EFFECTS OF NOREPINEPHRINE ON MEAN SYSTEMIC FILLING PRESSURE AND CARDIAC OUTPUT IN PATIENTS WITH SEPTIC SHOCK

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ABSTRACT

Objective: *To explore the regulation role of norepinephrine on the mean filling pressure and cardiac output in septic shock patients.*

Methods: *120 septic shock patients,who were treated from June 2020 to May 2022, were included in this experiment. They were divided into experimental group (treated withNE,60 cases) and control group (treated with DA,60 cases). The two groups general clinical data were collected. Cardiac output (CO) and left ventricular ejection fraction (LVEF) were checked by TTE, and PMSF was measured by the 12 s inspiratory retention method. Before and after treatment, the changes, adverse reactions and 28 day survival were compared and analyzed in two groups.*

Results: *The effective rates of the two groups were 93.33% and 80.00% in the experimental and control group. Before treatment,there was no difference in CO, LVEF, PMSF, and the adverse reactionsincidencebetween the two groups (P>0.05). After treatment, the CO, LVEF and PMSF of the were raisedin experimental group (P<0.05). The adverse reactions incidenceandthe 28 day mortality of the two groups with no significant difference (P>0.05).*

Conclusion: *Norepinephrine can significantly increase mean filling pressure and CO of patients with septic shock, but it does not have a significant effect on improving survival rate.*

Keywords: *Norepinephrine, septic shock, mean filling pressure, Cardiac output.*

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Introduction

Septic shock, characterized by sepsis complicated with hypotension[1]. In critically ill patients, it is still the major cause of morbidity and death[2]. Therefore, fluid resuscitation and vasopressors designed to correct blood volume insufficiency[3] and restore vascular tone are essential to keep early stages organ perfusion in good condition[4]. However, large volumes of fluid increase the risk of fluid overload[5]. In addition, fluid resuscitation did not further increase cardiac output (CO). Studies have also shown that NE alone administered early after ICU admission can restore MAP quickly, and NE has important therapeutic value in patients with septic shock by significantly increasing peripheral vascular resistance and mean arterial pressure. However, there are few studies on the effects of NE on systemic mean filling pressure and CO in septic shock patients. This article focuses on the mean the effects of NE on systemic filling pressure and CO in septic shock patients.

Table

Data and methods

General information

In this study, 120 septic shockpatients,who was admitted to our hospital from June 2020 to May 2022, were divided into experimental group (EG) and control group (CG), each group include 60 cases. The CG was treated with DA, and the EG was treated with NE.

Inclusion criteria:

• All patients met the septic shock diagnostic

criteria according for the surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021[6];

• The patients age, >18 years old;

• The patient had obvious infection and clinical manifestations of shock;

• Patients and their family members voluntarily participated in the experiment and signed informed consent.

Exclusion criteria:

• Unstable coronary syndrome and/or previous history of acute myocardial infarction;

• Diuretic treatment was performed within 6 hours after enrollment;

• Organ transplantation, patients with other immune system diseases, malignant tumors, and severe liver and kidney dysfunction were excluded;

• Exclusion of mental illness;

• Exclusion of intermediate transfer and discharge.

The gender, age, mean arterial pressure, BMI, underlying diseases, APACHE ii score, SOFA score, mechanical ventilation, and other general basic data of the two groups were no difference (P>0.05) (Table 1).

General information	Experimental group (EG) (n=60)	Control group (CG) (n=60)	t/χ^2	*P*
Gender			0.098	0.754
Male	33 (55.00%)	29 (48.33%)		
Female	27 (45.00%)	31 (51.67%)		
Age			2.217	0.136
<60 year	39 (65.00%)	36 (60.00%)		
≥60 year	21 (35.00%)	24 (40.00%)		
Mean arterial pressure	54.38±5.29	53.86±5.09	1.583	0.116
BMI	21.16±1.37	21.29±1.03	0.467	0.641
Basis of Disease			5.125	0.162
Biliary tract infection	18 (30.00%)	12 (20.00%)		
Peritonitis	17 (28.33%)	13 (21.67%)		
Severe pneumonia	13 (21.67%)	20 (33.33%)		
Gastrointestinal tract infection	10 (16.67%)	14 (23.33%)		
Other	2 (3.33%)	1 (1.67%)		
APACHE II score	67.57±10.63	66.96±11.07	0.505	0.614
SOFA score	12.38±4.68	11.76±4.68	0.162	0.871

Table 1: General data.

Treatment methods

After admission, patients received anti-infection, anti-shock, oxygen inhalation, expansion of blood volume, correction of acid-base water and treatment with electrolyte balance, and symptomatic support was given according to the conditions of the patients.

Control group

DA treatment based on conventional treatment. Central venous infusion was continued through an intravenous pump with an initial dose of 1 μg•kg-1•min-1, and the dose was increased every 2min until the termination dose was 15μg•kg-1•min-1.

In the EG, NE was treated based on conventional treatment. The initial dose was 0.05μg•kg-1•min-1, and the dose was increased every 2min until the termination dose was 0.50μg•kg-1•min-1. During treatment, the dose was adjusted timely manner according to mean arterial pressure (MAP), and the dose was reduced or stopped when the MAP reached 70-80 MMHG.

Observation indexes and efficacy judgment

• The general data were collected, including sex, age, mean arterial pressure, BMI, underlying diseases, APACHE ii score, and SOFA score.

• CO and LVEF were monitored and analyzed by TTE. TTE mainly adopts Philips IE33 color Doppler ultrasound, and the frequency of the heart phased probe is set to 2-8 MHZ. CO and LVEF was achieved before treatment and after 24 hours of treatment.

• The measurement of PMSF was achieved using the 12 s inhalation retention method according to Perishing et al. PMSF was achieved before treatment and after 24 hours of treatment.

• The survival rate was evaluated. The survival rate was = (number of surviving cases/number of cases) ×100%.

Statistical methods

All data were analyzed using the SPSS21.0 software.The data were represented by ($\bar{x}\pm s$), the comparison of data between groups was analyzed by the t-test, and all count data were represented by [n (%)]. The comparison of data was analyzed by χ^2 test, P<0.05 was used as the statistical standard.

Results

Clinical efficacy

In Table 2, the effective rates of the EG and the CG were 93.33% and 80.00%, with no significant difference (P>0.05).

Group	Excellent	Effective	Invalid	Total effective rate
Experimental group	36	20	4	56 (93.33)
Control group	26	22	12	48 (80.00)
χ^2				4.615
P				0.031

Table 2: Comparison of clinical efficacy.

Comparison of CO and LVEF indexes

Before treatment,there were no significant differences in CO and LVEF in EG and CG (P>0.05); but after treatment, CO and LVEF of EG were raised than those of the CG, (P<0.05) (Table 3).

Group	n	CO(L/min)		LVEF(%)	
		Before treatment	After treatment	Before treatment	After treatment
EG	60	3.46±1.08	5.15±1.32*	36.87±3.68	42.65±5.63*
CG	60	3.52±1.13	4.68±1.17*	37.23±3.81	40.26±4.64*
t		0.956	2.634	0.865	3.564
P		0.567	0.035	0.768	0.029

Table 3: Comparison of CO and LVEF indexes ($\bar{x}\pm s$).
*Note: *P<0.05.*

Comparison of PMSF

The PMSFof the EG was raised than that of the CG (P<0.05) (Table 4).

Group	n	Before treatment (mmHg)	After treatment (mmHg)
EG	60	22.35±3.24	30.69±2.86*
CG	60	23.65±3.61	26.84±3.57*
t		0.480	15.279
P		0.632	<0.001

Table 4: Comparison of PMSF ($\bar{x}\pm s$).
*Note: *P<0.05.*

Comparison of adverse reactions incidence and survival rate

The adverse reactions incidencein the EG was 21.67%and CG was 31.67% (P>0.05). The 28d mortality rates of the two groups were 30.00% and 35.00%, with no difference (P>0.05). Shown in Table 5.

Group	Adverse reactions						28d Mortality rate
	Arrhythmia	Shortness of breath	Chest pain	Nausea and vomiting	Heart palpitations	Total	
EG	3	2	3	2	3	13 (21.67)	18 (30.00)
CG	4	3	4	3	5	19 (31.67)	21 (35.00)
χ^2						1.534	0.341
P						0.215	0.558

Table 5: Comparison of the incidence of adverse reactions and survival rate.

Discussion

NE is an α1-adrenergic drug with β1-adrenergic properties. It has shown that NEadministration in the septic shock early stage could quickly obtain sufficient MAP can increase stroke volume[7]. Similar results have been found in septic shock patients and preload reactivity with positive passive leg lift tests[8]. This study found that CO and LVEF in the EG were significantly higher than those in the CG after treatment, suggesting that NE could promote cardiac preload and CO through its α1 adrenergic mediated effect in preload responsiveness patients in infected and after cardiac surgery patients, mean systemic filling pressure is increased[9, 10]. However, previous studies have not suggested that NE can increase CO, possibly because the high CO value caused by massive fluid administered before NE initiation leads to a low cardiac preload reserve.

In addition, NE can promotestroke output by raisingcardiac contractility. Septic shockpatients observed an improvement in measures of LVEF and CO after increasing NE dose. These results are also present in patients with a low LVEF[11]. Despite the increased left ventricular afterload, the present study found that NE promoted a significant increase in LVEF, indicating that NE enhanced left ventricular contractility. In the early stage of septic shock,the mechanism of action may be that NE increases myocardial contractility through β1-adrenergic stimulation. In general, septic shock is concerned to altered microcirculation, including preserved or corrected microcirculation patients[12]. However, in severe hypotensionpatients, correction of hypotension improves microvascular blood flow as a result of low organ perfusion pressurecorrection.

NE raised MAP from 54 to 77 mmHg, regulated tissue oxygen saturation (StO2), from 75% to 78% (normal value is about 82%).In septic shock patients, StO2 as a prognostic factor due to reflect the ability of microvessels responding to local hypoxia[13]. We hypothesized, increasing MAP in severe hypotension patients would improve microvascular blood flow in the pressure-dependent vascular bed, thus improving muscle oxygenation and microcirculatory recovery. It has reported, a good correlation between MAP and sublingual microcirculation index, 6 hours before resuscitation from septic shock[14]. So, hypothesis of microcirculatory injury due to NE-induced excessive vasoconstriction is not hold while MAP is low,even when it has reached 65 mmHg, raisingMAP to 85 or 90 mmHg does not affect microcirculation, but may

even stimulateit[15]. It has now been demonstrated that fluid balance status is associated with improved mortality from septic shock[16]. The mechanisms of excessive-fluid administration including risk with multiple organ dysfunction of peripheral tissue edema, risk, vascular permeability increase risk of endovascular candy calyx degradation, significantly increases venous pressure, especially in the case of preloaded without response) and reduce risks at the organ perfusion pressure and blood dilution[17]. Therefore, even in the initial stages of resuscitation, fluid administration can be limited by early administration of vasopressin.

Patients who received NE within two hours before resuscitation received less fluid than those who were given delayed NE[18]. Early initiation of NE to counteract the sepsis-induced reduce in vasomotor tone does not mean discontinuation of fluids, especially if in patients with severe hypovolemia and/or significant loss of fluid. The earlier the drug is administered, the more dramatic the effect may be.

In conclusion, NE can significantly increase the mean systemic filling pressure and CO in septic shock patients, but has no good effect on improving the survival rate.

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