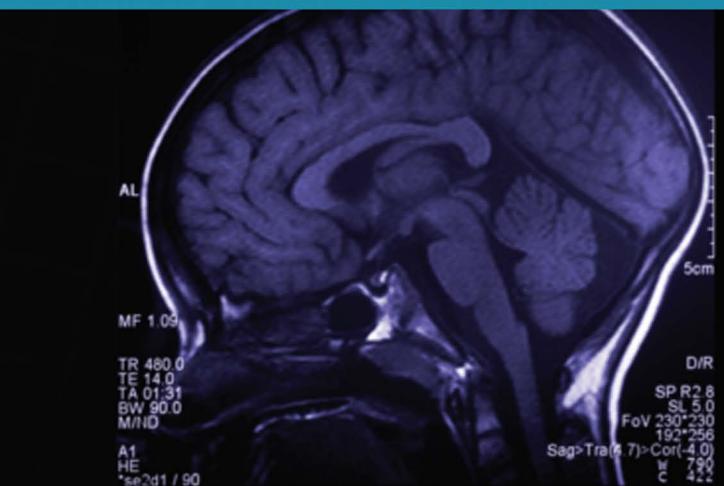


Medical Gas Research



Revisiting the expanded use of hyperbaric oxygen therapy for treatment of resistant migraines

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Abstract

There are currently 13 indications approved by the U.S. Food and Drug Administration for use of hyperbaric oxygen therapy. The European Consensus Conference on Hyperbaric Medicine has 28 indications approved for its use. However, neither includes the use of hyperbaric oxygen therapy for neurological conditions such as migraines with aura. Recent research has made the attempt to fully understand the use of hyperbaric therapy in treatment of neurological conditions, but results have so far been inconclusive. We report a 23-year-old female with an 11-year history of migraines with aura who has received inadequate pharmacological treatment for her migraines since she began having them. Migraines have led her to significant loss of function. The patient underwent treatment at 1.5 absolute atmospheres in a hyperbaric chamber Monday through Friday for 1 hour each day for a total of 40 sessions but reported missing a few sessions over the 8-week period. No more than 1 session during a given week was missed and the patient received no other treatments for her migraines throughout this time period. By her 24th treatment, the patient had only experienced a single migraine with aura but without debilitating pain. The patient stated she had never had a migraine with such little intensity prior to initiation of hyperbaric treatment and did not have to take any days off from work or school. Follow-up at the end of her 40-day treatment period revealed a highly-satisfied patient who had only experienced the single episode of a mild migraine during the entire course of treatment. Thus, we believe that further research needs to be done to realize the full potential of hyperbaric oxygen therapy in the treatment of neurological conditions as this case highlights the potential for using hyperbaric oxygen therapy as prophylaxis against attacks in patients with treatment resistant migraines with aura.

Key words: hyperbaric chambers; hyperbaric oxygen therapy; vascular headaches; migraines; aura; vasoconstriction; migraine with aura; indications for hyperbaric oxygen

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INTRODUCTION

The use of hyperbaric oxygen therapy (HBO) has been a widely-accepted form of treatment for certain conditions. Hyperbaric oxygen therapy involves the inhalation of 100% oxygen in a hyperbaric chamber at a pressure higher than 1 atm or 760 mmHg. The beneficial effects of HBO results from generating physiologic hyperoxia in tissue by fully saturating hemoglobin molecules and increasing the amount of oxygen dissolved in the plasma. This allows tissue to meet its oxygen demand through the dissolved oxygen alone without the need to utilize the oxygen linked to hemoglobin.¹⁻⁵ As a class II medical device, hyperbaric chambers are currently approved for 13 indications by the U.S. Food and Drug Administration (FDA) and Hyperbaric Medical Society.^{6,7} Indications currently include adjuvant therapy in wound ischemia, thermal burn treatment, blood loss anemia, air embolisms, carbon monoxide poisoning, clostridial myonecrosis, crush injury, decompression sickness, chronic refractory osteomyelitis, necrotizing soft-tissue infections, radiation tissue injury, ischemic skin grafts and flaps, and intracranial abscess (**Table 1**), but does not include neurologic conditions.^{5,8-10} The 2016 European Consensus Conference on Hyperbaric Medicine resulted in a list of 9 indications for HBO to be used as a primary therapy, with an additional 13 indications where there is acceptable evidence that HBO may be used as treatment, as well as 6 indi-

cations where HBO may be considered as an optional modality. Amongst the 13 FDA-approved indications and the 28 indications that resulted from the 2016 European Consensus Conference on Hyperbaric Medicine, neither group includes treatment for neurological conditions such as migraines with aura.^{5,8,9,11} Current treatments for migraines and other headaches are based around relieving the symptoms through the reduction of cerebral blood flow.¹² HBO substantially increases the amount of arterial oxygen and therefore effectively achieves cerebral vasoconstriction, thus treating the migraine.^{1,13} Based on this case report, we believe the current approved indications for HBO need to be expanded to include resistant migraines after further randomized control trials demonstrate efficacy in a larger patient population (**Table 1**).

CASE HISTORY

We present a 23-year-old female with a self-reported history of migraines with aura since the age of 12 with no other relevant medical history. She described her migraines as severe in nature lasting 4–6 hours, 3 times monthly on average. Her extreme pain and sensitivity to light and sound often impaired daily function, causing a loss of vision and inability to focus on tasks at hand. The patient also reported frequent abdominal pain leading to emesis during her migraine attacks. Overall, the migraines hindered her functional status as she had missed



Table 1: Current U.S. Food and Drug Administration approved indications and recommended update to the current indications for hyperbaric oxygen therapy^{6,7}

No.	Indications
Current U.S. Food and Drug Administration approved indications	
1	Gas embolism
2	Carbon monoxide poisoning
3	Gas gangrene
4	Crush injury/compartment syndrome
5	Decompression sickness
6	Healing of complicated wounds
7	Blood loss anemia
8	Intracranial abscess
9	Necrotizing fasciitis
10	Refractory osteomyelitis
11	Delayed radiation soft tissue injury
12	Compromised skin grafts
13	Thermal burns
Recommended update to the current indications	
14	Migraines
15	Stroke
16	Other neurological conditions

many days of school and work due to her condition. She had been managed by her primary care physician since the onset of her migraines at an early age; however, she experienced migraines refractory to Imitrix and adjustments to birth control. The patient would typically get mild relief using Excedrin, caffeine consumption, removal of light, and use of ice packs. Evaluation of this patient prior to initiation of treatment revealed no contraindications to HBO. The patient underwent treatment at 1.5 absolute atmospheres in a hyperbaric chamber Monday through Friday for 1 hour each day, for a total of 40 sessions, but reported missing a few sessions over the 8-week period. No more than one session during a given week was missed and the patient received no other treatments for her migraines throughout this time period. By her 24th treatment, the patient had only experienced a single migraine with aura but without debilitating pain. The patient stated she has never had a migraine with such little intensity prior to initiation of hyperbaric treatment and did not have to take any days off from work or school during treatment. Follow-up at the end of her 40-day treatment period revealed a highly-satisfied patient who had only experienced the single episode of a mild migraine during the entire course of treatment. It is important to indicate that the patient did not receive any additional therapy during HBO treatments.

DISCUSSION

The most recent guidelines for management of acute migraine attacks involve use of triptans, non-steroidal anti-inflammatory drugs and antiemetics. Prophylactic treatment often includes the use of beta blockers, tricyclic antidepressants, and anti-

convulsants. Response to such therapies is highly variable and is often effective only in a select group of patients. They are often prescribed based upon the patient's tolerability of the medication and comorbid conditions. Migraine attacks with aura are often less responsive to triptans and carry an even more differentiated response when compared to a migraine without aura.^{12,14} Thus, a great need for alternative treatments for migraines exists, especially for patients whose migraines are refractory to current pharmacologic therapies.

As illustrated by this report, HBO may provide a novel approach in reducing the disability of the migraineur by providing relief, and by reducing the frequency of attacks refractory to pharmacologic therapy. While the exact inflammatory mediators responsible for migraine headaches are still unknown, it is known that inflammation plays a role in the activation of the trigeminovascular system leading to migraines with the characteristic throbbing pain.^{13,15,16} The peripheral activation of the trigeminovascular nociceptors in the dura mater leads the release of vasoactive dilators including calcitonin gene-related peptide causing long lasting stimulation and vasodilation.¹⁶⁻¹⁸ The beneficial effects of HBO are caused through the physiologic consequences of 100% inspired oxygen and exposure to elevated atmospheric pressures. This leads to higher levels of dissolved oxygen in plasma and subsequent arterial constriction in the brain, thus aborting and preventing the migraine.^{1-4,15,19}

The current understanding of the pathophysiology behind migraines with aura combined with the increasing evidence supporting the anti-inflammatory and anti-vasodilatory effects of HBO, suggests that our patients' relief could be related to HBO decreasing the inflammatory response that leads to the activation of the trigeminovascular pathway.^{10,13,15,20} A study by Myers et al.²¹ demonstrated a significant reduction ($P < 0.05$) in migraine relief in patients undergoing HBO versus those who underwent normobaric oxygen therapy. Wilson et al.¹⁵ showed a significant decrease in subjective pain in those who underwent HBO versus the control group of females with migraine with aura. Other studies by Eftedal et al.^{1,22,23} showed insignificant prophylactic measure against migraines with the use of HBO. It is important to note that these studies have limited sample sizes. A Cochrane review on the usage of HBO to prevent migraines showed no evidence to suggest that HBO could prevent migraine attacks, reduce the incidence of nausea and vomiting, or reduce the requirement for rescue medication based upon 11 trials.²³ On the contrary, we present a patient who had a reduction in frequency, intensity, symptomatology, and need for rescue medications after HBO treatment. To truly judge the efficacy of HBO and take into account the inherent variability in response to different treatments, larger studies are needed. Our case of this 23-year-old female who experienced a reduction in the frequency and intensity of her migraines after HBO provides the evidence for the use of HBO in the management of chronic migraine. Of note, there has been a limited follow up time with the patient so we are unable to determine how long this treatment modality will remain effective in the long term. The purpose of this article is to expand the currently FDA-approved indications for HBO, such as migraine, headaches based on randomized controlled



studies addressing long lasting efficacy in large patient populations. While there has been progress both in the understanding of migraine pathophysiology and the mechanism of action of HBO over the past few years, further research is needed to expand our knowledge and create better treatments for patients with migraines.

Author contributions

DVM wrote the initial draft, and completed the final draft; DVM, BS, BL participated in the literature search; BS and BL participated in the proofread the initial draft. All authors read and approved the final manuscript for publication.

Conflicts of interest

None.

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Prior to publication, the Committee of Oxygen Oasis Hyperbaric Wellness Center, USA approved this study.

Declaration of patient consent

Prior to publication of this article, informed consent was obtained from the patient this study focuses on.

Copyright transfer agreement

The Copyright License Agreement has been signed by all authors before publication.

Data sharing statement

Datasets analyzed during the current study are available from the corresponding author on reasonable request.

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REFERENCES

1. Yildiz S, Uzun G, Kiralp MZ. Hyperbaric oxygen therapy in chronic pain management. *Curr Pain Headache Rep.* 2006;10:95-100.
2. Niinikoski JH. Clinical hyperbaric oxygen therapy, wound perfusion, and transcutaneous oximetry. *World J Surg.* 2004;28:307-311.
3. Tibbles PM, Edelsberg JS. Hyperbaric-oxygen therapy. *N Engl J Med.* 1996;334:1642-1648.
4. Leach RM, Rees PJ, Wilmshurst P. Hyperbaric oxygen therapy. *BMJ.* 1998;317:1140-1143.
5. Gill AL, Bell CN. Hyperbaric oxygen: its uses, mechanisms of action and outcomes. *QJM.* 2004;97:385-395.
6. Fife CE, Eckert KA, Carter MJ. An update on the appropriate role for hyperbaric oxygen: indications and evidence. *Plast Reconstr Surg.* 2016;138:107S-116S.
7. Jain KK. *Textbook of Hyperbaric Medicine.* Cham: Springer International Publishing. 2018.
8. Weaver LK. *Hyperbaric Oxygen Therapy Indications.* 13th ed. Durham, USA: Undersea and Hyperbaric Medical Society. 2014.
9. Bennett MH, Mitchell SJ. Emerging indications for hyperbaric oxygen. *Curr Opin Anaesthesiol.* 2019;32:792-798.
10. Al-Waili NS, Butler GJ, Beale J, et al. Hyperbaric oxygen in the treatment of patients with cerebral stroke, brain trauma, and neurologic disease. *Adv Ther.* 2005;22:659-678.
11. Mathieu D, Marroni A, Kot J. Tenth European Consensus Conference on Hyperbaric Medicine: recommendations for accepted and non-accepted clinical indications and practice of hyperbaric oxygen treatment. *Diving Hyperb Med.* 2017;47:24-32.
12. Goadsby PJ, Lipton RB, Ferrari MD. Migraine-current understanding and treatment. *N Engl J Med.* 2002;346:257-270.
13. Moskowitz MA. Neurogenic inflammation in the pathophysiology and treatment of migraine. *Neurology.* 1993;43:S16-20.
14. Charles A. The pathophysiology of migraine: implications for clinical management. *Lancet Neurol.* 2018;17:174-182.
15. Wilson JR, Foresman BH, Gamber RG, Wright T. Hyperbaric oxygen in the treatment of migraine with aura. *Headache.* 1998;38:112-115.
16. Celik O, Bay HH, Arslanhan A, et al. Effect of hyperbaric oxygen therapy on cerebral vasospasm: a vascular morphometric study in an experimental subarachnoid hemorrhage model. *Int J Neurosci.* 2014;124:593-600.
17. Dodick DW. A phase-by-phase review of migraine pathophysiology. *Headache.* 2018;58 Suppl 1:4-16.
18. Ferrari MD, Klever RR, Terwindt GM, Ayata C, van den Maagdenberg AM. Migraine pathophysiology: lessons from mouse models and human genetics. *Lancet Neurol.* 2015;14:65-80.
19. Bosco G, Vezzani G, Mrakic Sposta S, et al. Hyperbaric oxygen therapy ameliorates osteonecrosis in patients by modulating inflammation and oxidative stress. *J Enzyme Inhib Med Chem.* 2018;33:1501-1505.
20. Matchett GA, Martin RD, Zhang JH. Hyperbaric oxygen therapy and cerebral ischemia: neuroprotective mechanisms. *Neurol Res.* 2009;31:114-121.
21. Myers DE, Myers RA. A preliminary report on hyperbaric oxygen in the relief of migraine headache. *Headache.* 1995;35:197-199.
22. Eftedal OS, Lydersen S, Helde G, White L, Brubakk AO, Stovner LJ. A randomized, double blind study of the prophylactic effect of hyperbaric oxygen therapy on migraine. *Cephalgia.* 2004;24:639-644.
23. Bennett MH, French C, Schnabel A, Wasiak J, Kranke P, Weibel S. Normobaric and hyperbaric oxygen therapy for the treatment and prevention of migraine and cluster headache. *Cochrane Database Syst Rev.* 2015;CD005219.

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