

T.C.
ERCIYES ÜNİVERSİTESİ
BİLİMSEL ARAŞTIRMA PROJELERİ
KOORDİNASYON BİRİMİ



PROJE BAŞLIĞI

Karbonmonoksit Zehirlenme Şiddetinin Kan Copeptin Düzeyi ile Belirlenmesi

Proje No
3989

Proje Türü
N. Araştırma

SONUÇ RAPORU

Proje Yürütücüsü
Polat Durukan
Tıp Fakültesi/ Acil Tıp Anabilim Dalı

Araştırmacı
Polat Durukan
Tıp Fakültesi/ Acil Tıp Anabilim Dalı

Mayıs 2018
KAYSERİ

Bu Proje Erciyes Üniversitesi BAP birimi tarafından desteklenmiştir. Kendilerine teşekkür ederiz.

İÇİNDEKİLER

	Sayfa No
Özet	4
Abstract	4
Introduction	5
Material Methods	5
Results	6
Discussion	7
Conclusion	8

Özet

Giriş: Çalışmamızın amacı; karbonmonoksit zehirlenmesi ile acil servise başvuran hastalarda Copeptin plazma düzeylerinde bir değişiklik olup olmadığını ve karboksemoglobin, laktat ve copeptin düzeylerinin plazma düzeyleri arasında bir ilişki olup olmadığını belirlemektir.

Gereç ve Yöntem: Çalışmaya 18 yaşından büyük ve acil servise karbonmonoksit zehirlenmesi ile başvuran yedi hasta dahil edildi. Hastaların kan örnekleri, varışta, 6. ve 12. saatlerde, copeptin, laktat ve COHb düzeyleri için toplandı. Veriler SPSS-17 istatistik yazılımı kullanılarak analiz edildi.

Bulgular: Acil servise karbonmonoksit zehirlenmesi ile başvuran hastaların yaş ortalaması $37,2 \pm 16,1$ yılı, ve % 57,9'u kadındı. Bir ya da daha fazla semptom, hastaların% 89,5'inde görüldü ve en sık görülen semptom, baş ağrısıydı(% 73,7). Hastaların % 96,5 'i maruziyet kaynağı olarak bir kömür sobası bildirilmiştir. Hastaların serum copeptin düzeyleri sağlıklı bireylerin copeptin düzeyleri ile karşılaştırıldı ve aralarında istatistiksel olarak anlamlı bir fark bulundu. Bununla birlikte, sağlıklı bireylerin copeptin düzeyleri arasında anlamlı bir fark yoktu.

6. ve 12. saatlerde zehirlenmiş hastaların seviyeleri İstatistiksel olarak anlamlıydı

Copeptin varış seviyeleri ile 6, 12. saatlerde copeptin düzeyleri arasındaki fark vardı. 6. ve 12. saatlerde ise copeptin düzeyleri arasında anlamlı fark yoktu. Serum laktat seviyeleri açısından; varış ile 6. saat, varış ve 12. saat, 6. ve 12. saat arasında önemli bir fark vardı. Benzer şekilde, serum COHb seviyeleri açısından; varış ile 6. saat, varış ve 12. saat, 6. ve 12. saat arasında anlamlı bir fark vardı. Vardıklarında COHb ve laktat seviyeleri arasında pozitif bir korelasyon vardı. Bununla birlikte, serum copeptin düzeyleri ile COHb, laktat seviyeleri arasında bir ilişki saptanmadı.

Sonuç: Serum copeptin düzeyleri karbonmonoksit zehirlenmesinde artmış ve tedavi ile normal seviyelere gerilemiştir. Acil servise varışta serum laktat ve COHb düzeyleri arasında pozitif korelasyon vardır. Bununla birlikte, serum copeptin düzeyleri ile COHb ve laktat seviyeleri arasında korelasyon saptanmadı.

Anahtar Kelimeler: CO zehirlenmesi, copeptin, prognoz

Abstract

Introduction:The aim of our study is; determine whether there is a change in the plasma levels of copeptin and is there a relationship among the plasma levels of carboxyhemoglobin (COHb), lactate and copeptin levels in patients presenting to the emergency department with carbonmonoxide poisoning.

Material Methods: Fifty-seven patients who are older than 18 years old and admitted to the emergency department with carbonmonoxide poisoning were included in the study. The blood samples of the patients were collected on arrival (0th), 6th and 12th hours for copeptin, lactate and COHb levels. Data were analyzed by using SPSS-17 statistical software.

Results: Arrival serum copeptin levels of the patients were compared to copeptin levels of healthy individuals and a statistically significant difference was found between them. However, there was no significant difference between the copeptin levels of healthy individuals and copeptin levels of the poisoned patients at 6th and 12th hours. There was a

statistically significant difference between the arrival levels of copeptin and 6th, 12th hours levels of copeptin ($p < 0.05$). There was no significant difference between 6th and 12th hours copeptin levels ($p > 0.05$). In terms of serum lactate levels; there was a significant difference between arrival and 6th hours, arrival and 12th hours, 6th and 12th hours ($p < 0.05$). Likewise, in terms of serum COHb levels; there was a significant difference between arrival and 6th hours, arrival and 12th hours, 6th and 12th hours ($p < 0.05$). There was a positive correlation between COHb and lactate levels on arrival ($r = 0.52$; $p = 0.00$). However, there was no correlation detected between serum copeptin levels and COHb, lactate levels.

Conclusion: We believe that; plasma copeptin levels can be used in clinical diagnosis of acute CO poisoning in the emergency department.

Key Words: CO intoxication, copeptin, prognosis

Introduction

Carbon monoxide poisoning is still a significant cause of morbidity and mortality all around the world. Every year, especially in the fall and winter seasons, thousands of people die due to carbon monoxide poisoning. CO could show its toxic effect with several mechanisms. The most important of these is the tissue hypoxia. It shows this effect with binding to the respiratory pigments such as; hemoglobin and myoglobin and some enzymes which located in oxidative processes. Elevated serum lactate level is detected in CO poisoning in addition to ischemia. Copeptin is the precursor of arginine vasopressin (AVP). It is located on the C-terminal fragment of the pro-vasopressin. Copeptin is released concomitantly with vasopressin from the hypothalamus. Release of copeptin increases with stress response and there is a strong association between the level of copeptin and severity of illness (1,2). In the previous studies, it has been determined that; there is a relationship between the level of copeptin and severity of the diseases such as; respiratory tract infection, cardiac insufficiency, multiple organ failure and ischemia. There are also studies that show the association between copeptin level and subarachnoid hemorrhage (3), traumatic brain injury (4) and ischemic stroke (5). But there is limited data on serum copeptin level and CO poisoning. Copeptin results are available within one hour, which is crucial for any useful biomarker in the emergency department setting (2).

As a product of anaerobic glycolysis, lactic acid is related to insufficient oxygen supply and it may be used as a prognostic parameter for the patients with CO poisoning. There are also studies which concluded that; serum lactate level can be used as a prognostic biomarker in CO poisoning (6,7).

The main purpose of our study was to investigate whether there is any difference in serum levels of copeptin in the patients admitted to the emergency department with carbon monoxide poisoning. Our second objective is to determine whether there is a relationship between COHb, copeptin and lactate levels in CO poisoning.

Material Methods

This study was conducted at a tertiary care university hospital emergency department with an annual 90,000 patient admission. Fifty-seven patients who are older than 18 years old and

admitted to the emergency department with carbon monoxide poisoning were included in the study. As an inclusion criteria, CO poisoning was defined as COHb levels 5% in non smokers and 10% in smokers with clinical symptoms. Exclusion criteria were; patients younger than 18 years old, sepsis, heart and lung disease history, acute and chronic renal insufficiency, cardiovascular problems and cerebrovascular events.

The age, gender, vital signs, symptoms, blood parameters of the patients were recorded previously created form. Blood samples of the patients were collected on arrival, 6th and 12th hours for copeptin, lactate and COHb levels. Three milliliter blood sample was collected in a tube with ethylenediaminetetraacetic acid (EDTA). After shaking the tube, the blood was transferred to centrifuge tube and blood serum was separated by centrifuging for 10 minutes at 3,500 round per minute (rpm). The samples were stored in -70 ° C until the biochemical analysis. Human copeptin test kit (code: EK-065-32) of Phoenix Pharmaceuticals, Inc. Was used to analyse the copeptin level with sandwich ELISA method. Serum copeptin levels were measured quantitatively

Data of the study were analyzed using SPSS-17 statistical software. Normal distribution of data was evaluated by using One-Sample Kolmogorov-Smirnov test. Friedman test was used to compare the levels of copeptin, lactate and COHb in the study period (0th, 6th and 12th hours). $p < 0.05$ was considered statistically significant. Posthoc Bonferroni correction method was applied to the test. Pairwise comparisons of copeptin, lactate and COHb with in themselves were performed by using Wilcoxon test. $p < 0.017$ was considered statistically significant. In order to determine the correlation of copeptin, lactate and COHb with each other, Spearman correlation test was used.

Results

The mean age of the patients presenting to the emergency department with CO intoxication was $37,2 \pm 16,1$ year and 57.9% were female. 89.5% of the patients were symptomatic. When the patient were evaluated in terms of symptoms; 73.7% headache, 42.1% nausea and vomiting, 40.4% dizziness, 21.1% altered mental status, 15.8% dyspnea, 14% fainting, 8.8% blurred vision, 7% abdominal pain, 3.5% chest pain, 1.8% ataxia identified. 96.5% of the patients reported a coal stove as the sources of exposure (Table 1). Only 4 (7%) patients' electrocardiogram (ECG) were remarkable. The rests' ECG was normal. For the patients who underwent brain computerized tomography scan due to altered level of consciousness, there was no pathological findings. There was statistically significant difference between the serum copeptin level of patients' admission and healthy individuals ($p = 0.008$). But there was no significant difference between patients' 6th and 12th hour serum copeptin levels and healthy individuals' serum copeptin levels ($p > 0.05$) (Table 2). Patients' 0th, 6th and 12th hours serum copeptin levels were compared with each other by using Friedman test. There was no statistically significant difference ($p = 0.05$). When the groups were evaluated as pair; there was statistically significant difference between the 0th to 6th hours and 0th to 12th hours serum levels of copeptin ($p < 0.017$). But there was no significant difference between the serum levels of copeptin on 6th and 12th hours (Table 3).

0th, 6th and 12th hours serum lactate levels of the patients were compared to each other by using Friedman test. There was statistically significant difference among the groups (p

<0.05).When the groups were evaluated as pair; there was statistically significant difference between the 0th to 6th hours and 6th to 12th hours serum levels lactate ($p < 0.017$) (Table 3).

Patients' 0th, 6th and 12th hours serum COHb levels were compared with each other by using Friedman test. There was statistically significant difference ($p < 0.05$).When the groups were evaluated as pair; there was statistically significant difference between the 0th to 6th, 0th to 12th and 6th to 12th hours serum levels of COHb ($p < 0.017$) (Table 3).

When the correlation among copeptin, lactate and COHb levels were evaluated; there was just revealed a positive correlation between lactate and COHb levels in the arrival ($r = 0.52$; $p = 0.00$). There was no positive correlation observed between copeptin, lactate and COHb levels on 0th, 6th and 12th hours.

There was no statistically significant difference between the patients with and without changes in consciousness in terms of plasma copeptin levels ($p > 0.05$).A statistically significant difference was found between the patients with and without changes in consciousness in terms of COHb levels and blood lactate levels ($p < 0.05$) (Table 5).

Discussion

Carbonmonoxide poisoning is a medical emergency with high mortality among acute poisoning cases. This is the primary cause of tissue hypoxia and multiorgan failure (8). Copeptin consists of a 39 amino acid sequence of glycoprotein and serves as a new biomarker (8). Secretion of copeptin from the hypothalamus increases as part of a stress response (9). Its relatively high sensitivity but poor specificity (8). Copeptin may provide crucial information for risk stratification in a variety of clinical situations (2).In the literature, we could reach very limited study of plasma copeptin levels in CO poisonings.

In our study it was detected that; there is a significant difference between the serum copeptin levels of healthy individuals and poisoned patients' arrival copeptin levels.Pang et al. were reported that; plasma copeptin levels of patients with CO intoxication were significantly higher than those of healthy subjects (9).Li J. et al. have determined that; the first 2 hours plasma copeptin levels of the patients with acute CO poisoning had significantly higher than healthy subjects (8). Our result was compatible with these two studies.

When the patients groups were evaluated as pair; there was statistically significant difference between the 0th to 6th hours and 0th to 12th hours serum levels of copeptin ($p < 0.017$). But there was no significant difference between the serum levels of copeptin on 6th and 12th hours. Plasma copeptin levels increase in the early stages of acute developing diseases(10,11). Plasma copeptin levels may regress to normal levels in the early period of the treatment.We think that; this condition may be associated with a relative decrease in the copeptin levels with treatment.

Chai et al. Reported that; the level of plasma copeptin increased in 0-4 hours in acute MI, and decreased after the 6th hour (11).Ipekci et al. have shown that; plasma copeptin levels are high at the time of admission in patients with multitrauma and that they decreased in the early phase of treatment (10).In our study, plasma copeptin level was found to be high in the first hours of CO poisoning and started to decrease with treatment. Also in this study; it was observed that; increased plasma copeptin levels in CO poisoning were decreased to normal levels earlier than other parameters.

Carbon monoxide has an affinity to hemoglobin more than 200 times from oxygen. It causes tissue hypoxia because of lower oxygen delivery capacity of blood. This situation affects especially brain and heart, because these organs are very sensitive to hypoxia (12). In the study of Pang et al. (9) it has been reported that; there is a significant difference in plasma copeptin levels between unconscious and conscious groups. Also in the study of Pang et al. (9) it has been shown that; plasma copeptin levels could be used as a novel biomarker for predicting delayed neurological sequelae after acute CO poisoning. In our study; no significant difference was observed between the plasma copeptin levels of patients with altered mental status and without. We think that; low number of patients may be a factor in this situation, and also we did not investigate the delayed neurological sequelae of the patients.

The relationship between severity of clinical signs and increased serum lactate levels as an indicator of tissue hypoxia were investigated in CO poisoning. In the study of Benaissa et al. (13) it was reported that; there is a significant association between serum lactate levels and the severity of neurological impairment in CO poisoning although plasma lactate levels were mildly elevated in their study population. In another study, it has been reported that; lactate levels are significantly higher in severe CO poisoning compared to mild poisoning (14). Moon et al. (15) reported that; serum lactate levels could reflect the severity of CO poisoning. And also it is insisted that; COHb levels are not useful predictor in CO poisoning due to the reasons such as; delayed sampling and preoxygenization before arrival (13). In our study, it has been determined that; there are significant elevated lactate levels in patients with CO poisoning. However, in our study; significant difference was observed between the blood lactate levels of patients with altered mental status and without.

In the study of Icme et al, it was determined that; there is a positive relationship between blood lactate and COHb levels (16). This study, there was a positive correlation between arrival blood lactate and COHb levels of patients. This result was consistent with the results of Icme et al (16). However, there was no significant correlation between blood lactate and copeptin levels in terms of 6th and 12th hours in our study.

We also found no significant correlation between plasma copeptin levels and COHb-lactate levels in our study. This may be due to the fact that the level of copeptin decreases to the normal level earlier than the other two parameters. At the same time, the number of cases included in the study may also have affected the outcome. We couldn't find any other study related to this subject in the literature. All the patients included in the study were discharged from the emergency service with the complete healing after the treatment. We think that; early decrease to the normal levels of plasma copeptin levels compared to COHb and lactate levels in acute CO poisoning can be used to evaluate the early response to treatment.

In conclusion; serum copeptin levels increase in carbon monoxide poisoning and decrease to normal levels with treatment. There is a positive correlation between serum lactate and COHb levels in CO poisoning on arrival to the emergency department. However it was unable to observe a correlation between copeptin, COHb and lactate levels.

Quick decrease in plasma copeptin levels compared to COHb and lactate levels with treatment may allow early detection of response to treatment. We believe that; plasma copeptin levels can be used in clinical diagnosis of acute CO poisoning in the emergency department.