Review of the Literature • Hyperbaric Oxygen and Vision

Kerri Lyons, OD, MEd-VFL • Southern College of Optometry
Memphis, Tennessee

Kerri Lyons, OD
Memphis, Tennessee

Resident, Pediatrics & Vision Therapy at Southern College of Optometry

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MEd-VFL, Pacific University College of Optometry, 2020

ABSTRACT

Hyperbaric oxygen therapy is a medical treatment in which the ambient oxygen pressure is made greater than the atmospheric pressure. Initially, it was designed to help relieve deep-sea divers who returned to the surface too quickly, resulting in decompression sickness, otherwise known as the bends. It has been investigated as a possible treatment for numerous issues, both on- and off-label. It is approved for conditions such as, but not limited to, carbon monoxide poisoning, thermal burns, and necrotizing soft tissue infections. It is currently being investigated for use in conditions such as autism, brain injury, migraines, and HIV/AIDs. Essentially, patients lie or sit in a tube and undergo increased compression and decompression in a stepwise fashion for some preset amount of time. The pressure typically runs about 87 psi, and some set-ups can fit up to eight patients once. There are some risks, such as issues with eardrums and sinuses, as well as contraindications with conditions such as blood disorders, COPD, heart issues, and high fevers. This article review series summarizes three studies done on traumatic brain injury patients who underwent hyperbaric oxygen therapy. While no adverse effects were found in any of them, it is clear that more robust research is needed.

Effects of Hyperbaric Oxygen on Eye Tracking Abnormalities in Males After Mild Traumatic Brain Injury

Cifu DX, Hoke KW, Wetzel PA, Wares JR, Gitchel G, Carne W. J Rehabil Res Dev 2014;51(7):1047-56.

Hyperbaric chambers have been advocated as a treatment for numerous conditions. Some have FDA approval, such as decompression for deep-sea diving, anemia due to blood loss, and burns, while others remain off-label, such as Bell's palsy, depression, HIV, and brain injuries. A considerable number of veterans and service members have sustained one or more mild traumatic brain injuries (mTBIs), often resulting in post-concussive syndrome. The authors report that research on hyperbaric oxygen treatment (HBO2) of TBI has not demonstrated clinical significance but is still frequently used due to subjective reports. Research with animal models, however, demonstrates quantifiable changes and even offers potential mechanisms. The function of the central visual pathway provides a good indicator of cognitive function, and eye tracking is correlated with the integrity of these pathways. The authors of this paper seek to use an objective measure of eye tracking to measure changes in brain health for TBI patients undergoing hyperbaric treatment.

Common assessments of eye tracking include the measurement of saccades, smooth pursuit eye movement, and fixation. It is hypothesized that patients with moderate TBIs have decreased saccadic abilities and trouble with pursuits. Fixation changes in this population are not well studied at this time.

This study was a sham-controlled, blinded, randomized, three-arm trial of hyperbaric exposure on combat-related, symptomatic mTBI patients at the Naval Medicine Operational Training Center at Naval Air Station Pensacola. The sixty-one active duty military personnel who were recruited for this study had been diagnosed with mTBI with post-concussive symptoms for at least three months, had had the injury within the last three years, and had shown two months of stable psychiatric status. Specific to this analysis, no subjects

reported active difficulty with blurred vision, light sensitivity, or double vision.

Baseline eye tracking data was collected, after which the subjects went for two months of hyperbaric chamber exposure. Over ten weeks, each subject was delivered a series of 40, once-per-day, hyperbaric chamber compressions at a pressure of 2.0 atmospheres absolute (ATA). At each session, subjects breathed one of three preassigned oxygen fractions (10.5%, 75%, or 100%) for one hour, resulting in an oxygen exposure equivalent to breathing either surface air, 100% oxygen at 1.5 ATA, or 100% oxygen at 2.0 ATA, respectively. Eye tracking data was collected again immediately after treatment and then a third time three months post-treatment.

Eye movements (fixation, saccades, and smooth pursuits) were measured using a standardized, validated, computerized eye tracking protocol. Between- and within-group testing of pre- and post-intervention means revealed no significant differences in eye movement abnormalities. These variables were additionally compared for between- and within-group differences over the three time periods. At pre-treatment, there were no significant differences between groups for eye movement variables, verifying the efficacy of randomization. This same analysis was done three months post-treatment.

This study represents the first examination using objective eye tracking measurements to assess the potential effect of HBO2. There were no clinically significant between-group differences on any of the eye tracking variables following hyperbaric chamber compressions. While there were within-group differences on two of the saccade parameters for one of the oxygen condition groups, there were no clinical improvements seen in any of the HBO2 conditions. Interestingly, the changes seen between times 2 and 3 in the group receiving 1.5 ATA reflected saccadic slowing rather than improvements in eye functioning.

The authors mention a number of inherent limitations: small sample size, all subjects were a single gender (male), and atypical ability to follow up. Additionally, most mTBI patients have further symptoms, including emotional and other cognitive conditions, which have a yet-undetermined effect. This investigation does not support a therapeutic role for HBO2 for patients with persistent symptoms after mTBI or post-concussion syndrome.

Myopic Shift During Hyperbaric Oxygenation Attributed to Lens Index Changes

Evanger K, Pierscionek BK, Vaagbø G, Thorsen E, Haugen OH. Optom Vis Sci 2015;92(1):1076-84.

The crystalline lens is an avascular, transparent organ, and under normal physiological conditions, it is embedded in a low-oxygen environment. Hyperbaric oxygen (HBO2) therapy is used to increase the transfer from oxygen to tissue and has been a potential medical treatment for a number of conditions. Patients treated with HBO2 occasionally exhibit a temporary myopic shift. It only occurs in phakic, not in pseudophakic eyes, and the degree of the shift cannot be explained by any other optical elements of the eye other than the lens. The authors report that the effects are reversed after 10 weeks following treatment. Nuclear cataracts have been reported after extended HBO2 treatment.

The authors designed a study to look at the lens surface curvatures, axial thickness, and any structural changes in hopes of illuminating the mechanisms behind the myopic shift and any cataract-related changes. Ocular refraction, central corneal radius, intraocular pressure, anterior chamber depth, and axial length of the eye were also monitored in order to verify whether these variables were consistent with previously reported values.

Twenty Caucasian patients (10 males, 10 females) with an average age of 56 years (SD 7.7) were undergoing HBO2 treatment for radiation-induced osteonecrosis, proctitis, or cystitis. HBO2 therapy was given once daily for 20 days, 5 days per week. A total pressure of 240 kPA was given in a mono-place hyperbaric chamber for a period of 10-15 minutes. 100% of the O2 was breathed at this pressure for 90 min, in 3 cycles of 30 min, interrupted by breathing compressed air from an oronasal mask for 5 min between cycles. Then the patients were decompressed to normal atmospheric pressure over 7-10 min.

There was no time to complete baseline testing before the first HBO2 treatment, so data was collected after the first treatment. The eye examination included objective refraction, keratometry, measurements of forward-scattered light, intraocular pressure, axial length of the eye, Scheimpflug pictures (lens optical density, lens surface curvatures, anterior chamber depth, axial lens thickness, and pupil diameter), and backward-scattered light. A routine eye examination with slit-lamp biomicroscopy and ophthalmoscopy

was also undertaken. Follow-up measurements were taken within the same hour of treatment after 19 days of regular treatment.

A significant myopic shift occurred in 13 patients (65%) during treatment (-0.58D +/-0.39D), the majority spherical. The largest change in refractive error was -1.50D. There was a decrease in lens optical density, mostly in the nucleus, leading to the conclusion that the refractive power was not coming from an increase in nuclear refractive index. The researchers suggest that the power could be coming from a steepening of the gradient index of the cortex. There were not significant differences in the anterior or posterior lens surfaces or in the total axial thickness. The researchers measured a small but statistically significant reduction in the back-scattered light after HBO2 treatment. The best-corrected visual acuity was stable during therapy, and any refractive shift was not due to keratometry or axial length of the eye.

Overall, the researchers found that the significant changes after HBO2 therapy were in the reduction of backward-scattered light and the decrease in nuclear optical density, which suggested that the refractive change was due to media changes in the lens.

A few limitations exist with this study. The posterior surface of the lens was only visible in about 1/3 of the patients because of restricted pupil size. Despite only a few cases of reported cataracts, the majority (two from this study) were reversible, which is similar to the myopic refractive shift. The researchers suggest that more research is needed to understand the process and mechanisms.

This study demonstrates that the only measurable ocular change occurring with the reversible myopic shift during HBO2 therapy is the significant reduction in back-scattered light and the optical density of the lens. These findings indicate that the shift has to do with the structure of the lens tissue, leading to subtle alterations in the refractive index gradient.

The National Brain Injury Rescue and Rehabilitation Study – A Multicenter Observational Study of Hyperbaric Oxygen for Mild Traumatic Brain Injury with Post-Concussive Symptoms.

Mozayeni BR, Duncan W, Zant E, Love TL, Beckman RL, Stoller KP. Med Gas Res 2019;9(1):1-12.

The authors of this paper hope to contribute to the study of the effects of hyperbaric oxygen therapy (HBO2) on brain injury patients. In this paper, they argue that the health and financial cost of living from TBI is grossly underestimated, and overall, brain injuries are under-treated. HBO2 therapy is being explored as a therapy option for those diagnosed with TBI, post-traumatic stress disorder, and post-concussion syndrome. The authors note that the nuances and overlapping symptoms of these conditions make research difficult. The paper reviews some of the bureaucratic and political barriers that make narrowing down the treatment effects difficult.

The National Brain Injury Rescue and Rehabilitation Project was established as a preliminary study to test the safety and practicality of multi-center hyperbaric oxygen administration for the post-concussive symptoms of chronic mTBI as a precursor to a pivotal, independent, multi-center, controlled clinical trial. This paper presents the results of 32 subjects who completed a preliminary trial of HBO2. All subjects in this study had an mTBI and a history of at least 3 months of nonclinical improvement or deterioration. The subjects could be any gender, aged 18-65, history of mTBI with post-concussion symptoms/PTSD, and current symptoms or functional impairment attributable to TBI and/or PTSD. Subjects were not included if they had contraindicating health issues, pregnancy, severe anxiety, other neurological diagnoses, or any concurrent treatment.

Subjects underwent a battery of pretreatment tests, including medical history, neurological examination, Automated Neuropsychological Assessment Metrics (ANAM4™), Central Nervous System Vital Signs (CNSVS), and a variety of self-assessment tests. ANAM4™ is a library of neurocognitive tests for mood and cognitive ability. CNSVS is a series of tests that check verbal/visual memory, psychomotor speed, complex attention, reaction time, and cognitive flexibility.

Subjects received 40–82 one-hour treatments at 1.5 atmospheres with absolute 100% oxygen. Pressurization and decompression times were 3-7 min each. Subjects then spent either 45 min in a mono-place chamber or 50 min in a multi-place chamber at 1.5 ATA, which the authors suggest is equivalent. The subjects were evaluated for improvement after 40 sessions. If it was deemed that there were additional potential benefits, subjects could continue for another 20 or 40 sessions.

Twenty-nine males and 3 females completed the treatment. Outcome measures included repeated self-assessment measures and the listed automated neurocognitive tests. The subjects demonstrated improvement in 21 of 25 neurocognitive test

measures observed. The objective neurocognitive test components showed improvement in 13 of 17 measures. The sooner the administration of hyperbaric oxygen post-injury, a younger the age at the time of the brain injury, having military status, and a higher number of hyperbaric oxygen administrations were associated with improved outcomes. The authors acknowledge that although an observational study is not the strongest evidence-based approach, it is generally a good step. Additionally, as with many brain injury studies, the sample size is limited. However, there were no adverse events.

Outcomes of therapy were not as positive for subjects further removed from the time of their injury, but some improvement was still seen. The authors argue that the Hawthorn and placebo effects are less likely to impact longstanding injuries, and combined with no adverse effects, this supports the use of HBO2 as a valid means of treatment. Furthermore, there is no other known treatment demonstrating this degree of improvement for stable or deteriorating mTBI with post-concussive symptoms in other studies.

The researchers show that a diagnosis of PTSD seemed to contribute to better cognitive improvement; however, separating out mTBI from PTSD is a difficult task. The researchers list specific options that may be meaningful avenues for further study. Investigators should look at subjects with neuroimaging abnormalities, subjects who do not already live at either high or low elevation, data that is well-controlled for subjects on medications and in concurrent therapies, and data collected from objective (possibly imaging) testing.

The authors conclude that hyperbaric oxygen is safe, inexpensive, and worthy of clinical application for mTBI patients.

Correspondence regarding this article should be emailed to Kerri Lyons, OD, MEd-VFL at klyons@sco.edu.

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