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ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA MAKALESİ

Evaluation of Serial Lactate Measurements in Carbon Monoxide Poisoning

Karbonmonoksit Zehirlenmesinde Seri Laktat Ölçümünün Değerlendirilmesi

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ABSTRACT

Aim: Carbon monoxide is a gas that can cause acute poisoning and affect organs such as the brain, heart, and kidneys. The number of studies investigating lactate clearance in patients with CO poisoning is limited. The primary endpoint of our study is to determine whether there is a difference in lactate clearance according to demographic characteristics, hyperbaric oxygen therapy, and clinical outcomes.

Material and Methods: Our study was conducted retrospectively. Patients over the age of 18 with carboxyhemoglobin levels >10% and at least two venous blood gas results were included. Demographic characteristics, carboxyhemoglobin and lactate levels in the first and second blood gas analyses, the timing of blood gas sampling, whether or not they received hyperbaric oxygen therapy, and patient outcomes were recorded.

Results: A total of 272 patients were included in our study. The mean initial carboxyhemoglobin level was 22.8±8.6 (10.0-60.9). The mean initial lactate level was 2.3±1.8 (0.1-18.0). A decrease in lactate clearance of more than 20% was observed in 37 patients (51.4%) at the 1st hour, 43 patients (66.2%) at the 2nd hour, 75 patients (77.3%) at the 3rd hour, and 29 patients (76.3%) at the 4th hour. When grouped according to the timing of blood gas sampling, no significant difference was found between the first and second CO and lactate levels. A decrease in lactate clearance of more than 20% was not statistically significant in terms of age, gender, carboxyhemoglobin levels, and patient outcomes.

Conclusion: No statistically significant association was found between patient outcomes and lactate clearance.

Keywords: Carbon monoxide poisoning, lactate measurement, emergency medicine.

ÖZ

Amaç: Karbonmonoksit akut zehirlenmelere neden olabilen beyin, kalp, böbrek gibi organları etkileyen bir gazdır. CO zehirlenmesi hastalarındaki laktat klirensini araştıran çalışma sayısı kısıtlıdır. Çalışmamızın primer sonlanım amacı; laktat klirensinin demografik özellikler, hiperbarik tedavi ve sonlanım arasında fark olup olmadığını saptamaktır.

Gereç ve Yöntemler: Çalışmamız retrospektif olarak yapıldı. 18 yaş üstü karboksihemoglobin düzeyi >% 10 olan ve en az 2 venöz kan gazı sonucu bulunan hastalar dahil edildi. Hastaların demografik özelikleri, ilk ve ikinci kan gazında karboksihemoglobin, laktat değerleri, kan gazının alınma saatleri, hiperbarik tedavisi alıp almadıkları ve hastaların sonlanımı kaydedildi.

Bulgular: Çalışmamıza toplam 272 hasta dahil edildi. İlk karboksihemoglobin değeri ortalama 22,8±8,6 (10,0-60.9) saptandı. İlk laktat değeri ortalama 2,3±1,8 (0,1-18,0) saptandı. Kan gazında laktat klirensinde %20 den fazla düşme; 1. saatte 37 hastada (%51,4), 2. saatte 43 hastada (%66,2), 3. saatte 75 hastada (%77,3), 4. saatte 29 hastada (%76,3) saptandı. Kan gazı alınma saatlerine göre ayrılarak karşılaştırıldığında ilk ve ikinci CO ve laktat değerleri arasında anlamlı fark saptanmadı. Laktat klirensinde %20 den fazla düşmede; yaş, cinsiyet ve karboksihemoglobin değerleri ve hastanın sonlanımı ile istatiksel anlamsız saptandı.

Sonuç: Hastanın sonlanımı ile laktat klirensi arasında istatiksel anlamlılık saptanmamıştır.

Anahtar Kelimeler: Karbonmonoksit zehirlenmesi ,acil tıp, laktat ölçümü.

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Introduction

Carbon monoxide (CO) is a gas produced by incomplete combustion of carbon-based fuels and is a well-known cause of acute poisoning (1,2). In Türkiye, patients with CO poisoning frequently present to emergency departments, especially during the winter months due to the use of stoves and charcoal grills (2,3). CO poisoning primarily affects organs such as the brain, heart, and kidneys, leading to cardiovascular and neurological symptoms as major clinical manifestations (4,5).

Lactate levels increase particularly when oxygen delivery to tissues is impaired, and a serum lactate level of≥4 mmol/L has been associated with a more than 50% increase in mortality, especially in shock patients (6,7). The prognostic value of various indicators such as the duration of hyperlactatemia, serial lactate measurements, and lactate clearance has been investigated (8,9,10). Although a single lactate measurement may predict mortality, studies have shown that serial measurements assessing lactate clearance may provide greater clinical benefit (10).

Elevated lactate levels in blood gas analyses have been shown to be a valuable predictor of mortality in patients with CO poisoning (11,12). However, studies specifically evaluating the prognostic utility of lactate clearance in CO poisoning are limited. The primary outcome of our study was to determine whether there is a difference in lactate clearance according to demographic features, hyperbaric oxygen therapy, and clinical outcomes. The secondary aim was to evaluate the relationship between lactate measurements and other variables.

Material and Methods

This retrospective study was conducted with patients who presented to the emergency department between 01/01/2013 and 27/11/2018. The study was initiated after obtaining approval from the ethics committee (Approval No:2023/04-20).

Patients over the age of 18 who were diagnosed with CO poisoning in the emergency department, had carboxyhemoglobin levels ≥10%, and had at least two venous blood gas analyses during the same visit were included. Patients with only one venous blood gas analysis, or with carboxyhemoglobin levels below 10%, were excluded. Demographic characteristics (age, gender), initial and second carboxyhemoglobin and lactate levels, the timing of blood gas analyses, whether they received hyperbaric oxygen therapy, and clinical outcomes (hospitalization, discharge, death) were recorded. Temporary loss of consciousness, coma or seizures, ischemic ECG changes, focal neurological deficits, pregnant women with COHb levels > 15%, and individuals with headaches or nausea and COHb levels > 40% were considered as indications for hyperbaric oxygen therapy (13).

Lactate clearance was calculated as follows:

Lactate Clearance (%) = (Initial Lactate - Final Lactate) / Initial Lactate × 100.

Statistical Analysis

Statistical analysis was conducted using SPSS 22.0. Descriptive statistics were presented as mean ± standard deviation for continuous variables and frequency (percentage) for categorical variables. Normality was tested using the Kolmogorov-Smirnov test. For dependent continuous variables with normal distribution, the paired t-test was used; for independent continuous variables, the Student's t-test was used. Pearson correlation analysis was applied for continuous variables, and Spearman correlation for categorical ones. For categorical data, Fisher's exact test, the Fisher-Freeman-Halton test, and Pearson's chi-square test were used. A p-value <0.05 was considered statistically significant. Rho values were considered as follows: less than 0.30 as weak, between 0.30 and 0.70 as moderate, and greater than 0.70 as strong correlation.

Results

A total of 272 patients were included in the study. 12 patients were excluded due to being under 18 years old, 45 were excluded due to having only one blood gas measurement, and 8 patients were excluded due to having carboxyhemoglobin levels below 10. (Figure 1). Among them, 188 (69.1%) were female. The mean age was 41.05 ± 17.49 years (range: 18–87). Five patients (1.8%) received hyperbaric oxygen therapy. A total of 253 patients (93%) were discharged. Two patients (0.7%) died (Table 1). The mean initial carboxyhemoglobin (COHb) level was 22.83 ± 8.57 (range: 10–60.9). The mean initial lactate level was 2.26 ± 1.81 mmol/L (range: 0.11–18) (Table 2).

Among patients whose control blood gas was obtained at the 1st hour: A moderate correlation was observed between the initial COHb level and the initial lactate level (r = 0.629, p < 0.001). A moderate correlation was also found between the initial and second COHb levels (r = 0.485, p < 0.001), and between the second COHb level and the second lactate level (r = 0.534, p < 0.001).

	n (%)	Mean ± SD (min-max)
Age		41.1 ± 17.5 (14.0-87.0)
Gender		
Female	188 (69.1)	
CO_1		22.8 ± 8.6 (10.0-60.9)
CO_2		8.0 ± 5.2 (0.7-39.1)
Blood gas time		
1st hour	72 (26.5)	
2nd hour	65 (23.9)	
3rd hour	97 (35.7)	
4th hour	38 (14.0)	
Lactate_1		2.3 ± 1.8 (0.1-18.0)
Lactate_2		1.4 ± 1.3 (0.1-15.0)
Lactate clearance		30.0 ± 32.0 (-114.7-92.0)
Hyperbaric oxygen therapy		
Yes	5 (1.8)	
Outcome		
Discharge	253 (93.0)	
Admission	9 (3.3)	
Referral	2 (0.7)	
Exitus	2 (0.7)	
Left without permission	6 (2.2)	

Table 1. Demographic characteristics of the patients

CO_1: First measured carboxyhemoglobin level after admission CO_2: Second measured carboxyhemoglobin level after admission.

Lactate_1: First measured lactate level after admission, Lactate_2: Second measured lactate level after admission

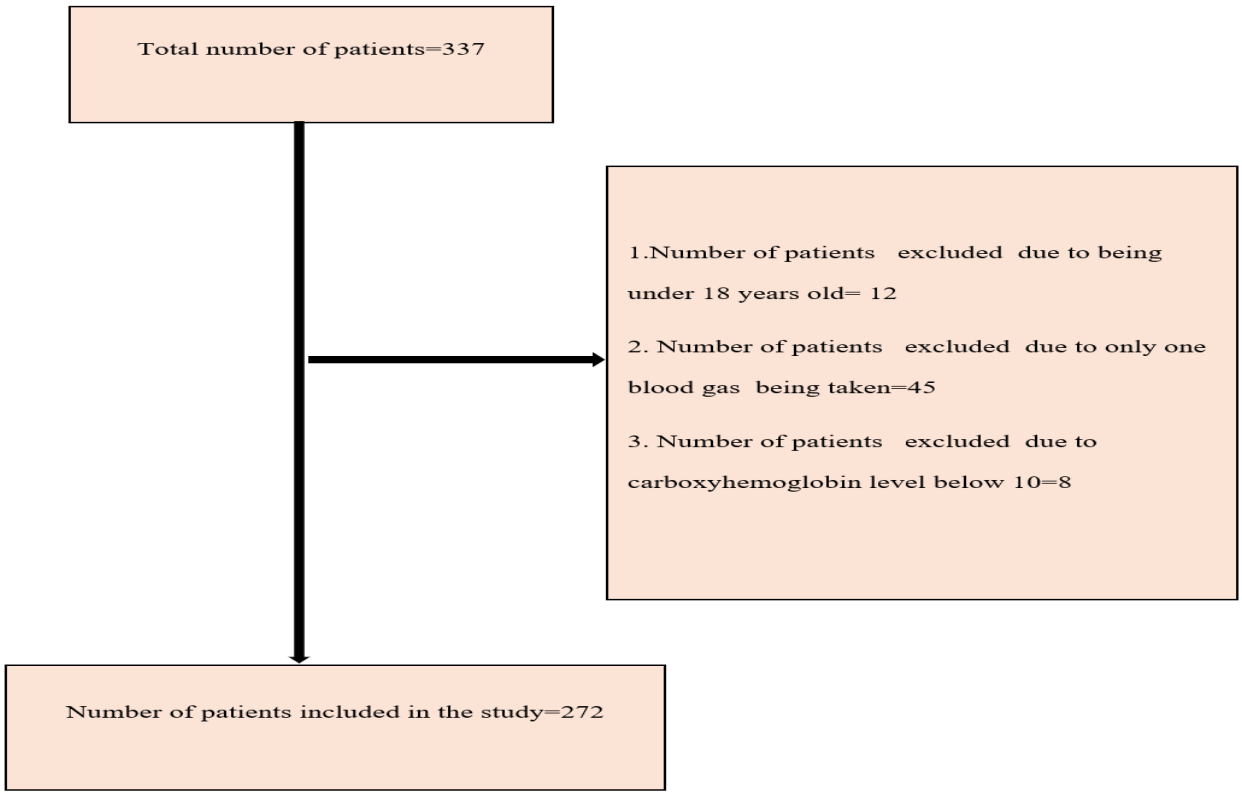

Figure 1. Flowchart of the study

Variable, mean ± SD (min-max)	1st hour (n=72)	2nd hour (n=65)	3rd hour (n=97)	4th hour (n=38)
CO_1	22.3 ± 10.7	21.7 ± 8.16	23.7 ± 7.6	23.4 ± 6.8
	(10.0-60.9)	(10.0-43.4)	(10.5 - 51.7)	(12.2-38.3)
	12.0 ± 6.5	7.63 ± 4.18	6.5 ± 3.3	4.6 ± 2.8
CO_2	(2.3-39.1)	(0.7-17.0)	(0.7 -17.1)	(0.8-14.5)
Lactate_1	2.5 ± 2.7	2.02 ± 1.26	2.2 ± 1.2	2.5 ±2.0
	(0.5-18.0)	(0.11-8.0)	(0.6-7.7)	(0.1-10.0)
Lactate_2	1.9 ± 2.2	1.23 ± 0.69	1.3 ± 0.6	1.2 ± 0.9
	(0.3-15.0)	(0.1-3.9)	(0.4-3.0)	(0.1-3.8)

Table 2. The first and second analysis results of carbon monoxide and lactate levels are grouped according to the time elapsed until the second blood gas analysis after admission

CO_1: First measured carboxyhemoglobin level after admission CO_2: Second measured carboxyhemoglobin level after admission

Lactate_1: First measured lactate level after admission, Lactate_2: Second measured lactate level after admission

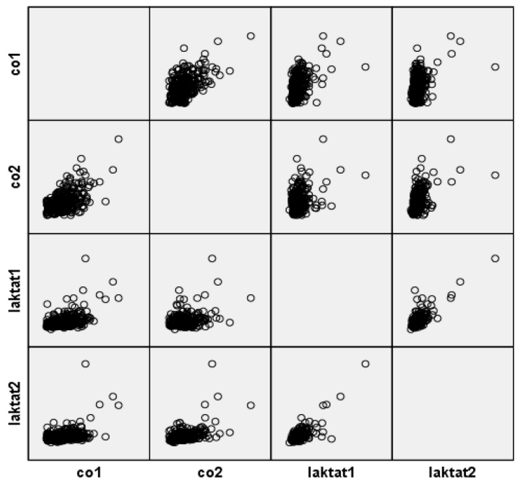

Figure 2. Correlation plots between carbon monoxide and lactate levels

A strong correlation was detected between the first and second lactate levels ($r = 0.948$, $p < 0.001$). Among patients with control blood gas at the 2nd hour, a moderate correlation was found between the first and second lactate levels ($r = 0.582$, $p < 0.001$) (Table 3, Figure 2).

Discussion

Carbon monoxide (CO) poisoning is a complex clinical condition characterized by hypoxia-induced cellular dysfunction and multiorgan involvement. In this study, we investigated the prognostic value of lactate levels in patients exposed to CO poisoning, with a particular focus on the impact of lactate clearance on clinical outcomes.

Lactate is widely used as an indicator of tissue perfusion, particularly in conditions such as sepsis and shock (14).

Time	Variable		Lactate_1	Lactate_2
	Age	rho	0.214	0.217
		p values	<0.001	<0.001
	Gender	rho	0.034	0.56
		p values	0.582	0.356
1st hour	**CO_1**	rho	0.629	0.617
		p values	<0.001	<0.001
	CO_2	rho	0.485	0.534
		p values	<0.001	<0.001
	Lactate_2	rho	0.948	
		p values	<0.001	
2nd hour	**CO_1**	rho	0.382	0.324
		p values	0.002	0.08
	CO_2	rho	0.352	0.402
		p values	0.004	<0.001
	Lactate_2	rho	0.582	
		p values	<0.001	
3rd hour	**CO_1**	rho	0.376	0.202
		p values	<0.001	0.048
	CO_2	rho	0.070	0.254
		p values	0.496	0.012
	Lactate_2	rho	0.378	
		p values	<0.001	
4th hour	**CO_1**	rho	0.448	0.192
		p values	0.005	0.247
	CO_2	rho	0.285	0.258
		p values	0.082	0.118
	Lactate_2	rho	0.596	
		p values	<0.001	

Table 3. The association of first and second lactate levels with other variables are grouped according to the time elapsed until the second blood gas analysis after admission

CO_1: First measured carboxyhemoglobin level after admission CO_2: Second measured carboxyhemoglobin level after admission

Lactate_1: First measured lactate level after admission, Lactate_2: Second measured lactate level after admission *Pearson correlation test

Numerous studies in septic patients have demonstrated a strong relationship between elevated lactate levels and increased mortality (15,16). In CO poisoning, hypoxic stress, mitochondrial dysfunction, and oxidative damage contribute to elevated lactate levels (2,17). Our study also observed significantly elevated lactate levels in patients presenting with CO poisoning, which may be associated with the severity of the clinical picture.

Previous studies have reported higher lactate levels in CO poisoning cases presenting with syncope, altered mental status, and those requiring hyperbaric oxygen therapy (18,19). A retrospective study by Eroğlu et al. involving 450 patients found significantly elevated lactate levels in hospitalized patients and those receiving HBO therapy (19), a finding consistent with our results.

On the other hand, the prognostic value of "lactate clearance," or the dynamic change in lactate levels over time, has been emphasized in the literature (20). Nguyen et al. reported that a lactate clearance of more than 10% was associated with improved prognosis (21). Similarly, Walker et al. showed that a 6-hour lactate clearance of over 36% was associated with reduced mortality (22). However, some studies argue that lactate clearance may have lower predictive power compared to the initial lactate value (23).

In our study, although we evaluated whether lactate clearance was associated with poor prognosis, no statistically significant difference was found. This may be related to variability in the timing of lactate measurements or the early initiation of supportive treatment. Lokhandwala et al. also reported that different lactate clearance thresholds yielded varying sensitivity and specificity (16). A meta-analysis by Zhang et al. concluded that lactate clearance is generally a useful mortality predictor, though study heterogeneity makes it difficult to define a precise cut-off value (10). BIS monitoring and lactate clearance rate have clinical value in the assessment of neurological damage and prognostic in severe carbon monoxide poisoning patients (24).

Similar results have been reported in pediatric populations. A prospective study by Scott et al. found that lactate normalization was inversely related to 48-hour organ dysfunction, but that lactate clearance alone was not a sufficiently strong predictor (23).

Meanwhile, emerging biomarkers such as the lactate/albumin ratio are proposed to offer better prognostic utility in sepsis and hypoxic conditions (15). However, their use in CO poisoning remains limited.

Limitations

The main strength of our study is its contribution to the limited literature specifically evaluating lactate clearance in CO poisoning. However, limitations include its retrospective design, variability in the timing of lactate measurements, and lack of standardized treatment protocols.

In our study, clinical outcomes were evaluated as hospitalization, mortality, and hyperbaric oxygen therapy administration. There is insufficient data regarding the parameters assessed in the clinical outcome (indications for admission and transfer). The patient numbers in the groups are limited to obtain statistically significant results. In our study, clinical outcomes such as the presence of delayed neurological sequelae, need for intensive care, and need for intubation were not evaluated. Since our study is retrospective, there is no data available regarding vital signs, physical examination, or Glasgow Coma Scale scores.

Conclusion

No statistically significant association was found between lactate clearance and clinical outcomes. Among patients with control blood gas obtained at the first hour, a mod Gerate correlation was observed between the initial COHb and initial lactate levels, as well as between the second COHb and second lactate levels.

Conflict of Interest: The authors declare that there is no conflict of interest.

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Authors' Contribution: GOY: Conceptualization, methodology, writing-final draft, supervision **AKA:** Conceptualization, methodology, writing-final draft, supervision. **EA:** Conceptualization, methodology, data curation, formal analysis, writing original draft

Ethical Approval: Ethical approval was obtained from the SBÜ Tepecik Training and Research Hospital Non-Interventional Clinical Research Ethics Committee before the study (Decision No. 2023/04-20.).

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