2016

Does Hyperbaric Oxygen Therapy Relieve Post-Concussion Symptoms and Improve Quality of Life?

Kevin (Sung Min) Lee
Philadelphia College of Osteopathic Medicine, sungminle@pcom.edu

Does hyperbaric oxygen therapy relieve post-concussion symptoms and improve quality of life?

Kevin (Sung Min) Lee, PA-S

A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

In Partial Fulfillment of the Requirements For

The Degree of Masters of Science

In

Health Sciences - Physician Assistant

Department of Physician Assistant Studies
Philadelphia College of Osteopathic Medicine
Philadelphia, PA

December 18, 2015

Abstract

Objective: The objective of this selective EBM review is to determine whether or not hyperbaric oxygen therapy relieves post-concussion symptoms and improve quality of life.

Study Design: Review of three randomized controlled trials published in English in peer review journals.

Data Sources: Three randomized controlled trials which evaluated the therapeutic benefits of hyperbaric oxygen therapy compared to control group that did not receive any treatment. All studies were found in PubMed database.

Outcomes Measured: All three studies analyzed the effect of hyperbaric oxygen therapy on quality of life. Rivermead Postconcussion Symptoms Questionnaire (RPQ) and EQ-VAS questionnaire were used to measure subjective improvements in quality of life.

Results: Two studies found that hyperbaric oxygen therapy had no statistically significant effect on quality of life. One study determined that treatments were effective and significantly improved quality of life.

Conclusions: Evidence is inconclusive and contradictory. Future studies should include large sample size and techniques to minimize placebo effect.

Key Words: “hyperbaric oxygen therapy” “post-concussion syndrome” “quality of life”

Introduction

Post-concussion syndrome (PCS) refers to a myriad of symptoms consisting mainly of a combination of fatigue, headache, dizziness, and difficulty in concentration and memory after a traumatic brain injury (TBI).[1] TBIs and concussions are relatively common and many are associated with increased morbidity and mortality. In 2010, TBI was the diagnosis in over 2.2 million emergency room visits.[2] The vast majority of TBIs are diagnosed and treated in the emergency room, where physician assistants commonly practice. Although most cases of TBI and concussion are managed in the emergency room and are discharged after a brief stay, up to 20% require hospitalization depending on the severity of the trauma, persistence of symptoms, and other comorbidities.[3] One study estimated that the treatment of traumatic brain injuries cost over $157 billion dollars per year or per-case cost of $2,772.[3] Many cases require follow-up with primary care provider, a neurologist, or a TBI specialist, especially with persistent debilitating symptoms.

The term concussion refers to a state of cognitive or perceptual changes after a physical injury to the head.[1] The patient may experience confusion and transient loss of consciousness with retrograde and/or anterograde amnesia.[1] Other common symptoms include headache, dizziness, lethargy, and nausea.[1] The mechanism of injury typically involves sudden deceleration of the head, causing physical damage to the brain within the skull.[1] The loss of consciousness may be attribute to a transient electrophysiologic dysfunction due to trauma.[1] In severe injury, the neuropsychological changes within the brain may cause persistent difficulties with concentration and memory, depression, anxiety, and insomnia.[1]

The usual methods of treating patients status post brain injury generally involve conservative and symptomatic approach. “Brain rest” devoid of unnecessary physical and

sensory stimulation for the first few days after the injury is considered the gold standard in treatment of TBIs. This involves restriction of activities such as exercising, watching television, and reading. As adjunctive therapy, acetaminophen and small doses of amitriptyline may be considered for headache symptoms.[1] For persistent dizziness, promethazine and vestibular exercises may alleviate some discomfort.[1] It is also important to educate patients that memory and cognitive dysfunction will resolve with time and provide adequate reassurance.

The studies in this review evaluated the potential of hyperbaric oxygen therapy to treat persistent symptoms of post-concussion syndrome refractory to traditional methods. The purpose of utilizing hyperbaric oxygen therapy is to increase oxygenation to supraphysiologic levels to encourage cellular growth and repair.[4] The goal of treatment is to reactivate damaged neurons after a traumatic brain injury to return to near normal function by stimulating metabolic and electrical pathways, thus ameliorating the negative symptomatology.[4]

Objective

The objective of this selective EBM review is to determine whether or not hyperbaric oxygen therapy can relieve post-concussion symptoms and improve quality of life.

Methods

The studies involved in this review consist of 3 randomized, blinded, sham-controlled clinical trials. The population consists of otherwise healthy men and women with diagnosed traumatic brain injury (TBI) suffering from post-concussion symptoms for a set period of time after their injury. Treatment was performed using hyperbaric oxygen chambers with above normal oxygen content and compared with placebo treatment with normal oxygen. In the Cifu et al[4,5] study, the intervention used was 60 minute treatment in hyperbaric oxygen chamber with 75% or 100% oxygen at 2.0 atmospheric absolute (ATA) pressure for a 10 week period.

Treatment group was compared to sham group who received treatment with 10.5% oxygen at 2.0 ATA. In the Boussi-Gross et al[6] study, the intervention was 60 minute treatment 5 days per week with 100% oxygen at 1.5 ATA for 8 weeks. Outcome was compared with a treatment group receiving intervention and with a crossover group who received hyperbaric oxygen treatment after the control period. Outcome was measured in both studies using quality of life questionnaires pre- and post-treatment period.

Key words used in search of peer reviewed articles used in this systemic review were "hyperbaric oxygen therapy" and "concussion" through PubMed and Cochrane Systematic Reviews database. All sources included in this systematic review were published in English in peer review journals. All research was performed by the author and articles were selected based on published date, relevance to topic in question, and if they included patient oriented outcomes (POEM).

Inclusion criteria involved otherwise healthy men and women with a confirmed diagnosis of traumatic brain injury and post-concussion syndrome for at least 3 months and up to 5 years. All subjects were otherwise healthy with no concurrent or stable psychiatric illness, or have any contraindication to hyperbaric oxygen treatment, such as any chest pathology, inner ear disease, and claustrophobia that may hinder their ability to receive treatment. Smoking was also prohibited for the duration of the study. The statistical analysis utilized in these studies included paired t-test and p-value. See Table 1 below for demographics of each study.

Table 1. Demographics and Characteristics of Included Studies

Study	Type	# of Pts	Age (yrs)	Inclusion Criteria	Exclusion Criteria	W/D	Interventions
Cifu[4] (2014)	Blinded, sham-controlled RCT	60	Mean age of 23.3	TBI specialist-confirmed diagnosis of mTBI for at least 3 months. Stable psychiatric stable for 2 months.	Presence of disorder that contraindicates hyperbaric exposure.	0	Treatment with 75% and 100% oxygen
Cifu[5] (2014)	Blinded, sham-controlled RCT	60	Mean age of 23.3	Diagnosis of post-concussion syndrome. 2 months of stable psychiatric history.	Previous exposure to or contraindication to hyperabaric therapy.	0	Treatment with 75% and 100% oxygen
Boussi-Gross[6] (2013)	Blinded, sham-controlled RCT	56	Mean age of 44	Age 18 or older. Experienced post-concussion syndrome for over 1 year.	Chest pathology incompatible with HBOT, inner ear disease, and claustrophobia	15	Treatment with 100% oxygen

Outcomes Measured

Outcome measures used included decrease in various post-concussion symptoms after hyperbaric oxygen treatment and were measured by Rivermead Postconcussion Symptoms Questionnaire (RPQ) and EQ-VAS questionnaire. The results of the questionnaire were compared with the baseline measures taken prior to the trials.

The RPQ comprises of symptom inventory to assess the somatic, cognitive, and emotional functioning of patients with PCS.[4] Subjects were asked to rate their symptoms on a

scale of 0 to 4, from no problem to severe problem, in categories such as headache, light sensitivity, noise sensitivity, fatigue, frustration/impatience, alertness, easily startled, and upset when reminded of stressful past event.[4]

The EQ-VAS questionnaire measures quality of life by recording the subjects' self-rated health on a scale of 0 to 100, from worst the best, in areas such as mobility, self-care, usual activities, pain/discomfort, and anxiety/depression.[6]

Results

The results of the 3 studies are evaluated and interpreted in this systemic review. All results are presented as continuous data and cannot be converted to dichotomous data. Statistical significance is determined by p-value of less than 0.05. The two Cifu et al[4,5] articles were based off the same study but one analyzed data gathered immediately after final treatment and the other evaluated data 3 months after conclusion of treatment.

Cifu et al[4,5] study compared the effect of hyperbaric oxygen therapy at 2 different oxygen concentrations of 75% (n=18) and 100% (n=21) to sham-controlled group (n=21) treated with 10.5% oxygen to stimulate placebo effect. Although the three groups were treated with different oxygen concentration, the hyperbaric oxygen chamber was pressurized to 2.0 ATA for all three groups to minimize the likelihood of the subjects noting differential pressures. All subjects included in the study were males with confirmed diagnosis of TBI due to a blast exposure. Other inclusion and exclusion criteria are described above in Table 1. Each subject underwent forty 60 minute treatments over a 10 week period. If a subject was unable to undergo a scheduled treatment due to a transient contraindication (acute illness, congestion, fever), he was allowed to make up the treatment at the earliest opportunity. Subjects' symptomatology was quantified using the RPQ pre- and post-compression and analyzed using paired t-test to establish between-

group and within-group differences. Data was gathered and analyzed immediately after final treatment and again 3 months afterwards. Although the 100% oxygen group showed greater improvement compared to 75% and 10.5% oxygen group, the results were not statistically significant (p=0.19). See Table 2 below for results.

Table 2. Change in RPQ Score after 10 Weeks of Treatment

	10.5% oxygen	**75% oxygen**	**100% oxygen**
Difference in RPQ Score between pre- and post-compression	p=0.98	p=0.61	p=0.19
Difference in RPQ Score between groups immediately post-compression	p=0.19		
Difference in RPQ Score between groups 3 months post-compression	p=0.41		

Boussi-Gross et al[6] study compared the effect of hyperbaric oxygen therapy with 100% oxygen at 1.5 ATA on treatment group (n=32) and crossover group (n=24). All subjects were over 18 years of age who suffered a mild TBI with varying etiology (MVA, falls, assault) within the last one to six years. They all suffer from post-concussion syndrome and impaired cognitive function for over one year. Other inclusion and exclusion criteria are described above in Table 1. Subjects in treatment group underwent forty 60 minute sessions 5x/week for 8 weeks of 100% oxygen at 1.5 ATA. The quality of life was evaluated using EQ-VAS questionnaire pre- and post-treatment. Subjects in the crossover group underwent an 8 week control period before participating in the same treatment protocol as the treatment group. The EQ-VAS was administered at baseline, after 8 week control period, and post-treatment. The data was analyzed using paired t-test for within-group comparison. Analysis showed that the EQ-VAS score

significantly improved following hyperbaric oxygen therapy in the treatment group and the crossover group after receiving treatment ($p<0.0001$). Furthermore, there was no significant improvement in the crossover group after the control period ($p=0.373$). See Table 3 below for results.

Table 3. Summary of results of EQ-VAS

Treatment Group			**Crossover Group**				
Pre-treatment	Post-treatment	p-value	Baseline	Control (pre-treatment)	Post-treatment	p-value (baseline vs control)	p-value (control vs post-treatment)
5.03	6.62	p<0.0001	5.26	5.21	6.39	p=0.373	p<0.0001

Discussion

Traumatic brain injuries and concussions are common and associated with increase in morbidity and mortality. Patients may experience severe and persistent symptoms lasting months to years after the initial injury. Due to the debilitating nature of certain symptoms of post-concussion syndrome such as headache, memory loss, difficulty in concentration, photophobia, and irritability, patients experience significant difficulties in attaining premorbid functioning. Treatment for post-concussion syndrome is mainly symptomatic and proves to be challenging to practitioners when symptoms are refractory to standard therapy and/or persistent over a prolonged period of time.

Both studies were limited by a small sample size (60 in Cifu et al[4,5] study, 56 in Boussi-Gross et al[6] study). The Cifu et al[4,5] study also only included men experiencing post-concussive symptoms after blast exposure due to the research affiliation with the military. The Boussi-Gross et al[6] study does not account for placebo effect of treatment with hyperbaric oxygen. As opposed to the Cifu et al[4,5] study which had a sham-controlled group treated with 10.5% oxygen at 2.0

ATA, the Boussi-Gross et al[6] utilized a control group that did not receive any form of treatment. Although this was ameliorated to some extent by employing a crossover study, placebo effect cannot be ruled out since subjects are able to objectively experience a change in pressure within the chamber.

Due to the high cost of operating and maintaining a hyperbaric oxygen chamber, insurances will only cover treatment of conditions approved by the FDA, such as burns, carbon monoxide poisoning, decompression sickness, and diabetic foot ulcers.[7] All non-FDA approved off-label uses, which include brain injury, are currently not covered by insurance and cost an average of $200 per 60 minute session.[7]

Conclusion

This systematic review of 3 randomized controlled trials studying the effects of hyperbaric oxygen therapy to relieve symptoms of post-concussion syndrome shows that treatment with hyperbaric oxygen is inconclusive and contradictory. The Cifu et al[4,5] study found no statistically significant decrease in symptoms according to the RPQ as opposed to the Boussi-Gross et al[6] study which did find statistically significant increase in quality of life based on the EQ-VAS. It is important to note that the Boussi-Gross et al[6] did not address the possibility of a placebo effect since treatment in a hyperbaric oxygen chamber produce noticeable changes in pressure. Further studying is required with larger sample size and utilization of techniques to account for placebo effect

References

1. Kasper D, Fauci A, Hauser Stephen, et al. Chapter 457e: Concussion and other traumatic brain injuries. In: *Harrison's principles of internal medicine.* 19th Edition ed. McGraw-Hill Education; 2015. Accessed October 10, 2015.

2. Basic information about traumatic brain injury and concussion. Centers for Disease Control and Prevention Web site. http://www.cdc.gov/traumaticbraininjury/basics.html. Updated 2015. Accessed October 10, 2015.

3. Edwards K. The cost of concussion in children. Advance Healthcare Network for Speech & Hearing Web site. http://speech-language-pathology-audiology.advanceweb.com/Features/Article-2/The-Cost-of-Concussion-in-Children.aspx. Updated 2010. Accessed October 10, 2015.

4. Cifu DX, Hart BB, West SL, Walker W, Carne W. The effect of hyperbaric oxygen on persistent postconcussion symptoms. *J Head Trauma Rehabil*. 2014;29(1):11-20. doi: 10.1097/HTR.0b013e3182a6aaf0 [doi].

5. Cifu DX, Walker WC, West SL, et al. Hyperbaric oxygen for blast-related postconcussion syndrome: Three-month outcomes. *Ann Neurol*. 2014;75(2):277-286. doi: 10.1002/ana.24067 [doi].

6. Boussi-Gross R, Golan H, Fishlev G, et al. Hyperbaric oxygen therapy can improve post concussion syndrome years after mild traumatic brain injury - randomized prospective trial. *PLoS One*. 2013;8(11):e79995. doi: 10.1371/journal.pone.0079995 [doi].

7. Gulati R. Conditions treated with and costs for hyperbaric oxygen therapy (HBOT). Patients Medical Website. http://www.patientsmedical.com/treatmentoptions/hyperbaricoxygentherapy/conditionstreated.aspx. Updated 2011. Accessed December 1, 2015.