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Original Article

Can lactate clearance used to as a determinant of survival in mechanical ventilation follow up of critically ill patients?

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Abstract

Aim: Serum lactate level is known to have prognostic value in critical patients. Tissue hypoxia is a cause of an increase in lactate levels. A decrease in excretion and metabolism of lactate can increase lactate levels. In this study, we have investigated whether clearance of serum lactate could be a predictor of mortality in critically ill intubated patients at the emergency room.

Materials and Methods: Study Groups. Data of 205 critically ill patients requiring intubation, admitted to the emergency department of Haydarpasa Numune Training and Research Hospital between January 2011 and December 2015 have been scanned retrospectively. The intubations were performed according to the latest rapid sequence intubation protocols.

Results: There were 100 (48.8%) male and 105 (51.2%) female patients. Median, minimum, and maximum age were 76,19, and 104, respectively. The number of patients who could not survive was 157 (76.6%). The median, maximum, and minimum age in the non-survivor group were 78,31, and 104, while they were 70,19, and 90 in the survivor group, respectively. The difference was statistically significant ($p<0.001$). Final diagnoses and mortality rates of the critically ill patients requiring intubation in the emergency department are shown in Table 1.

Conclusion: We have found out that lactate clearance has no statistically significant relationship with mortality ($p=0.5$). However, lactate levels were higher in the groups with mortality, and the difference was statistically significant for both referral time and 4th-hour blood samples ($p=0.024$ and 0.014, respectively).

Keywords: Lactate clearance; prognosis; intubated patient.

INTRODUCTION

Lactate is produced by the erythrocytes, hepatocytes, skeletal muscle myocytes, and skin at an amount of 0.8 mol/kg/hour as a result of glucose metabolism. Pyruvate, which is produced as an end product of the glucose metabolism, is converted by lactate dehydrogenase enzyme to lactate in the cytosol. In the situations of ischemia, exogenous glucose is not the only source of lactate, but also the myocardial glycogen (1). In cases of hypoxia, nicotinamide adenine-dinucleotide (NAD) production is altered, so the NADH/NAD ratio increases causing the accumulation of lactate. The ischemic zones of the myocardium can excrete serious amounts of lactate while normally perfused zones can continue lactate uptake and use (2). Lactate is cleared from the serum majorly by the liver and kidneys. Lactate is a strong ion when pH is within physiological limits (3). It is metabolized in the liver by gluconeogenesis. The hepatic metabolism rate of lactate usually is 100 mmol/hour, but in cases of acute renal insufficiency, it could fall to 0.6 mmol/hour (4). It is also turned to lactic acid in anaerobic conditions by lactate dehydrogenase enzyme. Lactic acid leaves a hydrogen ion to turn back to lactate form in aqueous solutions. These hydrogen ions either are used in the oxidative phosphorylation or cause acidosis when the oxidative metabolism is altered. Plasma lactate levels between 0.3-1.3 mmol/l show the healthy balance of production and metabolism of lactate. Among the reasons of hyperlactatemia are overproduction of

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lactate (due to tissue hypoxia, underlying disease, drugs, toxins or congenital metabolic disorders), increased glycolysis, metabolic disorders, decreased hepatic clearance, sepsis, chronic or critical diseases, decrease in hepatic metabolism, decrease in renal excretion, oral hypoglycemic medication and Hartmann's solution (5).

Increased lactate is known as a predictor of mortality (6).In addition to lactate level, base excess and gastric intramucosal pH can be used to determine mortality who critical ill patients. Lactate clearance is the rate of fall in lactate after resuscitation is started. Lactate clearance was calculated as followed: [(lactate initial- lactate delayed) / lactate initial] x 100%]. Lactate clearance might be altered even when serum lactate levels are within normal ranges.

In our study, we have investigated whether lactate clearance can be used to predict the outcome of critically ill patients in mechanical ventilation follow up in the emergency room.

MATERIAL and METHODS

Study Groups

Data of 205 critically ill patients requiring intubation, admitted to the emergency department of Haydarpasa Numune Training and Research Hospital between January 2011 and December 2015 have been scanned retrospectively. The intubations were performed according to the latest rapid sequence intubation protocols.

The patients who had died before all work-up was finished and been transferred to other hospitals or with a possible type B lactic acidosis were excluded from the study. The evaluated parameters were age, gender, date of admission, and lactate levels. The reasons for intubations, diagnosis, and mortality were recorded.

Blood samples

Blood gas samples were collected from all patients at admission and 4th hour. The evaluated parameters were lactate levels of referral time arterial blood gas analysis, 4th-hour blood gas analysis, and the lactate clearance at these hours. All assays were completed within 10 minutes in the emergency laboratory. Measurements of Systemic Markers The lactate levels are measured with a standard blood gas device (Rapidlab 1265; Siemens, North Rhine-Westphalia, Germany).

Statistical analysis

Categorical data were expressed as number and percentage, non-parametric numeric data were expressed as median, minimum, and maximum. In the evaluation of the normal distribution of numerical data, the Kolmogorov-Smirnov test was used. In the evaluation of the relationship between categorical data, Pearson Chi-Square and Fisher's Exact tests were used. Non-parametric numeric data were compared between groups with the Mann-Whitney U test. Statistical analysis was considered as significant if the p-value is lower than 0.05. Data has been analyzed by Statistical Package for Social Sciences (SPSS) version 23.0.

RESULTS

There were 100(48.8%) male and 105(51.2%) female patients. Median, minimum, and maximum age were 76,19, and 104, respectively. The number of patients who could not survive was 157(76.6%). The median, maximum, and minimum age in the non-survivor group were 78,31, and 104, while they were 70,19, and 90 in the survivor group, respectively. The difference was statistically significant (p<0.001). Final diagnoses and mortality rates of the critically ill patients requiring intubation in the emergency department are shown in Table 1.

Of the 205 patients included in the study, 123 had positive lactate clearance, and 79 had negative lactate clearance values. Of the patients with positive lactate clearance, 92(74.8%) could not survive, while the number was 63(79.75%) in the patients with negative lactate clearance. The difference was not significant between groups (p=0.416). The median, minimum and maximum first lactate level in the mortality group were 2.5 mmol/L, 0.5 mmol/L and 17 mmol/L, while the other group's levels were 1.95 mmol/L, 0,36 mmol/L and 32 mmol/L, respectively. The first lactate level was higher in the non-survivor group (p=0.024).

Fourth-hour lactate level median, minimum and maximum values were 2.3 mmol/L, 0.25 mmol/L and 22 mmol/L in the non-survivor group, while these levels were 1.4 mmol/L, 0.4 mmol/L and 17 mmol/L in the survivor group, respectively. The 4th-hour lactate level was higher in the non-survivor group (p=0.014).

Lactate clearance median, minimum and maximum values were 10.64 mmol/L, -300 mmol/L and 92.86 in the non-survivor group and 17.69 mmol/L, minimum-177.78 mmol/L and maximum 71.43 mmol/L in the survivor group, respectively. The difference was not significant between groups (p=0.5).

Table 1. Final diagnoses and mortality of the patients intubated in the emergency department

Diagnosis	Non-survivor	Survivor	p
Sepsis	60	11	0.051
CHF	43	12	0.744
Pneumonia	26	8	0.986
COPD	7	4	0.297
CRF	5	1	1.000
ICH	2	0	1.000
CVA	4	0	0.575
Pulmonary embolus	5	0	0.593
Drug abuse	0	5	0.001
Drug intoxication	0	3	0.012
Status epilepticus	2	1	0.553
Diabetic ketoacidosis	0	2	0.054

Abbreviations: CHF, Congestive Heart Failure; COPD, Chronic obstructive Pulmanary Disease; CRF, Chronic Renal Failure; ICH, Intracerebral Haemorrhage; CVA, Cardiovascular Attack

DISCUSSION

Our study aims to find the prognostic value of lactate clearance in intubated patients in the emergency room. We investigated the initial and the 4th-hour lactate levels to find the lactate clearance. Lactate clearance was compared in survivor and non-survivor groups. We found no statistically significant relationship between lactate clearance and mortality. However, we found higher initial and 4th-hour lactate levels in the non-survivor group.

Relations of age, fever, mean arterial pressure, pH, heart rate, respiratory rate, acute renal failure, electrolyte levels, urea creatinine ratio, neutrophil counts and many more values with mortality have been investigated in intensive care unit patients. After all these efforts, scoring systems like acute physiology and chronic health evaluation (APACHE) and sepsis-related organ failure assessment (SOFA) systems were created (7-8). Prognostic scoring systems commonly used in intensive care units; is used to estimate the severity of the disease and to estimate mortality. APACHE II and SOFA used in prognostic scoring systems are one of the primary criteria (9).

Lactate clearance is an essential marker of tissue hypoxia in sepsis patients without arterial hypotension. Many studies suggest that a single lactate value at an early stage of the disease is a predictor of mortality and morbidity (10-11). Besides, some studies suggest that consecutive lactate measurements have potential prognostic value (12-14). Lactic acidosis is mainly due to tissue hypoxia, but there are other metabolic reasons. It is also essential to determine whether the reason for lactic acidosis is hypoxia or any other metabolic condition in order to use the lactate clearance as a prognostic criterion (14).

In a prospective study conducted by Shapiro et al., 1278 patients over 18 years of age admitted to the emergency department with an infection-related disease were included. Venous blood lactate levels and mortality were compared. The mortality rate was 4.9% in patients with a lactate level of 0-2.5 mmol; 9% in patients with a lactate level of 2.5-4.0 mmol; and 28% in patients with a lactate level of > 4.0 mmol (15). Similarly, we found higher lactate levels in initial and 4th-hour evaluation in non-survivor group.

Callaway et al. 588 normotensive trauma patients who admitted to emergency department retrospectively evaluated the relationship between venous lactate levels and mortality. The cutoff value of lactate was accepted as 2.5 mmol, and every increase in lactate level was seen to increase mortality (16).

In a retrospective study of 2413 trauma patients conducted by Vandromme et al., capillary and venous lactate values were examined in normotensive patients. In that study, trauma patients with a systolic blood pressure of between 90-110 mm Hg were included (17). Mortality of lactate level 2.5 mmol and above systolic blood pressure was found to be more effective than pressure.

In a prospective study by Lee et al., 126 consecutive arterial blood lactate levels were taken into consideration. The lactate level had a cutoff value of 2.0 mmol. As a result of blood lactate sampling after 4 hours, no significant difference was found between mortality rates of patients with high lactate and normal lactate levels if the pH values were in normal ranges (18). All these studies show that there is no collective decision about the lactate cutoff value. In this study, cutoff value for mortality is not calculated. However, we found significant results for both initial and 4th-hour lactate levels in terms of predicting mortality.

In a study which adult patients with shock were evaluated, lactate clearance of <10% was found to be related to mortality and showed more promise in predicting mortality (19). As a result of the study, lactate clearance was associated with mortality.

In another study by Marie-Alix Regnier et al., 586 trauma patients were assessed. The lactate levels were measured at 0, 2, and 4 hours, and lactate clearances were calculated. However, the lactate clearance calculated from 0-2 hours, and the lactate clearance calculated from 0-4 hours were well correlated with each other (P <0.001) (20). In our study, similar data is taken into consideration next 4 hours values.

The medical conditions that are not related to tissue hypoxia, like malabsorption, are not the subject of our study. The value of lactate clearance in these diseases still needs to be investigated. The other possible reasons of lactic acidosis may limit the use of lactate clearance as a routine marker.

The results of our study show that lactate clearance is not a significant predictor of survival in critically ill patients, who require intubation. However, initial and 4th-hour lactate levels had both significantly higher values in the survivor group and can be used as a predictor of mortality. However, the study does not include a single specific disease; further studies are required for a better understanding of the value of this parameter.

This study has certain limitations. Firstly, the relatively low number of evaluated cases may be considered as a limitation. It is necessary to undertake a further study with a higher number of cases to obtain more reliable results. As the study is retrospective, the evaluation of blood gas analysis closest to the 4th hour is another limitation for this study.

CONCLUSION

Lactate clearance had no significant value in the prediction of mortality. Initial and 4th-hour lactate levels seem to be an important determinant of survival in critically ill patients, who require intubation.

Availability of supporting data

The data sets generated and/or analyzed during the current study are available at the University of Health

Sciences Haydarpaşa Numune Training and Research Center, Department of Emergency Medicine, Istanbul, Turkey.

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REFERENCES

1. Ferguson BS, Rogatzki MJ, Goodwin ML, et al. Lactate metabolism: historical context, prior misinterpretations, and current understanding. Eur J Applied Physiol 2018;118:691-728.
2. Cason BA, Wisneski JA, Neese RA, et al. Effects of high oxygen tension on function blood flow distribution, and metabolism in ischemic myocardium. Circulation 1992;85:828-38.
3. Siggaard-Andersen O, Fogh-Andersen N. Base excess or buffer base (strong ion difference) as measure of a non-respiratory aside-base disturbance. Acta Anaesthesiol Scand 1995;39:123-8.
4. Kellum JA. Recent advances in acid-base physiology applied to critical care. In Yearbook of Intensive Care and Emergency Medicine. Heidelberg; Berlin; 1998. p.577-87.
5. Juneja D, Singh O, Dang R. Admission hyperlactatemia: causes, incidence, and impact on outcome of patients admitted in a general medical intensive care unit. J Crit Care 2011;26:316–20.
6. Sargın G, Yavasoglu I, Kadıkoylu G, et al. Lactic acidosis: a short review of cases. J Med Surg Intensive Care Med 2011;63-7.
7. Ferreira FL, Bota DP, Bross A, et al. Serial evaluation of the SOFA score to predict outcome in critically ill patients. Jama 2001;286:1754-8.
8. Howell MD, Donnino M, Clardy P, et al. Occult hypoperfusion and mortality in patients with suspected infection. Intensive Care Med 2007;33:1892-9.
9. Knaus WA, Draper EA, Wagner DP, et al. APACHE II: a severity of disease classification system. Crit Care Med 1985;13:818-29.
10. Trzeciak S, Dellinger RP, Chansky ME, et al. Serum lactate as a predictor of mortality in patients with infection. Intensive Care Med 2007;33:970-7.
11. Bakker J, Coffernils M, Leon M, et al. Blood lactate levels are superior to oxygen-derived variables in predicting outcome in human septic shock. Chest 1991;99:956-62.
12. Bakker J, Gris P, Coffernils M, et al. Serial blood lactate levels can predict the development of multiple organ failure following septic shock. Am J Surg 1996;171:221-6.
13. Nguyen HB, Rivers EP, Knoblich BP, et al. Early lactate clearance is associated with improved outcome in severe sepsis and septic shock. Crit Care Med 2004;32:1637-42.
14. Andersen LW, Mackenhauer J, Roberts JC, et al. Etiology and therapeutic approach to elevated lactate levels. In: Mayo Clinic Proceedings. Elsevier, 2013.p.1127-40.
15. 15. Shapiro NI, Howell MD, Talmor D, et al. Serum lactate as a predictor of mortality in emergency department patients with infection. Ann Emerg Med 2005;45:524-8.
16. Callaway DW, Shapiro NI, Donnino MW, et al. Serum lactate and base deficit as predictors of mortality in normotensive elderly blunt trauma patients. J Trauma 2009;66:1040-4.
17. Vandromme MJ, Griffin RL, Weinberg JA, et al. Lactate is a beter predict orthan systolic blood pressure for determining blood requirement and mortality: could pre hospital measures improve trauma triage? J Am Coll Surg 2010;210:861-7.
18. Lee SW, Hong YS, Park DW, et al. Lactic acidosis not hyperlactatemia as a predictor of inhospital mortality in septic emergency patients. Emerg Med J 2008;25:659-65.
19. Arnold RC, Shapiro NI, Jones AE, et al. Multi-center study of early lactate clearance as a determinant of survival in patients with presumed sepsis. Shock 2009;32:35-9.
20. Régnier MA, Raux M, Le Manach Y, et al. Prognostic significance of blood lactate and lactate clearance in trauma patient. Anesthesiology 2012;117:1276-88.