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The safety of hyperbaric oxygen treatment – retrospective analysis in 2,334 patients

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ABSTRACT

Introduction: Hyperbaric oxygen (HBO_2) therapy is applied in a growing number of cases for patients with different comorbidities and is considered a generally safe therapy. The main side effects related to HBO_2 therapy are barotrauma, central nervous system- and pulmonary oxygen toxicity, claustrophobia, anxiety and visual disturbances. The aim of this study was to evaluate the incidence of side effects associated with HBO_2 therapy and risk factors in a large cohort of patients treated for different indications.

Methods: We conducted a retrospective analysis of 2,334 patients treated in the Sagol Center of Hyperbaric Medicine and Research, Assaf Harofeh, Israel, between June 2010 and December 2014. Patients were classified to one of three categories of indications:
Category A – non-neurological indications;
Category B – neurotherapeutic indications; and
Category C – acute indications.

Results: From a total of 2,334 patients, 406 (17.4%) experienced adverse event(s) (one or more) during HBO_2 therapy sessions. The overall per-session incidence was 721:100,000 events:sessions (0.72%). The main complication was middle ear barotrauma, which occurred in 9.2% of patients and in 0.04% of sessions. Females and children under the age of 16 years had increased risk for barotrauma. Other complications – hypoglycemia, oxygen toxicity, dizziness, anxiety reactions, dyspnea and chest pain – occurred in 0.5-1.5% of patients.

Conclusions: Strict operational protocols, including pre-HBO_2 therapy evaluations and in-chamber monitoring, are essential and improve patient safety. When applied, HBO_2 therapy can be considered one of the safest medical treatments available today.

INTRODUCTION

Hyperbaric oxygen (HBO_2) therapy is applied in a growing number of cases for patients with different comorbidities. Due to new indications such as idiopathic sudden sensorineural hearing loss [1] and recent clinical studies in medical conditions such as cerebral palsy, stroke and traumatic brain injury [2-4], the treated population has changed dramatically in both quantity and variety. Moreover, diabetic patients admitted to HBO_2 treatment for non-healing ulcers are older, with increasing numbers of comorbidities [5].

In general, HBO_2 therapy is considered to be safe with pressures lower than 3 atmospheres absolute (atm abs) when treatment sessions are shorter than two hours [1]. Accordingly, in recent years, HBO_2 protocols in clinical practice and studies have shifted to pressures lower than previously applied [1,6].

HBO_2 therapy-related complications can be di-

KEYWORDS: HBO, HBO_2, barotrauma, seizures, HBOT, HBO_2 therapy, safety, adverse events, complications

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vided into two major classes: pressure- or oxygen-related complications. Pressure-related complications include the following:

- middle ear barotrauma (MEB), the most common HBO2-therapy-related complication [1];
- sinus squeeze (SS), usually occurring in patients with upper respiratory tract infections or allergic rhinitis [7]; and
- pulmonary barotrauma with or without associated air embolism, occurring rarely during decompression [8,9].

Oxygen-related complications include:

- seizures induced by central nervous system (CNS) oxygen toxicity, more common at oxygen pressure higher than 2 atm abs;
- use of hoods instead of masks;
- inadequate air breaks and in patients suffering from carbon monoxide poisoning [10];
- reversible myopia, mostly in patients undergoing prolonged periods of daily HBO_2 sessions [11-13]; and
- pulmonary-related oxygen toxicity, considered to be very rare with the current protocols in use [14,15].

In addition, cardiovascular responses may include increased cardiac afterload and decreased cardiac output due to oxygen-induced peripheral vasoconstriction (increase in peripheral vascular resistance) [16,17]. These cardiovascular physiological changes are well tolerated by individuals with normal cardiac function, yet patients with compromised cardiac function have increased risk for pulmonary edema and/or cardiac ischemia [17,18].

The aim of this study was to evaluate the incidence of side effects associated with HBO_2 therapy and their risk factors in a large cohort of patients.

METHODS

A retrospective analysis was performed on patients treated in the Sagol Center of Hyperbaric Medicine and Research, Assaf Harofeh, Israel, between June 2010 and December 2014. Since June 2010, adverse events are strictly recorded in the medical files. Data collected from patients' medical files included age, sex, chronic diseases, medications, indication for HBO_2 therapy, hyperbaric pressure applied, number of sessions, side effects and reason for treatment termination. All patients were treated in a HAUX Starmed 2200 hyperbaric chamber, 2.2 meters wide by 11 meters in length divided into three compartments: Two are for treatment, including six and 12 patients seats; the third compartment, located between the two, is used for transition of patients and medical staff when needed.

Each patient was assigned to one of the following groups:

- **A.** Non-healing wounds, non-neurological radiation injury, osteomyelitis, AVN, fractures, Crohn's disease, idiopathic hearing loss.
- **B.** Stroke (both ischemic and hemorrhagic), traumatic brain injury, cerebral palsy, autism, radiation injury to the brain.
- **C.** Acute indications including decompression sickness, carbon monoxide (CO) intoxication, acute limb ischemia, central retinal artery occlusion.

Prior to the first session all patients were interviewed and examined by a hyperbaric physician. Chest X-ray was obtained from each patient. ECG was performed on patients with a history of cardiovascular diseases. History of epilepsy or seizures mandated a seizure-free interval of six months and normalized EEG prior to treatment. Before each session, heart rate, blood pressure and temperature were obtained in all patients, and blood glucose levels were measured in diabetic patients.

No patient with pneumothorax was accepted for treatment. Relative contraindications included bronchial asthma, obstructive pulmonary disease and pregnancy. Patients with fevers did not receive HBO_2 therapy until the fever was under control.

HBO_2 therapy was performed in a multiplace chamber equipped with video cameras and an intercom for observation of patients. In addition, a registered nurse certified for hyperbaric attendance was present inside the chamber each session for patient care. Patients were treated five times per week in different protocols:

1. 1.5 atm abs for 60 minutes with no air breaks and 0.8 meter-per-minute compression and decompression.
2. 2 atm abs for 90 minutes with five-minute air breaks every 30 minutes and 1 meter-per-minute compression and decompression.
3. 2.4 atm abs for 90 minutes with five-minute air breaks every 30 minutes and 1 meter-per-minute compression and decompression.
4. U.S. Navy Treatment Table 5 (TT5), Treatment Table 6 (TT6), Treatment Table 6A (TT6A) as described in the U.S. Navy Diving Manual [19].

Oxygen was supplied by masks or hoods.

Table 1: Basic patient characteristics.

			total number of sessions	average number of sessions
age	52.3 ± 22.5			
children <16	240 (10.3%)			
sessions	27 ± 22			
sex	males	1495 (64%)		
	females	839 (35%)		
indications	A	786 (33.7%)	25,072	32 ± 23
	B	1238 (53%)	36,195	29 ± 21
	C	310 (13.3%)	1,347	4 ± 5
atm abs	1.5	271 (11.6%)	12,303	45 ± 26
	2	1768 (75%)	49,049	28 ± 20
	>2	295 (12.6%)	1,262	4 ± 5

Table 2: Adverse events frequency and incidence per session

	patients	frequency (%)	sessions	incidence
subjective barotrauma	79	3.4	103	174:100,000
objective barotrauma				
MEB	215	9.2	242	410:100,000
SS	16	0.7	16	27:100,000
overall barotrauma	310	13.3	361	612:100,000
hypoglycemia	9	0.4	11	17:100,000
seizures	7	0.3	7	11:100,000
dizziness/weakness	36	1.5	36	57:100,000
claustrophobia	6	0.3	7	11:100,000
chest pain	22	0.9	22	35:100,000
dyspnea	8	0.3	8	13:100,000
visual changes	8	0.3		
TOTAL	406	17.4	452	0.77%

MEB = middle ear barotrauma SS =sinus squeeze

Approval from the Helsinki Ethics Committee of Assaf Harofeh Medical Center was obtained for retrospective analysis of all cases used in this study. No written consent was needed, according to the local ethics regulations. The study was registered in the U.S. National Institute of Health Clinical Trials registry.

Statistical analysis

Data are expressed as frequencies and percentages for non-parametric variables. Univariate analysis was performed using chi-square/Fisher's exact test to identify significant variables ($P<0.05$). Numeric variables analysis was performed using independent Student's t-test. Logistic regression was performed to control for potential confounders and to determine independent predictors for a specific side effect. Variables included: age, sex, number of sessions, hyperbaric pressure/protocol and diagnosis. Adjusted odds ratios (OR) and 95% confidence intervals (95% CI) were calculated. Methods were performed using the SPSS v.21 software (Armonk, N.Y., IBM Corp.).

RESULTS

Patients

The study included 2,334 patients with a total of 62,614 hyperbaric sessions. Mean age was 52.3 ± 22.5 years; 240 (10.3%) were children under the age of 16 years. The male-to-female ratio was 1.8:1 (Table 1).

The indications for treatment were as follows. The indications of:

- 786 (33.7%) patients, 25,072 sessions, were related to Category A;
- 1,238 (53%) patients, 36,195 sessions, were related to Category B;
- 310 (13.3%) patients, 1,347 sessions, had emergency indications under Category C (Table 1).

Univariate analysis of the adverse events per indication for treatment revealed that neurologic indications had a significantly lower rate of adverse events due to fewer barotrauma events ($p<0.0001$) (Table 3).

The hyperbaric pressures applied were as follows: 271 (11.6%) patients

Table 3: Adverse events per indication category

	Total	A	B	C	Comparison between A-B Groups#	Comparison between A-B-C Groups#
subjective barotrauma	79 (3.4%)	34 (4.4%)	42 (3.6%)	3 (1.0%)	P=0.44	P=0.137
middle ear barotrauma	215 (9.2%)	99 (12.8%)	107 (9.1%)	9 (3.0%)	P=0.009	P<0.0001
sinus squeeze	16 (0.7%)	3 (0.4%)	13 (1.1%)	0	P=0.087	P=0.54
hypoglycemia	9 (0.4%)	3 (0.4%)	6 (0.5%)	0	P=0.813	P=0.761
seizures	7 (0.2%)	2 (0.3%)	2 (0.3%)	3 (1.0%)	P=1.000	P=0.201
dizziness/ weakness	36 (1.5%)	13 (1.7%)	20 (1.5%)	3 (0.7%)	P=0.430	P=0.834
claustrophobia	6 (0.3%)	4 (0.5%)	1 (0.2%)	1 (0.3%)	P=0.141	P=0.078
chest pain	22 (0.9%)	9 (1.1%)	12 (!.0%)	1 (0.3%)	P=0.442	P=0.704
dyspnea	8 (0.3%)	4 (0.5%)	2 (+0.3%)	2 (0.6%)	P=0.272	P=0.222
vision	8 (0.3%)	2 (0.3%)	6 (0.5%)	0	P=0.421	P=0.372
total	406 (17.4%)	173(22.0%)	211 (17.0%)	22 (7.1%)	P=0.005	P<0.0001

Category A included patients with non-healing wounds, non-neurological radiation injury, osteomyelitis, AVN, fractures, Crohn's disease, idiopathic hearing loss.

Category B included patients with stroke (both ischemic and hemorrhagic), traumatic brain injury, cerebral palsy, autism and radiation injury to the brain.

Category C included patients with acute indications including decompression sickness, CO poisoning, acute limb ischemia, central retinal artery occlusion.

Inter-group differences significance was calculated using Chi-square test for non-parametric variables.

Category C patients, treated for emergency indications, were significantly different from the chronic subgroups A and B. Accordingly, post-hoc analysis comparing subgroups A and B was performed.

Statistical significance was considered as $p<0.05$.

were treated with 1.5 atm abs, 1,768 (75%) were treated with 2 atm abs and 295 (12.6%) were treated with pressures higher than 2 atm abs (Table 1). Univariate analysis of the adverse events per applied hyperbaric pressure revealed that patients treated by 1.5 atm abs had the highest rate of adverse events due to more barotrauma events ($p<0.0001$) (Table 4).

OVERALL ADVERSE EVENTS

From a total of 2,334 patients, 406 (17.4%) experienced an adverse event (one or more) during HBO_2 sessions. The overall per-session incidence was 721:100,000 events:sessions (0.72%). See Figure 1 for the relative frequency of each adverse event.

Barotrauma

Ventilation tube (VT) insertion or myringotomy was performed prior to treatment initiation in 79 (3.4%) patients who underwent a total of 3,563 sessions. Those patients were excluded from the barotrauma-related analysis.

Subjective symptoms of barotraumas (otalgia, sinus pain) were reported by 79 (3.4%) of patients, while 215 (0.36%) had objective signs of MEB per otoscopy and 16 (0.02%) had objective sinus barotrauma (tenderness and/or epistaxis). The overall incidence of objective barotrauma was 437:100,000 sessions (Table 2). Dental, inner ear or pulmonary barotrauma were not reported.

Most objective barotrauma events, 53%, occurred

Table 4: Adverse events per hyperbaric pressure applied

	total	1.5 atm abs	2 atm abs	>2 atm abs	significance
subjective barotrauma	79 (3.4%)	16 (7.3%)	60 (3.4%)	3 (1.1%)	P=0.011
middle ear barotrauma	215 (9.2%)	32 (14.5%)	174 (9.9%)	9 (3.2%)	P<0.0001
sinus squeeze	16 (0.7%)	3 (1.4%)	13 (0.7%)	0	P=0.183
hypoglycemia	9 (0.4%)	0	9 (0.5%)	0	P=0.576
seizures	7 (0.2%)	0	4 (0.2%)	3 (1.0%)	P=0.122
dizziness/ weakness	36 (1.5%)	3 (1.4%)	31 (1.8%)	2 (0.7%)	P=0.104
claustrophobia	6 (0.3%)	0	5 (0.3%)	1 (0.3%)	P=0.665
chest pain	22 (0.9%)	1 (0.4%)	20 (1.1%)	1 (0.3%)	P=0.252
dyspnea	8 (0.3%)	1 (0.4%)	5 (0.3%)	2 (0.7%)	P=0.751
vision	8 (0.3%)	1 (0.4%)	7 (0.4%)	0	P=0.558
total	406 (17.4%)	57 (21.2%)	328 (18.5%)	21 (7.1%)	P<0.0001

Frequency of patients is given in absolute numbers and percentage. Inter-group differences significance was calculated using Chi-square test for non-parametric variables.
Statistical significance was considered as p<0.05

in the first or second sessions, while 67% and 84% occurred during the first five and 10 sessions, respectively. More than 11% of the patients experienced barotrauma more than once. All patients were treated with rest and oxymetazoline nasal spray for few days. Of those patients who experienced barotraumas, 5% underwent uni/bilateral VT insertion in order to complete HBO_2 treatment.

Multivariate analysis related to objective MEB revealed that females (p=0.001, adj.OR=1.673 CI95% [1.249-2.242]) and children under 16 years of age (p=0.005, adj.OR=2.729 CI 95% [1.352-5.505]) are at increased risk for MEB. On the other hand, patients treated for neurological indications had lower risk for MEB (p=0.004, adj.OR=0.615 CI 95% [0.443-0.855]). The same increased risk was demonstrated by multivariate analysis of the overall barotrauma events (objective signs and/or subjective symptoms) in females (p=0.001, adj.OR=1.518) and children under 16 years of age (p=0.008, adj.OR=2.254). Likewise, neurologic diagnosis lowered the risk for overall barotrauma (p=0.019, adj.OR=0.709).

Seizures

Seven patients (0.3%) experienced seizures during or after HBO_2 therapy, with a total incidence of 11:100,000. However, only one patient (0.04%) had a true oxygen toxicity event (Table 2). No significant risk factors were found in univariate analysis.

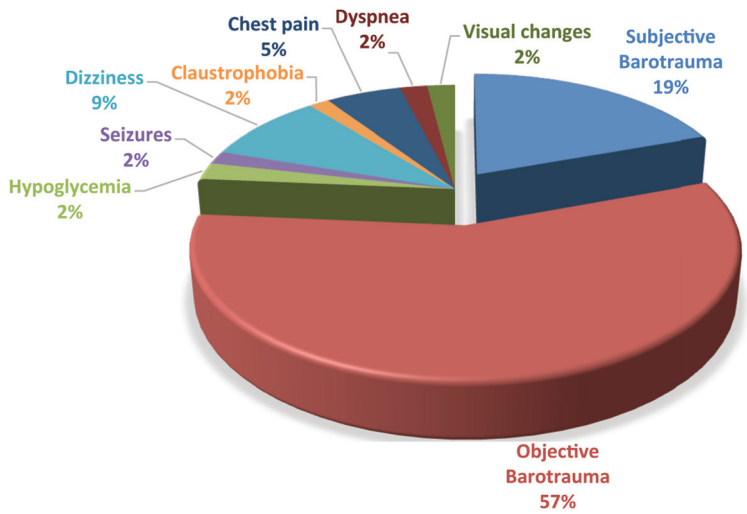
Hypoglycemia

Nine patients (0.4%) experienced hypoglycemia during HBO_2 therapy, with an incidence of 17:100,000 (Table 2). All patients were diabetic and were treated successfully by oral glucose administration. No significant risk factors were found in univariate analysis.

Dizziness/Weakness

Thirty-six patients (1.5%) experienced dizziness and/or weakness during HBO2 sessions, with an incidence of 57:100,000 (Table 2). No significant risk factors were found in univariate analysis. All patients recovered shortly after being taken out of the chamber. Further pulmonary and cardiac evaluations were normal in all cases.

Figure 1: Adverse events relative frequency



Barotrauma was the main adverse event (76%) where 55% had objective signs in otoscopy.

Claustrophobia

Six patients (0.3%) experienced claustrophobia during HBO_2 therapy, with an incidence of 11:100,000 (Table 2). No significant risk factors were found in univariate analysis.

Chest pain

A total of 22 patients (0.9%) experienced chest pain during HBO_2 therapy, with an incidence of 35:100,000 (Table 2). Multivariate analysis showed increased age was a weak risk factor (p=0.01, adj.OR=1.036 [1.006-1.067]. Cardiac evaluation revealed that only one patient had acute coronary syndrome.

Dyspnea

Eight patients (0.3%) experienced dyspnea during HBO_2 therapy, with an incidence of 13:100,000 (Table 2). No significant risk factors were found in univariate analysis.

Visual changes

Eight patients (0.3%) reported visual deterioration (Table 2). Six patients regained visual acuity a short time after HBO_2 therapy completion. No significant risk factors were found in univariate analysis.

Termination of HBO_2 therapy

A total of 58 (2.5%) patients did not complete the scheduled HBO_2 sessions due to side effects (Table 5). The main reason for treatment termination was middle ear barotrauma (55%).

DISCUSSION

Due to the growing number of patients being treated with HBO_2 therapy, it is crucial to reassess and analyze its safety within the new variety of patients and indications. The study summarized one of the largest cohorts of patients treated with HBO_2 therapy. From a total of 62,614 HBO_2 sessions, 452 adverse events were recorded – calculated incidence of 721:100,000 (0.72%). Most of the adverse events were benign, with no long-term residual unwanted effects.

Barotrauma-related side effects

The main complication during the course of HBO_2 is barotrauma, which affects the middle ear and, with a lower incidence, the sinuses. Barotrauma is the mechanical tissue damage produced by the environmental pressure changes. According to Boyle's law, which states that the pressure and the volume of a gas are inversely proportional, enclosed air cavities are susceptible to barotrauma. The pneumatic sockets in the cranium, which include the middle ear, inner ear and sinuses, are most frequently involved in the pressure stress caused by compression and decompression maneuvers during exposure to altered pressures in the hyperbaric chamber.

Table 5: Distribution of adverse events that caused patients to stop HBO_2 therapy

barotrauma		
MEB	32	(55.2%)
sinus squeeze	2	(3.4%)
seizures	2	(3.4%)
hypoglycemia	1	(1.7%)
dizziness/weakness	4	(6.9%)
claustrophobia	1	(1.7%)
chest pain	5	(8.6%)
dyspnea	8	(13.7%)
vision changes	3	(5.2%)
TOTAL	58	

In order to prevent or minimize barotrauma during compression in HBO_2 therapy, equilibration of the pressure in the enclosed air cavities must be achieved. This can be done by either compensatory maneuvers (autoinflation techniques) or use of ventilation tubes for those who cannot perform these maneuvers. During decompression, the gas in the enclosed cavities expands and is expelled passively.

Middle ear barotrauma has a wide reported incidence of 2%-82% [1,20-23]. The large variability can be attributed to the heterogeneous population sampled in different studies as well as the difference between subjective otalgia and objective barotrauma. Previous prospective studies reported incidence of 1.9%-2% sessions [24] of objective barotrauma, which is considerably higher than the incidence in our study (0.41%). A recent retrospective study on a small cohort by Heyboer, et al. found that 43% of the patients had objective middle ear barotrauma [25], which is higher than 3.8%-8% reported in other studies [24,26] and 9.2% in our study.

Although our study included children and neurologic patients (such as patients with stroke and traumatic brain injury), we had low incidence of barotrauma. This could be explained by our standard of operation: All intubated patients undergo myringotomy, and patients who are expected to have problems in equalization (such as young children or disabled and elderly patients) undergo uni/bilateral VT insertion prior to HBO_2 therapy. Each patient is evaluated and briefed by a qualified hyperbaric physician. Patients are also instructed to report any nasal congestion prior to session. Moreover, during each HBO_2 session, a qualified nurse inside the chamber keeps a strict surveillance for equalization difficulties.

In agreement with our study, Commons, et al. found that females are at increased risk for middle ear barotrauma [27]. The pathophysiology behind this finding is yet to be determined. Ambiru, et al. showed that the female gender and that ages older than 60 increase the risk for middle ear barotraumas [28]. In the current study, age above 60 did not serve as a risk factor for barotrauma. However, children under the age of 16, even though seen to equalize sufficiently in pretreatment, remained a significant concern (OR=2.2).

Plafki, et al. found that patients with sensory deficits involving the outer ear area may be at increased risk for middle ear barotrauma (and tympanic membrane rupture) due to lack of sensory inputs [24]. This should not be extrapolated to other neurologic conditions. On the contrary, in our study, patients with neurologic indications (such as stroke, traumatic brain injury, cerebral palsy) had significantly lower risk compared to patients with non-neurologic indications (OR=0.7). This finding might be due to tighter surveillance taken with former patients.

Prior studies have shown most of the equalization difficulties occur in the first sessions. However, in this study, more than a third of the patients had objective barotrauma after their fifth session [7]. This strengthens the need for an in-chamber attendant to guide and assist in equalization for all patients. In the case of a patient having trouble in equalizing, the compression is halted, and the attendant can assist the patient.

Lung barotrauma was not observed in this study, most probably due to proper lung evaluation prior to HBO_2 therapy. Baseline chest X-ray was performed prior to HBO_2 therapy in patients who had one of the following indications:

- age older than 60 for non-smokers and above 40 for smokers;
- any abnormal chest-related findings in the physical examination;
- any history of known lung pathology.

Patients with lung pathology and/or findings in physical examination performed a lung function test and underwent evaluation prior to treatment. Patient with severe obstructive disease, restrictive disease or focal finding were not treated unless it was acute lifesaving treatment.

Oxygen-related toxicity

CNS oxygen toxicity has been reported in varying incidence of 0.01%-0.03% and can increase up to 1:600 in hyperbaric pressure higher than 2.4 atm abs [29,30]. In our study, although seven seizures were recorded, only one was considered a pure cerebral oxygen toxicity while the rest were related to epilepsy or air embolism [31]. The pure oxygen toxicity was 1:62,614 which is significantly lower than previous studies [32]

Lung oxygen toxicity, which was reported in 15%-20% of the patients in the past, was not a concern in our series due to the limited oxygen pressures (up to 2 atm abs in the chronic treatments) and air breaks (five minutes, every 30 minutes) [33]. Previous studies have shown pulmonary symptoms are not produced by daily exposures to oxygen at 2 atm abs or 2.4 atm abs for 120 or 90 minutes, respectively [14,15]. Nevertheless, lung functions were not recorded before and after HBO_2 therapy completion, which may have revealed new findings in the elderly or neurologic patients. Subjective dyspnea events were extremely rare (0.013%). Some of these events may have been related to the increased ventilatory effort needed in order to overcome the dead space in the mask tubes.

Hypoglycemia

Hypoglycemia events during HBO_2 therapy were rare (0.017%), probably since our standard of operation includes glucose measurement in all diabetic patients. A previous study has shown that blood glucose may decrease during an HBO_2 session, yet this should not be attributed entirely to the hyperbaric environment [34].

Claustrophobia

Claustrophobia is considered to be relatively common in the general population (≈2%), and with anxiety-related reactions associated with magnetic resonance imaging examinations even higher (4%-30%) [35]. Claustrophobia is more commonly expected in a small monoplace than in the multiplace chamber [6]. In our study pure claustrophobic reactions were reported by 0.3% of the patients compared to previous reports of 4% [24]. However, some of the dizziness/weakness, chest pain and dyspnea events may be attributed to anxiety as well. Clark, et al. found that anxiety levels increase during the first sessions but decrease significantly after the treatment. Their study points out the importance of communication and explaining the procedure to the patient [36].

Dizziness and weakness

These conditions – i.e., dizziness and weakness – are the second most frequent adverse event (0.06%) in HBO_2 therapy. No clear pathophysiology for these events has been described, and there were no specific characterizations of those patients who experienced them.

Cardiovascular-related events

In the current study there were 35 (0.035%) events, where one of them was the presentation of myocardial infarction (MI). An MI event during HBO_2 session is considered a coincidental medical event, which is not attributed to the hyperbaric environment [6]. However, hyperbaric oxygen has been shown to increase systemic vascular resistance and, as a consequence, decreases cardiac output and increases the risk for pulmonary edema in congestive heart failure patients [17]. Accordingly, our center's policy is to exclude patients with severe systolic heart failure (ejection fraction <30%) or severe diastolic heart failure.

Myopia

Myopia caused by repeated hyperbaric exposures is presumed to be due to changes in the lens [37] and usually resolves within three months following the last treatment in most cases. In this series, 0.3% of the patients reported visual deterioration, which is considerably lower than 20% reported in the literature [12]. Previous studies found that the average myopic shift during chronic HBO_2 therapy is around 0.5-0.6 diopters [38-40], a difference that may go unnoticed by the patients. In addition, the incidence of myopia increases with the use of hoods compared to masks and hyper-

baric pressure higher than 2 atm abs [39]. Cataract screening was not performed routinely, so we cannot contribute information regarding the possible effect of HBO_2 therapy on cataract formation/acceleration.

Overall recorded events

In a recent study by a large multicenter wound care registry, HBO_2 performed in monoplace chambers [7] reported an overall incidence rate of side effects of 0.37%-0.44% compared to 0.72% in our study. The differences may be explained by different patient characteristics and by different policies regarding actively recording any possible side effects during treatment.

STUDY LIMITATIONS

The study has several limitations. Most of the limitations are related to the fact that data were collected retrospectively. Retrospective data collection may increase the risk for selection bias. However, in order to eliminate this risk, all patients treated in our institute in the past five years were included without any selection. In addition, patients' chronic medical conditions were not adjusted for in multivariate analysis. Also, middle ear barotitis severities (in the TEED scale, for instance), which were not rigorously recorded, were excluded from the analysis. However, none of the patients had a TEED 5 score or needed any surgical intervention. With regards to visual disturbance, it should be noted that no objective vision tests or eye evaluation performed routinely before and after HBO_2 treatment, but rather after patients' complaints.

CONCLUSION

Strict operational protocols including pre-HBO_2 therapy evaluations and in-chamber monitoring are essential and improve patient safety. When applied, HBO_2 therapy can be considered one of the safest medical treatments available today. Most of the adverse events can be prevented and, if they do happen, treated by simple measures.

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Conflict of interest statement

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

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