Turkish Archives of Pediatrics

ORIGINAL ARTICLE
DOI: 10.5152/TurkArchPediatr.2023.22189

How to Decide Oxygen Therapy in Childhood Carbon Monoxide Poisoning?

Metin Uysalol, Sühelya Gümüş, Raif Yıldız

[1]Division of Pediatric Emergency, Department of Pediatrics, İstanbul University, İstanbul Faculty of Medicine, İstanbul, Turkey

What is already known on this topic?

- *Carbon monoxide (CO) poisoning is an important cause of morbidity and mortality worldwide. Evaluation of clinical findings and laboratory results to provide appropriate treatment is still controversial. In children, signs and symptoms are different, not correlated with laboratory values, and the first choice of treatment is not clearly known.*

What this study adds on this topic?

- *In our study, CO exposure duration, carboxyhemoglobin levels, neurological symptoms, and lactate levels were determined as guiding parameters in determining the indication for hyperbaric oxygen therapy (HBOT). It is important to determine relevant clinical and laboratory factors that may help in making HBOT treatment decision and to evaluate patients according to these parameters.*

ABSTRACT

Objective: Carbon monoxide poisoning is an important cause of morbidity and mortality all over the world. In our study, it was aimed to determine the clinical and laboratory parameters that may be effective in deciding the need for hyperbaric oxygen therapy in the management of cases.

Materials and Methods: From January 2012 to the end of December 2019, 83 patients who applied to a university hospital pediatric emergency department in İstanbul with the diagnosis of carbon monoxide poisoning were included. Demographic characteristics, carbon monoxide source, exposure duration, treatment approach, physical examination findings, Glasgow Coma Score, laboratory results, electrocardiogram, cranial imaging, and chest x-ray were evaluated from the records.

Results: The median age of the patients was 56 (37.0–100.0) months and 48 (57.8%) of them were male. The median time of exposure to carbon monoxide was 5.0 (0.5–3.0) hours in those who received hyperbaric oxygen therapy and was significantly higher than those who received normobaric oxygen therapy ($P < .001$). Myocardial ischemia, chest pain, pulmonary edema, and renal failure were not detected in any of the cases. The median lactate level was detected as 1.5 (1.0–2.15) mmol/L in those who received normobaric oxygen therapy and 3.7 (3.17–4.62) mmol/L in those who received hyperbaric oxygen therapy, and the difference between them was statistically significant ($P < .001$).

Conclusions: A guideline containing precise clinical and laboratory parameters for hyperbaric oxygen therapy in children has not been developed yet. In our study, carbon monoxide exposure duration, carboxyhemoglobin levels, neurological symptoms, and lactate levels were found to be guiding parameters in determining the need for hyperbaric oxygen therapy.

Keywords: Carbon monoxide, hyperparic oxygen therapy, normobaric oxygen therapy, poisoning

INTRODUCTION

Carbon monoxide (CO) poisoning is an important cause of morbidity and mortality all over the world.[1] Epidemiological data are necessary to develop organized efforts to reduce the cumulative effect of CO poisoning.

Evaluation of clinical findings and laboratory results in order to make a diagnosis and to provide appropriate treatment is still controversial and unclear.[2] It is very important to make decision immediately on the appropriate treatment by evaluating current conditions in order to prevent dramatic consequences of CO poisoning, which may be severe enough to cause multiple deaths.

Corresponding author:
Metin Uysalol
✉ uysalol@istanbul.edu.tr
Received: July 27, 2022
Accepted: January 3, 2023
Publication Date: May 2, 2023

Cite this article as: Uysalol M, Gümüş S, Yıldız R. How to decide oxygen therapy in childhood carbon monoxide poisoning? *Turk Arch Pediatr.* 2023;58(3):282-288.

Carbon monoxide (CO) can cause cellular hypoxia followed by oxidative stress and inflammation, neurological, cerebrovascular or cardiovascular disorders, including encephalopathy, ischemia, and peripheral nerve damage.[3] First symptoms are usually seen in neurological and cardiovascular system because of the need for high amounts of oxygen for these systems functions. Although the risk is higher in patients with cardiac disease, tachycardia, cardiac enzyme elevation, myocardial damage, and arrhythmias can often be seen after exposure to CO.[4] On the other hand, in children, unlike adults, signs and symptoms are different; they do not correlate with laboratory values, and the first treatment choice is not clearly known.

The basis of treatment for CO poisoning is to remove patients from the source and to ensure adequate oxygenation.[5] Normobaric oxygen therapy (NBOT) can be achieved by delivering 100% oxygen at a rate of 10-15 L/min with a non-rebreather reservoir mask. It is recommended to continue the treatment until the symptoms regress or blood carboxyhemoglobin (COHb) level decreases below 5% in patients in a good general condition, with no unconsciousness, no additional complaints, or mild symptoms.[6] Hyperbaric oxygen therapy (HBOT) is a medical treatment in which patients breath 100% oxygen intermittently in a hyperbaric chamber, at a pressure higher than the atmospheric pressure at sea level (1 ATA = 1 atmosphere absolute = 1 Bar = 760 mmHg). Hyperbaric oxygen therapy increases dissolved oxygen in blood regardless of oxygen carried by hemoglobin, thus decreases tissue hypoxia and leads to regression of intoxication symptoms. Although there is no clear difference in results of studies comparing HBOT and NBOT in the literature, there are studies indicating that HBOT reduces the risk of cognitive sequelae.[3,7] Retrospective observational evidence shows that HBOT is associated with reduced short- and long-term mortality in cases of severe CO poisoning, especially in those with acute respiratory failure and in patients under 20 years of age. Hyperbaric oxygen therapy indication in CO poisoning is determined according to clinical signs, symptoms, and laboratory findings of the case. Although controversial, HBOT is recommended for neurological symptoms such as syncope, coma, seizure, mental status change, resistant metabolic acidosis, pregnant women with COHb level above 15%, history of ischemic heart disease and COHb level >20%, patients with COHb level above 40%, sign of cardiac ischemia or arrythmia, and proven end-organ damage findings.[8,9] The treatment of CO poisoning in children is a race against time. The main discussion is deciding whether and when to use HBOT or NBOT. Patients in need of HBOT should be carefully selected and closely observed within the first few hours. Late signs and symptoms such as neurological sequelae can be prevented with early diagnosis and rapid decision for HBOT administration.[10]

Although the number of HBOT centers is relatively high in our country, it is limited in the world, and transportation difficulties may be experienced in patient referral. For this reason, it is important to determine the appropriate predictor factors in pediatric population for HBOT need and evaluate the parameters that can help in making a referral decision.

In our study, the determination of clinical and laboratory parameters that can be effective in deciding on the need for HBOT during the management of cases admitted to a university hospital, Pediatric Emergency Department with a suspicion of CO poisoning has been planned. In addition, this study aimed to reveal demographic, clinical, and laboratory characteristics, to examine the systemic involvement, to determine the degree and prognosis of intoxication, and to investigate the effects of these data during the treatment process.

MATERIALS AND METHODS

Patients

From January 2012 to the end of December 2019, 83 patients who applied to a university hospital pediatric emergency department in İstanbul with the diagnosis of CO poisoning were included in our study. The data of the patients were extracted and analyzed retrospectively from the patient's records in the division's achieve. Patients who had incomplete records were excluded from the study. Demographic characteristics at the time of admission, CO source, exposure duration to carbon monoxide, treatment approach, physical examination findings, Glasgow Coma Score (GCS), laboratory results, electrocardiogram (ECG), cranial imaging, and chest x-ray were evaluated from the records.

Hyperbaric Oxygen Therapy Method

Hyperbaric oxygen therapy was applied in a multiplace hyperbaric chamber, at the treatment pressure of 2.4 ATA, by sessions with three 25-minute oxygen periods with 5-minute air breaks for 5 minutes, with a total session duration of 120 minutes including compression and decompression time. The total number of HBOT sessions varied according to the clinical condition of each case.

Statistical Analysis

Statistical Package for the Social Sciences (IBM Corp.; Armonk, NY, USA) Windows 21.0 package program was used for the analysis of the data. The variables were investigated using visual (histograms, probability plots) and analytical methods (Kolmogorov–Smirnov/Shapiro–Wilk's test) to determine whether they are normally distributed. Categorical variables were given as numbers (n) and percentages (%). Categorical variables were evaluated using Pearson Chi-square, Fisher, or Freeman–Halton test. The Mann–Whitney *U* test was performed to compare the significance of pairwise differences. The correlation coefficients and their significance were calculated using the Spearman test. Diagnostic decision-making variables in predicting treatment were analyzed using receiver operating characteristics (ROC) curve analysis. Logistic regression analysis was used to determine independent predictors. Hosmer-Lemeshow goodness of fit statistics were used to assess model fit. A 5% type-I error level was used to accept a statistically significant predictive value of the test variables.

Ethics Statement

This study was approved by the ethics committee of İstanbul University (approval date: 26.01.2018 and number 02) and was conducted according to the guidelines of the Declaration of Helsinki.

RESULTS

From January 2012 to the end of December 2019, 83 patients who applied to a university hospital pediatric emergency department in İstanbul with the diagnosis of CO poisoning were included in our study. The median age of the patients was 56 (37.0-100.0) months, and 48 (57.8%) of them were male. While CO source was 43.9% coal stoves, 46.3% gas was detected in those who received NBOT, 59.5% coal stoves and 16.7% gas were detected in those who received HBOT, and there was no significant difference between the treatment approach. The median time of exposure to CO was 5.0 (0.5-3.0) hours in those who received HBOT and was significantly higher than those who received NBOT ($P < .001$). Median COHb level was found to be 2.6 (1.2-10.75) in those who received NBOT and 28.95 (13.88-33.25) in those who received HBOT, and the difference between them was significant ($P < .001$). Demographic and clinical characteristics and laboratory data of the patients are shown in Table 1. Myocardial ischemia, chest pain, pulmonary edema, and renal failure were not detected in any of the cases. Chest x-ray was evaluated as normal in all patients. There was no significant difference between the NBOT and HBOT groups in terms of complaints of acute gastroenteritis, nausea, vomiting, and weakness. A statistical significance was found between restlessness and HBOT ($P = .012$). The median lactate level was detected 1.5 (1.0-2.15) mmol/L in those who received NBOT and 3.7 (3.17-4.62) mmol/L in those who received HBOT and the difference between them was statistically significant ($P < .001$). In the presence of any of the Babinski sign, hyperactive deep tendon reflex or signs of meningeal irritation, the neurological examination finding was considered positive and a significant relationship was found with HBOT ($P = .004$).

Factors predicting HBOT were CO exposure duration, COHb level, and lactate level. When the cut-off point of CO exposure duration was calculated as 3 and 4 hours separately area under the curve (AUC) = 0.804, 95% CI 0.706-0.901, $P < .001$), the sensitivity was 83.3% and 71.4% and specificity was 56.1% and 78.0%, respectively. When the cut-off points of COHb values to predict HBOT were calculated as 9%, 20%, and 25%, respectively (AUC = 0.857, 95% CI 0.775-0.940, $P < .001$), the specificity was 73.2%, 85.4%, and 90.2%; sensitivity was 85.7, 64.3%, and 64.3%, respectively. When lactate level in predicting HBOT was calculated as 2.6 mmol/L (AUC = 0.909, 95% CI 0.842-0.975, $P < .001$), the specificity was 90.2% and the sensitivity was 88.1% (Table 2 and Figure 1).

The comparison between neurological and cardiological symptoms and treatment is shown in Table 3. It was found statistically significant that patients with symptoms such as blurred

Table 1. Comparison of Study Population in the Different Treatment Groups

	NBOT (n = 41)	HBOT (n = 42)	Total (n = 83)	*P*
Age (month) (median) (IQR, 25-75 percentiles)	56.0 (37.5-102.5)	56.5 (35.5-87.25)	56.0 (37.0-100.0)	.946*
Sex (n, %)				
Male	19 (46.3)	29 (69.0)	48 (57.8)	**.036****
Female	22 (53.7)	13 (31.0)	35 (42.2)	
CO Source (n, %)				.08***
Coal stoves	18 (43.9)	25 (59.5)	43 (51.8)	
Gas	19 (46.3)	7 (16.7)	26 (31.3)	
Fire	3 (7.3)	3 (7.1)	6 (7.2)	
Liquefied petroleum gases	1 (2.4)	7 (16.7)	8 (9.6)	
CO exposure duration (hour) (median) (IQR, 25-75 percentiles)	2.0 (0.5-3.0)	5.0 (0.5-3.0)	3.0 (1.0-5.0)	**< .001***
COHb level (%) (median) (IQR, 25-75 percentiles)	2.6 (1.2-10.75)	28.95 (13.88-33.25)	12.9 (1.8-29.3)	**< .001***
Lactate (mmol/L) (median) (IQR, 25-75 percentiles)	1.5 (1.0-2.15)	3.7 (3.17-4.62)	2.5 (1.4-3.8)	**< .001***
Cardiac enzyme (median) (IQR, 25-75 percentiles)				
CK-MB (U/L)	28.0 (15.5-33.1)	28.0 (22.25-36.0)	28.0 (17.0-34.0)	.366*
Troponin (pg/mL)	6.1 (0.3-13.9)	4.5 (2.5-12.2)	5.2 (2.4-12.4)	.967*
Neurological symptoms (n,%)				
Present	4 (9.8)	26 (61.9)	30 (36.1)	**< .001****
Absent	37 (90.2)	16 (38.1)	53 (63.9)	
Pathological neurological examination (n, %)				**.004****
Present				
Absent	1 (2.4)	10 (23.8)	11 (13.3)	
	40 (97.6)	32 (76.2)	72 (86.7)	
GCS (median) (IQR, 25-75 percentiles)	15.0 (15.0-15.0)	15.0 (14.75-15.0)	15.0 (15.0-15.0)	**<.001***
Cranial imaging (n, %)				**<.001[ß]**
Normal	39 (95.1)	22 (72.4)	61 (73.5)	
Absent	0 (0.0)	10 (23.8)	10 (12.0)	
Abnormal	2 (4.9)	10 (23.8)	12 (14.5)	

CK-MB, creatine kinase-myoglobin binding; CO, carbon monoxide; COHb, carboxyhemoglobin; GCS, Glasgow Coma Score; HBOT, hyperbaric oxygen therapy; IQR, interquartile range; NBOT, normobaric oxygen therapy.
*Mann–Whitney *U* Test; **Pearson chi-square test; ***Likelihood Ratio [ß]Freeman Halton Test.

Table 2. ROC Curve Analysis of Factors Predicting Hyperbaric Oxygen Therapy

	AUC	95% CI	Cut-Off	Sensitivity	Specificity	*P*
CO exposure duration (hour)	0.804	0.706-0.901	4	71.4%	78.0%	**<.001**
			3	83.3%	56.1%	
COHb level (%)	0.857	0.775-0.940	9	85.7%	73.2%	**<.001**
			20	64.3%	85.4%	
			25	64.3%	90.2%	
Lactate (mmol/L)	0.909	0.842-0.975	2.6	88.1%	90.2%	**<.001**

AUC, Area under the curve; CO, Carbon monoxide; COHb, carboxyhemoglobin; ROC, Receiver Operating Characteristic.

vision, syncope, seizures, altered consciousness, weakness, and confusion received HBOT ($P = .039$, $P = .001$, $P = .006$, $P = .001$, $P = .028$, $P = .022$). In comparison of headache and treatment, the patient group with headache received more NBOT and this difference was found to be statistically significant ($P = .041$). No patients had chest pain or myocardial ischemia among the cardiological symptoms. A significant relationship was found between hypotension and HBOT ($P = .012$).

Correlation analysis was performed between frequently used parameters of blood gas and COHb levels (Table 4). Although there was a significance between pH and COHb level, a very weak correlation was found ($r = 0.020$, $P < .001$). Similarly, although there was a significance between pCO_2 and COHb level, a weak correlation was found ($r = 0.236$, $P = .03$). Both significance and very high correlation were found between lactate level and COHb level ($r = 0.803$, $P < .001$).

DISCUSSION

Carbon monoxide poisoning is an important cause of morbidity and mortality all over the world and has a significant place among poisoning cases in emergency admissions of children. Since HBOT centers are few in the world and in our country, access difficulties can be encountered and patients may experience problems during referral.[10] Therefore, it is important to determine relevant clinical and laboratory predictor factors that can help in making HBOT decision and evaluate patients according to these parameters. Thus, it will be possible to determine the patients who need HBOT in CO poisoning who are admitted to the pediatric emergency department, taking into account clinical and laboratory predictive findings as soon as possible.

Carbon monoxide poisoning is more common in winter. Increase in the use of CO sources during this period, the inadequate quality of fuels used for heating, insufficient ventilation of the heating systems, and deficiencies in maintenance are among the possible reasons.[2] In our study, coal stoves and gas are among the main sources of poisoning. There was no significant difference between the sources and treatment. Mendoza and Hampson[11] found exhaust fumes of motor vehicles and coal as the most common causes of poisoning. In our country, gas cylinder or gas-fired water heaters used in baths and coal

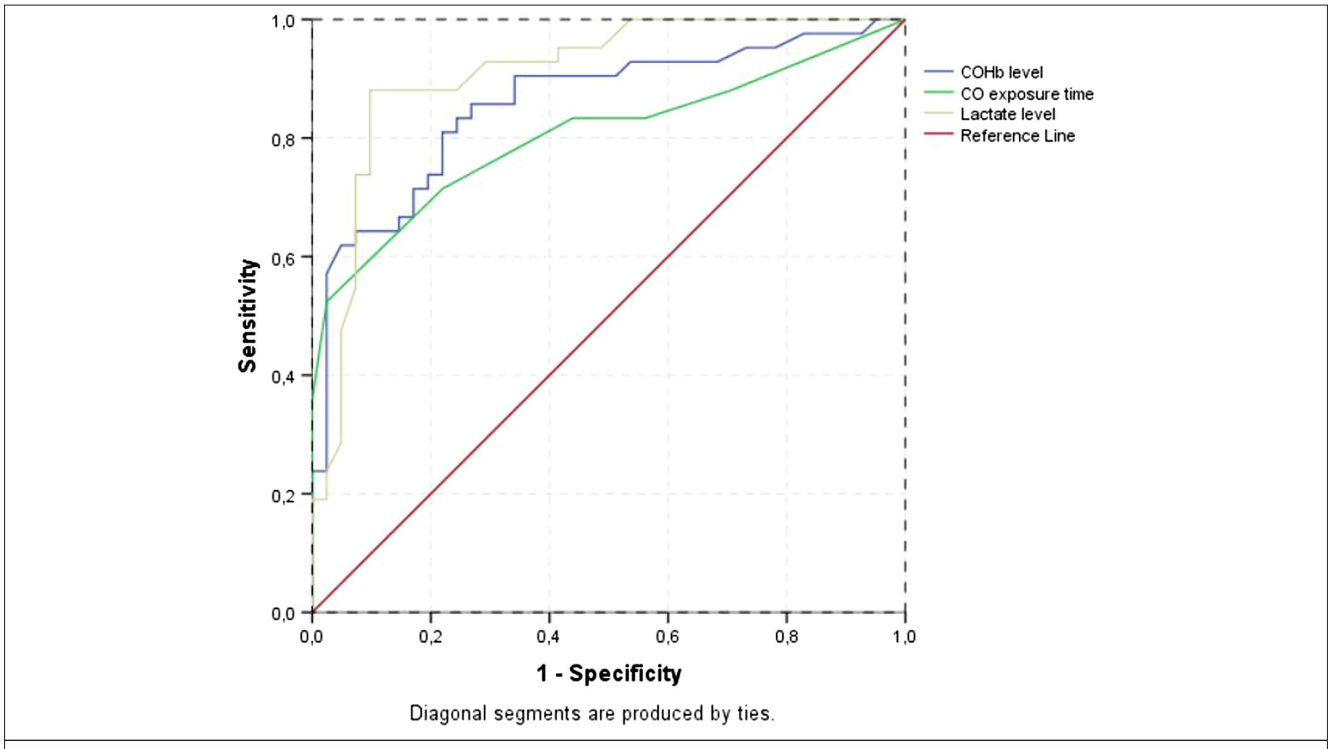

Figure 1. ROC curve analysis of factors predicting hyperbaric oxygen therapy.

Table 3. Comparison of Therapy with Neurological and Cardiac Symptoms

Symptoms	NBOT	HBOT	*P*	Logistic Regression *P* Value	OR (95% CI)
Neurological symptoms (n, %)					
Blurred vision	5 (12.2)	13 (31.0)	**.038****	-	-
Syncope	4 (9.8)	17 (40.5)	**.001****	**0.036**	4.840 (1.109-21.103)
Seizures	0 (0.0)	7 (16.7)	**.012**&&	-	-
Altered consciousness	1 (2.4)	12 (28.6)	**.001****	0.056	9.586 (0.941-97.683)
Ataxia	0 (0.0)	1 (2.4)	-	-	-
Weakness	1 (2.4)	7 (16.7)	.057&&	-	-
Headache	11 (26.8)	4 (9.5)	**.041****	0.217	0.381 (0.082-1.763)
Dizziness	7 (17.1)	9 (21.4)	.615**	-	-
Confusion	3 (7.3)	11 (26.2)	**.022****	0.999	1.001 (0.157-6.392)
Cardiological symptoms (n, %)					
Palpitation	11 (26.8)	13(31.0)	.679**	-	-
Chest pain	0 (0.0)	0 (0.0)	-	-	-
Tachycardia	3 (7.3)	9 (21.4)	.068**	-	-
Dysrhythmia	3 (7.3)	9 (21.4)	.060**	-	-
Hypotension	0 (0.0)	6 (14.3)	**.026**&&	0.888	0.868 (0.121-6.229)
Myocardial ischemia	0 (0.0)	0 (0.0)	-	-	-

HBOT, hyperbaric oxygen therapy; NBOT, normobaric oxygen therapy; OR, odds ratio.
**Pearson chi-square test; &&Fisher's exact test.

stoves are reported to be among the main causes of accidental CO poisoning.[12,13] In line with the results found in our study, the importance of raising awareness with intermittent warnings and trainings should be emphasized in our country where the use of wood-coal stoves is common.

Carbon monoxide may cause systemic effects that can lead to lactate production by mechanisms such as seizure, hyperventilation, and cardiac dysfunction.[14] In our study, statistical significance was found in the group that received HBOT comparing treatment with CO exposure duration and COHb and lactate levels. It has been thought that as the CO exposure duration increased, COHb values rise and high COHb levels caused an increase in neurological symptoms and therefore in the need for HBOT. We found that blood lactate level could provide more accurate information about the duration and degree of hypoxia, and lactate could be considered as an indicator of severe intoxication and would help in deciding the need for HBOT. When evaluating the severity of intoxication, duration of treatment, and patients' follow-up, it was concluded that the blood lactate level was more significant than the COHb level. Benaissa et al[15] reported that plasma lactate level was significantly associated with the initial severity of neurological impairment and COHb level at presentation. Damlapinar et al[16] reported that high lactate levels were found in most of the patients and no significant correlation was found between the patients' COHb levels and their clinical conditions. Lactate levels were found to be more significant than COHb levels in terms of loss of consciousness and convulsions, and it was concluded that lactate levels may be important in evaluating the severity of intoxication and treatment. Different studies reported that there is no correlation between the initial degree of intoxication and clinical outcome of the patients.[9,14] Reasons such as contact with normal atmospheric oxygen after leaving the source of poisoning, giving 100% oxygen treatment in ambulance before admission to hospital, delay in admission after exposure may cause the initial COHb level to be measured lower than expected. Sokal and Kralkowska[17] reported a significant correlation between COHb level and lactate level in their study and suggested that this poor correlation could be explained by their different half-lives under oxygen treatment and tissue hypoxia caused by COHb formation and other lactate formation mechanisms. When the results of our study are evaluated together with the literature, it has been thought that lactate level may be a more useful prognostic factor than COHb level and may be effective in determining the treatment process. Evaluation of lactate level together with parameters specified among the indications for HBOT will be useful in defining the patients who need the treatment.

Table 4. Correlation of Carboxyhemoglobin Level and Blood Gas Parameters#

Parameters	*r*	*P*
pH	0.020	< **.001**
pCO_2	0.236	**.03**
HCO_3	0.137	.22
Lactate	0.803	< **.001**
Base excess	−0.095	.392

HCO_3, bicarbonate; pCO_2, partial pressure of carbon dioxide; pH, potential of hydrogen
#Spearman's rho correlation was used.

Carbon monoxide poisoning can present with a diverse range of spectrum of neurological signs. Although there are studies reporting that there is no relationship between clinical status of patients at the time of admission and COHb levels,[8,18] there are also articles reporting that COHb level is related to severity of clinical signs.[12,14] In our study, a significant correlation was found between the presence of blurred vision, syncope, seizure, altered consciousness, weakness, confusion, restlessness, or pathological neurological examination and HBOT. Moon et al[14] evaluated the presence of neurological symptoms as an indicator of severe CO intoxication and reported COHb levels to

be significantly higher in patients who presented with lethargy and confusion. Tissue hypoxia and metabolic acidosis developed as a result of prolonged exposure to CO were thought to cause cerebral ischemia leading to clinical effects.

Keleş et al[9] reported that there is a correlation between the severity of neurological symptoms and COHb level. There are studies stating that HBOT administration as soon as possible in patients presenting with moderate and severe CO poisoning may be beneficial in preventing neuropsychiatric sequelae.[7,19] In our study, a significance was found between low GCS and HBOT and it was evaluated as one of the indicators of severe neurological impairment. Grieb et al[19] found a significant negative correlation between GCS at the time of admission and severity of intoxication and stated that it should be evaluated together with other parameters in determining the severity of poisoning. Serious neurological symptoms should be considered as a sign of severe intoxication, and HBOT decision should not be delayed. None of the patients had chest pain or myocardial ischemia among cardiological symptoms in our study. A significant correlation was found between hypotension and HBOT. Carbon monoxide can cause vasodilation and hypotension through the activation of guanylate cyclase and the release of nitric oxide from platelets. The retrospective study of Huysal et al[20] reported that troponin levels increased significantly in patients with high COHb levels. Seçilmiş and Öztürk[12] reported that there was no significant difference between the clinical condition of the patient, need for intensive care, and COHb level. They stated that as the exposure duration to CO increased, COHb level, cardiotoxicity, and neurological symptoms increased.

The limitation of our study is the small sample size. However, despite being a single center, our unit is a center that accepts these patients.

CONCLUSION

A guideline containing precise clinical and laboratory parameters for HBOT in children has not been developed yet. Although many studies agree on the use of HBOT in severe poisoning, there are differences in treatment of mild and moderate cases. However, considering the unpredictability of delayed neurological sequelae, it is also suggested that the use of HBOT only in severe cases is too limiting. In our study, the duration of CO exposure, COHb levels, neurological symptoms, and lactate levels were found to be guiding parameters in determining the need for HBOT. More research is needed to develop guidelines to determine which pediatric patients admitted with CO poisoning should be referred to an HBOT center.

Ethics Committee Approval: This study was approved by the ethics committee of İstanbul University (Approval date: 26.01.2018 and number 02).

Informed Consent: Informed consent was not required because of the retrospective nature of the study and the analysis used is anonymous clinical data.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – M.U., S.G., R.Y.; Design – M.U., S.G., R.Y.; Supervision – M.U.; Materials – M.U., S.G., R.Y.; Data Collection and/or Processing – M.U.; Analysis and/or Interpretation – M.U., S.G., R.Y.; Literature Review – M.U., S.G., R.Y.; Writing – M.U., S.G., R.Y.; Critical Review – M.U., S.G., R.Y.

Acknowledgments: The authors thank the division of pediatric emergency nurses and hyperbaric oxygen therapy unit staff for their assistance in the treatment of patients.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: This study received no funding.

The manuscript has been presented at the 57th Turkish Pediatrics Congress on 22-26 May 2022 in Cyprus.

REFERENCES

1. Prockop LD, Chichkova RI. Carbon monoxide intoxication: an updated review. *J Neurol Sci*. 2007;262(1-2):122-130. [CrossRef]
2. Gozubuyuk AA, Dag H, Kacar A, Karakurt Y, Arica V. Epidemiology, pathophysiology, clinical evaluation, and treatment of carbon monoxide poisoning in child, infant, and fetus. *North Clin Istanb*. 2017;4(1):100-107. [CrossRef]
3. Chang YC, Lee HY, Huang JL, Chiu CH, Chen CL, Wu CT. Risk factors and outcome analysis in children with carbon monoxide poisoning. *Pediatr Neonatol*. 2017;58(2):171-177. [CrossRef]
4. Huzar TF, George T, Cross JM. Carbon monoxide and cyanide toxicity: etiology, pathophysiology and treatment in inhalation injury. *Expert Rev Respir Med*. 2013;7(2):159-170. [CrossRef]
5. Uysalol M, Uysalol EP, Saraçoğlu GV, Kayaoğlu S. A retrospective analysis of pediatric patients admitted to the pediatric emergency service for carbon monoxide intoxication. *Balk Med J*. 2011;28:237-243. [CrossRef]
6. Gorman D, Drewry A, Huang YL, Sames C. The clinical toxicology of carbon monoxide. *Toxicology*. 2003;187(1):25-38. [CrossRef]
7. Weaver LK, Valentine KJ, Hopkins RO. Carbon monoxide poisoning risk factors for cognitive sequelae and the role of hyperbaric oxygen. *Am J Respir Crit Care Med*. 2007;176(5):491-497. [CrossRef]
8. Ernst A, Zibrak JD. Carbon monoxide poisoning. *N Engl J Med*. 1998;339(22):1603-1608. [CrossRef]
9. Keleş A, Demircan A, Kurtoğlu G. Carbon monoxide poisoning: how many patients do we miss? *Eur J Emerg Med*. 2008;15(3):154-157. [CrossRef]
10. Casillas S, Galindo A, Camarillo-Reyes LA, Varon J, Surani SR. Effectiveness of hyperbaric oxygenation versus normobaric oxygenation therapy in carbon monoxide poisoning: a systematic review. *Cureus*. 2019;11(10):e5916. [CrossRef]
11. Mendoza JA, Hampson NB. Epidemiology of severe carbon monoxide poisoning in children. *Undersea Hyperb Med*. 2006;33(6):439-446.
12. Seçilmiş Y, Öztürk MA. Factors that affect prognosis and morbidity in pediatric patients with carbon monoxide poisoning. *J Pediatr Emerg Intensive Care Med*. 2018;5(3):113-118. [CrossRef]
13. Aslan S, Erol MK, Karcıoğlu O, Meral M, Cakır Z, Katırcı Y. The investigation of ischemic myocardial damage in patients with carbon monoxide poisoning. *Anadolu Kardiyol Derg*. 2005;5(3):189-193
14. Moon JM, Shin MH, Chun BJ. The value of initial lactate in patients with carbon monoxide intoxication: in the emergency department. *Hum Exp Toxicol*. 2011;30(8):836-843. [CrossRef]
15. Benaissa ML, Mégarbane B, Borron SW, Baud FJ. Is elevated plasma lactate a useful marker in the evaluation of pure carbon monoxide poisoning? *Intensive Care Med*. 2003;29(8):1372-1375. [CrossRef]
16. Damlapinar R, Arikan FI, Sahin S, Dallar Y. Lactate level is more significant than carboxihemoglobin level in determining prognosis

of carbon monoxide intoxication of childhood. *Pediatr Emerg Care*. 2016;32(6):377-383. [CrossRef]
17. Sokal JA, Kralkowska E. The relationship between exposure duration, carboxyhemoglobin, blood glucose, pyruvate and lactate and the severity of intoxication in 39 cases of acute carbon monoxide poisoning in man. *Arch Toxicol*. 1985;57(3):196-199. [CrossRef]
18. Piantadosi CA. Diagnosis and treatment of carbon monoxide poisoning. *Respir Care Clin N Am*. 1999;5(2):183-202.
19. Grieb G, Simons D, Schmitz L, Piatkowski A, Grottke O, Pallua N. Glasgow Coma Scale and laboratory markers are superior to COHb in predicting CO intoxication severity. *Burns*. 2011;37(4):610-615. [CrossRef]
20. Huysal K, Ustundag Budak YU, Aydin U, Demirci H, Turk T, Karadag M. COHb level and high-sensitivity cardiac troponin T in 2012 in Bursa, Turkey: a retrospective single-center study. *Iran Red Crescent Med J*. 2016;18(5):e27061. [CrossRef]