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# Evaluation of Hyperbaric Oxygen Therapy in the Treatment of Traumatic Brain Injuries

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## Abstract

Traumatic brain injuries (TBIs) affect approximately 2.5 million people each year (Brain, 2014). The most current treatment options for TBIs include extensive long-term rehabilitation and therapy services, in which many only gain little improvement of their overall health (Traumatic, 2019). New trends in treating TBIs with hyperbaric oxygen therapy (HBOT) are emerging due to increased accessibility to hyperbaric oxygen chambers.

The purpose of this research and systematic literature review is to evaluate the safety and efficacy of using HBOT to improve the treatment outcomes of TBIs. This review included the search of four databases including PubMed, Cochrane Review, Clinical Key, and DynaMed. The search included randomized control trials, systematic reviews, and meta-analyses that were published within the last 20 years.

Several of the presented studies show evidence to support the use of HBOT in TBIs, however the majority of research suggests overall insufficient evidence to support the efficacy of HBOT in the treatment of TBIs. Several studies also address the concern for safety and side effects with the use of HBOT in treating TBIs, as individuals are exposed to increased pressures for long lengths of time. Ultimately, more research and clinical trials are needed in order to claim safety and efficacy in the use of HBOT for the treatment of TBIs.


*Key Terms:* hyperbaric oxygen therapy and traumatic brain injuries, hyperbaric oxygen effectiveness, hyperbaric oxygen safety, hyperbaric oxygen side effects, hyperbaric oxygen contraindications, hyperbaric oxygen mechanism of action, and hyperbaric oxygen evidence.

## Introduction

In hyperbaric oxygen therapy (HBOT), air is pressurized to three times higher than normal atmospheric pressure. These conditions allow for more oxygen to gather in the lungs than would be possible at normal air pressure. The increased amount of delivered oxygen and pressure enhances the amount of oxygen your blood can carry and ultimately promotes healing. Hyperbaric oxygen therapy has been a well-established treatment for conditions such as decompression sickness, infections, burns, and wounds (Mayo, 2018). The previously listed conditions have well-studied trials to demonstrate the efficacy of HBOT as a treatment. Hyperbaric oxygen therapy has also been used as an attempt to treat many neurological conditions, such as traumatic brain injuries (TBIs). This research paper will investigate several studies, clinical trials, and meta analyses in attempt to prove or disprove the use of HBOT as an effective treatment of TBIs.

## Statement of the Problem

Approximately 2.5 million people suffer from traumatic brain injuries (TBIs) each year, with 80,000 of them suffering permanent disabilities (Brain, 2014). While CT and MRI scans of these individuals may be normal, those with TBIs suffer from a multitude of cognitive problems throughout their life. Most current treatment for TBIs involve extensive and time-consuming rehabilitation and therapy services, with varying results (Traumatic, 2019). Many patients with TBIs undergo years of extensive therapy treatments and rehabilitations to only gain little improvement in their overall health. Hyperbaric oxygen therapy could be an adjunct, or alternative, to traditional TBI treatments. Medical providers should be informed of the most recent literature on hyperbaric oxygen therapy in the treatment of TBIs so they can provide their patients with another possible option for treatment.

## Research Questions

In adult patients with a traumatic brain injury, does treatment with hyperbaric oxygen therapy compared to no hyperbaric oxygen therapy improve recovery and cognitive outcomes?

## Methodology

Methods used to search the included themes consisted of a thorough PubMed, Cochrane, DynaMed, and Clinical key search. The keywords and mesh terms for this search included: *hyperbaric oxygen therapy and traumatic brain injuries, hyperbaric oxygen effectiveness, hyperbaric oxygen safety, hyperbaric oxygen side effects, hyperbaric oxygen contraindications, hyperbaric oxygen mechanism of action, and hyperbaric oxygen evidence.* Searches were limited to current articles in the last 20 years. PubMed was the main database used to find reliable articles and studies. Several articles were excluded from this literature review due to their primary focus being on HBOT in health conditions other than brain injuries. A Cochrane review search of hyperbaric oxygen in traumatic brain injuries demonstrated relevant comprehensive studies that were also included.

## Review of the Literature

A review of literature has been conducted which shows both effective and ineffective research of HBOT in the treatment of TBIs. The literature review does include research in which HBOT improves cognitive outcomes in those with TBIs, however the majority of the studies have overall insufficient evidence. The literature also demonstrates that although hyperbaric oxygen therapy is generally deemed safe for most patients, it is not without risks and complications.

The drawbacks to the studies include: small participant groups, variability in TBIs, studies deemed of poor quality, comorbidities altering trial results, and sham/control groups being exposed to low levels of pressure.

**Mechanism of action of hyperbaric oxygen therapy**

Hyperbaric oxygen therapy is a treatment in which a patient breathes 100% oxygen while inside a chamber that is pressurized to approximately 1.4-3 atmospheric pressure. HBOT is known to accelerate impaired healing by increasing the amount of oxygen dissolved in a patient's blood serum. This is supported by Henry's Law which states that the amount of ideal gas dissolved in a solution is directly proportional to its partial pressure. HBOT promotes healing by supporting an oxygen-rich supply of blood to the site of injury and progressing an injury from the inflammatory phase to the proliferative phase. HBOT also creates a driving force for neovascularization, or formation of new blood vessels, as it creates a higher tissue oxygen gradient which allows for new blood vessel formation. (Lam, 2017). These mechanisms are extensively studied and well demonstrated in HBOT treatment for decompression sickness, infections, burns, and wounds (Mayo, 2018).

A 2016 article by HuQ et al. identifies and evaluates the mechanisms of neuroprotection that HBOT may contribute to TBI treatment. Results of researched mechanisms of HBOT that may improve TBIs include increased tissue oxygenation, reduced inflammation, inhibition of apoptosis, reduced intracranial pressure (ICP), and angiogenesis/neurogenesis promotion. Results of further reviewed clinical and experimental HBOT TBI trials concluded the demonstration of neuroprotective effects, without oxygen toxicity as a side effect, when administered at pressures less than 3 atmospheric pressure (ATA).

A Tal et al. 2015 study evaluated the mechanism of action of HBOT in TBIs through imaging and extensive testing on their subjects. Tal et al. had the primary goal of assessing the neurotherapeutic effect of HBOT in post-mild TBI patients using both clinical cognitive function tests and brain perfusion imaging. Inclusion criteria for patients was two brain MRIs and two neurocognitive tests pre- and post- HBOT. All patients applied at their own interest for this HBOT trial. A total of ten patients were treated with 60 HBOT sessions, five days a week, for a total of 12 weeks. Each session was 60 minutes at 1.5 atmospheric pressure. After two weeks of treatment, brain MRIs as well as computerized cognitive tests were repeated. Test-retest reliability for the cognitive tests were found to be very high, increasing the strength of the study results. All areas of testing were compared to the pre-HBOT results for both cognitive testing and MRI brain imaging.

Through extensive testing, Tal eta la. noted that HBOT was found to have induced a significant improvement in the overall global cognitive scores ($p=0.007$). There was a statistically significant improvement found for memory indices after treatment ($p=0.015$). The areas of most improvement in cognitive testing was processing speed, visual spatial processing, and motor skill indices ($p=0.005$, $p=0.0043$, $p=0.013$). MRI analysis before and after HBOT was used to assess cerebral blood flow (CBF), cerebral blood volume (CBV), and mean transit time (MTT). After HBOT, there was an increase seen in the CBF, CBV, and a decrease in the MTT (2015).

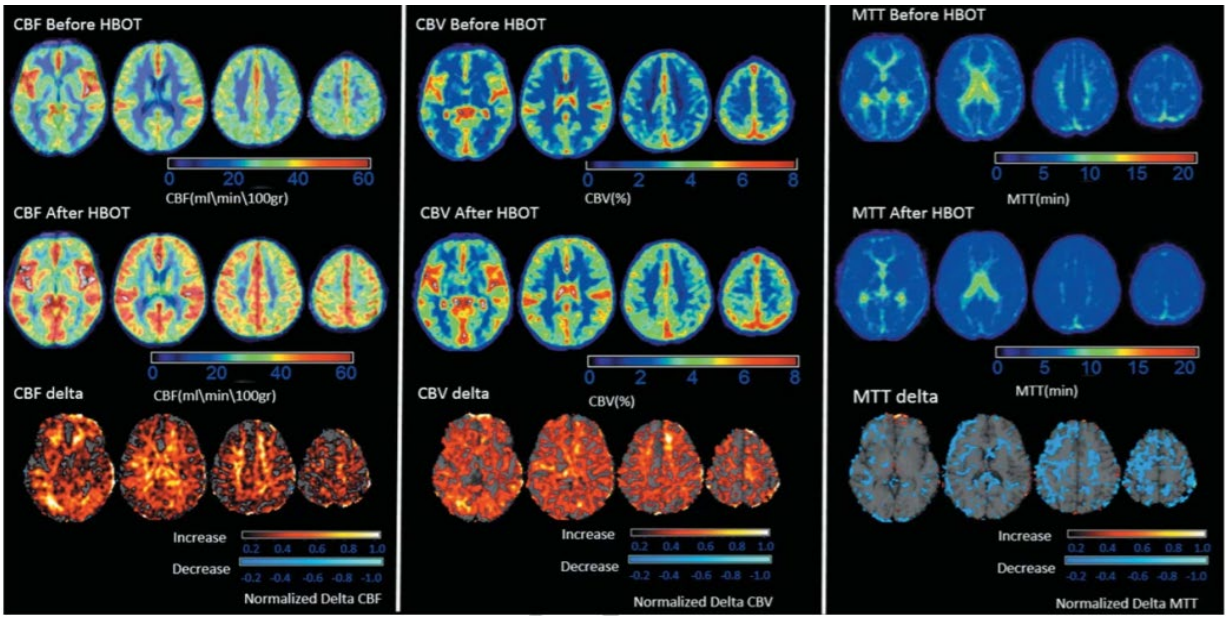


*Figure 1.* MRI technique known as dynamic susceptibility contrast (DSC) used to measure cerebral blood flow (CBF). CBF, CBV, and MTT shown before and after HBOT in Tal et al. clinical studies (2015).

Guedes et al. states that hypoxia of the brain plays a main role in the cause of TBIs, and in the absence of oxygen neurons revert to anaerobic metabolism. These negative changes to the neurons make it hard for cells to survive and therefore increase free oxygen radicals. It is thought that improving oxygen in the brain post-TBI with HBOT may improve long-term outcomes. HBOT is also thought to reduce swelling in the brain via osmotic effects and as a result may improve cognitive outcomes. Guedes et al. notes that, despite 50 years of studies and interest, the use of HBOT in TBI patients is overall lacking evidence of clinical effectiveness (2016).

**Efficacy of Hyperbaric Oxygen in Traumatic Brain Injuries**

Hyperbaric oxygen therapy has well established efficacy when used to treat conditions such as: anemia, air emboli, burns, wounds, decompression sickness, gangrene, and infections. However, most research suggests that there is overall insufficient data to demonstrate any official claims that it can effectively treat brain injuries at this time (Mayo, 2018).

In 2012, Barrett et al. conducted a systematic review which included seven studies and a total of 571 individuals. Barrett et al. assessed the effects of adjunctive hyperbaric oxygen therapy for traumatic brain injuries. The methods to compile articles and studies for review included an electronic search including the following databases: CENTRAL, MEDLINE, EMBASE, CINAHL, DORCTHIM. Relevant journal articles were hand searched and researches were also directly contacted. Their selection criteria included randomized studies of TBIs that compared the effects of therapeutic regimens including hyperbaric oxygen therapy to those excluding hyperbaric oxygen therapy. From there, three authors independently evaluated the quality of the trials and extracted data to be included in the review.

Of the 571 people, approximately half were receiving HBOT while the other half were part of the control group. Two of the included studies used the Glasgow coma sale (GCS) and showed a significant decrease in the number of people with unfavorable outcomes one month after HBOT ($p=0.001$). Those studies also showed a significant reduction in the risk of death when HBOT was used ($p=0.003$). Another two trials showed lower intracranial pressure (ICP) in those receiving HBOT who had myringotomies performed compared to the control group. A myringotomy is a procedure where an incision is placed in the eardrum to relieve pressure of the middle ear. A negative result of HBOT treatment was demonstrated in this systematic review when two studies showed a 13% incidence for significant pulmonary impairment in the HBOT group versus 0% in the non-HBOT group ($P=0.007$) (Bennett et al., 2012). This identified risk of pulmonary impairment with HBOT will be covered in more detail provided by both Mayo Clinic and Johns Hopkins later within the review of literature.

A limitation to the studies included in Bennet et al.'s systematic review involve room for bias due to small sample sizes. None of the studies disclosed randomization, and the patients and

staff involved were not blinded to treatment. As noted by the authors, higher methodological clinical studies are required to define which patients, if any, will benefit the most from HBOT. The conclusions of this review show evidence that HBOT may reduce the risk of death and lower GCS scores, however little evidence supports that survivors have overall improved outcomes in terms of their TBIs (Bennett et al., 2012).

A systematic review performed by Crawford et al. in 2017 evaluated the efficacy of HBOT for TBIs with the goal of making evidence-based recommendations for its current recommended use and for future research. Methods that were used to select studies for this review included specific eligibility criteria. To be included in this review, studies had to be in English, peer-reviewed, involve subjects suffering from TBIs, and have HBOT as an intervention for patients without other preexisting conditions. All clinical outcomes were evaluated closely and considered for inclusion to ensure the capture of all relevant research studies. The databases searched by Crawford et al. included: PubMed, CINAHL, PsycInfo, Cochrane, and the Database of Randomized Controlled Trials in Hyperbaric Medicine. This included human studies through December 2014. Using these search strategies, 12 research-controlled trials met the inclusion criteria. An additional 27 studies were classified as non-research-controlled trials met the eligibility criteria and were also described within the systematic review.

The results of Crawford et al.'s systematic review demonstrated that for patients with mild TBIs, HBOT is no more effective than the sham treatment, in which patients were not provided with HBOT. However, moderate-to-severe TBIs showed mixed results, with the majority favoring HBOT compared to "standard care" (2017). Standard care, as previously mentioned includes treating TBIs with extensive rehab and therapy services.

Limitations that were encountered during this systematic review included a study of low quality in which adverse events and relevant outcomes were not properly reported. Adverse events are an important consideration when choosing to go forward with HBOT, and without proper reporting a study's credibility comes into question. The placebo analysis was also limited by a lack of details regarding the sham and control arms of the studies. It was noted that HBOT therapy may show effectiveness within populations suffering from moderate to severe TBIs, however studies showed good evidence to support the theory that mild TBIs will likely not benefit from HBOT (Crawford et al., 2017).

A systematic review performed by McDonagh et al. in 2004 identified 7 studies to evaluate. Two of the studies were randomized controlled trials which were identified as having fair quality. The other 5 studies were observational studies. The first randomized controlled trial studied 60 patients with coma/head injury, in which they were randomized to receive HBOT or standard therapy. After 12 months, the overall mortality was similar in both groups (48.3% HBOT vs 55.2% control). However, the rate of recovery of consciousness at one month was higher in the HBOT group (42% HBOT vs 28% control). A limitation to this trial is the failure to include information of other medical factors in each patient that could mask or enhance outcomes.

A second trial included in McDonagh et al.'s review studied 168 patients with acute, closed head trauma. This study used the Glasgow Coma Scale (GCS) to follow the progression of TBIs while using HBOT. After assessing GCS scores pre and post treatment, variables did not seem to favor either the HBOT or control group in this study (2004). This study did not report if the patients were evenly distributed amongst the two evaluated groups after they enrolled in the

study. The prognoses of TBIs vary greatly, and this could create potential bias in the trail and limit its credibility.

The observational studies included in McDonagh et al's review include two of fair quality, and three of low quality. The main goal of these studies was to examine the short-term effect of HBOT on physiologic parameters (ICP and GCS) with the goal of examining if there is a correlation between patient outcomes. The results could not claim evidence of effectiveness or adverse events. Although some patient's ICP initially decreased, some patients showed rebound elevations higher than pretreatment levels. Adverse events such as seizures, neurologic deterioration, and pulmonary impairment were also reported. The low quality of these observational studies creates a limitation for the overall review by limiting its credibility. Overall, McDonagh et al. reported that evidence for HBOT in treating TBIs is insufficient to prove effectiveness or ineffectiveness, and more high-quality studies will be needed in the future (2004).

A Wolf et al. 2015 randomized trial was conducted with a goal of assessing changes in cognitive and post-traumatic stress disorder (PTSD) symptoms in those with TBI exposed to 2.4 atmospheres of HBOT pressure vs. a sham control group. The methods of this clinical trial included 50 randomize subjects who all completed 30 HBOT sessions. They were evaluated at baseline, post-series, and 6 weeks follow-up. They also had a concussion history evaluation done prior to treatment. To assess the effectiveness of HBOT, patients completed cognitive testing, brain checkers, and PTSD checklists. The results showed that there were no statistical differences between the two groups, but both groups improved. Limitations to the study include the placebo effect, which could be a valid rationale as to why there was no statistical difference in this study. Another limitation to this study is that the sham group was also exposed to low

levels of atmospheric pressure in the HBOT chamber, which could also contribute to the lack of statistical evidence.

Although there are many resources and studies reporting insufficient and unsupportive data to claim that HBOT as an effective treatment for TBIs, there are also many resources claiming the opposite.

Daly et al.'s 2018 article in Department of Physical Medicine and Rehabilitation summarizes over 40 years of clinical and pre-clinical research on the treatment of HBOT in TBIs through the Hyperbaric Oxygen Brain Injury Treatment Trial. Thirty studies that administered HBOT within 30 days of a TBI were found through PubMed searches. The pre-clinical studies involved animals and the clinical studies involved humans. Studies that had less than a sample group of 6 people were excluded. Studies were also excluded if HBOT was initiated more than 30 days after the initial TBI.

The pre-clinical animal models included in Daly's article showed evidence for neuroprotective effects of HBOT after TBI, reporting reduced lesion size, severity, brain water content, and apoptosis. They also included findings of reduced blood-brain barrier permeability and dysfunction. Many studies also found increased neuronal density, neuronal integrity, neurogenesis, synaptogenesis, and axonal integrity. There was only one pre-clinical study that reported neutral treatment effects, but it was solely measuring cerebral edema as an outcome assessment. Main limitations of the studies, that could cause inconsistency in the literature, include heterogenous pathophysiology of TBIs and inconsistent methodologies being employed by the HBOT studies (2018).

Daly et al.'s systematic review looks back to the early years of HBOT treatment with TBI and summarizes both animal and human pre-clinical and clinical trials involved. While looking

at many involved studies, it provides an in-depth analysis of the efficacy of HBOT in TBIs and touches on many of the above listed pathophysiological reasons that HBOT may or may not work (2018).

Figueroa et al.'s 2016 article in a neurology-focused journal demonstrates that B-level evidence exists for the use of HBOT as an effective treatment in mild to moderate TBIs/persistent post-concussion syndrome (PPCS). The authors extensively reviewed published, peer-reviewed articles of HBOT clinical trails involving TBIs and PPCS. Several studied trials demonstrated reparative effects in TBI/PPCS symptoms with HBOT. Other trials including varying doses and pressures elicited a clear indication of HBOT having a drug-like effect in brain injury repair. Studies included in this journal article also suggested that pressures less than 2 ATA and oxygen levels less than 100% may be potentially better for the treatment of TBIs, as it decreases the chances of complications such as oxygen toxicity.

Limitations to the studies of Figueroa et al.'s article include the current use of low levels of pressurized air as a placebo/sham in clinical trials because it biases the results due to biological activity that favors healing. In some of the studies, the sham groups were exposed to small amounts of pressure and oxygen above atmospheric conditions, but still showed improvement. Figueroa et al. argue that a true control sham group should be exposed to the chamber, but not exposed to extra pressure or increased oxygen. This causes a double-bind to be difficult, however not impossible with this type of sham (2016).

A 2016 research article by HuQ et al. identifies and evaluates the mechanisms of neuroprotection that HBOT may contribute to TBI treatment. It also discusses the issues that may affect the efficacy of HBOT in TBI patients. HuQ et al. evaluates the results of HBOT in

clinical and experimental TBI, elaborates on the mechanisms of therapy, and touches on current and future understandings of studies.

The methods used by the HuQ et al. to select research articles to analyze were through searches using the keywords: traumatic brain injury, hyperbaric oxygen therapy, tissue oxygenation, inflammation, and apoptosis. The authors then evaluated clinical studies within each mechanism to evaluate its efficacy in relation to HBOT and TBIs. They broke it down further to the levels of atmospheric pressures that were used in these clinical studies and provided information on these clinical studies and their therapeutic effects (2016).

HuQ et al.'s results of reviewing clinical and experimental HBOT TBI trials supported the demonstration of neuroprotective effects, without oxygen toxicity, when administered at pressures less than 3 atmospheric pressure (ATA). However, similarly to other pieces of literature on this topic, HuQ et al. found that due to the heterogeneity of human TBIs, the efficacy of HBOT remains controversial (2016).

Some limitations to the studies HuQ et al. evaluated were: delayed treatment time, subjective methods for measuring outcomes, and inappropriate HBOT patterns. All of which could contribute to misinterpretation of the results (2016).

Hypoxia of the brain plays a main role in TBIs, and in the absence of oxygen neurons revert to anaerobic metabolism. These negative changes to the neurons make it hard for cells to survive and increase the free oxygen radicals. It is thought that improving oxygen in the brain post-TBI with HBOT may improve long-term outcomes. HBOT is also thought to reduce swelling in the brain via osmotic effects, and can improve outcomes (Guedes et al., 2016). Guedes et al.'s article in *Expert Review of Neurotherapeutics* notes that, despite 50 years of studies and interest, the use of HBOT in TBI patients is lacking evidence of clinical

effectiveness. The use of HBOT also remains controversial due to the risk of releasing free radicals as such high levels of oxygenation (2016).

A meta-analysis by Wang et al. in 2016 evaluated the outcomes of HBOT studies comparing HBOT vs. control patients ranging from mild to severe TBIs. Methods used to search for articles and studies included searching "hyperbaric oxygen therapy, traumatic brain injury, and post-concussion syndrome" from medical databases including: Medline, Cochrane EMBASE, and google scholar. The main outcome assessed to evaluate efficacy included the Glasgow coma scale (GCS). Secondary outcomes assessed were overall mortality and changes in PTSD scores. The average age of patients in the included studies were 23-41 years old.

Wang et al. reported the results of eight studies including 519 participants revealing a higher post-treatment GCS score in the HBOT group ($p<0.001$). The studies also revealed a decrease in the overall mortality rate. No significant change in the PTSD score was observed. After two studies were removed from the meta-analysis pool, the pooled odds ratio for the GCS improvement rate became insignificant. This indicates that the meta-analysis has overall poor reliability which creates a limitation to the article. Overall, Wang et al.'s favorable results demonstrate that HBOT may be an effective therapy to utilize for patients with TBIs (2016).

**Safety and Side Effects of Hyperbaric Oxygen Therapy**

When evaluating the efficacy of HBOT in treating TBIs, the safety and side effects must also be considered. Treating TBIs with HBOT is not a one-time treatment. It can be an extensive process, oftentimes lasting several months. This puts patients at a greater risk for experiencing side effects, as they are exposed to multiple rounds of HBOT.

An expert review article published in The Expert Review of Neurotherapeutics details the current safety concerns that have been evaluated from hyperbaric oxygen therapy. The article

focuses on the safety and side effect profiles of therapy rather than efficacy and outcomes. The authors compiled data from clinical and pre-clinical trials. Hadanny et al. note that a serious concern with recent HBOT TBI clinical trials include the lack of its safety profile. It is important that this article is included within the literature review as it focuses primarily on research and data involving the safety and side effects of HBOT (Hadanny et al., 2016).

Hadanny et al. identifies central nervous system oxygen toxicity, lung toxicity, and claustrophobia as some possible side effects of HBOT. Oxygen toxicity is more likely at higher doses, and since TBIs are usually treated with less than 2 ATA, the occurrence rate has been found to be around 1:10,000 for toxicity. Lung toxicity also rarely occurs, however in patients with certain pre-disposing pulmonary conditions (emphysema, etc.), it is more common. Claustrophobia can be a very debilitating adverse event, as patients typically do not return for another HBOT session after this occurs.

According to John Hopkins Medicine, the most common side effect after HBOT is fatigue and lightheadedness. It identifies some more severe problems with HBOT as lung damage, middle ear rupture, sinus damage, vision changes, and oxygen poisoning. Likelihood of side effect occurrence depend on length of therapy as well as the atmospheric pressure in the chamber. This resource is beneficial to not only providers contemplating hyperbaric oxygen therapy, but also patients. This source also identifies preexisting conditions that would classify patients as high risk for hyperbaric oxygen therapy. These preexisting conditions include a history of lung disease, recent viral illness, recent fever, recent ear surgery or injury, and history of claustrophobia. Hopkins Medicine also encourages those seeking treatment to ensure that they are being treated by board-certified healthcare providers, since HBOT is not yet FDA approved and regulated at regular healthcare standards (Johns, 2019). Since many HBOT clinical studies

and trials only include patients that are at low risk for adverse effects, this article is of great value. This article highlights patients that are potentially high risk or more likely to experience adverse effects from HBOT. Strengths of this article include the strong credibility of the source as a well-known research hospital. A weakness of this source is that there are no related studies that are mentioned to enforce their provided facts.

The Mayo Clinic most commonly uses HBOT to treat gas embolisms, decompression sickness, carbon monoxide poisoning, nonhealing wounds, burns, and infections. Through use of HBOT to treat the above conditions, they identify potential risks of hyperbaric oxygen including: myopia, middle ear injuries, barotrauma, seizures, and a risk of fire in the oxygen-rich environment (Mayo, 2018). The Mayo Clinic provides a list of conditions that hyperbaric oxygen therapy has been found to be beneficial for, and conditions in which HBOT lacks sufficient claims for use. It also shares potential risks that patients and providers must be aware of and how a patient can prepare for the therapy. This source is extremely beneficial to my topic as it not only educates the reader regarding risks, but it also gives an inside look of what therapy entails and what the patient can expect. This article is strong in its credibility as it is from a top research hospital in the United States.

## Discussion

In adult patients with a traumatic brain injury, does treatment with hyperbaric oxygen therapy as compared to no hyperbaric oxygen therapy improve recovery and cognitive outcomes?

HBOT has a long history of being a well-established and effective treatment for conditions such as wound healing, decompression sickness, infections, and burns (Mayo, 2018). Because of HBOT's demonstrated effectiveness in the above conditions, it has also been used "off label" for other conditions, one of which includes traumatic brain injuries. Despite the lack of consistent

data to support the use of HBOT, as it becomes more affordable and available, there are increasing trends in using HBOT in the treatment of brain injuries.

After an extensive literature review, several articles support the use of HBOT in the treatment of TBIs. As previously noted, a systematic review by Barrett et al. demonstrated efficacy of HBOT in TBIs through a decrease in the number of individuals with unfavorable outcomes (i.e. damage to lungs, ears, and sinuses) and a reduction in the risk of death. Two studies of Barrett's systematic review noted lower intracranial pressures associated with improved outcomes in those receiving HBOT. Another systematic review performed by Crawford et al. concluded that HBOT showed no efficacy in those with mild TBIs, however moderate-severe TBIs showed mixed results that ultimately favored HBOT compared to "standard care" (2017).

Daly et al's article in *Department of Physical Medicine and Rehabilitation* journal summarizes over 40 years of clinical and pre-clinical research on the treatment of HBOT in TBIs through the Hyperbaric Oxygen Brain Injury Treatment trial. These trials showed evidence for neuroprotective effects of HBOT after TBI, reporting reduced lesion size, severity, brain water content, and apoptosis. They also included findings of reduced blood-brain barrier permeability and dysfunction. Many studies also found increased neuronal density, neuronal integrity, neurogenesis, synaptogenesis, and axonal integrity (2018).

Figueroa et al's 2016 journal article claimed B-level evidence for the use of less than 2 ATA HBOT as an effective treatment in mild to moderate TBIs, as it had a drug-like effect in brain injury repair demonstrating protective measures against neuronal loss.

Noted within the review of literature, there were also many systematic reviews and studies that showed little, or controversial, clinical efficacy for HBOT in TBIs. A systematic review performed by McDonagh et al. in 2004 as well as a randomized control trial by Wolf et al. in 2015 both failed to show statistical differences between the groups exposed to HBOT and the control groups. McDonagh et al. evaluated cognitive testing, brain checkers, and PTSD checklists to evaluate pre and post HBOT treatment in TBIs. The post-treatment tests showed improvement in both the control group as well as the HBOT group, supporting evidence that HBOT cannot be deemed clinically effective.

A 2016 Wang et al. study including 519 participants reported that GCS scores were increased in the HBOT group as compared to the control group. PTSD scores were also evaluated in the patients involved in these studies, and no significant change was noted after HBOT and more future data is needed to demonstrate HBOT's effectiveness in TBI treatment.

A 2016 Huq et al. study reported that even after having identified some neuroprotective effects at pressures less than 3 ATA in clinical trials of TBIs, the efficacy of HBOT still remains controversial. This was because of the subjective means of measuring outcomes as well as the inconsistency in HBOT patterns that patients were exposed to. As previously stated, Guedes et al. also noted that despite 50 years of studies and interest, the use of HBOT in TBI patients is lacking evidence of clinical effectiveness.

As with any experimental treatment, the risks and side effects must be evaluated just as closely as the efficacy. Even though there were some trials that demonstrated efficacy, treating TBIs requires numerous exposures to HBOT which also increases the likelihood of risks and side effects. John Hopkins Medicine identifies side effects to include: fatigue, lightheadedness, lung damage, middle ear rupture, sinus damage, vision changes, and oxygen poisoning. John Hopkins

also identifies patients at high risk due to pre-existing conditions including lung disease, viral illness, recent fever, recent ear surgery/ear injury, and claustrophobia (2019).

The review of the literature ultimately demonstrates that there is not yet enough consistent evidence to claim the overall efficacy of HBOT in the treatment of TBIs. However, since there have been instances of improved outcomes, patients and providers can still consider HBOT as an option for treatment of TBIs if the patient is a good candidate and the benefits outweigh the risks.

## Applicability to Clinical Practice

With the information provided in this literature review, the medical provider will be aware of alternative treatments in the management of patients with traumatic brain injuries. Treating patients with TBIs can be very difficult due to their complexity, thus further knowledge of potential treatment options is important. HBOT may not be a first-line treatment for TBIs, but it can be considered as a possible adjunct or alternative when rehabilitation and therapy are not providing patients with their desired results.

Despite insufficient evidence to support the use of HBOT in TBIs, many patients have found benefit from HBOT as an adjunct or primary treatment for treating their head injury. With that being said, the side effects and risks as noted above are very real and can decrease quality of life. If patients are appropriately educated and informed of what HBOT entails, HBOT will remain an experimental treatment that can be trialed in those hoping to see an overall improvement in their recovery and cognitive function after suffering from a traumatic brain injury.

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