Therapy Development for TBI and Related Symptoms

US Army HBO2 Clinical Trial

HBO2 clinical trials currently focus on treatment development using HBO2 for chronic PCS after mTBI in active duty Service Members. Many of the trial participants had deployment related mTBI due to blast. While HBO2 is approved by FDA for 13 conditions, the treatment of PCS is not a currently approved condition.

I. A pilot phase II study of HOPPS after mTBI (Miller et al., 2014) study of low dose HBO2 was completed and analyzed, and results were published in the Journal of the American Medical Association—Internal Medicine in January 2015, and the clinical study report was submitted to the FDA in June 2015. The HOPPS study was a DoD, multi-center, Phase II trial conducted at Fort Gordon, Georgia; Fort Carson, Colorado; Camp Lejeune, North Carolina; and Camp Pendleton, California, with assistance of research staff from the Denver VA Medical Center, Colorado, and Latter Day Saints Hospital, Salt Lake City, Utah. This study consisted of three arms with a total of 72 volunteer Service Members with PCS following mTBI. All subjects continued to receive routine local care. One arm received 1.5 ATA pressurization breathing 100 percent oxygen, one arm received 1.2 ATA pressurization breathing room air (21 percent oxygen), and one arm received no chamber procedures as a supplement to local care. From the standpoint of study design, the 100 percent oxygen breathing group (HBO2) was considered to be the treatment intervention. The room air breathing group was a comparative sham exposure and the routine care group was a non-chamber exposure control. The focus was on the evaluation of PCS symptoms and neurocognitive improvement. The results of the study showed that HBO2 oxygen provided no differential benefit relative to room air breathing in terms of short-term relief (six weeks post-treatment) for PCS after mTBI. Researchers did note that some participants (20 to 30 percent) treated in the hyperbaric chambers with either HBO2 or room air (i.e. which is associated with no significant increase in body oxygen levels) did report short-term improvements in TBI symptoms compared to patients treated with TBI standard of care (control group; no chamber time). However, researchers believe the improvements were most likely due to placebo effects or participant expectations coupled with intensive involvement with the research team as part of the chamber procedures. The DoD-sponsored trials are the first ever placebo-controlled studies of HBO2 for PCS after mTBI. The DoD remains committed to researching and providing evidenced-based solutions for our wounded Service Members. The DoD is actively investigating a number of alternate potential treatments for wounded Service Members for the treatment of PCS and PTSD.

II. The HBO2 LTFU study was a single-survey, observational cohort research study of participants who participated in US Navy and Army interventional trials evaluating the efficacy of HBO2 therapy as a treatment for PCS after mTBI with or without PTSD. This research study, conducted from 2009 to 2010, was designed to provide follow-up at a single point in time, more than one year (HOPPS trials and DARPA-funded Virginia Commonwealth University) after intervention. The results showed no consistent trends to support the hypothesis that chamber exposure with either 1.5 ATA HBO2 or the study sham condition was associated with long-term improvement in PCS or PTSD symptoms. Within-group trends seen among LTFU participants from the Navy study (Cifu et al., 2014) were dissimilar to within-group trends seen among LTFU participants from the HOPPS study. For the sham groups, modest improvement was seen in PCS and PTSD symptoms in Navy LTFU participants, but worsened in HOPPS LTFU participants. In the 1.5 ATA HBO2 groups, worsening from baseline was seen in PCS and PTSD symptoms in Navy LTFU participants while minor improvement in PCS and worsening in PTSD symptoms was seen in HOPPS LTFU participants. In a statistically invalid sample of three participants receiving 2.0 ATA HBO2, there was modest improvement of PTSD symptoms. The final report was disseminated to senior leadership at the USAMRMC in July 2015 and the study officially closed September 2015.