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USE OF LACTATE CLEARANCE IN DETERMINING SERUM LACTATE LEVELS AND EFFECTIVENESS OF TREATMENT IN CARBON MONOXIDE POISONINGS

Karbon Monoksit Zehirlenmelerinde, Serum Laktat Düzeyleri ve Tedavinin Etkinliğinin Belirlenmesinde Laktat Klirenslerinin Kullanılması

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ABSTRACT

Objective: This study aims to determine the feasibility of using the rate of lactate clearance to evaluate the metabolic response to treatment in patients with carbon monoxide (CO) poisoning after their lactate levels were measured on initial presentation to the emergency department (ED).

Material and Methods: Patients older than 18, who presented with CO poisoning to the ED of Ankara Training and Research Hospital between November 2010 and February 2011 were enrolled in the study. Lactate levels upon admission (Lactate-1) and after 6 hours of treatment (Lactate-2) were compared to calculate the lactate clearance rate. Lactate levels of 1.7 mmol/l or greater were considered as positive.

Results: A total of 100 patients were enrolled in the study (62 females and 38 males). We found that 94% of patients had elevated lactate levels on admission to the ED. When lactate levels and CO values were compared, the CO values were found to be significantly higher in the elevated lactate level group compared to non-elevated patients. The rate of lactate clearance was 52% in the standard oxygen therapy group compared to 64% in the hyperbaric oxygen therapy (HOT) group, which suggests a faster removal of lactate with this treatment modality.

Conclusion: We conclude that lactate levels increase in patients with CO poisoning, and that those levels are correlated with carboxyhemoglobin (COHb) levels. The rate of lactate clearance can be used to evaluate the effectiveness of therapy. Patients with metabolic acidosis and significantly increased lactate should be referred for HOT in early phases of management.

***Keywords**: Lactate, lactate clearance, carbon monoxide poisoning*

ÖZ

Amaç: Bu çalışmanın konusu karbon monoksit (CO) zehirlenmelerinde, başvuru anındaki laktat düzeylerinin ölçülmesi ve 6 saat sonra alınan laktat düzeylerine göre laktat klirens hızına bakarak tedavide metabolik cevabı değerlendirilmesindeki kullanılabilirliğini belirlemektir.

Gereç ve Yöntemler: Ankara Eğitim ve Araştırma Hastanesi Acil servise, Kasım 2010- Şubat 2011 tarihleri arası CO zehirlenmesi nedeniyle başvuran 18 yaş üstü hastalar dâhil edildi. Geliş laktatı (laktat 1) ve 6. saatteki laktat (laktat 2) sonuçlarından laktat klirensi hesaplandı. Laktat> 1.7 mmol/lt ve üzeri pozitif kabul edildi.

Bulgular: Çalışmaya 100 hasta dâhil edilmiştir. Hastaların %62'si kadın, %38'i erkektir. Hastaların %94'ünde hastaneye başvuru anlarındaki laktat oranları yüksekti. Hastaların laktat düzeyleri ile CO seviyelerine bakıldığında, laktat düzeyi yüksek olan grupta, normal olan gruba göre CO düzeyi anlamlı olarak daha büyüktü. Standart oksijen tedavisi alan grupta laktat klirensi %52 iken hiperbarik alan grupta %64 idi ve bu durum hiperbarik oksijen tedavisi alan grupta laktatın ortadan kaldırılması daha hızlı olduğunu göstermektedir.

Sonuç: Bizim çalışmamıza göre CO zehirlenmelerinde laktat yükselmektedir ve düzeyleri karboksi hemoglobin (COHb) düzeyleri ile koreledir. Tedavi etkinliğini değerlendirmede laktatklirens hızı kullanılabilir. Özellikle belirgin laktat yüksekliği ve metabolikasidozu olan hastalar erken dönemde hiperbarik oksijen tedavisine gönderilmelidir.

***Anahtar Kelimeler**: Laktat, laktat klirensi, karbon monoksit zehirlenmesi*

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INTRODUCTION

Carbon monoxide (CO) poisonings are among the clinical problems seen in emergency departments (ED) with significant mortality and morbidity rates. CO poisoning causes hypoxia because the CO molecule binds to hemoglobin with high affinity of oxygen, reduces the oxygen-carrying capacity of the blood, and finally damages delivery of the oxygen to tissue (1,2). The partial oxygen pressure (PaO2) and partial carbon dioxide pressure (PaCO2) levels in the blood gas analysis and oxygen saturation levels are usually measured as normal; however, this condition does not accurately reflect the tissue hypoxia (1,5-7). Metabolic acidosis can develop secondary to lactic acidosis, which is seen following ischemia in CO poisonings (5). This study aims to determine the feasibility of using the rate of lactate clearance to evaluate the metabolic response to treatment in patients with CO poisoning after their lactate levels were measured on initial presentation to the ED.

MATERIALS AND METHODS

Patients, older than 18, who consecutively presented with CO poisoning to the emergency department of Ankara Training and Research Hospital between November 2010 and February 2011, and who consented to participate, were accepted into the study. Patients with venous blood carboxyhemoglobin levels greater than 8 upon presentation were considered as suffering from CO poisoning. All blood analysis used a Roche Cobas 221. All study patients were initially evaluated in the ED and those with indications of hyperbaric oxygen therapy (HOT) were referred to specialty centers. Others with no indication for HOT were treated with supplemental O_2 via non-rebreather masks at 10 lpm. Blood lactate levels were measured following 6 hours of treatment. 2.5 atmospheres absolute pressure (ATA) was used during HOT for three sessions which were one day apart, and a second round of blood lactate levels were measured in these patients after the HOT. Lactate levels upon admission (Lactate-1) and after 6 hours of treatment (Lactate-2) were compared to calculate the lactate clearance rate. Six-hour lactate clearance was calculated as (Lactate start − lactate 6 hour) / lactate start (%). Lactate levels of 1.7 mmol/l or greater were considered as positive.

Statistical Analysis

Data analyses were performed with SPSS for Windows (v.11.5). Distribution of continuous variables was analyzed with the Shapiro-Wilk test. Descriptive statistics are presented as mean ± standard deviation, mean ± standard deviation (minimum-maximum) or median (minimum-maximum), whereas categorical variables are shown as number of cases and percentages. The significance of inter-group means was analyzed using Student's t-test, and the significance of variations in inter-group median values was analyzed using the Mann-Whitney U test. Nominal variables were tested with Fisher's exact test. Spearman's correlation test was used to test for statistically significant correlation in continuous variables. A value of $p<0.05$ was considered significant in all tests.

RESULTS

A total of 100 patients were enrolled in the study (62 females and 38 males). The most common main complaint on admission was headache. Fifteen percent of the patients were referred for HOT. Patient demographics are given in Table 1.

When lactate levels and CO values were compared, the CO values were found to be significantly higher in high-lactate group ($p=0.013$) (Table 2).

There was a significant positive correlation between the Lactate-1 levels and CO values ($r=0.588$ and $p<0.001$). There was also a positive correlation

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between lactate clearance level and CO values (r=0.310 and p=0.002) (Table 3).

The median Lactate-1 and lactate clearance levels in the group receiving HOT were significantly higher compared to the group not receiving HOT (p<0.05). However, there was no significant difference noted between groups in terms of the Lactate-2 levels as well as levels of Lactate-1 and-2 being above 1.7 (p>0.05) (Table 4).

A significant reduction was observed in Lactate-2 levels compared to Lactate-1 in the group that received standard oxygen therapy (p<0.001). Similarly, a significant reduction in Lactate-2 levels compared to Lactate-1 was also detected in the group that received HOT (p<0.001). The amount of reduction in the HOT group was significantly higher than that of the non-HOT group (p=0.018) (Table 5).

Table 1: Patient distribution based on age, sex GCS, clinical findings, hyperbaric oxygen therapy, CO and lactate levels

Variables	n=100
Age [mean±SD (minimum-maximum)]	41.8±16.0 (19-82)
Sex M/F	n=62/n=38
GCS [median (minimum-maximum)]	15 (3-15)
Clinical Findings	
Headache [n (%)]	58 (58)
Dizziness [n (%)]	40 (40)
Syncope [n (%)]	18 (18)
Nausea/Vomiting [n (%)]	32 (32)
Hyperbaric oxygen therapy [n (%)]	15 (15)
CO levels [mean±sd (minimum-maximum)]	27.2±8.9 (4.1-56.2)
1st Lactate > 1.7 [n (%)]	94 (94)
2nd Lactate > 1.7 [n (%)]	39 (39)

SD: standard deviation GCS: Glasgow coma scale

Table 2: CO values based on lactate levels

Variables	CO value	p-value
Lactate level on admission		
≤1.7	18.5±6.38	0.013
>1.7	27.7±8.76	

Table 3: Correlation coefficients and levels of significance between lactate, lactate clearance and CO levels

Variables	Correlation coefficient	p-value
Lactate 1	0.588	<0.001
Lactate clearance	0.310	0.002

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Table 4: Levels of Lactate-1, Lactate-2 and lactate clearance in HOT and non-HOT groups

Variables	Did Not Receive HOT (n=85)	Received HOT (n=15)	p-value
Lactate 1	3.2 (0.9-11.2)	5.4 (2.1-19.1)	<0.001
Lactate 1 >1.7	79 (92.9%)	15 (100.0%)	0.587
Lactate 2	1.6 (0.6-4.7)	1.5 (0.7-5.9)	0.411
Lactate 2 >1.7	32 (37.6%)	7 (46.7%)	0.509
Lactate clearance (%)	52 (-21 – 84)	64 (32 – 87)	0.030

HOT: Hyperbaric oxygen therapy

Table 5: Percentage change in initial and follow-up lactate levels

Variables	Lactate 1	Lactate 2	p-value *	Lactate change	p-value **
Not received HOT	3.2 (0.9-11.2)	1.6 (0.6-4.7)	<0.001	-50.0 (-84.8 – 21.7)	0.018
Received HOT	5.4 (2.1-19.1)	1.5 (0.7-5.9)	<0.001	-64.9 (-86.8 – 25.7)	

* Comparisons of Lactate-1 and Lactate-2 in groups

** Comparisons in groups based on percentage changes between Lactate-2 and Lactate-1.

DISCUSSION

In patients with carbon monoxide (CO) poisoning, there was a correlation between initial clinical severity on admission and blood lactate levels. Recently, it is suggested that lactate level may be a useful prognostic factor in a case report (5). Other studies have also discussed the relationship between lactate increase and clinical findings in tissue hypoxia resulting from CO poisoning. Benaissa et al. detected significantly elevated lactate levels in CO poisoning cases accompanied by neurological symptoms; however, they determined that the clinical significance of this finding is questionable, as the level of increase was low (8). Sokal et al. reported that lactate levels were significantly higher in severe CO poisoning compared to mild cases (9). We found that 94% of patients had elevated lactate levels on admission to the ED. When lactate levels and CO values were compared, the CO values were found to be significantly higher in the elevated lactate level group compared to non-elevated patients. This indicates that metabolic dysfunction is more severe in patients exposed to greater levels of CO for longer duration. Inoue et al. reported that initial lactate levels can be related to the clinical course and outcome, and can therefore be used as a useful marker for the clinical course of the patients (10).

Following the concept of "Early-Goal-Directed-Therapy" (EGDT), therapeutic approaches should aim to achieve a lactate clearance greater than 20% within 6 hours of treatment (11-13). This metabolic goal is acceptable when the lactate overproduction reflects a hypermetabolic state, as in septic patients or acute cardiorespiratory failure. However, LACT-6h-clearance is less useful in assessing the response to treatment when an increase in lactate occurs rapidly. When we evaluated the response to therapy in our study group, we observed that the 'Lactate-2' levels, measured 6 hours after initial presentation, were significantly reduced in both the standard oxygen therapy group (treated with 100% oxygen at 10 lpm) and HOT group compared to their initial 'Lactate-1' levels ($p<0.001$). The rate of lactate clearance was 52% in the standard oxygen therapy group compared to 64% in the HOT group, which suggests a faster removal of

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lactate with this treatment modality. Indeed, the amount of lactate reduction in HOT group was found to be significantly higher than the standard oxygen therapy group (p=0.018). HOT is indicated in severe CO poisonings, determined by the patient's clinical presentation and COHb levels. The purpose of HOT is not only to treat the acute symptoms, but also to prevent late-term neuropsychiatric conditions. The mechanisms for faster clearance of lactate in HOT are as follows: its ability to promptly normalize mitochondrial oxidative reactions, to improve tissue oxygenation by removing carbon monoxide molecules from hemoglobin, and to reduce the formation of free radicals (14). This shows that patients with elevated lactate levels and metabolic acidosis on initial evaluation can be referred to specialty centers for early HOT, even when there are no clinical indications for such therapy.

We conclude that lactate levels increase in patients with CO poisoning, and that those levels are correlated with COHb levels. The rate of lactate clearance can be used to evaluate the effectiveness of therapy. Patients with significantly increased lactate and metabolic acidosis should be referred for HOT in early phases of management.

Limitations

We have not differentiated the source of CO in our study. Cyanide poisoning can simultaneously present with CO poisoning in patients suffering from smoke inhalation. The literature indicates that lactate levels are even more elevated in smoke inhalation patients suffering from both CO and cyanide poisoning. We did not measure blood cyanide levels in our patients and did not differentiate the source of poisoning in the present study.

Conflict of Interest

The authors declare that there is no actual or potential conflict of interest.

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