

# Hyperbaric Oxygen Therapy in Children with Epilepsy: A Review of the Evidence

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**Abstract:** We aim in this study to review the current evidence pertaining to the efficacy of the hyperbaric oxygen (HBO) therapy in the treatment of children with epilepsy and to report adverse events.

**Methodology:** We conducted a descriptive systematic review using the preferred reporting items for systematic reviews and meta-analysis (PRISMA) guidelines for all clinical trials concerning the use of HBO for the treatment of epilepsy attacks in children aged from birth-21 years. Primary outcome assesses the effects of HBO therapy for the treatment of epilepsy. Secondary outcome measures evaluated any reported adverse events of HBO therapy.

**Results:** Thirty-one abstracts were identified out of which 22 were excluded and one was a duplicate. Eight full text articles were included in this study with three retrospective analyses, three case reports, one non-blinded randomized clinical trial, and one was a prospective observational study.

**Conclusion:** No study has evaluated the effect of HBO therapy on epilepsy in children. With the rare complication of oxygen toxicity seizures, HBO therapy may complicate epilepsy. However, new evidence showing that seizures not secondary to oxygen toxicity could be safely relieved by HBO therapy. Further randomized clinical trials assessing the effect of HBO therapy in children and adolescents with epilepsy is recommended.

**Keywords:** HBO Therapy (Hyperbaric Oxygen), Evidence Pertaining.

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## 1. INTRODUCTION

Hyperbaric oxygen (HBO) therapy is a treatment modality in which patients receive 100% O<sub>2</sub> at a high atmospheric pressure Treatment duration is usually 90-120 minutes long depending on the indication, and can be repeated two to three times daily(1). According to the Undersea Hyperbaric Medicine Society, the minimum pressure of 100% oxygen for HBO therapy should be 1.4 atm. (2) Hyperbaric oxygen therapy has many physical, biomedical, and physiological effects.

With the increase in oxygen pressure, the volume of gas bubbles in blood vessels and the half-life of carboxyhemoglobin are reduced. (3) This avoids air embolism and decompression sickness. Vasoconstriction is another rationale behind the use of HBO. It reduces edema and heals damaged tissues. HBO also activates fibroblasts, stimulates angiogenesis, and regulates the activity of osteoclasts. (4) HBO is also bactericidal on specific species of *Pseudomonas aeruginosa* and *Escherichia coli* and improves neutrophil-mediated defense against bacterial infections. (5)

Epilepsy is a neurological condition characterized by recurrent unprovoked seizures. This condition affects an estimated 2.2 million people in the United States and 65 million worldwide. (6) In Saudi Arabia, the prevalence of epilepsy is 6.5 per 1,000. (7) While epilepsy tends to be more prevalent among males, pediatric studies have found inconsistent results by gender. Some researchers identified a higher prevalence among young girls (0–9 years) and older boys (10–19 years), whereas other researchers found higher prevalence in younger boys and older girls. (8)

The present study is a systematic review of the current literature regarding the efficacy of HBO therapy for treating children with epilepsy. There are two objectives: 1) assessment of the effects of HBO therapy for the treatment of epilepsy, and 2) reporting adverse effects of HBO therapy in these children and adolescents.

## 2. METHODS

This descriptive systematic review was conducted using the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines for searching the literature and reporting the results. (9) The author reviewed the titles and abstracts of the retrieved articles in order to assess if they met the established inclusion criteria.

### Types of studies:

The current study aimed to review all non-randomized and randomized clinical trials concerning the use of HBO for the treatment of epilepsy attacks. PubMed, Google Scholar, and the Database of Randomised Controlled Trials in Hyperbaric Medicine (HBOEvidence; <http://hboevidence.unsw.wikispaces.net>), were electronically searched. In addition, medical subject heading terms and text words for 'hyperbaric oxygen therapy' AND 'epilepsy' OR 'seizure'. These databases were searched from their starting date to January 2017.

### Types of Participants:

Pediatric participants (from birth to 21 years of age) from both genders with epilepsy were included in the present study.

### Types of Outcome Measures:

The primary outcome measures assessed the outcomes with a valid and reliable instrument of the effects of HBO therapy for the treatment of epilepsy in children and adolescents. Besides, the secondary outcome measures evaluated any reported adverse events of HBO therapy.

### Data extraction and validity scoring:

Both the titles and the abstracts were evaluated for inclusion based on the participants, the design of the study, intervention, and outcomes assessment. The articles which did not meet the inclusion criteria were excluded from the study. A summary of the flow of information is displayed in Figure 1. Also, the information about the specific diagnosis, HBO therapy and its duration and protocols, seizure symptoms as outcome, and secondary outcomes (adverse effects) were collected.

## 3. RESULTS

### Trial flow:

In this study, a total of 31 abstracts were identified. One article was duplicated, and 22 were deemed irrelevant (Figure 1). Eight full text articles were retrieved for additional information. All retrieved papers were published in English.

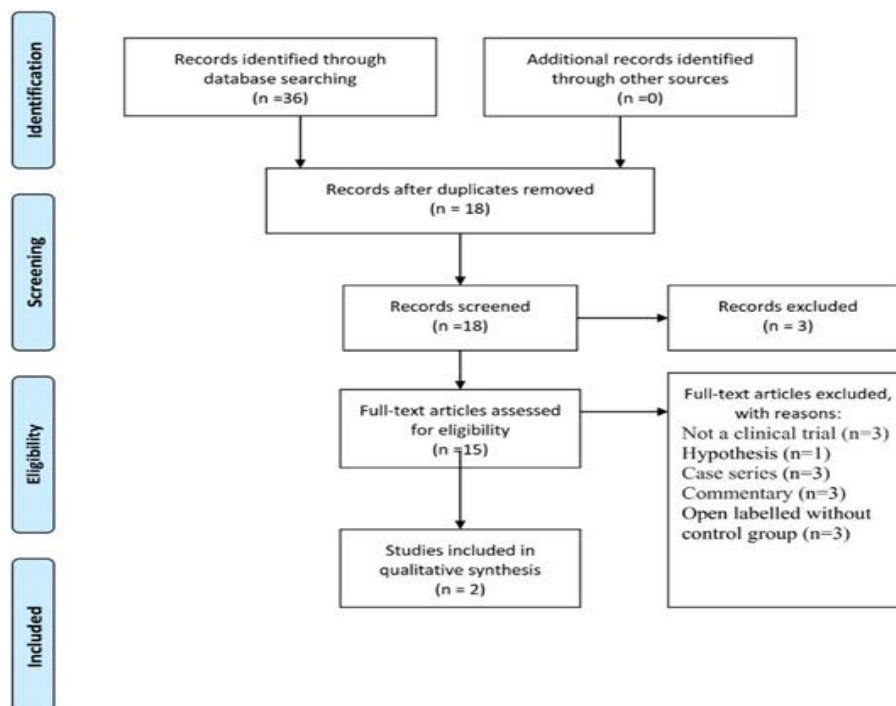


Figure 1. Flowchart indicating the exclusion process

Of the studies reviewed, three were retrospective analyses, three were case reports, one was a non-blinded randomized clinical trial, and one was a prospective observational study (Table 1).

Table 1. Summary of included studies

| Ref | Methods  | N   | Objective  | Outcome and adverse effects   | Conclusion  |
|-----|--|---|--|---|---|
| 10  | Retrospective analysis   | 2,334 patients                                    | Determine the incidence of seizures, evaluate whether chronic neurological disorders increase risk   | Incidence of seizures: 0.011%   | Seizures induced by oxygen toxicity during HBO <sub>2</sub> therapy are extremely rare  |
| 11  | Retrospective analysis   | 931 patients                                      | To determine overall incidence of seizure and identify risk factors  | overall incidence of seizure: five per 10,000   | statistically significant increased risk of seizure with increasing treatment pressure  |
| 12  | Retrospective analysis   | seven cases of seizures in five patients          | explore whether the patients who experienced seizures in the hyperbaric chamber had other medical comorbidities or were on medications which lowered their seizure threshold | All patients had a risk factor for seizure, including: COPD, narcotic withdrawal, alcohol dependence, and drug use                                | patients who experience oxygen toxicity seizures may have other factors which contribute to the development of these seizures |
| 13  | Observational study  | 71 children; 47 aged 2-4 years, 24 aged 4-6 years | Safety and efficacy of HBO in treating SRBD in patients with CP  | sleep improvement after 10 sessions; two children developed a seizure during decompression  | HBO therapy is beneficial to improve sleep and is safe for children with CP   |
| 14  | Non-blinded randomised controlled trial without intention-to-treat | 195 patients                                      | does addition of hyperbaric oxygen therapy to cerebrolysin improve symptom resolution  | HBO therapy was superior to medication treatment alone in the recovery of clinical symptoms, control of epilepsy, and resolution of hydrocephalus | Significant resolution of post injury syndrome with hyperbaric oxygen   |
| 15  | Case report  | 20-year old male                                  | Case report of epilepsy during diving test   | neurotoxic effects of oxygen while the patient was in a hyperbaric chamber, not epileptic seizures  | Reexposure to hyperbaric conditions leads to recovery   |
| 16  | Case report  | 1-year old boy                                    | Case report of CO poisoning presenting with seizure  | CO toxicity completely resolved with HBO  | patient presenting with an afebrile seizure, carbon monoxide poisoning should always be considered as one of the etiologies   |
| 17  | Case report  | 13-year old boy                                   | Treatment of cerebral gas embolism   | Accidental helium inhalation from pressurized tank treated with HBO   | hyperbaric oxygen therapy successfully alleviated symptoms  |

In a retrospective review that included 62,614 HBO sessions in 2,334 patients, (10) it was found that Seizures induced by oxygen toxicity during HBO<sub>2</sub> therapy are extremely rare. Moreover, in relation to oxygen-induced seizures, HBO therapy can be considered safe for patients suffering with chronic neurological disorders. However, the authors warned that HBO therapy may not be safe in patients with uncontrolled epilepsy.

In another study that compared seizure incidence according to treatment pressure in patients receiving HBO therapy, 931 patients underwent 23,328 treatments. The overall incidence of seizure was one in 2,121 sessions (0.05%). There were no seizure episodes reported when HBO was set at 2.0 atmospheres absolute (atm abs), 15 per 10,000 at 2.4-2.5 atm abs, and 51 per 10,000 at 2.8 atm abs. This difference in incidence in different pressures was statistically significant. The authors concluded that oxygen toxicity seizures are highly proportional to the increased HBO pressure. (11)

Seidel, et al. conducted a retrospective review at multiple HBO therapy centers to identify risk factors associated with oxygen toxicity. The group found seven cases of seizures in five patients, and upon reviewing the medical history, it was found that each patient had at least one identifiable risk factor. This included hypercapnia secondary to chronic obstructive pulmonary disease, narcotic withdrawal, alcohol dependence, and antidepressant, tramadol or cephalosporin/ceftriaxone use. The study authors believe that oxygen toxicity after HBO is highly unlikely to present unprovoked. (12)

An observational study by Long and colleagues aimed to find out whether HBO therapy is safe and effective in improving sleep-related breathing disorders (SRBD) in children with cerebral palsy (CP). While the study did not demonstrate significant improvement in SRBD parameters, the incidence of seizure disorder in this group was extremely low. Two episodes were observed in 419 sessions (0.5%). (13).

A clinical trial from China randomized 320 patients to two to four courses of HBO therapy and/or medications. Assessment was made with (99m)Tc-ethyl cysteinate dimer [(99m)Tc-ECD] single photon emission computed tomography (SPECT) before and after treatment. The study concluded that HBO therapy has precise curative effects on patients with postbrain injury neural status and was superior to the stand-alone medication treatment in the relief of clinical symptoms, resolution of hydrocephalus and control of epilepsy. (14)

As for the case reports available in the literature, (15) a one-year old boy developed seizures secondary to carbon monoxide toxicity. This boy was successfully managed with HBO therapy, and no oxygen toxicity seizure was observed. (16) Another report of a 13-year old boy found that seizures secondary to cerebral gas embolism were successfully treated with HBO therapy. (17)

#### 4. DISCUSSION

This systematic review of published articles on the efficacy of HBO therapy for children with epilepsy did not find any articles supportive of HBO therapy as a treatment modality for childhood seizure disorder. The studies reviewed suggest that oxygen toxicity seizures are a recognized complication of HBO therapy. For this reason, the medical community avoided this treatment modality for fear of aggravating an already present seizure disorder. Nevertheless, oxygen toxicity seizure has a unique pathophysiology, and its risk can be reduced through lowering treatment pressure. (11)

This review found that the incidence of seizures secondary to HBO therapy is extremely low at 0.01%. Additionally, HBO therapy was successful at alleviating seizures secondary to some of the more common indications for HBO therapy. In the case report by Mori and Nagai, the one-year old boy who presented with seizures secondary to carbon monoxide toxicity was safely treated with HBO. (16)

Long, et al. observed the effect of HBO therapy on SRDB in young children with CP. No significant improvement in SRDB symptoms was observed in the study group. Interestingly, however, is the observation that CP, which is commonly associated with seizure disorder, did not appear to be a significant risk factor for seizures. Only 2 of 419 HBO sessions (0.5%) were complicated by seizures. Additionally, oxygen toxicity seizures did not recur in the two children after being reinstated in the program. (13) Interestingly, a randomized clinical trial by Shi et al. found that postbrain injury, addition of HBO therapy to medications was superior to medication treatment alone in the recovery of clinical symptoms, control of epilepsy, and resolution of hydrocephalus. (14)

In a large, multicenter chart review at hyperbaric oxygen centers in the Milwaukee, Wisconsin, USA, it was found that all patients who developed oxygen toxicity seizures were had identifiable risk factors for oxygen toxicity. Namely, these patients had: hypercapnia secondary to chronic obstructive pulmonary disease, narcotic withdrawal, alcohol dependence, and antidepressant, tramadol or cephalosporin/ceftriaxone use. It is hypothesized that the risk of oxygen toxicity seizures may be nullified by excluding identifiable risk factors for oxygen toxicity, including hypercapnia, alcohol dependence and antibiotic use. (12)

## 5. CONCLUSIONS

No previous studies evaluated the effect of HBO therapy on pediatric epilepsy. Oxygen toxicity seizure is a rare but recognized complication of this treatment modality. Accordingly, it is thought that HBO therapy may only complicate epilepsy. However, emerging evidence shows that seizures that are not secondary to oxygen toxicity can be safely alleviated using HBO therapy. This review supports executing a randomized clinical trial that assesses the effect of HBO therapy in children and adolescents with epilepsy.

## REFERENCES

- [1] Thom SR. Hyperbaric oxygen – its mechanisms and efficacy. *Plast Reconstr Surg.* 2011;127(Suppl 1):131S-41S.
- [2] Shah J. Hyperbaric Oxygen Therapy. *J Am Col Certif Wound Spec.* 2010. p. 9-13.
- [3] Blumenthal I. Carbon monoxide poisoning. *J R Soc Med.* 942001. p. 270-2.
- [4] Bhutani S, Vishwanath G. Hyperbaric oxygen and wound healing. *Indian J Plast Surg.* 452012. p. 316-24.
- [5] Bumah VV, Whelan HT, Masson-Meyers DS, Quirk B, Buchmann E, Enwemeka CS. The bactericidal effect of 470-nm light and hyperbaric oxygen on methicillin-resistant *Staphylococcus aureus* (MRSA). *Lasers Med Sci.* 2015;30(3):1153-9.
- [6] Sauro KM, Wiebe S, Dunkley C, Janszky J, Kumlien E, Moshe S, et al. The current state of epilepsy guidelines: A systematic review. *Epilepsia.* 2016;57(1):13-23.
- [7] Benamer HT, Grosset DG. A systematic review of the epidemiology of epilepsy in Arab countries. *Epilepsia.* 2009;50(10):2301-4.
- [8] Camfield P, Camfield C. Incidence, prevalence and aetiology of seizures and epilepsy in children. *Epileptic Disord.* 2015;17(2):117-23.
- [9] Stewart LA, Clarke M, Rovers M, Riley RD, Simmonds M, Stewart G, et al. Preferred Reporting Items for Systematic Review and Meta-Analyses of individual participant data: the PRISMA-IPD Statement. *Jama.* 2015;313(16):1657-65.
- [10] Hadanny A, Meir O, Bechor Y, Fishlev G, Bergan J, Efrati S. Seizures during hyperbaric oxygen therapy: retrospective analysis of 62,614 treatment sessions. *Undersea Hyperb Med.* 2016;43(1):21-8.
- [11] Heyboer M, 3rd, Jennings S, Grant WD, Ojevwe C, Byrne J, Wojcik SM. Seizure incidence by treatment pressure in patients undergoing hyperbaric oxygen therapy. *Undersea Hyperb Med.* 2014;41(5):379-85.
- [12] Seidel R, Carroll C, Thompson D, Diem RG, Yeboah K, Hayes AJ, et al. Risk factors for oxygen toxicity seizures in hyperbaric oxygen therapy: case reports from multiple institutions. *Undersea Hyperb Med.* 2013;40(6):515-9.
- [13] Long Y, Tan J, Nie Y, Lu Y, Mei X, Tu C. Hyperbaric oxygen therapy is safe and effective for the treatment of sleep disorders in children with cerebral palsy. *Neurol Res.* 2017:1-9.
- [14] Shi XY, Tang ZQ, Xiong B, Bao JX, Sun D, Zhang YQ, et al. Cerebral perfusion SPECT imaging for assessment of the effect of hyperbaric oxygen therapy on patients with postbrain injury neural status. *Chin J Traumatol.* 2003;6(6):346-9.
- [15] Rabrenovic M, Tresnjic S, Rabrenovic V, Cikiriz N, Masic S, Matunovic R. Neurotoxic effects of oxygen in hyperbaric environment: A case report. *Vojnosanit Pregl.* 2015;72(9):827-30.
- [16] Mori T, Nagai K. Carbon-monoxide poisoning presenting as an afebrile seizure. *Pediatr Neurol.* 2000;22(4):330-1.
- [17] Pao BS, Hayden SR. Cerebral gas embolism resulting from inhalation of pressurized helium. *Ann Emerg Med.* 1996;28(3):363-6.