Complications and Side Effects of Hyperbaric Oxygen Therapy

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Background: Despite ongoing controversy, hyperbaric oxygen (HBO) therapy is frequently administered in various clinical situations. Probably because of the unique atmospheric conditions to which the patient is exposed, there are concerns about the safety aspects of this therapy. Possible complications during HBO therapy include barotraumatic lesions (middle ear, nasal sinuses, inner ear, lung, teeth), oxygen toxicity (central nervous system, lung), confinement anxiety, and ocular effects (myopia, cataract growth). ***Methods:*** To analyze the medical safety of HBO therapy, this report reviewed complications and side effects of 782 patients treated for various indications with a total of 11,376 HBO therapy sessions within a multiplace chamber. The absolute treatment pressure was 240 or 250 kPa (14 or 15 msw). The compression was performed in a linear manner with 14 to 15 kPa (1.4 to 1.5 msw) · min^{-1}. All data were gathered prospectively within a special database. ***Results:*** More than 17% of all patients experienced ear pain or discomfort as an expression of problems in equalizing the middle ear pressure. Most episodes were not related to a persistent eustachian tube dysfunction since they only occurred once. Barotraumatic lesions on visual otological examinations (ear microscopy) were verified in 3.8% of all patients. Patients with sensory deficits involving the ear region need special attention, because they seem to be at risk for rupture of the tympanic membrane (three cases documented). A barotrauma of the nasal sinuses occurred rarely and no barotraumatic lesions of the inner ear, lung, or teeth were noted. Oxygen toxicity of the CNS manifested by generalized seizures affected four patients without any recognizable risk factors or prodromes. None of the patients suffered recurrences or sequelae. Regular checks of the blood glucose in diabetics failed to reveal episodes of hypoglycemia as a cause for seizures. Lung function tests of patients undergoing prolonged treatment (average 52.8 sessions) did not deteriorate. ***Conclusion:*** Patients scheduled for HBO therapy need a careful pre-examination and monitoring. If safety guidelines are strictly followed, HBO therapy is a modality with an acceptable rate of complications. The predominant complication is represented by pressure equalization problems within the middle ear. Serious complications rarely occur.

Keywords: hyperbaric oxygen therapy, complications, barotrauma, oxygen toxicity, ocular side effects, confinement anxiety.

THE THERAPEUTIC VALUE of hyperbaric oxygen (HBO) therapy has been extensively reviewed and discussed (23). Despite many questions and ongoing research, its use is widespread with thousands of patients treated daily worldwide. A great deal of uncertainty still exists concerning risks and side effects (3,10). Major concerns address the patients' exposure to pressures exceeding the normal 100 kPa at sea level and the application of a dramatically raised oxygen partial pressure of about 1,500–2,000 mmHg.

Patient safety during HBO therapy is always related to technical and medical issues. Technical aspects of hyperbaric chamber safety have been discussed before (21). Knowledge of the incidences of medical complications may contribute to patient counseling and help to define a risk-benefit ratio in certain cases.

In general, possible complications of HBO therapy are divided into the following categories:

1. Barotraumatic lesions by the compression or expansion of enclosed gas volumes:
   - Middle ear (5,10,22);
   - Nasal sinuses (5);
   - Inner ear (13);
   - Lungs (17);
   - Teeth (13).
2. Oxygen-toxicity:
   - *Central nervous system (Paul Bert Effect)*: In spite of nonspecific early symptoms, generalized seizures are the cardinal symptom (24). Suspected risk factors include conditions that generally reduce the seizure threshold, such as epilepsy, hypoglycemia, hyperthyroidism, high fever and several drugs (e.g., penicillin,) (7,24) and specific risk factors, e.g., hypercarbia, secondary to acetazolamide therapy (increase in cerebral blood flow (1,14)) or disulfiram medication (11). Up to now there has been no report on sequelae in patients with oxygen-induced seizures.
   - *Lung (Lorraine Smith Effect)*: Occasional dry cough and burning substernal sensations may occur. Prolonged hyperoxia causes alveolar exudation and edema followed by a proliferation of type II pneumocytes and fibroblasts (9,16).

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TABLE I. EXAMINATIONS PERFORMED IN EACH PATIENT PRIOR TO THE HBO THERAPY.

Examination	Main Consequences/Exclusions
Health questionnaire and patient's history	
General physical examination with respect to the hyperbaric exposure	
Pulmonary function tests (PFTs): Vital capacity (VC), Forced vital capacity (FVC), Forced exspiratory volume in 1 s (FEV1)	VC and/or FVC and/or FEB1 < 70% of individual normal value
ECG at rest	Exclusion of patients with acute ischemia, indication for ECG-monitoring during HBOT in patients with bradycardia < 60 bpm and AV-block grade III
Thorax X-ray at least a.p., preferably also lateral projection	Exclusion of patients with pleural adhesions and/or intrapulmonary irregularities
Ear microscopy with observation of the pressure equalization	Insertion of tymanostomytubes if the ears could not be cleared actively
Tympanometry	Documentation of a healthy tympanic membrane pre HBOT, further diagnostics in case of middle ear effusions

This results in fibrosis clinically expressed by restrictive changes with a reduced vital capacity (4). The Unit Pulmonary Toxic Dose (UTPD) concept has been introduced to estimate the decrease in the vital capacity by the exposure to elevated oxygen partial pressures for a certain time period (13,16). Experimentally oxidative stress to the lung has been verified by the measurement of lipid peroxidation (18). Elevated levels of malondialdehyde and exhaled alkanes were reduced by the administration of α-tocopherol (Vitamin E) that may have an undetermined protective effect (8). The time for recovery after hyperoxic exposure is not known (16). Therefore, the UPTD-limit in HBO therapy cannot be defined. However, oxygen toxicity of the lung remains a theoretical complication that is considered inconsequential in most cases (13). Caution is only warranted, if a patient is ventilated with elevated oxygen in the intervals between two HBO therapies (13) or if HBO therapy is very intense (more than one treatment a day for a longer period) or prolonged (one treatment per day for a long course).

3. Confinement anxiety.
4. Ocular effects: There have been conflicting reports concerning ocular side effects of HBO therapy in different studies (2,6,15,19). Reports focus mainly on myopia and cataract growth.

This prospective study was designed to evaluate the incidence of side effects and complications during HBO therapy in a large population of patients, who were considered fit for HBO therapy and treated for various conditions.

METHODS

In the first series, consecutive patients receiving HBO therapy during the period from November 1994 to December 1997 at two hyperbaric centers were included in the study. Irregularities and complications during the HBO therapy were documented in a special database. Indications for treatment included sudden deafness and acute tinnitus, problem wounds, bone infections, radiation side effects, osteonecrosis and diving accidents in the postacute phase. All patients signed informed consent to this type of monitoring.

All patients were examined prior to their HBO therapy according to the guidelines of the German Diving and Hyperbaric Medical Society, including the measures listed in **Table I**. Fitness for HBO therapy was confirmed by a qualified hyperbaric physician after the screening program.

The HBO therapy was performed in a multiplace chamber equipped with video cameras and an intercom system to observe the patients and to keep in contact with them. Transcutaneous oxygen partial pressures were monitored in the upper chest region in all patients (Kontron Instruments Ltd., Great Britain). ECG monitoring was instituted in patients with a history of cardiovascular diseases not representing contraindications to the HBO therapy. Blood glucose was checked in diabetics before and after HBO therapy, if the pretreatment level was below 130 mg $\cdot$ dl^{-1}.

Patients were treated usually five to six times per week with two different schemes according to the recommendations of the German Diving and Hyperbaric Medical Society. Patients with inner ear disorders received two oxygen intervals of 30 min each at 250 kPa (15 msw) (a), compression rate was 15 kPa (1.5 msw) $\cdot$ min^{-1}. The chamber was decompressed with 10 kPa (1.0 msw) $\cdot$ min^{-1} with continued oxygen breathing. Patients with other indications were treated with three oxygen intervals of 30 min each at 240 kPa (14 msw) (a). Compression and decompression rates were not altered; air breaks lasted 10 min each in either scheme. The patients were supplied with oxygen by tight fitting masks or hoods.

Otological inspection was routinely performed after every five HBO therapy sessions and in cases of patient complaints. During prolonged courses of HBO therapy, serial pulmonary function tests (PFTs) were done after every 10 treatment days after the 30th HBO therapy. Treatment was to cease if a reduction of vital capacity (VC) and forced vital capacity (FVC) exceeded the $\pm$ 2% measurement accuracy listed by the spirometer manufacturer (Schiller, Switzerland). Increase or no change of one value accompanied by a decrease of the other was attributed to problems in the patient's compliance and not regarded as significant.

TABLE II. DATA OF THE PATIENTS WHO WERE SCREENED OUT DUE TO PULMONARY IRREGULARITIES.

No.	Age	Sex	VC (%)	FVC (%)	FEV1 (%)	History	X-rays
1	35	m	59	64	66	Sarcoidosis	Pulmonary sarcoidosis
2	28	m	100	103	99	Thorax trauma	Pleural adhesions
3	57	f	109	87	92	—	Intrapulmonary calcifications
4	56	f	99	85	92	—	Pleural adhesions
5	58	m	59	55	34	Smoker, pneumonia	Fibrosis
6	74	m	115	99	113	—	Suspected tumor
7	68	m	39	36	42	—	Fibrosis
8	65	f	47	42	31	Smoker	—
9	72	m	66	63	55	Smoker	—
10	85	f	62	59	55	—	—

In a second series, the value of pulmonary screening was evaluated in consecutive patients between June 1998 and April 1999 by clinical examination, PFTs, and thoracic X-rays.

The data of both series were collected prospectively within a specially designed database. Data were entered exclusively by physicians taking part in this survey according to a standardized code. Complications were documented in a real time manner immediately after their occurrence. The statistical data analysis was performed with the help of the χ^2-test.

RESULTS

Within the observation period of the first series 782 patients (38.6% females and 61.4% males) were treated with HBO therapy. The average age was 45.4 yr (range 13–83). A total of 11,376 hyperbaric exposures was performed during the observation period and included in this study; mean of 14.5 (range 1–85) treatments per patient.

In the second series 179 patients were evaluated concerning their pulmonary screening. The average age was 47.8 yr (range 14–79), 42% were female and 58% were male.

Pulmonary Screening

Of the 179 patients, 10 (5.6%) were screened out due to pulmonary irregularities (**Table II**). Three had abnormal PFTs while the X-rays were normal. Four patients just revealed changes on X-rays (pleural adhesions, scar formations, foreign bodies) without significant reduction of the PFT values and three patients had changes of both PFTs and X-rays (residual change status post severe pneumonia, sarcoidosis). Only in three of these patients was the significance of the disease predicted from the medical history.

Middle Ear Barotrauma

Pressure equalization problems of the middle ear expressed by pain or discomfort during compression were observed in 139 patients (incidence 17.8%). A total of 216 episodes were recorded (1.9% of all 11,142 exposures in patients without tympanostomy tubes or membrane ruptures). Problems occurred once in 88 (64.0%), twice in 34 (24.5%) and more than twice in 16 (11.5%) patients. The patients older than 60 yr more frequently suffered pressure equalization problems than the younger ones ($p < 0.05$, Chi Square Test). Often (60.2%) the problem occurred during the first HBO therapy, 23.7% were recorded between the second and fifth session, while only 16.1% were noted after the fifth HBO therapy.

All patients reporting pressure equalization problems received repeated ear microscopy and tympanometry. These examinations revealed barotraumatic lesions defined as a pathologic tympanometry (flat curve and/or underpressure) and/or pathologic appearance of the tympanic membrane (erythema/hemorrhage of the membrane; serous or bloody effusions within the middle ear cavity; ruptures) in 30 patients (incidence 3.8%). Three patients (incidence 0.4%) suffered ruptures of a tympanic membrane. All of these patients had underlying neurological diseases (radiation-induced anesthesia of the ear region, polyneuropathy, diffuse palsies of cranial nerves as an expression of multiple sclerosis). None of them reported major pain sensations and all ruptures were detected on routine inspections. No sequelae were noted at follow up examinations.

The patients affected by pressure equalization problems required the following procedures:

- A modification of the compression schedule, usually in combination with an application of topical nasal decongestant, allowed a further compression and treatment in 153 (70.8%) of the 216 incidents. Compression was halted for 3–5 min until the patient reported an effect of the topical decongestant. Compression was restarted at half of the usual rate (7.5 kPa $\cdot$ min^{-1}) and slowly accelerated up to 20 kPa $\cdot$min^{-1}, if the patient confirmed a proper pressure equalization. If there were a serous or hematous effusion within the middle ear cavity HBO therapy was interrupted for 2 d and oral secretolytics were administered. Oral decongestants were not used.
- HBO therapy was continued after bilateral placement of tympanostomy tubes in 12 patients with persistent dysfunctions of the eustachian tube (1.5% of all patients). All tubes worked well up to the end of the patient's HBO therapy. None of the patients had tubes inserted before HBO therapy.
- In 13 patients (1.7% of all patients) the HBO therapy had to be stopped, because they refused the placement of tympanostomy tubes or a therapeutic alternative was tried and the patient was, therefore, lost to follow up.

TABLE III. PULMONARY FUNCTION TESTS IN PATIENTS UNDERGOING PROLONGED HBO THERAPY. NONE OF THESE CHANGES IS STATISTICALLY SIGNIFICANT.

Patients (n)	10
Mean HBO therapy-sessions	52.8 (30–85)
Mean age (yr)	49.6 (13–78)
Vital capacity (mean change post HBO therapy/pre HBO therapy)	+1.15%
Forced vital capacity (mean change post HBO therapy/pre HBO therapy)	+2.78%
Forced exspiratory volume in one second (mean change post HBO therapy/pre HBO therapy)	+1.56%

Sinus Barotrauma

Nine patients (incidence 1.2%) suffered a barotraumatic lesion of their nasal sinuses during compression. The cardinal symptom was headache localized to the frontal (two patients) or maxillary sinuses (seven patients). In six events nose bleeding followed the decompression. All symptoms could be resolved by the use of topical nasal decongestants and secretolytic agents. One patient discontinued the HBO therapy.

Oxygen Toxicity

Oxygen induced seizures were noted once in four patients (incidence 0.5% of all patients 1:2,844 treatments) at average pO_2-values of 1,340 (1,120–1,570) mmHg measured transcutaneously. No heralding signs were noted. None of the patients were diabetic and none had high fever or a history of epilepsy. After decreasing the oxygen concentration, the convulsions terminated within 2–5 min. No injuries or tongue bites were documented. Anticonvulsive drug administration was not necessary. Risk factors were not detected in any of these patients. All patients were examined by a neurologist and received an EEG as well as a CT- or MRI-scan of the cranium. None of the patients revealed an underlying neurological disease. Therefore, all four seizures were regarded as random events and the patients were encouraged to continue their HBO therapy, but three of them refused further treatments. Prophylactic diazepam was used in two patients with risk for a lowered seizure threshold (both were receiving penicillin medication). None of them seized.

The lung function was routinely checked regarding the values for VC, FVC, and FEV1 after the 30th HBO therapy as described in Methods, above. The results of 10 patients undergoing a very prolonged HBO therapy with a mean of 52.8 HBO therapy-sessions are listed in **Table III**. None of the group means revealed a significant reduction. Only one patient (non-smoker, no intercurrent pulmonary disease) presented a significant reduction of the VC by 3.0% as well as of the FVC by 10.3% measured 1 h after HBO therapy. HBO therapy was not terminated in this patient as these values were obtained after his 51st and final HBO therapy session. Follow up data are not available. The others did not show any hints for restrictive lung alterations.

Confinement Anxiety

A total of 34 (incidence 4.3%) patients reported problems which, by a diagnosis of exclusion, were labeled confinement anxiety, during the treatment. The problems were expressed in a variety of different symptoms; e.g., unexplainable feeling of dyspnea despite well adjusted breathing apparatuses, non-specific nausea, uncontrollable fear, palpitations and other non-specific heart reactions, and hyperventilation.

Of these patients, 25 had to be taken off the current treatment: 10 (1.3% of all patients) stopped the HBO therapy completely; 5 of the 15 patients continuing the HBO therapy needed an orally administered sedative medication (e.g., 5 mg diazepam 30 min before the treatment).

Barotrauma of the Inner Ear, Lungs and Teeth

None of these complications was observed within this series. Pulmonary contraindications for elective HBO therapy are listed above.

A summary of the incidences of major complications and side effects with respect to the whole patient group is expressed in **Table IV**.

TABLE IV. COMPLICATIONS AND SIDE EFFECTS DURING HBO THERAPY (N = 782 PATIENTS WITH 11.376 TREATMENTS).

Complication	Incidence	Comment
Pressure equalization problems within the middle ear	1:5.7 patients 1:52.7 exposures	In most cases occurring once
Middle ear barotrauma	1:26.1 patients	No sequelae noted
Ruptures of the tympanic membrane	1:260.7 patients	Only in patients with sensory deficits in the ear region
Placement of tympanostomy tubes	1:65.2 patients	
Sinus barotrauma	1:86.9 patients	
Confinement anxiety	1:23 patients	Various symptoms
Oxygen toxicity of the CNS	1:195.5 patients 1:2,844 treatments	Anecdotal, literature quotes risk between 1:10,000 and 1:20,000 treatments
Ocular effects	Not verified	Controversial results within the literature
Oxygen toxicity or barotrauma of the lung, inner ear barotrauma	Note noted	
Incomplete HBO therapy courses on account of ENT complications	1:55.9 patients	
Incomplete HBO therapy courses on account of confinement anxiety	1:78.2 patients	
Incomplete HBO therapy courses—total	1:290.0 patients	

DISCUSSION

The therapeutic value of HBO therapy remains the subject of much discussion and research. Most probably because of the special environment to which the patient is exposed, potential complications are identified more readily, and recently HBO therapy has been termed "complication prone" (3). Another reason for this uncertainty may be that the current literature provides little information on the whole spectrum of incidents during HBO therapy. To keep the medical community from irrational speculation, an analysis not only of the efficacy, but also of the safety aspects, seems advisable.

All the results of this study were obtained in a multiplace chamber setting, and therefor we cannot comment on the environment occurring within a monoplace chamber. Differences may occur concerning the management of complications and possibly in the incidence of confinement anxiety.

Complications during the course of a HBO therapy predominantly affect the middle ear and, with a lower incidence, the nasal sinuses. At first review, the percentage of patients who suffered pressure equalization problems appears considerably high. As most of these cases occurred only once, the percentage of cases with pressure equalization problems is only 1.9% of all 11,142 exposures in patients with an intact tympanic membrane. Furthermore, the complication of a pressure equalization problem has to be distinguished from a manifest barotrauma, as only every fifth patient with pressure equalization problems showed definite signs of barotrauma on examination. This percentage matches a barotrauma incidence of 2% reported previously in a military setting (22). However, there may be differences regarding the patient groups, as within this series, almost exclusively, civilians without SCUBA-diving experience were treated.

The majority of problems can be resolved by simple means and minor invasive procedures and termination of the HBO therapy rarely becomes necessary. Patients with reduced sensibility because of underlying neurological diseases need special care, because they seem to be at risk for ruptures of the tympanic membrane. The insertion of tympanostomy tubes prior to the HBO therapy is advisable in order to avoid incurring middle ear damage. Also older patients seem to be more prone to these problems. Obviously the majority of equalization problems happens during the first HBO therapy. Therefore every new patient needs to be educated regarding procedures. If possible, the compression rate may be lowered, which seems to be easier in a monoplace than in a multiplace setting. Since we use a multiplace chamber, we prefer an individual approach, i.e., in case of a problem we quickly interrupt the compression and continue with a slower rate.

Sinus barotrauma also plays a minor role, according to our current data. Barotraumatic lesions of the lung, the inner ear or the teeth were not observed within this series. Occasional reports (17) show that there is the possibility of lung barotrauma not only in scuba-diving, but also in HBO therapy. Because of possible deleterious consequences, every hyperbaric physician must bear this complication in mind and exclude patients at risk, e.g., patients with major obstructive or restrictive lung diseases, from an elective HBO therapy.

Several authors have reported incidences of hyperoxic seizures of 1:10,000 exposures or less (12,20,24). This rate can be lowered by a careful preexamination and attendance of the patients in order to identify possible risk factors (7,13,24). However, up to now none of these suspected risk factors has been verified in a prospective human trial. In particular, patients with a history of epilepsy, hyperthyroidism and other factors that reduce the seizure threshold (several drugs, e.g., penicillin, disulfiram, sleep deficit or elevated blood alcohol) should be excluded from HBO therapy or given prophylactic anticonvulsive treatment. The authors use 2.5 mg of diazepam 30 min before HBO therapy in patients at risk, if there is no possibility of changing the medication, compensating the hyperthyroidism or interrupting the HBO therapy for some days. In patients with fever (body temperature exceeding 37.5°C) a break or seizure prophylaxis is advisable accordingly. However, we only check body temperature in cases of suspected fever and not routinely. Hypoglycemia as a reason for seizures may be excluded by proper blood glucose monitoring in diabetics. The incidence of one hyperoxic seizure in 2,844 treatments noted here seems to exceed the numbers published previously, but the survey did not include enough patients to determine a reliable incidence. This seems to be possible only by a multicentric approach. However, seizures during or after HBO therapy may not always originate from hyperoxia (10). Hence a thorough neurological examination including EEG and/or CT- or MRI-scans of the cerebrum is advisable after an incident.

The oxygen toxicity of the lungs does not play a role in current HBO therapy with limited treatment pressures and oxygen exposure times (13). In this study HBO therapy was divided into intervals of 30 min with air breaks of 10 min in between. Any of these intervals produces a UPTD of approximately 90, which gives a total UPTD of 270 (180 for the short schedule) plus 16 during decompression making 286 (196) per day. None of the patients treated in a prolonged course suffered significant PFT changes. Therefore, the UPTD we administered did not produce remarkable pulmonary changes, nor was it expected to based on standard calculations. Despite this, the results of Clark and Lambertsen show remarkable individual differences in the susceptibility to pulmonary oxygen toxicity (4). Therefore, an analysis of HBO therapy patients is useful, keeping in mind that these are not healthy young volunteers.

PFTS is mainly a screening tool to detect patients at risk for a pulmonary barotrauma. We screened out more than 5% of the patients tested, but a risk estimation is still not possible. In suspicion of a pulmonary risk PFTS and thoracic X-rays should be added to the clinical examinations. On the other hand, serial PFT evaluations are only indicated if a patient reports symptoms such as cough, shortness of breath, thoracic pain, etc.

Confinement anxiety during HBO therapy is an inevitable condition in predisposed patients, although the

rate of therapy terminations as a result of it is acceptable in a multiplace chamber setting. Attention has to be paid to the variety of symptoms, and organic causes for them must be excluded by appropriate diagnostics.

Based on our data, we cannot contribute meaningful information concerning the controversy on ocular side effects of HBO therapy. This question must be left open to another prospective analysis.

In conclusion, HBO therapy can be regarded as a procedure with an acceptable rate of complications as long as safety guidelines concerning preexaminations, contraindications, therapeutic schemes, and monitoring of the patients are followed. The vast majority of incidents can be managed by simple measures so that major complications represent rare events. Despite this reassurance, every hyperbaric facility needs to be prepared for the worst case scenario including the appropriate emergency equipment and well trained medical personnel.

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