Clinical Experience

**Effect of Shen-Fu Injection (参附注射液) on Hemodynamics in Early Volume Resuscitation Treated Septic Shock Patients**

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**ABSTRACT**  
Objective: To investigate the hemodynamic effect of Shen-Fu Injection (SFI) in early volume resuscitation treated septic shock patients by monitoring pulse indicator continuous cardiac output (PICCO).  
Methods: All septic shock patients admitted in the Intensive Care Unit of the Affiliated Hospital of Shandong University of Traditional Chinese Medicine from January 1st, 2014 to December 31th, 2015, were reviewed, and totally 65 were enrolled in this study. They were assigned to SFI group (33 cases) and control group (32 cases). All 65 patients underwent conventional treatment mainly including volume resuscitation, antibiotics and vasoactive drugs therapy. The patients of the SFI group received additional 100 mL of SFI intravenously every 12 h. In all 65 patients, the PICCO arterial catheter and vein catheter were implanted within 1 h after the diagnosis of septic shock. In the course of early volume resuscitation, hemodynamic data of patients were recorded by PICCO monitor at 0, 12, and 24 h after the catheter implantation. Results: The hemodynamic indices of the two groups showed no significant differences at the beginning of 0 h (P>0.05). At 12 and 24 h, the hemodynamic indices of SFI group were significantly improved in comparison with the control group (P<0.05), including cardiac index (CI), global end diastolic volume index (GEDI), mean arterial pressure (MAP) and heart rate (HR). In addition, there was no significant change of extra-vascular lung water index between the two groups (P>0.05). Conclusion: SFI significantly improved hemodynamic indices such as CI, GEDI, MAP and HR in early volume resuscitation treated septic shock patients.

**KEYWORDS** septic shock, hemodynamic, Shen-Fu injection, Chinese medicine, pulse indicator continuous cardiac output

With the development of survival sepsis campaign (SSC) and the application of sepsis management guidelines, the treatment of sepsis and septic shock become more and more standardized. Nevertheless, the morbidity and mortality is still high in sepsis and septic shock patients.

Shen-Fu Injection (参附注射液, SFI) extracted from Chinese medicine (CM) Radix Ginseng Rubra and Radix Aconiti Lateralis Preparata, this formula has been used in clinic for over 2,000 years in treating cardiac diseases such as coronary heart disease, myocardial ischemia and heart failure in China, Korea and Japan.

The major active ingredients of red ginseng are ginsenosides also known as triterpene glycosides. Modern pharmacological research shows that ginsenosides confer beneficial effects on cardiovascular system through various mechanisms such as adjusting blood pressure, modifying vasomotor function, and influencing ion channels.¹⁻² The major active ingredient of aconite is higenamine (HG) that has positive inotropic and chronotropic action in the heart.³⁻⁴ Moreover, HG plays a protective role in myocardial cells, being responsible for the anti-infection, anti-shock, and anti-endotoxin effects.⁵⁻⁶

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improvement of hemodynamics. HG can improve coronary circulation, and thus decrease the injury of acute myocardial ischemia.

As a well-known CM, SFI has been widely used in clinic showing a curative effect during shock and resuscitation. Previous study shows that SFI can improve microcirculation, aiding in an inflammatory reaction and protecting ischemic myocardial cell. Additionally, SFI enhances heart contractility and improves coronary circulation that helps elevate blood pressure and improve hemodynamics. Therefore, SFI may have a great potential in treating septic shock though lack of supporting data from evidence-based medicine. The current clinical trial has been designed to investigate the effect of SFI on hemodynamics in early volume resuscitation treated septic shock patients by monitoring pulse indicator continuous cardiac output (PICCO).

**METHODS**

**Diagnostic, Inclusion and Exclusion Criteria**

The international consensus definition of septic shock was used according to 2012 SSC guidelines for management of severe sepsis and septic shock. The diagnostic criteria consists of a serious infection plus two or more systemic inflammatory response syndrome (SIRS) and shock criteria. The presence (probable or documented) of infection, SIRS criteria include: (1) heart rate >90 beats/min, (2) body temperature >38.3 °C or <36 °C, (3) tachypnea (>20 breaths/min) or PCO₂ >32 mm Hg, and (4) leukocytosis [white blood cell (WBC) >12.0 × 10⁹/L, or 4.0 × 10⁹/L or >10% bands]; persisting sepsis-induced hypotension (hypotension, elevated lactate, or oliguria) despite adequate fluid resuscitation; with organ failure.

Inclusion criteria include: (1) patients should meet the diagnostic criteria for septic shock; (2) aged 18–80 years old; (3) onset time within 24 h; (4) patients should be hospitalized.

Exclusion criteria include: (1) patients combined with diseases that may affect monitoring data of PICCO, such as intra-cardiac shunt, aortic aneurysm, aortic stenosis, and pulmonary lobectomy; (2) patients combined with other diseases that may affect lactic acid level, such as diabetic ketoacidosis and severe liver disease; and (3) patients presented other cause of shock, such as cardiac shock, neurogenic shock, and allergic shock.

**Study Design**

All septic shock patients admitted in the Intensive Care Unit (ICU) of the Affiliated Hospital of Shandong University of Traditional Chinese Medicine were reviewed from January 1st, 2014 to December 31th, 2015, and totally 65 septic shock patients were enrolled. They were assigned to SFI group (conventional therapy + SFI, 33 cases) and control group (conventional therapy alone, 32 cases). All patients underwent conventional treatment mainly including the volume resuscitation, antibiotics and vasoactive drugs according to 2012 SSC International Guidelines for Management of Severe Sepsis and Septic Shock. The SFI group underwent conventional therapy plus SFI (10 mL per piece, Ya’an San-jiu Pharmaceutical Co., Ltd., Sichuan Province, China; batch No.130903010) 100 mL intravenous drip every 12 h SFI was administered within 1 h after septic shock diagnosis.

In all 65 patients enrolled in this study, the PICCO arterial catheter and vein catheter were implanted within 1 h after the diagnosis of septic shock. In the course of early volume resuscitation, hemodynamic data of patients were monitored by PICCO monitor at 0, 12, 24 h after the catheter implantation. The hemodynamic and blood gas data were analyzed and compared to investigate the effects of SFI on hemodynamics in early volume resuscitation treated septic shock patients. Hemodynamic data include cardiac index (CI), global end diastolic volume index (GEDI), extra-vascular lung water index (ELWI), mean arterial pressure (MAP) and heart rate (HR).

**Resuscitation Goals**

The initial resuscitation goals of all the enrolled patients should meet the following criteria during the first 6 h of resuscitation according to the strategy of early goal-directed therapy: (1) central venous pressure 8–12 mm Hg, (2) MAP ≥65 mm Hg, (3) urine output ≥0.5 mL/kg/h, and (4) superior vena cava oxygenation saturation (Scvo₂) or mixed venous oxygen saturation (Svo₂) 70% or 65%, respectively.

**Statistical Analysis**

Statistical analysis was performed using the SPSS 17.0 software (SPSS, Inc., Chicago, IL, USA) via a normal distribution test (Kolmogorov Smirnov test) and homogeneity test for variance (Levene’s t-test). The data are presented as the mean ± standard deviation (x ± s). Statistical differences