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Analysis of patients presenting to the emergency department with carbon monoxide intoxication

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ABSTRACT

Objectives: Carbon monoxide is a potentially fatal form of poisoning. The exact incidence is unclear, due to cases being undiagnosed or reported as fewer than the real number. Hyperbaric oxygen therapy (HBOT) is of proven efficacy in the treatment of CO intoxication.
The purpose of this study was to describe the general characteristics of carbon monoxide (CO) intoxications presenting to the emergency department and to investigate troponin I values and the effectiveness of hyperbaric oxygen therapy (HBOT) in these patients.
Material and methods: Patients presenting to the emergency department with CO intoxication over one year and patients with such intoxications receiving HBOT were examined retrospectively.
Results: One hundred seventy-one patients were included; 140 (81.9%) were poisoned by stoves, 18 (10.5%) by hot water boilers and 10 in (5.8%) by fires. COHb levels were normal in 49 of the 163 patients whose values were investigated, and were elevated in 114 patients. Mean COHb value was 16.6. Troponin I values were investigated in 112 patients. These were normal in 86 patients and elevated in 26. Mean troponin I value was 0.38 ng/ml. One hundred twenty-three of the 171 patients in the study were discharged in a healthy condition after receiving normobaric oxygen therapy, while 48 patients received HBOT. Forty-two (87.5%) of the patients receiving HBOT were discharged in a healthy condition while sequelae persisted in five (10.4%). One patient died after 15 session of HBOT.
Conclusion: Although elevated carboxyhemoglobin confirms diagnosis of CO intoxication, normal levels do not exclude it. Troponin I levels may rise in CO intoxication. No significant relation was observed between carboxyhemoglobin and receipt of HBOT. A significant correlation was seen, however, between troponin I levels and receipt of HBOT.

1. Introduction

Carbon monoxide (CO) is a potentially fatal form of poisoning. The exact incidence is unclear, due to cases being undiagnosed or reported as fewer than the real number. Hyperbaric oxygen therapy (HBOT) is of proven efficacy in the treatment of CO intoxication.[1]

During respiration of oxygen at high pressure, levels of oxygen dissolved in plasma independent of hemoglobin are raised. More oxygen is thus enabled to reach the tissues. Comparing HBOT with normobaric oxygen therapy (NBOT), time to improvement of intoxication symptoms is shorter and the incidence of mortality and late neuropsychiatric findings is lower.[2]

The heart is one vital organ affected in CO intoxication. Myocardial damage induced by acute CO intoxication can be shown biochemically by an increase in cardiac markers and creatine phosphokinase (CPK) levels. Serum cardiac troponin I (cTnI) level is a test with high sensitivity and specificity in showing myocardial

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damage.[3] Studies in recent years have suggested that serum cTnI levels may be an important marker in showing cardiac injury in CO intoxication and deciding to initiate HBOT.[3]

This study investigated the demographic characteristics of patients presenting with CO intoxication, their cardiac enzyme findings and the effect of HBOT used in the treatment of intoxication on both clinical and biochemical markers. Findings obtained regarding successful treatment of this significant public health problem may provide clues regarding this intoxication that can be used in emergency practice.

2. Materials and methods

This study was performed under local ethical committee approval (no. 2013/94). The research was conducted as a joint study between the Underwater and Hyperbaric Medicine Clinic, the sole hyperbaric oxygen treatment center in the Eastern Black Sea region of Turkey, and the emergency medicine clinic of the Kanuni Training and Research Hospital. The study was performed retrospectively among patients presenting to the emergency department within the first 24 h of CO intoxication between 1 March, 2011 and 1 March 2012. Data for the patients enrolled in the study were obtained from patient files and computer records with ICD-10 code starting with T.58.XX (Toxic effect of carbon monoxide). Missing information was completed by contacting patients or their families by telephone. Data obtained were transferred onto a study form. Patients presenting after more than 24 h following exposure to CO, undergoing infarction within the previous month, diagnosed with pulmonary embolism in the previous month, attending due to COPD attack, with acute cerebrovascular disease, with acute and chronic renal failure and undergoing simultaneous trauma and pulmonary injury (pneumothorax, hemothorax or pulmonary contusion) were excluded. One hundred seventy-one patients with no exclusion criteria were included. Patients with severe neurologic symptoms, syncope, seizure, continued neurologic symptoms after NBO therapy, having evidence of myocardial ischemia, cardiac arhtythmias, elevated troponin values, high carboxyhemoglobin (COHb) levels (CoHb > 40%), pregnancy with COHb level > 15% were treated with HBOT.

3. Statistical analysis

Data obtained were subjected to statistical analysis on SPSS 18.0. Data compatibility with normal distribution was determined on the basis of the Kolmogorov–Smirnov test. The Mann–Whitney U test was used to investigate the presence of variation of non-normally distributed variables between groups. $P < 0.05$ was regarded as statistically significant. Patients' age, gender, time of presentation, sources of CO exposure, troponin I and COHb levels and levels of persistence of post-treatment sequelae were subjected to descriptive statistical analysis. Pearson correlation analysis was performed for normally distributed data in order to determine correlation between variables, and Spearman's rho correlation was used for non-normally distributed data. Biserial correlation analysis was also performed in examining correlation between COHb and receipt of HBOT and between troponin I and receipt of HBOT.

4. Results

One hundred seventy-one patients presenting to the training and research hospital were included in the study, 84 (49.1%) men and 87 (50.9%) women. Total number of presentations to the emergency department during the study period was 256,674. CO intoxications represented 0.06% of all emergency department presentations. No significant difference was determined between gender and COHb values ($p > 0.05$). Mean age of the 171 patients was 34.91 ± 23.5. CO intoxication was the most common in the 15–20 age group, with 19 patients (11%). No significant difference was determined between patients' ages and COHB values ($p > 0.05$).

In terms of months in which patients exposed to CO presented to the emergency department, the most common was March, with 67 cases. There were no CO intoxication-related presentations in June or August. Seventeen (9.9%) patients presented in January, 19 (11.1%) in February, 67 (39.2%) in March, 8 (4.7%) in April, 19 (11.1%) in May, 3 (1.8%) in July, 1 (0.6%) in September, 4 (2.3%) in October, 15 (8.8%) in November and 18 (10.5%) in December.

In terms of sources of CO intoxication, 140 (81.9%) patients were poisoned by stoves, 18 (10.5%) by hot water boilers, 10 (5.8%) by fires and 3 (1.8%) from other causes.

In terms of COHb values, 49 of the 163 patients had normal COHb values (0–5%) and 114 high. Mean COHb value was 16.6 ± 13.4. The lowest value was 0.1, while COHb levels were above 50 in two patients. The highest value was 55.8 of 171 patients' COHb value was not measured because they had treatment in another center.

Troponin I values were investigated in 112 patients. These were normal (0–0.1 ng/ml) in 86 (%76.8) patients and elevated in 26 (% 23.2). A reverse but non-significant correlation was determined between COHb and troponin I levels ($p = 0.511$, $r = -0.64$). The highest troponin I value measured was 50 ng/ml. Mean troponin I after exclusion of extreme values was 0.39 ± 1.15 ng/ml.

One hundred twenty-three of the 171 patients included in the study were discharged in a healthy condition after receiving normobaric oxygen therapy (NBOT) in the emergency department. Forty-eight patients were taken for HBOT. Twenty (41.7%) of these were treated on an outpatient basis and 28 (58.3%) were hospitalized and monitored for 1–15 days. Mean number of HBOT sessions received was 3.25. The lowest number of sessions was one and the highest 15. Forty-two (87.5%) of the 48 patients receiving HBOT were discharged in a healthy condition while sequelae persisted in five (10.4%). One patient (2.1%) who was transferred to intensive care unit died after 15 HBOT sessions on the 180th day of treatment because of sepsis and multiple organ dysfunction syndrome. Impaired vision developed in two patients following CO intoxication. Full vision was restored in both after HBOT, although neurological sequelae persisted in one. Paresthesia persisted in the upper extremity after HBOT in one patient brought to the emergency department in a tetraparesic state (3/5 loss of strength). Two intubated patients referred from external centers were extubated after HBOT and discharged in a healthy condition. No sequelae persisted in either patient. HBOT-related complications were investigated, with bilateral hemotympanum developing in three patients receiving HBOT.

Correlation analysis was performed to determine the association between patients' COHb values and HBOT. No significant correlation was determined between patients' COHb values and receipt of HBOT ($p > 0.05$). The same statistical technique was performed for correlation between patients' troponin I values and receipt of HBOT, and a positive significant correlation was determined ($p < 0.05$). No significant difference was determined between COHb and troponin I ($r = -0.064$, $p > 0.05$). Twenty-five patients had elevated troponin I. Wall motion disorder was determined with echocardiography (ECO) in 11 of these, while ECO was normal in the other 14. No significant correlation was determined between troponin I values and wall motion disorder ($p > 0.05$).

Magnetic resonance imaging (MRI) was performed on 22 patients, and was normal in 16. MR findings secondary to CO intoxication were determined in six. Globus pallidus involvement was present in two patients. Widespread involvement was seen in

three. Involvement of both cerebellar hemispheres and bilateral parieto occipital lobes were seen in one patient. The Mann–Whitney U test was performed to investigate variations between COHb values depending on the presence or absence of a finding developing secondary to CO intoxication in patients' MRs. No statistically significant difference was determined in terms of COHb levels between patients with normal MRs and those with findings secondary to CO intoxication ($p > 0.05$).

5. Discussion

Since CO intoxications are generally misdiagnosed the true incidence is unknown. In a study from Turkey in 2010, Metin S et al. reported an incidence of CO intoxication of 0.0137%.[4] To our study number of patients with CO intoxication is equivalent to 0.06% of all patients attending the emergency department during that time.

CO intoxication may have various sources. Motor vehicle exhausts are the most common cause of intoxication resulting in death in the USA.[5] In Spain, water boilers and central heating systems using propane gases are implicated in more than half of cases of intoxication.[6] Similarly, sources of exposure in Turkey vary according to region, geographical conditions, socioeconomic status and season. In a study of CO intoxication performed in Erzurum, Turkey by Kandiş et al., 68.3% of cases were poisoned by hot water boilers, 15.4% by stoves, 13.1% by fires and 3.2% by vehicle exhausts.[7] In a study of 192 cases by Çevik et al., sources of poisoning were stoves at 74.7% and water heaters using propane or natural gas at 21.4%.[8] Arıcı et al. reported stoves as source of intoxication in 48.3% of cases and hot water boilers in 44%.[9] The level of CO intoxications originating from water heaters in our study was quite low. We attribute this to greater popular awareness following mass deaths due to water boiler poisonings in recent years and greater security precautions being taken.

Accident-related intoxications are common in winter months, while intoxications for purposes of suicide are equally distributed throughout the year.[10] All the patients in our study had been poisoned accidentally. In contrast to the literature, the most intoxication in our study was seen in spring. Patients presented to hospital most commonly in spring, (55%) and particularly in March (39.2%). The fewest presentations were in summer (1.8%). We attribute this variation to the geographical conditions of the province of Trabzon and in particular to sudden changes of wind direction in spring increasing the number of stove-related poisonings.

Elimination of blood CO can be accelerated by increasing the concentration of oxygen in respiration air or by increasing atmospheric pressure. The mean half life of CO, 4–5 h in room air, decreases to a mean 60 min with 100% oxygen therapy and a mean 20 min with HBOT. In addition, when oxygen is administered, the level of dissolved oxygen in blood rises and the half life of CO decreases.[11] COHb values were normal in 49 (30%) of the patients in our study. We attribute this to patients presenting late to the emergency department, lengthy transportation procedures and oxygen therapy being provided by medical teams during transportation.

The heart is one of the organs most affected by oxidative stress caused by CO intoxication. Hypoxia occurring with a rise in COHb levels may cause ventricular dysrhythmias, and CO intoxication-related acute mortality may develop. T. Wocka-Marek et al. showed that troponin I can be used to show cardiac damage arising in acute CO intoxication.[12] The presence of a reverse and non-significant correlation between COHb and troponin I levels is due to COHb gradually decreasing as troponin I increases. Clinical studies have shown that there is not always a significant correlation between COHb levels and myocardial injury. Myocardial damage can even develop in low COHb levels.[1] A negative and non-significant correlation was also determined between COHb and troponin I in our study, and this was compatible with the literature. This study also examined the Echocardiograms of patients with elevated troponin I and sought to establish the relationship between wall motion disorder and elevated troponin I. No statistically significant correlation was determined between troponin I elevation and wall motion disorder determined at ECO.

Early HBOT is recommended in the acute period of intoxication. If possible, first HBOT should be administered within the first 6 h after intoxication.[13,14] If loss of consciousness persists after administration, HBOT should be repeated in 6–8 h. Gorman et al. showed that repeated administrations had a better effect on prognosis.[13,14] Hay et al. reported a mean HBOT session number of 3.8, and Kandiş et al. of 3.4.[7,15] Mean number of HBOT sessions in our study was 3.25, in agreement with the literature. Hampson reported that clinical improvement was possible with NBOT alone even in the event of loss of consciousness in CO intoxication. Mortality is lower in patients receiving HBOT in the short term compared to those receiving NBOT. Neuropsychiatric findings have also been shown to decrease in the long term.[16] All the patients arriving with impaired consciousness in our study received HBOT. Neurological deficits may persist after HBOT. Forty-eight patients received HBOT in our study, and 42 were discharged in a healthy condition, while neuropsychiatric sequelae persisted in five. One patient died.

Yarar et al. noted that barotrauma may be observed in the middle ear, sinus and lungs due to high pressure after HBOT.[17] Bilateral hemotympanum was seen in 3 patients in our study. No sinus or pulmonary barotrauma were encountered.

Fetal hemoglobin has a greater affinity for CO than adult hemoglobin. Since fetal or neonatal levels are higher than maternal levels, the risk of toxicity is greater. Additionally, since CO gas elimination time between mother and fetus in pregnant patients is approximately five times greater in the fetus, it has been shown while maternal CO levels are not at the toxic levels, the fetus is at risk of hypoxia.[18] In the first prospective and multicenter study in the literature concerning acute CO intoxication, Koren et al. monitored 32 pregnant women exposed to CO gas and determined that the fetal effect in severe CO toxicity led to significantly greater fatal effects compared to moderate and mild CO intoxication.[19] In our study, two pregnant patients presented with CO intoxication. One was transferred to our emergency department after NBOT in the emergency department at an external center and received one session of HBOT, despite COHb being normal on admission, for reasons of respiratory difficulty and lethargy. The other pregnant woman presented to our emergency department directly. Her COHb level was 18.3. The patient had no symptoms apart from headache. After NBOT she was sent for HBOT in order to protect the fetus against possible toxic effects. Her clinical picture improved and no problems were seen in the fetus. No HBOT-related complications were observed. After one-day hospitalization she was discharged in a healthy condition.

A decrease in density in white matter and the globus pallidus and findings of cerebral edema may be seen at cranial CT in the first 6 h in intoxications resulting in coma. At autopsy, other regions of the brain have also been shown to be affected, however. The presence of low density areas in the globus pallidus has been reported as the most important finding indicating poor prognosis.[20,21] MR is more effective in detecting cerebral lesions, hemorrhages and permanent cerebral atrophies seen in CO intoxications.[22] MR was performed on 22 patients in our study, of which 16 were evaluated as normal. MR findings secondary to CO intoxication were determined in the other six. Globus pallidus involvement was present in two patients. Widespread involvement

was seen in three patients and both cerebellar hemispheres and bilateral parieto occipital lobe involvement in one.

In conclusion, although elevated COHb is diagnostic of CO intoxication, normal levels do not exclude the diagnosis. Troponin I levels may rise in CO intoxication. A significant correlation was not observed between COHb levels and receipt of HBOT. A significant correlation was observed between troponin I levels and receipt of HBOT.

As a conclusion we think that the findings from this study provide important preliminary information regarding approaches to diagnosis and treatment.

6. Limitations

The study center is a research and education center, and some of the patients were referred from other hospitals. The patients referred from other hospitals were treated with oxygen during the transfer. So these patients' COHb values may be lower than the actual COHb values.

References

1. Hardy KR, Thom SR. Pathophysiology and treatment of carbon monoxide poisoning. *J Toxicol Clin Toxicol*. 1994;32:613–629.
2. Weaver LK, Hopkins RO, Chan KJ, et al. Hyperbaric oxygen for acute carbon monoxide poisoning. *N Engl J Med*. 2002;347:1057–1067.
3. Gök H. *Akut Miyokard İnfarktüsü*. Ankara: Nobel Tıp Kitabevi; 2002 [Book in Turkish].
4. Metin S, Yıldız S, Cakmak T, et al. 2010 Yılında Türkiye'de Karbonmonoksit Zehirlenmesinin Sıklığı [Article in Turkish] *TAF Prev Med Bull*. 2011;10:587–592.
5. Varon J, Marik P. Carbon monoxide poisoning. *Internet J Emerg Intensive Care Med*. 1997;1(2).
6. Harper A, Croft-Baker J. Carbon monoxide poisoning: undetected by both patients and their doctors. *Age Ageing*. 2004;33:105–109.
7. Kandis H, Katırcı Y, Çakır Z, et al. Acil Servise Karbonmonoksit İntoksikasyonu ile Başvuran Olguların Geriye Dönük Analizi [Article in Turkish] *J Acad Emerg Med*. 2007;5:21–25.
8. Cevik AA, Unluoglu I, Yanturali S, et al. Interrelation between the Poisoning Severity Score, carboxyhaemoglobin levels and in-hospital clinical course of carbon monoxide poisoning. *Int J Clin Pract*. 2006;60:1558–1564.
9. Arıcı AA, Demir Ö, Özdemir D, et al. Acil Servise Başvuran Karbonmonoksit Maruz Kalımları: On Dört Yıllık Analiz [Article in Turkish] *DEÜ Tıp Fak Derg*. 2010;24:25–32.
10. İnal V. Karbonmonoksit Zehirlenmesi ve Tedavisi [Article in Turkish] *Turk Klin J Anest Reanim*. 2005:34–41.
11. Kao LW, Nanagas KA. Carbon monoxide poisoning. *Emerg Med Clin N Am*. 2004;22:985–1018.
12. Wocka-Marek T, Klopotowski J, Kicka M, et al. The usefulness of troponin I in the diagnosis of cardiac damage in acute carbon monoxide poisoning. *Med Pr*. 2002;53:119–123.
13. Gorman DF, Clayton D, Gilligan JE, et al. A longitudinal study of 100 consecutive admissions for carbon monoxide poisoning to the Royal Adelaide Hospital. *Anaest Intensive Care*. 1992;20:311–316.
14. Gorman DF, Runciman WB. Carbon monoxide poisoning. *Anaest Intensive Care*. 1991;19:506–511.
15. Hay PJ, Denson LA, van Hoof M, et al. The neuropsychiatry of carbon monoxide poisoning in attempted suicide: a prospective controlled study. *J Psychosom Res*. 2002;53:699–708.
16. Hampson NB. Hyperbaric oxygen: a plea for uniform nomenclature. *Undersea Hyperb Med*. 1999;26:267.
17. Yarar C, Yakut A, Akin A, et al. Analysis of the features of acute carbon monoxide poisoning and hyperbaric oxygen therapy in children. *Turk J Pediatr*. 2008;50:235–241.
18. Gabrielli A, Layon AJ. Carbon monoxide intoxication during pregnancy: a case presentation and pathophysiologic discussion, with emphasis on molecular mechanisms. *J Clin Anesth*. 1995;7:82–87.
19. Koren G, Sharav T, Pastuszak A, et al. A multicenter, prospective study of fetal outcome following accidental carbon monoxide poisoning in pregnancy. *Reprod Toxicol*. 1991;5:397–403.
20. Ernst A, Zibrak JD. Carbon monoxide poisoning. *N Engl J Med*. 1998;339:1603–1608.
21. Saracel M, Ozen H, Ozcelik UT. Karbon monoksit zehirlenmesi [Article in Turkish] *Katkı Pediatri Derg*. 1990;11:327–333.
22. Raub JA, Mathieu-Nolf M, Hampson NB, et al. Carbon monoxide poisoning–a public health perspective. *Toxicology*. 2000;145:1–14.