

Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration

ISSN: 2167-8421 (Print) 2167-9223 (Online) Journal homepage: <http://www.tandfonline.com/loi/iafd20>

ALS Untangled No. 35: Hyperbaric Oxygen Therapy*

The ALSUntangled Group

To cite this article: The ALSUntangled Group (2016): ALS Untangled No. 35: Hyperbaric Oxygen Therapy*, Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, DOI: [10.3109/21678421.2016.1172818](https://doi.org/10.3109/21678421.2016.1172818)

To link to this article: <http://dx.doi.org/10.3109/21678421.2016.1172818>



Published online: 18 Apr 2016.



Submit your article to this journal [↗](#)



Article views: 345



View related articles [↗](#)



View Crossmark data [↗](#)

Full Terms & Conditions of access and use can be found at
<http://www.tandfonline.com/action/journalInformation?journalCode=iafd20>

RESEARCH ARTICLE

ALS Untangled No. 35: Hyperbaric Oxygen Therapy*

The ALSUntangled Group

ALSUntangled Update 35

ALSUntangled reviews alternative treatments for patients with ALS (PALS). Here we review hyperbaric oxygen therapy (HBOT) for ALS, a topic for which we have had 90 requests (1).

Overview

HBOT involves treating patients with 100% oxygen at pressures several times higher than atmospheric pressure. This is accomplished by placing patients in a sealed, pressurized chamber (2). HBOT was initially used to treat decompression sickness after diving. There are currently 14 approved, evidence-based indications for HBOT including treatment of air embolism, carbon monoxide poisoning, non-healing wounds (such as diabetic wounds), burns, gangrene, brain abscess, and radiation injury (3). Numerous websites advertise off-label HBOT for a wide variety of other conditions including multiple sclerosis, dementia, stroke and ALS (4,5). Meta-analyses conclude that there is insufficient evidence to support the use of HBOT in multiple sclerosis (6), dementia (7) and stroke (8). The FDA has warned patients against such off-label use (9).

Mechanism

Oxidative stress (10,11), mitochondrial dysfunction (11,12) and neuroinflammation (13) are believed to play key roles in ALS pathophysiology. HBOT has been shown to modify all of these processes, albeit in small studies. In a small human study, HBOT increased the synthesis of heat shock protein

HSP70, which plays a role in cellular protection against oxidative stress (14). In a small study of the Wobbler mouse model of motor neuron disease, HBOT improved mitochondrial respiration in the motor cortex (15). In rat models of stroke, HBOT reduced post-ischemic markers of inflammation such as COX-2 and MMP, and reduced infarct size (16). Based on all of this, ALSUntangled assigns a TOE ‘Mechanism’ grade of B (Table I).

It should be noted that trials of other agents that target oxidative stress, mitochondrial dysfunction and neuroinflammation have been unsuccessful to date in patients with ALS. Unfortunately many of these studies never addressed CNS penetration and target engagement.

Pre-clinical data

HBOT is reported to delay onset of motor neuron disease in the Wobbler mouse model (15). This study looked at the effects of HBOT both in mice with phenotypic motor disease and in newborn mice prior to onset of disease phenotype. For the first part, Wobbler mice with motor dysfunction were treated for 28–30 days with 100% oxygen at 2 ATA (1 h per day). The treated mice were compared to both Wobbler and wild-type controls that did not receive HBOT. For the second part the investigators treated newborn Wobbler mice with HBOT for 1 h per day, six days per week for 350 days. Onset and progression of motor neuron disease was significantly delayed in the treated Wobbler mice compared to untreated controls. The results of this paper

*The ALSUntangled Group currently consists of the following members: Emma Fixsen, Richard Bedlack, Colin Quinn, Chafic Karam, Alex Sherman, Lyle Ostrow, Orla Hardiman, Terry Heiman-Patterson, Laurie Gutmann, Mark Bromberg, Gregory Carter, Edor Kabashi, Tulio Bertorini, Tahseen Mozaffar, Peter Andersen, Josep Gamez, Mazen Dimachkie, Yunxia Wang, Paul Wicks, James Heywood, Steven Novella, L. P. Rowland, Erik Pioro, Lisa Kinsley, Kathy Mitchell, Jonathan Glass, Sith Sathornsumetee, Jon Baker, Nazem Atassi, Dallas Forshev, John Ravits, Robin Conwit, Carlayne Jackson, Kate Dalton, Katherine Tindall, Ginna Gonzalez, Janice Robertson, Larry Phillips, Michael Benatar, Eric Sorenson, Christen Shoesmith, Steven Nash, Nicholas Maragakis, Dan Moore, James Caress, Kevin Boylan, Carmel Armon, Megan Grosso, Bonnie Gerecke, Jim Wymer, Bjorn Oskarsson, Robert Bowser, Vivian Drory, Jeremy Shefner, Noah Lechtzin, Melanie Leitner, Robert Miller, Todd Levine, James Russell, Khema Sharma, David Saperstein, Leo McClusky, Daniel MacGowan, Jonathan Licht, Ashok Verma, Michael Strong, Catherine Lomen-Hoerth, Rup Tandan, Michael Rivner, Steve Kolb, Meraida Polak, Stacy Rudnicki, Pamela Kittrell, Muddasir Quereshi, George Sachs, Gary Pattee, Michael Weiss, John Kissel, Jonathan Goldstein, Jeffrey Rothstein, Dan Pastula, Gleb Levitsky, Mieko Ogino, Jeffrey Rosenfeld, Efrat Carmi, Christina Fournier, Paul Barkhaus, Brett Morrison, Lorne Zinman, Eric Valor, Neta Zach, Ahmad Ghavanini, Yvonne Baker, Kristiana Salmon, Steve Perrin, Rob Goldstein, Fernando Vieira, Merit Cudkowicz, Hiroshi Mitsumoto.

Note: this paper represents a consensus of those weighing in. Every investigator in this group does not necessarily share the opinions expressed in this paper.

seem promising, but several aspects are problematic. First, the numbers of mice studied were small ($n=18$ for the first experimental group and $n=9$ for the second). In addition, delayed onset and progression of disease was seen in mice treated since birth with HBOT. This effect may not translate to humans who do not begin HBOT treatment until after they have developed symptomatic ALS. ALSUntangled assigns a TOE ‘Mechanism’ grade of C based on this information (Table I).

Clinical data

Cases

Within the online community ‘PatientsLikeMe’, seven people report trying HBOT for ALS (17). There is only one individual patient review, which states that no improvement was noted after three weeks of HBOT (18). In addition, the patient developed ‘eyesight deterioration’ coincident with HBOT treatment (18). Google search identified the website of Kim Cherry, who reports that his ALS has been reversing on a regimen of HBOT in addition to I.V. ozone treatments, various vitamins and supplements, detox, special diets and attitude changes (19). We contacted Mr. Cherry via email and he kindly sent us his medical records. These confirm a history of insidious onset slowly progressive painless weakness starting in 2010. His neurologist documented upper and lower motor neuron signs, progressing to involve bulbar, cervical and lumbar segments. His EMG studies demonstrated a mild sensory neuropathy with a superimposed progressive motor axonopathy, eventually affecting bulbar, cervical, thoracic and lumbar segments. Neuroimaging of his brain and spine as well as blood tests including CK, ganglioside antibodies and paraneoplastic antibodies failed to find an explanation for his presentation and he was diagnosed with ALS in November 2011. A second opinion confirmed this diagnosis (19). He slowly

Table I. TOE grades for HBOT in ALS.

	Grade	Explanation
Mechanism	B	Shown in a peer reviewed publication to act on a relevant mechanism in a pre-clinical ALS model
Pre-clinical	C	One flawed publication reports benefit in an ALS rat model
Cases	C	One unpublished case report with validated diagnosis and improvements (though HBOT was part of a large number of treatments used)
Trials	F	The best available trial showed no benefit
Risks	D	More than 0% but less than 5% of those exposed to HBOT experience serious side-effects

progressed to his nadir in January 2012 at which time his ALSFRS-R score was 31. His most recent ALSFRS-R score in August 2015 had improved to 47 (20). Based on all this, ALSUntangled assigns a TOE ‘Cases’ grade of C (Table I).

Trials

No large clinical trials have been published on the use of HBOT for ALS. A small phase I clinical safety study was performed in which five ALS patients were treated with HBOT for eight weeks (21). Four patients reported decreased fatigue after HBOT treatment, while one patient reported increased fatigue and dropped out of the trial. In addition, a statistically significant improvement maximum isometric voluntary contraction (MVIC) of all muscle groups except the right hand was observed. However, a phase II single-blinded placebo-controlled study by the same group showed no benefit from HBOT in patients with ALS (22). In this study five patients with ALS were treated for eight weeks with actual HBOT, while another group of five ALS patients was treated with sham HBOT. Based on all this, ALSUntangled assigns a TOE ‘Trials’ grade of F.

Risks and costs

HBOT can temporarily increase certain markers of oxidative stress in humans (23); theoretically this could accelerate ALS progression. The most common side-effects of HBOT are otological and include ear pain, hearing loss, and tinnitus; approximately 15% of patients receiving HBOT experience otological side-effects (24). Rare but serious potential complications of HBOT can include barotrauma (of the middle ear, nasal sinuses, inner ear, lung and teeth), ocular damage, and seizures (25). Based on all this, ALSUntangled assigns a TOE ‘Risks’ grade of D.

HBOT costs \$100–\$200 per session (26). It is not clear what the dosing is for ALS but one website mentions 4–5 treatments per week (27). It is also possible to buy a home hyperbaric chamber for between \$5000 and \$15,000 (27).

Conclusions

Although there are plausible mechanisms by which HBOT could work in ALS and a flawed pre-clinical study showing benefit in a mouse model, the best available human trial of HBOT showed no benefit. Given this negative human trial and the fact that HBOT has potentially serious complications, we do not recommend HBOT for patients with ALS at this time.

Kim Cherry’s ALS reversal, which occurred on HBOT and several other alternative treatments, appears very interesting. We do not think this is

due to HBOT alone. There are other rare examples of ALS reversals on different (or sometimes no) treatments (28). Other explanations for these reversals include undetected ALS mimics syndromes or endogenous mechanisms that confer resistance to the disease (28). We look forward to further study of cases like this (29).

Declaration of interest: ALSUntangled is sponsored by the ALS Association and the Motor Neurone Disease Association.

References

1. URL:<http://www.alsuntangled.com/open.php>. Accessed: 2016-03-21. (Archived by WebCite® at <http://www.webcitation.org/6gAiF5zJg>).
2. URL:<http://emedicine.medscape.com/article/1464149-overview>. Accessed: 2016-03-21. (Archived by WebCite® at <http://www.webcitation.org/6gAiQQS02>).
3. URL:<https://www.uhms.org/resources/hbo-indications.html>. Accessed: 2016-03-21. (Archived by WebCite® at <http://www.webcitation.org/6gAiVoN58>).
4. URL:<http://balancedhealthtoday.nocelltowers.com/Amyotrophic-Lateral-Sclerosis.html>. Accessed: 2016-03-21. (Archived by WebCite® at <http://www.webcitation.org/6gBA5Nmsr>).
5. URL:<http://mettahealthcare.com/hyperbaric-oxygen-chamber-has-its-first-birthday/>. Accessed: 2016-03-21. (Archived by WebCite® at <http://www.webcitation.org/6gBABpIoC>).
6. Bennett M, Heard R. Hyperbaric oxygen therapy for multiple sclerosis. *CNS Neurosci Ther*. 2010;16:115–24.
7. Xiao Y, Wang J, Jiang S, Luo H. Hyperbaric oxygen therapy for vascular dementia. *Cochrane Database Syst Rev*. 2012;7:CD009425.
8. Bennett M, Weibel S, Wasiak J, Schnabel A, French C, Kranke P. Hyperbaric oxygen therapy for acute ischemic stroke. *Cochrane Database Syst Rev*. 2014;11:CD004954.
9. URL:<http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm364687.htm>. Accessed: 2016-03-21. (Archived by WebCite® at <http://www.webcitation.org/6gBAHbKfU>).
10. Barber S, Shaw P. Oxidative stress in ALS: key role in motor neuron injury and therapeutic target. *Free Radical Biology & Medicine*. 2010;48:629–41.
11. Carri M, Valle C, Bozzo F, Cozzolino M. Oxidative stress and mitochondrial damage: importance in non-SOD1 ALS. *Front Cell Neurosci*. 2015;9:41.
12. Wiedemann FR, Manfredi G, Mawrin C, Beal MF, Schon EA. Mitochondrial DNA and respiratory chain function in spinal cords of ALS patients. *Journal of Neurochemistry*. 2002;80:616–25.
13. Zhao W, Beers D, Appel S. Immune-mediated mechanisms in the pathoprogession of amyotrophic lateral sclerosis. *J Neuroimmune Pharmacol*. 2013;8:888–99.
14. Denny C, Rademacher P, Barnett Y, Speit G. Antioxidant status in humans after exposure to hyperbaric oxygen. *Mutation Research: Fundamental and Molecular Mechanisms of Mutagenesis*. 1999;428:83–9.
15. Dave K, Prado R, Busto R, Raval A, Bradley W, Torbati D, Perez-pinzon M. Hyperbaric oxygen therapy protects against mitochondrial dysfunction and delays onset of motor neuron disease in Wobbler mice. *Neuroscience*. 2003;120:113–20.
16. Ding Z, Tong W, Lu X, Peng H. Hyperbaric oxygen therapy in acute ischemic stroke: a review. *Intervent Neurol*. 2013;2:201–11.
17. URL:<https://www.patientslikeme.com/treatments/show/754-hyperbaric-oxygen-therapy-hbo-side-effects-and-efficacy#overview>. Accessed: 2016-03-21. (Archived by WebCite® at <http://www.webcitation.org/6gBAO9DGd>).
18. URL:https://www.patientslikeme.com/treatment_evaluations/browse?condition_id=9&id=754-hyperbaric-oxygen-therapy-hbo-side-effects-and-efficacy. Accessed: 2016-03-21. (Archived by WebCite® at <http://www.webcitation.org/6gBAMvku>).
19. URL:<http://www.alswinners.com>. Accessed: 2016-03-21. (Archived by WebCite® at <http://www.webcitation.org/6gBC6LLco>).
20. Emails between ALSUntangled and Mr. Kim Cherry, 2015.
21. Steele J, Matos LA, Bradley WG. A phase I safety study of hyperbaric oxygen the EU-Joint Programme for Neurodegeneration (JPND) SOPHIA project therapy for amyotrophic lateral sclerosis. *Amyotroph Lateral Scler Other Motor Neuron Disord*. 2004;5:250–4.
22. Steele J, Zutshi D, Bradley WG. Negative results of a phase II study of hyperbaric O₂ therapy for amyotrophic lateral sclerosis. *Amyotroph Lateral Scler*. 2007;8:274–5.
23. Gurdol F, Cimsit M, Oner-Iyidogan Y, Korpınar S, Yalcinkaya S, Kocak H. Early and late effects of hyperbaric oxygen treatment on oxidative stress parameters in diabetic patients. *Physiol Res*. 2008;57:41–7.
24. Yamamoto Y, Noguchi Y, Enomoto M, Yagishita K, Kitamura K. Otological complications associated with hyperbaric oxygen therapy. *European Archives of Oto-Rhino-Laryngology*. 2015; Dec 9 [Epub ahead of print].
25. Plafki C, Peters P, Almeling M, Welslau W, Busch R. Complications and side-effects of hyperbaric oxygen therapy. *Aviation Space Environmental Medicine*. 2000;71:119–24.
26. URL:<http://www.perrybaromedical.com/hbot-reimbursable.html>. Accessed: 2016-03-21. (Archived by WebCite® at <http://www.webcitation.org/6gBCCA9yQ>).
27. URL:<http://www.balancedhealthtoday.com/Amyotrophic-Lateral-Sclerosis.html>. Accessed: 2016-03-25. (Archived by WebCite® at <http://www.webcitation.org/6gHX3wa6A>).
28. Bedlack RS, Vaughan T, Wicks P, Heywood J, Sinani E, Selsov R, et al. How common are ALS plateaus and reversals? *Neurology*. 2016;86:808–12.
29. URL:<http://www.alsreversals.org>. Accessed: 2016-03-21. (Archived by WebCite® at <http://www.webcitation.org/6gBCIHEiV>).