

The use of hyperbaric oxygen therapy for carbon monoxide poisoning in Europe

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ABSTRACT

Background: The aim of this survey was to identify practice differences in the treatment of carbon monoxide (CO) poisoning with hyperbaric oxygen (HBO₂) therapy among centers in Europe.

Materials and methods: Using a commercial online survey website (surveymonkey.com), we created a questionnaire and invited the medical directors of hyperbaric centers in Europe by email to complete the survey.

Results: Sixty-eight centers from 23 countries participated in the survey. While transient or prolonged unconsciousness was unanimously recognized as an indication for HBO₂ therapy, positive neurological findings, ECG suggesting acute ischemia and pregnancy were considered important indications of HBO₂ therapy in more than 95% of the centers.

Twenty-three (44%) centers reported that they used carboxyhemoglobin (COHb) levels as a criterion for patient selection. Among responders, 39% (18/46) reported delivering a single session within the first 24 hours of CO poisoning, and nine (19%) reported delivering three sessions in the first day. The majority of the centers (52%) replied that they initially gave a single session per patient, which was repeated if symptoms persisted. We identified a total of 21 different HBO₂ profiles used in European centers.

Conclusion: Our results showed that the indications of CO poisoning for HBO₂ therapy are still not universally recognized. Additionally, HBO₂ therapy protocols used at European hyperbaric centers varied significantly, suggesting a need for more education regarding the published guidelines.

INTRODUCTION

Carbon monoxide (CO) poisoning is an important healthcare problem worldwide. CO binds to heme proteins such as hemoglobin, myoglobin and mitochondrial cytochrome oxidase and causes tissue hypoxia. It also impairs cellular metabolism, eventually affecting, particularly, the cardiovascular and central nervous system functions [1-3]. Historically CO poisoning has been managed with normobaric oxygen (NBO₂), which was used specifically to accelerate the

elimination of CO. Since the 1960s hyperbaric oxygen (HBO₂) therapy has increasingly been used in the treatment of CO poisoning. HBO₂ therapy has been shown not only to further enhance CO clearance but also to provide additional treatment benefits such as inhibition of lipid peroxidation, impairment of leukocyte-endothelium adhesion, improvement of mitochondrial function and resolution of cerebral edema [2-4].

Scientific societies such as the Undersea and Hyperbaric Medical Society (UHMS) and the European

KEYWORDS: carbon monoxide poisoning, hyperbaric oxygen therapy

Committee for Hyperbaric Medicine (ECHM) have published guidelines on the use of HBO₂ in patients with CO poisoning. In the current study, we sought to identify the level of adherence to these guidelines by European HBO₂ centers and to determine variances in the treatment practices among these centers. While similar surveys have been performed previously in the United States [5-8], to our knowledge, this is the first to be conducted in Europe.

MATERIALS AND METHODS

This study was conducted between February 2015 and April 2015. Using a commercial online survey website (surveymonkey.com), we created a questionnaire in five languages (English, French, German, Italian and Turkish). We identified the medical directors of HBO₂ centers in Europe through an online registry [9] and invited them to participate in this study using an e-mail containing a link directing the responders to the survey website. Non-responders were reinvited to participate to the survey at Weeks 2 and 4 after study onset; the survey was closed one month after the last invitation. The questionnaire comprised the following questions.

1. Do you use HBO₂ therapy for CO poisoning?
2. What is the type of chamber used for HBO₂ treatment?
3. What is the number of patients treated for CO poisoning in 2014 (or during the last 12 months)?
4. Do you adhere to any of the published guidelines on the treatment of CO poisoning with HBO₂?
5. Which criteria do you consider as an indication for HBO₂ therapy in patients with CO poisoning?
6. Is carboxyhemoglobin (COHb) level utilized as an indication criterion for HBO₂ therapy?
7. What is the time delay allowed prior to HBO₂ therapy?
8. What is the number of HBO₂ treatments (dives) delivered within the first 24 hours after admission?
9. What is the total number of HBO₂ treatments (dives) administered per patient?
10. Describe the pressure (P; atm abs) and the duration of oxygen inhalation (t; minutes) of the treatment protocol used in your center (Figure 1).

The results were assessed using basic descriptive analyses. We calculated the percentages of each question by using the number of responding centers to that particular question as a denominator.

RESULTS

A total of 179 centers received the invitation to participate. Of these, 68 centers from 23 countries responded. Six centers (8%) replied that they did not use HBO₂ for CO poisoning. The majority of centers (45/52, 86%) used multiplace chambers. Overall, 2,778 patients (mean: 61.73 ± 94.63; median: 32, min 1 – max 430) were treated during 2014 in these centers. Overall, 14 (14/52; 26%) centers reported that they treated 50 or more patients in the past year. The distribution of the number of centers and patients by countries is shown in Figure 2.

A total of 49 of the centers (94%) reported they followed published guidelines. Among these, 32 (61%) were using the ECHM consensus report and 29 (55%) used the UHMS committee report. Additionally, 19 (36%) of the centers noted they used criteria established by their own center; and six (11%) reported use of other guidelines.

The presence of transient or prolonged unconsciousness was used as a patient selection criterion in all the participant centers. In addition, positive neurological findings (98%), ECG suggesting acute ischemia (96%) and pregnancy (94%) were also frequently used as indications for HBO₂ therapy. Of note, 23 (44%) centers reported that they used COHb level as a criterion for patient selection. The most frequently used COHb level was 25% (Figure 3). A complete list of the indications used for patient selection and their rate of acceptance is presented in Table 1.

While 17 (32%) centers reported that they accepted patients for HBO₂ treatment only if they were referred within the first six hours of exposure, seven (13%) did so within 12 hours and 16 (30%) within 24 hours. Altogether 40 (77%) centers did not accept patients with CO poisoning for HBO₂ treatment if they were referred 24 hours after exposure (Table 2).

Forty-six centers responded about the frequency and total number of HBO₂ sessions delivered. While 18 centers (18/46; 39%) applied a single HBO₂ session within the first 24 hours, 16 (34%) applied two, and

Figure 1: Template HBO₂ protocol where “p” denotes pressure and “t” duration

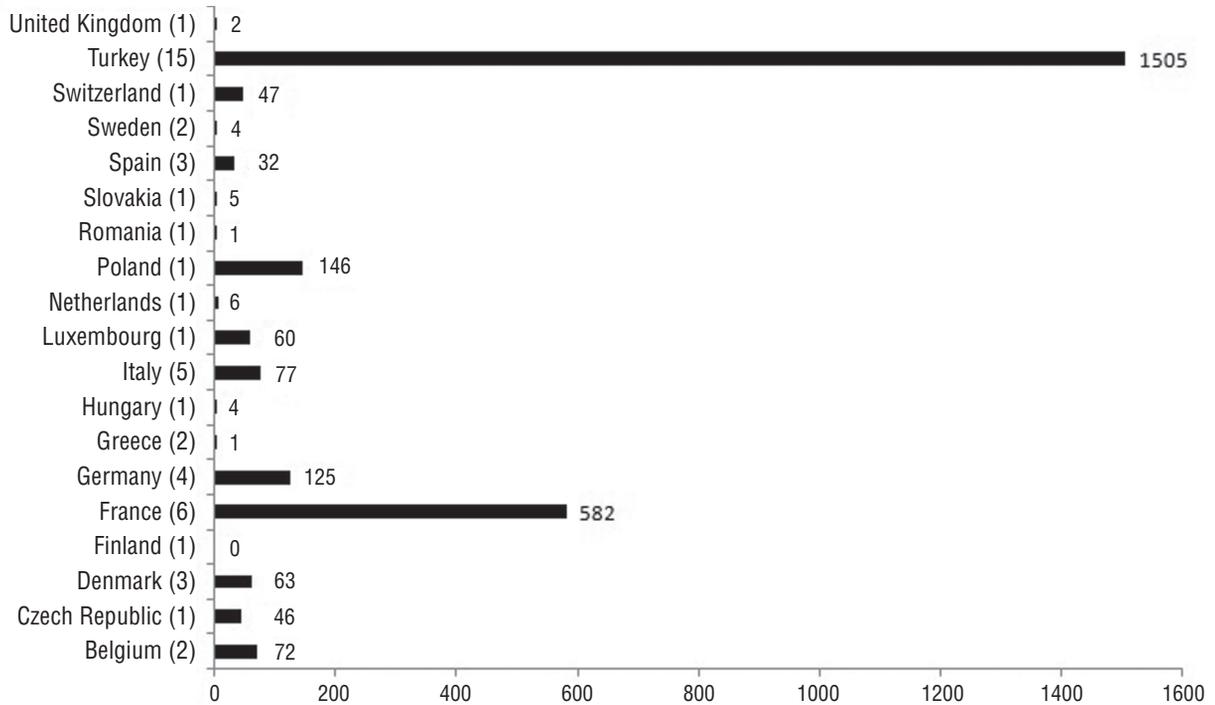
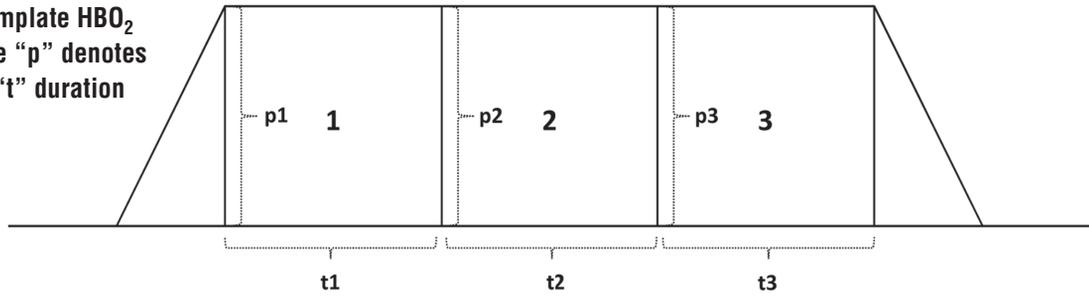


Figure 2: Bars represent the number of patients treated in 2014 in each country and the number of participant centers by country is presented in parenthesis

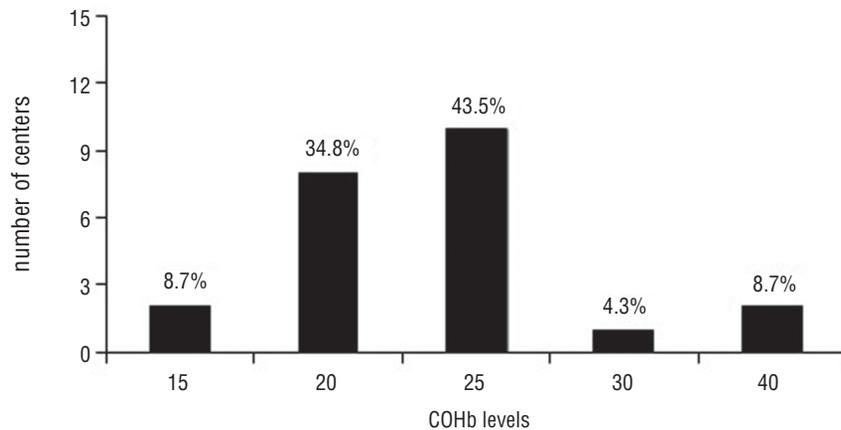


Figure 3: Carboxyhemoglobin levels and their acceptance rate

Table 1: Criteria used for HBO₂ indications in CO poisoning and their acceptance rate

CRITERIA	YES	NO
1 transient or prolonged unconsciousness	52 (100%)	0 (0%)
2 positive neurological findings	51 (98.1%)	1 (1.9%)
3 ECG suggesting acute ischemia	50 (96.2%)	2 (3.8%)
4 pregnancy	49 (94.2%)	3 (5.8%)
5 severe acidosis	42 (80.8%)	10 (19.2%)
6 persistent symptoms after 4 hours of normobaric oxygen therapy	36 (69.2%)	16 (30.8%)
7 normal ECG but elevated cardiac enzymes (ck-mb, troponin etc.)	35 (67.3%)	17 (32.7%)
8 abnormal psychometric testing	31 (59.6%)	21 (40.4%)
9 exposure to CO for 24 hours or longer	30 (57.7%)	22 (42.3%)
10 carboxyhemoglobin	23 (44.2%)	29 (45.8%)
11 age >36 years	7 (13.5%)	45 (86.5%)

Table 2: Maximum time delay allowed prior to HBO₂ therapy

TIME	N	%
<6 hours	17	32.7
<12 hours	7	13.5
<24 hours	16	30.8
<48 hours	4	7.7
>48 hours	8	15.4
Total	52	100

Table 3: Total number of HBO₂ sessions applied per patient

# SESSIONS	N	%
1	1	2.17
1, repeated if symptoms persist	24	52.17
2	3	6.52
3	7	15.21
3, repeated if symptoms persist	1	2.17
5	5	10.86
5, repeated if symptoms persist	5	10.86
Total	46	100

nine (19%) applied three sessions in the first day. Three (6%) of the centers replied that they delivered a single session but also provided additional session(s) depending on the patient’s clinical status; two other centers did not specify a particular number of treatments but instead noted that they decided the number of treatments based solely on the patient’s clinical condition. With regard to the total number of sessions applied per patient, 24 (52%) centers reported that they gave a single session per patient, which was repeated if symptoms persisted. Seven of the centers (15%) reported to routinely deliver three sessions per patient, regardless of the patient’s clinical condition (Table 3).

Finally, we identified a total of 21 different profiles used in 42 centers (Table 4), the most commonly used of which involved a total of 90 minutes of oxygen breathing at 2.5 atm abs (7/42; 16%).

DISCUSSION

We found that there were considerable variances in criteria used for patient selection among HBO₂ centers in Europe. Additionally, HBO₂ treatment profiles used to treat patients with CO poisoning showed wide variation. In the current study we did not, in any sense, aim to criticize any practice pattern in the management of CO poisoning with HBO₂. Instead we sought to demonstrate the diversity of the patterns and thereby point to the need for further studies which, hopefully, in the future will help establish universally recognized practice guidelines.

Although quite similar, the fact that UHMS guidelines are followed as frequently as ECHM guideline in European treatment centers is notable (61% vs. 55%, respectively). While UHMS recommends the use of HBO₂ therapy for all cases of acute symptomatic CO poisoning [1], ECHM recommendations include: unconsciousness at or before admission, clinical neurological, cardiac, respiratory or psychological signs or

symptoms and pregnancy [10]. Among the criteria stated in these guidelines, the presence of transient or prolonged unconsciousness, positive neurological findings, ECG suggesting acute ischemia and pregnancy were highly rated as indications for HBO₂ treatment (100%, 98%, 96% and 94%, respectively). The least accepted criterion, on the other hand, was the state of being older than 36 years (13%). The latter is actually a relatively new indication added to the UHMS committee report in the 2008 update one year after a study, conducted by Weaver, et al., revealed that patients older than 36 years had significantly higher risk of developing delayed neurologic sequelae than those under 36 [11].

Another less accepted criterion for patient selection was the COHb level (44%). This finding was in contrast with a previous survey conducted in North American HBO₂ centers, which revealed that 62% of the centers used COHb as an independent criterion for patient selection [5] as well as with another similar study conducted in Midwestern American HBO₂ centers (65%) (8). Findings from recent research demonstrating that COHb and clinical symptoms do not correlate [12] may partly account for the low acceptance rate of COHb as an independent criterion for patient selection in European centers. Nevertheless, among those accepting COHb as an indication for HBO₂ therapy, the most frequently used COHb level (25%) was in accordance with the UHMS guideline. The study by Hampson, et al. also revealed that a COHb level of 20% or 25% was being used by the majority of North American HBO₂ centers [5]. Of note, patients with a normal ECG but elevated cardiac enzymes (e.g., CK-MB, troponin) were interestingly reported as candidates for HBO₂ by almost two-thirds of the centers. We believe that this issue warrants further research.

Table 4: HBO₂ treatment protocols used in European centers

protocol	P1 (atm abs)	t1 (min)	P2 (atm abs)	t2 (min)	P3 (atm abs)	t3 (min)	n center	n patient
1	1.5	30	1.5	30	1.5	30	1	60
2	2	30	2	30	1.8	30	1	1
3	2.4	25	2.4	25	2.4	25	4	590
4	2.4	30	2.4	30	2.4	30	4	368
5	2.5	20	2.5	20	2.5	20	3	224
6	2.5	30	2.5	30	2.5	30	7	490
7	2.5	25	2.5	25	2.5	25	4	133
8	2.5	40	2.5	40			1	145
9	2.5	40	2.5	40	2.5	40	1	47
10	2.8	60	2	60			1	2
11	2.8	30	2.8	30	2.8	30	3	65
12	2.8	30	2.5	30			1	327
13	2.8	70	1.9	10	1.3	15	1	2
14	2.8	30	2.4	30	2.4	30	1	34
15	2.8	60	2.4	60	1.8	60	1	30
16	2.8	20	2.8	20	2.8	20	1	12
17	2.8	25	2.4	25	2.2	25	1	25
18	2.8	30	2.8	30			1	60
19	3	30	3	30	3	30	3	90
20	3	45	2	45			1	14
21	3	40	3	40	3	40	1	1

Early treatment with HBO₂ therapy is a challenging issue affecting treatment success in CO poisoning. ECHM does not recommend treatment with HBO₂ beyond 24 hours after CO exposure if the patient has become symptom-free [10]. While one-third of the centers (32%) in the current study reported that they accepted patients only within the first six hours, around one-third (30%) did so within 24 hours, and the rest reported to accept even delayed casualties. Hampson, et al. has also surveyed the same issue and determined that the majority of hyperbaric physicians allowed a delay of a maximum of 12 hours in patients with only transient loss of consciousness [5]. Delayed diagnosis, delayed indication for HBO₂ therapy and low number of HBO₂ centers may account for treatment delay.

Treatment frequency was an important conflicting issue among European centers. While a typical HBO₂ treatment protocol for the majority of indications involves the delivery of a single daily session, in certain conditions, such as in CO poisoning, patients are likely to benefit further from multiple sessions given within the first 24 hours. While no study has yet compared outcome results between one vs. multiple sessions delivered within the first day, one ongoing blinded randomized trial comparing one to three HBO₂ sessions in 24 hours will hopefully provide some important results on this issue [13]. This issue has, indeed, been more frequently discussed within the hyperbaric medicine community, particularly, following the Weaver study, which demonstrated that patients receiving three sessions per day of HBO₂ had significantly fewer neurologic sequelae when compared with those who did not receive HBO₂ treatment [14]. In the current survey, while the majority of centers (39%) reported to deliver a single session of HBO₂ therapy within the first 24 hours, 19% of the participants reported that they gave three daily sessions. Given the relative difficulty in doing so – i.e., staying on duty for almost the entire day – this rate is noteworthy.

The total number of HBO₂ sessions delivered in patients with CO poisoning also differed among centers. We identified that roughly half (24/46, 52%) of the HBO₂ centers in Europe tended frequently to apply a single session per patient, but gave a repeat session depending on the patient's clinical condition. Only one center replied that they never retreated patients. Two previous surveys [6,7], both conducted by Hampson, et al. on North American HBO₂ centers, surveyed the same issue and revealed that while in 1992, 24% of the centers never offered a repeat HBO₂ treatment for patients with CO poisoning, 10 years later this rate decreased to 8%. Taken together, physicians seem to be more likely to give multiple HBO₂ treatments in patients with CO poisoning in recent years. Further supporting this assumption is the fact that 21% of the centers in the current survey reported that they gave five or more HBO₂ treatments. This issue has been addressed by Gorman, et al., who, in a retrospective and non-randomized trial, have shown that the frequency of sequelae was significantly higher in patients who were

given a single HBO₂ session than in those who had two or more sessions (15). It is evident that more studies on this topic are needed.

We identified 21 different profiles used for the treatment of CO poisoning in European HBO₂ centers. Treatment profile no. 6 (Table 1: 2.5 atm abs, 90 minutes) was most commonly used [16%]. While the ECHM guideline does not state any recommendation on any specific treatment profile for CO poisoning, the UHMS guideline recommends the use of a pressure between 2.5 and 3.0 atm abs for a duration of 90 to 120 minutes per session [1].

While in the majority of HBO₂ indications, treatment is delivered using a pressure between 2.0-2.5 atm abs, some specific indications such as CO poisoning have been shown to benefit more with pressures between 2.8 and 3.0 atm abs. In his seminal work, Thom [16] has shown that oxygen at 3 – but not 1 – atm abs prevented brain lipid peroxidation, and 2 atm abs had an intermediate effect. This was followed by randomized controlled clinical trials reporting beneficial effects for HBO₂ therapy when used at pressures between 2.8 and 3.0 atm abs [14,17]. Studies lacking efficacy for HBO₂ for CO poisoning used 2.0 atm abs [18,19], a pressure that may be ineffective for CO poisoning, or had limitations prohibiting efficacy inferences from the trial [20-23]. Overall, these studies have probably influenced hyperbaric physicians' practice patterns toward applying 2.8 or 3.0 atm abs instead of 2.4 or 2.5 atm abs.

Two previous surveys conducted in northern [6] and Midwestern [8] American HBO₂ centers have indeed supported this assumption and demonstrated that the majority of these centers (83% and 55%, respectively) started HBO₂ treatment with either 2.8 or 3.0 atm abs. In contrast, in the current study, we observed that only around one-third of the centers (38%) used 2.8 or 3.0 atm abs pressure. The study with the best design of all randomized trials of this regard is the one by Weaver, et al [14]. This study showed a dramatic reduction in brain injury. In this study, patients were mostly treated promptly (four hours) and aggressively with a 3-atm abs session initially followed by two 2-atm abs sessions, all given in 24 hours. It is surprising that no surveyed center uses this specific

treatment protocol. It is unknown if protocols other than that of Weaver, et al. have equivalent, better or worse outcomes.

Given the participation rate, these results may not be generalizable throughout the whole European continent; nevertheless considering the number of participant countries and centers, the results are interesting.

CONCLUSION

Our results show that the indications of CO poisoning for HBO₂ therapy are still not universally recognized. Additionally, HBO₂ treatment profiles used at European hyperbaric centers varied significantly, suggesting a need for more education regarding the published guidelines.

Acknowledgments

We are grateful to the directors of European HBO₂ centers, who responded to our survey. This study could not be completed without their volunteer contribution.

Conflict of interest

The authors have declared that no conflict of interest exists with this submission. ■

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