

COMMENTARY

Hyperbaric Oxygen Therapy for Traumatic Brain Injury: Promising or Wishful Thinking?

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A recent [review by Hadanny and colleagues](#) recommends [hyperbaric oxygen therapy](#) (HBOT) for acute moderate to severe [traumatic brain injury](#) (TBI) and selected patients with prolonged [postconcussive syndrome](#).

This article piqued my curiosity because I trained in HBOT more than 20 years ago. As a passionate scuba diver, my motivation was to master treatment for air embolism and decompression illness. Thankfully, these diving accidents are rare. However, I used HBOT for nonhealing wounds, and its efficacy was sometimes remarkable.

Paradoxical Results With Oxygen Therapy

Although it may seem self-evident that "more oxygen is better" for medical illness, this is not necessarily true. I recently interviewed [Ola Didrik Saugstad, MD](#), who demonstrated that the traditional practice of resuscitating newborns with 100% oxygen was more toxic than resuscitation with air (which contains 21% oxygen). His counterintuitive discovery led to a lifesaving change in [the international newborn resuscitation guidelines](#).

The US Food and Drug Administration (FDA) has [approved HBOT for a wide variety of conditions](#), but some practitioners enthusiastically promote it for off-label indications. These include [anti-aging](#), [autism](#), [multiple sclerosis](#), and the aforementioned TBI.

More than 50 years ago, [HBOT was proposed for stroke](#), another disorder where the brain has been deprived of oxygen. Despite obvious logic, [clinical trials have been unconvincing](#). The FDA has not approved HBOT for stroke.

HBOT in Practice



During HBOT, the patient breathes 100% oxygen while the whole body is pressurized within a hyperbaric chamber. The chamber's construction allows pressures above normal sea level of 1.0 atmosphere absolute (ATA). For example, The [US Navy Treatment Table](#) for [decompression sickness](#) recommends 100% oxygen at 2.8 ATA. Chambers may hold one or more patients at a time.

The frequency of therapy varies but often consists of 20-60 sessions lasting 90-120 minutes. For off-label use like TBI, patients usually pay out of pocket. Given the multiple treatments, costs can add up.

Inconsistent Evidence and Sham Controls

The unwieldy 33-page evidence review by Hadanny and colleagues cites multiple studies supporting HBOT for TBI. However, many, if not all, suffer from methodological flaws. These include vague inclusion criteria, lack of a control group, small patient numbers, treatment at different times since injury, poorly defined or varying HBOT protocols, varying outcome measures, and superficial results analysis.

A sham or control arm is essential for HBOT research trials, given the potential placebo effect of placing a human being inside a large, high-tech, sealed tube for an hour or more. In some sham-controlled studies, which consisted of low-pressure oxygen (ie, 1.3 ATA as sham vs. 2.4 ATA as treatment), all groups experienced symptom improvement. The review authors argue that the low-dose HBOT sham arms were biologically active and that the improvements seen mean that both high- and low-dose HBOT is therapeutic. The alternative explanation is that the placebo effect accounted for improvement in both groups.

The late Michael Bennett, a world authority on hyperbaric and underwater medicine, [doubted that conventional HBOT sham controls](#) could genuinely have a therapeutic effect, and I agree. The upcoming HOT-POCS trial (discussed below) should answer the question more definitively.

Mechanisms of Action and Safety

Mechanisms of benefit for HBOT include increased [oxygen availability and angiogenesis](#). Animal research suggests that it may reduce secondary cell death from TBI, through [stabilization of the blood-brain barrier and inflammation reduction](#).

HBOT is generally safe and well-tolerated. A retrospective [review of 1.5 million outpatient hyperbaric treatments](#) revealed that < 1% were associated with adverse events. The most common were ear and [sinus barotrauma](#). Because HBOT uses increased air pressure, patients must equalize their ears and sinuses. Those who cannot because of altered consciousness, anatomical defects, or congestion must undergo [myringotomy](#) or terminate therapy. Claustrophobia was the second most common adverse effect. Convulsions and tension pneumocephalus were rare.

Perhaps the most concerning risk of HBOT for patients with TBI is the potential waste of human and financial resources.

Desperate Physicians and Patients

As a neurologist who regularly treats patients with TBI, I share the review authors' frustration regarding the limited efficacy of available treatments. However, the suboptimal efficacy of currently available therapy is insufficient justification to recommend HBOT.

With respect to chronic TBI, it is difficult to imagine how HBOT could reverse brain injury that has been present for months or years. No other therapy exists that reliably encourages neuronal regeneration or prevents the development of [post-traumatic epilepsy](#).

Frank Conidi, MD, a board-certified sports neurologist and [headache](#) specialist, shared his thoughts via email. He agrees that HBOT may have a role in TBI, but after reviewing Hadanny and colleagues' paper, he concluded that there is insufficient evidence for the use of HBOT in all forms of TBI. He would like to see large multicenter, well-designed studies with standardized pressures and duration and a standard definition of the various types of [head injury](#).

Ongoing Research

There are [at least five ongoing trials](#) on HBOT for TBI or postconcussive syndrome, including the well-designed placebo-controlled [HOT-POCS](#) study. The latter has a novel placebo gas system that addresses Hadanny and colleagues' contention that even low-dose HBOT might be effective.

The placebo arm in [HOT-POCS](#) mimics the HBO environment but provides only 0.21 ATA of oxygen, the same as room air. The active arm provides 100% oxygen at 2.0 ATA. If patients in both arms improve, the benefit will be due to a placebo response, not HBOT.

Conflict of Interest

Another concern with the review is that all three authors are affiliated with Aviv Scientific. This company has an exclusive partnership with the world's largest hyperbaric medicine and research facility, the Sagol Center at Shamir Medical Center in

Israel.

This conflict of interest does not a priori invalidate their conclusions. However, official HBOT guidelines from a leading organization like the [Undersea and Hyperbaric Medicine Society](#) or the [American Academy of Neurology](#) would be preferable.

Conclusion

There is an urgent unmet need for more effective treatments for postconcussive syndrome and chronic TBI. Despite tantalizing theoretical mechanisms as to why HBOT might promote brain healing after trauma, its efficacy remains unproven.

The review authors' recommendations for HBOT seem premature. They are arguably a disservice to the many desperate patients and their families who will be tempted to expend valuable resources of time and money for an appealing but unproven therapy. Appropriately designed placebo-controlled studies such as HOT-POCS will help separate fact from wishful thinking.

*Andrew Wilner is a seasoned neurologist and [epilepsy](#) expert who has mastered the less conventional locum career path. He is the author of four books, including *Bullets and Brains*, and hosts the podcast *The Art of Medicine with Dr. Andrew Wilner*.*

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