

Traumatic Brain Injuries and the Potential of Hyperbaric Oxygen Therapy

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“The cost of Traumatic Brain Injuries (TBI) is approximately \$56 billion, and more than 5 million Americans alive today have had TBI related injury resulting in a permanent need for help in performing daily activities. Survivors of TBI are often left with significant cognitive, behavioral, and communicative disabilities, and some patients develop long-term medical complications, such as epilepsy.” (National Institutes of Neurological Disorders and Stroke, NIH, 2010)

INTRODUCTION

Traumatic Brain Injuries (TBI) are becoming one of the leading causes of death and life-long disabilities in infants, adolescents, adults and senior citizens ⁽¹⁾. Consequently, there is an increasing concern among parents and health care providers regarding the prevalence of brain injuries in commonly practiced sports; car related accidents, worker injuries as well as increasing number of brain-injured soldiers returning from war theaters. Approximately 1.7 million Americans will experience a brain injury annually, with ~80% of those patients diagnosed with mild-to-moderate TBI ⁽¹⁾. Limited medical and technological tools to address this urgent concern have created a strong need to develop new approaches to treat TBI sufferers.

Hyperbaric Oxygen Therapy (HBOT) has been used for more than a 100 years to increase oxygen intake in damaged or oxygen-starved tissues. By increasing atmospheric pressure around the damaged tissue and applying 100% oxygen, the total amount of oxygen in the blood and organs increases, ensuring that all cells are supplied with this life sustaining gas.

Evidence of the benefits of HBOT in the treatment of Traumatic Brain Injury has been accumulating for the last 30 years with encouraging results. Recent clinical reports and animal studies support the idea that patients with mild-to-moderate brain injury can greatly accelerate their recovery and reverse damage with HBOT. Currently medications focus on controlling brain injury symptoms rather than brain recovery. HBOT has shown positive benefits for mild-to-moderate TBI now and can reverse damage that is untreatable with drugs.

What is Traumatic Brain Injury?

Traumatic brain injury is defined as brain damage that results in the disruption or loss of some of its functions. One of the reasons for such a broad definition for TBIs is the variety of different accidents that can produce this trauma. Sports injuries, car accidents, work accidents and blast wounds can result in a very complex pattern of brain damage and behavioral changes ⁽²⁻⁶⁾, making TBI difficult to diagnose and treat.

In the U.S. alone approximately 2 million cases of mild-to-moderate TBI go unreported yearly, with 1.7 million people being admitted into hospitals and resulting in annual deaths of 50,000 per year ^(1, 15-18). A subset of TBI called Sports Brain Injury (SBI), is responsible for 300,000 hospital admissions ⁽¹⁹⁾, highlighting the ease by which TBIs can be sustained in everyday sports activities. Not included in the statistics above are armed service men and women that are returning to the nation with serious brain trauma. Current estimates are that 360,000 are now suffering from traumatic brain injuries, creating a significant social and mental health issue ⁽²⁰⁾. To put this in perspective, it is estimated that a minimum of 1% of the U.S. population is suffering from mild-to-moderate TBI ^(15, 21) with inadequate medical support and complete lack of awareness about this national problem.

TBI can be divided into four major types of injury: blunt (a blow to the head), penetrating (material entering past the skull), blast (shock waves compressing the brain) and toxins (chemicals, drugs or gases

directly affecting the brain). Damage caused by TBIs includes, among others, loss of neuronal connections (7-9), brain bruising, swelling, bleeding into the brain (9, 10) and direct disruption of neuron functions (11-14).

For those that suffer from mild-to-moderate TBI, the clinical symptoms may range from depression (22-24), blurred vision (25), headaches, impaired decision making, diminished motor skills (26-28) and post-traumatic stress disorder (29). Associated with the direct suffering of individuals are the societal and economic costs of TBIs. Current estimates are that \$50-60 billion a year are lost due to medical costs and lost productivity (1, 30), coupled to the incalculable emotional turmoil and distress that directly affects the sufferer of TBI and those around them.

Why Use Hyperbaric Oxygen Therapy?

Hyperbaric oxygen therapy (HBOT) has been in use for over 100 years, safely treating a variety of medical condition (31-33). HBOT is a treatment in which the entire body is exposed to 100 % oxygen under increased pressure. By augmenting total gas pressure, oxygen levels in all body organs can be increased dramatically (31, 33) sparing and maintaining organs that are oxygen deprived, removing obstructions in blood flow caused by gas bubbles, and inhibiting certain types of bacteria (34-36).

Recent studies reveal that HBOT has other beneficial effects. In TBI studies of rats and mice treated with HBOT, behavioral and neurological damage is spared or reversed (37-44). In humans, clinical reports show similar effects. Armed service personnel that were diagnosed with mild-to-moderate TBI shows that repeated HBOT exposures produce beneficial effects in terms of brain functioning (45, 46). Single photon emission computer tomography (SPECT) imaging of TBI - affected brain regions reveals improvement in brain blood flow. From a neuro- psychological viewpoint, changes observed in the SPECT imaging of the brain correlates with improved mental conditions (46, 47). Psychological and cognitive tests taken prior to HBOT reveal improvements in almost all areas during and after HBOT. Symptoms, such as headaches, disturbed sleep and PTSD (Post Traumatic Stress Disorder) are alleviated (45-47) and positive outcomes are long-lasting.

How is it that a single therapy can produce such remarkable changes? Given the role that oxygen plays in the cellular function of the brain, it should not be surprising that HBOT provides healing and protection. HBOT probably produces all these beneficial effects through multiple, parallel pathways. In rats, data demonstrates that HBOT promotes new neuron (48) and blood vessel regrowth (49-51). Cellular metabolism and cell survival is improved (11, 13, 52) and cellular death (40, 52) is inhibited. Inflammation of the brain after TBI is a common response to damage (53), but inflammation is reduced (54) by HBOT, as well as brain bleeding (55, 56) and brain swelling (14, 57). It is still not known if these are all the benefits that HBOT provides or just the most obvious that have been observed to date. It seems apparent that the synergistic effect that HBOT has with other treatments (58, 59), strongly suggests that combining therapies with HBOT could yield better results than either alone.

Treating TBI with HBOT

Patients with TBI or SBI have few options for rehabilitation. Drug treatments have been inadequate to provide significant recovery (60, 61), and no proven treatments emerging in the last 30 years have been considered to be effective (21). In almost all cases, the proper course of action is to provide mental and physical rehabilitation, expecting for healing to occur spontaneously. Doctors and patients are looking for alternative treatments and HBOT is emerging as an attractive and effective alternative. Given the large number of military personnel and civilians suffering from TBI or SBI, the field of HBOT offers a potential to alleviate symptoms and reverse damage with minimal risk. Recent advances in diagnostic tests, brain imaging and telemetry for assessing trauma to the body and brain, will improve targeting specific TBI and SBI lesions for HBOT. In the near future, as advances in drug therapy or other alternatives come into play, the integration of HBOT and drug, physical or behavioral treatments could provide better prognosis for recovery to all forms of TBI that are considered today too severe to heal.

References:

1. Faul M, Xu L, Wald MM, VG C. Traumatic brain injury in the United States: emergency department visits, hospitalizations, and deaths. Centers for Disease Control and Prevention, National Center for Injury Prevention and Control. 2010.
2. Grady MF. Concussion in the adolescent athlete. *Curr Probl Pediatr Adolesc Health Care*. 2010;40(7):154-69.
3. Dewall J. The ABCs of TBI. Evidence-based guidelines for adult traumatic brain injury care. *JEMS*. 2010;35(4):54-61; quiz 3.
4. Powell JW, Barber-Foss KD. Traumatic brain injury in high school athletes. *JAMA*. 1999;282(10):958-63.
5. Nolan S. Traumatic brain injury: a review. *Crit Care Nurs Q*. 2005;28(2):188-94.
6. Kocsis JD, Tessler A. Pathology of blast-related brain injury. *J Rehabil Res Dev*. 2009;46(6):667-72.
7. Levin HS, Wilde E, Troyanskaya M, Petersen NJ, Scheibel R, Newsome M, et al. Diffusion tensor imaging of mild to moderate blast-related traumatic brain injury and its sequelae. *J Neurotrauma*. 2010;27(4):683-94.
8. Caeyenberghs K, Leemans A, Geurts M, Taymans T, Vander Linden C, Smits-Engelsman BC, et al. Brain-behavior relationships in young traumatic brain injury patients: fractional anisotropy measures are highly correlated with dynamic visuomotor tracking performance. *Neuropsychologia*. 2010;48(5):1472-82.
9. Galloway NR, Tong KA, Ashwal S, Oyoyo U, Obenaus A. Diffusion-weighted imaging improves outcome prediction in pediatric traumatic brain injury. *J Neurotrauma*. 2008;25(10):1153-62.
10. Povlishock JT, Katz DI. Update of neuropathology and neurological recovery after traumatic brain injury. *J Head Trauma Rehabil*. 2005;20(1):76-94.
11. Soustiel JF, Larisch S. Mitochondrial Damage: A Target for New Therapeutic Horizons. *Neurotherapeutics*. 2010;7(1):13-21.
12. Rockswold SB, Rockswold GL, Zaun DA, Zhang X, Cerra CE, Bergman TA, et al. A prospective, randomized clinical trial to compare the effect of hyperbaric to normobaric hyperoxia on cerebral metabolism, intracranial pressure, and oxygen toxicity in severe traumatic brain injury. *J Neurosurg*. 2010;112(5):1080-94.
13. Zhou Z, Daugherty WP, Sun D, Lévassieur JE, Altememi N, Hamm RJ, et al. Protection of mitochondrial function and improvement in cognitive recovery in rats treated with hyperbaric oxygen following lateral fluid-percussion injury. *J Neurosurg*. 2007;106(4):687-94.
14. Al-Waili NS, Butler GJ, Beale J, Abdullah MS, Hamilton RW, Lee BY, et al. Hyperbaric oxygen in the treatment of patients with cerebral stroke, brain trauma, and neurologic disease. *Adv Ther*. 2005;22(6):659-78.
15. Summers CR, Ivins B, Schwab KA. Traumatic brain injury in the United States: an epidemiologic overview. *Mt Sinai J Med*. 2009;76(2):105-10.
16. Rutland-Brown W, Langlois JA, Thomas KE, Xi YL. Incidence of traumatic brain injury in the United States, 2003. *J Head Trauma Rehabil*. 2006;21(6):544-8.
17. Langlois JA, Rutland-Brown W, Wald MM. The epidemiology and impact of traumatic brain injury: a brief overview. *J Head Trauma Rehabil*. 2006;21(5):375-8.
18. Bruns J, Jr., Hauser WA. The epidemiology of traumatic brain injury: a review. *Epilepsia*. 2003;44 Suppl 10:2-10.
19. Thurman DJ, Branche CM, Snizek JE. The epidemiology of sports-related traumatic brain injuries in the United States: recent developments. *J Head Trauma Rehabil*. 1998;13(2):1-8.
20. Disability NCo. Invisible Wounds: Serving Service Members and Veterans with PTSD and TBI. 2009:73.
21. Editorial LE. Traumatic brain injury: time to end the silence. *Lancet Neurol*. 2010;9(4):331.
22. Lin MR, Chiu WT, Chen YJ, Yu WY, Huang SJ, Tsai MD. Longitudinal changes in the health-related quality of life during the first year after traumatic brain injury. *Arch Phys Med Rehabil*. 2010;91(3):474-80.
23. Bryant RA, O'Donnell ML, Creamer M, McFarlane AC, Clark CR, Silove D. The psychiatric sequelae of traumatic injury. *Am J Psychiatry*. 2010;167(3):312-20.
24. Bombardier CH, Fann JR, Temkin NR, Esselman PC, Barber J, Dikmen SS. Rates of major depressive disorder and clinical outcomes following traumatic brain injury. *JAMA*. 2010;303(19):1938-45.
25. Lew HL, Garvert DW, Pogoda TK, Hsu PT, Devine JM, White DK, et al. Auditory and visual impairments in patients with blast-related traumatic brain injury: Effect of dual sensory impairment on Functional Independence Measure. *J Rehabil Res Dev*. 2009;46(6):819-26.
26. Sheedy J, Geffen G, Donnelly J, Faux S. Emergency department assessment of mild traumatic brain injury and prediction of post-concussion symptoms at one month post injury. *J Clin Exp Neuropsychol*. 2006;28(5):755-72.
27. Rees PM. Contemporary issues in mild traumatic brain injury. *Arch Phys Med Rehabil*. 2003;84(12):1885-94.
28. Davis AE. Cognitive impairments following traumatic brain injury. Etiologies and interventions. *Crit Care Nurs Clin North Am*. 2000;12(4):447-56.
29. King NS. PTSD and traumatic brain injury: folklore and fact? *Brain Inj*. 2008;22(1):1-5.
30. Boake C, McCauley SR, Pedroza C, Levin HS, Brown SA, Brundage SI. Lost productive work time after mild to moderate traumatic brain injury with and without hospitalization. *Neurosurgery*. 2005;56(5):994-1003; discussion 994-.
31. Edwards ML. Hyperbaric oxygen therapy. Part 1: history and principles. *J Vet Emerg Crit Care (San Antonio)*. 2010;20(3):284-8.
32. Biddle C. Oxygen: the two-faced elixir of life. *AANA J*. 2008;76(1):61-8.
33. Sheridan RL, Shank ES. Hyperbaric oxygen treatment: a brief overview of a controversial topic. *J Trauma*. 1999;47(2):426-35.
34. Gill AL, Bell CN. Hyperbaric oxygen: its uses, mechanisms of action and outcomes. *QJM*. 2004;97(7):385-95.
35. Edwards ML. Hyperbaric oxygen therapy. Part 2: application in disease. *J Vet Emerg Crit Car*. 2010;20(3):289-97.
36. Bitterman H. Bench-to-bedside review: oxygen as a drug. *Crit Care*. 2009;13(1):205. PMID: 2688103.
37. Voigt C, Forschler A, Jaeger M, Meixensberger J, Kuppers-Tiedt L, Schuhmann MU. Protective effect of hyperbaric oxygen therapy on experimental brain contusions. *Acta Neurochir Suppl*. 2008;102:441-5.
38. Rockswold SB, Rockswold GL, Defillo A. Hyperbaric oxygen in traumatic brain injury. *Neurol Res*. 2007;29(2):162-72.

39. Harch PG, Kriedt C, Van Meter KW, Sutherland RJ. Hyperbaric oxygen therapy improves spatial learning and memory in a rat model of chronic traumatic brain injury. *Brain Res.* 2007;1174:120-9.
40. Liu Z, Jiao QF, You C, Che YJ, Su FZ. Effect of hyperbaric oxygen on cytochrome C, Bcl-2 and Bax expression after experimental traumatic brain injury in rats. *Chin J Traumatol.* 2006;9(3):168-74.
41. Vlodavsky E, Palzur E, Feinsod M, Soustiel JF. Evaluation of the apoptosis-related proteins of the BCL-2 family in the traumatic penumbra area of the rat model of cerebral contusion, treated by hyperbaric oxygen therapy: a quantitative immunohistochemical study. *Acta Neuropathol.* 2005;110(2):120-6.
42. Palzur E, Vlodavsky E, Mulla H, Arieli R, Feinsod M, Soustiel JF. Hyperbaric oxygen therapy for reduction of secondary brain damage in head injury: an animal model of brain contusion. *J Neurotrauma.* 2004;21(1):41-8.
43. Niklas A, Brock D, Schober R, Schulz A, Schneider D. Continuous measurements of cerebral tissue oxygen pressure during hyperbaric oxygenation--HBO effects on brain edema and necrosis after severe brain trauma in rabbits. *J Neurol Sci.* 2004;219(1-2):77-82.
44. Rosenthal RE, Silbergleit R, Hof PR, Haywood Y, Fiskum G. Hyperbaric oxygen reduces neuronal death and improves neurological outcome after canine cardiac arrest. *Stroke.* 2003;34(5):1311-6.
45. Wright JK, Zant E, Groom K, Schlegel RE, Gilliland K. Case report: Treatment of mild traumatic brain injury with hyperbaric oxygen. *Undersea Hyperb Med.* 2009;36(6):391-9.
46. Harch PG, Fogarty EF, Staab PK, Van Meter K. Low pressure hyperbaric oxygen therapy and SPECT brain imaging in the treatment of blast-induced chronic traumatic brain injury (post-concussion syndrome) and post traumatic stress disorder: a case report. *Cases J.* 2009;2:6538. PMID: 2740054.
47. Harch PG, Andrews SR, Fogarty E, Lucarini J, Aubrey C, Staab PK, et al. Hyperbaric Oxygen Therapy Treatment of Chronic Mild-Moderate Blast-Induced Traumatic Brain Injury/Post Concussion Syndrome with Post Traumatic Stress Disorder: Pilot Trial. International Hyperbaric Medical Foundation. 2010.
48. Zhang T, Yang QW, Wang SN, Wang JZ, Wang Q, Wang Y, et al. Hyperbaric oxygen therapy improves neurogenesis and brain blood supply in piriform cortex in rats with vascular dementia. *Brain Inj.* 2010.
49. Milovanova TN, Bhopale VM, Sorokina EM, Moore JS, Hunt TK, Hauer-Jensen M, et al. Hyperbaric oxygen stimulates vasculogenic stem cell growth and differentiation in vivo. *J Appl Physiol.* 2009;106(2):711-28. PMID: 2644249.
50. Liu ZJ, Velazquez OC. Hyperoxia, endothelial progenitor cell mobilization, and diabetic wound healing. *Antioxid Redox Signal.* 2008;10(11):1869-82. PMID: 2638213.
51. Velazquez OC. Angiogenesis and vasculogenesis: inducing the growth of new blood vessels and wound healing by stimulation of bone marrow-derived progenitor cell mobilization and homing. *J Vasc Surg.* 2007;45 Suppl A:A39-47. PMID: 2706093.
52. Palzur E, Zaaroor M, Vlodavsky E, Milman F, Soustiel JF. Neuroprotective effect of hyperbaric oxygen therapy in brain injury is mediated by preservation of mitochondrial membrane properties. *Brain Res.* 2008;1221:126-33.
53. Morganti-Kossmann MC, Satgunaseelan L, Bye N, Kossmann T. Modulation of immune response by head injury. *Injury.* 2007;38(12):1392-400.
54. Vlodavsky E, Palzur E, Soustiel JF. Hyperbaric oxygen therapy reduces neuroinflammation and expression of matrix metalloproteinase-9 in the rat model of traumatic brain injury. *Neuropathol Appl Neurobiol.* 2006;32(1):40-50.
55. Jadhav V, Ostrowski RP, Tong W, Matus B, Chang C, Zhang JH. Hyperbaric oxygen preconditioning reduces postoperative brain edema and improves neurological outcomes after surgical brain injury. *Acta Neurochir Suppl.* 2010;106:217-20.
56. Veltkamp R, Siebing DA, Sun L, Heiland S, Bieber K, Marti HH, et al. Hyperbaric oxygen reduces blood-brain barrier damage and edema after transient focal cerebral ischemia. *Stroke.* 2005;36(8):1679-83.
57. Niklas A, Brock D, Schober R, Schulz A, Schneider D. Continuous measurements of cerebral tissue oxygen pressure during hyperbaric oxygenation - HBO effects on brain edema and necrosis after severe brain trauma in rabbits. *Journal of the Neurological Sciences.* 2004;219(1-2):77-82.
58. Yuan LJ, Niu CC, Lin SS, Chan YS, Yang CY, Chen WJ, et al. Additive effects of hyperbaric oxygen and platelet-derived growth factor-BB in chondrocyte transplantation via up-regulation expression of platelet-derived growth factor-beta receptor. *J Orthop Res.* 2009;27(11):1439-46.
59. Michalski D, Kuppers-Tiedt L, Weise C, Laignel F, Hartig W, Raviolo M, et al. Long-term functional and neurological outcome after simultaneous treatment with tissue-plasminogen activator and hyperbaric oxygen in early phase of embolic stroke in rats. *Brain Res.* 2009;1303:161-8.
60. Maas AI, Steyerberg EW, Marmarou A, McHugh GS, Lingsma HF, Butcher I, et al. IMPACT recommendations for improving the design and analysis of clinical trials in moderate to severe traumatic brain injury. *Neurotherapeutics.* 2010;7(1):127-34.
61. Narayan RK, Michel ME, Ansell B, Baethmann A, Biegon A, Bracken MB, et al. Clinical trials in head injury. *J Neurotrauma.* 2002;19(5):503-57. PMID: 1462953.