

Influence of Hyperbaric Oxygen Therapy on Central Corneal Thickness

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Key Words

Cornea · Hyperoxia · Hyperbaric oxygenation · Ultrasonic pachymeter · Diabetes mellitus

Abstract

Background/Aims: Hyperbaric oxygen (HBO) therapy is used in the treatment of several disorders. Little is known about the effects of HBO treatment on corneal thickness. The aim of this study was to investigate the effect of HBO treatment on central corneal thickness. **Methods:** Thirty-two subjects (18 males and 14 females, mean age 57.3 ± 16.7 years) undergoing HBO treatment were consecutively enrolled. The subjects were assigned into diabetic ($n = 16$) and nondiabetic groups ($n = 16$). Best-corrected visual acuity was recorded before HBO treatment, and anterior and posterior segment examinations were performed on a slit lamp biomicroscope. Central corneal thickness was measured with an ultrasonic pachymeter before and immediately after HBO treatment, which lasted 120 min at 2.4 atmospheres absolute with three 30-min oxygen and two 5-min air breathing periods. **Results:** HBO treatment did not change the central corneal thickness in diabetic subjects (547.6 ± 34.5 vs. $548.6 \pm 34.6 \mu\text{m}$; $p = 0.606$). In nondiabetic subjects, however, the

central corneal thickness was significantly reduced after HBO treatment (576.5 ± 34.8 vs. $569.0 \pm 34.8 \mu\text{m}$; $p < 0.001$). **Conclusion:** A single exposure to HBO treatment reduced the central corneal thickness in nondiabetic subjects but not in diabetic subjects. However, the change in central corneal thickness was minor.

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Introduction

The corneal endothelium plays an important role in regulating stromal hydration and thus maintaining the transparency of the cornea. Reduced oxygen tension at the corneal epithelium during contact lens wear causes increased hydration and stromal acidosis, resulting in an increase in central corneal thickness (CCT) [1]. Alterations in the structure of the cornea lead to refractive error and a reduction in visual acuity. Environmental factors may alter the corneal structure. Hypoxia alone and with altitude exposure has been shown to increase corneal thickness [2–4].

Hyperbaric oxygen (HBO) therapy, which is the inhalation of pure oxygen at >1 atmosphere of pressure, is

used in the treatment of several disorders including carbon monoxide poisoning, decompression sickness, arterial gas embolism, gas gangrene, problem wounds, refractory osteomyelitis, and compromised flaps and grafts. Under hyperbaric conditions, much more oxygen is dissolved in the plasma and delivered to all tissues. Although extensive clinical studies are still lacking, adjunctive HBO therapy is suggested in the treatment of some ophthalmologic disorders such as central retinal artery occlusion, anterior segment ischemia, corneal edema, and diabetic macular edema [5]. Ophthalmologic complications such as myopic shift and nuclear cataract formation may develop in patients receiving HBO treatment [6–9].

Although HBO is suggested in the treatment of corneal edema [5], to the best of our knowledge, the effect of HBO treatment on CCT has not been investigated previously. Additional studies designed to evaluate the effects of HBO treatment on ocular systems are needed to better understand the possible therapeutic effects of HBO in ophthalmologic disorders and to enhance the safety of patients receiving HBO treatment.

A significant portion of the patients receiving HBO treatment consists of diabetic subjects with problem wounds. Diabetes mellitus is associated with corneal structural and functional alterations [10, 11]. The effect of exposure to HBO treatment on CCT in diabetic subjects is not known. The aim of this study was 2-fold: first, to investigate the effect of clinical HBO treatment at 2.4 atmospheres absolute (ATA) on CCT and second, to evaluate whether HBO-induced CCT changes differ between diabetic and nondiabetic subjects.

Materials and Methods

The study population consisted of 32 adult patients receiving HBO treatment at the Department of Underwater and Hyperbaric Medicine at Güllhane Military Medical Academy, Istanbul, Turkey. Ethical approval was obtained from the Local Ethics Committee and all subjects gave informed consent before participation. The study adhered to the Declaration of Helsinki. Subjects with any of the following were excluded: uncontrolled hypertension, poor metabolic control, congestive heart failure, previous refractive surgery or any other ocular surgery, ptosis, keratoconjunctivitis sicca, superficial corneal disorders, contact lens use for any reason, topical ocular medication use in the last month, and use of systemic medications that can affect corneal thickness. Patients with an acute condition requiring immediate HBO treatment such as carbon monoxide poisoning, decompression sickness, and arterial gas embolism were also excluded. All remaining patients who had unremarkable ophthalmic examinations at presentation were consecutively enrolled into the study.

Best-corrected visual acuity was recorded before HBO treatment, and anterior and posterior segment examinations were per-

formed on a slit lamp biomicroscope. Bilateral CCT was measured using an ultrasonic pachymeter (65 MHz, Accupach V; Accutone, Inc., Malvern, Pa., USA) before HBO treatment at 1 ATA (room air) and immediately after HBO treatment by the same physician. Measurements were made before and after the first HBO treatment in all patients. Pachymetry is an efficient and accurate method for measuring corneal thickness [12]. The measurement is made by touching a probe including an ultrasonic transducer into the center of the cornea. Topical anesthesia was maintained by topical administration of 0.5% proparacaine (Alcaine; Alcon Laboratory, Fort Worth, Tex., USA). The mean of 9 consecutive measurements was accepted as the corneal thickness. The measurement was repeated if the standard deviation (SD) of 9 measurements was 8 μ m or more.

HBO treatment was carried out in a multiplace hyperbaric chamber. The atmospheric pressure was gradually increased from 1 to 2.4 ATA (equivalent to 13.6 m of sea water) inside the hyperbaric chamber over 10 min. Thereafter, the patients began breathing 100% oxygen for three 30-min periods interspersed with 5-min air breaks. Following treatment, the hyperbaric chamber was decompressed to 1 atmospheric pressure over 10 min. The total duration of the HBO treatment was 120 min. All HBO treatments were performed between 9:30 and 11:30 a.m.

Data are presented as means \pm SD. Statistical analyses were performed using SPSS 11.0 statistical software (SPSS, Inc., Chicago, Ill., USA). Pre- and posttreatment values were compared using a paired samples t test. $p < 0.05$ was considered statistically significant.

Results

Of the 32 subjects, 18 (56%) were male and 14 (44%) were female, with an average age of 57.3 ± 16.7 years (range 25–80). The subjects were prescribed HBO treatment for problem wounds ($n = 22$), radionecrosis ($n = 4$), sudden hearing loss ($n = 4$), chronic osteomyelitis ($n = 1$), and avascular necrosis of the femoral head ($n = 1$).

Since diabetes mellitus affects corneal structure and function, subjects were further grouped according to the presence of diabetes. There were 16 diabetic subjects (9 males and 7 females) and 16 nondiabetic subjects (9 males and 7 females). The mean age of the diabetic and nondiabetic subjects was 62.6 ± 13.9 and 51.4 ± 16.7 years, respectively. Diabetic subjects were significantly older than nondiabetic subjects ($p = 0.049$). The mean duration of diabetes was 8.4 ± 4.6 years and the mean HbA1c level was $8.1 \pm 1.3\%$. The mean serum fasting glucose level was 130 ± 36 mg/dl in diabetic subjects and 78 ± 17 mg/dl in nondiabetic subjects. None of the diabetic subjects had proliferative diabetic retinopathy. Of the diabetic patients, 6 had background retinopathy, 7 had mild nonproliferative retinopathy, and 3 had moderate nonproliferative retinopathy.

CCT was measured with an ultrasonic pachymeter before and after HBO treatment (table 1). In diabetic subjects, HBO treatment did not change the CCT significantly (547.6 ± 34.5 vs. $548.6 \pm 34.6 \mu\text{m}$; $p = 0.606$). In nondiabetic subjects, however, the CCT was significantly reduced after HBO treatment (576.5 ± 34.8 vs. $569.0 \pm 34.8 \mu\text{m}$; $p < 0.001$).

Discussion

To our knowledge, this is the first study to investigate the acute effects of HBO treatment on corneal thickness. The mechanism underlying the HBO-induced reduction of CCT is not clear. The cornea does not have blood vessels. It takes oxygen directly from the atmosphere and also from the aqueous humor that fills the anterior chamber [13]. Fluid and nutrients diffuse slowly from tears and the anterior chamber into the corneal stroma [13]. A thin layer of endothelial cells forms the inner layer of the cornea, and these cells pump the excess fluid out of the stroma into the anterior chamber to maintain corneal transparency. Endothelial pump function is an energy-driven process. HBO-induced hyperoxia in the anterior chamber may increase corneal metabolism and endothelial pump function. This may account for the observed changes in corneal thickness in our patients. Secondly, reduced aqueous production secondary to the hyperbaric hyperoxia-induced vasoconstriction and decreased intraocular pressure (IOP) may also contribute to the response of the corneal tissue [14, 15].

The ocular effects of HBO treatment are not extensively known. We have previously shown that IOP decreases during HBO treatment and returns to pretreatment values immediately after the treatment [14]. Refractive changes have been reported in patients receiving HBO treatment. Fledelius et al. [6] found a myopic shift (mean 0.58 diopters, range 0–1.5) after 20 sessions of HBO treatment. They also found that the central corneal curvature radius was reduced, indicating a slightly more peaked central cornea after 20 HBO sessions [6]. Anderson and Farmer [8] investigated the refractive error and IOP before and after 40 HBO sessions. They found a myopic shift of 0.25 diopters per week. They also found that the mean change in corneal dioptric power was 0.05 diopters flatter (not significant) and the IOP decreased by a mean of 0.8 mm Hg (not significant) [8]. Both studies concluded that the observed change in the cornea cannot account for the changes in the refractive state [6, 8].

Table 1. CCT was measured with an ultrasonic pachymeter before and after HBO treatment in diabetic and nondiabetic subjects

	CCT, μm		P
	Pre-HBO	Post-HBO	
Diabetic subjects (n = 16)	547.6 ± 34.5	548.6 ± 34.6	0.606
Nondiabetic subjects (n = 16)	576.5 ± 34.8	569.0 ± 34.8	<0.001

Values are presented as means \pm SD.

In contrast with the results in nondiabetics, we failed to find a significant change in the CCT of diabetic subjects after HBO treatment. Diabetes is known to impair corneal endothelial function. It has been shown that Na^+/K^+ -ATPase activity is reduced in diabetic rats [11]. Since this enzyme is the main component of the endothelial pump, impairment of the activity of the enzyme leads to a decreased corneal swelling response and slower recovery from hypoxic edema in diabetics compared to nondiabetics [10]. We think that diabetes-related endothelial dysfunction may be the reason for the nonsignificant response to HBO treatment observed in this study. It is plausible that diabetic corneas necessitated longer or repeated HBO treatment to observe a significant response.

This study had some limitations. The time of measurement of the corneal thickness may affect the results because of the diurnal variation in corneal thickness. All HBO treatments were between 9:30 and 11:30 a.m. CCT has a diurnal variation and changes significantly only during sleep [16]. Because the treatment was only 2 h long in the morning and the subjects did not sleep during the treatment, we think that time cannot explain the CCT changes in this study.

In conclusion, our results suggest that a single HBO treatment session reduces CCT in nondiabetic subjects. The change observed was minor and clinical and the physiological importance of this change is not known. Further studies should also investigate the duration of this effect.

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