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Investigation of the Relationship between Blood Gas Parameters and Thirty-day Mortality in Elderly Patients Diagnosed with Sepsis

Sepsis Ön Tanılı Yaşlı Hastalarda Kan Gazı Parametreleri ve Otuz Günlük Mortalite Arasındaki Ilişkinin Araştırılması

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ABSTRACT

Introduction: Although sepsis is one of the most important causes of death in hospitalized patients, information on early predictive factors for predicting mortality and morbidity is limited. The aim of this study was to determine the relationship between defined arterial blood gas parameters and 30-day mortality in adult patients aged 65 years and older who were admitted to the emergency department and diagnosed with sepsis.

Methods: Arterial blood gas parameters of patients older than 65 years who were diagnosed with sepsis in the emergency department during the 5-month period between March and August 2017 were analyzed retrospectively. The relationship between pH, lactate, anion gap, bicarbonate and base-excess and 30-day mortality was analyzed.

Results: A total of 103 elderly patients with sepsis were included in the study. Fifty-eight patients (56.3%) were female and the mean age was 77.74±8.45 years (range: 65-99 years). Twenty-two patients (21.4%) died within 30 days. The admission "Quick Sepsis-related Organ Failure Assessment" values were found to be 2 or more in 32 patients (31.1%). Bicarbonate (p=0.001), lactate (p<0.001), anion gap (p=0.007) and base-excess (p=0.001) values were found to be significantly associated with 30-day mortality.

Conclusion: In our study, we found that the levels of lactate, bicarbonate, anion gap and base-excess in arterial blood gas were associated with 30-day mortality in elderly patients diagnosed with sepsis. These parameters should be closely monitored in septic patients. Monitoring of these parameters may help early clinical decision-making in emergency department patients with sepsis and may affect the outcome of sepsis.

Keywords: Blood gas analysis, mortality, sepsis, elderly patient

ÖZ

Amaç: Sepsis hastanede yatan hastalarda en önemli ölüm nedenlerinden biri olsa da mortalite ve morbiditeyi öngörmeye yönelik erken prediktif faktörlerle ilgili bilgiler sınırlıdır. Bu çalışmada acil servise başvuran ve sepsis ön tanılı 65 yaş ve üzeri erişkin hastalarda tanımlanmış arteriyel kan gazı parametreleriyle 30 günlük mortalite arasındaki ilişkinin belirlenmesi amaçlandı.

Yöntemler: Mart-Ağustos 2017 tarihleri arasındaki 5 aylık süreçte acil serviste sepsis ön tanısı konulmuş 65 yaş üzeri hastaların arteriyel kan gazı parametreleri retrospektif olarak incelendi. Kan gazı parametrelerinden pH, laktat, anyon açığı, bikarbonat ve baz açığı ile 30 günlük mortalite arasındaki ilişki analiz edildi.

Bulgular: Sepsis tanılı 103 yaşlı hasta çalışmaya dahil edildi. Hastaların 58'i (%56,3) kadındı ve yaş ortalaması 77,74±8,45 yıl (aralık: 65-99) olarak saptandı. Hastaların 22 (%21,4) tanesi 30 gün içerisinde öldü. Başvuru "Hızlı Sepsisle İlgili Organ Yetmezliği Değerlendirmesi" değerleri 32 (%31,1) hastada 2 veya daha üzeri olarak saptandı. Parametrelerden bikarbonat (p=0,001), laktat (p<0,001), anyon açığı (p=0,007) ve baz açığı (p=0,001) değerlerinin 30 günlük mortalite ile anlamlı olarak ilişkili olduğu bulundu.

Sonuç: Çalışmamızda 65 yaş ve üzeri sepsis ön tanılı hastalarda arteriyel kan gazında saptanan laktat, bikarbonat, anyon açığı ve baz fazlalığı düzeylerinin 30 günlük mortalite ile ilişkili olduğunu saptadık. Septik hastalarda bu parametreler yakından izlenmelidir. Bu parametrelerin izlenmesi, sepsis ön tanılı acil servis hastalarında erken klinik karar almaya yardımcı olabilir ve sepsis sonucunu etkileyebilir.

Anahtar Kelimeler: Kan gazı analizi, mortalite, sepsis, yaşlı hasta

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Introduction

Sepsis is a life-threatening organ dysfunction syndrome resulting from an inappropriate host response to infection (1-3). Sepsis and septic shock, which affects millions of people around the world every year and cause the death of one in four people, is an important health problem (4,5). Early diagnosis and initiation of appropriate treatment in the first hours after sepsis improve outcomes. Especially in the last guidelines, dynamic measurements instead of static are recommended for evaluation of response to fluid treatment and determination of subsequent fluid treatment. Sepsis-induced hypoperfusion is manifested by acute organ dysfunction and/or ± a decrease in blood pressure and an increase in serum lactate levels. Although serum lactate level is not an indicator of direct tissue perfusion, increased lactate levels have been reported to be associated with poor outcome regardless of source (6,7). When the studies evaluating lactate-guided resuscitation in septic shock patients are examined, it is also known that there is a significant decrease in mortality in lactate-guided resuscitation compared to resuscitation without lactate monitoring (8,9). The use of lactate is also recommended in the follow-up of patients' response to treatment in sepsis. Blood lactate levels can be evaluated in arterial or venous blood gas examinations in many health facilities and blood gas examinations are used almost routinely in sepsis patients.

Population over 65 years of age is increasing day by day in developing and developed countries and in parallel with this; the number of emergency service admissions is increasing in this age group. Elderly patients have the highest hospitalization rate, the longest hospital stay, and the highest resource utilization rate compared to other age groups (10). Due to the high frequency of atypical presentations, weakened physiological responses, complex medical backgrounds and the presence of chronic diseases, these patients have higher mortality during hospitalizations compared to all other age groups (11).

Although sepsis is one of the most important causes of death in hospitalized patients, information on early predictive factors for predicting mortality and morbidity is limited. The aim of this study was to determine the relationship between 30-day mortality and defined arterial blood gas parameters in adult patients aged 65 years and older who were admitted to the emergency department with the diagnosis of sepsis.

Methods

This study was planned as retrospective, cross-sectional and observation-based in our emergency department. After the approval of the İstanbul Training and Research Hospital Local Ethics Committee (decision no: 2011-KAEK-50), five-month data between March 1, 2017 and August 1, 2017 were retrospectively reviewed. Patients who were 65 years or older and were admitted to the emergency department within this date range and who underwent blood gas analysis in the emergency room were detected using the laboratory computer system. The medical files of these patients were examined using the infection-related ICD diagnostic codes and the patients with a prediagnosis of sepsis constituted the study cohort. According to the Third International Consensus, sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection (1). In our study, patients diagnosed with sepsis by clinician were confirmed in each case using Third International Consensus definitions. Quick Sepsis-related Organ Failure Assessment (qSOFA) score was calculated retrospectively for patients with registered respiratory rate, systolic blood pressure (SBP), and consciousness on admission to the emergency department. Patients with a score of 2 or more were evaluated as sepsis at the emergency department and patients with a score of less than 2 were included in the study if their qSOFA score increase to 2 or more within 24 hours after verifying with respiratory rate, SBP and consciousness. Among the patients who were clinically thought to have sepsis, patients who were 65 years or older and who had arterial blood gas analysis within the first 4 hours in the emergency department with available results in the laboratory software system were selected for the study. Patients under the age of 65 years, patients with qSOFA score less than two in the first 24 hours, patients without arterial blood gas analysis within the first 4 hours or patients with no blood gas analysis due to technical reasons were excluded from the study. Considering these criteria, 103 patients were included in the study. The demographic, laboratory and clinical data of the patients were retrospectively reviewed and recorded from the hospital software system. The patients were asked whether they were alive on the 30th day either by screening from the population registry system or by telephone. The relationship between pH, bicarbonate, lactate, anion gap and base-excess and 30-day mortality was investigated. The study was carried out in accordance with the Helsinki Declaration with the data obtained from the patient file and laboratory software system.

SPSS 16.0 was used for statistical analysis (SPSS Inc., Chicago, IL, USA). The normality of continuous variables was evaluated by Shapiro-Wilk test. Continuous variables were expressed as mean ± standard deviation, and categorical variables were expressed as number and percentage. Chi-square test was used for comparisons between categorical variables. Student's t-test was used for comparison of the normally distributed parameters and Mann-Whitney U test was used for the comparison of non-normally distributed parameters. The receiver operating characteristic (ROC) curve was plotted to calculate the probability of predicting mortality and the area under the curve was calculated. Statistical significance was accepted as $p<0.05$.

Results

The mean age of 103 patients included in the study was 77.74±8.45 years (range: 65-99 years). Fifty-eight patients (56.3%) were female and 45 (43.7%) were male. Thirty-two patients (31.1%) had a qSOFA score of 2 or more on admission to the emergency department and the remaining 71 patients (68.9%) had a qSOFA score of 2 or more within 24 hours although they had a score less than 2 on admission. On admission to the emergency department, 41 patients (39.8%) had a Glasgow Coma scale score of 13 or less, 23 (22.3%) had SBP of 100 mmHg and less, and 20 (19.4%) had respiratory rate of 22 and above per minute. Of the 103 patients included in the study, 22 (21.4%) died within 30 days. On admission, median respiratory rate was 15/min, mean SBP was 131.6±30.7 mmHg, mean diastolic blood pressure was 70.6±14.0 mmHg, and mean arterial pressure 90.9±18.2 mmHg, mean heart rate was 88.7±17.5 beats/minute, mean body temperature was 36.8±1.0 °C and mean peripheral oxygen saturation was 94.0±4.7 (Table 1). When the sources of infection were examined, it was found that 49 (47.6%)

were due to respiratory system, 23 (22.3%) were due to urinary system and the remaining 31 (30.1%) were due to other infections.

In all patients, the mean lactate was 2.2±1.6 mmol/L (range: 0.1-7.7), base-excess was 1.5±4.9 mmol/L (range: -17.3-23.4), anion gap was 1.9±4.8 mmol/L (range: -20.4-17.1), bicarbonate was 25.8±5.0 mmol/L (range: 9.5-48.2), ionized calcium was 1.12±0.08 mmol/L (range: 0.62-1.33) and pH was 7.41±0.68 (range: 7.18-7.61). Lactate ($p<0.001$) and anion gap ($p=0.007$) values were higher, and base-excess ($p=0.001$) and bicarbonate ($p=0.001$) values were lower in the mortality group and these differences were statistically significant. Ionized calcium values were found to be significantly higher in the mortality group, but this value had no clinical significance. There was no significant correlation between pH and mortality ($p=0.913$) (Table 2).

Regarding ROC curve and areas under the curve, lactate (0.825), bicarbonate (0.742), base-excess (0.733) and anion gap (0.687) were found to predict mortality. The ROC curves of the parameters are shown in Figure 1.

Discussion

Sepsis is defined as a life-threatening organ dysfunction caused by an abnormal host response to infection and is one of the leading causes of death. The prevalence of sepsis is increasing in the whole world. Although there are many factors contributing to this increase, the increase in the proportion of the elderly population plays an important role in this and mortality is higher in this age group. Blood gas assessment is almost routinely used in the management of patients with sepsis. The aim of this study was to determine the relationship between defined arterial blood gas parameters and 30-day mortality.

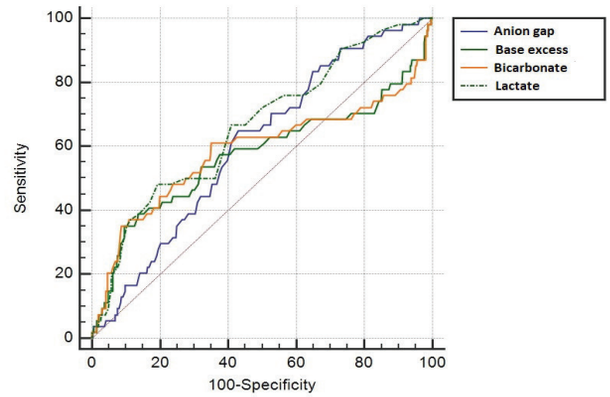

Figure 1. ROC analysis of defined parameters for predicting 30-day mortality
ROC: receiver operating characteristic

Table 1. Comparison of the cases included in the study with all variables according to mortality

Variable	Study cohort (n=103)	30-day mortality		p
		Yes (n=22)	No (n=81)	
Age, Mean ± SD	77.74±8.45	79.86±1.44	77.16±0.98	0.147
Female, n (%)	58 (56.3%)	12 (20.7%)	46 (79.3%)	0.519
Male, n (%)	45 (43.7%)	10 (22.2%)	35 (77.8%)	
Admission qSOFA ≥2, n (%)	32 (31.1%)	8 (25%)	24 (75%)	0.220
24th hour qSOFA ≥2, n (%)	71 (68.9%)	14 (19.7%)	57 (80.3%)	
GCS score ≤13, n (%)	41 (39.8%)	12 (29.3%)	29 (70.7%)	0.090
SBP mmHg, Mean ± SD	131.6±30.7	127.1±6.4	132.9±3.4	0.267
DBP mmHg, Mean ± SD	70.6±14.0	70.6±3.3	70.5±1.5	0.587
MAP mmHg, Mean ± SD	90.9±18.2	89.6±4.0	91.3±2.0	0.385
Heart rate/min, Mean ± SD	88.7±17.5	89.9±3.9	88.4±1.9	0.834
Respiratory rate/min, median (IQR)	15 (13-17)	14.5 (12-19)	15 (13-16.5)	0.874
Body temperature °C, Mean ± SD	36.8±1.0	36.6±0.2	36.9±0.1	0.301
SpO2 %, Mean ± SD	94.0±4.7	93.4±1.2	94.2±0.5	0.926

SD: standard deviation, qSOFA: Quick Sepsis-related Organ Failure Assessment, GCS: Glasgow Coma scale, SBP: systolic blood pressure, DBP: diastolic blood pressure, MAP: mean arterial pressure, IQR: interquartile range, SpO2: peripheral oxygen saturation

Table 2. Relationship between blood gas parameters and 30-day mortality

Variable, Mean ± SD	Study cohort (n=103)	30-day mortality		p
		Yes (n=22)	No (n=81)	
Lactate, mmol/L	2.2±1.6	4.0±0.4	1.8±0.1	<0.001
Base-excess, mmol/L	1.5±4.9	-1.1±0.8	2.2±0.6	0.001
Anion gap, mmol/L	1.9±4.8	4.0±0.9	1.3±0.5	0.007
Bicarbonate, mmol/L	25.8±5.0	22.8±0.8	26.6±0.6	0.001
Ionized calcium, mmol/L	1.12±0.08	1.13±0.02	1.12±0.01	0.001
pH	7.41±0.68	7.42±0.02	7.41±0.01	0.913

SD: Standard Deviation

Respiratory and genitourinary tract infections are the most common sepsis foci in the elderly (12). In our study, respiratory tract infections were found to be the most common (47.6%) etiologic cause in accordance with the literature. Increased awareness of sepsis and significant improvements in diagnosis and management have led to improvements in outcomes in all age groups. However, despite all developments, the overall mortality rate remains high in elderly adults. In-hospital mortality rate in patients 65 years and older is reported to be 30-60% in the literature and this rate increases to 40-80% in patients 80 years and older (4,13,14). In our study, 30-day mortality was 21.4%. This result may be due to the fact that sepsis cases with less severe clinical severity were retrospectively included in our study. When our cohort was examined, it was seen that the number of cases with a qSOFA score of 2 or more on admission was 32 (31.1%).

Sepsis may cause respiratory failure, acute kidney damage, organ dysfunction and metabolic acidosis associated with shock and multiple organ failure. Therefore, assessment and careful management of acid-base status is often necessary (4,15). Blood gas analysis is not only used for this, but also it has the advantages of performing analyzes such as sodium, potassium, glucose, hemoglobin, lactate, ionized calcium and ionized magnesium on the sample taken. It has been well defined that serum lactate levels are predictors of mortality in trauma and sepsis (16-18), and the importance of lactate in the treatment of sepsis is often emphasized and it has been also stated that some treatment approaches have to be made dependent on lactate levels (19). In our study, higher serum lactate levels were found in patients who died due to sepsis. Although it has been proved that serum lactate levels may help to manage septic shock treatment and the necessity of routine study is recommended, lactate level may not be evaluated routinely in all centers due to lack of technical infrastructure. In these cases, anion gap has traditionally been used as an indicator for lactate levels. Bakker et al. (20) reported that high anion gap is a good but not perfect indicator for high lactate levels in emergency department patients at risk of sepsis. In our study, higher anion gap levels were found in patients with sepsis who died on the 30th day compared to the survivors.

Shock is best described as organ dysfunction resulting from inadequate tissue perfusion due to inadequate oxygen delivery. Inadequate oxygen supply to tissues often causes metabolic acidosis, and therefore metabolic acidosis is a common finding in patients with septic shock. In many studies, it has been reported that metabolic acidosis evaluations in the first days of hospitalization in patients with septic shock are associated with good clinical outcomes (21). Carrara et al. (22) reported that there was a significant association between decreased blood pH and oxygenation and mortality in patients with severe sepsis and septic shock (22). There are also studies reporting that neither bicarbonate, lactate and base deficit nor regional perfusion endpoints are superior to each other in the diagnosis of shock (23). In our study, low bicarbonate level was found to be significantly associated with mortality, but we found no significant relationship between blood pH and mortality.

Base-excess represents the additional base amount that should be added to one liter of blood to normalize the pH. It has been reported that base-excess is a predictor of morbidity and mortality in critically ill and trauma patients (24,25). Similarly, in our study, the base-excess level was found to be lower in patients who died.

We had some limitations in the study. It was a single-center, retrospective study and the sample size was relatively small. Intensive care treatment processes (inotropic initiation, antibiotherapy, interventions, etc.) in some sepsis patients could not be monitored and recorded due to referral to other centers for intensive care unit stay. When we examined the reports in the literature in our age group, our mortality values were lower. This may be due to diagnosis-related deficiencies, or to the fact that the selected patients were clinically better patients with sepsis.

Conclusion

Regardless of clinical severity, the majority of sepsis patients are first examined in the emergency department. Therefore, it is important for emergency physicians to accurately evaluate disease severity and mortality risk when confronted with these patients. In our study, we demonstrated that the levels of lactate, bicarbonate, ionized calcium, anion gap, and base-excess in the arterial blood gas were associated with 30-day mortality in patients aged 65 years and older. These parameters should be closely monitored in septic patients. Monitoring of these parameters may help early clinical decision-making in emergency department patients with sepsis and may affect the outcome of sepsis.

Ethics Committee Approval: After the approval of the İstanbul Training and Research Hospital Local Ethics Committee (decision no: 2011-KAEK-50), five-month data between March 1, 2017 and August 1, 2017 were retrospectively reviewed.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

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