Hyperbaric oxygen therapy in autism: Is there evidence?

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To the Editor:

We read with great interest the article by Rossignol and colleagues published in BMC Pediatrics (1), which investigated the effect of hyperbaric oxygen (HBO²) therapy on oxidative stress, inflammation, and symptoms in children with autism. The use of HBO² therapy in children with autism is the subject of debate in medical community. Autism is not approved as an indication for HBO² therapy neither by Undersea and Hyperbaric Medical Society nor European Committee for Hyperbaric Medicine (2,3). However, there are a number of centers which applies HBO² therapy for children with autism. These HBO² centers proclaim the efficacy of the treatment but they accept that there are not sufficient controlled trials to support the beneficial effects of HBO² therapy in autism. We appreciate the effort of Rossignol et al. to conduct a clinical study on such a controversial issue. This study, though a small one, is important as being the single study published in a peer-reviewed journal. However, we feel that the terms hyperbaric treatment and HBO² therapy is confused throughout the article which affected both the interpretation of the results and conclusions drawn.

Autism is a pervasive developmental disorder of the brain which always begins in childhood. Children with autism usually develop impairment in at least three of the following areas: social relationship, language, behavior, and sometimes intelligence. The pathophysiology of the autism is not fully understood. A number of factors have been proposed as a possible cause of autism, including genetic, infectious, endocrine and toxic etiologies.

Several treatment modalities including HBO² therapy have been suggested in the treatment of autism. However, an effective treatment modality has not been found yet. Rossignol and colleagues published two hypothetical articles which explains the possible beneficial effects of HBO² therapy in autism (4,5). Some studies showed cerebral hypoperfusion, neuroinflammation and gastrointestinal inflammation in autistic children. Since HBO² therapy is shown to increase tissue oxygen tension and reduce inflammation in some experimental studies, it is proposed that HBO² therapy may decrease the hypoperfusion, neuroinflammation and gastrointestinal inflammation.
and improve symptoms in autistic children (4,5).

In the recent study, Rossignol et al. included eighteen children with autism (ages 3 to 16 years). The patients received 40 sessions (45 minutes each) of hyperbaric treatment with either 100% oxygen at 1.5 atmosphere (n=12) or 24% oxygen at 1.3 atmosphere (n=6). HBO\textsubscript{2} therapy is the breathing of 100% oxygen at a pressure higher than 1 atmosphere (2). Since the patients in the second arm of the study received only 24%, not 100%, of oxygen at 1.3 atmospheres, the therapy undertaken in this group cannot be accepted as HBO\textsubscript{2} therapy. A therapy at 1.3 atmospheres with 24% oxygen could be assessed as hyperbaric treatment rather than HBO\textsubscript{2} therapy. Therefore, this study investigated the effect of HBO\textsubscript{2} therapy and hyperbaric treatment in children with autism. However, the authors failed to compare the results of two different treatments. The authors justified not comparing these two different treatments because of the low numbers of patients involved in the treatment groups. We believe that the effectiveness of both treatments should be assessed separately.

The effect of the treatments on inflammation was determined by measuring serum C-reactive protein (CRP) levels before and after 40 sessions. Rossignol et al. report that although mean CRP declined by 60% in the HBO\textsubscript{2} group, the difference did not reach a statistically significant level (p=0.084). Similarly, CRP levels did not significantly change in hyperbaric treatment group (p=0.123). They have pooled the data for CRP levels from all patients and found a significant reduction after treatments (p=0.021). Based on this finding, the authors conclude in the abstract that HBO\textsubscript{2} therapy significantly reduces inflammation as measured by CRP levels in children with autism. However, since one group received HBO\textsubscript{2} therapy and the other group did not (as we explained above), the data from all patients cannot be polled. Therefore, we think that the conclusion that HBO\textsubscript{2} therapy significantly reduces inflammation is not correct.

Clinical outcomes of the patients were assessed with Aberrant Behavior Checklist-Community (ABC-C), Social Responsiveness Scale (SRS), and Autism Treatment Evaluation Checklist (ATEC). These tests have a total of 14 subscales. The authors also calculated aggregated scores for each test. Total ATEC and SRS scores, but not ABC-C score, significantly improved after 40 treatments in both groups. In the HBO\textsubscript{2} group, significant improvement was observed in 4 of 14 subscales (ABC-C social withdrawal, SRS social motivation, ATEC speech/language/communication, and ATEC sensory/cognitive awareness). In the hyperbaric treatment group, significant improvement was observed in 6 of 14 subscales (SRS social communication, SRS social motivation, SRS autistic mannerism, ATEC speech/language/communication, ATEC sensory/cognitive awareness, and ATEC health/physical/behavior). From this point of view, one could conclude that HBO\textsubscript{2} therapy is not superior to hyperbaric treatment at 1.3 atmospheres with 24% of oxygen.

Finally, we think that there is not enough evidence to support the use of HBO\textsubscript{2} therapy in the treatment of children with autism. Since breathing 24% oxygen at 1.3 atmospheres is the same as the breathing of 31.2% of oxygen at normal atmospheric pressure (1 atmosphere), future studies should also include a normobaric hyperoxic treatment group.

REFERENCES

To the Editor UHM:

I read the recent case reports by Weisher with interest. These 2 cases are a timely reminder that neurological decompression illness (DCI) responds favorably to hyperbaric oxygen treatment (HBOT) even when treatment is substantially delayed. This has been well established in the literature for over 20 years.2-5

Because neurological DCI so often responds to HBOT, even when treatment has been delayed several days,6-9 the therapeutic value of lidocaine in the two reported cases should be viewed as speculative, notwithstanding promising but limited animal research on the subject10,11 and a few case reports showing a good outcome when adjunctive lidocaine was used12-14

As noted by Weisher, controlled studies of lidocaine’s role in the treatment of neurological DCI are needed. In considering the efficacy of adjunctive lidocaine we should remember the numerous other agents proposed as adjuncts to HBOT (e.g., dextran 40, heparin and other anticoagulants, nonsteroidal anti-inflammatory drugs, corticosteroids, terbutaline and sodium lactate, to name some) which were enthusiastically supported initially but turned out to be of no significant benefit when subjected to appropriately rigorous assessment.

Kenneth W. Kizer, M.D., M.P.H.

REFERENCES


**Response from Dr. Weisher to Dr. Kizer**

10/13/08

To the Editor UHM.

Response to Kenneth W. Kizer, regarding my case report on lidocaine adjunctive therapy (J. UHMS Vol 35, No. 3 May/June 2008)

Dr Kizer’s comments are well taken and appreciated. I agree that these two case reports in no way prove the benefits of lidocaine adjunctive therapy in acute neurological decompression therapy. However, I would disagree that this study data is mere “speculative.” There is a broad spectrum between compelling and speculative. I would classify this as provocative, intriguing and indicative of further examination. These two cases were remarkable not only because of treatment delays 12 and 24 hrs but also because of their substantial recovery from a serious neurological impairment.

Nonetheless, there is another reason for my interest in lidocain therapy. I have been using lidocaine adjunctive therapy at cardiac doses in most of my serious neurological cases including head trauma, intracranial bleed and impending central herniation for the last two years; pediatric as well as adult cases. I realize that this is only anecdotal, but I do believe that lidocaine has been helpful in many successful outcomes and further investigation should be done.

Although I may be a bit more enthusiastic, I agree with Kenneth Kizer that further research is needed.

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