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Hyperbaric Oxygen Therapy Treatment of Chronic Mild-Moderate Blast-Induced Traumatic Brain Injury/Post Concussion Syndrome with Post Traumatic Stress Disorder: Pilot Trial

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Objectives

Mild-moderate blast-induced traumatic brain injury (TBI) and post-traumatic stress disorder (PTSD) affect 11-28% and 13-17%, respectively, of U.S. combat troops returning from Iraq and Afghanistan. Protracted treatment for PTSD exists, but there is no effective treatment for the post-concussion syndrome (PCS) of mild-moderate TBI nor the combined diagnoses of PCS and PTSD. Based on previous case experience with PCS and an animal model we investigated the effect of hyperbaric oxygen therapy (HBOT 1.5) on symptoms, cognition, and SPECT brain blood flow in military veterans with blast-induced TBI/PCS with/without PTSD.

Method

Fifteen symptomatic U.S. military veterans with blast-induced PCS(2) or PCS/PTSD(13), diagnosed by military and/or civilian neuropsychologists and neurologists, who were average: 29.7y (21-45), 2.6y (1.24-4.75) post injury, 1 minute (13 subjects; 2 subjects 4.5 & 9h) loss of consciousness, with 3 blast TBI's (1-8) completed the study. All subjects completed cognitive testing, symptom and quality of life questionnaires, and affective measures pre and immediately post a course of forty bid, 5d/week, 1.5ATA/60 minute hyperbaric oxygen therapy treatments (HBOT). Subjects underwent SPECT brain blood flow imaging (Picker Prism 3000, 25mCi Ethyl Cysteinate Dimer) pre and post a single HBOT and post 40 HBOT's. SPECT was analyzed with Osiris software; relative standard deviation of the mean on a histogram analysis of counts in left centrum semiovale region of interest was taken pre/post Rx. Paired Student t test and Wilcoxon Signed-Ranks test (non-normally distributed data) were used for all cognitive/questionnaires.

Results

All subjects reported symptomatic improvement in the 35 day study period. Pre, post, difference, confidence interval, and p values for cognitive tests and questionnaires were: FSIQ: 95.8+/-8.4; 110.6+/-10.3, 14.8+/-7.4, 10.7-18.9, <0.001; Wechsler Memory Scale (WMS) IV delayed memory: 97.7+/-13.3, 106.9+/-15.4, 9.2+/-14.3, 1.3-17.1, =0.026; WMS Working Memory: 97.0+/-13.6, 106.9+/-13.1, 9.9+/-10.3, 4.1-15.6, =0.003(np); Stroop Color/Word: 84.3+/-12.2, 95.3+/-12.8, 11.1+/-9.2, 6.0-16.2, <0.001; TOVA variability: 64.4+/-28.7, 75.3+/-24.6, 10.9+/-20.2, -0.2-22.1, =0.045(np); Rivermead Post Concussion Symptom Questionnaire: 39.7+/-6.0, 24.1+/-12.6, -15.6+/-12.8, -22.7-(-8.5), =0.002(np); PTSD Checklist Military: 67.4+/-10.5, 47.1+/-16.0, -20.3+/-18.2, -30.4-(-10.2), <0.001; Modified Perceived Quality of Life: 81+/-37, 114+/-36, 33+/-36, 13-53, =0.003; Personal Health Questionnaire 9-Depression Index: 16.6+/-4.9, 8.2+/-4.7, -8.4+/-7.4, -12.5-(-4.3), <0.001; GAD-7 Anxiety Rating: 12.7+/-5.8, 7.9+/-5.3, -4.8+/-5.8, -8.0-(-1.6), =0.007; Percent Back to Normal: [Cognitive: 49.6+/-17.6, 67.0+/-19.4, 17.4+/-17, 7.5-27.2, =0.002], [Physical: 46.8+/-23.0, 66.3+/-18.6, 19.5+/-16, 10.3-28.7, <0.001], [Emotional: 32.5+/-20.6, 61.3+/-19.8, 28.8+/-20.9, 16.7-40.9, <0.001]. SPECT analysis on the first 5 subjects showed a reduction in the standard deviation of the mean on counts in the left centrum which corresponded to a pattern shift from heterogeneity (abnormal) to homogeneity (more normal).

Conclusions

A thirty day course of forty 1.5 ATA HBOT's demonstrated significant symptomatic, cognitive, and affective improvements in 15 U.S. military veterans with chronic blast-induced post-concussion syndrome and post-traumatic stress disorder. These findings were reinforced by quantitative and qualitative SPECT improvements.

Lay Interpretation of Preliminary Data in LSU IRB #7051 Pilot Trial Hyperbaric Oxygen Therapy (HBOT) in Chronic Traumatic Brain Injury (TBI)/Post-Concussion Syndrome (PCS) and TBI/Post-Traumatic Stress Disorder (PTSD)-Pilot Trial

The preliminary data from the LSU Pilot Trial of Hyperbaric oxygen therapy in blast-induced chronic traumatic brain injury (TBI) and post-traumatic stress disorder (PTSD) represents the first organized body of information that suggests a significant treatment effect on the conditions that present the greatest challenge to the integrity of our armed forces.

The Rand Report of 4/2008 indicated that about 33% of our military that have served in Iraq and Afghanistan have been injured or affected by TBI or PTSD or major depression. That is nearly 600,000 individuals. Traditional treatment is protracted counseling and off-label, unapproved use of FDA-black labeled psychoactive drugs that have significant side effects such as increased suicide rates. Epidemic suicide rates currently seen in war veterans from recent conflicts are consistent with the use of such medications.

In this seminal report at the 8th World Congress on Brain Injury Harch and colleagues from LSU School of Medicine, New Orleans demonstrated significant improvements in cognition, symptoms, and quality of life in 15 U.S. veterans with TBI and PTSD an average 3 years after their injury. The physicians and researchers showed that with 4 weeks of treatment using a low dose of hyperbaric oxygen therapy, a treatment used for nearly 100 years in divers and 50 years for wounds, they were able to treat these wounds in the brains of injured U.S. servicemen. Specifically, the veterans achieved substantial improvements in memory, concentration, executive function, and quality of life, and a reduction in headaches, concussion symptoms, depression, and anxiety. Specifically, the veterans achieved substantial improvements in memory, concentration, executive function, and quality of life, and a reduction in headaches, concussion symptoms, depression, and anxiety.

The average veteran experienced clinically meaningful and highly significant improvements. Their IQ increases 15 points -- a nearly 35 percentile increase. This is the IQ difference between a construction worker and an engineer. Other cognitive improvements averaged 25 percentile points. Quality of life measures, concussion symptoms, depression and anxiety indices, and the veterans own estimates of their cognitive, physical, and emotional improvements improved by 30-90%. Surprisingly, the veterans showed a 30% reduction in PTSD symptoms, a 40% reduction in post-concussion syndrome and a 51% decrease in depression and anxiety indexes. All results were clinically and statistically significant. The treatment effects are lasting and reduced or eliminated the need for other medications.

While the study did not include a control group, the magnitude of the improvement measured was striking and never before reported in the medical literature. The time course of symptoms and clinical response over the course of therapy followed a consistent pattern and was of such magnitude that the treatment results cannot be attributed to a placebo effect. Moreover, the outcome measures were supported by functional brain imaging data. This imaging data was very similar to a previous study by Harch where HBOT improved memory and blood vessel density in an animal model of traumatic brain injury. In gauging benefit relative to risk, it is notable that in both the case reports and the LSU pilot study there was no significant side effect to the treatment apart from a temporary emotional flare-up in some patients. The scientific report at the International Brain Injury Association's 8th World Congress reaffirmed earlier published peer-reviewed case reports of Harch and USAF Col. Jim Wright on brain injured U.S. servicemen.

The implication of this preliminary study is that U.S. veterans with the same conditions can safely begin treatment with this established modality, HBOT, by physician direction privately or under a national program approved by Western Institutional Review Board. This program, the National Brain Injury Recovery and Rehabilitation Project (N-BIRR) will incorporate the latest statistical design methodology that is favored by the FDA, the Bayesian Adaptive Design, to continually improve the care pathway for TBI and PTSD by comparing the efficacy of the HBOT doses and other therapies in different treatment 'arms' of the study .

With these strong positive benefits of treatment without risk, the group finds that it would not be ethical in future studies to have a control arm with sham treatment. We believe that an Institutional Review Board that is made aware of this pilot data would will find it unethical to approve sham treatment for these patients in other similar studies they may review. Therefore, our group has concluded that we must use Bayesian Adaptive Design to compare the efficacy of different doses and modalities of treatment. This will provide internal control groups for the study while optimizing in an ongoing way, the care pathway for TBI / PTSD.

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