

# Comparison of clinical effect of dopamine and norepinephrine in the treatment of septic shock

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**Abstract:** This study aims to compare the clinical effect of dopamine and nor epinephrine in the treatment of septic shock. Fifty cases with septic shock were randomly divided into two groups. Patients in both two groups revived after taking effective liquid. Then dopamine was pumped into central veins of patients in the research group (group DA) in  $2\mu\text{g}/(\text{kg}\cdot\text{min})$  upon the conventional treatment, while nor epinephrine was pumped into patients in the control group (group NE) in  $0.1\mu\text{g}/(\text{kg}\cdot\text{min})$ , besides conventional treatment. The improvement of haemodynamics and microcirculation perfusion indexes were compared between two groups before and after treatment, as well as the improvement of tissue oxygen metabolism. The results demonstrated that, central venous pressure (CVP), mean arterial pressure (MAP), urine volume and central venous oxygen saturation ( $\text{Scv O}_2$ ) in both groups before treatment was not statistically significant ( $P>0.05$ ); 6 h after treatment, CVP, MAP, urine volume and  $\text{Scv O}_2$  of group NE were higher than group DA; 12h and 24h after treatment, blood lactic acid clearance of group NE was superior than group DA ( $P<0.05$ ). All the above findings suggested that, both dopamine and nor epinephrine are beneficial to improve microcirculation and tissue oxygen metabolism in the treatment of septic shock, and the clinical effect of nor epinephrine was distinctly better than dopamine.

**Keywords:** Dopamine; nor epinephrine; septic shock.

## INTRODUCTION

Septic shock is a kind of clinical syndrome with microcirculation disturbance caused by pathogenic microorganism and their toxin. It is likely to induce metabolic disorders, histanoxia, cell damage and multiple organ dysfunction syndromes (MODS) if shock cannot be reversed in the early stage (Yang *et al.*, 2012). Treatment methods for septic shock all aim at improving hypotension and vascular activity. Vasopressor is commonly used for treating septic shock. Dopamine and nor epinephrine as the first line vasoactive agents are widely applied in treating septic shock (Feihu and Qing, 2013).

While studying the clinical effect of dopamine and nor epinephrine in the treatment of septic shock, Feng Shiyan and Xiao Xu found that, dopamine, nor epinephrine combined with dobutamine are both able to enhance hemodynamic status throughout the whole body of patients with septic shock; however, the latter was distinctly better than the former in improving blood perfusion of visceral organs (Shiyan and Xu, 2005). Moreover, it was found that, dopamine excited adrenergic receptor in sympathetic nervous system and dopamine receptor that locates in kidney, mesentery, coronary artery and cerebral artery, and the effect had dose dependency; certain dose of dopamine could promote oxygen transplanted, enhance pH value of intestinal mucosa and improve organ perfusion, however, single use or

small dose is not satisfactory in enhancing blood pressure of shock patients. In addition, nor epinephrine could help shrink artery and vein so as to reduce shunt, improve visceral ischemia and decrease lactic acid generation. At the same time, after blood supply of organs improved, the concentration of lactic acid lowered down for blood flowing through liver increased and lactic acid metabolism of liver strengthened. Wang Shanshan and Cui Wei found that, septic shock patients had severe imbalance in tissue oxygen metabolism. During 6-hour resuscitation, treatment with dopamine could not improve tissue oxygen metabolism effectively, while for treatment with nor epinephrine, indexes such as  $\text{DO}_2$ ,  $\text{VO}_2$  and  $\text{O}_2$  ext were remarkably enhanced (Shanshan and Wei, 2014). It is known that, tissue oxygen metabolism imbalance reflects microcirculation disturbance and cell metabolism disorder, and the latter has been regarded as the important treatment objective of serious infection and shock (Vanina S.K. *et al.*, 2011). It follows the advantage of nor epinephrine in tissue oxygen metabolism is considered to be beneficial to improve clinical effect and prognosis. This study primarily studied the comparison of clinical effect of dopamine and nor epinephrine.

## MATERIALS AND METHODS

### Study design

Fifty patients with septic shock who were admitted to the First Affiliated Hospital of Zhengzhou University from Oct., 2012 to Nov., 2014, were recruited in this study, among which, 28 were male and 22 were female, ranging in age from 18~72 years (mean  $45.6\pm 2.12$  years). All

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patients or their family members have signed informed consent and this experiment has been approved by the Medical Ethics Committee. All the patients were conforming to the diagnosis criteria of septic shock, with typical clinical presentation of clear focus of infection or positive blood cultures. The selected patients all followed by International Guidelines for Management of Severe Sepsis and Septic Shock 2008. Patients who had severe diseases in organs such as heart, liver and kidney and who were suffering from malignant tumor, mental disease and conscious disturbance were excluded. Based on random number table, 50 patients were randomly divided into dopamine group (group DA) and nor epinephrine group (group NE). Of 25 patients in-group DA, 10 had abdominal infection, 9 pulmonary infection, 4 catheter-related infection and 2 soft tissue infection; of 13 patients in group NE, 13 had abdominal infection, 10 pulmonary infection, 1 catheter-related infection and 1 soft tissue infection. General conditions such as gender, age and infection site were of no statistical significance, hence, these cases were comparable.

Inclusive criteria: tissue perfusion insufficiency and/or urine volume  $<0.5\text{mL}/(\text{h}\cdot\text{kg})$ ; systolic pressure  $<90\text{mmHg}$ ; with clear focus of infection or positive blood cultures; temperature  $\square 38.5^{\circ}\text{C}$  or  $\square 35^{\circ}\text{C}$  (Peng *et al.*, 2010).

### Methods

Therapeutic method: after admitted into the hospital, the patients were treated with early goal directed therapy (EGDT) based on positive controlling primary infection and thorough drainage on focus of infection. Vasoactive agent was pumped into central vein upon micro pump once they came back to life by positive liquid: group DA was given dopamine at  $2\mu\text{g}/(\text{kg}\cdot\text{min})$  while group NE was given norepinephrine at  $0.1\mu\text{g}/(\text{kg}\cdot\text{min})$ . Dose of drug was regulated as per blood pressure, until  $\text{MAP} \geq 65\text{mmHg}$ ,  $\text{CVP}$  from  $8\sim 12\text{mmHg}$ , urine volume  $\geq 0.5\text{mL}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ ,  $\text{Scv O}_2$  in central vein  $\geq 70\%$  or  $\text{Scv O}_2$  in mixed vein  $\geq 65\%$ .

Observation indexes: concentration of lactic acid of arterial blood of patients was recorded before taking drugs. All of the patients excluded influence from blood glucose, dysphoria and blood transfusion on lactic acid of arterial blood.  $\text{Scv O}_2$  of pulse should remain above 95%. 12 h and 24 h after drug administration, concentration of lactic acid in arterial blood was detected using GEM Premier 3000 analyzer and then recorded. 12 h and 24 h before and after treatment, heart rate (HR), CVP, MAP, urine volume per hour,  $\text{Scv O}_2$  in central vein were detected respectively.

Statistical processing: statistical software SPSS 18.0 was applied, count data was expressed by percentage;  $\chi^2$  test was also used; measurement data was expressed by mean

$\pm$  SD; comparison between groups used t test;  $P < 0.05$  was considered to be statistical significant.

### RESULTS

Before treatment, differences of HR, CVP, MAP and urine volume were of no statistical significances ( $P > 0.05$ ). Six hours after treatment, HR, CVP, MAP, urine volume per hour and  $\text{Scv O}_2$  in group NE was significantly superior than group DA ( $P < 0.05$ ), as shown in table 1. Before treatment, clearance rate of lactic acid and  $\text{Scv O}_2$  in central vein of those patients were of no statistical significance ( $P > 0.05$ ). Clearance rate of group NE after treatment was much higher than group DA, as shown in table 2.

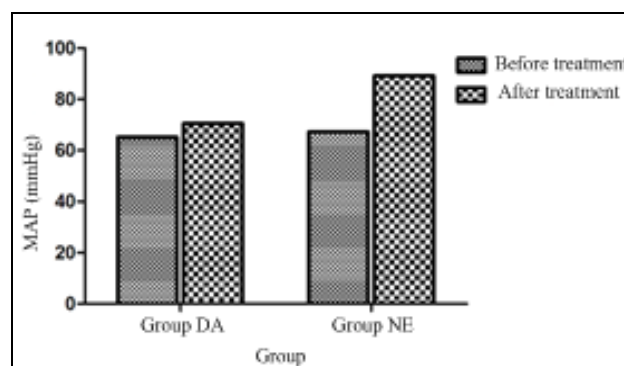


Fig. 1: Comparison of MAP of two groups before and after treatment

From fig. 1, it was found that MAP of group DA and NE were of no statistical significance before treatment ( $P > 0.05$ ); MAP of group NE increased faster than group DA.

### DISCUSSION

Septic shock, a kind of distributive shock, is featured by disordered haemodynamics, reduction of effective capillary perfusion, increase of vascular permeability, hence, haemodynamics support is considered as an important treatment method for septic shock. Currently, circulation support still bases on anabiosis with sufficient liquid and vasoactive drugs. There are lots of drugs for treating septic shock, among, which vasoactive drugs dominate. Ideal vasoactive drugs should be able to enhance blood pressure rapidly and improve blood perfusion of heart and brain, increase blood perfusion of visceral organs such as kidney and intestinal tract, correct tissue hypoxemia, as well as prevent MODS, thus to prevent disease progress and decrease mortality. Dopamine and nor epinephrine are commonly used drugs in the treatment of septic shock clinically at present. Results of this study demonstrated that, indexes such as haemodynamics and tissue oxygen metabolism of patients in group NE after treatment were superior than group DA

**Table 1:** Comparison of haemodynamics, microcirculation perfusion and tissue oxygen metabolism between two groups after treatment

Group DA	HR (time/min)	CVP (mmHg)	MAP (mmHg)	Urine volume per hour (mL)	Scv O <sub>2</sub> (%)
Before treatment	123.2±7.0	6.3±2.4	60.1±16.3	68.2±42.1	49.2±21.3
After treatment	125.3±7.0	9.8±1.9	78.2±13.2	90.3±42.8	70.3±4.8
Group NE					
Before treatment	121.1±8.2	6.1±2.3	62.5±12.0	66.3±45.6	50.4±15.9
After treatment	90.2±	11.2±2.2	82.3±14.5	82.7±14.5	77.8±10.1
t value	0.71	0.85	3.12	5.58	5.24
p value	<0.05	<0.05	<0.05	<0.05	<0.05

**Table 2:** Comparison of concentration and clearance rate of lactic acid between two groups (mean ± SD)

Group	Case number	Concentration of lactic acid /(mmol · L <sup>-1</sup> )			Clearance rate of lactic acid/%	
		Before treatment	12 h after treatment	24 h after treatment	12 h after treatment	24 h after treatment
Group DA	25	4.92±1.34	3.26±1.05	2.85±0.89	28.34±9.55	47.88±7.69
Group NE	25	4.88±1.38	2.74±1.23	2.13±0.72	48.02±13.89	65.77±16.58
t value	-	0.72	0.89	3.08	5.18	5.09
p value	-	>0.05	>0.05	<0.05	<0.05	<0.05

Clearance rate of lactic acid wherein is calculated according to formula (1).

$$\text{Clearance rate of lactic acid} = \frac{\text{concentration of lactic acid before treatment} - \text{concentration of lactic acid after treatment}}{\text{concentration of lactic acid before treatment}} \times 100\% \quad (1)$$

( $P < 0.05$ ), which is consistent with the results of literature (Peng *et al.*, 2010). Both dopamine and nor epinephrine are catecholamine drugs and can increase vascular resistance, cardiac output, blood flow of kidney, organs and brain, with little influence on HR. A foreign study (Olfa *et al.*, 2010) demonstrates that, dopamine has a much higher risk of arrhythmic events in treating septic shock compared to nor epinephrine (Chenping, 2014). It has also been reported that, improvement of hypo perfusion and anoxia of patients with septic shock treated by nor epinephrine was better than using dopamine (Weihua, 2013).

Dopamine is a dose associated drug mainly acting on  $\alpha$  and  $\beta$  adrenergic receptor and dopamine adrenergic receptor. This study also found dopamine has a higher risk of arrhythmic events in treating septic shock than nor epinephrine and many previous studies suggest that, dopamine is able to increase occurrence rate of arrhythmic events when treating septic shock. A intensive care experimental group from Australia found increase of arrhythmic events increase is correlated with dopamine. Meanwhile, Argalious *et al.* (2005) believe dopamine is an independent risk factor for occurrence of a trial fibrillation. Dopamine acts on cardiac muscle through activating  $\beta$  receptor and meanwhile improves heart rate. These may be the causes of high risk of arrhythmic events in the application of dopamine. Thus arrhythmic events become the important factor limiting application of

dopamine. Research results of this study suggested that, various levels and urine volume per hour of patients in research group was better than control group, and there was a statistically significant difference ( $P < 0.05$ ); lactate clearance of patients in research groups was also better than control group and the difference was statistically significant ( $P < 0.05$ ); occurrence rate of adverse effects in research group was much lower than control group, and there was also a statistically significant difference ( $P < 0.05$ ).

As to the limitation of this experiment, limited data obtained from the experiment reduces the reliability of evaluation of mortality of septic shock patients treated with nor epinephrine and dopamine, and moreover, related data concerning arrhythmic events have not been demonstrated, which is also the cause of heterogeneity.

## CONCLUSION

To sum up, nor epinephrine is considered to be more suitable to be used in septic shock as it can effectively sustain hemodynamic state of shock patients, improve tissue oxygenation and enhance systemic vascular resistance index and oxygen uptake rate. Thus it is clinically worth popularizing.

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