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Investigation of The Relationship Between Carboxyhemoglobin Level and End-Tidal Carbon Dioxide In Carbon Monoxide Poisoning

Ramazan Sami Aktaş[1*], Polat Durukan[2], Sadi Elasan[3]

[1]Department of Emergency Medicine, Faculty of Medicine, Van Yüzüncü Yıl University, Van, Turkey
[2]Department of Emergency Medicine, Medical Faculty Hospital, Erciyes University
[3]Department of Biostatistics, Medical Faculty Hospital, Yuzuncu Yıl University

ABSTRACT

Carbon monoxide (CO) poisoning makes up an important part of deaths due to poisoning in the world. It may be hard to diagnose CO poisoning if it is not suspected because the clinical features are non-specific. We wanted to investigate the effects of end-tidal carbon dioxide ($ETCO_2$) measurement in expirium on the diagnosis and follow-up of CO poisoning.
After the patients were diagnosed as having CO poisoning by taking arterial blood gas from patients who were suspected of having CO poisoning, $ETCO_2$ was measured using the sidestream method. The data were analyzed using the SPSS (IBM SPSS for Windows, ver.23) statistical package program.
One hundred fourty six146 patients, 106 with CO poisoning and 40 control cases, were included in the study. After the demographic data were evaluated, the relationship between $ETCO_2$ and carboxyhemoglobin (COHb) was analyzed. No statistically significant difference was found.
To the best of our knowledge, this is the first study to look for a relationship between $ETCO_2$ and COHb. More studies are required to investigate the relationship between $ETCO_2$ and COHb.
The study was conducted in a single centre with a few patients. Only the sidestream method was used in the measurement of $ETCO_2$. The parameters affecting respiratory physiology could not be excluded completely.

Keywords: Emergency service, carbon monoxide poisoning, capnometer

Introduction

Carbon monoxide (CO) poisoning constitutes an important part of deaths due to poisoning in the world. Carbon monoxide poisoning handles about two-thirds of accidental poisoning. In the United States of America, approximately 50,000 patients with CO poisoning are admitted to hospitals every year, and 1000-2000 of them are reported to have died (1). The toxic effect of CO gas on tissues was first demonstrated by Bernard in 1957, and later the pathophysiologic mechanism of CO poisoning was described by Haldane in 1895 (2). Poisoning can be seen in every region but is more common in areas where ventilation is inadequate and in cold climates (3). The CO gas that is inhaled from the outside quickly passes into the intravascular area and rapidly binds to hemoglobin (Hb) because CO's affinity to Hb is about 200-240 greater than oxygen (O_2). Thus, partial oxygen pressure (PO_2) decreases, and hypoxia occurs (3-4). Although mortality and morbidity rates vary according to the severity and duration of poisoning, the mortality rate was 4.3% in a study conducted in the USA in 2018 (1). In severe poisoning, the mortality rate could increase up to 30%, and the rate of permanent damage was determined as 11% in patients who survived (5). Clinical findings in CO poisoning are quite broad and nonspecific. Patients may be admitted to the emergency room with various symptoms ranging from headache to coma (6). The most common symptoms are headache, dizziness, nausea/vomiting, confusion, fatigue, chest pain, and tachypnea (7).

The amount of carbon dioxide (CO_2) in respiration is measured with end-tidal carbon dioxide ($ETCO_2$) (8). The measurement of CO_2 density at the end of the expirium is performed using a capnometer. Capnography comprises continuous analysis and recording of CO_2 in

***Corresponding Author:** Ramazan Sami Aktaş, Department of Emergency Medicine, Faculty of Medicine, Van Yüzüncü Yıl University, Van, Turkey
E-mail: ramazansamiaktas@gmail.com
ORCID ID: Ramazan Sami Aktaş: 0000-0003-1072-382X, **Polat Durukan:** 0000-0002-8388-7166, **Sadi Elasan:** 0000-0002-3149-6462
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respiratory gases. Capnometry suggests measurement (ie, analysis alone) without a continuous written record or waveform (9). There are two types of measurements of CO_2 as sidestream and mainstream. The mainstream method is a measurement technique using a CO_2 sensor placed directly in the patient's airway. The sidestream method is the measurement technique performed from samples taken through a catheter (10). This non-invasive method, first used by Smallhout and Kalenda in the 1970s, was reported to give information about the patient's metabolic status, perfusion, and ventilation, instantaneously (11).

Capnography is more commonly used in emergency service for various conditions such as cardiopulmonary resuscitation, airway management, sedo-analgesia, pulmonary diseases, heart failure, shock, metabolic diseases, gastroenteritis, and trauma (12). The American Heart Association (AHA) has stated that it is one of the valid methods to be used besides clinical evaluation for confirmation of intubation in the 2015 guideline for resuscitation (13).

We wanted to investigate the effects of $ETCO_2$ measurement on the diagnosis and treatment of patients with CO poisoning, which is based on the negative effect of decreased production of CO_2 gas due to hypoxia on $ETCO_2$ in CO poisoning, and which is increasingly used in emergency services because of its ease of use, high reliability, low cost, and the possibility of instantaneous evaluation it gives.

Materials and Methods

This study was conducted prospectively in patients admitted to a tertiary emergency department with CO poisoning over a 15-month period. The patients were informed about the study after obtaining approval from the ethics committee, with approval no. 2014/50 study data were collected by one physician, and the patients were followed up by the same physician.

Our study did not include patients aged under 18 years, those with lung disease, and those with other conditions (fever, pregnancy) that could affect respiratory physiology.

In this study, 106 patients who were admitted with CO poisoning were included in the study group and 40 patients who were admitted because of other causes were included in the control group. Patients who were admitted to the emergency department and were suspected of having CO poisoning had their diagnosis confirmed according to the results of blood gas got from radial and/or femoral arteries. Blood gas was taken using an insulin injector washed with heparin and was immediately assessed without delay using a 'Siemens brand rapidlab 1265' blood gas device located in the emergency service.

After the diagnosis of CO poisoning was made in the patients, $ETCO_2$ measurement was performed using the sidestream method via a cannula connected to "PM-9000GTA" model headboard monitors and recorded as numeric data. The average of the maximum values seen at the end of 5 expiriums was used in the measurement of $ETCO_2$. The treatment was started using normobaric oxygen therapy (NBOT) given with a reservoir mask. Patients were monitored and both COHb and $ETCO_2$ levels were measured in blood gas at 0 (admission), 6, 12, and 24 hours. The demographic data of the patient were got on admission, and vital findings were recorded simultaneously. The medical history of the patients was questioned and those with diseases affecting CO_2 production were excluded from the study; those with other diseases were included. The source of CO in the patients, occupations, and symptoms were recorded. In order to confirm that there was no CO poisoning in the control group, arterial blood gas was taken and COHb levels were measured, and the patients were included in the study if the results were normal.

Statistical Analysis: In the sample's calculation size of our study, the power of test was taken at least 80% and the Type-1 error was 5%. The normality distributions of the measurements were examined with Shapiro-Wilk ($n<50$) and Skewness-Kurtosis tests, and since the measurements showed normal distribution, parametric tests were applied. The descriptive statistics for continuous (quantitative) variables in the study were expressed mean and standard deviation. The independent (student's) T-Test was used in the mean's comparison of the continuous variables between the groups. Pearson's correlation coefficients were calculated separately in each group to determine the relationship between the variables. The statistical significance level in calculations was taken as 5% and the SPSS (IBM SPSS for Windows, ver.23) statistical package program was used in the calculations.

Results

One hundred forty-six patients (106 patients with CO poisoning and 40 patients as controls) were included in the study. The mean age of the patients with CO poisoning and control group was 40.3±15.7 and 60.5±14.9 years, respectively. The male/female ratio was 1/3 in the patients with CO poisoning. Of the patients with CO poisoning, 16 had hypertension, 12 had diabetes mellitus, 2 had coronary artery disease, 2 had a stroke, 21 had other diseases, including rheumatologic and hematologic diseases and skin diseases. The means of the vital signs at admission are summarized in Table 1.

According to the results in Table 1, there was a statistically significant difference between the groups in terms of "respiratory rate" and "body temperature" ($p<0.05$). According to this, while the "respiratory rate" was higher in the "patient" group, the "body temperature" was higher in the "control" group. However, no significant difference was observed between the groups in the "TA" and "pulse rate" measurements.

Most of the patients admitted to the emergency service with CO poisoning had a few nonspecific symptoms. The frequency of symptoms is summarized in the chart below. The most common symptom was a headache.

Of the patients with CO poisoning, 49 (46.2%) were unemployed, 12 (13.2%) were students, 4 (3.8%) were civil servants, 18 (17%) were manual workers, and 21 (19.8%) were from other professions. There were no cases of occupational injury.

In 97 (91.5%) of the patients, a stove was the source of CO poisoning. CO poisoning was due to fire in 6 (3.8%) and narghile (water pipe) smoking in 3 (2.9%) patients.

According to the results in Table 2, there was a statistically significant difference between the groups in terms of "COHb % at admission" and "COHb % at 6 hours" ($p<0.05$). According to this; COHb % at admission" and COHb % at 6 hours" measurements were higher in the Patients" group. However, no significant difference was observed between the groups in the "COHb % at 12 hours" and "COHb % at 24 hours" measurements. When these results are considered, it is understood that the COHb" value decreases with time.

According to the results in Table 3, there was a statistically significant difference between the groups in terms of "ETCO2 at 6 hours" and " ETCO2 at 12 hours " ($p<0.05$). According to this, ETCO2 at 6 hours" and ETCO2 at 12 hours" measurements were higher in the Control" group. However, no significant difference was observed between the groups in the " ETCO2 at admission " and " ETCO2 at 24 hours" measurements.

In Table 4, the results of the correlation analysis between the "COHb" and "ETCO2" measurements are given. According to this, A 7% relationship between COHb at admission" and ETCO2 admission" was not statistically significant ($p>0.05$). Similarly, no statistically significant relationship was found between these binary variables measured in all other periods.

Discussion

Carbon monoxide poisoning makes up an important part of the poisonings in the world. Because of factors such as climate characteristics of countries and regions, heating systems, fossil fuel use, industrialization, and motor vehicle use rate, the true incidence is not clearly known. Especially during the winter months, large numbers of poisoning cases are reported where fossil fuels are used frequently (7-14). According to a study conducted in South Korea, 67.8% of the cases of poisoning involved men (15). In a multi-center study conducted in 2012 in 2417 patients over a 10-year period (16). concluded that the incidence was 35 in 10,000, and the male/female ratio was reported as 2/3 (16). The male/female ratio was 1/3 in our study. Sex distribution differs according to the study area in the literature. There are differences due to the source of poisoning, the characteristics of the region where the study is conducted, and the status of men and women in working life.

The mean age of patients with CO poisoning was 40 years. According to the literature, the mean age ranges from 30 to 50 years (15-17-18). These results suggest that patients who are admitted to the emergency service are often young adults.

In a study from England, it was concluded that hyperventilation and tachycardia occurred first to compensate for the relative hypoxia, and hypoventilation was observed in later stages (5). We found no difference between the study and control groups in terms of the respiratory rate at admission. We did not include patients with disturbances that could directly affect the respiratory rate in the control group. However, the first vital parameters in patients who are admitted to the emergency service are usually

Table 1. Comparison Of Patients Vital Signs According To Groups

	Patients (n=106) (Mean±SD)	Controls (n=40) (Mean±SD)	p
TA (mm Hg)	89.981 ± 12.722	87.125 ± 14.702	0.249
Pulse rate (min)	90.405 ± 17.570	92.850 ± 23.084	0.494
Respiratory rate (min)	20.971 ± 3.258	19.725 ± 3.038	0.038
Body temperature (°C)	36.277 ± 0.439	36.525 ± 0.645	0.009

SD: Standard Deviation

Table 2. Comparison of COHb Measurements By Groups

	Patients (Mean±SD)	Controls (Mean±SD)	p
COHb % at admission	19.923 ± 9.395 (n: 106)	0.757 ± 0.706 (n: 40)	0.001
COHb % at 6 hours	2.384 ± 3.180 (n: 105)	0.820 ± 0,720 (n: 40)	0.003
COHb % at 12 hours	1.054 ± 1.273 (n: 33)	0.752 ± 0.623 (n: 40)	0.190
COHb % at 24 hours	0.540 ± 0.658 (n: 5)	0.737 ± 0.653 (n: 40)	0.528

SD: Standard Deviation

Table 3. Comparison of $ETCO_2$ Measurements By Groups

	Patients (Mean±SD)	Controls (Mean±SD)	p
$ETCO_2$ at admission (mm Hg)	31.434 ± 8.542 (n: 106)	33.650 ± 5.303 (n: 40)	0.128
$ETCO_2$ at 6 hours (mm Hg)	31.104 ± 4.988 (n: 105)	34.020 ± 4.022 (n: 40)	0.001
$ETCO_2$ at 12 hours (mm Hg)	31.727 ± 5.964 (n: 33)	34.375 ± 4.246 (n: 40)	0.030
$ETCO_2$ at 24 hours (mm Hg)	36.600 ± 5.412 (n: 5)	34.600 ± 4.493 (n: 40)	0.363

SD: Standard Deviation

measured high because of anxiety. We evaluated the vital signs at admission only, and follow-up values were not recorded. Including follow-up values and collecting more data in future studies is required.

Patients with CO poisoning are often admitted to emergency services with multiple nonspecific symptoms. The most common cause of admission to the emergency service was headache (6). Headache was the most common cause of admission to hospital with a rate of 55% in the study by Rose et al., and headache, nausea/vomiting, lethargy, altered consciousness level, and weakness were the most common causes of admission in a study from Italy (18-19). In a review published in 2007, the symptoms seen in CO poisoning, from most frequent to less frequent, were headache, dizziness, irritability, confusion, disorientation, nausea, vomiting, and chest pain (20). The symptoms, from the most frequent to less frequent in our study, were headache, dizziness, nausea, fatigue, syncope, vomiting, and chest pain. Considering these findings, although the symptoms of patients with

Table 4. The Correlation Between COHb and $ETCO_2$ in CO Poisoning

		$ETCO_2$ at admission (mm Hg)	$ETCO_2$ at 6 hours (mm Hg)	$ETCO_2$ at 12 hours (mm Hg)	$ETCO_2$ at 24 hours (mm Hg)
COHb at admission time %	Patients r (p)	0.070 (0.937)			
	Controls r (p)	0.156 (0.111)			
COHb at 6 hours admission %	Patients r (p)		0.034 (0.685)		
	Controls r (p)		0.119 (0.227)		
COHb at 12 hours admission %	Patients r (p)			-0.125 (0.293)	
	Controls r (p)			-.144 (.425)	
COHb at 24 hours admission %	Patients r (p)				0.123 (0.420)
	Controls r (p)				-0.135 (0.829)

r: Pearson correlation coefficients

CO poisoning varies; it can be concluded that the most affected system is the nervous system and then the gastrointestinal system. CO poisoning should also be considered in differential diagnoses in patients admitted to the emergency service with nonspecific neurologic and gastrointestinal symptoms.

The most common source of CO was stoved in our study. In a retrospective study performed in the Aegean region of Turkey, the most common sources of CO were stoves and water heaters (17). Aslan et al. also showed that the most common causes of CO poisoning were water heaters (77.5%) and stoves (22.5%) (21). CO sources vary because income levels, heating systems, and climate characteristics vary. CO sources are often reported as stoves or water heaters in the literature. Here, regular maintenance of heating/heating systems should be performed, careful extraction of carbon waste in windy, cold weather should be observed, and people should be informed about CO poisoning.

When poisoning cases are evaluated according to professional groups, the results of studies in different regions vary. According to a 10-year retrospective study conducted in the USA, 61% of poisoning cases were from the general population, 27.7% were manual workers, and 7.6% were students (1). In our study, of the patients with CO poisoning, 49 (46.2%) were unemployed, 12 (13.2%) were students, 4 (3.8%) were civil servants, 18 (17%) were manual workers, and 21 (19.8%) were from other professions. We had no cases of occupational injury. People living in more rural areas often have stoves or water heater heating systems and the patients most frequently admitted to hospital with CO poisoning are housewives, farmers, children, and the elderly. Patients with CO poisoning in more centralized residential areas, which are predominantly industrial, are typically manual workers and young adults. Therefore, the occupational profile varies according to the level of development of the society. It is necessary to take measures to prevent household and work accidents, and the public should be informed accordingly.

Most cases of CO poisoning are accidental. The rates of CO poisoning due to occupation or suicide are lower. Sutupa et al. showed that most cases of CO poisoning were accidental, and CO poisoning for suicide or because of illegal ways constituted only 1.8% of cases (1). In a study published in 2010, 111 cases were accidental, four were occupational, and one was for suicide (17). In view of these results, it can be said that patients with poisoning who are admitted to the emergency room are usually due to accidental poisoning, and one way of suicide is self-CO poisoning. Suicide rates may be higher than the rate of emergency room admissions because these patients are not brought to emergency rooms when they die.

Parameters such as age, body mass index, lung diseases, metabolic disorders, and psychological state affect the metabolism and production of CO_2, as well as the measurement of $ETCO_2$. $ETCO_2$ at admission was not different between the study and control groups in our study. In our study, it was found that in patients with CO poisoning, the use of $ETCO_2$ measurements would not be appropriate for diagnosis and follow-up; however, performing larger studies and eliminating parameters that affect $ETCO_2$ measurement in the study and control groups would give better results.

We found no relationship between COHb and $ETCO_2$ in both the study and the control groups. To our knowledge, our study is the first in the literature to search for a relationship between COHb and $ETCO_2$.

This study had some limitations. The study was conducted in a single center with a few patients. Only the sidestream method was used in the measurement of $ETCO_2$. All parameters that affect respiratory physiology could not be completely excluded.

In this study, there was a statistically significant difference between the groups in terms of "respiratory rate" and "body temperature. While the "respiratory rate" was higher in the "Patient" group, the "body temperature" was higher in the "Control". While the COHb% in the first 6 hours was higher in the "patient" group, it resulted in a similar level in the "patient and control" group at 12-24 hours. In the patient group, COHb decreased over time and returned to normal. While the ETCO2 value was similar in the two groups at the beginning, it was significantly higher in the patient" group at 6-12 hours. However, the ETCO2 value increased to the normal level again at the 24th hour. The ETCO2 value showed an increasing trend as time passed and returned to the normal level. As a result, there was no significant correlation between COHb levels and $ETCO_2$ measurement in the blood gas of patients with CO poisoning. According to our findings, we believe that $ETCO_2$ measurements cannot be used as an alternative method of blood gas in patients with CO poisoning. More studies with larger numbers of patients and more data are needed about this topic.

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