Ocular refractive changes in patients receiving hyperbaric oxygen administered by oronasal mask or hood

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ABSTRACT.

Purpose: **The aim of this study was to quantify ocular refractive changes after a standard hyperbaric oxygen (HBO) treatment protocol and to characterize the time period of recovery.**

Patients and Methods: **Hyperbaric oxygen therapy was given for 90 min daily at a pressure of 240 kPa for 21 days. Oxygen was administered to 20 patients using an oronasal mask and to 12 patients using a hood. Follow-up examinations were carried out 2–4 days after treatment, and thereafter regularly for up to 10 weeks in both groups. Refraction was assessed automatically and by the monocular subjective refraction method. A subgroup of nine of the 20 patients to whom oxygen was administered by an oronasal mask underwent a separate eye examination, which included crystalline lens opacity measurements and LOCS III gradings.**

Results: **In the patients given oxygen by mask, there was a significant myopic shift in the mean spherical equivalent, which was largest 2–4 days after treatment. The shift was -0.55 ± 0.40 D in the right eye and -0.53 ± 0.42 D in the left eye. In the patients given oxygen by hood, the largest shift was observed after 12–16 days, and was -1.06 ± 0.52 D in the right eye and -1.10 ± 0.57 D in the left eye. The refractive changes returned to baseline 6 weeks and 10 weeks after HBO treatment, respectively. No significant changes in crystalline lens transparency were revealed.**

Conclusions: **The myopic shift after HBO therapy recovers within 10 weeks and may be more pronounced when patients are given oxygen using a hood compared with using an oronasal mask.**

Key words: hyperbaric oxygen therapy – myopic shift – lens opacification

Acta Ophthalmol. Scand. 2004: 82: 449–453

doi: 10.1111/j.1600-0420.2004.00290.x

Introduction

Recompression and hyperbaric oxygen (HBO) have been used for many years to treat diving-related diseases, such as decompression sickness and arterial gas embolism. Hyperbaric oxygen has also been shown to be effective in carbon monoxide poisoning and anaerobic infections, and, further, to have effects in the treatment of other disorders characterized by local ischaemia.

An increase in local oxygen supply due to an increased gradient for diffusion is achieved by increasing the partial pressure of oxygen (PO_2) in the inspired gas. This results in local stimulation of fibroblast proliferation and collagen synthesis, capillary angiogenesis and enhanced granulocyte function and peroxidase activity in ischaemic tissue. An extensive review of the mechanisms of and indications for HBO treatment is given by the Undersea & Hyperbaric Medical Society (1999). Hyperbaric oxygen therapy is considered to be an effective adjunct in the treatment of osteoradionecrosis, chronic ostemyelitis, diabetic leg ulcers and radiation-induced proctitis and cystitis. In this setting HBO treatment is usually given for 90 min daily at a PO_2 of 200–280 kPa for 20–30 days.

A myopic shift has frequently been described as an ocular side-effect of

HBO treatment, and, occasionally, in divers exposed to an increased PO_2 (Anderson & Farmer 1978; Lyne 1978; Palmquist et al. 1984; Ross et al. 1996; Fledelius et al. 2002). Development of cataract has been described in patients who have received HBO therapy for extended periods, which may be related to the large cumulative oxidative stress (Palmquist et al. 1984). Lens opacification has been described in guinea pigs exposed to hyperoxia, corresponding to the exposure given with HBO therapy (Nichols et al. 1972; Padgaonkar et al. 1999; Borchman et al. 2000).

The aim of this study was to quantify the refractive changes in the eye after a standard HBO treatment protocol, and to characterize the time period of recovery.

Patients and Methods

Initially the study was planned to include 20 patients. An interim analysis identified two patients whose responses appeared to differ, and who had had oxygen administered using a hood. The study was then expanded to finally include 20 patients to whom oxygen was administered by oronasal mask and 12 patients to whom oxygen was administered by hood. Oxygen was administered by hood to patients for whom a proper fit of an oronasal mask could not be accomplished. All patients had HBO therapy for radiation-induced osteonecrosis, proctitis or cystitis. In patients with mandibular osteoradionecrosis, the orbitae were shielded during radiation therapy. The median time between radiation therapy and HBO treatment was 3 years (range 1–12 years).

Patients meeting the inclusion criteria were consecutively invited to take part in the study.

The inclusion criteria were: an ametropia within −5.00 D to +5.00 D; a normal anterior segment of the eye, and age less than 70 years. Those wearing contact lenses on a regular basis, having mature cataract, crystalline lens extraction, any previous corneal surgery, or having diabetes mellitus were excluded. Furthermore, patients who would have needed to travel for more than 1 hour to attend follow-up examinations were not invited to take part in the study. Assessments of refraction were carried out on each patient individually by the most experienced optometrist in one of the three optometry clinics participating in the study. The characteristics of the patients in the two groups and their baseline refractive indices are given in Table 1.

Assessment of refraction was performed within 1 week prior to HBO therapy and within 2–4 days of completion of HBO therapy in both groups. Thereafter, follow-ups were carried out every second week for 16 weeks and then every fourth week up to 36 weeks in the group of patients whose oxygen was administered by oronasal mask. The patients whose oxygen was administered by hood underwent follow-up examinations every second week for 6 weeks, and then again after 10 weeks.

Hyperbaric oxygen treatment was given daily in the morning on 21 consecutive days. The patients were compressed in a multiplace hyperbaric chamber with air to a total pressure of 240 kPa within 10–15 min. They were then given 100% oxygen (PO_2 240 kPa) in three cycles of 30 min interrupted by breathing air (PO_2 50 kPa) for two periods of 5 min between each cycle. Thereafter, they were decompressed to normal atmospheric pressure in 7–10 min. The outline of the daily oxygen exposure is given in Fig. 1.

Table 1. Characteristics of patients given hyperbaric oxygen using either an oronasal mask or a hood, and their baseline refractive state.

Patients	Oxygen given using a mask ($n=20$)	Oxygen given using a hood ($n=12$)
Age (years)	55.1 ± 6.4	57.5 ± 8.9
Sex (M/F)	1/19	6/6
Current smokers ($n=$)	7	4
Never smokers ($n=$)	8	5
Previous smokers (n =)	5	3
Mean refractive state (D)	0.27 ± 1.58	0.48 ± 1.68

The eye examination consisted of determination of visual acuity (VA), measurement of the power of corrective lenses for patients wearing distance spectacles, and slit-lamp examination of the anterior segment. The refractive state was first assessed with an autorefractor (Nidek AR-1000) on each eye (Rosenberg 1991), and thereafter by the standard subjective refraction method at distance (Freeman 1955; Polasky 1991; Borish & Benjamin 1998; Viner 2004), without the use of cycloplegia.

A subgroup of nine of the 20 patients (mean age 53.8 ± 7.1 years) having oxygen administered by an oronasal mask underwent separate examinations, including crystalline lens opacity and density measurements, as well as nuclear, cortical and posterior subcapsular cataract gradings. Such examinations were carried out before, immediately after and 1 year of completion of HBO therapy. These examinations were performed 30 min after administration of cyclopentolate 1% eye drops, but never on the same day as examination of refraction.

An Interzeag Opacity Lensmeter 701 (Interzeag, Schlieren, Switzerland) was used to quantify lens opacity. The operation principle involves the projection of a modulated red (700 nm) lightbeam of 1.5 mm in diameter directed along the optical axis into the eye (Elliott & Hurst 1988; Wegener & Hockwin 1988; Jones & Kratz 1990). The instrument measures by a photometer the intensity of the light scattered back from the lens and displays it in a unidimensional scale from 0 to 99. On this scale a normal lens ranges from 4 to 25, depending on the age of the patient.

Axial lens density was measured with a Nidek Model EAS-1000 anterior eye segment analysis system (Nidek, Gamagori, Japan), based on computerized analysis of photographs according to the Scheimpflug principle (Scheimpflug 1906; Drews 1964), in combination with slit-lamp illumination. A well focused image of the sagittal plane from the cornea to the posterior lens surface is produced and transmitted to a monitor screen. From this image, the examiner is able to calculate various aspects of the crystalline lens through an on-line computer equipped with special analysis programs (Sasaki et al. 1990; Baez et al. 1992; Sakamoto et al. 1992; Sakamoto & Sasaki 1994).

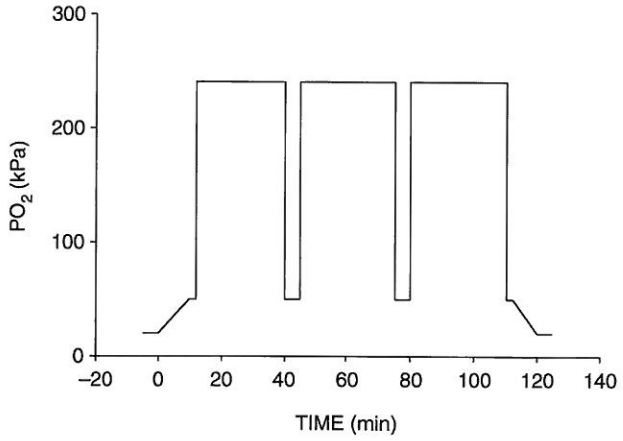

Fig. 1. Outline of the daily hyperbaric oxygen exposure.

Lens density was examined in the axial densitometry program as the computer automatically chose a point just in front of the anterior lens capsule (defined as density = 0) and compared different locations within the lens nucleus to this reference point. Lens density was thus measured in the centre of the lens, 1 mm anterior and posterior to the centre.

The nine subjects in the subgroup were assessed with respect to nuclear, cortical and posterior subcapsular opalescence at a biomicroscope slit-lamp (Nikon FS-3) and retroillumination, and compared with the Lens Opacity Classification System (LOCS) III (Chylack et al. 1989, 1993; Karbassi et al. 1993).

The study followed the tenets of the Declaration of Helsinki for research involving human subjects. Informed consent was obtained from the patients, and the Regional Ethics Committee approved the study.

Statistics

The results obtained by the monocular subjective refractive method were used in the analysis and the refractive values were converted into spherical equivalents for further analysis. For comparison of results between initial eye examination and post-HBO treatment eye examinations, a paired student's *t*-test was used. Changes in astigmatic correction were analysed within the with-the-rule and against-the-rule concepts (Naeser 1990). For comparison of patients given oxygen by oronasal mask and hood, respectively, unpaired *t*-test was used. The sign test and Wilcoxon sign ranks test were used to compare LOCS III scores of nuclear, cortical and posterior subcapsular opacification gradings between the initial and follow-up examinations. The results were given as mean values and one standard deviation (mean ± 1 SD). $P < 0.05$ was considered to be the level of statistical significance.

Results

Individual refractive changes ranged from 0.00 D to −1.75 D in the mask group, and from 0.00 D to −2.87 D in the hood group on the first examination 2–4 days after completion of HBO therapy. A significant myopic shift (≥ 0.50 D) was found in 24 (60%) single eyes in the mask group individuals and in 20 (83%) single eyes in the hood group.

The maximal changes in the spherical equivalents for patients given oxygen by mask had mean values of −0.55 ± 0.40 D (range 0.00 D to −1.37 D) and −0.53 ± 0.42 D (range 0.00 D to −1.75 D) in the right and left eyes, respectively ($p < 0.001$), and were observed 2–4 days after cessation of HBO treatment. Refraction had returned to baseline 6 weeks after HBO treatment for both eyes separately, and remained unchanged over the next 30 weeks of follow-up. For the patients given oxygen by hood, the maximal change was observed on day 12–16 after treatment, and showed mean values of −1.06 ± 0.52 D (range 0.00 D to −1.75 D) and −1.10 ± 0.57 D (range 0.00 D to −1.87 D) in the right and left eyes ($p < 0.001$). Refraction had returned to baseline 10 weeks after treatment.

The myopic shift in the patients given oxygen by hood was larger than that in the patients given oxygen by mask ($p < 0.01$). The changes in the mean spherical equivalents are shown in Figs 2 and 3.

The refractive changes occurred symmetrically in the right and left eyes within a margin of ≤ 0.25 D for 16 (80%) patients in the mask group and eight (66%) patients in the hood group. Large individual variation was revealed as two temporary exceptions only. The largest myopic shift of −2.87 D was found at the first eye examination 2 days after completed HBO treatment in a subject who had oxygen supplied by hood. This patient also had a refractive difference of 0.87 D between the right and left eyes. Another patient showed a major difference of 1.00 D between each eye. At eye examination

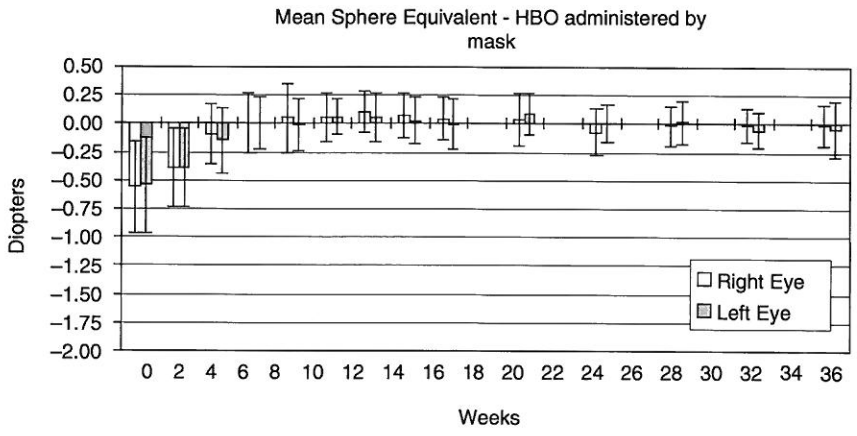

Fig. 2. Refractive changes in 20 patients after termination of hyperbaric oxygen (time 0) administered using an oronasal mask.

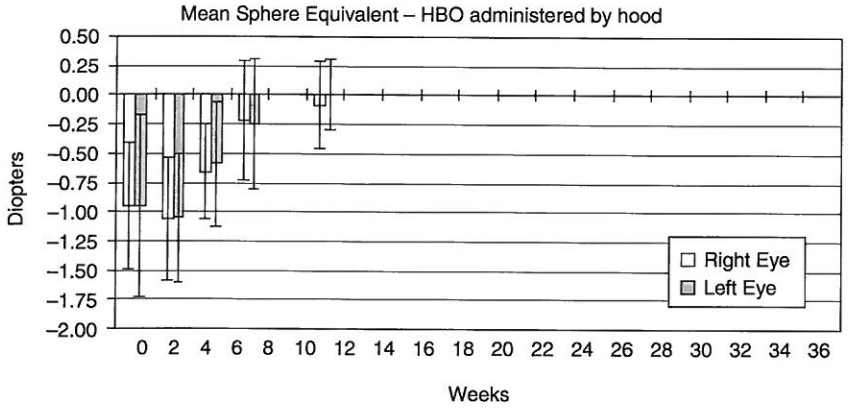

Fig. 3. Refractive changes in 12 patients after termination of hyperbaric oxygen (time 0) administered using a hood.

2 weeks later, the side differences in these two patients were reduced to 0.50 D and 0.25 D, respectively.

No changes in total astigmatism (cylinder power) larger than 0.50 D were found. A total of 38 (95%) single eyes in the mask group and 22 (92%) single eyes in the hood group showed no significant shifts in cylinder power (≤ 0.25 D). The calculated polar value revealed only minute fluctuations in the balance between the with-the-rule and against-the-rule components for both groups.

No changes were found regarding the lens parameters. Neither axial lens density measurements, lens opacity measurements, nor the LOCS III grading scores for the nine patients who had oxygen administered by oronasal mask showed any significant changes during HBO therapy or 1 year after completed therapy (Table 2).

Discussion

In this study a significant mean myopic shift (≥ 0.50 D) was found in HBO-exposed patients. There were large individual variations in the degree of refractive changes (range 0.00 D to − 2.87 D), but this was not related to age or gender. No significant changes in best corrected visual acuity were found. Furthermore, there was no evidence in the data that the myopic shift was different among eyes that were myopic or hypermetropic before HBO therapy.

Previous reports have excluded corneal power changes, changes in axial length or accommodative tonus as the main cause of the myopic shift in HBO-exposed patients (Anderson & Farmer 1978; Lyne 1978; Anderson & Shelton 1987; Ross et al. 1996; Fledelius et al. 2002). Reports focus on alterations within the structure of the crystalline lens.

The refractive index of the lens is a function of its protein concentration (Pierscionek & Chan 1989). It has been suggested that myopic shifts may be initiated by lenticular refractive index changes resulting from oxidative damage to lens proteins (Giblin et al. 1995). An increase of the lens nucleus index from Gullstrand's value of 1.406–1.416 would be sufficient to create a myopic shift of − 3.00 D (Atchinson & Smith 2000). One subject in the present study showed a myopic change of − 2.87 D. Unfortunately we have no LOCS data on this patient. In addition, in those nine patients examined regarding lens changes, we were unable to show any increase in the LOCS III grading.

Oxygen supply to the lens is provided by diffusion from the ciliary processes through the aqueous humour, and by diffusion from the retinal and choroideal circulation through the vitreous body. Oxygen also reaches the aqueous humour from atmospheric air through the cornea. Increased PO_2 in the aqueous humour has been reported when the rabbit corneal surface was exposed to increased PO_2 (760 mmHg) while maintaining the animals' normal respiration with room air (Heald & Langham 1956). When oxygen is supplied by hood there will be larger gradients for diffusion from the arterial blood, as well as from the atmosphere within the hood, which is pure oxygen at a pressure of 240 kPa. When oxygen is supplied by oronasal mask, the cornea is exposed to compressed air only with a PO_2 of 50 kPa at a total pressure of 240 kPa. It has been suggested that the effect of exposure to oxygen results in a larger oxygen load in the aqueous and the lens tissue when both blood oxygen tension and oxygen tension at the corneal surface are markedly elevated (Anderson & Shelton 1987).

Extensive clinical experience indicates that new cataracts rarely develop during the commonly used series of 20–30 daily treatments of 90 min oxygen breathing at 240 kPa (Davis et al. 1988). However, very often 2–3 repeated treatment series are considered. Observations suggest that there is a threshold of cumulative oxygen exposure, after which damage to the lens nucleus takes place (Schaal et al. 2003).

The HBO regime used in this study appears to be a safe treatment, with no increased risk of irreversible changes in refraction or transparency of the lens. The myopic shifts gradually resolved

Table 2. Lens opacity measurements and LOCS III gradings in nine patients receiving hyperbaric oxygen administered using an oronasal mask.

Patients		Opacity	Nuclear score	Cortical score	Posterior subcapsular score
Before HBO therapy	Right eye	16.84 ± 3.55	2.33 ± 0.94	1.22 ± 0.41	1.11 ± 0.31
	Left eye	17.15 ± 3.94	2.33 ± 0.94	1.22 ± 0.41	1.11 ± 0.31
After HBO therapy	Right eye	17.22 ± 4.47	2.44 ± 0.83	1.33 ± 0.47	1.11 ± 0.31
	Left eye	17.22 ± 4.43	2.55 ± 0.83	1.22 ± 0.41	1.11 ± 0.31
1 year after HBO therapy	Right eye	17.66 ± 4.15	2.44 ± 0.95	1.27 ± 0.41	1.00 ± 0.00
	Left eye	17.55 ± 4.12	2.44 ± 0.95	1.16 ± 0.33	1.00 ± 0.00

within 6 weeks and 10 weeks after HBO treatment, respectively. Refractive changes were mainly found in the spherical part of the ametropia. Patients are advised to wait at least 10 weeks before ordering a new spectacles prescription and should be provided with this information when they are asked to give informed consent for HBO therapy.

Acknowledgements

This study was supported by grants from the Norwegian Optometry Research Institute.

Thanks are due to optometrists A. Strøm-Gundersen, P. A. Olsen and H. Nordvik, who performed the eye refraction assessments, and ophthalmologist R. Piatkowski, who performed the lens opacity measurements and the LOCS III gradings.

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Received on October 13th, 2003.
Accepted on April 10th, 2004.

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