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ORIGINAL RESEARCH

Clinical Effect of Norepinephrine Combined with Esmolol Treatment in Patients with Septic Shock and Its Impact on Prognosis

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Objective: To unveil the influence of norepinephrine (NE) combined with esmolol treatment on cardiac function, hemodynamics, inflammatory factor levels, and prognosis in patients with septic shock.

Methods: Ninety-six patients with septic shock admitted to our hospital from January 2021 to June 2023 were retrospectively analyzed and divided into the control and observation groups according to the different treatment methods. The control group was treated with standard anti-infection and fluid resuscitation, followed by NE administration [with an infusion rate of 0.1–0.5 μg/(kg-min)]. The observation group was treated with esmolol [starting pumping rate of 50 μg/(kg-min) and adjusting the pumping rate according to the target heart rate] in combination with the control group. Changes in hemodynamic parameters, including heart rate, mean arterial pressure, central venous pressure, cardiac index, stroke volume index, and systemic vascular resistance index, were monitored by pulse-indicating continuous cardiac output monitors before treatment (T0), 24h after treatment (T1), and 72h after treatment (T2); changes in cardiac function before and after 72h of treatment, indicators of inflammatory factors before and after treatment, and indicators of oxygenation metabolism were assessed; and adverse drug reactions during treatment were recorded in both groups.

Results: NE combined with esmolol treatment improved the efficacy of patients with septic shock; was beneficial for the enhancement of blood perfusion in patients; improved the patient's cardiac function, reduced myocardial injury, and suppressed the inflammatory response in patients; improved the oxygenation metabolism and the prognosis of patients; did not significantly increase the adverse drug reactions of patients and had a better safety profile.

Conclusion: NE combined with esmolol treatment can improve the efficacy of patients with septic shock, improve their cardiac function and hemodynamic indices, reduce myocardial injury and inflammatory response, and have a better safety profile, which is conducive to improving patient prognosis and reducing mortality.

Keywords: norepinephrine, esmolol, septic shock, cardiac function, hemodynamics, myocardial injury, inflammatory factor levels, prognosis

Introduction

Sepsis is defined as life-threatening organ dysfunction resulting from a dysregulated host response to infection. Septic shock is defined as a subset of sepsis in which particularly severe circulatory, cellular, and metabolic abnormalities are associated with a higher risk of death than sepsis alone.[1] Treatment of sepsis/septic shock is challenging and involves different pathophysiologic aspects, including empiric antimicrobial therapy (administered promptly after microbiological testing), fluid (crystalloid) replacement (determined by fluid tolerance and fluid responsiveness), and vasoactive drugs (eg, norepinephrine (NE)), the use of which maintains mean arterial pressure (MAP) above 65 mmHg and reduces the risk of fluid overload.[2] Relevant guidelines indicate that for adult patients with septic shock on vasopressor medications, an initial target MAP of 65 mmHg is recommended rather than a higher MAP target; for adults with suspected sepsis or septic shock but undiagnosed infection, ongoing reassessment and search for an alternative diagnosis are recommended;

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and for adults with probable sepsis but no shock, a rapid assessment of acute illness is recommended of infectious versus non-infectious etiologies; and for adults with sepsis or septic shock, recommendations for optimizing antimicrobial dosing strategies based on accepted pharmacokinetic/pharmacodynamic principles and specific drug properties.[3] It is evident that the treatment of septic shock is very important.

Norepinephrine (NE), as an α1- and β1-agonist, is capable of enhancing vascular tone and contractility.[4] The data demonstrate that NE is superior to other vasopressors in reducing the incidence of arrhythmias and is therefore safe for use in septic shock.[5] NE, as a vasopressor, is often used in dilution for the treatment of hypotension and shock in the intensive care unit,[6] however, NE used in patients with septic shock at doses above 1 μg/ kg/min results in a mortality rate of more than 80%, suggesting the need for adjunctive strategies before this dose is reached.[7] Vasoactive drugs are crucial to maintain hemodynamic stability and ensure the perfusion of chief organs for the treatment of septic shock.[8] β-blockers are essential drugs for the treatment of a wide range of cardiovascular diseases such as heart failure, acute and chronic ischemic heart disease, tachyarrhythmias, and hypertension.[9] β-blockers can mediate cardiovascular changes in sepsis, and generate great changes at immunologic, metabolic, and coagulation levels.[10,11] Esmolol is known as a highly selective β1 receptor blocker, and it has the advantages of fast onset, good tolerance and convenient adjustment, which is the frequently-used drug in critical care medicine.[12] Esmolol has been examined by researchers in sepsis-related animal studies, which exhibits promising outcomes in animal models.[13,14] Nevertheless, the negative inotropic impact of the β-receptor is able to decrease myocardial contractility and cardiac output, posing a potential risk of subsequent aggravating shock.[15] Therefore, we conducted this research to unveil the influence of NE combined with esmolol treatment on the clinical outcome and prognosis in patients with septic shock.

Materials and Methods

Ethical Approval

The study complied with the Declaration of Helsinki and was approved by the Ethics Committee of Dongying People's Hospital (Ethic Approval No.:20210302), and the patients and their families signed the informed consent form.

Participants

Ninety-six patients with septic shock admitted to Dongying People's Hospital from January 2021 to June 2023 were retrospectively analyzed. Inclusion criteria: patients meeting the definition of sepsis-3 in septic shock;[1] those ≥ 18 years of age; those who did not in the pregnancy or lactation period; those without contraindications to the drug in this study; those with complete clinical data. Exclusion criteria: patients who had a previous history of pulmonary heart disease, acute coronary syndrome, heart valve disease, chronic cardiac insufficiency, and congenital heart disease; those with a history of asthma; those with extremely unstable vital signs; those combined with autoimmune lesions, hematologic diseases, and malignant tumors; the patient died within 24 h of admission. The patients were divided into a control group and an observation group according to the treatment method. Patients in the control group (n = 48) were treated with standardized anti-infection and fluid resuscitation, followed by NE application. Patients in the observation group (n = 48) were treated with esmolol on the basis of the control group. There was no marked difference in the general data of subjects in the two groups ($P > 0.05$; Table 1).

Treatment Methods

Patients in the control group were treated with standardized anti-infection and fluid resuscitation with reference to the international guidelines for the management of septic and sepsis shock.[16] On this basis, patients were given NE (Guangzhou Baiyunshan Mingxing Pharmaceutical Co., Ltd., Guangdong, China; No. H44022396; specifications: 1 mL: 2 mg) to maintain blood pressure with an infusion rate of 0.1–0.5 μg/(kg · min) to maintain MAP between 65–70 mmHg. Patients in the observation group were treated with esmolol in addition to the control group, and NE was administered as in the control group. Esmolol (Qilu Pharmaceutical Co., Ltd., Shandong, China; No. 20140109) was pumped continuously through a central vein at a starting rate of 50 μg/(kg · min), and the pumping rate of esmolol was adjusted to achieve the target heart rate (HR) within 20 min, and then the target HR was maintained at this rate.

Table 1 Analysis of the Patient's General Data

Item	Control group (n = 48)	Observation group (n = 48)	*P* value
Gender (n, %)			0.675
Male	28 (58.33%)	31 (64.58%)	
Female	20 (41.67%)	17 (35.42%)	
Age (years, $\bar{x}\pm$ s)	50.88 ± 4.07	51.08 ± 4.50	0.814
Temperature (C, $\bar{x}\pm$ s)	38.42 ± 0.21	38.45 ± 0.18	0.410
Type of primary disease (n, %)			0.953
Bloodstream infection	4 (8.33%)	5 (10.42%)	
Purulent biliary tract infection	10 (20.83%)	12 (25.00%)	
Abdominal infection	7 (14.58%)	6 (12.50%)	
Intestinal perforation	8 (16.67%)	9 (18.75%)	
Pulmonary infection	19 (39.58%)	16 (33.33%)	

Observation of mechanical ventilation time, intensive care unit (ICU) length of stay, and resuscitation success rate within 6h

The mechanical ventilation time, the ICU length of stay, and the resuscitation success rate within 6 h were recorded separately for comparison between the two groups. The criteria for successful resuscitation were: improvement in perfusion, reduction in HR, a manifestation of improved mental status and skin color, urine output exceeding 1 mL/(kg · h), capillary refill time less than 2 s, blood lactate (Lac) level less than 4 mmol/L, mixed venous oxygen saturation exceeding 0.7, and the central venous pressure (CVP) values returned to normal.

Monitoring of Hemodynamic Indicators

Hemodynamics, including changes in HR, MAP, CVP, cardiac index (CI), stroke volume index (SVI), and systemic vascular resistance index (SVRI), were measured in both groups at the time of dosing (T0), 24 h after dosing (T1), and 72 h after dosing (T2) using a pulse-indicated continuous cardiac output (PiCCO) monitor. Patients were monitored with an indwelling PiCCO (Philips Medical Systems). Central venous access was first established in the jugular or subclavian vein, and the main lumen of the catheter was connected to a temperature sensor for temperature measurement and a transducer for pressure measurement, respectively. A PiCCO-specific monitoring catheter was placed in the patient's femoral artery and connected to the electrocardiogram monitor with the PiCCO module via a transducer. Next, 10–15 mL of cold saline was injected from the central vein and the relevant hemodynamic parameters were calculated.

Indicators of Cardiac Function and Myocardial Injury

Changes in cardiac function, including left ventricular ejection fraction (LVEF), left ventricular end-systolic internal diameter (LVESD), and left ventricular end-diastolic internal diameter (LVEDD), were measured before and after 72 h of treatment using a PHILIP IE-33 echocardiograph (probe frequency of 2.5–3.5 MHz) bedside and were recorded by the same physician to prevent errors. B-type natriuretic peptide (BNP) values, serum creatine kinase isoenzyme MB (CK-MB) and serum cardiac troponin I (cTnI) were assessed by enzyme-linked immunosorbent assay (ELISA) with the corresponding kits (Roche, Switzerland). Fasting venous blood was acquired from patients and the supernatant blood was centrifuged.

Inflammatory Factor Levels

Fasting venous blood was acquired from both groups of subjects before and after treatment, and interleukins (IL-1β, IL-6) and tumor necrosis factor (TNF-α) values were estimated by ELISA with the corresponding kits (Abcam, USA).

Changes in Oxygen Metabolism Indicators

Arterial blood was harvested before and after treatment for blood Lac monitoring. Blood Lac levels were measured by conventional biochemical methods, and femoral artery blood was drawn from patients, centrifuged and placed on a fully automated biochemical analyzer. Central venous blood was collected on a fully automatic analyzer to determine central venous oxygen saturation (ScvO2).

Prognostic Analysis

The sequential organ failure assessment (SOFA) and Acute Physiology and Chronic Health Evaluation II (APACHE II) scores were recorded in patients before and after treatment. The SOFA score covered 6 systems: respiratory, hematologic, hepatic, cardiovascular, central nervous system, and renal systems, each with a score of 0–4 points, up to a maximum of 24 points, with the higher the score, the more severe the symptoms. The APACHE II score included acute physical, age, and chronic health components, with a maximum score of 71 points, with higher scores associated with more severe symptoms. Besides, the mortality rate of the patients was recorded within 28 d.

Occurrence of Adverse Drug Reactions

The adverse drug reactions, including bradycardia, hypotension, nausea and vomiting, and dizziness, were observed and recorded during the treatment of patients in both groups. By comparing the occurrence of adverse reactions in the two groups, the safety of treatment in the two groups was assessed.

Statistical Analysis

SPSS 22.0 software (SPSS Inc, Chicago, IL, USA) and GraphPad Prism 6.0 software (Graph Pad Inc., La Jolla, CA, USA) were applied to process and analyze the data. Numeration data were expressed as n (%), and the χ^2 test was employed for comparison between groups. Measurement data conforming to normal distribution were indicated as mean ± standard deviation. The independent samples *t*-test was implemented for comparison between groups, and the paired *t*-test was adopted for comparison within groups. A *P*-value less than 0.05 meant a statistical significance.

Results

Mechanical Ventilation Time, ICU Length of Stay, and Resuscitation Success Rate Within 6h

Shortened mechanical ventilation time and ICU length of stay and increased resuscitation success rate within 6 h were found in the observation group versus the control group ($P < 0.05$; Table 2).

Hemodynamic Parameters

No marked difference was noted in hemodynamic parameters between the two groups of patients at the T0 time point ($P > 0.05$). HR and SVRI at T1 and T2 time points were lower and MAP, CVP, CI and SVI were higher than those at T0 time point in both groups ($P < 0.05$). Reduced HR and SVRI and elevated SVI and CI were observed at T1 and T2 time points after treatment in the observation group in comparison to the control group ($P < 0.05$), and the differences in MAP and CVP changes were not statistically significant ($P > 0.05$) (Table 3).

Table 2 Comparison of Clinical Efficacy Between Two Groups of Patients

Group	Mechanical ventilation time (d, $\bar{x} \pm s$)	ICU length of stay (d, $\bar{x} \pm s$)	Resuscitation success rate within 6h (n, %)
Control group (n = 48)	8.17 ± 1.03	11.58 ± 1.04	32 (66.67%)
Observation group (n = 48)	5.83 ± 0.77	8.40 ± 0.95	42 (87.50%)
P value	< 0.001	< 0.001	0.027

Note: ICU, intensive care unit.

Table 3 Comparison of Hemodynamic Parameters Between Two Groups of Patients (n, $\bar{x}\pm$ s)

Group	Time	HR (time/min)	MAP (mmHg)	CVP (mmHg)	CI [L/(min m^2)]	SVI (mL/m^2)	SVRI [(Kpa s)/(L m^2)]
Control group (n = 48)	T0	114.42 ± 6.21	70.85 ± 3.48	11.98 ± 2.19	2.64 ± 0.47	17.48 ± 4.78	218.14 ± 46.33
	T1	107.52 ± 4.86[a]	72.71 ± 4.68[a]	13.94 ± 2.85[a]	2.91 ± 0.58[a]	21.26 ± 6.07[a]	196.27 ± 39.32[a]
	T2	102.15 ± 4.22[a]	73.15 ± 4.95[a]	14.10 ± 2.84[a]	2.95 ± 0.52[a]	20.83 ± 6.00[a]	183.95 ± 35.14[a]
Observation group (n = 48)	T0	112.98 ± 6.49	70.98 ± 3.82	12.04 ± 2.24	2.59 ± 0.39	17.35 ± 4.71	215.83 ± 49.52
	T1	98.25 ± 2.46[ab]	72.63 ± 3.69[a]	13.44 ± 2.72[a]	3.65 ± 0.72[ab]	35.21 ± 7.08[ab]	158.90 ± 38.41[ab]
	T2	94.42 ± 2.01[ab]	72.88 ± 4.85[a]	13.98 ± 2.51[a]	3.66 ± 0.70[ab]	25.54 ± 7.22[ab]	160.31 ± 31.90[ab]

Note: [a]$P < 0.05$ vs T0 within the same group; [b]$P < 0.05$ vs Control group; HR, heart rate; MAP, mean arterial pressure; CVP, central venous pressure; CI, cardiac index; SVI, stroke volume index; SVRI, systemic vascular resistance index.

Indicators of Cardiac Function and Myocardial Injury

No distinct difference was witnessed in left ventricular ultrasound parameters (LVEF, LVESD, and LVEDD) and myocardial injury indices (BNP, CK-MB, and cTnI) before treatment in both groups ($P > 0.05$). After treatment, increased LVEF and reduced LVESD, LVEDD, BNP, CK-MB, and cTnI were detected in both groups; higher LVEF and lower LVESD, LVEDD, BNP, CK-MB, and cTnI were found in the observation group in comparison to the control group ($P < 0.05$) (Table 4–5).

Inflammatory Factor Levels

Compared with the pre-treatment period, the inflammatory indices such as IL-1β, IL-6, and TNF-α were reduced in both groups after treatment ($P < 0.05$). The degree of reduction of each index was more significant in the observation group versus the control group ($P < 0.05$) (Table 6).

Oxygenated Metabolic Therapy Changes

After treatment, Lac levels in both groups were lower than before treatment, and Lac levels in the observation group were notably lower than those in the control group after treatment ($P < 0.05$). ScvO2 levels in both groups were higher than

Table 4 Comparison of Cardiac Function Before and After Treatment Between Two Groups of Patients

Group	LVEF (%)		LVESD (mm)		LVEDD (mm)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group (n = 48)	59.42 ± 3.07	61.98 ± 2.19[a]	47.85 ± 2.90	43.27 ± 2.24[a]	55.17 ± 3.05	53.08 ± 2.28[a]
Observation group (n = 48)	59.73 ± 3.27	65.29 ± 3.04[a]	47.77 ± 2.86	39.83 ± 2.20[a]	55.83 ± 3.12	50.60 ± 1.70[a]
P value	0.634	< 0.001	0.889	< 0.001	0.297	< 0.001

Note: [a]$P < 0.05$ vs Before treatment within the same group; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic internal diameter; LVEDD, left ventricular end-diastolic internal diameter.

Table 5 Comparison of Myocardial Injury Indicators Before and After Treatment Between Two Groups of Patients

Group	BNP (pg/mL)		CK-MB (U/L)		cTnI (ng/mL)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group (n = 48)	751.83 ± 59.01	201.73 ± 24.00[a]	25.19 ± 2.26	22.94 ± 2.17[a]	0.23 ± 0.05	0.12 ± 0.03[a]
Observation group (n = 48)	749.72 ± 59.11	141.89 ± 20.83[a]	25.03 ± 2.44	19.21 ± 1.81[a]	0.22 ± 0.04	0.09 ± 0.02[a]
P value	0.863	< 0.001	0.743	< 0.001	0.235	< 0.001

Note: [a]$P < 0.05$ vs Before treatment within the same group; BNP, B-type natriuretic peptide; CK-MB, creatine kinase isoenzyme MB; cTnI, cardiac troponin I.

Table 6 Comparison of Inflammatory Factor Levels Before and After Treatment Between Two Groups of Patients

Group	IL-1β (ng/L)		IL-6 (ng/L)		TNF-α (ng/L)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group (n = 48)	22.19 ± 4.61	19.03 ± 3.29[a]	38.93 ± 3.43	26.28 ± 3.38[a]	25.51 ± 2.98	20.86 ± 2.33[a]
Observation group (n = 48)	21.69 ± 4.44	15.18 ± 2.89[a]	39.02 ± 3.11	21.26 ± 2.08[a]	25.18 ± 2.89	16.62 ± 2.81[a]
P value	0.594	< 0.001	0.894	< 0.001	0.588	< 0.001

Note: [a]*P* < 0.05 vs Before treatment within the same group; IL-1β, interleukin-1β; IL-6, interleukin-6; TNF-α, tumor necrosis factor.

before treatment, and the ScvO2 levels in the observation group were markedly higher than those in the control group after treatment ($P < 0.05$) (Figure 1).

Prognostic Analysis

In contrast to the pre-treatment period, SOFA score and APACHE II score decreased in both groups after treatment ($P < 0.05$). After treatment, the degree of reduction of each index was more obvious in the observation group versus the control group, and the 28-d mortality rate was lower than that of the control group ($P < 0.05$) (Table 7).

Occurrence of Adverse Reactions

During the treatment, one case of bradycardia and one case of hypotension occurred in the observation group, which was relieved after adjusting the drug administration rate and did not affect this treatment. No significant adverse reactions occurred in the control group. The difference between the two groups was not statistically significant ($P > 0.05$).

Discussion

Sepsis and septic shock are the leading causes of death in hospitalized patients. The septic state is due to a dysregulated host response to infection, resulting in inflammatory damage to virtually all organ systems.[17] When sepsis is associated with severe hypotension, septic shock occurs and leads to massive mortality.[18] Based on this, it is imperative to find more effective treatment approaches for septic shock. Herein, we conducted this research to unveil the influence of NE combined with esmolol treatment on the clinical efficacy and prognosis in patients with septic shock.

In this study, we found that NE combined with esmolol treatment could shorten the duration of mechanical ventilation and ICU hospitalization in septic patients, and it could improve the success rate of resuscitation within 6 h in patients.

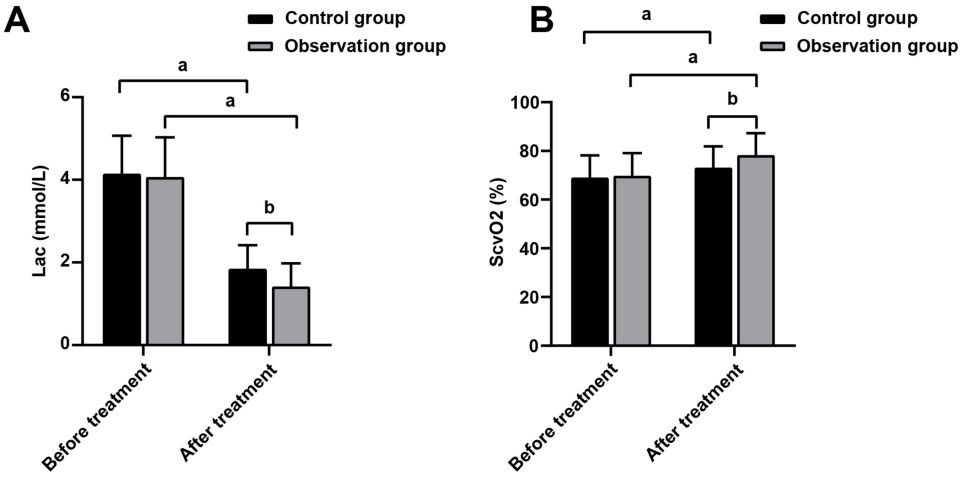

Figure 1 Changes in oxygenated metabolic therapy in both groups. (**A**) Comparison of Lac levels. (**B**) Comparison of $ScvO_2$ levels. Note: Lac, blood lactate; $ScvO_2$, central venous oxygen saturation.

Table 7 Prognostic Analysis of Patients in Both Groups

Group	SOFA score (point)		APACHE II score (point)		28 d mortality rate (%)
	Before treatment	After treatment	Before treatment	After treatment	
Control group (n = 48)	12.10 ± 1.12	4.98 ± 0.72[a]	28.19 ± 3.34	16.08 ± 1.89[a]	12 (25.00%)
Observation group (n = 48)	11.83 ± 1.05	3.38 ± 0.56[a]	28.79 ± 3.52	12.83 ± 1.55[a]	3 (6.25%)
P value	0.230	< 0.001	0.396	< 0.001	0.022

Note: [a]*P* < 0.05 vs Before treatment within the same group; SOFA, sequential organ failure assessment; APACHE II, Acute Physiology and Chronic Health Evaluation II.

This suggests that NE combined with esmolol treatment can improve the outcome of septic shock patients. Hemodynamic assessment is an integral part of the diagnosis and treatment of cardiovascular disease.[19] Hemodynamic parameters are important indicators for assessing cardiac and vascular function. Resuscitation in sepsis focuses on systemic hemodynamics.[20] Septic shock is usually characterized by tachycardia and a hyperactive hemodynamic profile.[21] NE is recommended as a first-line vasopressor for stabilizing hemodynamics in cardiogenic shock;[22] β-blockers impact hemodynamics and metabolic and immune modulation in sepsis,[23] and the utilization of the β-antagonist esmolol has been regarded as a therapy to decrease HR, resulting in improved diastolic filling time and cardiac output, thereby reducing vasopressor support.[21] In healthy hearts, sympathetically released NE positively modulates the chronotropic, inotropic, and ectotropic directions, resulting in a significant increase in cardiac output.[24] A statistically significant reduction in the release of troponin T, CK, CK-MB and n-terminal brain natriuretic peptide as surrogate indicators of myocardial injury in patients with ST-segment elevation myocardial infarction is statistically demonstrated with esmolol treatment.[25] In this study, we observed that HR, SVRI, MAP, CVP, CI, and SVI at T1 and T2 time points of patients in both groups changed after treatment, in which HR and SVRI at T1 and T2 time points of patients in the observation group decreased markedly after treatment, and SVI and CI increased significantly. In addition to this, we also found that the LVEF of both groups increased after treatment, and the observation group was higher than the control group; LVESD, LVEDD, BNP, CK-MB and cTnI decreased in both groups, and the observation group was lower than the control group. This discloses that in the state of septic shock, NE can elevate blood pressure and increase myocardial contractility, while esmolol can reduce HR and decrease myocardial oxygen consumption. The combination of the two may produce a synergistic effect, which is able to maintain blood pressure stabilization and reduce cardiac burden, improve patients' cardiac function and reduce myocardial injury.

NE treatment can facilitate infection and exert immunosuppressive effects. For instance, NE is able to make the leukocyte phenotype more anti-inflammatory when exposed to bacterial agonists, with reduced pro-inflammatory cytokine production and elevated anti-inflammatory cytokine production, as well as advanced bacterial growth.[26] β-blockers decrease HR, exert anti-inflammatory effects, and mitigate myocardial oxygen supply in sepsis[23] Lac and ScvO2 levels generally reflect oxygen metabolism and tissue infusion at an early stage of sepsis.[27] In this study, we revealed that after treatment, inflammatory indicators such as IL-1β, IL-6, and TNF-α were reduced in both groups, and the degree of reduction of each indicator was more obvious in the observation group. In addition, Lac and $ScvO_2$ levels changed in both groups; Lac levels in the observation group were obviously lower versus those in the control group, and $ScvO_2$ levels were obviously higher versus those in the control group. As discussed above, NE in the treatment of septic shock can increase peripheral vascular resistance, increase cardiac contractility and HR, thereby raising blood pressure and ensuring the blood supply to the brain and other vital organs. This mechanism of action helps to improve tissue perfusion in patients with septic shock, which in turn improves oxygenation metabolism. At the same time, the use of esmolol can effectively reduce the HR and reduce the burden on the heart, while improving the balance of oxygen supply and demand in the myocardium. In addition, esmolol also has the effect of regulating the body's inflammatory response, which helps to diminish the systemic inflammatory response syndrome caused by sepsis. Some studies have confirmed that the combination therapy of milrinone and esmolol improves cardiac function and 28-day survival in patients with severe sepsis.[28] Liu et al have supported that esmolol can notably shorten the ICU stay and decrease 28-day mortality.[29] The results of the study found that the SOFA score and APACHE II score of the two groups of patients

were reduced after treatment; after treatment, compared with the control group, the degree of reduction of each index in the observation group was more obvious, and the 28d mortality rate was lower than that of the control group.

In conclusion, NE combined with esmolol treatment can enhance blood perfusion, ameliorate cardiac function, reduce myocardial injury, inhibit inflammatory response, and improve oxygen metabolism and patient prognosis. This paper highlights the practicability of NE combined with esmolol in the clinical treatment of septic shock. However, the few patient numbers and low quality of evidence of this work warrant further verification. Meanwhile, specific treatment protocols should be adapted and optimized according to the patient's specific situation.

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The authors have no conflicts of interest to declare that are relevant to the content of this article.

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