ORIGINAL ARTICLE

PLASMA LACTATE AS PROGNOSTIC MARKER OF SEPTIC SHOCK WITH ACUTE RESPIRATORY DISTRESS SYNDROME

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ABSTRACT

The present study was conducted to study the significance of lactate as a prognostic marker in patients of septic shock with acute respiratory distress syndrome. This study was conducted on 50 critically ill patients of septic shock with acute respiratory distress syndrome between the age group of 20-60 years and 50 controls. Plasma lactate and serum electrolytes were determined among controls and patients. Arterial blood gas analysis for pO_2 , pCO_2 and pH was carried out among patients. Arterial base excess and anion gap were calculated and lactate was correlated with base excess, anion gap and pCO_2 at 5% level of significance. Higher lactate, negative arterial base excess, high anion gap, low pO_2 and high pCO_2 were observed among patients. Lactate was positively correlated pCO_2 and anion gap and negatively with pO_2 and base excess among patients. Hyperlactatemia increasing with progression of septic shock with acute respiratory distress syndrome may suggest that lactate may be used as noninvasive prognostic marker or guide to resuscitation.

KEY WORDS

Lactate, Acute respiratory distress syndrome, Base excess, Anion gap, Hyperlactatemia, pCO_2 .

INTRODUCTION

Acute respiratory distress syndrome (ARDS) is a clinical and pathophysiologic entity commonly caused by sepsis, characterized by the development of new bilateral pulmonary infiltrates and severe hypoxemia without congestive heart failure. The main characteristics of the syndrome are diffuse inflammation and increased microvascular permeability that cause diffused interstitial and alveolar oedema and persistent refractory hypoxemia (1). Serum lactate levels may be used as a surrogate marker of tissue hypoxia in critically ill patients. Few studies indicate increased lactate levels in septic ARDS while some studies indicate that there was no significant relation between lactate levels and severity of lung disease

(2). The aim of this study was to determine lactate as prognostic tool in patients of septic shock with ARDS.

MATERIALS AND METHODS

This study was conducted at J.S.S. Medical College and Hospital, Mysore. The patient group included critically ill patients with sepsis (temperature higher than $39^{\circ}C$, white blood cell count of $12.0 \times 10^9/l$ (12,000/dl) or more, 20% or more band forms, or a known or strongly suspected source of infection, along with anion gap of more than 20 mmol/l or base excess lesser than -5 mmol/l) between the age group of 20-60 years [38 males and 12 females], who developed ARDS [tachycardia (>90 bpm), tachypnea (>20 breaths per min), hypoxemia with $PaO_2 < 72$ mm Hg, oxygen saturation $< 80\%$, hypotension with a systolic blood pressure of 90 mm Hg or less for more than 2 hours, diffuse bilateral pulmonary infiltrates involving more than 50% of at least 3 lung quadrants on chest X-ray] in the I.C.U within 24 hrs of admission. Patients with diabetes mellitus, liver diseases, renal diseases, cardiac diseases and who were on medications causing hyperlactatemia at the time of admission were excluded from the study. The control group consisted of 50 age and sex

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matched, normal healthy volunteers (38 males and 12 females) without any systemic illnesses or any chronic diseases and who were not on any medications causing hyperlactatemia. This was a prospective, matched, parallel cohort study. The study was conducted after informed consent was obtained from them and the study has been approved by the ethical committee of the institution.

4 ml of venous blood drawn aseptically was immediately placed in oxalate fluoride tubes, put on ice, and centrifuged for 10 min at 3,000 rpm. The plasma was then stored at -18°C until analysis. The lactate concentration was determined five times on each plasma sample and averaged. Lactate was determined by lactate oxidase method (3) using RX Daytona Randox Autoanalyzer. Lactate is oxidized by the enzyme lactate oxidase to give pyruvate and hydrogen peroxide. In the presence of peroxidase, hydrogen oxidatively couples with 4 amino antipyrine and N-ethyl-N-2 hydroxy-3-sulphopropyl m-toluidine to produce purple coloured complex which is measured at 550 nm, the intensity of the colour formed is directly proportional to the concentration of lactate in the sample. Na^+ , K^+ and Cl^- were measured from the serum samples collected in a serum separator tube in the central laboratory with the use of a direct ion-selective electrode technique (4). Arterial blood gas analysis using AVL Compact 3 analyzer for pO_2 , pCO_2 and pH was carried out on the arterial blood samples from the patients collected in a sodium heparin syringe (5). From the measured pH and pCO_2 we calculated $[\text{HCO}_3^-]$ using the Henderson-Hasselbalch equation, and base excess (BE) with Siggaard-Andersen's formulas (6). Anion gap (AG) was calculated as $([\text{Na}^+] + [\text{K}^+] - ([\text{Cl}^-] + [\text{HCO}_3^-]))$ (7). Lactate was correlated with base excess, anion gap and PCO_2 at 5% level of significance.

Statistical Analysis: Statistical comparisons were carried out using student's 't' test and correlations were tested using pearson's correlation test. $P < 0.05$ was considered statistically significant. All the statistical operations were done through SPSS for Windows (Version 15 evaluation version, 2006), SPSS Inc. New York.

RESULTS

Patients developing ARDS had higher lactate (22.3 ± 4.1 mg/dl on 1st day and on 26.6 ± 8.0 mg/dl on 5th day) compared to controls (14.10 ± 3.7 mg/dl) [$p < 0.05$] (Table 1). Negative BE (-10.3 ± 2.8 mmol/l on 1st day and -14.2 ± 2.3 mmol/l on 5th day), high AG (23.7 ± 8.0 mEq/l on 1st day and 26.2 ± 6.4 mEq/l on 5th day), low pO_2 (62.7 ± 11.3 mm Hg on 1st day and 46.6 ± 11.4 mm Hg on 5th day) and high pCO_2 (43.7 ± 4.8

Table 1 : Lactate values (mg/dl) in plasma of controls and patients

Subjects	Mean $\pm$ SD	P value
Controls (n=50)	14.10 ± 3.66	$<0.01^*$
Patients (n=50)	22.3 ± 4.1 (day 1) 26.6 ± 8.08 (day 5)	

Table 2 : Measured parameters in patients of septic shock with ARDS

PARAMETERS	1 ST DAY	5 TH DAY	P value
Lactate (mg/dl)	22.3 ± 4.1	26.6 ± 8.08	$<0.05^*$
Anion gap (mEq/l)	23.7 ± 8.0	26.2 ± 6.4	$<0.05^*$
Base excess (mmol/l)	-10.3 ± 2.8	-14.2 ± 2.3	$<0.05^*$
pO_2 (mmHg)	62.7 ± 11.3	46.6 ± 11.4	$<0.05^*$
pCO_2 (mmHg)	43.7 ± 4.8	56.5 ± 12.1	$<0.05^*$
pH	7.10	6.95	$<0.05^*$

mm Hg on 1st day and 56.5 ± 12.1 on 5th day) were observed among the patients (Table 2). Positive correlations were observed between lactate and pCO_2 ($r = 0.11$, $p > 0.05$) and between lactate and AG ($r = 0.07$, $p > 0.05$) among the patients. Negative correlations were observed between lactate and pO_2 ($r = -0.21$, $p > 0.05$) and between lactate and BE ($r = -0.06$, $p > 0.05$) among the patients. None of these correlations were statistically significant (Table 3).

Table 3 : Correlation between measured parameters in patients of septic shock with ARDS

	r value	p value
Lactate and pCO_2	0.11	>0.05
Lactate and PO_2	-0.21	>0.05
Lactate and Anion gap	0.07	>0.05
Lactate and Base excess	-0.06	>0.05

DISCUSSION

ARDS is characterized by severe acute injury, directly or indirectly via the blood, to the endothelial and epithelial surfaces of the lung leading to noncardiogenic respiratory failure (1). Determination of pCO_2 , BE and plasma lactate concentration may be useful as metabolic markers of tissue hypoxia (8).

Some studies demonstrated hyperlactatemia (lung is the main lactate-producing organ in septic ARDS patients) in patients with ARDS which is proportional to the severity of the lung injury and few studies indicate that there is no significant relation between lactate levels and severity of lung disease

(9, 10). Hyperlactatemia may be caused by an inadequate tissue perfusion-induced oxygen debt on exposure to endotoxin, inhibition of pyruvate dehydrogenase activity and increased anaerobic glycolysis, which would lead to pyruvate and lactate accumulation in the cell, deranged oxidative phosphorylation with consequent spillage of excess lactate into the circulation causing increase in blood lactate level (11). In the present study, the patients demonstrated hyperlactatemia which is increasing with the progression of septic shock with ARDS.

AG has been used as indicator of metabolic acid-base disturbances. BE is thought to represent the presence of unmeasured anions and is usually taken as a surrogate marker of lactic acidosis (12). Several studies have demonstrated an association between BE and severity in ARDS patients but most of the studies have usually failed to identify the effects that causative anions like lactate have on their resulting BE, AG, pO_2 and pCO_2 in critically ill patients (13, 14). In our study, lactate correlating positively with anion gap and negatively with BE shows that lactate, like BE would be a marker of tissue hypoxia and illness severity in patients of septic shock with ARDS. Although BE measurement serves as prognostic marker as well as to guide resuscitation or therapy in patients of septic shock with ARDS (15), its measurement requires an arterial puncture or placement of an indwelling arterial catheter which has been associated with significant pain and complications such as infection, pseudoaneurysm, distal embolization (16).

Thus, the early serial measurement of lactate as a biomarker may serve as an independent non-invasive prognosticator of the disease outcome in septic shock with ARDS providing equivalent information to the arterial BE and may be used as an alternative predictive marker or guide to resuscitation. Out of 50 patients of septic shock with ARDS, on 5th day when severe hypoxia and hypercarbia were observed, pressure controlled-low tidal volume-mechanical ventilation with gradually increasing FiO_2 (fraction of inspired oxygen) was started. 38 patients showed improvement at 90% FiO_2 and by 8th day started recovering from ARDS. Remaining 12 patients developed severe ARDS with multiple organ failure.

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