Original research

The effect of fluid therapy on hemodynamic and venous blood gas parameters in patients with septic shock

Sahar Mirbaha[1], Abdelrahman Ibrahim Abushouk[2], Ahmed Negida[3], Alaleh Rouhipour[4], Alireza Baratloo[5]*

1. Department of Emergency Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
2. Faculty of Medicine, Ain Shams University, Cairo, Egypt.
3. Faculty of Medicine, Zagazig University, Zagazig, El-Sharkia, Egypt.
4. Pediatric Specialist, Private Researcher, Tehran, Iran.
5. Department of Emergency Medicine, Tehran University of Medical Sciences, Tehran, Iran.

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Abstract: ***Background:*** Hemodynamics and venous blood gas (VBG) may be used to guide fluid therapy in septic shock patients. However, the influence of fluid therapy on hemodynamic and blood gas parameters is not fully understood. In this study, we aimed to investigate the effect of fluid therapy on hemodynamic and VBG parameters.

Methods: This cross-sectional study was conducted from January to April 2016. All patients with diagnosis of severe sepsis were enrolled in the study. Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), central venous pressure (CVP) shock index, VBG parameters, serum sodium (Na) and chloride (Cl) levels, anion gap, and oxygen saturation (O2sat) were assessed before fluid resuscitation, after resuscitation, and after fluid challenge test.

Results: A total of 100 patients were included (mean age were 72.54 ± 12.77 years, 66% male). Fluid therapy significantly increased DBP (df: 2; F= 4.17; p = 0.017), MAP (df: 2; F= 6.06; p= 0.003), and CVP (df: 2; F= 27.54; p < 0.001), while the shock index was significantly reduced After fluid challenge test (df: 2; F= 7.6; p= 0.001). In addition, fluid therapy had no effect on pH (p= 0.90), HCO3 (p= 0.23), base excess (p= 0.13), SCVO2 (p= 0.73), O2sat (p= 0.73), anion gap (p= 0.96), serum Na level (p= 0.71), and serum Cl level (p= 0.64).

Conclusion: Administration of fluid therapy in septic shock patients had no significant effect on SBP, heart rate, or blood gas parameters. Future studies on a larger sample of patients should confirm these findings and correlate them to clinical outcomes.

Keyword: Hemodynamic parameters; Blood Gas Analysis; Fluid Therapy; Shock, Septic

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1. Introduction

Septic shock is defined as inadequate tissue perfusion, secondary to severe sepsis (1). It has a yearly incidence of 50 to 95 cases per 100,000 individuals, and accounts for 2% of hospital admissions (2). Mortality from septic shock ranges from 35% to 70% depending on the presence of comorbidities, acute lung injury, or renal failure (3, 4). While the incidence of septic shock has been increasing over the past decades, its associated mortality has remained constant or slightly decreased (5). To diagnose septic shock, the infection must be recognized and linked to organ failure (6). Treatment of this type of shock requires fluid therapy (colloids or crystalloids), combined with antibiotics and corticosteroids (7). However, septic shock may be associated with cardiac dysfunction and therefore, accurate assessment of fluid depletion status and monitoring circulatory volume and left ventricular preload during fluid resuscitation are essential to guiding fluid therapy (8).

Hemodynamic parameters including central venous pressure (CVP), mean arterial pressure (MAP), and shock index have been used in this regard for decades in emergency departments (ED) and intensive care units

* **Corresponding author:** Alireza Baratloo; Department of Emergency Medicine, Tehran University of Medical Sciences, Tehran, Iran. Tel: +989122884364;
Email: alirezabaratloo@yahoo.com

(ICU) (9, 10). Monitoring these parameters usually requires insertion of invasive arterial and venous lines, which require special equipment, physician's expertise, and knowing the coagulation profile of the patient (11). Moreover, Rady et al. reported that early stages of hypoperfusion are insufficient to significantly influence the vital signs, especially in previously healthy individuals (12). Several studies have suggested that blood gas parameters including oxygen saturation, blood PH, and base excess can serve as monitoring tools for the severity of shock and adequacy of fluid therapy (13, 14).

In a former study we performed, using data of 40 patients, we suggested that CVP can be directly proportional to anion gap (AG) and inversely proportional to base deficit (BD) and bicarbonate (15). In this study, we aimed to investigate the effect of fluid therapy on venous blood gas (VBG) parameters, using a larger sample of patients, to determine if these parameters can be used to guide fluid therapy in septic shock patients.

2. Method

2.1. Study design

This cross-sectional study was conducted from January to April 2016. The study protocol was approved by the ethical committee of Shahid Beheshti University of Medical Sciences. The authors adhered to the Helsinki ethical principles throughout this research.

2.2. Study population

All patients with diagnosis of severe sepsis (2016/17 ICD-10-CM Diagnosis Code R65.2) were enrolled in the study. Those with known history of heart failure and/or renal failure and intubated patients were excluded.

2.3. Measurements

Detailed methods of the blood pressure measurements are presented in previous studies (16). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were assessed via a standard mercury sphygmomanometer (Model 1002/ Presameter, Riester, Germany). MAP was calculated based on the following formula:

$$MAP = \frac{(2 \times DBP) + SBP}{3}$$

Shock index was calculated based on the following formula:

$$Shock\ index = \frac{Heart\ rate}{SBP}$$

For eligible patients, peripheral blood sample was taken for testing VBG [measurement of pH, base excess (BE), central venous oxygen saturation ($SCVO_2$), and HCO_3], sodium (Na) and chloride (Cl). Anion gap and oxygen saturation (O_{2sat}) were also calculated. These data along with demographic data were registered in a prepared checklist.

Following initial resuscitation of 20 ml/kg crystalloid solutions, all measurements were repeated for the second time. If the patient was still hypotensive and/or had serum level lactate of more than 4 mmol/l, central venous line was inserted in the internal jugular vein and those with CVP less than 8 cmH_2O were candidates of participation in the rest of the study. Fluid challenge test with infusion of 500 cc of normal saline 0.9% in about 1 hour was performed and those with more than 3 cmH_2O raise in CVP were excluded. All mentioned parameters were measured again for the remained patients.

2.4. Statistical analysis

Based on the previous study of the authors, correlation coefficient of serum bicarbonate level and CVP of patients in septic shock was -0.456 (15). Therefore, considering the 95% statistical confidence interval ($\alpha = 5\%$) and 90% power of the study ($\beta = 10\%$), sample size of about 90 participants is enough for the study. Data were analyzed using STATA 11.0 statistical software. After making sure data had normal distribution applying Kolmogorov–Smirnov test, to compare evaluated factors before and after fluid therapy, quantitative data were compared using repeated measures ANOVA. P-value <0.05 was considered significant.

3. Result

A total of 100 patients were included. The mean and standard deviation of the patients' age was 72.54 ± 12.77 years. Our sample included 34 females (34%) and 66 males (66%). Fluid therapy had no effect on SBP (df: 2; F= 1.68; p= 0.19) or heart rate (df: 2; F= 2.17; p= 0.12). However, fluid therapy significantly increased DBP (df: 2; F= 4.17; p = 0.017), MAP (df: 2; F= 6.06; p= 0.003), and CVP (df: 2; F= 27.54; p < 0.001), while the shock index was significantly reduced After fluid challenge test (df: 2; F= 7.6; p= 0.001). Table 1 shows the effect of fluid therapy on the measured values of hemodynamic parameters.

In addition, fluid therapy had no effect on pH (p= 0.90), HCO_3 (p= 0.23), base excess (p= 0.13), $SCVO_2$ (p= 0.73), O_{2sat} (p= 0.73), anion gap (p= 0.96), serum Na level (p= 0.71), and serum Cl level (p= 0.64). Table 2 shows the effect of fluid therapy on venous blood gas parameters.

4. Discussion

This diagnostic study was designed to investigate the effect of fluid therapy on blood gas parameters in septic

Table 1: Mean and standard deviation of hemodynamic parameters before and after fluid therapy

Variable	Before fluid therapy	After initial fluid resuscitation	After fluid challenge test	p
Systolic blood pressure (mmHg)	117.73 ± 29.45	119.26 ± 28.17	119.61 ± 27.37	0.19
Diastolic blood pressure (mmHg)	67.10 ± 18.42	68.11 ± 22.35	71.96 ± 17.09	0.017
Mean arterial pressure (mmHg)	83.98 ± 21.14	85.32 ± 21.42	88.60 ± 20.22	0.003
Heart rate (beat/minute)	86.82 ± 18.75	87.28 ± 19.5	84.73 ± 18.96	0.12
Shock index (beat/mmHg)	0.80 ± 0.31	0.78 ± 0.29	0.75 ± 0.26	0.001
Central venous pressure (mmHg)	8.11 ± 6.63	8.18 ± 6.68	10.3 ± 6.77	<0.001

Table 2: Mean and standard deviation of venous blood gas parameters before and after fluid therapy

Variable	Before fluid therapy	After fluid challenge test	p
pH	7.34 ± 0.10	7.35 ± 0.13	0.90
HCO3 (mmol/L)	24.21 ± 6.59	27.96 ± 31.67	0.23
Base excess (mEq/L)	0.21 ± 7.99	1.31 ± 7.72	0.13
Anion gap (mEq/L)	13.48 ± 15.98	13.56 ± 10.03	0.96
Na (mEq/L)	141.42 ± 8.26	140.66 ± 18.92	0.71
Cl (mmol/L)	105.53 ± 10.96	106.26 ± 13.57	0.64
SCVO2 (%)	32.68 ± 23.79	30.68 ± 24.54	0.38
O2sat (%)	77.90 ± 19.07	78.4 ± 17.24	0.73
pH	7.34 ± 0.10	7.35 ± 0.13	0.90

HCO3: Bicarbonate; SCVO2: central venous oxygen saturation; O2sat: oxygen saturation

shock patients. To assess the usefulness of these novel monitoring parameters, they must be compared to hemodynamic parameters that serve as the gold standard in this regard. Our results show that administration of fluid therapy in septic shock patients markedly elevated DBP, MAP, and CVP and produced a significant reduction of the shock index three hours after the intervention. No significant effect of fluid therapy was noted on SBP, heart rate, or blood gas parameters.

Recognition and early treatment of sepsis and septic shock are essential to improve the clinical outcomes of shock management because the condition can progress to serious illness after a few hours, the so-called "Golden hours" (17). Goal directed therapy primarily targets relieving global tissue hypoxia by achieving a balance between oxygen delivery and oxygen demand (18). Hemodynamic measures fail to recognize early changes in tissue oxygenation during the pathogenesis of sepsis and in response to therapy (12). Therefore, resuscitation endpoints usually include arterial lactate, pH, and base deficit (19). Being a surrogate of cardiac index, mixed venous saturation is another valuable parameter; however, if inserting a pulmonary artery catheter is not feasible, venous oxygen saturation is a valid alternative (20).

There are conflicting results in the literature about the optimal endpoints for fluid therapy in septic shock patients. CVP is a commonly used parameter in this regard; however, several studies doubted its efficacy because its normalization was accompanied by persistent elevation of shock index (21-24). Other studies suggested that dynamic parameters such as pulse pressure or stroke volume variation are superior to static parameters such as CVP in monitoring fluid resuscitation in critically ill patients (10, 25). Different studies have shown that elevated base deficit correlates with a higher incidence of shock-related complications and a longer ICU stay (14, 25, 26). We formerly published a diagnostic study of 40 patients with septic shock, which concluded that venous O_2 saturation can be a valuable indicator of response to fluid therapy (17). However, our results on a larger sample of patients showed no significant effect of fluid therapy on these parameters.

Sevransky et al. conducted a systematic review to identify the hemodynamic goals, commonly used in clinical trials on patients with sepsis. The authors concluded that restoring MAP is the most commonly used treatment goal in sepsis clinical trials, with a fewer number of trials choosing pulmonary artery occlusion pressure, CVP, or cardiac index as a hemodynamic endpoint (27). Several sepsis clinical trials used SBP as a hemodynamic monitoring tool and assigned a 90 mmHg value as the

treatment endpoint (28, 29). In our study, administration of fluid therapy did not significantly affect SBP, adding to the controversy regarding its value as a hemodynamic endpoint.

Our study has the following limitations: 1) small sample size limits the generalizability of our results, 2) we did not evaluate the correlation between the reported hemodynamic and blood gas parameters in this study and the clinical status of patients; therefore, we cannot comment on the benefit of these parameters in predicting clinical improvement, 3) the use of vasopressors or mechanical ventilation may interfere with the effect of fluid therapy on the reported outcomes, and 4) we measured our outcomes at two points (1 hour and 3 hours) following the intervention. The sensitivity and specificity of these measures may not be adequate; therefore, serial measurement of hemodynamic and blood gas parameters may be of a higher prognostic benefit than single measurements.

Future studies should consider recording serial measurements of hemodynamic and blood gas parameters during fluid resuscitation, and correlate these parameters to mortality or clinical outcomes such as length of ICU stay and incidence of organ dysfunction. Correlation with clinical outcomes is essential to draw conclusions over the clinical benefits of monitoring these parameters. To exclude the effect of the cause of shock on the hemodynamic or blood gas response, future studies are recommended to include patients with the same causes or risk factors of shock.

Findings of the present study showed that strength training leads to an increase in EMG parameters or an

5. Conclusion:

Administration of fluid therapy in septic shock patients markedly elevated DBP, MAP, and CVP and produced a significant reduction of the shock index three hours after the intervention. No significant effect of fluid therapy was noted on SBP, heart rate, or blood gas parameters. Future studies on a larger sample of patients should confirm these findings and correlate them to clinical outcomes.

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7. Conflict of interest

No conflict of interest was declared.

8. Funding source

None.

9. Author contribution

Conception or design of the work: AB, AIA, AN; data gathering: SM; data analysis: AB, AR; drafting the work: SM, AB; critically revised the manuscript: All authors. All authors approved final version of the paper to be published and agreed to be accountable for all aspects of the work.

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