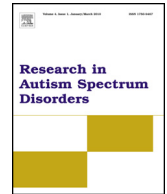




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Research in Autism Spectrum Disorders

journal homepage: <http://ees.elsevier.com/RASD/default.asp>



Hyperbaric oxygen therapy for the treatment of children and youth with Autism Spectrum Disorders: An evidence-based systematic review



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ARTICLE INFO

Article history:

Received 20 January 2016
 Received in revised form 16 April 2016
 Accepted 16 May 2016
 Number of reviews completed is 2
 Available online 1 June 2016

Keywords:

Autism
 Hyperbaric oxygen therapy
 Treatment
 Review

ABSTRACT

Background: Autism Spectrum Disorder (ASD) is a common disorder that has a complex and heterogeneous etiology. Some evidence suggests that inflammation and oxidative stress may have a pathophysiological link. Hyperbaric Oxygen Therapy (HBOT) has been proposed as a possible therapy. Because HBOT is an expensive treatment with significant commercial opportunity, it is essential for it to have a research evidence base prior to widespread use. **Objective:** To conduct a systematic review of the literature evaluating the clinical impact of HBOT on behavior and development in ASD with a view to inform practice. **Methods:** A literature search of electronic scientific databases focusing on clinical outcomes of HBOT in ASD was performed. Articles meeting inclusion criteria were independently assessed by reviewers and were classified according to the American Academy of Neurology Guidelines. Recommendations were made based on the evidence. **Results:** Five articles were reviewed with data extraction. Based on the AAN Classification of Recommendations the data supported a rating of "A", indicating that HBOT is not effective for treating children and youth with ASD. **Conclusions:** Current evidence does not support HBOT as an effective treatment for children and youth with ASD.

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1. Introduction

Autism Spectrum Disorder (ASD) is a neurodevelopmental condition with persistent impairment in social communication and interaction with restricted and repetitive patterns of behavior and interests. This condition can substantially limit an individual's participation in everyday activities and functioning in the community.

ASD affects a large number of children with most recent estimates suggesting prevalence as high as 1/68 (Centers for Disease Control and Prevention [CDC], 2012). The underlying pathophysiological mechanisms for autism are still not clear, and researchers are striving to fully understand the range of possible etiologies for ASD (Pardo and Eberhart, 2007). A large body of literature has emerged identifying genetic correlates of ASD (Neale et al., 2012). Other proposed theories have looked at increased inflammation or oxidative stress as a cause of ASD (James et al., 2004; Sajdel-Sulkowska, Lipinski, Windom, Audhya, & McGinnis, 2008). There is some theoretical support for these concepts and many researchers are working to elucidate the connection. At the present time there is not yet conclusive evidence supporting a causal link between inflammation/oxidative stress and ASD.

Hyperbaric Oxygen Therapy (HBOT) is a treatment that involves having the recipient inhale up to 100% oxygen at a pressure greater than one atmosphere. It is administered in an enclosed pressurized chamber. HBOT is used to treat decompression sickness, as well as inflammatory conditions such as chronic diabetic ulcers (Kranke, 2004). In these conditions, the pressurization of oxygen allows high concentrations of oxygen to be delivered deeper into tissues than would normally occur.

Studies in both humans and animals have reported a decrease in production of pro-inflammatory cytokines as a result of HBOT (Rossignol et al., 2012). In a study of children with ASD, C-reactive protein (a general marker of inflammation) was found to drop significantly following HBOT. Several case reports of children with ASD have demonstrated improvements in cerebral perfusion following HBOT as measured by SPECT scans. Antioxidant enzymes such as catalase and glutathione peroxidase have been found to increase following HBOT treatment of a group of children with ASD (Rossignol et al., 2012).

Because of the theoretical possibility that inflammation or increased oxidative stress may have an etiologic role in ASD, and because some studies have suggested that there can be a decrease in inflammatory and oxidative stress markers and increase in cerebral perfusion in children with ASD treated with HBOT (Rossignol et al., 2012), researchers familiar with HBOT have wondered if treating ASD with HBOT might result in improvements in clinical presentation. Similar postulations have been made regarding chronic disabling conditions such as cerebral palsy (Mitchell & Bennett, 2014) and multiple sclerosis (Bennett & Heard, 2004). Well executed, randomized controlled trials have shown no benefit of HBOT in cerebral palsy (Mitchell & Bennett) and multiple sclerosis (Bennett & Heard).

A recent systematic review of randomized controlled trials of HBOT use in Autism concluded that there was no evidence supporting the clinical efficacy of its use (Ghanizadeh, 2012). It was noted that there were limitations to the review as there were only 2 randomized trials, each of which had some limitations. Subsequent to the publication of the 2012 systematic review, a third controlled trial was published which attempted to address some of the identified limitations (Sampanthavivat, Singkhwa, Chaikyakul, Karoonyawanich, & Ajpru, 2012).

The present report includes a review of the two trials looked at in the Ghanizadeh (2012) systematic review, along with the more recent trial from Sampanthavivat et al. (2012). The latter trial addressed a number of methodological concerns, but also was especially relevant as it used the same measures as were used in the first randomized HBOT trial, thus allowing for the possibility of replication of positive findings. Using widely accepted classification of evidence and recommendation systems relies on having a certain number of studies to achieve conclusions. The addition of the Sampanthavivat et al. trial provided sufficient evidence to avoid an indeterminate conclusion.

ASD is a highly heterogeneous condition and it is possible that physiological differences related to inflammation/oxidative stress may play a role for a subset of individuals with it. It is important to explore possible treatments that address these physiological differences. Because HBOT is an expensive treatment with significant commercial opportunity, it is essential that a well-established research base be available to guide treatment decisions.

This article reviews and evaluates up-to-date published evidence of the efficacy of HBOT in the treatment of children and adolescents with ASD.

2. Methods

Comprehensive computer-assisted literature searches of MEDLINE, CINAHL, Embase and PsycINFO were conducted for all relevant articles published until April 2013 using the following subject terms and text words: Autism, Asperger Syndrome,

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