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Changes in End-Tidal Carbon Dioxide (ETCO2) vs. Changes in Central Venous Oxygen Saturation (ScvO2) and Lactate Clearance as a Quantitative Goal Parameter in Treatment of Suspected Septic Shock Patients

Sayed Hamed Khajebashi*, Tayebeh Cholmaghani, Mohamad Nasr-Esfahani

Department of Emergency Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.

***Corresponding author:** Sayed Hamed Khajebashi; **Email:** drkhajebashi@gmail.com

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Abstract

Introduction: Physiologic indexes for therapeutic assessment of shock were introduced long time ago. Recent studies have evaluated central venous pressure (CVP), central venous oxygen saturation (ScvO2), lactate and end-tidal carbon dioxide (ETCO2) levels in this regard.

Objective: To understand the potential diagnostic capability of ETCO2 in comparison with ScvO2, CVP and lactate in patients with suspected septic shock, we aimed to compare these parameters through a quantitative resuscitation treatment approach.

Methods: In this cross-sectional study, 84 patients with suspected septic shock were selected randomly. All patients underwent quantitative resuscitation treatment approach. The following parameters were measured and recorded at baseline: ETCO2, CVP, ScvO2, mean arterial pressure (MAP), percentage of arterial oxygen saturation (SatO2), blood lactate levels, heart rate (HR), respiratory rate (RR), and the exact amount of urine output. At the time of treatment, and 3 hours and 6 hours after, all of the tests and measurements were re-implemented and registered by an emergency medicine specialist.

Results: There was a significant positive correlation between ETCO2 and ScvO2 at all times (baseline: $r=0.566$, $p<0.001$; after 3 hours: $r=0.409$, $p<0.001$; after 6 hours: $r=0.170$, $p>0.05$). Furthermore, there was a significant inverse correlation between ETCO2 and lactate at all times (baseline: $r= -0.538$, after 3 hours: $r= -0.677$, after 6 hours: $r= -0.799$). There was no significant correlation between ETCO2 and CVP at any time ($p>0.05$).

Conclusions: All parameters significantly changed over time, and the correlation between changes in ETCo2, ScvO2 and lactate clearance was significant.

Key words: Central Venous Oxygen Saturation; Central Venous Pressure; End-Tidal Carbon Dioxide; Shock, Septic; Patient Management

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Introduction

Recently, sepsis has been demarcated as a life-threatening phenomenon representing body destruction of its own tissues and organ dysfunction while confronting an infection (1). If cellular, circulatory and metabolic dysfunctions aggravate, it can be concluded that suspected septic shock has occurred (2). Physiologic indexes for quantitative resuscitation of shock were introduced long time ago. The primary goals of this treatment approach are maintaining adequate vascular oxygen, blood pressure and urinary output based on the hypothesis that supports provided by these interventions might reduce and limit tissue hypoperfusion and endothelial damage (3, 4). Quantitative resuscitation is defined as early recognition and initiation of fluid therapy (1000 ml of normal saline) and antibiotic therapy along with close monitoring (3, 5, 6). Some studies suggest that quantitative resuscitation has significant effects on lowering mortality rates in patients with sepsis, whereas others have found no significant changes in survival rates (7, 8). Recent studies have evaluated central venous pressure (CVP), central venous oxygen saturation (ScvO2), lactate and end-tidal carbon dioxide (ETCO2) levels in this regard (5, 9, 10). Lactate clearance and ScvO2 are the two main indexes introduced for assessing the proper treatment of shock. However, measuring them needs some invasive procedures or time consuming laboratory analysis. However, ETCO2 is a simple, rapid, non-invasive method (3, 5, 6, 9). Although, studies evaluated the association of ETCO2, lactate clearance and ScvO2 with sepsis, but their predictor value have yielded contradictory results. Given the contradictory results and limited studies available, this research aimed to compare the changes in ETCO2 level with those of ScvO2 and lactate clearance in patients with suspected septic shock, who underwent quantitative resuscitation to evaluate the diagnostic role of the mentioned parameters.

Methods

Study design and setting

This was a diagnostic accuracy study conducted in the emergency departments (EDs) of Amin and Al-Zahra hospitals in Isfahan during 2016-2018. After obtaining the code of ethics from Isfahan University of Medical Sciences (Approval Number: IR.MUI.MED.REC.1397.202) and obtaining written consent from the patients or their relatives, broad-spectrum antibiotic therapy was initiated for all patients.

Study population

The study population consisted of all patients with suspected septic shock presenting to the mentioned hospitals. Assuming correlation coefficient of 0.3 between ETCO2 and ScvO2, lactate level or CVP, and type-I error of 0.05, and a test power of 80%, at-least of 84 patients were required for this correlation coefficient to be significantly different from zero. The sample was selected from the target population using convenience sampling. Inclusion criteria were suspected septic shock cases (patients with hypotension and unresponsive to intravenous fluids and positive systemic inflammatory response syndrome (SIRS)) with age of 18 years and older. The exclusion criteria were pregnancy, intubation before admission, chronic obstructive pulmonary disease (COPD).

Data gathering

Patients underwent accurate cardiac monitoring, and their oxygen saturation was controlled. For all patients with suspected septic shock, a central venous catheter (CVC) was first embedded in their internal jugular vein or subclavian vein. The following parameters were measured at baseline: ETCO2 (measured by capnography), CVP (measured through manometer), ScvO2 (measured by the blood sampling of a CVC), mean arterial pressure (MAP), percentage of arterial oxygen saturation (SatO2), blood lactate levels, heart rate (HR), and respiratory rate (RR).

The nasal cannula tubes were inserted for patients with spontaneous breathing, and the amount of expiratory CO2 was measured by the sidestream capnography method for intubated patients. All patients were non-intubated and obeying, so we used capnograph (Med Lab Manufacturer, Karlsruhe, Germany) with sidestream method. At the 3rd and 6th hours during the treatment, an emergency medicine specialist performed all the tests and measurements, and documented them. The values of ScvO2 more than 70%, or lactate clearance of more than 10% are the primary objectives of the Early Goal Directed Therapy (EGDT) protocol during the first 6 hours.

Statistical analysis

The obtained data was entered into SPSS software, Version 20. The results are presented as mean ± standard deviation (SD) or frequency (percentage). According to the results of Kolmogorov–Smirnov test indicating normal distribution of data, repeated measures ANOVA was used to compare the changes in variables over time. Moreover, Pearson's correlation coefficient was used to evaluate the linear correlation between variables at 95% confidence interval. The changes in ETCO2, ScvO2, lactate levels and CVP were calculated at three time intervals of baseline, 3 hours and 6 hours. We also present regression equation of significant change of correlation based on linear regression. Significance level of less than 0.05 was considered significant in all analyses.

Results

In this study, 84 patients (45 male / 39 female) with the mean age of 60.73±12.37 years enrolled. Baseline information of the study patients are presented in table 1. The mean values were 114.42±10.85 beats/min for PR, 24.33±4.94 breaths/min for RR, 38.63±0.46 ˚C for body temperature, and 64.40±16.40 mmHg for MAP.

The values of ETCO2, ScvO2, lactate, and CVP at the baseline, 3 hours and 6 hours after starting the resuscitation process are reported in table 2. Based on the findings, the changes in ETCO2, ScvO2, lactate, and CVP were statistically significant. The mean values of ETCO2, ScvO2, and CVP increased

Table 1: Baseline information of the study patients; Data shows in mean± SD or n(%).

Variables		Values
Gender	Male	45 (53.6%)
	Female	39 (46.4%)
Age (years)		60.73±12.37
Pulse rate (/min)		114.42±10.85
Respiratory rate (/min)		24.33±4.94
Temperature (˚C)		38.63±0.46
Mean arterial pressure (mmHg)		64.40±16.40

Table 2: The values of ETCO2, ScvO2, lactate, and CVP at the baseline, 3 hours and 6 hours

Variables	Times			P-value
	Baseline	After 3h	After 6h	
	mean± SD			
End-tidal carbon dioxide (mmHg)	19.58±4.63	25.88±4.48	29.20±3.98	<0.001
Central venous oxygen saturation (%)	41.71±10.57	65.08±9.15	73.55±7.93	<0.001
Lactate (mg/dL)	23.17±6.47	18.38±4.85	17.28±4.35	<0.001
Central venous pressure (cmH2O)	1.10±2.07	4.02±2.22	6.91±2.09	<0.001

Table 3: Correlation of ETCO2 (baseline, after 3 and 6h) with SVO2, lactate, and CVP at the baseline, 3 hours and 6 hours

Time	Variables	ETCO2		ScvO2		Lactate		CVP	
		r	P	r	P	r	P	r	P
Baseline	**ETCO2**	1		0.566	<0.001	-0.538	<0.001	0.028	0.797
	ScvO2			1		-0.505	<0.001	0.294	0.007
	Lactate					1		-0.162	0.142
	CVP							1	
After 3h	**ETCO2**	1		0.409	<0.001	-0.677	<0.001	0.029	0.796
	ScvO2			1		-0.405	<0.001	0.044	0.688
	Lactate					1		-0.087	0.433
	CVP							1	
After 6h	**ETCO2**	1		0.170	0.123	-0.799	<0.001	0.054	0.626
	ScvO2			1		-0.123	0.265	0.116	0.293
	Lactate					1		-0.065	0.559
	CVP							1	

ETCO2: End-Tidal Carbon Dioxide, ScvO2: Central venous oxygen saturation, CVP: central venous pressure

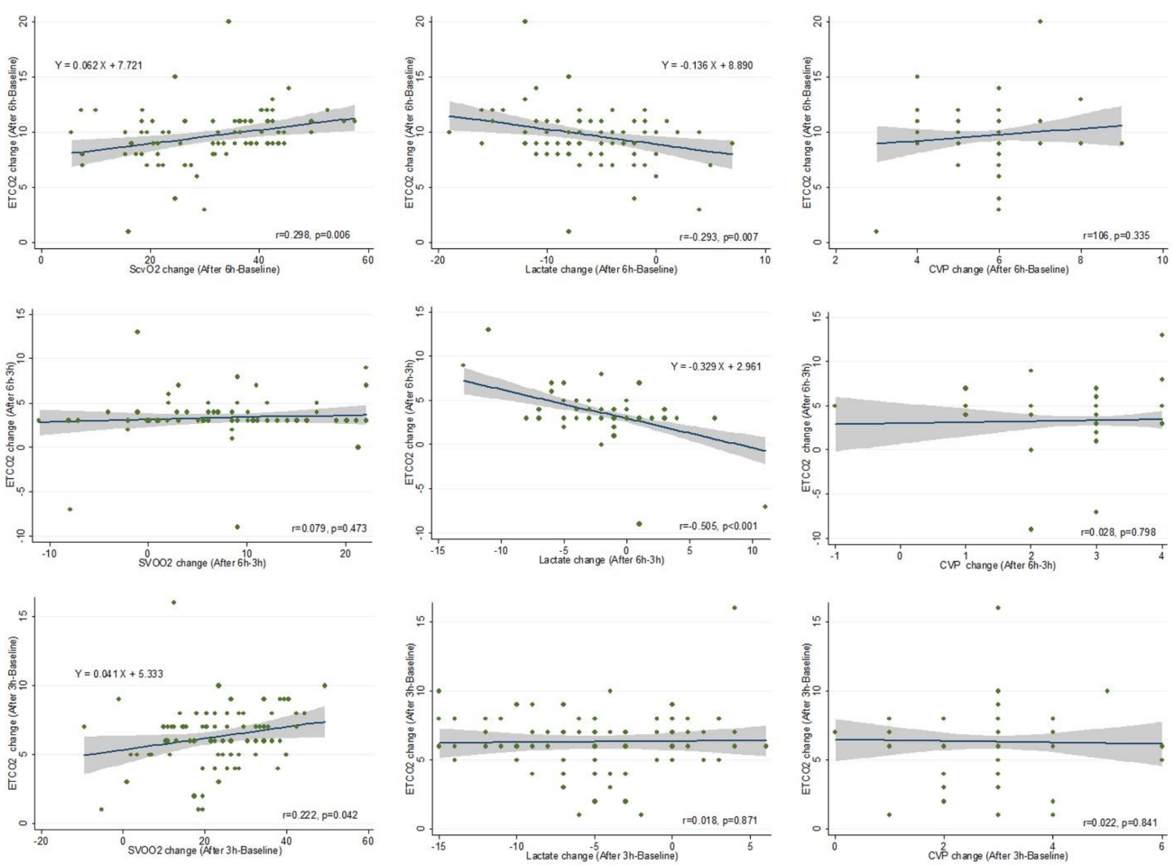

Figure 1: Scatter plot of correlation and linear regression equation of ETCO2 changes against ScvO2, lactate, CVP changes at baseline, 3 hours and 6 hours after starting resuscitation

significantly after 6 hours, while the mean value of lactate decreased significantly after 6 hours. In addition, the correlation of ETCO2 with ScvO2, lactate level, and CVP indicated that the correlation coefficient of ETCO2 with ScvO2 was direct and significant at baseline, and after 3 hours with the values of 0.566 (95% CI: 0.385 to 0.747), and 0.409 (95% CI: 0.208 to 609), respectively ($p<0.01$). Furthermore, the correlation coefficient of ETCO2 with lactate level was inverse and significant at baseline, after 3, and 6 hours with the values of -0.538 (95% CI: -0.723 to -0.353), -0.677 (95% CI: -0.839 to -0.515), and -0.799 (95% CI: -0.931 to -0.667), respectively ($p<0.001$). However, ETCO2 did not correlate significantly with CVP at any of the three time points ($p>0.05$). Other relationships between the variables are presented in table 3. Changes in ETCO2, ScvO2, lactate level and CPV were calculated at three time intervals of baseline, 3 hours and 6 hours. The correlation of changes in ETCO2 with ScvO2 was statistically significant 6 hours after and at baseline (r = 0.298, P=0.006), and 3 hours after and at baseline (r=0.222, P=0.042). furthermore, the correlation of changes in ETCO2 with lactate level was statistically significant at 6 hours and at baseline (r =-0.293, P= 0.007), and at 3 hours and at baseline (r=-0.505, P<0.001). The correlation of changes in ETCO2 with CPV was not significant at any of the three time points (Figure 1).

Discussion

Our results showed that ETCO2, ScvO2, lactate and CVP were changed significantly at 3 and 6 hours after the initiation of resuscitation in suspected septic shock patients. ETCO2, CVP, and ScvO2 showed an increasing pattern with a decrease in lactate amounts. Findings of this study revealed the positive correlation between ETCO2 and ScvO2 and inverse correlation between ETCO2 and lactate amounts, and showed no significant relationship between ETCO2 and CVP. These findings indicate that in a quantitative resuscitation approach in suspected septic shock, ETCO2 elevation is associated with the rise in ScvO2 levels and lactate clearance. Hunter et al. also found an inverse correlation between exhaled ETCO2 levels and lactate in a study of patients with suspected sepsis (6). Permpikul et al. reported no relationship between ScvO2 and lactate levels generally, but dividing ScvO2 levels into three groups revealed that ScvO2 more than 85% was related with significantly higher levels of lactate (11). Guirgis et al. demonstrated that ETCO2 and ScvO2 had no significant relationship with different measure times, but the correlation of ETCO2 and lactate was almost significant (5). In a study by McGillicuddy et al., a weak inverse correlation was reported between ETCO2 and lactate in febrile patients (12). Varied results from similar studies or different settings indicate the complicated relationship between the regulating mechanisms of metabolism especially in sepsis and related conditions. The underlying mechanism that adjusts the rates of lactate clearance and ETCO2 are yet to be discussed, but since ETCO2 could be altered quickly and measured more simply, it may be considered as a reliable predictor of metabolic acidosis in individuals suspected of sepsis, although further studies are required to establish the firm predictive scales (6).

Limitations

One of the limitations of this study was its rather small sample size. Another weakness was failure to follow the patients for assessing the outcome of suspected septic shock treated by quantitative resuscitation such as mortality. ScvO2 is a diagnostic marker for low cardiac output, but this parameter was not measured in our participants. Another limitation of this study was failure to measure the parameters more than 3 times. Comparing the amounts of these parameters at the time of discharge or death might express if the rates persist after treatment or worsen only during the suspected septic shock period. Therefore, it is suggested to conduct further studies with larger sample sizes to determine detailed and reliable findings. In addition, given that the present study revealed the association of ETCO2, ScvO2, and lactate amounts, it may be concluded that these variables are effective in the early detection and treatment of this disease. Therefore, it is suggested that further studies be conducted on the diagnostic value of these variables in septic shock.

Conclusions

ETCO2, ScvO2, and CVP show elevated rates at 3 and 6 hours after the baseline measurement in EGDT setting whereas lactate levels decline. We observed a positive correlation between ETCO2 and ScvO2 and an inverse correlation between ETCO2 and lactate levels whereas ETCO2 and CVP revealed no significant correlation over the measured time, indicating that ETCO2, ScvO2, and lactate clearance may correlate with one another at different times. The changes in these parameters with time in patients suspected of septic shock may correlate with their proper diagnostic value, although CVP and ETCO2 may not be correlated at different times.

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Authors' contribution
All the authors met the standards of authorship based on the recommendations of the International Committee of Medical Journal Editors.

Conflict of interest
None declared.

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