Research Article

Comparison between central venous and arterial gases level versus lactate clearance as an indicator of initial resuscitation in septic patients in intensive care unit

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Abstract

Objective: Aim of this study: was to compare the central venoarterial carbon dioxide difference/arterial-central venous oxygen difference (P(va)CO2/C(a-v)O2) ratio versus lactate clearance as an indicator to evaluate the steps of initial resuscitation in septic patients. **Patients and methods:** Our study was conducted in the ICU,Minia University Hospital. Eighty patients with severe sepsis or septic shock**. Results:** There was improvement in CVP, MAP, or Scvo2 at T8 after early resuscitation with no significant differences between group1 and group 2 and inside each group. There were no significant difference in $P(v\text{-}a)CO_2/C(a\text{-}v)O_2$ ratio at T0 and at T8 at **group 1.** However there was higher lactate level at T0 and exhibited significantly lower at T8 in **group 2. Conclusion:** Further clinical trials are needed to conclusively establish lactate clearance as a resuscitation endpoint and an outcome measure to be targeted during the most proximal phases of severe sepsis and septic shock.

Keywords: CVP; MAP; Scvo2

Introduction

Sepsis is one of the most common causes of death in the intensive care unit (ICU). It is difficult to be diagnosed due to multiple comorbidities and underlying diseases in these patients[1, 2].

Sepsis is considered a complex syndrome characterized by presence of organ dysfunction mediated by different mechanisms of cell damage resulting in more than 30% mortality rate [3,4]. Although sepsis involve microvascular anomalies and constitute a central element of such organ dysfunction through decrease in oxygen supply and/or deficient utilization of the available oxygen[5].

Severe sepsis and septic shock is a life-threatening condition for patients of intensive care unit (ICU)[6,7]. Promoted practice for septic shock therapy is largely based on a study by Rivers et al., which developed a protocol known as early goal-direeted therapy (EGDT [8].

The initial resuscitation of the septic patients includes anticipation for the need for fluid resuscitation, antimicrobials, and possibly vasoactive medications (vasopressors)[9,10].

In a cellular hypoxia anaerobic carbon dioxide increases as hydrogen ions generated by anaerobic sources of energy are buffered by bicarbonate[11]. Consequently, a rise in the respiratory quotient (VCO_2/VO_2 ratio) reflects the presence of global anaerobic metabolism [12].

The $P(v\text{-}a)CO_2/C(a\text{-}v)O_2$ ratio is calculated from several parameters based on a known formula that mainly involves $ScvO_2$, hemoglobin (Hb), arterial oxygen saturation (SaO2), and P(v-a)CO[13]. Therefore, a simple and rapid method for identification of a high $P(va)CO_2/C(a\text{-}v)O_2$ ratio would be of substantial benefit, and the factors contributing to a high $P(v\text{-}a)CO_2/C(a\text{-}v)O_2$ ratio are worthy of consideration in the clinical setting [14].

Sepsis is a disease characterized by hypercatabolism with increased demand for oxygen due to elevated consumption in tissue[15]. Early therapy with optimization of blood volume, hemoglobin levels and/or use of inotropic agents favors the patient's prognosis[16].

Despite questioning relating to the mechanisms of hyperlactatemia,[17-19] this is a well-recognized instrument for diagnosing hypoperfusion and occult tissue hypoxia, and it is also used as a prognostic index among septic patients[20]. However, although hype rlactatemia is generally measured in the arterial blood, the ideal collection site has not been clearly established [21].

Patients and methods

Our study was conducted in the ICU ,Minia University Hospital. Eighty patients with severe sepsis or septic shock were divided into two groups: **group 1**, resuscitated to normalize CVP, MAP, and $(P(va)CO_2/C(a-v)O_2)$ ratio; and group 2, resuscitated to normalize CVP, MAP, and lactate clearance. Whereas mortality was followed up for 28 days. Inclusion criteria

o septic adult patients who were sequentially admitted to ICU and required central venous catheters for resuscitation and met the criteria of sepsis were eligible for the study.

***Age: ≥ 18 to ≤ 65 years.**

*** Sex: male and female .**

Exclusion criteria

* Patints less than 18 years or more than 65 years
* Patients who were unable to complete the assessment tools
* Patients with no relatives to sign the consent
* Patients admitted to intensive care unit not due to sepsis
* Patients had a contraindication to central venous catheterisation
* pregnancy

Parameters to be assessed

- The admission characteristics, pre-existing conditions and acquired complications in the intensive care unit will be recorded
- The inclusion time (T0) and study enrollment will be defined as the moment at which central venous pressure (CVP) monitoring begin after intensive care unit (ICU) admission.
- The demographic characteristics including the Acute Physiology and Chronic Health Evaluation II (APACHE II) score, the Sequential Organ Failure Assessment (SOFA) score, use of inotropes and type of organism.
-The global hemodynamic including HR, MAP, CVP, arterial, and central venous blood gas analyses were simultaneously performed on the T0 and T8.

- Measurements in this study included determination of the following variables:
- Pao2.
- arterial carbon dioxide tension (Paco2) - central venous oxygen tension (Pvo2) - central venous carbon dioxide tension (Pvco2) - Sao2, and Scvo2 - The Hb and lactate level were measured from the arterial blood.

- The arterial oxygen content (Cao2) =(1.34 × Sao2 × Hb) + (0.003 × Pao2) -central venous oxygen content (Cvo2) =(1.34 × Svo2 × Hb) + (0.003 × Pvo2) –arterio-venous oxygen content difference (C(a-v) O2) -venoarterial CO_2 tension differ-ence $(P(v-a)CO_2)$ -$P(va)CO_2/C(a-v)O_2$ ratio - Lactate clearance rat = (T0 lactate − T8 lactate)/(T0 lactate) × 100%
- Prediction of ICU mortality at day 28.

Statistical analysis

The patients were divided into 2 groups: group 1; $P(v-a)CO_2/C(a-v)O_2$ ratio group and group 2; Lactate clearance group. A descriptive analysis was performed. All data are expressed as the mean s ± SDs and medians (25^{th}-75^{th} percentiles) unless otherwise specified. Mann-Whitney tests were used to compare the groups in terms of the continuous variables, and $\chi 2$ and Fisher exact tests were used to compare the categorical variables between groups.

Pairs of continuous variables were analyzed using linear regressions. All comparisons were 2 tailed, and P<05 was required to exclude the null hypothesis. Statistical analyses were performed with the SPSS 13.0 software package (SPSS Inc, Chicago, Ill) and Med Calc 11.4.3.0 software (Mariakerke, Belgium).

Results

The relevant hemodynamic and global oxygen metabolic parameters at T0 and T8 for the LC and non-LC groups are shown in Tables 1 and 2, respectively. There was improvement in CVP, MAP, or Scvo2 at T8 after early resuscitation with no significant differences between group1 and group 2 and inside each group. There were no significant difference in $P(va)CO_2/C(a\text{-}v)O_2$ ratio at T0 and at T8 at group 1. However there was higher lactate level at T0 and exhibited significantly lower at T8 in group 2.

Table (1): Hemodynamic and related variables in group 1 at T0 and T8

Variables	T0	T8	*P*
HR (beats/min)	98 ± 27	99 ± 22	0.563
MAP (mm Hg)	89 ± 21	85 ± 14	0.512
CVP (mm Hg)	10 ± 3.5	9.7 ± 4	0.089
$Scvo_2$ (%)	76 ± 9	75 ± 13	0.123
$C(a\text{-}v)O_2$ (mm Hg)	3.48 ± 2.05	3.7 ± 1.6	0.132
$P(v\text{-}a)\ CO_2$ (mm Hg)	6.4 ± 5.1	7.3 ± 4.5	0.978
$P(v\text{-}a)\ CO_2/C(a\text{-}v)O_2$ ratio (mm Hg/mL)	1.87 ± 1.55	2.1 ± 1.0	0.538
No. of patients with NE (%)	20/34 (59)		0.797
NE dose ($\mu g\ kg^{-1}\ min^{-1}$)	0.18 ± 0.25	0.32± 0.6	0.588

HR indicates heart rate; CVP , central venous pressure; MAP, mean arterial pressure; $(P(v-a)co2)$ veno-arterial gradient in carbon dioxide tension, $(C(a-v)O_2)$ arteriovenous gradient in oxygen content; NE, norepinephrine;
P value is significant if less than 0.05

Table (2): Hemodynamic and related variables in group 2 at T0 and T8.

Variables	T0	T8	P
HR (beats/min)	98 ± 22	92 ± 21	0.123
MAP (mm Hg)	90 ± 17	90 ± 15	0.215
CVP (mm Hg)	9 ± 3	8.5 ± 3	0.334
$Scvo_2$ (%)	72 ± 11	77 ± 9	0.760
Lactate (mmol/L)	2.9 ± 2.2	1.3 ± 0.8	0.007
No. of patients with NE (%)	28/50 (56)		
NE dose ($\mu g\ kg^{-1}\ min^{-1}$)	0.15 ± 0.25	0.24 ± 0.31	0.904

HR indicates heart rate; CVP, central venous pressure; MAP, mean arterial pressure; NE, norepinephrine.
 $P < 0.05$ is significant between T0 and T8 inside **(group 2)**

Discussion

Severe sepsis and septic shock are leading causes of death in the world [22]. mortality rate remains high in septic shock [23].There is a need to test the prognostic value of factors that could be used for guiding therapy after the initial resuscitation.

The results of our study reported that a protocol targeting lactate clearance of at least 10% or more, as an evidence of adequate tissue oxygen delivery and a measurement of total body oxygen metabolism and was compared with the $P(v\text{-}a)CO_2/C(a\text{-}v)O_2$ ratio when resuscitating the septic patients at time of admission and 8hours after the initial resuscitation.

Our results on $P(v\text{-}a)CO_2/C(a\text{-}v)O_2$ ratio dem onstrated that, although the target indicator of the initial resuscitation of $P(v-a)CO_2/C(a-v)O_2$ ratio around 1.68 or low was achieved in 85% of patients in (**group 1)**, 45% mortality was recorded, with no statistically significant difference between survivors and nonsurvivors ($P > 0.05$).

Our results demonstrated that target indicatorof lactate clearance of 10% or more was achieved in 70% of patients in **(group 2)**. On comparing it with $P(v-a) CO_2/C(a-v)O_2$ ratio as goals of the initial sepsis resuscitation, we found that targeting lactate clearance of at least 10%, as evidence of adequate tissue oxygen delivery and a measure of total body oxygen metabolism when resuscitating patients with severe sepsis and septic shock.

The present research showed discrepancy between lactate and $P(v-a)CO_2/C(a-v)O_2$ ratio as regards their correlation with mortality and, as we demonstrated, the target goal of lactate clearance of 10% or more was achieved in 70% of patients in **(group 1**), but with a mortality of 30%. Hence, this group had 15% lower in-hospital mortality than those resuscitated to $P(v-a)CO_2/C(a-v)O2$ ratio around 1.68 or low (30 vs. 45%, respectively), with a statistically significant difference. In our study, basal lactate was significantly higher ($P < 0.05$) in nonsurvivors compared with survivors.

Monnet et al.,[24] also reported that the $P(v-a)CO_2/C(a-v)O_2$ ratio is predictive of increases in VO2, but the Scvo2 value is not. These authors demonstrated that a $P(v-a)CO_2/C(a-v)O_2$ ratio greater than 1.8 is predictive of VO2 increases of more than 15% in response to increases in DO2 when the Scvo2 is greater than 70%.

The arterial lactate level is well known to lect ongoing metabolism and serves as an refindicator of anaerobic metabolism, and LC is associated with mortality in critically ill patients [25,26]. Although the use of LC is limited to a certain degree, it has generally been accepted for use as an indicator of oxygen debt in clinical practice, and LC is particularly well accepted for this purpose. Therefore, it was relatively reasonable to use LC as an indicator of anaerobic metabolism in our study.

Thus, VO2/DO2 dependence has been considered to be a hallmark of tissue hypoxia and the activation of anaerobic metabolism[25,27], although it has been challenged because of the methodological limitations (mathematical coupling) in the VO2/DO2 relationship assessment [28].

Conclusion

Lactate clearance provide useful information for assessing the initial resuscitation of the septic patients in ICU after 8 hours, than $P(v-a)CO_2/C(a-v)O_2$ ratio.in addition to its simplicity in measurement away from miscalculation of $P(v-a)CO_2/C(a-v)O_2$ ratio assessment parameters. Further clinical trials are needed to conclusively establish lactate clearance as a resuscitation endpoint and an outcome measure to be targeted during the most proximal phases of severe sepsis and septic shock.

Disclosure

The authors report no conflicts of interest in this work.

Source of funding: by self.

Ethical clearance: Taken from faculty of medicine – Minia University Committee.

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