**Online Supplement A: Evidence table of RCT studies**

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| **Reference** | **Population Description** | **Study arm # assigned (drop out rate)\*** | **Treatment Dosages\*** | **Relevant Outcome** | **Adverse Events** | **Author's Main Conclusions\*\*** | **SIGN SCORE** |
| **HBO2 for MILD TBI** |
| Cifu, 201417,18,22 | 61 active service members with at least 1 mTBI, with the most recent TBI occurring at a mean of 8.5 months prior to the baseline assessments (61M, 0F) with a mean age\* of 23.2 +/- 2.95b***Note:*** Mean-age reported on by authors reflects only 60 patients due to one drop-out. | 1.5 ATA HBO2 equivalent 21(0%)2.0 ATA HBO2 equivalent 19(5%)Sham Compression 21(0%)Overall 61(1.6%)d | HBO2 at 1.5 ATA equivalent: 60 min sessions of 75% O2 at 2.0 ATA x 40 sessions over 10 weeks.HBO2 at 2.0 ATA equivalent: 60 min sessions of 100% O2 at 2.0 ATA x 40 sessions over 10 weeks.Sham Compression: 60 min sessions of 10.5% O2 at 2.0 ATA x 40 sessions over 10 weeks.*For HBO2 & Sham arms:* Compression: less than 3 min; Plateau: 60 min; Decompression: less than 3 min. | Time points: baseline, immediate post-interventionPOST-CONCUSSIVE SYMPTOMS: **Rivermead Post-concussion Symptom Questionnaire (RPQ).** NS bt groups at post-intervention. Within group the 1.5 ATA equivalent (2.0 ATA-75% O2) group showed a statistically significant increase (ie, worsening) on item 14 (light sensitivity) (p=0.04); the 2.0 ATA equivalent (2.0 ATA-100% O2) group showed a statistically significant decrease on items 4 (noise sensitivity) (p=0.04) and 9 (frustration, impatience) (p=0.05). Other items, subscale and total scores between baseline and post-intervention were NS.PSYCHOLOGICAL: **Posttraumatic Disorder Checklist-Military Version (PCL-M)**. NS bt groups at post-intervention. Within groups the sham group (2.0 ATA-10.5% O2) significantly decreased statistically for items 16 (being super alert; watchful) (p=0.03) and 17 (easily startled) (p=0.03); the 1.5 ATA equivalent (2.0 ATA-75% O2) group showed a statistically significant decrease on item 16 (being super alert; watchful) p=0.05); the 2.0 ATA equivalent (2.0 ATA- 100% O2) group demonstrated a statistically significant decreases on items 4 (upset when reminded of stressful past event) (p=0.02) and 16 (being super alert; watchful) (p=0.04) and total score (p=0.05). No other significant differences were noted between baseline and post-intervention.Time points: baseline, post-intervention (within 1 week after last exposure), FU: 3 monthsPOST-CONCUSSIVE SYMPTOMS: **Rivermead Post-concussion Symptom Questionnaire (RPQ)**. NS bt groups at 3 month FU.COGNITION: **Wechsler Adult Intelligence Scale; Trail-Making B; Stroop; Continuous Performance Test; California Verbal Learning Test; Paced Auditory Serial Addition Test; Benton Visual Memory Test; Controlled Oral Word Association Test; Grooved Peg Board**. NS bt groups at 3 month FU.PSYCHOLOGICAL: **Centers for Epidemiological Studies Depression Scale**. NS bt groups at 3 month FU.GOS & MORTALITY: **Glasgow Outcome Scale Extended (GOSE).** NS bt groups at 3 month FU.NEUROPHYSIOLOGICAL: **Balance Sensory Organization Test**. NS bt groups at 3 month FU. | Not reported. | This study, which used a randomized, controlled, double blinded design conducted at total oxygen doses most commonly used by clinicians, did not demonstrate significant effects of HBO2 in individuals with symptoms of chronic mTBI when compared with sham compression.17 This study found no beneficial effect of HBO2 exposure 3 months post-compression for symptoms, functional status, or cognitive or psychomotor performance at either 1.5 or 2.0ATA equivalent oxygen breathing compared to sham intervention. Within-group changes were noted for the entire sample in both primary and secondary (neuropsychological testing) measures, and interactions were noted between primary and secondary measures and within secondary measures; however, none of these were noted to be related to HBO2. These results parallel those of Wolf et al19,20 and do not support the use of HBO2 to treat post-concussion syndrome (PCS) after combat-related mTBI even at typical treatment pressures advocated by hyperbaric clinicians for mTBI.18This study demonstrated that neither 1.5 nor 2.0 ATA equivalent HBO2 had an effect on post-concussive eye movement abnormalities after mTBI when compared with a sham-control.22 | (+) |
| Wolf, 2012 19,20 | 50 military service members with at least one combat-related, mTBI (48M, 2F) with a mean age of 28.3 +/- 7.7b | HBO2 25(4%)Sham Compression 25(4%)c | HBO2: 117 min sessions of 100% oxygen at 2.4 ATA x 30 sessions over 8 weeks.Sham Compression: 117 min sessions of air (21% O2) at 1.3 ATA (with a slow drift to 1.2 ATA) x 30 sessions over 8 weeks.*For HBO2 & Sham arms:*  Compression: 7 min; Plateau 90 min; Decompression: 20 min***Note:*** 90 min sessions were broken into three 30 min sessions with 10 min air breaks where the hood was removed. | Time points: baseline, FU: 6 weeks PSYCHOLOGICAL: **Post-Traumatic Disorder Check List-Military Version (PCL-M**). NS composite scores bt groups at any time. Within groups both HBO (t = 3.90, p = 0.001) and sham (t=3.76, p=0.001) showed statistically significant improvements over the course of the study.COGNITION: **Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT)**. NS total scores bt groups at anytime. Within groups sham-control and HBO2 groups revealed statistically significant downward trends over the course of the study for both the sham-control group (t = 3.76, p = 0.001) and the HBO2 group (t = 3.90, p = 0.001). Ten ImPACT symptom subscale scores in the sham-control group were significantly different statistically from baseline to 6 week FU: headaches (p=0.02), fatigue (p=0.05), sleeping more than usual (p=0.038), sleeping less than usual (p=0.038), irritability (p=0.032), sadness (p=0.029), nervousness (p=0.046), emotionality (p=0.46), slower than usual (p=0.01). Two ImPACT symptom scale scores in the HBO2 group were significantly different statistically from baseline to 6 week FU: sleep onset problems (p=0.03) and sleeping less than usual (p=0.01). | (# of HBO2; # of sham patients) Ear barotrauma (n=10; n= 4); sinus squeeze (n=1; n=0); confinement anxiety (n=1; n= 1); headache (n=4; n= 3); nausea (n=2; n= 1); numbness (n=1; n= 0); heartburn (n=0; n= 1); latex allergy (n=0; n=1); musculoskeletal chest pain (n=1; n= 0); and hypertension (n=0; n=1);Of the 52 ear blocks 8 of were diagnosed with a TEED2 in severity. Others were either 0 or 1. | Hyperbaric oxygen is a potent intervention for acute ischemic injuries that has a sound theoretical underpinning and demonstrated efficacy in dive-related injuries, soft tissue healing, and carbon monoxide poisoning. Human research trials with acute severe TBI have been inconclusive. The current study in participants with post-concussive syndrome from chronic mTBI demonstrates no efficacy in symptom relief with HBO2 at an exposure pressure of 2.4 ATA for 90 min given once daily for 30 treatments; however, both groups improved more than would be expected greater than 6 months after mTBI. Given that HBO2, in this controlled study, demonstrates no therapeutic value, requires long treatment series, is expensive, exposes patients to potential side effects, and has limited availability, clinical usage is not warranted for the management of symptoms of chronic mTBI at this treatment pressure. It is recommended that larger, multicenter, randomized, controlled (both sham-control and wait-list), double-blinded clinical trials be conducted at lower total oxygen doses as recommended by Agency for Healthcare Research and Quality (AHRQ).19,20Given the infrequent, mild side effect profile, the authors feel that the study demonstrated that HBO2 was safe at a relatively high treatment pressure in traumatic brain injury subjects and that, subsequently, these data can be used to alter the risk/benefit calculation when deciding whether to utilize HBO2 in the treatment of various diseases in the TBI population. Per the AHRQ, the standard of proof of HBO2 efficacy should be lowered.19 | (+) |
| Miller, 201521 | 72 military service members with mTBI and ongoing symptoms of at least 4 months (69M, 3F) with a mean age of 31 +/- NDa | HBO2 + TBI-care 24(4.2%)Sham + TBI-care 25(16%)Routine TBI-care only 23(13%)c | HBO2: 60 min sessions at 100% O2 at 1.5 ATA daily x 40 sessions over 10 weeks.Sham: 60 min sessions at 1.2 ATA of room air daily x 40 sessions over 10 weeksRoutine TBI-care only: ND*For HBO2 and Sham arms:* Compression: 5 min +/- 1min; Plateau 50 min +/- 2 min; Decompression: 5 min +/- 1 min | Time points: baseline, post-interventionPOST-CONCUSSIVE SYMPTOMS: **Rivermead Post-Concussion Symptoms Questionnaire-3 subscale (RPQ-3):** NS bt groups at post-intervention. Within groups at post-intervention: "TBI-care" had no change during 3-month observational period; HBO2 group had statistically significant improvements symptomatically (p=0.04) as did the sham group (p=0.03). **Change of at least 2 points on RPQ-3 scale** (indicating clinically relevant change): NS bt groups.**Rivermead Post-Concussion Symptoms Questionnaire-total score (RPQ):** NS bt HBO2 & sham at post-intervention. Within groups at post-intervention: "TBI-care" no change during 3-month observational period; HBO2 group had statistically significant improvements symptomatically (p=0.008), as did the sham group (p=0.02).POST-CONCUSSIVE SYMPTOMS: **Neurobehavioral Symptom Inventory scores (NSI):** NS bt groups at post-intervention.**NSI subscales (cognitive, affective, somatic):** NS bt HBO2 and sham at post-intervention.Time points: baseline, after 20 sessions, post-interventionCOGNITION: **Automated Neuropsychological Assessment Metrics (ANAM4 TBI-MIL)**: NS bt HBO2 and sham at post-intervention.**ANAM subscales**: Simple reaction: HBO2 and sham achieved slight improvements; Procedural reaction time & code substitution learning: both TBI-care and sham worsened, while HBO2 improved; Mathematical processing & matching to sample: both intervention groups improved with sham performing better than HBO2 in the former and HBO2 performing better in the latter. (Mean change scores were reported for individual subscales but p-values were not reported.PSYCHOLOGICAL: **PTSD Checklist - Civilian Version (PCL-C);** Improvements in mean change scores tended to favor sham vs. HBO2 at post-intervention. P-values not reported.PSYCHOLOGICAL: **Center for Epidemiologic Studies – Depression Scale (CES-D); Beck Anxiety Inventory (BAI); SF-36 mental health subscale**: Mean change scores for “TBI-care” group worsened while improvements in mean change scores for the HBO2 and sham groups tended to favor sham at post-intervention. P-values not reported. | (# of HBO2; # of sham patients) Middle ear pain (n=1; n=1); Tooth pain (n=1; n=0); Inner ear barotrauma (n=2; n=0); Inner ear barotrauma, TEED Grade 2 (n=1; n=0);Onset migraine headache (n=1; n=0); Increase frequency and intensity of headaches (n=1; n=0); Change in headache frequency (n=0; n=1);Transient worsening of myopia (n=1; n=0); Sinus pain (n=0; n=3); Claustrophobia/anxiety (n=0; n=1). | Among service members with persistent post-concussive symptoms (PCS), HBO2 showed no benefits over an air sham compression procedure, but symptoms in both groups improved compared to mTBI care without supplemental chamber interventions. This suggests that the observed improvements are not oxygen-mediated, but may reflect non-specific improvements related to placebo effects. Our study, taken with results from other concurrent DoD trials, does not support Phase III trials of HBO2 for the treatment of PCS at this time.  | (+) |
| Boussi-Gross, 201323 | 67 patients with mTBI1-6 years prior to their inclusion and experience of post-concussion syndrome (PCS) and impaired cognitive functions for over a year (24M, 37F) with a mean age of 44 years (+/- ND)***Note:*** Gender balance and mean-age reported on by authors reflects only 56 patients included in the final analysis after drop-outsa. | Treated36 (11.1%)Crossover 31(22.6%)c | Treated: 60 min HBOT sessions of 1.5 ATA daily x 40 sessions 5 days per week over 8 weeks.Compression times NDCrossover: 2 month control period with no treatment followed by 60 min HBOT sessions of 1.5 ATA daily x 40 sessions 5 days per week over 8 weeks. | Time points: baseline; 2 months; 4 months (crossover group only)COGNITION: **Mindstreams - Information Processing Speed Index**: NS bt groups endpoint scores following treatment of both groups. Statistically significant improvements at post-intervention for both treated group (t(31) = 4.20, p<0.0001; effect size: Cohen’s d = 0.74) and crossover group (t(23) = 1.98, p<0.05; effect size: Cohen’s d =0.40).COGNITION: **Mindstreams –Attention-related index**: NS bt groups endpoint scores following treatment of both groups. Statistically significant improvements at post-intervention for both treated group (t(31) = 3.26, p<0.005; effect size: Cohen’s d = 0.57) and crossover group (t(23) = 2.29, p<0.05; effect size: Cohen’s d =0.47).COGNITION: **Mindstreams – Memory-related index**: NS bt groups endpoint scores following treatment of both groups. Statistically significant improvements at post-intervention for both treated group (t(31) = 4.13, p<0.0005; effect size: Cohen’s d = 0.73) and crossover group (t(23) = 3.21, p<0.005; effect size: Cohen’s d = 0.65).COGNITION: **Mindstreams – Executive Functions index**: NS bt groups endpoint scores following treatment of both groups. Statistically significant improvements at post-intervention for both treated group (t(31) = 3.72, p<0.0005; effect size: Cohen’s d = 0.66) and crossover group (t(23) = 2.26, p<0.05; effect size: Cohen’s d = 0.46). | One participant dropped out due to ear problems, however this event was not further described. | This study provides, for the first time, convincing results based on a crossover study, demonstrating that HBOT can induce neuroplasticity and significant brain function improvements in mild TBI patients with prolonged PCS at late chronic stage, years after injury. The results call for better understanding of how to set the optimal HBOT protocol for the specific patients and how to determine which patients benefit the most from this treatment. The findings reported here bear the promises that HBOT can be effective in treating other brain impairments, like easing post-traumatic stress disorder symptoms or repairing radiation damage. It is also reasonable to expect that HBOT can help slow down or even reverse metabolic disorders associated neurodegenerative diseases. | (+) |
| **HBO2 for MODERATE-TO-SEVERE TBI** |
| Lin, 200826 | 44 patients with sub-acute, moderate to severe TBI (38M, 6F), 20 with a GCS score of 9-12 and 24 with a GCS of 3-8, with an age range of 25-64 years (mean age ND)a | HBOT 22 (0%)No HBOT Treatment 22 (0%)e | HBOT: 120 min sessions of 100% O2 at 2.0 ATA x 20 sessions over 4 wks.Compression: 15 min; Plateau: 90 min; Decompression: 15 min.No HBOT Treatment | Time points: time of TBI, baseline (after TBI stabilized), post-interventionCONSCIOUSNESS: **Glasgow Coma Scale (GCS)**. HBO2 group achieved statistically significant better GCS scores than the control group post-intervention (p<0.05).Time points: time of TBI, baseline (after TBI stabilized), FU: 3 & 6 monthsGOS & Mortality: **Glasgow Outcome Scale (GOS**). Patients were stratified according to GOS score at baseline. NS bt groups at 3 & 6 months; NS bt those groups stratified to GOS=2 or 3 at baseline; Statistically significant improvement bt HBO2 group versus control in group stratified to GOS=4 at baseline (p<0.05).  | Seizures resolved by anticonvulsants (n=2); severe ear pain resolved by tympanostomy (n=2).Authors also report the following minor side effects were well tolerated by patients: tinnitus; aural fullness; disequilibrium; vertigo; nausea. (n=ND). | With incorporation of rehabilitation, HBO2 can help patients with mild neurological deficits to recover and return to normal life. In this prospective study, we can conclude that HBO2 can help TBI patients in GCS recovery and also help patients with mild functional disability to lead a better life. | (+) |
| Ren, 200127,31  | 55 patients with severe brain injury (SBI) as defined as GCS score less than 8 (42M, 13F) with a mean age of 34.9 +/- 1.27b | HBO + Standard care 35(0%)Standard care 20(0%)e | HBO: 40-60 min sessions of pure O2 at 0.25 MPa daily x 30-40 sessions.Compression & decompression times ND.Standard care: Dehydrating, cortical steroid, and antibiotic therapy in the neurosurgery department.***Note:*** One course was 10 days long, each patient received 3-4 courses with a 4-day intermission between courses. | Time points: baseline, after 1 course of HBO2 (at 2 weeks), after 3 courses of HBO (at 3 months).CONSCIOUSNESS: **Glasgow Coma Scale (GCS)**. HBO2 group showed statistically significant improvement over control group (p<0.01). Within groups HBO groups GCS scores significantly improved statistically both after 1 course (p< 0.01) & 3 courses of treatment (p<0.001); NS results for control group.GOS & MORTALITY: **Glasgow Outcome Scale (GOS)**. HBO2 group showed statistically significant improvement over control group at 6 months after injury (p<0.001). Within group HBO2 significantly improved statistically at 6 months after injury (p< 0.01). | Not reported. | From all these results, we find that HBO2 not only effectively attenuates the cranial vascular vasospasm during the acute period after SBI, but also decurate clinical course of brain vascular vasospasm. HBO2 can improve clinical GCS score, Brain Electric Earth Map (BEAM) and prognosis of the SBI patients. HBO2 treatment can reduce SBI patient mortality and morbidity, through decreasing blood endothelin (ET) levels, retarding middle cerebral artery (MCA) blood flow rate, and diminishing brain vascular resistance, which can alternate cranial vascular vasospasm.  | (+) |
| Xie, 200729 | 60 patients with craniocerebral injury selected from the Department of Neurosurgery at the Second Affiliated Hospital, Medical College of Shantou University (37M, 23F) with a mean age of 26 +/- NDa | Hyperbaric oxygenation + routine neurosurgical therapy 30(0%)Routine neurosurgical therapy 30(0%)e | Hyperbaric oxygenation: 105-120 min sessions of ND% O2 at 0.2 to 0.25 MPa daily x 10 sessions.Compression: 15-20 min; Plateau 70-80 min; Decompression: 20 min.Routine neurosurgical therapy after hospitalization, including protecting brain, desiccation, decreasing craniocerebral pressure, anti-infection and related operative therapies. | Time points: baseline, post-interventionCONSCIOUSNESS: **Glasgow Coma Scale (GCS)**. There was a statistically significant difference between HBO2 group and control group after treatment (t=9.21, P < 0.01). Within groups both HBO2 and control groups, scores were increased after treatment with statistically significant mean change scores (t =9.92, 2.51, P < 0.01, 0.05 respectively) | Not reported. | Hyperbaric oxygenation can remarkably decrease content of plasma C-reactive protein in patients with craniocerebral injury at the phase of stress. | (+) |
| Rockswold, 199225 | 168 patients with severe brain injury, as defined as GCS score of 9 or less for at least 6 hours, admitted to Level 1 Trauma Center at Hennepin County Medical Center, with a mean age of 32.5 +/- NDa | Hyperbaric Oxygen Treatment + Standard care 84(ND)Standard care 84(ND)e | Hyperbaric Oxygen Treatment: 60 min sessions (plus compression and decompression times) of 100% O2 at 1.5 ATA every 8 hours over 2 weeks or until patient recovered (alert and oriented) or declared brain dead. Compression: 1 psi / min; Plateau: 60 min; Decompression: 1 psi / min.Standard care: Neurosurgical care, medical treatment, and management of Intracranial pressure. | Time points: HBO2 group - every 15 minutes during 60-minute treatment and then hourly for the next 7 hours until next treatment for 2 weeks; Control group - hourly for 2 weeks.VITAL: **Intracranial pressure (ICP)**. NS bt groups. Time points unclear.Time points: UnclearGOS & MORTALITY: **Mortality rate**. The mortality rate was 17% for the 84 hyperbaric oxygen-treated patients and 32% for the 82 control patients, a statistically significant difference. (chi-squared test, 1 df, p = 0.037). The difference in mortality rate between the hyperbaric oxygen-treated and control patients with GCS scores of 4 to 6 was statistically significant by the chi-squared test (1 df, p = 0.04). Hyperbaric oxygen-treated patients with ICP's higher than 20 mm Hg for over 20 minutes had a mortality rate of 21%, as compared to 48% for the control group (chi-squared test, 1 df, p = 0.02). | Increasing FIO2 requirement and infiltrates detected on chest x-ray studies (n=1); generalized seizure treated with phenytoin sodium (n=2); hemotympanum (n=2).Researchers performed bilateral myringotomies on the last 46 of the 84 HBO2 patients because of higher-than-expected intracranial pressure possibly due to inner ear pain. | Analysis of the outcome of survivors reveals that hyperbaric oxygen treatment did not increase the number of patients in the favorable outcome categories (good recovery and moderate disability). The possibility that a different hyperbaric oxygen treatment paradigm or the addition of other agents, such as a 2 l-aminosteroid, may improve quality of survival is being explored.  | (+) |
| Rockswold, 201028 | 69 patients treated for severe TBI (defined as GCS score of 8 or less) at Hennepin County Medical Center, after resuscitation (58M, 11F) with a mean age of 35 +/- NDa | HBO2 + Standard care 26(ND)Normobaric hyperoxia + Standard care (NBH) 21(ND)Standard care 22(ND)e | HBO2: 94 min sessions of 100% FiO2 at 1.5 ATA daily x 3 sessions Compression: 17 min; Plateau 60 min; Decompression: 17 min.1) NBH: 3-hour sessions of 100% FiO2 at 1 ATA daily x 3 sessions2) Standard care: Intensive neurosurgical care closely paralleling Brain Trauma Foundation’s “Guidelines for the Management of Severe TBI, 3rd Edition”, including stabilization with early intubation, surgical evacuation of significant hematomas, continuous monitoring of ICP, and treatment of ICP > 15 mm Hg and prophylactic phenytoin sodium. | Time points: baseline, 24 hours post-interventionVITAL SIGNS: **Intracranial Pressure (ICP)**. ICP was significantly lower statistically after HBO2 until the next treatment session (p < 0.001) in comparison with levels in the control group. The post-treatment effect was the same for all 3 days. The NBH group’s ICP measures did not differ significantly from those in the control group following each treatment session. | Not reported. | Data in this study can be summarized by the following 7 major points: 1) Hyperbaric O2 had a significantly greater positive post-treatment effect than NBH on oxidative cerebral metabolism and ICP. 2) Although the treatment effect was not an all-or-nothing phenomenon, a critical brain tissue pressure of oxygen (PO2) level of 200 mm Hg seemed important to achieve a robust positive effect on cerebral metabolism, especially cerebral metabolic rate for oxygen (CMRO2), which reflects mitochondrial function. Brain tissue PO2 monitoring to determine O2 delivery in the injured brain during O2 therapy appeared to be important as well. 3) Hyperbaric O2 had a post-treatment effect lasting at least 6 hours, which means that HBO2 can be delivered intermittently to maintain the treatment effect over many days and reduce potential O2 toxicity. 4) The treatment effect was as great on Day 3 as it was in the first 24 hours that is, the treatment effect was the same after the first treatment as after the third— which implies that HBO2 is effective in improving mitochondrial function even when ischemia is not overtly present. 5) Intracranial pressure was reduced after HBO2 treatments in comparison with levels following standard care. The decrease in the therapeutic intensity level (TIL) score also indicated that ICP was treated less aggressively after the HBO2 sessions. The NBH group did not demonstrate a reduction in ICP. 6) There was no evidence of cerebral or pulmonary O2 toxicity in either the HBO2 or NBH treatment paradigms administered. 7) Monoplace HBO2 chambers are practical, straightforward to install, and adaptable to severe TBI care. | (0) |
| Artru, 197624 | 60 patients with head injuries and in a coma (mean Jouvet scale score of 9.49) (60M, 0F) with a mean age of 29.8 +/-5.6b  | OHP 31(ND)Standard care 29(ND)e | OHP: 60 min sessions of 2.5 ATA daily x ND number of sessions over ND wks.Compression: 10 min; Plateau 60 min; Decompression: 20 min.Standard care: ND***Note:*** After 10 daily sessions, there was a four-day intermission. This cycle was repeated until patient recovered consciousness or died. | Time points: 1 month; FU: 1 yearGOS & MORTALITY: **Mortality.** NS bt groups overall and for subgroup 5 (<30 years, not reacting in an adapted manner to painful stimuli, not operated on) at 1 year FU.CONSCIOUSNESS: **Consciousness recovery rate.** In subgroup 5 HBO2 group had statistically significant higher rates of recovered consciousness at 1 month (p<0.03).Time points: 1 monthCONSCIOUSNESS: **Persistent Coma Rate in survivors**. NS bt groups at 1 month. In subgroup 5 HBO2 group had statistically significant lower rates of persistent coma at 1 month (p<0.03). | Polypnea with expiratory dyspnea; cyanosis at exit of the chamber; and reduced SaO2 value (all subsided after decompression and sometimes coexisted with an improved neurological condition after the session); hyperoxic pneumonia interrupting treatments (n=5). | Overall mortality and mean duration of coma in survivors were not different in both groups, indicating that OHP was either ineffective or too intermittently applicated. Analysis of results in subgroups revealed that, in one subgroup (18 patients), the rate of recovered consciousness at 1 month was significantly higher when OHP was used. These patients were under 30 and had a brain stem contusion without supratentorial mass lesion. The view is defended that, besides its toxic action on the normal nervous tissue, OHP can counteract edema and ischemia in the zones of brain injuries.  | (0) |
| Rockswold, 198530 | 30 patients with severe brain injury, defined as persisting unconsciousness with inability to obey commands or express recognizable words and GCS score of less than 10, with a mean age of NDa | Overall 30(ND)HBO ND(ND)Standard Hospital Treatment ND(ND)e | HBO: 60 min sessions of 100% O2 at 1.5 ATA every 4 or 8 hours over 2 weeks (or until patient recovered being alerted and oriented or declared brain dead).Standard Hospital Treatment: ND***Note:*** Sessions were given every 8 hours if ICP was normal or every 4 hours is ICP elevated greater than 15 mm Hg until normalized for 48 hours. | Time point: not describedGOS & MORTALITY: **Mortality.** NS bt groups for survival rate in those with GCS scores of 3 or 7-9. Among patients with GCS scores between 4-6 increased survival occurred in the HBO group compared with the control group but difference was NS (p=0.100) | Not reported. | Based on the experience in the literature cited previously and on our own initial experience, we hope in the future to convincingly demonstrate that the treatment of severe brain-injured patients with HBO will result in an overall beneficial response in terms of long-term functional recovery and decreased mortality rate. Completion of this clinical trial will hopefully demonstrate whether the treatment of head-injured patients with HBO should be pursued further. | (0) |
| **HBO2 for TBI SEVERITY NOT DESCRIBED** |
| Shi, 200332 | 320 patients with post-brain injury neural status treated at a hospital (215M, 105F) with a mean age of 38.5 +/-NDb | HBO + Medication 195(0%)Medication Only 125(0%)e | HBO plus medication: 90 min sessions of 96% O2 at 0.1 MPa daily x 20-40 sessions.Standard medication group: Cerebroblysin (20ml) mixed with glucose (250ml, 10%) intravenously daily over 7 to 10 days. A vasodilating agent such as nimodipine was administered orally.***Note:*** One course consisted of 10 days; each patient received 2-4 courses. | Outcomes not relevant to this review. | Not reported. | HBO therapy has specific curative effects on patients with post-brain injury neural status, and TcECD SPECT could play an important role in diagnosing post-brain injury neural status and monitoring the therapeutic effects of HBO. | (0) |

*\* Name of study arms reported as written by original authors; \*\* Author’s conclusions as reported in authors’ words.*

*aInformed consent received; bInformed consent not reported; cAuthors report power achieved; dAuthors report power not achieved; eAuthors do not report on power.*

Abbreviations: ATA, atmospheres absolute; bt, between; FIO2, fraction of inspired oxygen; FU, follow-up; GCS, Glasgow Coma Scale; GOS, Glasgow Outcome Scale; HBO2 / HBO / HBOT, hyperbaric oxygen therapy; MPa, Megapascal; mTBI, mild traumatic brain injury; NS, not significant; ND, not described; 02, oxygen; TBI, traumatic brain injury; TcECD SPECT, Tc-ethyl cysteinate dimer single photon emission computated tomography