ORIGINAL ARTICLE

Correlation between Blood Lactate Levels and Hospitalization and Prognosis in Drug Intoxication Patients in the Emergency Medicine Department

ADNAN TURK[1,*], ASIM KALKAN[1], ŞEREF EMRE ATİŞ[1], MEHMET ALI TOPAL[1], BORA ÇEKMEN[1], ÖNER BOZAN[1], HAKAN TOPAÇOĞLU [2]

[1]University of Health Sciences, Okmeydani Training and Research Hospital, Department of Emergency Medicine, Istanbul, Turkey
[2]Düzce University Faculty of Medicine Department of Emergency Medicine, Düzce, Turkey

Abstract

Background: Several drug intoxications can affect both pulmonary and cellular respiration. We therefore think that assessing blood lactate levels can provide information about prognosis. Blood lactate levels have provided information about prognosis in several diseases involving hypoxia at the cellular level, such as sepsis and trauma. The purpose of this study was to determine whether there is any relation between blood lactate levels and mortality, morbidity, and prognosis in patients presenting to the emergency department with drug intoxication.
Methods: This retrospective cross-sectional study involved patients admitted to the emergency department due to suicidal drug intoxication over a one-year period (January to December 2016). The primary outcome measure was the relationship between serum lactate concentrations and patient discharge or hospitalization, and if hospitalized, the duration of stay. The secondary outcome measure was the relationship between serum lactate concentrations and toxic dose intake in single-drug intoxication.
Results: We enrolled 372 patients, of whom 192 were analyzed after exclusion criteria application. The mean blood lactate level in the total patient group was 2.6±1.46, and 2.7±1.9 in the single drug group and 2.5±1.3 in the multidrug group. Also, blood lactate levels in the overdose group and toxic dose group were 3.4±3.0 and 2.4±0.9, respectively. No significant differences were determined in the lactate level, discharge, hospitalization and the length of hospital stay between the single drug and multidrug groups. In the toxic dose group, patient ages and number of admissions to intensive care unit were significantly higher than in the overdose group. The number of discharges was significantly lower in the toxic dose group. No correlation was determined between the serum lactate level and the length of hospital stay.
Conclusion: Lactate level is not a useful parameter for predicting hospitalization in drug intoxication patients.

Keywords: Drug Toxicity; Hospitalization; Lactic Acid

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INTRODUCTION

Intoxication is defined as a living organism encountering a substance that adversely affects its vital functions (1, 2). The problem emerged as more significant following the establishment of emergency departments (EDs) and records (3). Intoxications may present to the emergency department in the form of single-drug or multidrug intake. Although the toxic doses of many drugs are known and their blood levels can be assessed, there are still drugs whose blood levels cannot be investigated and whose toxic effects cannot be predicted. Various methods are therefore required to manage and assess the prognosis of drug intoxications in emergency departments receiving frequent presentations (4).

Lactate, a breakdown product of anaerobic respiration, is a useful prognostic marker in various clinical conditions (5). Lactate levels have been proved to be a useful biomarker in determining mortality and morbidity in different diseases including sepsis and trauma (6, 7). It is also a good indicator of respiratory impairment at the cellular level. Lactate is known to affect respiration at the cellular level. Animal experiments have shown that at low levels, lactate increases respiration rates by affecting receptors in the carotid, while at high levels it suppresses respiration (8). In addition, several studies have reported that blood lactate levels increase in drug intoxications causing metabolic acidosis (9, 10). It may therefore be concluded that oxidative stress will develop in drug intoxications. Evaluation of hypoxia in cases in which the drug dosage is unknown and in patients in whom blood drug levels cannot be measured may provide information about prognosis. The principal aim of our study was to determine the values at which mortality or morbidity

[*]Correspondence to: Adnan Turk; MD. Kaptanpasa Mah, Darulaceze Cad, No:25, Okmeydani Training and Research Hospital Kağıthane, Istanbul, Turkey
Tel: +905323911792, Email: dradnanturk@gmail.com
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may occur by measuring blood lactate levels in drug intoxications. Additionally, we also intended to determine the values at which we can determine admission to the ward or intensive care, or mortality, if a cut-off value can be identified.

METHODS

Study design and setting

This retrospective cross-sectional study involved patients admitted to University of Health Science Okmeydani Training and Research Hospital ED, Istanbul, Turkey, due to suicidal drug intoxication. In our ED, patients admitted due to drug intoxication are transferred from the triage room to yellow or red zones. Approximately 100,000 patients per year are admitted to the yellow and red zones in our ED, and all are examined by an emergency physician. Data were obtained from patients admitted to hospital between 01.01.2016 and 31.12.2016 (a one-year period). The study was conducted after the receipt of local ethic committee approval (ethical committee approval No. 773).

Selection of participants

The study population consisted of adults presenting to the ED with drug intoxication. Data were collected by screening registration records according to International Classification of Disease codes X44 and X49. Exclusion criteria included presence of alternative diagnosis (trauma, infection), chronic drug use, nondrug intoxication (such as CO or pesticide), intoxication due to non-oral exposure (dermal, inhalation, intravenous), age under 16, pregnancy, referral from an external institution emergency or intensive care department, incomplete data, out-of-hospital cardiac arrest, or unavailability of lactate data.

Data collection

Demographic characteristics (age and gender) and history of intoxication (drug type and dose), venous blood gas results and serum lactate concentrations of the patients enrolled in the study were collected from electronic and medical records. Data were also obtained for hospitalization requirements and the duration and type of admission if applicable (inpatient or intensive care). Patients were divided into two groups - single-drug intoxication and multi-drug intoxication cases. Patients in the single-drug intoxication group were divided into two subgroups on the basis of the dose of drug ingested. The first group consisted of patients with toxic doses and the second of "overdose" patients, defined as drug intake exceeding the daily dose but not as high as toxic doses. Serum lactate concentrations were analyzed using an AKINLAB Radiometer ABL800 (Istanbul, Turkey) analyzer.

Outcome measures

The primary outcome measure was the relationship between serum lactate concentrations and patient discharge or hospitalization, and length of stay if applicable. The secondary outcome measure was the relationship between serum lactate concentrations and toxic dose drug intake in single-drug intoxications.

Statistical analysis

Data are presented as mean±standard deviation, median value with interquartile range, frequency and proportion. The Kolmogorov-Smirnov test was used for testing normal distribution of variables. The Kruskal-Wallis and Mann-Whitney-U tests were used to compare non-normal distributions. The chi-square test was used to compare the qualitative data. Spearman correlation analysis was used for testing the relations. P values < 0.05 were considered statistically significant. Computer analysis was performed on SPSS version 22.0 software (SPSS, Inc., Chicago, IL, USA).

RESULTS

A total of 372 patients were screened, 192 of whom met the inclusion criteria. One hundred eighty patients were excluded due to missing lactate data (125 patients), missing drug data (51 patients), non-oral drug exposure (intravenous, or transdermal) (two patients), pregnancy (one patient) and out-of-hospital cardiac arrest (one patient).

One hundred forty-six (76%) of the patients included in the study were women and 46 (24) were men. Patients' mean age was 32.6±11.5 years. The mean blood lactate level in the total patient group was 2.6±1.6 (range: 0.8-16.0). Overdose was determined in 60 of these patients (68.2) and toxic doses in 28 (31.8%). Single drug use was present in 88 patients (45.8%), and multidrug use in 104 (54.2%). Mean length of stay in intensive care was 2.6±1.6 days (range: 1-7), and mean length of stay on the ward was 2.6±3.7 days (range: 2-22). Demographic characteristics, serum lactate levels and drug intoxication types are shown in Table 1.

Table 1. Patients' demographics and distribution of patients based on hospitalization and ingested drug dose.

		n (%)	Mean±SD	Range
Age			32.6±11.5	16.6-78.4
Age group	≤ 25	65 (33.9)		
	26-35	58 (30.2)		
	36-45	39 (20.3)		
	46-55	23 (12.0)		
	≥56	7 (3.6)		
Female		146 (76.0)		
Lactate level (mmol/L)			2.6±1.6	0.8-16.0
Discharged		134 (69.8)		
ICU		28 (14.6)		
Inpatient care		41 (21.4)		
ICU duration			2.6±1.6	1.0-7.0
Inpatient care duration			2.6±3.7	1.0-22.0
Ingested dose	Over dose	60 (68.2)		
	Toxic dose	28 (31.8)		
Single drug		88 (45.8)		
Multi drug		104 (54.2)		

Mean blood lactate levels were 2.7±1.9 in the single drug group and 2.5±1.3 in the multidrug group. Mean lengths of stay in the single drug group were 2.3±1.8 days in intensive care and 3.5±5.6 days on the ward. In the multidrug group, mean lengths of stay were 2.8±1.6 days in intensive care and 2.1±1.9 days on the ward. Patients' ages and sex, serum lactate levels, discharge or hospital stay rates (inpatient care or intensive care) were not significantly different between the single and multi-drug groups (Table 2).

Mean ages were 31.1±10.5 years in the overdose group and 37.6±13.1 in the toxic dose patients. Blood lactate levels were 2.4±0.9 in the overdose group and 3.4±3.0 in the toxic dose patients. The difference in blood lactate levels between the overdose and toxic dose groups was not statistically significant. Mean lengths of stay among the overdose patients were 1.5±1.0 days in intensive care and 1.6±0.96 on the ward. Patients' ages and length of in-hospital stay in the intensive care unit were significantly higher in the toxic dose

Table 2. Comparison between single drug and multidrug group demographics, lactate levels and outcomes.

	Single drug			Multi drug			
		n (%)	Mean±SD	n (%)	Mean±SD	p	
Age			33.2±11.7		32.1±11.4	*0.448*	*m*
Age group	≤ 25	27 (30.7)		38 (36.5)		*0.722*	*X²*
	26-35	30 (34.1)		28 (26.9)			
	36-45	18 (20.5)		21 (20.2)			
	46-55	9 (10.2)		14 (13.5)			
	≥56	4 (4.5)		3 (2.9)			
Male		23 (26.1)		23 (22.1)			
Lactate level (mmol/L)		63 (71.6)	2.7±1.9		2.5±1.3	*0.486*	
Discharged		11 (12.5)		73 (68.3)		*0.617*	
ICU				11 (16.3)		*0.452*	
ICU duration		15 (17.0)	2.3±1.8		2.8±1.6	*0.222*	*m*
Inpatient care				26 (25.0)		*0.180*	*X²*
Inpatient care duration		63 (71.6)	3.5±5.6		2.1±1.9	*0.953*	*m*

m Mann-Whitney U test / x² chi-square test

Table 3. Comparison between overdose and toxic dose group demographics, lactate levels and outcomes.

	Over Dose			Toxic Dose			
		n (%)	Mean±SD	n (%)	Mean±SD	p	
Age			31.1±10.5		37.6±13.1	*0.014*	*m*
Age group	≤ 25	23 (38.3)		4 (14.3)		*0.026*	*X²*
	26-35	21 (35.0)		9 (32.1)			
	36-45	9 (15.0)		9 (32.1)			
	46-55	5 (8.3)		4 (14.3)			
	≥56	2 (3.3)		2 (7.1)			
Male		16 (26.7)					
Lactate level (mmol/L)			2.4±0.9		3.4±3.0	*0.190*	*m*
Discharged		47 (78.3)		16 (57.1)		*0.040*	*X²*
ICU		4 (6.7)		7 (25.0)		*0.015*	*X²*
ICU duration			1.5±1.0		2.7±2.1	*0.228*	*m*
Inpatient care		8 (13.3)		7 (25.0)		*0.175*	*X²*
Inpatient care duration			1.6±0.9		5.6±7.9	*0.412*	*m*

m Mann-Whitney u test / x² chi-square test

group than in the overdose group. Discharge numbers were significantly lower in the toxic dose group. No significant difference was observed between the groups in terms of sex, serum lactate levels, hospital stay for inpatient treatment, duration of hospitalization for inpatient treatment or in the intensive care unit (Table 3).

Mean blood lactate levels were 2.47±1.15 in the discharged patients and 2.88±2.38 in the hospitalized patients. Serum lactate levels were not significantly different between the discharged and hospitalized patients (Table 4).

Table 4. Correlations between lactate levels, hospitalization and discharge.

	Lactate	
	Mean±SD	p
Overall hospitalization	2.88±2.38	p>0.05
Discharge	2.47±1.15	p>0.05
Mann Whitney U test		

DISCUSSION

The mean age of the patients was 32.6±11.5 years, a figure consistent with the previous literature. O'Donovan et al. also reported that patients admitted to the intensive care unit due to drug intoxication tended to be younger (11). In a national multicenter study from Spain, the mean age of patients was 33 (12). An association has been shown between hyperlactatemia and mortality in medical and surgical patients in various studies (13-15). In one observational, prospective, cohort study performed at two urban teaching hospitals over a five-year period, 1,500 patients were evaluated, and a mean serum lactate concentration of 2.31 mmol/L was determined (5). Similarly, in a case-control study involving fewer patients, the mean serum lactate concentration was approximately 3 mmol/L. In our study, the mean serum lactate concentration was 2.2 mmol/L, a figure consistent with previous reports.

In our study, 69.8% of all patients admitted to the ED with drug intoxication were discharged following initial assessment and appropriate follow-up. Previous studies have reported a wide variation, from 5.1% to 64% (16, 17). Lionte et al.'s prospective cohort study of 120 drug intoxication patients and the drugs detected reported that 30% involved combinations of toxins (18). Flomenbaum et al. reported that 50% of patients presented with multi-drug intoxication (19). In our study, 45.8% of patients were admitted to the ED with single-drug intoxication. This disparity with the previous literature may be due to comorbidities and related drug intake of the patients which cause facility to reach drugs.

We compared age and gender, serum lactate levels, discharge/hospital stay rates and duration of hospitalization between the single- and multi-drug intoxication groups, but observed no statistically significant difference in any of these parameters. Our study is the first in the literature to compare single- and multi-drug intoxications.

Although suicide rates are 6-8 times higher among the elderly, more young people than elderly individuals die from suicide, and the age group in which most suicides are successfully committed is 35-44 years (20). Similarly, the World Health Organization describes 20-35 years as the age group with the highest suicide rates (21). In our study, the mean age of patients in the single drug toxic dose group was 37.6, higher than that in the overdose group. It may therefore be hypothesized that suicidal tendencies arise with increasing age.

In our study, discharge rates were lower and hospital stay rates in the intensive care unit were higher in the toxic dose group. Physicians tend to follow up these patients for longer in the ED because the signs and symptoms are generally more severe in this group, and national poison counseling centers advise that these patients be kept under surveillance.

Shapiro et al. reported that a high serum lactate concentration is a predictor of mortality in ED patients with infection (13). Correlation between serum lactate concentrations and risk scoring, clinical severity and hospitalization in carbon monoxide intoxicated patients has also been shown in several studies (22). In our study, there was no statistically significant difference between serum lactate levels in the discharged and hospitalized patients. No statistically significant difference was also observed between the durations of hospitalization (intensive care or inpatient care). One prospective study reported a mean serum lactate concentration of 8.1 mmol/L in fatal cases, significantly higher than in non-fatal cases (5). In another study of drug intoxicated patients, hyperlactatemia was identified as a predictor of unfavorable outcomes (19). In contrast, Megarbane et al. reported that the mean serum lactate concentration in beta blocker intoxication cases, 3 mmol/L, was not an exact predictor of mortality (23).

LIMITATIONS

The principal limitation of our study is the low patient number. However, we think that further studies with larger patient numbers will support our conclusions. Another limitation is that no mortality occurred in any of the patients enrolled. One patient died, but we considered that this would not be statistically significant, and this patient was excluded. Although we initially set out to investigate whether any relation exists between lactate levels and mortality, the fact that none of our patients died meant that no information concerning mortality could be obtained. The purpose of the study was therefore revised in the light of our findings. We think that multi-center studies in which cases involving mortality are also included will provide better information concerning blood lactate levels and mortality in drug intoxications. Another limitation of our study is that 125 patients were excluded. The exclusion of such a large number of patients in this research, as in other various studies, may be attributed to difficulties in data recording. Appropriate histories cannot be obtained in some cases presenting due to drug intoxication. Cheung et al. support this view. They examined 3,739 patients but were only able to include 1,406 in their study. They attributed this to data insufficiency, absence of acute intoxication, suspicion of

anaphylaxis, hronic intoxications and plant poisonings (5).

CONCLUSION

In conclusion, blood lactate levels do not affect admissions to intensive care or the ward in patients with drug intoxications. However, they are a good marker for deciding on discharge or admission when toxic doses are involved. Cases of drug intoxication with high blood lactate levels should be admitted to hospital. Further studies with larger numbers will support our thesis. In addition, evaluation of lactate levels will be more useful in the management of patients with specific drug indications.

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