FACTORS THAT INFLUENCE THE DECISION FOR HYPERBARIC OXYGEN THERAPY (HBOT) IN CASES OF CARBON MONOXIDE POISONING: A RETROSPECTIVE STUDY

INDICATION D’OXYGÉNOthéRAPIE HYPERBARE (OHB) EN CAS D’INTOXICATION AU MONOXYDE DE CARBONE: ÉTUDE RÉTROSPECTIVE

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SUMMARY. Carbon monoxide poisoning (COP) is one of the most common types of potentially fatal poisoning throughout the world. Hyperbaric oxygen therapy (HBOT) is an effective and quick response modality that clears symptoms and prevents sequelae. HBOT should be administered within 4-6 hours after poisoning. The aim of this study was to contribute COP treatment protocols by retrospectively examining the results of COP cases who were administered HBOT according to clinical and laboratory findings at the Emergency Department.

Keywords: hyperbaric oxygen treatment, carbon monoxide poisoning, carboxyhemoglobin, emergency medicine

RÉSUMÉ. L’intoxication au monoxyde de carbone (ICO), potentiellement létale, est une des intoxications les plus courantes au monde. L’OHB permet de réverser rapidement les symptômes d’ICO et d’en prévenir les séquelles. Elle doit être réalisée dans les 4 à 6 heures suivant l’intoxication. Le but de cette étude est de contribuer à l’amélioration des protocoles d’OHB en cas d’ICO après examen rétrospectif des dossiers recueillis dans un service d’accueil des urgences.

Mots-clés: oxygénothérapie hyperbare, intoxication au monoxyde de carbone, carboxyhémoglobine, médecine d’urgence

Introduction

Carbon monoxide poisoning (COP) is a significant health problem. Carboxyhemoglobin (COHb) levels are usually used to diagnose COP. As well as rapid changes in consciousness and widespread neurological symptoms after CO exposure, there may also be atypical symptoms. Neurological symptoms can persist for up to 20 days after poisoning, and cognitive sequelae for up to a month.1 Failure to determine the degree of damage sustained in the brain after rapid recovery from high COHb levels with oxygen treatment in the first 4 hours after poisoning is one of the most important reasons for COP-related death.2,3 Early diagnosis is the most important factor in COP, and when a rapid decision is taken to administer HBOT, late symptoms and signs together with neurological sequelae can be prevented. During treatment in the first intervention, 100% oxygen is used as normobaric oxygen therapy (NBOT) and hyperbaric oxygen therapy (HBOT).4 NBOT is generally administered with a reservoir mask, diffusion mask, and various other face-covering masks. Although mortality rates for cases reaching the ED are low, with the use of NBOT and HBOT together to treat COP, the frequency of neurological complications in particular is currently reducing throughout the world. HBOT has been found to be successful in preventing late complications in COP patients.

HBOT should be administered to patients with syncope as soon as possible, especially those who have experienced convulsions, lengthy loss of consciousness or neurological deficit, have clinical signs of myocardial involvement, or have highly resistant acidosis. In patients with symptoms that do not clear after 4 hours of NBOT, HBOT can be administered to those with a COHb level of 30% and above, even if there are few clinical symptoms in the first evaluation. Several studies have compared the effect of HBOT on COHb level, lactate and other parameters.2,5,6 Generally, HBOT is preferred for patients with severe COP.1 As the most significant advantage of HBOT is the increase in dissolved oxygen in the blood, so it contributes to the treatment through several mechanisms. The first of these mechanisms is the elimination of carbon monoxide. The second is the prevention of lipid peroxidation in the brain. Thirdly, HBO contributes to ATP levels remaining high in tissues exposed to CO. The main disadvantages of HBOT are the need for transportation to the treatment centre, hyperoxic attacks and barotrauma.1 When making the decision to administer HBOT, the advantages and disadvantages should be taken into consideration. In several studies, there are conflicting data regarding the decision to administer HBOT to patients.1,7,8

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In this study, the clinical and laboratory findings of patients who were given HBOT were compared, according to COHb levels. The aim is to contribute to decision-making concerning HBOT, which is extremely important in the follow-up and treatment of severe COP cases.

**Materials and methods**

**Patient selection**

A retrospective examination was made of the data of 217 patients who presented to the adult and paediatric Emergency Departments (ED) of our hospital between 1 January 2016 and 1 January 2018. Approval for the study was obtained from the Local Ethics Committee. Patients who were administered NBOT only were excluded from the study. Four of the remaining patients were excluded due to incomplete data, 2 abandoned treatment early, 2 were pregnant, and 1 did not attend the second HBOT session or continuing multiple treatments, leaving a total of 100 patients receiving HBOT to be included in the study.

The diagnosis of COP was made with findings in the patient history of poisoning following exposure to a source of CO, such as stove, boiler or fire, and the determination of >10% COHb in peripheral blood. The evaluation was made with data from patient records on age, gender, residence in the same region or transfer from another region, symptoms, findings at the time of presentation, CO source, arterial blood gas pH, COHb, lactate level, single or multiple sessions of HBOT, and prognosis. After data collection, the patients were divided into two groups: Group I was made up of patients with COHb level of 0-30% and Group II >30%. Data collection and preparation of this paper was conducted according to Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. A flowchart of the patients included in and excluded from the study is provided in Fig. 1.

**Treatment protocol applied in the Emergency Department**

The data of patients who presented to the ED were examined, and they were followed up with normal pressure oxygen treatment, or with HBOT, confirmed by an ED specialist and administered by a paediatric ED specialist and a hyperbaric specialist working together. HBOT was administered in single or multiple sessions, and the results were examined together with the results of the physical and neurological examinations. HBOT was administered (Baroks® O₂multi machine, Mul32, standard, 90 mins at 2.7 pressure) and as it continued, patients were kept under observation to ensure O₂ saturation remained >90%. Patients showing full clinical recovery were discharged after 24 hours with medication, and those who did not respond to a single session were discharged and re-admitted for multiple HBOT sessions, maintaining 100% oxygen between each one. The study was completed by recording data from the 3-week follow-up examination of the patients. Any patient with data that did not conform to the treatment protocol was excluded from the study.

**Statistical analysis**

Data obtained from patient records were transferred to a computer and a statistical analysis was performed using SPSS v22.0 software. The study was retrospective and descriptive. A frequency table was created, and conformity of the data to normal distribution was assessed with the Kolmogorov Smirnov test; those conforming to the normal distribution were checked with the One Sample Kolmogorov Smirnov test. Descriptive statistics for the measurement values were stated as mean±standard deviation, and for the numerical values, as number (n) and percentage (%). In the comparative analyses, when parametric test assumptions were met, the Student’s t-test was applied to determine the difference between the measured variables of the two groups. When parametric test assumptions were not met, the Mann-Whitney U test was applied. To compare the difference between the two percentages, Chi-square analysis was applied. For the analysis of more than two groups that met the parametric assumptions, One-Way Variance Analysis (ANOVA) and the post hoc Bonferroni were used, and when parametric assumptions were not met, Kruskal Wallis variance analysis was used. Spearman Correlation Analysis was applied to examine the relationships between variables. All statistical analyses were performed two-way at a 95% confidence interval. A value of p<0.05 was accepted as statistically significant.

**Results**

The patients comprised 41 males (41%) and 69 females (69%), with a mean age of 34.43±21.42 years (range, 6 months-92 years). The age distribution of the patients is shown in Fig. 2.
A total of 48 patients (48%) were resident in the region and presented directly to our hospital, while 52 (52%) were transferred from EDs outside the region. Ninety-eight cases (98%) were recorded as accidental poisoning and 2 (2%) as attempted suicide. Four patients (4%) had no history of contact with a CO source. In 95% of cases, the source of poisoning was associated with coal, and in the remaining 5% with natural gas.

Glasgow Coma Score (GCS) on presentation was 15 for 90 patients (90%) and ≤14 for the remaining 10 (10%). Forty-eight patients complained of a headache, 17 listlessness, 54 nausea, 16 vertigo, and 9 flu-like symptoms, cough and blurred vision. Nausea and vomiting were determined at the highest rate in both groups. Details of symptoms and COHb levels are shown in Table I.

When patient symptoms were examined, change in consciousness was determined in 49 patients (49%), convulsions in 24 (24%), loss of balance in 16 (16%), syncope in 24 (24%), speech impairment in 9 (9%), and dizziness in 10 (10%). Other findings were determined in 66 patients (66%). Seizures and syncope were determined at a statistically significant high rate. A single session of HBOT was administered to 89 patients (89%) and 2 or more sessions to 11 (11%).

In arterial blood gases, mean COHb levels were 35.13±10%, pH values 7.34±0.10, and lactate values 4.40±3.51. Lactate values were 2.89±1.98 in Group I and 5.10±3.84 in Group II. Lactate values for Groups I and II are compared in Fig. 3. Group II values were found to be statistically significantly higher. A total of 5 patients in Group II were determined to have severe metabolic acidosis and pH<7.2.

No statistically significant differences were detected between the groups with respect to patient symptoms. Comparison of patients in the two groups with respect to headache, weakness, nausea/vomiting and vertigo is shown in Fig. 4.

![Fig 3 – The distribution of lactate levels according to groups.](image)

![Fig 4 – The distribution of symptoms according to COHb level (0 = no symptoms, 1 = symptom-positive).](image)

### Table I - Patient characteristics and statistical comparison of data according to COHb levels

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patient number = 100 mean ± SD or n (%)</th>
<th>COHb 0-30% (patient n = 31) mean ± SD or n (%)</th>
<th>COHb &gt;30% (patient n = 69) mean ± SD or n (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>34.43±21.42</td>
<td>28.91±18.59</td>
<td>36.91±22.25</td>
<td>0.048</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>41 (41)</td>
<td>12 (38.7)</td>
<td>29 (42)</td>
<td>0.755</td>
</tr>
<tr>
<td>Hospital</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Direct</td>
<td>48 (48)</td>
<td>28 (90.3)</td>
<td>3 (9.7)</td>
<td>0.628</td>
</tr>
<tr>
<td>Transfer from other centres</td>
<td>52 (52)</td>
<td>67 (97.1)</td>
<td>2 (2.9)</td>
<td>0.788</td>
</tr>
<tr>
<td>Suicide attempt</td>
<td>2 (2)</td>
<td>1 (3.2)</td>
<td>1 (1.4)</td>
<td>0.557</td>
</tr>
<tr>
<td>GCS &lt;14</td>
<td>10 (10)</td>
<td>3 (9.7)</td>
<td>7 (10.1)</td>
<td>0.597</td>
</tr>
<tr>
<td>Source</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coal</td>
<td>95 (95)</td>
<td>28 (90.3)</td>
<td>67 (97.1)</td>
<td>0.159</td>
</tr>
<tr>
<td>Natural gas</td>
<td>5 (5)</td>
<td>5 (8.7)</td>
<td>2 (2.9)</td>
<td>0.170</td>
</tr>
<tr>
<td>Symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>48 (16)</td>
<td>14 (45.2)</td>
<td>34 (49.3)</td>
<td>0.703</td>
</tr>
<tr>
<td>Weakness</td>
<td>17 (17)</td>
<td>5 (16.1)</td>
<td>12 (17.4)</td>
<td>0.876</td>
</tr>
<tr>
<td>Nausea</td>
<td>54 (54)</td>
<td>16 (51.6)</td>
<td>38 (55.1)</td>
<td>0.748</td>
</tr>
<tr>
<td>Vertigo</td>
<td>16 (16)</td>
<td>5 (16.1)</td>
<td>11 (15.9)</td>
<td>0.981</td>
</tr>
<tr>
<td>Other</td>
<td>9 (9)</td>
<td>5 (16.1)</td>
<td>4 (5.8)</td>
<td>0.307</td>
</tr>
<tr>
<td>Findings</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transient loss of consciousness</td>
<td>49 (49)</td>
<td>11 (35.5)</td>
<td>35 (50.7)</td>
<td>0.207</td>
</tr>
<tr>
<td>Seizures</td>
<td>24 (24)</td>
<td>3 (9.7)</td>
<td>21 (30.4)</td>
<td>0.010</td>
</tr>
<tr>
<td>Postural instability</td>
<td>16 (16)</td>
<td>5 (16.1)</td>
<td>11 (15.9)</td>
<td>0.597</td>
</tr>
<tr>
<td>Syncope</td>
<td>24 (24)</td>
<td>3 (9.7)</td>
<td>21 (30.4)</td>
<td>0.046</td>
</tr>
<tr>
<td>Speech impairment</td>
<td>9 (9)</td>
<td>3 (9.7)</td>
<td>6 (8.7)</td>
<td>0.874</td>
</tr>
<tr>
<td>Dizziness</td>
<td>10 (10)</td>
<td>3 (9.7)</td>
<td>7 (10.1)</td>
<td>0.943</td>
</tr>
<tr>
<td>Other findings</td>
<td>66 (66)</td>
<td>11 (35.5)</td>
<td>38 (55.1)</td>
<td>0.070</td>
</tr>
<tr>
<td>HBO treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single session</td>
<td>89 (89)</td>
<td>28 (90.3)</td>
<td>61 (88.4)</td>
<td>0.777</td>
</tr>
<tr>
<td>Multiple sessions</td>
<td>11 (11)</td>
<td>3 (9.7)</td>
<td>8 (11.6)</td>
<td>0.082</td>
</tr>
<tr>
<td>Lactate (mmol/L) (n = 54)</td>
<td>4.40±1±5.1</td>
<td>2.89±1.98</td>
<td>5.10±3.84</td>
<td>0.030</td>
</tr>
<tr>
<td>pH (n=66)</td>
<td>7.34±0.10</td>
<td>7.37±0.05</td>
<td>7.32±0.12</td>
<td>0.047</td>
</tr>
<tr>
<td>Severe metabolic acidosis (pH&lt;7.2)</td>
<td>5 (5)</td>
<td>0 (0)</td>
<td>5 (5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Outcome</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discharged with medication</td>
<td>89 (89)</td>
<td>28 (90.3)</td>
<td>61 (88.4)</td>
<td>0.858</td>
</tr>
<tr>
<td>Partial response</td>
<td>6 (6)</td>
<td>2 (6.5)</td>
<td>4 (5.8)</td>
<td>0.331</td>
</tr>
<tr>
<td>No change</td>
<td>5 (5)</td>
<td>1 (3.2)</td>
<td>4 (5.8)</td>
<td>0.307</td>
</tr>
<tr>
<td>EX</td>
<td>1 (1)</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>0.134</td>
</tr>
</tbody>
</table>
The comparison of treatment with single or multiple sessions of HBOT for patients in Groups I and II is shown in Fig. 5.

![Fig. 5 – The distribution of single and multiple sessions of HBOT according to COHb levels.](image)

The distribution of cases according to month of presentation is shown in Fig. 6. Most cases presented in the months of November, December, January and February, and the lowest numbers were seen in July, August and September.

![Fig. 6 – Patient distribution according to month of presentation.](image)

**Discussion**

According to this study, COHb level alone is not sufficient to diagnose COP and plan treatment. A significant difference was found in neurological findings according to the COHb levels of the patients in this study. Thus, symptoms and findings are important when making a decision to give HBO. In addition, a significant difference was found between the groups with respect to patients with low pH and high lactate. However, lactic acidosis should not be treated or care must be taken to avoid sudden changes in pH.

The aim of COP treatment is to rapidly remove the toxic substance and quickly recover cellular damage by increasing oxygen transport and capacity. Vital signs and cardiac function must be monitored. Hydration, NBOT and HBOT are the basic techniques used to treat hypoxia. The binding of CO to hemoglobin is reversible, and oxygen competes with CO to bind to it. The half-life of CO is 5 hours at room temperature and with 100% oxygen treatment it is 90 minutes. The half-life of CO with HBOT at 3 ATA is 25 minutes. This duration is important, particularly for its cardiac effect. HBOT reduces the half-life of COHb. Free oxygen radical production is reduced and mitochondrial functions and capillary platelet activation are strengthened. The period of recovery from symptoms is shortened. Compared to NBO treatment, HBOT reduces long-term neurological complications. In unconscious patients, HBOT should certainly be the first choice. Its effect is to block the hypoxia induced by CO in the cells. As far as possible, HBOT should be administered within the first 6 hours. In the current study, all the patients were first started on NBOT, and patients suitable for HBOT were admitted directly for HBOT. In patients where loss of consciousness continues, HBOT can be administered again after 6-8 hours. To be able to provide 100% oxygen performance in the body, HBOT at 2.7-3 ATA for 30-90 minutes is sufficient. In maintenance, it should be given for 90 minutes at a reduced pressure of 2.2 ATA. In accordance with previous reports in the literature, patients in the current study presenting to the ED were administered direct NBOT, and suitable patients were administered standard HBOT at 2.7-3 ATA. With NBOT at 10-15 lt/min with a diffusion mask, and with masks impermeable to air covering the face, COHb levels are brought down to <5% in 4-6 hours. Generally, pH falls and lactic acidosis may be seen. As lactic acidosis is increased by oxygen penetration, the acidosis must be corrected. In the comparisons of the current study, lactic acidosis was found to be significant, according to COHb levels.

Misdiagnosed COP cases and delayed initiation of HBO treatment for COP can result in significant complications. As most cases are deceased before they are brought to the ED, the actual incidence is not exactly known. The causes of COP show significant variations from country to country and season to season. In the USA, suicide is the leading cause of COP, followed by accidental poisoning. Among the accidental reasons, the most common is motor vehicle exhaust fumes. Several studies have reported that the vast majority of poisonings occur accidentally. In our study, 98 (98%) out of 100 patients who presented to the ED and were administered HBOT were accidental COP cases. In a study by Mendoza et al., it was determined that in the USA rates of accidental COP were higher, and in young children poisoning was from coal stoves. Although this is a preventable cause of COP, there continue to be cases of poisoning in the same months every year. Similarly, in the current study, most cases were seen in the winter months of November to February, constituting 88% of total cases. Mendoza et al. reported 51% of total cases in the same months due to coal stove poisonings. This difference could be attributed to a greater use of coal in Turkey in those months. Public education on the use of coal, as well as inspections, could be significant factors in reducing morbidity and mortality associated with this cause of poisoning.

A wide range of findings and symptoms of acute COP are seen. Symptoms of COP include listlessness, headache, dizziness, nausea, vomiting, cough, respiratory problems and tachypnea. Findings may also include arrhythmia and tachycardia of the cardiovascular system, and ataxia, confusion, syncope, convulsions and coma associated with its effects on the
central nervous system.\textsuperscript{12} Patient symptoms and findings in the current study were similar to those reported in other studies.\textsuperscript{5,6,8} No relationship has been found between clinical findings at the time of presentation with COP and COHb levels.\textsuperscript{4,15,17} Keles et al.\textsuperscript{13} reported that there was a relationship between severity of neurological findings and COHb level. In the current study, seizures and syncope (p=0.04) were seen to be statistically significant in the comparison between the groups according to COHb level. As for other symptoms and findings, the difference between the groups was not statistically significant.

The relationship between COHb level and prognosis in COP has not yet been clarified.\textsuperscript{1,12} The results of both groups in the current study were examined and no significant difference was determined. Although there are studies showing that COHb levels could be affected by length of exposure with respect to the development of neurological sequelae, full consensus has not been reached. Ernst et al. reported that there could be early or late neurological findings in COP cases with a COHb level of >30% at the time of presentation.\textsuperscript{3} Early neurological findings may be short-term loss of consciousness, convulsions, brain edema and coma.\textsuperscript{4} In the current study, two groups - one made up of patients with a COHb level of over 30% and the other of 30% or below - were compared, and no statistically significant difference was found. In studies of children affected by COP, acute neurological symptoms have been reported at rates of 65.0%-86.7%.\textsuperscript{18}

In the current study, neurological findings in the form of non-response to stimulus were found in 49% of cases. Several studies have reported that if there are neurological findings in patients presenting with moderate and severe COP, the administration of HBOT as soon as possible could be useful in preventing the formation of neuropsychiatric sequelae.\textsuperscript{15,18,19} Eighty-nine (89%) of the patients receiving HBOT in this study made a full recovery, while 6 made a partial recovery and 5 showed no response to treatment. One patient died. The results of the current study are consistent with data published previously in the literature.

In addition to all these positive effects, HBOT can also cause complications, such as seizures related to hyperoxia, barotrauma in the ears, anxiety and oxidative stress.\textsuperscript{1} Physicians must take these complications into consideration when deciding for HBOT, and also during the follow-up.\textsuperscript{6,20,22} In the current study, only 1 patient suffered anxiety. Also in the literature, no difference has been shown between single or multiple sessions of HBO treatment as far as complications are concerned.\textsuperscript{1}

HBO treatment should be planned not only on the basis of COHb level but also according to the clinical status of the patient. Poor general status on presentation, being unconscious, cardiac arrest, coma, metabolic acidosis and a high COHb level increase mortality.\textsuperscript{17} If the patient shows any of these problems, HBOT is necessary. Changes in clinical status may necessitate changing treatment choices. From these findings it can be concluded that treatment for COP is determined by clinical status rather than COHb levels, and that treatment applications can be changed following a change in clinical status.\textsuperscript{21,22} As in the current study, patients can be followed up with 100% NBOT and saturation of ≥90%, they can be observed for a minimum of 24 hours and discharged when social needs are met, and neurological and other symptoms have cleared.\textsuperscript{2,5} In cases where symptoms persisted or did not diminish and lead to a full recovery, multiple HBO sessions were administered with successful results.

Contraindications for HBOT are the presence of pneumothorax, prolonged CPR, hemodynamically unstable patients and those with emphysema or bronchitis. Side-effects of HBOT include tympanic membrane rupture, ear pain, tension pneumothorax, hypotension, dysrhythmia, seizures, oxygen toxicity and several negative conditions that can occur during transportation of unstable patients to the treatment unit.\textsuperscript{12} In the current study, HBOT was not administered to patients with contraindications, and the COP patients’ files showed that only 1 patient suffered from anxiety.

\section*{Conclusion}

HBO therapy should certainly be administered to patients with obvious symptoms, low pH, high lactate levels and evident neurological findings. Multiple sessions of HBOT should be planned for patients with persistent symptoms that do not clear. Although it is recommended that patients are followed up for at least 24 hours, a follow-up 3 weeks later is also advised. The results of the study showed no significant difference between the COHb level groups, and it must be kept in mind that in COP there is no difference between age groups. The treatment of COP is a race against time. Patients needing HBOT must be carefully selected within the first few hours, and kept under close observation.

\section*{BIBLIOGRAPHY}