INFORMATION PAPER ON HYPERBARIC OXYGEN THERAPY AND TRAUMATIC BRAIN INJURY

RELEVANCE TO THE DEPARTMENT OF DEFENSE

As described in detail below, evidence from both military and civilian studies does not support using hyperbaric oxygen therapy to manage TBI. Studies on HBOT for TBI vary considerably in methodology, rigor, and sample population. DOD-sponsored studies of active duty service members with mild TBI history have collectively shown either 1) no significant differences in symptoms between those who underwent HBOT and those who completed a sham control treatment; or 2) improvements observed after HBOT diminish in the months after treatment ends.

PURPOSE

HBOT is considered an effective treatment for a variety of indications, but evidence regarding its efficacy for the treatment of TBI and post-concussion symptoms remains inconclusive. The purpose of this information paper is to summarize evidence from clinical studies investigating the use of HBOT for treatment of TBI and post-concussion symptoms.

Information is current as of March 2025 and may be subject to change as new findings become available.

BACKGROUND

HBOT is a treatment during which an individual breathes oxygen in a hyperbaric chamber to increase oxygen levels in the blood and tissues. The hyperbaric chamber's atmospheric pressure is greater than sea level pressure, which is 1 atmosphere absolute (ATA). For clinical purposes, according to The Undersea & Hyperbaric Medical Society, the procedure must involve near-100% oxygen and pressure of at least 1.4 ATA.[1] To date, the FDA has cleared both the oxygen and chambers used in HBOT to treat 13 medical disorders and conditions (Table 1).[2] However, HBOT is considered a first-line treatment for only two of these indications—decompression sickness and arterial gas embolism—and an adjunct to standard of care for the remaining indications.[3] The FDA has not indicated or cleared HBOT for the treatment of TBI or post-concussion symptoms.[4]

Findings from over two decades of non-DOD funded preclinical studies suggest that HBOT protects the brain in several ways. Studies of rodent models of TBI have found that those treated with HBOT had much less activity in genes that cause cell death (a process known as apoptosis) than control animals. This difference was seen within a few days of the injury.[5,6] Some studies have also shown more activity in anti-apoptosis genes and neurotrophic factors than control animals within seven days post injury, which may improve neuroplasticity.[5] Other preclinical studies using rodent models of TBI have found that HBOT reduced neuron loss,[6,9-11] inflammatory gene activity,[7-10] and mitochondrial dysfunction.[6] It also increased cerebral levels of ATP,[11] which can improve metabolic function in the brain, and reduced the number of astroglial cells, which promote neuroinflammation.[6,8,9] Collectively, these findings suggest HBOT inhibits pathways contributing to neurologic damage, such as those involved in neuronal loss and glial scarring, while activating those that promote neurologic repair and regeneration.

These findings appear promising, but evidence regarding HBOT's effectiveness in treating TBI and post-concussion symptoms in humans remains inconclusive. However, based on anecdotal testimonies and case reports, some researchers and clinicians advocated for clearance to use HBOT for these indications.[3] In response to these efforts, the DOD sponsored five randomized, prospective studies to evaluate the efficacy of HBOT among military service members with mild TBI (Table 2). Four of the trials consistently found that HBOT was no more effective than sham treatment for improving post-concussion symptoms in military personnel, leading to a 2018 memorandum from the Office of the Assistant Secretary of Defense for Health Affairs concluding that HBOT should not be prescribed for the treatment of persistent post-concussion symptoms.[3] While the fifth study showed positive findings, it had notable limitations such as no sham-control group and a crossover-control design that prevented blinding of the participants and researchers to the allocated treatments.[12] Given the low quality and inconsistency of available scientific evidence, the *2021 VA/DOD CPG for the Management and Rehabilitation of Post-Acute Mild Traumatic Brain Injury* recommends against the use of HBOT for the treatment of patients with symptoms attributed to mild TBI.[4]

HYPERBARIC OXYGEN FOR TBI TREATMENT

Due to extensive media and research interest, studies investigating the use of HBOT for TBI and post-concussion symptoms have continued since the 2018 memorandum, showing conflicting results (Table 3; Table 4). Some studies report significant positive effects, including improvements in pain intensity,[13,14] cognitive function,[15-19] levels of oxidative stress markers in blood,[20] and blood flow to the brain[13-15,19,21,22] within days after HBOT treatment; however, these improvements generally decrease by later posttreatment timepoints in the few studies with 3- to 12-month follow-up.[16,18,23] Additionally, the long-term follow-up of patients enrolled in previous DOD clinical studies, through 36 months posttreatment found no significant benefit of HBOT on post-concussion symptoms or TBI pathologies.[24-28] One of these studies confirmed the safety of HBOT and the adequacy of subject blinding,[24] but another found no differences in global symptom scores immediately after HBOT.[25] A follow-up of a DOD-sponsored study demonstrated significant improvements in postural control immediately after HBOT in those with mild TBI and PTSD; however, these differences were not significant at the 6-month follow-up.[26] Similarly, other follow-up studies have revealed no long-term differences in eye tracking measures, white matter features, pain, or emotional symptoms at 6 to 36 months posttreatment, and minimal improvement in sleep.[27-31] Collectively, these studies indicate that any potential benefits of HBOT for TBI are likely transient.

The discrepancies in study findings are likely due to the heterogeneity of HBOT study designs[32,33] and a lack of consensus on an appropriate control treatment (or sham) group.[34] Studies with more rigorous methodology, control conditions, and low potential for bias have not found significant cognitive or neurologic benefits from HBOT relative to sham treatment, consistent with the DOD-sponsored studies.[33] Most recent studies that do indicate a benefit of HBOT for post-concussion symptoms have considerable methodological concerns or have been conducted with non-negligible financial conflicts of interest or other potential sources of bias. Other common features of studies with low evidence strength that have reported benefits of HBOT include small sample sizes (N<50),[14,15,18,20,21] a cohort or retrospective study design,[14-21,23,35] and no appropriate control groups.[12-23,35,36]

Notably, although the Undersea & Hyperbaric Medical Society indicates that clinical HBOT involves the use of at least 1.4 ATA pressure, HBOT proponents have raised concerns over the definition of a true sham condition. Many studies with a sham control use 1.2 ATA pressure, which is considered hyperbaric.[37] However, as evidence suggests that patients perceive a therapeutic effect merely from entering the HBOT chamber,[38,39] it is important to incorporate a sham control to account for potentially confounding placebo effects.[40] Studies that compared HBOT treatment with both this sham control and a no-chamber control to address this concern have found no significant differences in TBI outcomes among these three groups. [9-13] Most other studies conducted to date—including those showing positive HBOT effects—used only one of these control conditions (typically a no-treatment control). And unlike other studies of HBOT for approved indications, most studies of HBOT's effect on TBI to date were conducted at a single site, limiting generalizability to larger populations.[41] The lack of consistency in HBOT regimens among different studies—such as the duration of treatment and number of sessions—also limits our ability to determine the precise effect of HBOT on TBI and post-concussion symptoms. Finally, evidence suggests that the effect of HBOT may depend on the severity of the TBI; studies of moderate-to-severe TBI tend to show more positive findings, but only a few such studies have been conducted since 2018.[15,16,19,22,35,36]

Additional studies investigating the efficacy of HBOT for TBI and post-concussion symptoms are currently underway; however, most focus on severe TBI. One study anticipated to be completed in 2027 will investigate different HBOT regimens to determine an optimal HBOT course for patients with severe TBI.[42] A retrospective study completed in February 2025 evaluated the efficacy of delayed HBOT intervention for severe TBI; however, the results were not publicly available at the time of this writing.[43] To assess potential companion biomarkers that could identify severe TBI patients who would benefit from HBOT, one study will measure molecular biomarkers of TBI and assess their ability to predict response to HBOT.[44] Finally, a study at the University of South Florida will investigate using HBOT to treat veterans with mild to moderate TBI. The study will assess whether HBOT reduces neurobehavioral and PTSD symptoms in these individuals and how many HBOT sessions are needed to see results.[45]

CONCLUSION AND IMPACT TO THE WARFIGHTER

Studies on using HBOT for TBI or post-concussion symptoms exhibit widespread differences in methodological rigor and study design. However, those that were conducted using multiple control conditions and clearly defined outcome measures indicate that HBOT has limited beneficial effects in treating TBI or post-concussion symptoms.[46] Furthermore, both the FDA and the Undersea & Hyperbaric Medical Society have not changed their position on clearing HBOT for TBI or post-concussion symptoms. Also, HBOT is not covered through VA eligibility or TRICARE given the limited clinical findings and lack of FDA approval, as well as its high cost and lengthy treatment duration.[4,47] Recommending a treatment with insufficient clinical evidence has considerable potential to lead to patient mistrust when expected clinical outcomes are not met. Collectively, available evidence does not support the use of HBOT as an off-label or evidence-based therapy for TBI or post-concussion symptoms in military service members or civilian populations.

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DISCLAIMER

TABLES

Table 1: FDA Indications of Use for Hyperbaric Oxygen Therapy[48]

- Air gas bubbles in blood vessels
- Anemia (severe anemia when blood transfusions cannot be used)
- Burns (severe and large burns treated at a specialized burn center)
- Carbon monoxide poisoning
- Crush injury
- Decompression sickness (diving risk)
- Gas gangrene
- Hearing loss (complete hearing loss that occurs suddenly and without any known cause)
- Infection of the skin and bone (severe)
- Radiation injury
- Skin graft flap at risk of tissue death
- Vision loss (when sudden and painless in one eye due to blockage of blood flow)
- Wounds (non-healing, diabetic foot ulcers)

Table 2: DOD-Sponsored Studies on HBOT for the Treatment of Post-Concussion Symptoms after Mild TBI among Active Duty Service Members

Study	Sample Size	Timepoint(s) for Outcome Assessment	HBOT Regimen	Control Group(s)	Key Findings
Air Force-Sponsored study[38,49,50]	N=50	Baseline, after every 5 exposures, 6 weeks	2.4 ATA (100% oxygen), 30 sessions	Sham treatment (1.3 ATA, room air)	• No major adverse effects; no significant differences in PTSD symptoms or cognitive function between groups • Both groups showed improvements after the study
Navy/Defense Advanced Research Projects Agency Study[51-53]	N=60	Baseline, 1 week	2.0 ATA (100% oxygen) or 1.5 ATA (100% oxygen), 60-minute sessions, 40 sessions total over 10 weeks	Sham treatment (room air), 60-minute sessions, 40 sessions total	• No significant benefits of either 1.5 ATA or 2.0 ATA HBOT treatment on measures of balance, fine motor speed, PTSD symptoms, post-concussion symptom questionnaires, or cognitive function relative to sham treatment
Army-Sponsored Hyperbaric Oxygen for Persistent Post-Concussive Symptoms after Mild Traumatic Brain Injury (HOPPS) Study[54]	N=72	Baseline, immediately posttreatment	1.5 ATA (100% oxygen), 60-minute sessions, 40 sessions total over 10 weeks	Sham treatment (1.2 ATA, room air, 40 sessions) or no HBOT (standard TBI care)	• No significant differences between the sham and HBOT groups on a post-concussion symptom questionnaire

Study	Sample Size	Timepoint(s) for Outcome Assessment	HBOT Regimen	Control Group(s)	Key Findings
Army-Sponsored Brain Injury and Mechanisms of Action of HBO_2 for Persistent Post-Concussion Symptoms after Mild TBI (BIMA) Study[31]	N=71	Baseline, 13 weeks, 6 months, 12 months	1.5 ATA (>99% oxygen), 60-minute sessions, 40 sessions total over 12 weeks	Sham treatment (1.2 ATA, room air, 60 minutes), 40 sessions total over 12 weeks	• HBOT associated with improvements in PTSD neurobehavioral symptoms, cognitive function, balance, sleep quality, immediately after treatment, but effects regressed at 6 months and 12 months
Army-Sponsored Louisiana State University study[12]	N=60	Baseline, immediately posttreatment, 2 months	150 kilopascal (~1.5 ATA), 1-hour sessions once daily, 5 days per week for 8 weeks, 40 sessions total	No treatment	• Improvements in cognitive, sleep, mood, and PTSD symptoms observed immediately posttreatment and at 2 months

Table 3: Summary of Recent Studies Investigating Hyperbaric Oxygen Therapy for TBI Treatment—Follow-up to 2018 ASD Report

Study	Sample Size	Population	Timepoints for Outcome Assessments	HBOT Regimen	Control group	Key Findings
Churchill et al., 2019; Meta-analysis of 2 randomized controlled trials (RCTs; HOPPS and BIMA)[24]	N=143	Active duty service members and veterans	Baseline, immediately posttreatment, 6 months, 12 months	• HOPPS: 1.5 ATA (>99% oxygen), 40 sessions over 10 weeks • BIMA: 1.5 ATA (>99% oxygen), 40 sessions over 12 weeks	• HOPPS: No treatment or sham treatment (1.2 ATA, room air, 40 sessions) over 10 weeks • BIMA: sham treatment (1.2 ATA, room air, 40 sessions) over 12 weeks	• Adverse event rates of 1.1% in HOPPS and 2.2% in BIMA • Adequate blinding (participants unable to accurately determine whether they received treatment or sham)
Weaver et al., 2019; Meta-analysis of 2 RCTs (HOPPS and BIMA)[25]	N=143	Active duty service members and veterans	Baseline, immediately posttreatment	• HOPPS: 1.5 ATA (>99% oxygen), 40 sessions over 10 weeks • BIMA: 1.5 ATA (>99% oxygen), 40 sessions over 12 weeks	• HOPPS: No treatment or sham treatment (1.2 ATA, room air, 40 sessions) over 10 weeks • BIMA: sham treatment (1.2 ATA, room air, 40 sessions) over 12 weeks	• No differences in composite symptom scores between sham and HBOT groups in either trial

Study	Sample Size	Population	Timepoints for Outcome Assessments	HBOT Regimen	Control group	Key Findings
Meehan et al., 2019; Follow-up study of BIMA RCT[26]	N=146	Active duty service members and veterans	Baseline, immediately posttreatment, 6 months	1.5 ATA (>99% oxygen), 60 minutes, 40 sessions	No treatment or sham treatment (1.2 ATA air, 60 minutes), 40 sessions over 12 weeks	• No significant improvements in balance/postural control with HBOT at 6 months • Most benefits observed in those with concomitant PTSD
Hart et al., 2019; Follow-up study of BIMA RCT[30]	N=54	Active duty service members	Baseline, immediately posttreatment, 24 months, 36 months	1.5 ATA (>99% oxygen), 40 sessions over 12 weeks	Sham treatment (1.2 ATA room air, 60 minutes), 40 sessions over 12 weeks	• Improvements observed immediately posttreatment resolved by 6 months • No significant improvements in symptoms by 36 months
Wetzel et al, 2019; Follow-up study of BIMA RCT[27]	N=146	Active duty service members and veterans	Baseline, immediately posttreatment, 6 months	1.5 ATA (>99% oxygen), 40 sessions over 12 weeks	No treatment or sham treatment (1.2 ATA, room air, 40 sessions) over 12 weeks	• No significant differences immediately posttreatment or at 6 months
Cartwright et al., 2019; Prospective RCT[28]	N=146	Active duty service members and veterans and civilians	Baseline, immediately posttreatment, 6 months	1.5 ATA (>99% oxygen), 60-minute sessions, 40 sessions total over 13 weeks	No treatment or sham treatment (1.2 ATA, room air, 60-minute sessions) over 13 weeks	• No differences in white matter metabolite ratios between patients and controls or changes in these ratios over time
Walker et al., 2018; Follow-up study of BIMA RCT[29]	N=146	Active duty service members and veterans	Baseline, immediately posttreatment, 6 months	1.5 ATA, >99% oxygen, 60 minutes, 40 sessions over 12 weeks	Sham treatment (1.2 ATA), 40 sessions over 12 weeks	• Improvements in one sleep measure, no effect of HBOT on other measures

Study	Sample Size	Population	Timepoints for Outcome Assessments	HBOT Regimen	Control group	Key Findings
Weaver et al., 2018; Follow-up study of BIMA RCT[31]	N=71	Active duty service members	Baseline, immediately posttreatment, 6 months, 12 months	1.5 ATA, 60-minute sessions, 40 sessions total over 12 weeks	Sham treatment (1.2 ATA, room air, 40 sessions) over 12 weeks	• Improvements in neurobehavioral and PTSD symptoms observed immediately posttreatment regressed at 6 and 12 months

Table 4: Summary of Recent Studies Investigating Hyperbaric Oxygen Therapy for TBI Treatment—Other Clinical Studies

Study	Sample Size	Population	Timepoints for Outcome Assessments	HBOT Regimen	Control group	Key Findings
Doenyas-Barak et al., 2024; RCT sham controlled study[55]	N=56	Male veterans	Baseline; immediately posttreatment	2.0 ATA (100% O2), 90-min sessions, 60 daily sessions	1.02 ATA (21% O2), 90 min sessions, 60 daily sessions	• HBOT group showed a significant decrease in mean CAPS-5 total score • Sham group demonstrated a significant increase in CAPS-5 total score • Significant improvement in the depression domain of the DASS-21 and BDI-II • Stress and anxiety domains of DASS-21 did not differ
Ablin et al., 2023; RCT[13]	N=58	Civilians	Baseline, immediately posttreatment	2.0 ATA (100% oxygen), 1x daily, 90-minute sessions, 5 sessions per week, 60 sessions total	No HBOT with standard medication for fibromyalgia syndrome	• Significant improvement in pain intensity and blood flow in HBOT group • All side effects resolved after treatment stopped
Miskin et al., 2023; Retrospective study[15]	N=12	Civilians	Baseline, immediately posttreatment, 3 months	1.5 ATA (100% oxygen), 60 minutes, 5 sessions per week, 40 sessions total	None	• Improvements in cognitive function, increased cerebral blood flow and oxygen metabolism
Wright et al., 2023; RCT[56]	N=100	Civilians	Baseline, immediately posttreatment, 12 months	2.0 ATA (100% oxygen), 20 sessions	Sham treatment (20 sessions of 10.5% oxygen and 89.5% nitrogen at 2.0 ATA)	• Not published (in progress)

Study	Sample Size	Population	Timepoints for Outcome Assessments	HBOT Regimen	Control group	Key Findings
Betsted et al., 2022; Case series[14]	N=39	Veterans	Baseline, immediately posttreatment	1.5 ATMs (100% oxygen), twice daily 90-minute sessions for 20 days, 40 sessions total	None	• Significant improvement in blood flow to the brain • Improvement in pain, mood, and sleep symptoms
Chen et al., 2022; Cohort study[16]	N=84	Civilians	Baseline, immediately posttreatment, 3 days, 10 days, 20 days, 6 months	2.0 ATA, 60-minute sessions, 20 treatments total	No treatment	• Improved consciousness and cognitive function 10 and 20 days after treatment • Reduced hematoma volume 3 and 10 days after treatment • Decreases in pathologic biomarker levels and increases in regenerative marker levels • No significant difference in 6 month outcome
Liu et al., 2022; RCT[36]	N=58	Civilians	Baseline, 1 week, 2 weeks, 4 weeks	1.8 to 2.0 megapascal (99.5% oxygen), once daily 60-minute sessions, 20 sessions total with transcranial magnetic stimulation	No HBOT with transcranial magnetic stimulation alone	• HBOT group woke from coma faster and at a higher rate • Improved Glasgow Coma Scale scores, and CNS function after HBOT • Increased CSF levels of norepinephrine and decreased blood flow velocity with HBOT
Duan et al., 2021; Cohort study[35]	N=78	Civilians	Baseline, 20 days	970 milliliter per liter oxygen + ≤30 milliliter per liter CO_2, once daily 20-minute sessions, 10 days with standard medication	No HBOT with standard medication	• Increased P2 waveform extraction rate with HBOT • Differences in P2 latency after HBOT

Study	Sample Size	Population	Timepoints for Outcome Assessments	HBOT Regimen	Control group	Key Findings
Lu et al., 2021; Multicenter prospective randomized case-controlled study[23]	N=158	Civilians	Baseline, immediately posttreatment, 3 months	3 courses of 2.0 ATA, 1-hour daily sessions for 20 days per course with routine or intensified rehabilitation	No HBOT with routine or intensified rehabilitation training	• No difference between routine rehabilitation and routine rehabilitation with HBOT at 3 months • Effect of HBOT dependent on intensity of rehabilitation training
Ma et al., 2021; Prospective cohort study[21]	N=28	Firefighters	Baseline, immediately posttreatment	1.3 ATA (100% oxygen), 45-minute sessions, 5 sessions per week, 20 sessions total	No treatment	• Increased blood flow in and around the hippocampus
Wang et al., 2021; Cohort study[20]	N=10	Civilians	Baseline, immediately posttreatment	2.5 ATA (100% oxygen), 100 minute-sessions, 30 sessions total over 6 weeks	None	• Serum levels of some markers of oxidative stress decreased after HBOT treatment
Zhong et al., 2020; Randomized trial[22]	N=88	Civilians	Baseline, immediately posttreatment	0.20 MPa to 0.25MPa for 80 minutes, once daily for 2 weeks	No treatment	• Higher cerebral blood flow and oxygen uptake in treated group • Higher GCS scores and lower National Institutes of Health Stroke Scale scores in treated group
Mozayeni et al., 2019; Multicenter cohort study[17]	N=32	Civilians and active duty service members and veterans	Baseline, immediately posttreatment	1.5 ATM (100% oxygen), 40 to 82 one-hour sessions	None	• Improvements in cognitive function and symptoms

Study	Sample Size	Population	Timepoints for Outcome Assessments	HBOT Regimen	Control group	Key Findings
Shytle et al., 2019; Case series[18]	N=3	Civilians and active duty service members	Baseline, immediately posttreatment, 12 months	Case 1: 1.75 ATA, once daily, 5 days per week, 20 sessions total Case 2: 1.5 ATA twice daily, 5 days per week, 30 sessions total Case 3: 1.5 ATA twice daily, 5 days per week, 25 sessions total followed by 1.5 ATA once daily, 5 days per week, 10 sessions total	None	• Immediate improvements in symptoms, cognitive function and mood • Improvements resolved by the 1-year follow up
Hadanny et al., 2018; Retrospective cohort study[19]	N=154	Civilians	Baseline, immediately posttreatment	1.5 or 2.0 ATA, once daily 60- or 90-minute sessions, 5 days per week, 40-70 sessions total	None	• Significant improvements in cognitive function; minor improvements in blood flow to the brain • More improvements in SPECT metrics in individuals with improved cognitive function

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