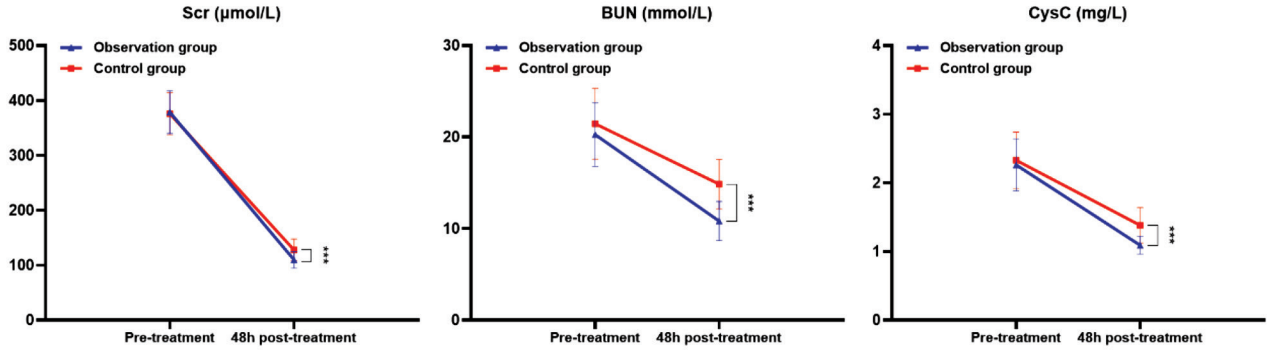

Figure 3. Comparison of Renal Function Related Indicators Before and After 48 Hours of Treatment in Both Groups ([***]*P* < .001)

Table 5. Comparison of Occurrence of Bleeding Events Across Both Groups example (%)

Groups	Skin and mucous membrane bleeding	Gastrointestinal bleeding	Puncture site bleeding	Total occurrence
Observation group (n = 40)	1 (2.50)	0 (0.00)	1 (2.50)	2 (5.00)
Control group (n = 40)	4 (10.00)	1 (2.50)	3 (7.50)	8 (20.00)
χ^2				4.114
P				.043

Table 6. Comparison of Occurrence of Adverse Reactions Across Both Groups example (%)

Groups	Diarrhea	Hyperkalemia	Nausea/vomiting	Hypocalcemia	Total occurrence
Observation group (n = 40)	1 (2.50)	1 (2.50)	1 (2.50)	0	3 (7.50)
Control group (n = 40)	1 (2.50)	0	2 (5.00)	2 (5.00)	5 (12.50)
χ^2					0.139
P					.709

Table 7. Comparison of Length of Stay and 28-day Survival Rate Across Both Groups

Groups	Length of stay ($\bar{x} \pm s$, d)	28-day survival rate example %)
Observation group (n = 40)	14.86 ± 2.17	38 (95.00)
Control group (n = 40)	19.35 ± 2.89	32 (80.00)
Statistic value	*t* = 7.858	χ^2 = 4.114
P	< .001	.043

Comparison of Occurrence of Adverse Reactions Across Both Groups

The occurrence of adverse reactions was comparable across both groups (*P* > .05) (Table 6).

Comparison of Length of Stay and 28-day Survival Rate Across Both Groups

The observation group exhibited a shorter duration of hospital stay and a higher 28-day survival rate in comparison to the control group (*P* < .05) (Table 7).

DISCUSSION

Continuous Renal Replacement Therapy (CRRT) is an important therapeutic modality in the clinical management of critically ill patients with Acute

Kidney Injury (AKI). It functions by processes including adsorption, diffusion, and convection to eliminate metabolic waste products and toxic substances from the body, thereby attaining fluid and electrolyte balance.[12,13] However, during CRRT, blood comes into contact with the extracorporeal circuit, increasing the risk of thrombus formation within the tubing.[14] Therefore, effective anticoagulant medications and methods are necessary to mitigate this risk.

Anticoagulation therapy is an important part of CRRT. When the patient's blood comes into contact with the filter and extracorporeal tubing, it can activate coagulation factors, cause platelet adhesion, lead to thrombosis, affect blood flow, and reduce treatment effectiveness. In this study, Nafamostat Mesilate (NM) and systemic unfractionated heparin were used for anticoagulation in critically ill AKI patients with AKI undergoing CRRT. The results showed that compared to baseline, both the observation and control groups exhibited decreased levels of FIB and PLT count and increased levels of APTT, PT, TT, and INR after 48 hours of treatment. However, the observation group had higher levels of FIB and PLT count and lower levels of APTT, PT, TT, and INR, indicating that the use of NM has less disruptive effect on coagulation system in critically ill AKI patients undergoing CRRT. Heparin, derived from porcine intestinal mucosa or bovine lung, is a glycosaminoglycan sulfated polysaccharide anticoagulant. It has favorable effects on increasing protein C activity, enhancing the affinity of antithrombin III (AT-III) for thrombin,[15,16] and inhibiting platelet adhesion and aggregation, thereby improving vascular permeability and stimulating the release of fibrinolytic and anticoagulant substances from vascular endothelial cells (VECs) to achieve anticoagulant effects.[17,18] However, heparin has a strong anticoagulant effect and carries a higher risk of bleeding, which limits its clinical application. NM is a serine endopeptidase inhibitor, selective inhibition of trypsin and trypsin serine endopeptidase of the classical pathways of phospholipase A2, trypsin, peptide releasing enzyme (angiotensin), fibrinolysin, Brinase (a fibrinolytic enzyme), and the complement system, by inhibiting the expression of the above-mentioned enzymes involved in the coagulation process of enzyme activity, to achieve a good anticoagulant effect. Additionally, NM exerts potent inhibitory effects on coagulation factors XIIa and Xa.[19] These coagulation factors, as protein components, play a vital role in hemostasis by rapidly activating and adhering to platelets at the site of vascular injury, thus participating fully in the blood clotting process and exerting anticoagulant effects.[20] In CRRT, approximately 40% of NM can be removed from the extracorporeal circuit by dialysis and/or convection. Subsequently, NM undergoes esterase degradation in the blood and liver, resulting in a milder anticoagulant effect and modulation of coagulation function indicators.[21]

Mendrala K et al[22] found that most metabolic waste and drugs can be excreted from the body through the kidneys, which are important excretory organs. Critically ill AKI patients, release a considerable amount of inflammatory mediators in a short period, due to the influence of a large amount of toxins, bacteria, and other factors, which lead to varying degrees of damage to renal function and elevation of renal function indicators such as SCr, BUN, and CysC levels in the body. The findings of this study indicate that compared to baseline, both the observation and control groups exhibited decreased levels of SCr, BUN, and CysC after 48 hours of treatment, with lower levels observed in the observation group. This suggests that NM anticoagulation has less adverse effects on renal function in patients with severe AKI compared with heparin CRRT. The reasons are as follows: Nm can inhibit the release of inflammatory mediators and oxygen free radicals, protect the integrity and continuity of VEC, thereby improving the coagulation function and microcirculation function, and further reducing the damage of renal function; Moreover, the effect of dialysis was better and the interruption of CRRT was less after the application of NM anticoagulation. Also, the effect of dialysis was better after using NM anticoagulation, and the interruption of CRRT was less, which is beneficial to ensure the therapeutic effect and reduce the damage to renal function.

The control group had 1 case of diarrhea, 2 cases of nausea and vomiting, and 2 cases of hypocalcemia, while the observation group had 1 case of diarrhea, 1 case of nausea and vomiting, and 1 case of hyperkalemia. The adverse reaction areas of the two regimens were consistent. Analyse the reasons behind it: (1) Heparin, after intravenous injection, acts rapidly, and upon absorption, it

distributes in the blood cells and plasma. It can bind to plasma low-density lipoproteins, globulins, and fibrinogen to form complexes. Under the action of the mononuclear phagocyte system, it is taken up into the liver where it undergoes enzymatic degradation by heparinase, producing metabolites such as urinary heparin, which are then excreted by the kidneys. Additionally, the half-life of intravenous heparin is short, averaging 1.5 hours, which contributes to its high safety profile.[23] (2) Although NM does not have a specific antagonist, its half-life is only about 8 minutes on average. After absorption, it is rapidly metabolized by esterase in the liver; therefore, it does not accumulate in the body. Moreover, NM has a relatively small molecular weight, facilitating its clearance by CRRT treatment. It exerts its anticoagulant effect locally in the ECC circuit, thereby minimizing systemic reactions. Hence, NM exhibits good safety in clinical use. Studies have reported that timely anticoagulation measures and the use of effective anticoagulants can effectively prevent premature clotting in the ECC circuit, maintaining its patency, and achieving a balance between coagulation and bleeding risks.[24] Furthermore, the results of this study showed that the observation group had a longer duration of the first filter use, fewer filters used after 72 hours of treatment, a lower incidence of bleeding events, shorter hospital stay, and higher 28-day survival rate in comparison with the control group. This suggests that NM anticoagulant therapy is beneficial for extending the duration of filter use, reducing the number of filters used, shortening hospital stay, lowering the incidence of bleeding events, and improving the patient prognosis. Considering that the half-life of NM is significantly shorter than that of heparin, and its anticoagulant effect is superior to heparin, the use of NM as an anticoagulant in AKI patients treated with CRRT at high risk of bleeding, significantly reduces the risk of bleeding compared to systemic anticoagulation with unfractionated heparin. This, in turn, prolongs filter use duration and reduces the number of filters used. Additionally, compared to systemic unfractionated heparin, NM is more conducive to accelerating body metabolism, improves microcirculation, thereby shortening patient hospital stay and improving prognosis. However, this study still has limitations including: (1) the study sample size was small(3) The source of research subjects is limited by region, which affects the research results. Therefore, in future studies, it is recommended to include larger sample size, extend the study period, expand the source of the sample size, and further conduct multicenter randomized controlled trial to confirm the results of this study.

In summary, compared to systemic unfractionated heparin, NM demonstrates superior effects on coagulation activity in critically ill patients with AKI who are treated with CRRT. It extends filter use duration, reduces the number of filters used, shortens hospital stay, lowers the incidence of bleeding events, and improves prognosis. Moreover, NM does not increase adverse reactions and exhibits a higher level of safety.

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AUTHORS' CONTRIBUTIONS

Xiaofeng Zhan, Xiaolei Qu: Conceptualization, methodology, writing original draft preparation. Di Wu, Guangpu Wang: Investigation, software, statistical analysis. Tingting Ji, Shoujun Bai: Reviewing and editing, funding acquisition, supervision. All authors read and approved the final manuscript.

CONFLICT OF INTERESTS

The authors declared no conflict of interest.

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