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Correlation of End Tidal CO_2 ($ETCO_2$) Level with Hyperlactatemia in Patient with Hemodynamic Disturbance

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Abstract

Background: Critically ill and hemodynamically unstable patients usually have perfusion disturbance that causes anerobic metabolism, causing increased lactate production. Hyperlactatemia induces metabolic acidosis, which then compensated by hyperventilation. Decreased $PaCO_2$ as the consequence of hyperventilation can be measured as end-tidal CO_2 ($ETCO_2$). High $ETCO_2$ was hypothesized as related to hyperlactatemia, thus monitoring of $ETCO_2$ could be a non-invasive monitoring in hemodynamically unstable patients.

Objective: This study aimed to search the correlation between $ETCO_2$ level and hyperlactatemia in patients with hemodynamic disturbance.

Method: This was observational, cross sectional study conducted on January to February 2017 in Sanglah General Hospital, Bali, Indonesia. Subjects were hemodinamicaly unstable patients aged 13-90 years old without primary pulmonary diseases recruited by consecutive sampling. $ETCO_2$ measurement by capnograph, lactate level measurement, and blood good analysis were done to all eligible patients. We did an association test to determine ther relation between $ETCO_2$ level and lactate level in such patients.

Results: There were 70 subjects analyzed with median age 55 years old. Subjects' case was 35.7% called for resuscitation, 32.9% was septic shock with surgery, 17.1% was septic shock without surgery, and 14.3% was hypovolemic shock with surgery. Most of most of the patients had compensated metabolic acidosis (82.9%). Correlation analysis between $ETCO_2$ and lactate level showed significantly strong negative correlation (correlation coefficient [r]=-0.852, p=0.001). Linear regression analysis of correlation showed that an increase of 1 mmol/L lactate was associated with decrease of 3.42 mmol/L $ETCO_2$ (p<0.001).

Conclusion: $ETCO_2$ was related to serum lactate level in patients with hemodynamic disturbance. $ETCO_2$ measurement by capnograph was a non-invasive and fast method to detect hyperlactatemia.

Keywords: End-tidal CO_2 ($ETCO_2$); Hyperlacatatemia; Lactate; Hemodynamic disturbance

Introduction

Serum lactate measurement is one of the most commonly used laboratory parameter in patients with hemodynamic disturbance, sepsis, severe asthma, post-operation, brain injury, liver failure, acute lung injury, and poisoning [1]. Lactate acid is an end result of metabolism and a total of 1400 mmol/L lactate acid is produced daily. Conditions increasing lactate production or declining its elimination capacity will result in hyperlactatemia. Normal lactate value in healthy individual is 1 ± 0.5 mmol/L [2].

High lactate value is correlated with decreased blood pH and led to lactate acidosis. Lactate acidosis is defined as metabolic acidosis with lactate level >2 mmol/L [3,4]. Using lactate as diagnostic adjunct takes time, approximately 72 min in emergency triage setting. This could result in treatment delay for septic patients [4-6].

Patients with metabolic acidosis compensated with deep and rapid breathing, causing decreased CO_2 alveolar pressure and CO_2 arterial pressure. End-tidal CO_2 ($ETCO_2$), an invasive test to indirectly measure $PaCO_2$, can be used to determine acidosis severity in metabolic acidosis patients [7].

A previous prospective study stated that decresed level of $ETCO_2$ was correlated with high lactate level. It wass mentioned in the study that lactate level >4 mmol/L was correlated with $ETCO_2$ of <25 mmHg [8].

This study intended to search the correlation between $ETCO_2$ level and hyperlactatemia in patients with hemodynamic disturbance. We expect that this study could help such patients to get earlier treatment and also predict morbidity and mortality.

Methods

This was an observational, cross sectional study conducted on January to February 2017 in Sanglah General Hospital, Bali, Indonesia. Subjects were patients aged 13-90 years old with hemodynamic disturbance (mean arterial pressure [MAP]<65 mmHg) with or without support. Exclusion criteria was patients with pulmonary diseases. Subjects was recruited by consecutive sampling method.

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Eligible patients was recruited as subjects until the minimum sample was accomplished. Based on sample calculation, minimal sample should be 70 subjects. Informed consents were given by the first-degree family member of the patients. In all subjects, laboratory test of lactate level and blood good analysis were done, and capnography was used to monitor $ETCO_2$ simultaneously. Lactate level measurement was done with Accutrend®.

The minimum sample calculation was as follow:

$$n = \left(\frac{(Z\alpha + Z\beta)}{0,5 \quad \ln\{(1+r)/(1-r)\}}\right)^2 \quad + 3$$

$$n = \left(\frac{(1,64 + 1,64)}{0,5 \quad x\, 0,84}\right)^2 \quad + 3$$

$$n = \left(\frac{3,28}{0,42}\right)^2 \quad + 3$$

$$n = (7,8)^2 \quad + 3$$

$n = 69,5$

Statistical analysis

The data collected will be analyzed data include analysis of descriptive statistics. The descriptive statistical analysis describes the characteristics of the study subjects and all the variables studied, mean variables, deviations, minimum values, and maximal values. Categorical scale variables are displayed using relative frequency (number and percentage). The results of the descriptive statistical analysis are presented in a single distribution table.

Data analysis in this research is divided into several stages: descriptive statistical analysis, normality test, and correlation test. All stages of data analysis using of computer programs.

Descriptive statistical analysis

This analysis aims to describe the characteristics of subjects and research variables. Variables that are numerical scale data will be described using the mean and standard deviation or median values using the interquantil range. Categorical-scale variables will be described in relative frequency. The results of descriptive statistical analysis are presented using a single distribution table.

The data result from the study was analyzed for normality test by using Kolmogorov Smirnov from which based on the result analysis that shows the data is not normally distributed. Correlation test then analyzed by using Spearman Correlation.

Results

There were 70 subjects recruited with no drop out. Subjects' characteristic was shown in Table 1. Median age of the subjets was 55 years old, 54.2% was male and 45.8% was female. Subjects' case was 35.7% called for resuscitation, 32.9% was septic shock with surgery, 17.1% was septic shock without surgery, and 14.3% was hypovolemic shock with surgery. Most of the patients (55.7%) used 1 kind of support (inotropic or vasopressor), 35.7% used >1 support, and 8.6% without support. Based on hemodynamic parameter, median heart rate was 110.5 beats per minute, respiratory rate was 24 breaths per minute and mean arterial pressure (MAP) 70 mmHg. In blood gas analysis (BGA), most of the patients had compensated metabolic acidosis (82.9%).

Characteristic	**n=70**
Age (yr), median (IQR)	55 (28)
Sex	
Male, n (%)	38 (54,2)
Female, n (%)	32 (45,8)
BMIkg/m^2), median (IQR)	21,05 (6,0)
Case	
Calling Resucitation, n (%)	25 (35,7)
Septic Shock without surgery, n (%)	12 (17,1)
Septic Shock with surgery, n (%)	23 (32,9)
Hypovolumic shock with surgery, n (%)	10 (14,3)
Hemodynamic	
Heart rate (per minutes), median (IQR)	110,50 (15)
Respiratory rate (per minutes), median (IQR)	24,00 (6)
MAP (mmHg), median (IQR)	70,00 (7)
Hemodynamic support	
Without support, n (%)	6 (8,6)
Using 1 support, n (%)	39 (55,7)
Using >1 support, n (%)	25 (35,7)
Blood Gas Analysis	
Without metabolic acidosis, n (%)	11 (15,7)
metabolic acidosis without compensation,n (%)	1 (1,4)
metabolic acidosis with compensation, n (%)	58 (82,9)

Table 1: Study Subject Characteristic.

Variable	**Normality Result**	**Median (IQR)**	**Correlation Coefficient (r)**	**P value**
$EtCO_2$	0,130	24,00 (8)		
Lactate Level	0,117	3,50 (1,6)	-0,852	0,001

Table 2: Correlation Test Result Between $ETCO_2$ and Lactate Level.

Variable	**β**	**95% CI**	**P value**	**R^2**
Lactate	-3,420	-3,991-(-2,849)	<0,001	0,678
Constant	36,170	34,053-38,160	<0,001	

Table 3: Linier Regression Analysis Result of $ETCO_2$ and Lactate Correlation.

Normality test by Kolmogorov-Smirnov test showed that $ETCO_2$ and lactate level data was normally distributed (p=0.005 and p=0.019, resprectively). Correlation analysis between $ETCO_2$ and lactate level showed significantly strong negative correlation (correlation coefficient [r]=-0.852, p=0.001), Table 2.

This means that high level of lactate was associated with low level of $ETCO_2$. Linear regression analysis of correlation showed that an increase of 1 mmol/L lactate was associated with decrease of 3.42 mmol/L $ETCO_2$ (p<0.001), Table 3.

Discussion

This study aimed to asses the correlation between $ETCO_2$ and lactate level in patient with hemodynamic disturbance. In patient with hemodynamic disturbance, there would be a darrangement of tissue perfusion that lead to anaerobic metabolism that increased lactate level. Long term tissue perfusion derangement would eventually lead to imbalance of production and elimination of lactate. Hyperlactatemia reduced blood pH, therefore lead to lactic acidosis. Lactic acidosis is metabolic acidosis with lactate level ≥ 5 mmol/L and arterial pH<0.35. Kussmaul breathing as compensation would commence academia with signs of perfusion disturbance (eg hipotensi, oligouria, sensoric disturbance, and hypothermia). These signs could be used as predictor of acidemia severity. Based on this correlation, $ETCO_2$ could be used to determine academia severity in patient with metabolic acidosis. It was expected that $ETCO_2$ measurement by capnograph could be an indirect sign of increased lactate level in patients with hemodynamic disturbance.

Our finding of significantly negative correlation between $ETCO_2$ and lactate level was in accordance with previous studies. This means that low $ETCO_2$ was correlated with high lactate level. We found that an increase of 1 mmol/L lactate was associated with decrease of 3.42 mmol/L $ETCO_2$ (Figure 1).

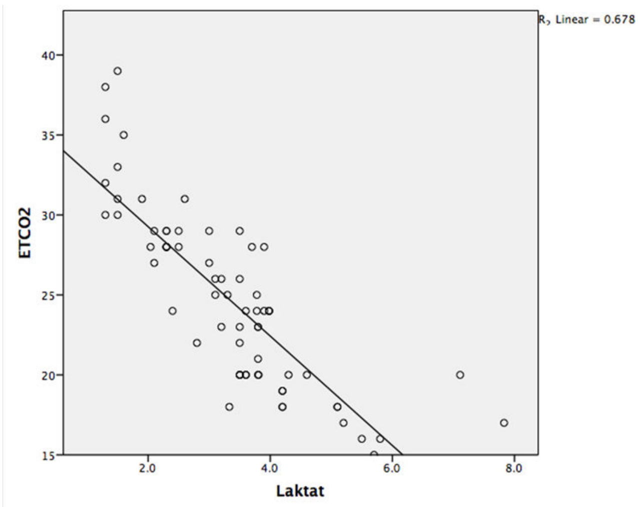

Figure 1: Scatterplot correlation between $ETCO_2$ and lactate level.

A previous prospective study by Christopher in 2014 showed that decresed level of $ETCO_2$ was correlated with high lactate level. It wass mentioned in the study that lactate level >4 mmol/L was correlated with $ETCO_2$ of <25 mmHg [8]. Another study using Pearson correlation calculation demonstrated that increased lactate level was correlated with decreased $ETCO_2$ (95% of confidence interval) [9].

It is expected that the use of $ETCO_2$ monitoring as non-ivasive and fast method to detect hyperlactatemia. A study by Goyal M in 2010 stated that serum lactate measurement could take time up to 72 minutes. This required time could delay initial treatment for septic patients. Althoug there were other tools to detect lactalte level in faster time, they had not been widely used [5].

This study was a cross-sectional study and could barely describe the progression of diseases precisely.

Conclusion

$ETCO_2$ was related to serum lactate level in patients with hemodynamic disturbance; a decrease of 3.42 mmol/L $ETCO_2$ was associated with the increase of 1 mmol/L lactate. $ETCO_2$ measurement by capnograph was a non-invasive and fast method to detect hyperlactatemia.

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