The effects of blood lactate level on mortality in patients developing sepsis in intensive care unit

Yoğun bakım ünitesinde sepsis gelişen hastalarda kan laktat düzeyinin mortalite üzerine etkisi

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Abstract

Aim: Sepsis is a serious condition with high mortality and morbidity in intensive care units (ICUs). Mortality decreases with early and appropriate antimicrobial treatment. We aimed to investigate the relationship between lactate levels and mortality in the ICU of our hospital.

Methods: Patient records > 18, hospitalized in the ICU of Meram State Hospital between January 2022 and January 2024, were retrospectively examined. All patients microbiologically confirmed to have positive blood culture results and diagnosed sepsis were included in the study. Age on admission, gender, diagnoses at hospitalization, Apache II, length of stay, and mortality in ICU were obtained from patients' medical records. In the presence of suspicion of sepsis in a patient hospitalized in intensive care and in the first 72 hours after antibiotic treatment, the lactate level was recorded. Lactate clearance was defined as the percent decrease in lactate from ICU department presentation to hour 72. Mortality rates within the first 28 days were recorded. Lactate levels were compared in patients with and without mortality. The value of lactate in predicting mortality was evaluated statistically.

Results: Of 56 patients included in the study, whose diagnoses of sepsis were microbiologically proven, 38 (67.9%) died. The area under a receiver operating characteristic (ROC) curve Area under curve (AUC) of lactate in predicting mortality was 0.738 [95% confidence interval (CI): 0.590 –0.886, (p=0.004)]. Threshold lactate value for mortality was 1.7 mmol/L (sensitivity: 73.7%, specificity: 61.1%). While lactate levels, lactate clearance, length of hospital stay, Acute Physiologic and Chronic Health Evaluation (APACHE II) score were statistically significant between sepsis patients with and without mortality (p=0,004, p = 0.03 p= 0,00 p=0.003). Baseline lactate was in survivors 2.05±1.37 and in nonsurvivors 1.33±0.98 mmol/L. Survivors compared with nonsurvivors had a lactate clearance of 48.2 ± 24.4 vs. 22.06 ± %, respectively (p = 0.007). It showed lactate clearance to have a significant relationship with mortality (p = 0.03).

Conclusion: Here, we found that lactate level and, lactate clearance may be a significant place in the early treatment and follow-up of sepsis patients in ICUs.

Keywords: Intensive care unit; lactate; mortality; sepsis

Öz

Amaç: Sepsis yoğun bakım ünitesinde (YBÜ), mortalitesi ve morbiditesi yüksek önemli bir durumdur. Mortalite, erken ve uygun antimikrobiyal tedavi ile azalmaktadır. Çalışmamızda hastanemiz 3. basamak yoğun bakım ünitelerinde yatan hastaların kan laktat düzeyleri ile mortalite oranları arasındaki ilişkiyi incelemeyi amaçladık.

Yöntemler: Meram Devlet Hastanesi YBÜ'de yatan Ocak 2022'den Ocak 2024'e kadar olan 2 yıllık süreçte 18 yaş üstü hastaların kayıtları retrospektif olarak incelendi. Sepsis tanısı alan mikrobiyolojik olarak (pozitif kan kültürü sonuçları) doğrulanan tüm hastalar dahil edildi. Hastaların yatış anında yaşları, cinsiyetleri, yatış tanıları, Acute Physiologic and Chronic Health Evaluation (APACHE II), yatış süresi, YBÜ mortalite verileri tıbbi dosya kayıtlarından elde edildi. Yoğun bakıma yatırılan bir hastada sepsis şüphesi varlığında ve antibiyotik tedavisi sonrası ilk 72. saatte laktat düzeyi kaydedildi. Laktat klirensi, yoğun bakıma başvurudan 72. saatte olan laktatta azalma olarak tanımlandı. Hastalarda ilk 28 gün içindeki mortalite kaydedildi. Mortalite gelişen ve gelişmeyen hasta grubunda laktat düzeyleri karşılaştırıldı. Laktatın mortaliteyi öngörmedeki değeri istatistiksel olarak değerlendirildi.

Bulgular: Çalışmaya 56 hasta alınmıştır. Araştırma grubuna dâhil edilen sepsis tanısı mikrobiyolojik olarak kanıtlanan hastaların (%67,9)'i ölüm ile sonuçlanmıştır. Laktatın mortaliteyi öngörmedeki Receiver Operating Characteristic (ROC) eğrisi altında kalan alan (AUC) 0,738 idi [% 95 güven aralığı (GA): 0,590 –0,886] p=0,004). Mortalite için eşik laktat değeri 1,7 mmol/L (duyarlılık: % 73,7, özgüllük: % 61,1 olarak bulundu. Mortalite olan ve olmayanlar sepsis hastaları arasında laktat düzeyi, laktat klirensi, hastanede kalış süresi ve APACHE II istatistiksel olarak anlamlı bulunurken (p=0,004, p = 0.03 p= 0,00 p=0.003), Başlangıç laktat düzeyi hayatta kalanlarda 2,05±1,37, ölen hastalarda 1,33±0,98 mmol/L idi. Hayatta kalanların, hayatta kalmayanlarla karşılaştırıldığında laktat klerensi sırasıyla %48,2 ± 24,4 ve %22,06 ± idi (p = 0,007). Laktat klerensinin mortalite ile anlamlı bir ilişkiye sahip olduğunu gösterdi (p = 0.03).

Sonuç: Çalışmamızda laktat düzeyinin ve laktat klirensinin yoğun bakım ünitelerinde sepsisin erken tedavi ve takibinde önemli bir yeri olabileceği düşünülmüştür.

Anahtar Sözcükler: Laktat; mortalite; sepsis; yoğun bakım ünitesi

Received/*Geliş* : 18.07.2024
Accepted/*Kabul*: 18.10.2024

DOI: 10.21673/anadoluklin.1518446

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INTRODUCTION

Sepsis is a serious condition with high mortality and morbidity among those staying in the intensive care unit (ICU). Even so, mortality decreases with early and appropriate antimicrobial treatment (1,2). Considering the high mortality of sepsis, it is considered that to make a timely diagnosis, the pre-evaluation of simple and easily accessible biomarkers will support the decision-making process about the clinical status of the patient in the future. Serum lactate levels have been suggested to be a marker of hypoperfusion and tissue hypoxia in sepsis. Even before patients develop significant hypotension, tissue perfusion deteriorates due to myocardial depression, injury-associated hypovolemia, an increase in metabolic activity, and impaired vasoregulatory mechanisms. For this reason, oxygen demand increases, and the production of anaerobic lactate occurs (3). Regardless of the mechanism of lactate production, the mortality rate has been witnessed to increase in patients presenting with the diagnosis of sepsis and with high serum lactate levels (> 4 mmol/L) (4). Measuring the levels of lactate provides beneficial information about the progression of the disease and the effectiveness of the treatment. For those suspected to have sepsis, measuring the levels of lactate provides useful information about the severity of the disease and allows the course of the disease to be monitored (5). Additionally, after a 6-hour-treatment in septic patients, mortality rates have been reported to decrease in those with high lactate clearance (6). In sepsis, elevated lactate levels are associated with increased mortality, independent of shock and organ failure (7). This study aims to investigate the relationship between blood lactate levels and mortality rates of patients hospitalized in the tertiary ICU of our hospital.

MATERIAL AND METHODS

This study was approved by Clinical Research Ethics Committee of the Faculty of Medicine at Karatay University (date: 28.06.2024, decision no: 2024/033). The study was conducted in accordance with the principles stated in the Declaration of Helsinki. Patients' medical records over 18 years of age and hospitalized in the ICU of Konya Meram State Hospital between January 2022 and January 2024 were retrospectively investigated. Diagnosed with sepsis, all patients confirmed microbiologically to have positive blood culture results were included in the study. Blood samples were examined through the BACTEC 9240 fully automatic blood culture device (Becton Dickinson, Diagnostic Device System, Spark, USA). In the presence of suspicion of sepsis in a patient hospitalized in intensive care and in the first 72 hours after antibiotic treatment, the lactate level was recorded. Lactate clearance was defined as the percent decrease in lactate from ICU department presentation to hour 72. Patients' age rates on admission, gender, diagnoses on admission to the hospital, Acute Physiologic and Chronic Health Evaluation (APACHE II) scores, length of stay, and mortality rates in ICU data were obtained from medical file records in the automation system of the hospital. Mortality rates of the patients within the first 28 days were also recorded, and lactate levels were compared in the patient groups with and without mortality. Then, the value of lactate in predicting mortality was evaluated statistically.

Statistical analyses

Statistical analyses of the study findings were evaluated with the Statistical Package for the Social Sciences software for Windows, version 24.0 (SPSS Inc., Chicago, IL, USA). While the nominal data were described as ratios and percentages, mean and standard deviation (±, SD) were used to describe continuous numerical data. Additionally, median and interquartile ranges were used to describe non-normally distributed continuous numerical data. The presence of normal distribution was evaluated using statistical tests and graphical methods. While the Pearson chi-square test was used to compare the categorical data, the Mann-Witney U test was utilized to compare non-normally distributed numerical data in pairs, and the student's *t*-test was used in independent groups to compare normally distributed continuous numerical variables. The receiver-operating characteristic (ROC) analysis was performed to evaluate the ability of laboratory tests to predict whether the sepsis-causing bacterium is a Gram-negative bacterium and to predict mortality. A *p*-value of <0.05 was accepted to be statistically significant.

RESULTS

Fifty-six patients were included in the study, and 29 (51.8%) and 27 (48.2%) of the cases were male and female. The average age was 75.45±11.77. Of 56 patients in the study with the diagnosis of sepsis proven microbiologically, 38 (67.9%) died within 28 days. The ROC analysis was performed to determine the predictive diagnostic value of lactate levels in terms of mortality in patients with sepsis. The area under the ROC curve (AUC) of lactate in predicting mortality was found as 0.738 [95% confidence interval (CI): 0.590 –0.886 (p=0.004)] (Figure.1). The threshold value of lactate for mortality was determined to be 1.7 mmol/L (sensitivity: 73.7%, specificity: 61.1%). Baseline lactate was in survivors 2.05±1.37 and in nonsurvivors 1.33±0.98 mmol/L. Survivors compared with nonsurvivors had a lactate clearance of 48.2 ± 24.4 vs. 22.06 ± %, respectively (p = 0.007). It showed lactate clearance was significantly related to mortality (p = 0.03). Lactate levels, lactate clearance and length of hospital stay were found to be statistically significant between sepsis patients with and without mortality (p=0.004, p = 0.007, p= p=0.00) (Table 1). When the mortality rates of those with lactate levels < 2 mmol and those with lactate levels of ≥ 2 mmol were compared, mortality was found to be significantly higher in those with lactate levels of ≥ 2 mmol. The effects of lactate levels on mortality are given in Table 2.

DISCUSSION AND CONCLUSION

Sepsis is among the leading causes of death in patients staying in ICUs (8). High lactate levels in sepsis have been associated with poor prognosis (9). In our study, while the mortality rates were found as 66% in patients with lactate levels < 4 mmol/L and 83.3% in those with ≥ 4 mmol/L, the mortality rates in ICU were detected to increase 1.5 times. Additionally, the mortality rates in ICU were reported to be 54.8% in patients with lactate levels of < 2 mmol/L and 84% in those with lactate levels between 2-3.99 mmol/L. Mortality rates were seen to be higher in patients with high Apache II scores; Apache II score was 27.87±6.8 in nonsurvivors and 17.21±3.9 in survivors. It showed a significant relationship with mortality

In a study carried out by Shapiro et al. where the relationship between lactate levels and mortality rates was investigated in 1278 patients, the researchers found mortality rates as 4.9% in those with lactate levels of 0-2.4 mmol/L, 9% in those with lactate levels of 2.5-3.9 mmol/L levels, and 28.4% in those with lactate levels of > 4 mmol/L. In the same study, it was also revealed that the evaluation of lactate clearance with serial measurements would help decrease the rates of morbidity and mortality (6). Mortality was found to be high in patients with a lactate level of 4 mmol/L at baseline. These results support our study findings that as lactate levels increase, the mortality rates in ICU also elevate (6). In another

Table 1. Demographic characteristics of patients under mortality rates

	Exitus	**Survival**	***p***
	Median (Q1-Q3)	**Median (Q1-Q3)**	
Age	78±14	76±21	0.97
Gender (F/M)	18/20	9/9	0.85
Lactate (0. day)	2.05±1.37	1.33±0.98	***0.004***
Lactate (3. day)	1.42±1.06	0.82±0.8	***0.007***
Length of hospital stay	22±28 (2-278)	83±87 (28-420)	***0.003***
Apache II score	27.87±6,8	17.21±3,9	***0.003***

Q1-Q3: Quartile 1-3, F/M: Female/Male, Acute Physiologic and Chronic Health Evaluation (APACHE II)

Table 2. Relationship between lactate levels and mortality

Lactate levels	**Mortality rates, % n**
<2 mmol/L	54 (17)
2-3.99 mmol/L	84 (16)
≥ 4 mmol/L	83.3 (5)

n: Number, %: Percentage

study conducted in our country, the mortality rate was found to be 75.6% in patients with a lactate level of < 4 mmol/L and 24.4% in those with a lactate level of > 4 mmol/L (10). In the study evaluating lactate levels among the patients admitted to the emergency department, the researchers demonstrated that a 20% or more decrease in lactate level of > 3 mmmol/L in ICU within the first 8 hours led to a definite decrease of 9.6% in mortality (11). Early Goal-Directed Therapy (EGDT) is a hemodynamic algorithmic approach used for patients with suspected severe sepsis or septic shock, who are admitted to the emergency department in patients. According to EGDT, the early treatment plan and the target of the treatment should be to normalize lactate levels in patients with sepsis-induced tissue hypoperfusion (continuing hypotension despite initial fluid therapy or blood lactate level ≥ 4 mmol/L) and in those with increased tissue blood lactate levels (12). In our study; baseline lactate was in survivors 2.05±1.37 and in nonsurvivors 1.33±0.98 mmol/L. Survivors compared with nonsurvivors had a lactate clearance of 48.2 ± 24.4 vs. 22.06 ± %, respectively. It showed lactate clearance to have a significant relationship with mortality (p = 0.03). Similar to our study, in a study conducted APACHE II score was 20.2 ± 6.8 and lactate 6.9 ± 4.6 mmol/L. Survivors compared with nonsurvivors had a lactate clearance of 38.1 ± 34.6 vs. 12.0 ± 51.6%, respectively (13).

In the 2018 update of the sepsis survival campaign care packages, a significant decrease was demonstrated in mortality through lactate-guided resuscitation. If the lactate level measured first is > 2 mmol/L, the level should be remeasured within 2-4 hours, and the resuscitation should be directed, considering the later measurement. In other words, the normalization of lactate, which is an indicator of tissue hypoperfusion, should be targeted (8). As emphasized in the guidelines of sepsis treatment, lactate level is emphasized as an important indicator of mortality in sepsis. In our study, it was found that lactate level and lactate clearance could be an important biomarker in the early treatment and follow-up of sepsis in ICUs.

Limitations

It was conducted retrospectively and our study included a limited number of sepsis cases.

Conflict-of-interest and financial disclosure

The authors declare that they have no conflict of interest to disclose. The authors also declare that they did not receive any financial support for the study.

REFERENCES

1. Armstrong BA, Betzold RD, May AK. Sepsis and septic shock strategies. Surg Clin North Am. 2017;97(6):1339-79.
2. Seymour CW, Liu VX, Iwashyna TJ, et al. Assessment of clinical criteria for sepsis: For the third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA. 2016;315(8):762-74.
3. Bota DP, Ferreira FL, Melot C, et al. Body temperature alterations in the critically ill. Intensive Care Med. 2004;30:811-16.
4. Yang SL, Chung CS, Ayala A, et al. Differential alterations in cardiovascular responses during the progression of polymicrobial sepsis in the mouse. Shock. 2002; 17(1):55-60.
5. Freund Y, Delerme S, Goulet H, et al. Serum lactate and procalcitonin measurements in emergency room for the diagnosis and risk-stratification of patients with suspected infection. Biomarkers. 2012;17(7):590-96.
6. 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;45:524-528.
7. Chebl RB, Tamim H, Dagher GA, Sadat M, Al Enezi F, Arabi YM. Serum lactate as an independent predictor of in-hospital mortality in intensive care patients. J Intensive Care Med. 2020;35(11):1257-64.
8. Levy MM, Evans LE, Rhodes A. The Surviving Sepsis Campaign Bundle: 2018 update. Intensive Care Med. 2018;44(6):925-28.
9. Shankar-Hari M, Phillips GS, Levy ML, et al. Developing a new definition and assessing new clinical criteria for ceptic shock: For the third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA. 2016;315(8):775–87.
10. Yakışık Çakır E, Özkoçak Turan I. Yoğun bakım ünitesinde laktat ve mortalite. Ahi Evran Med J. 2022;6(2):115-20.
11. Jansen TC, van Bommel J, Schoonderbeek FJ, et.al. LACTATE study group. Early lactate-guided therapy in intensive care unit patients: a multicenter, open-label, randomized controlled trial. Am J Respir Crit Care Med. 2010;182(6):752-61.
12. Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med. 2001;345(19):1368-1377.
13. Nguyen HB, Rivers EP, Knoblich BP, et.al. Early lactate clearance is associated with improved outcome in severe sepsis and septic shock*. Critical Care Medicine 2004;32(8):1637-1642.