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CORRELATION OF PROCALCITONIN VS SERUM LACTATE AT ADMISSION AND LACTATE CLEARANCE AS A PROGNOSTIC MARKER IN SEPSIS

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ABSTRACT

Background: Severe sepsis and septic shock, are the major cause of emergency room admission and are associated with high morbidity and mortality worldwide. Similarly mortality rate of sepsis in asia found to be 40%, so sepsis is still the leading cause of death. Delayed identification and inadequate resuscitation in severe sepsis and septic shock leads to the high mortality. Lactate clearance is a marker of tissue hypoxia and can be used as an indicator of mortality in sepsis, hyperlactemia and lactic acidosis is a biomarker for disease severity. **Methods:** It is a retrospective study conducted on 100 subjects age more than 18 years who were admitted with sepsis and septic shock in KIMS hospital, Bengaluru. Serum Procalcitonin, serum lactate at admission, at 24 hours and at 48 hours was measured. Lactate clearance was calculated as (latctate at admission – delayed lactate)/lactate at admission *100. Lactate clearance was defined as lactate decline of >40% or lactate normalization. APACHE 2 score was calculated as a control. **Results:** Out of the 100 patients 65 survived and 35 died**,** The blood lactate acid and procalcitonin levels at different time points were significantly lower among the patients in the survival control group than those in the death group, a substantial reduction in the APACHE II score was noted among those in the survival control group. Patients with lactate >5 mmol/L at admission and poor lactate clearance at 24 hours (i.e lactate decline <40%) had poor outcome. APACHE II score was positively correlated with the blood lactate acid level and the procalcitonin level. **Conclusion:** In the very busy emergency room where calculating APACHE 2 score or other scoring systems for sepsis is time consuming and expensive, serum lactate levels at admission and lactate clearance can be used as alternative marker to predict mortality in severe sepsis and septic shock. High lactate at admission and poor lactate clearance is an indicator of poor prognosis and correlates well with serum procalcitonin levels and APACHE 2 score.

KEYWORDS: Sepsis, Septic shock, Lactate, lactate clearance, procalcitonin.

1. INTRODUCTION

Sepsis is one of the oldest and most elusive syndromes in medicine. Hippocrates claimed that sepsis was the process by which flesh rots, swamps generate foul air. Galen later considered sepsis a laudable event, necessary for healing of wound. With the confirmation of germ theory by Semmelweis, Pasteur and others, sepsis was recast as a systemic infection, often described as “blood poisoning,” and assumed to be the result of the host's invasion by pathogenic organisms that then spread in the bloodstream.

Lactate is a crucial source of energy, especially while starving. So, when lactate is not produced, humans cannot survive. Lactate also contributes to acidic environment by converting to lactic acid. Next, lactate is converted to bicarbonate and becomes a main source of alkalemia under normal conditions. Lactate of 1400–1500 mmol/L/day is formed from the reduction of pyruvate which is generated largely by anaerobic glycolysis. In tissue hypoxia, lactate is overproduced by increased anaerobic glycolysis. Lactate clearance typically occurs in the liver (60%), followed by the kidney (30%) and to a lesser extent by other organs (heart and skeletal muscle). Lactate clearance cannot overcome production of lactate and may be worsened during critically ill conditions. Septic shock status with liver dysfunction and acute kidney injury increase lactate levels due to decreased lactate clearance. Lactate clearance at a distinct time point is a vital prognostic factor compared to initial serum lactate level in severe sepsis. Few patients recovering from septic shock display normalized serum lactate levels although vasopressors are still needed to maintain a MAP of ≥65 mmHg. In addition, decreasing or normalized lactate levels are vital signs of recovery from septic shock. Although there is no data related to this, we generally detect lactate levels before stopping vasopressor treatment or detect normalized inflammatory markers such as C-reactive protein. This clinical finding supports that serum lactate level is a more sensitive vital sign reflecting anaerobic metabolism and acidosis than Blood Pressure (BP).

In today's clinical practice, lactate levels are usually used to detect tissue hypoxia; however, increased lactate levels reflect more than just this aspect. The finding of hyperlactatemia in patients with normal tissue perfusion and oxygen delivery additionally suggests that an overstimulation of the Na+-K+-ATPase leads to an increased lactate production in septic patients similar to hypokalemia. It has been shown that activation of the skeletal muscle Na+-K+-ATPase pump is a relevant factor in lactate production, as it has been observed that lactate is released from muscular tissue in septic shock patients. Several studies have proven that lactate levels are a dependable parameter in diagnosis, therapy evaluation, and prognosis in circulatory shock.

2. METHODS

This was a hospital based retrospective, cross sectional study. Initial work up consisting of detailed general and systemic examination, an active search for the underlying infection, routine hematological, and biochemical profile were noted. To assess the severity of illness and organ dysfunction, APACHE II score was calculated. Lactate levels measured in arterial blood by blood gas analyzer were labeled as L1, L2, L3. Acute physiological and chronic health evaluation (APACHE) II score was calculated by using APACHE II scoring system calculator –MD Calc. Serum procalcitonin was measured. The associations outcome with APACHE II score, serum lactate value at admission, serum lactate clearance and serum procalcitonin levels were noted and comparision made to assess the prognosis. Lactate clearance was calculated as followed: (lactate initial – lactate delayed)/ lactateinitial] x 100%].

3. RESULTS

100 patients diagnosed with sepsis and septic shock were included in the study, out of the 100 patients 35 were male and 65 were female, 35 of the 100 patients died 17 male and 18 female. All patients initial lactate levels at admission, serum procalcitonin were noted. APACHE 2 score was calculated as control.(table 1).

Data collection

The data collected from the patients were as follows: basic data of patients, including age, sex, mean time to onset, source of infection, etiology, and underlying diseases; the blood lactate acid levels which were defined as the blood lactate acid values obtained from all the patients at 0 h, 24 h and 48 h after admission to the ICU, respectively; the procalcitonin levels which were defined as the procalcitonin values obtained from all the patients at 0 h after admission to the ICU. The APACHE II scores which were pooled and calculated.

Outcome measures

The correlations of the blood lactic acid, procalcitonin levels and the APACHE II score with prognosis, as well as the blood lactic acidand procalcitonin levels with the APACHE II score were analyzed among the patients in the two groups.

Statistical analysis

Measurement data were represented as mean ± standard deviation (x ±s); the comparisons between the groups were made by the t-test, and the comparisons within the same group in the blood lactic acid and procalcitonin levels at different time points were conducted with the use of the repeated measures analysis of variance. Data were represented as percentages, and the comparisons between the groups were made with the chi square test. Pearson correlation analysis was utilized for detection of the prognostic correlations and APACHE II score correlations. A P value of less than 0.05 was considered statistically significant.

Table 1: Basic data of patients.

VARIABLES	SURVIVAL GROUP	MORTALITY GROUP
CASE	65	35
AGE	56.3+/-4.1	60.3+/-4.2
GENDER(M/F)	28/37	17/18

Majority of the patients in study group and mortality group had pulmonary disorder(66%), followed by GI (11%), urinary tract infections(10%), skin and soft tissue(9%) and CNS(4%). In the mortality group majority (50%) patients had pulmonary manifestations. (table 2).

Table 2: Etiology of sepsis.

ETIOLOGY	SURVIVAL GROUP	MORTALITY GROUP
PULMONARY	44	22
ABDOMINAL	7	4
URINARY TRACT	6	4
SKIN AND SOFT TISSUE	6	3
CNS	2	2
TIME TO ONSET(DAYS)	5+/-2.0	6.6+/-1.4

Table 3: The correlation of serum lactate, procalcitonin and APACHE 2 scores.

VARIABLES	CORRELATION COEFFICIENT	P VALUE
SERUM LACTATE	0.72	0.010
PROCALCITONIN	0.80	0.014
APACHE 2	0.76	0.008

Blood lactate acid and procalcitonin levels The blood lactic acid and procalcitonin levels of patients at 0 h, 24 h and 48 h after admission to the ICU respectively were significantly lower among the patients in the survival control group than those in the death group (All P=0.000). The blood lactic acid levels and the procalcitonin levels of patients at 0 h, 24 h and 48 h respectively after admission to the ICU showed a dropping trend over time among the patients in the survival control group, where as insignificantly reduced blood lactic acid levels but rising procalcitonin levels were observed among those in the death group.

Table 4: Serum lactate at admission and clearance at 24 hours in survival and mortality group.

VARIABLES	SURVIVAL GROUP	MORTALITY GROUP
SERUM LACTATE	2.2+/-0.66	5.6+/-2.2
LACTATE CLEARANCE (24 HOURS)	46%+/-12.2%	8%+/-6.6%

The prognosis of the patients was negatively correlated with the blood lactate acid and pro calcitonin levels, and the APACHE II scores ($P< 0.05$) whereas the APACHE II score was positively correlated with the procalcitonin and blood lactate acid levels.

4. DISCUSSION

Septic shock is a clinical complication with high mortality caused by the worsening health conditions in patients with sepsis, primarily as the result of the interactions between bacterial infection and immune defense mechanisms. Currently, although growing advances have made in medical treatment, the mortality of septic shock remains high. Therefore, assessment of the severity of sepsis in the patients encourages early intervention in a timely manner, reducing the mortality of the patients.

The APACHE II score is one of the measures for assessing the severity of diseases in critically ill patients, and is extensively used in clinical practice. Monitoring the APACHE II score can not only assess the patient's conditions, but also predict the mortality of the patients. The results of the present study demonstrated that the mean APACHE II score in the survival control group was significantly lower than that in the death group ($P<0.05$).

Moreover, the APACHE II score was negatively correlated with the prognosis of patients, with lower APACHE II scores indicating better prognosis. This may be due to the fact that the APACHE II score is involved in a sea of clinically physiological and laboratory indicators, and the patients with septic shock frequently have a variety of underlying diseases, leading to hypoxia, acidosis, and electrolyte disturbances. All these are associated with the abnormality in the indicators, and concurrently suggest that more severe organ dysfunction indicates worse prognosis. The results were basically similar to those in the previous reports.

Procalcitonin is a calcitonin precursor substance that is synthesized and secreted by thyroid C cells. A study suggested that trauma, medullary thyroid carcinoma, burns, and early postoperative development are associated with elevated procalcitonin levels.

Multiple studies worldwide have shown that procalcitonin can effectively induce the effect of ant-infection in critically ill patients. Besides, procalcitonin can be used as an early indicator for the diagnosis and assessment of bacterial infectious diseases. The present study found that, as compared to the death group, the procalcitonin levels decreased significantly among the patients in the survival control group; over time, the procalcitonin showed a dropping trend; in addition, the procalcitonin level was negatively correlated with prognosis of the patients, but positively correlated with the APACHE II score. It suggests higher procalcitonin level indicating worse prognosis.

The blood lactate acid and procalcitonin levels predicting the mortality of patients with septic shock on the ROC curves showed the areas under the curves of greater than 0.5, with significant differences. In the present study, the area under the curve was calculated as including the blood lactate acid and procalcitonin levels of all patients, but no subgroup analysis was performed.

In conclusion, monitoring of the blood lactate acid at admission, lactate clearance are better indicators than serum procalcitonin in sepsis and septic shock.

5. CONCLUSION

In the very busy emergency room where calculating APACHE 2 score is time consuming and expensive, serum lactate could be used as alternative marker to predict mortality in severe sepsis and septic shock. And subsequent lactate clearance can be used for further prognostication.

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