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Is Hyperbaric Oxygen Therapy Effective For Treating Autism?

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Abstract

Autism spectrum disorder (ASD) is characterized as a developmental disability caused by abnormalities in brain function. Studies link ASD with various physiological abnormalities, such as cerebral hypoperfusion, oxidative stress, inflammation, and mitochondrial dysfunction. Studies show that diminished blood flow to the brain demonstrates a connection between several core autistic behaviors, and the hypoperfusion generally worsen with age, growing more prevalent in older children. Although hyperbaric oxygen therapy (“HBOT”) is not yet approved by the United States Food and Drug Administration (“FDA”), several studies performed internationally have proven its efficacy in treating people with autism. Even so, the FDA does approve of its use for other medical conditions such as decompression sickness (the bends) experienced by divers, treatment of air or gas embolism, carbon monoxide poisoning, and thermal burns. Hyperbaric oxygen therapy chambers expose the patient to 100% oxygen (unlike the 21% oxygen found in the air we breathe) by increasing the air pressure in the chamber up to three times higher than normal air pressure of 1 atm. This allows the lungs to take in more than the expected amount of oxygen and thus be distributed throughout the body to the cells that are deprived of oxygen. This paper examines the effectiveness of HBOT in children with ASD, by reviewing the available research.

Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by “persistent deficits in social communication and social interaction across multiple contexts and restricted repetitive patterns of behavior, interests, or activities,” (APA, 2013). ASD includes autistic disorder, pervasive developmental disorder, and Asperger syndrome. Approximately 1 out of 110 people in the United States are currently affected by ASD (Rice, 2006). The cause of ASD is unclear. Although several genetic syndromes, such as Fragile X and Rett syndromes, have been linked with ASD, the majority of ASD cases are not due to a simple single gene or chromosomal disorder; studies have estimated that genetic syndromes only account for 6-15% of ASD cases (Schaefer & Mendelsohn, 2008). Recently, research and clinical studies in ASD have linked physiological abnormalities, such as cerebral hypoperfusion, inflammation, oxidative stress, mitochondrial dysfunction and immune dysregulation (Rossignol & Frye, 2012). With this perspective, ASD may consist of physiological irregularities rather than merely a CNS disorder (Herbert, 2005). Treating ASD is not a simple matter; there are a limited number of treatments. The behavioral aspects of ASD are manageable with the help of behavioral therapies. Applied behavioral analysis (ABA), specifically, has been proven to lead to advances in certain children with ASD. In two years, ABA brought about remarkable improvements in the IQ and behavioral issues of several children with ASD (Lovaas, 1987). After four years, ABA researchers at the Wisconsin Early Autism project found analogous results of improved IQ and behavior (Sallows & Graupner, 2005). Conversely, researchers in Norway found that eclectic therapy (a form of psychotherapy) was successful in the treatment of children with ASD who were observed for only one year. The results proved to supersede the effective outcomes of ABA (Eikeseth, et al., 2002). When it comes to cognitive and behavioral

transformations in children with ASD, behavioral therapies are not an ideal approach, as they are quite time demanding. Additional treatments for ASD that aim to treat physiological irregularities have been conveyed, yet, a majority of these forms of treatments have not been critically assessed. However, many studies were performed to test the effects of HBOT to treat the physiological abnormalities possessed by people with ASD, many of which have shown promising results.

Methods

The research incorporated in this paper was retrieved from original research papers and scholarly articles obtained through Touro College’s library of databases, such as ProQuest and EBSCO. Google scholar, and PubMed were also used to acquire data. The articles chosen were critically assessed, compared, and analyzed to evaluate if hyperbaric oxygen therapy is effective for treating autism

History of Hyperbaric Chambers

Hyperbaric air or “air under pressure” is a medical treatment that dates back over 150 years. In 1662, a British physician created a sealed chamber in which the air was compressed and decompressed using valves and oxygen. This was extraordinary; it preceded the discovery of oxygen and was utilized as a treatment for respiratory diseases (Clarke, 2008). The idea of employing pressurized environments developed further in 1879, when the French surgeon, Fontaine, built a pressurized mobile operating room. He observed that inhaled nitrous oxide had greater efficacy when used under pressure. Patients treated in an increased pressure environment were not as cyanotic as those treated in standard conditions. Additionally, his patients experienced improved oxygenation (Fontaine, 1879). In the early 1900’s, Dr. Orville Cunningham, a professor of anesthesia, found a greater improvement in heart disease victims when they resided

closer to sea level than when they were living at higher altitudes. Later, hyperbaric chambers were utilized by the military, in the 1940's, to treat deep-sea divers who experienced decompression sickness. In the 1950's, physicians first used HBOT during lung and heart surgery, which steered to its use for carbon monoxide poisoning in the 1960's. Since then, over 10,000 clinical trials and case studies have been achieved for several other health-related purposes, with the great majority reporting successful outcomes (Ohnishi, et al. 2000).

Hyperbaric oxygen therapy (HBOT)

Hyperbaric oxygen therapy (HBOT) is the medical use of oxygen in a pressurized environment, and involves breathing 100% oxygen while inside a hyperbaric chamber that exhibits pressures greater than sea level (1 atmosphere). The increased pressure permits oxygen to dissolve and saturate the blood plasma (autonomous of hemoglobin), which yields an extensive array of valuable physiological and cellular outcomes. This noninvasive therapy is the most reliable way to provide ample oxygen to all organs of the body. The standard treatment lasts for 60-90 minutes, during which the patient lies down and breathes regularly (Feldmeier, 2003). The use of hyperbaric oxygen treatment (HBOT) was implemented as a treatment method for numerous clinical disorders. It has been proven in several clinical studies to enhance the body's inherent ability to regenerate and repair. It is used as a therapy to facilitate the healing process in both chronic and acute disorders. Decompression sickness, stroke victims, arterial gas embolism, healing of wounds, severe carbon monoxide poisoning and smoke inhalation are only some of the common uses of HBOT. However, in 2005, researchers began to consider using HBOT to improve behavioral and physiological abnormalities found in individuals with ASD (Leach, et al. 1998). This paper will evaluate the current data on treating ASD with HBOT. First, the effects of HBOT on physiological irregularities in children with ASD will be evaluated. Then, the effects on autistic behaviors will be examined. Finally, the apparent contrary effects of HBOT in ASD and restrictions of studies will be assessed.

Cerebral Hypoperfusion in ASD and the Effects of HBOT

Cerebral hypoperfusion is characterized as insufficient blood flow in the brain and is one of the common physiological abnormalities possessed by individuals with ASD. Positron emission tomography (PET) and single-photon emission computed tomography (SPECT) were used in studies to discern hypoperfusion exhibited in the brains of

people with ASD versus normal healthy brains (Björklund, et al. 2018). Both PET and SPECT scans are types of nuclear imaging tests that utilize radioactive tracers to create three-dimensional images. However, they differ in the radiotracers used. Studies have proven these scans to be a reliable measure of cerebral blood flow in observing what areas of the brain are receiving more blood flow. (Amen, et al. 2011; NIH CC, 2002). Common autistic behaviors such as need for consistency (Ohnishi, et al. 2000), habitual behaviors (Starkstein, et al. 2000), disability in processing emotions and facial expressions (Critchley, et al. 2000), and delayed language development (Wilcox, et al. 2002), are linked to hypoperfusion. Moreover, hypoperfusion is related with increasing age in children with ASD (Wilcox, et al. 2002). It is possible that HBOT could improve cerebral hypoperfusion in ASD. Numerous studies were completed that evaluated the effects of HBOT to treat various neurological disorders, such as chronic brain injury and traumatic brain injury. The results of the SPECT scans were evaluated before and after the delivery of HBOT at low pressures (1.3 to 1.5 atm). These studies showed significant results (Harch, et al. 2012), (Golden, et al. 2002). Histograms correlated to the pre and post SPECT scans were analyzed with a widely used medical images software called Osirix DICOM. Results from both scans showed significant pattern differences beneath the cerebral cortex in the central area of white matter, known as the centrum ovale. The pre-HBOT images displayed a larger array of counts in the histograms than in the post-HBOT. The narrower range of counts in the post-HBOT corresponded to the increase of perfusion to the lacking areas. The effectiveness was studied through many areas in addition to SPECT: physical exam, symptoms, and psychological measurement (Harch, et al. 2012). Moreover, numerous case studies have reported enhancements in cerebral perfusion after HBOT treatment. One study involved a child with ASD who received one hour of HBOT at 1.3 atm and 24% oxygen per day for ten days (Heuser, et al. 2002). The SPECT scans revealed increased perfusion. However, the effects of ten treatments only lasts several months. For longer lasting effects (6-18 months) more treatments are necessary (20-60 treatments). Behavioral improvements were detected in this child including cognitive and memory functions. The child became sympathetic, started to point and articulate, and interact with others. Another child with ASD, who received 40 treatments of HBOT at 1.3 atm and 24% oxygen, also presented behavioral improvements, such as, improvements in speech and communication and fine motor skills (Rossignol, 2008).

Another study involved 108 children with ASD who

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experienced decreased perfusion in their temporal lobes as measured by SPECT scans (Kinaci, et al. 1970). They received HBOT at 1.5 atm with 100% oxygen for an hour a day for 50 days. After their treatments, SPECT scans revealed that 82.40% showed improvements in their temporal lobes, 85.26% in their frontal lobes, and 75.75% in other areas. Furthermore, clinicians did an Autism Treatment Evaluation Checklist (ATEC) on 54 of the individuals and significant improvements were noted: 85.5% in Sociability, 79% in Speech/Language/Communication, 75.2% in Health/Physical/Behavior, and 87% in Sensory/Cognitive Awareness. This study revealed major improvements in the physical, behavioral and cerebral perfusion of children with ASD after HBOT (Kinaci, et al. 1970). This study is reliable due to the large sample size, unbiased SPECT imaging, and therapist assessments.

Oxidative Stress in ASD and the Effects of HBOT

Oxidative stress is defined as an imbalance between the production of reactive oxygen species (free radicals) and antioxidant defenses. Some children with ASD experience oxidative stress. Some researchers believe that HBOT indirectly causes an increase in oxidative stress due to the amplified production of reactive oxygen species (“ROS”) from the elevated oxygen levels (Alleva, et al. 2005). Therefore, they are reluctant to use HBOT on children with ASD, since some of them already have elevated oxidative stress levels (Rossignol, et al. 2007). A contributing factor to their increased oxidative stress levels might be due to the excessive amounts of oxygen supply to their cell's mitochondria, which can escalate the production of ROS. In contrast, HBOT has proven to upregulate antioxidant enzyme production that can aid with detoxification issues found in children with ASD such as glutathione peroxidase, superoxide dismutase (Gulec, et al. 2004), and catalase (Nie, et al. 2006). The antioxidant enzyme level increase can protect against harm initiated by ROS (Rossignol, 2007). Additionally, minor elevations in ROS created by HBOT can be advantageous, as they increase mitochondrial biogenesis (Gutsaeva, et al. 2006).

Two studies have observed the influences of HBOT on oxidative stress in children with autism (Audhya, 2007; Rossignol, et al. 2007). The first study included administering HBOT at 1.3 atm daily to 48 children with autism. Catalase, glutathione peroxidase and superoxide dismutase (SOD) levels were screened before beginning HBOT and again after day 1 and day 32 of HBOT (Audhya, 2007). Results demonstrated a 1.9-fold increase of the original catalase levels after the first day and a 90% improvement after 32 days. Glutathione peroxidase showed a 1.4-fold increase after 1 day and a 1.2-fold increase after

32 days from the initial HBOT. Finally, a 4.5-fold increase of SOD was observed after 1 day and a 4.7-fold increase after 32 days of starting HBOT. The results of HBOT on antioxidant enzymes can be considered conditioning.

The second study involved 18 autistic children from ages 3-16. This open label, prospective study included administering 40 treatments of HBOT, with 24% oxygen, at 1.3 atm, to 12 children, and 100% oxygen at 1.5 atm to 6 children. Blood markers were taken before and after 40 treatments (Rossignol, et al. 2007). Researchers noticed dramatic improvements in speech, socialization, GI function, and strength. The effects persisted months after the study was completed. Furthermore, insignificant changes were seen in plasma-oxidized glutathione levels. This proves that oxidative stress markers did not worsen because oxidized glutathione is transported from within the cells when intracellular levels surpass the redox capacity (Dickinson and Forman, 2002). However, the intracellular oxidative stress levels in the children with ASD did not diminish with the lower HBOT pressures (Rossignol, et al. 2007). The open-label nature of this study and the two diverse treatment groups (one group who received 24% oxygen at 1.3 atm versus the other group who received 100% oxygen at 1.5 atm), as well as the absence of a control group, are some of the limitations of this study. Nonetheless, the prospective nature of this study strengthens it.

Inflammation in ASD and the Effects of HBOT

Some individuals with ASD experience inflammation, such as neuroinflammation, gastrointestinal inflammation and immune dysregulation as supported by recent studies. Numerous studies have conveyed atypical inflammatory indicators in children with ASD. For instance, increases in Tumor Necrosis Factor-alpha (TNF-alpha) (Chez, et al. 2007), and neopterin (cellular immune system activation marker) (Messahel, et al. 1998), were related in studies of children with ASD. Additionally, studies showed that children with ASD, who reported having gastrointestinal inflammation, have analogous symptoms to one suffering from inflammatory bowel disease (IBD) (Ashwood, et al. 2003). Anti-inflammatory results were reported after treatment with HBOT. A decrease in pro-inflammatory cytokines (including TNF-alpha, IL-1 and IL-6) (Weisz, et al. 1997), and an increase in counter-inflammatory IL-10 levels were reported after HBOT (Buras, et al. 2006). Moreover, improvements in IBD were reported in a systematic review that used HBOT (Rossignol 2012). A study reported a decrease in production of interferon-gamma by lymphocytes with HBOT at 2.0 atm/10.5% oxygen, but an increase in interferon-gamma with 100%

oxygen administered at 1.0 atm (Granowitz, et al. 2002). Therefore, it is concluded that the result of HBOT on reducing inflammation is facilitated through the pressure-related component and not particularly on the delivery of oxygen.

Unfortunately, a series of recurring events can cause amplified inflammation which can lead to escalated cerebral hypoperfusion. This may cause hypoxia, which leads to production of HIF-1 α (hypoxia-inducible factor-1 α) which induces inflammation (Nathan, 2003). HIF-1 α is fundamental in the innate immune system, as it triggers inflammation by myeloid cells (Cramer, et al. 2003).

The effects of HBOT on biomarkers of inflammation in children with ASD were inspected in two prospective studies. The first study included 12 children who were given 40 treatments of HBOT at 1.3 atm/24% oxygen and 6 children who were given HBOT at 1.5 atm/100% oxygen. Biomarkers were measured before and after the treatments by testing the participants' blood specimens taken before and after the treatments (Rossignol, et al. 2007). Improvements were seen in C-reactive proteins (non-specific inflammation markers), as their levels decreased in the total study population ($p=0.021$). The most significant decrease was seen in children with the highest levels of C-reactive proteins prior to the study. These children also showed behavioral improvements. SRS (Social Responsiveness Scale), ABC-C (Aberrant Behavior Checklist – Community), and ATEC (Autism Treatment Evaluation Checklist) were filled out by the parents and were used to calculate the scores for each child before and after their treatments.

The second study measured plasma cytokine levels, including some related to inflammation prior to and after HBOT. Ten children with ASD participated in this 20 week study with 80 sessions of HBOT given to them at 1.5 atm/100% oxygen (Bent, et al. 2012). Although the study reported behavioral improvements, negligible modifications were observed in cytokines. Yet, the authors mentioned that none of the children actually had irregular cytokine levels prior to the study, so notable variations could not be seen.

In another study, a child with ASD who suffered from eczema and bowel inflammation, with a distended abdomen, displayed significant improvements after 40 treatments of HBOT at 1.5 atm and 100% oxygen over the course of a month (Rossignol 2008).

Mitochondrial Dysfunction in ASD and the Effects of HBOT

Mitochondrial dysfunction is observed in some people with ASD (Rossignol & Frye, 2011; Frye & Rossignol, 2011).

HBOT is considered a possible treatment for mitochondrial dysfunction, although treatments for this condition are minimal (Rossignol & Frye, 2011). The outcomes of HBOT on mitochondrial dysfunction were measured in various studies.

In a controlled study HBOT at 1.5 atm and 100% oxygen was administered to 69 patients who obtained severe traumatic brain injury (TBI), within 24 hours of injury. Significant increases in brain oxygen concentrations were seen, as well as increases in cerebral blood flow and reduced CSF lactate levels (elevated CSF lactate is an indicator of mitochondrial dysfunction). Results also showed improvements in mitochondrial function and brain metabolism after contrasting both room air treatment of 21% oxygen and 100% oxygen given at normal pressure (1 atm) (Rockswold, et al. 2010).

HBOT can make more electron transport chains in mitochondria. In 2008, a study was conducted on healthy rat tissue (Kurt, et al. 2008). HBOT was done on the rat and the tissues were looked at before and after the treatment. Results showed that the mitochondria were working more efficiently. Mitochondria work more efficiently through physical exercise. During exercise, the cells are stressed and mitochondria are making more electron transport chains. Similarly, with HBOT, the cells are slightly stressed and they make more electron transport chains thereby working more efficiently and experiencing less oxidative stress.

Furthermore, a study was conducted in 2006, which showed it is possible to increase the number of mitochondria in the brain cells of rats. This phenomenon is called mitochondrial biogenesis (Gutsaeva et al. 2006). This was not demonstrated in humans, because it would require risky brain biopsies to be performed on patients. This can be one possible mechanism as to why HBOT is working. Although these results seem promising, no clinical studies were performed to test the effects of HBOT on mitochondrial dysfunction in children with ASD.

Behavioral Measurements in ASD and the Effects of HBOT

Most of the studies performed using HBOT for children with ASD have inquired behavioral rather than physiological factors. In a current systematic review, two double-blind, arbitrary, controlled trials were reviewed regarding the use of HBOT in children with ASD (Ghanizadeh, 2012). The first study examined the outcome of giving 33 children with ASD, 40 treatments of HBOT with 24% oxygen at 1.3 atm, which included 2 treatments each day for 5 days a week, over the course of 4 weeks. This study was performed in comparison to 29 control

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children with ASD who were given room air that was slightly pressurized (1.03 atm/21% oxygen) (Rossignol, et al. 2009). Noteworthy improvements were detected in the treated children on the ATEC scales (questionnaire that measures changes in severity of ASD in response to treatment) by the caregiver, as well as on the CGI scales (Clinical Global Impression rating scales: measures the severity of symptoms, treatment response and the effectiveness of treatments) by the clinicians and parents. The results showed improvements in language, eye contact, cognitive attentiveness and overall functioning. Strengths of this study comprise of the involvement of 6 medical centers (which limited possible biases correlated to a specific site study), assessments by blinded parents and clinicians and the use of a control group.

The second study examined the outcome of giving 18 children with ASD, 80 treatments of HBOT with 24% oxygen at 1.3 atm, within a 15 week duration. These results were compared to 16 children who were treated with a placebo, involving air flowing through a chamber at normal pressure. Subsequently, ABA therapy was given to both groups, yet insignificant changes were observed using various behavioral scales (Granpeesheh, et al. 2010). These undesirable results can be attributed to the fact that rigorous ABA therapy was given during the administration of HBOT which did not seem successful (Ghanizadeh, 2012). On the other hand, this study is reliable because of the blinded evaluators as well as the control group. The contrasting results can be ascribed to the discrepancies among the two controlled trials (Ghanizadeh, 2012). For example, the age and quantity differences of the participants, as well as the magnitude of treatments. One study delivered 10 hours of HBOT per week (Rossignol, et al. 2009). While the other study provided 5 hours per week (Granpeesheh, et al. 2010). There were also probable distinctions in ASD severity.

Antagonistic Properties of HBOT in ASD

Among the many studies performed, minimal unfavorable outcomes were reported of HBOT usage for people with autism. One study stated that "HBOT was safely administered to autistic children and all participants were able to finish 40 HBOT sessions without any major adverse events" (Rossignol, et al. 2007). A different study informed minor antagonistic effects, including 4 kids with earaches, 2 kids with otitis media and other individuals who were autonomously affected with insomnia, seizures, lethargy, amplified vocal sensitivity and hyperactivity (Bent, et al. 2012). In a controlled study, one of the participants experienced frequent urination and a skin rash which the doctor attributed to yeast as the causing factor. Other

participants withdrew from the study, specifically one child who experienced regressing symptoms of asthma after several HBOT treatments. The physicians did not think the two were related, but removed the child as a safeguard. Another child withdrew from the study before completing it due to anxiety. One participant in the control group experienced diarrhea and abdominal swelling, yet still completed the experiment. In addition, another control group participant experienced worsening of pre-existing eczema. Seizures or barotrauma, however, were not detected in neither the treatment nor control groups (Rossignol, et al. 2007). In a study performed on the effects of HBOT in Thai autistic children, it was reported in the data analysis that "there was no serious adverse effect in any case and tinnitus was a mild side effect in one case and it went away in one week" (Chungpaibulpatana, et al. 2008).

According to the FDA, "patients receiving HBOT are at risk of suffering an injury that can be mild (such as sinus pain, ear pressure, painful joints) or serious (such as paralysis, or air embolism). Since hyperbaric chambers are oxygen rich environments, there is also a risk of fire" (FDA commissioner, 2013).

Restrictions of the Studies Performed

Most of the studies performed contain restraints that contribute to the erratic results among them, including the retrospective approaches, the absence of control participants and the minimal amount of participants. Moreover, the open trials increase bias, as both the participants and the researchers are aware which treatment is being given. However, two of the controlled studies did not contain these restraints. Furthermore, other studies utilized observational methods which are not efficient when analyzing modifications in memory and attentiveness (Jepson, et al. 2011). Unfortunately, the long-term effects of HBOT are unknown because once the study was complete researchers did not follow up on the long-lasting effects. Additionally, a majority of the studies focused on behavioral modifications rather than physiological modifications. Earlier studies proved that ABA therapy in individuals with autism is only effective when done over a substantial period of time. For example, ABA therapy studies displayed significant behavioral changes over a one to four year duration (Lovaas, 1987; Sallows & Graupner, 2005).

It is common for the physiological modifications seen in autistic children treated with HBOT to be observed before intellectual and developmental enhancements due to the intricacies of brain maturation. Studies have found significant physiological improvements after a short time

in participants who were treated with HBOT, specifically modifications with cerebral hypoperfusion. While most of the studies noted behavioral enhancements in several children with autism, the studies only persisted for a few months. This short duration of time is not enough to determine the influence HBOT has on development. Further studies are necessary to investigate the long lasting results of HBOT in people with autism.

Many studies noted behavioral and physiological advances when treating autistic children using HBOT. Yet, noteworthy developments were not found when researchers from a common group performed two studies (Granpeesheh, et al. 2010; Jepson, et al. 2011), and insignificant results were noticed in a different minor study (Lerman, et al. 2009). The inconsistent outcomes among the studies may be attributed to the autistic children's opposing responses to HBOT (Jepson, et al. 2011). To illustrate, children who possess certain physiological abnormalities such as mitochondrial dysfunction, cerebral hypoperfusion and inflammation might be more prone to display improvements. Nevertheless, most of the studies performed to test behavioral aspects did not analyze the chemical aspects such as levels of oxidative stress or inflammatory markers. However, one behavioral study did analyze alterations in the levels of cytokine, but insignificant modifications in cytokines were seen because all the participants already had regular cytokine levels prior to their HBOT treatment (Bent, et al. 2011).

Further investigation is required including participants with ASD who possess specific physiological abnormalities and which analyze variations in these physiological issues such as cerebral hypoperfusion and inflammation. Noteworthy improvements were related in studies which administered HBOT sessions more frequently. This also seemed true in studies that used HBOT to treat patients with traumatic brain injuries, (Harch, et al. 2012). More studies, however, are needed to analyze several HBOT factors, such as the ideal oxygen and pressure limits required to treat patients with ASD.

HBOT in Thailand

In 2008, the first study in Thailand was performed to determine the effects of HBOT to treat autistic children and whether it is safe or not (Chungpaibulpatana, et al. 2008). The study included 7 Thai autistic children who received 10 sessions of HBOT once a week at 1.3 atm. Before and after the treatments, five areas were evaluated: "1. Social development 2. Fine motor and Eye-hand coordination 3. Language development 4. Gross motor development 5. Self - help skills" (Chungpaibulpatana, et al. 2008). Results showed advances within these five domains with 75% of

children who displayed progress while 25% showed no reaction to the treatment.

FDA Approval

Although HBOT is currently being used as a treatment method to treat various disorders in Thailand such as autism, it has not been clinically verified or cleared by the FDA to cure or be successful in the treatment of autism, cancer, or diabetes (FDA, 2013). However, the FDA did approve the use of HBOT for several other conditions. These include "treatment of air or gas embolism (dangerous 'bubbles' in the bloodstream that obstruct circulation), carbon monoxide poisoning, decompression sickness ('the bends'), and thermal burns (caused by heat or fire)," (FDA, 2013).

Disadvantages

Dr. Paul Claus, medical director of Mayo Clinic's Hyperbaric and Altitude Medicine Program, relates risk factors of HBOT. The increased oxygen of the chamber supports combustion which poses a risk for fires in the facility. Therefore, necessary precautions are taken. The patients are required to remove their street clothes since polyester is fuel for fire. The patients are provided with cotton blend clothing instead. Additionally, the treatments are quite expensive; they are approximately \$1,500 an hour in most hospital settings (Claus, 2017). However, if more studies are done documenting improvements of HBOT, then hopefully the cost will be covered by the healthcare system or insurance companies to further benefit those with autism. .

Conclusion

"There is no one-answer for many questions but there are many answers for one question. Multiple factors are the possible causes of autism. The curative factors may be from multidisciplinary approaches," (Chungpaibulpatana, et al. 2008). Numerous studies have demonstrated that HBOT is an effective treatment for children with autism. The pressures utilized during treatment with HBOT (1.5 atm/100% oxygen maximum) are proven to improve the common physiological abnormalities in individuals with ASD; such as, cerebral hypoperfusion, oxidative stress, inflammation and mitochondrial dysfunction. Furthermore, studies that targeted the behavioral measurements in ASD also showed positive results even though most of those studies did not use control groups. The two studies that did utilize control groups however related opposing outcomes. However, multiple crucial variations between the trials were noted. Taken together, the studies imply that the use of HBOT in children with autism correlates

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with marginal antagonistic effects and is handled well. In conclusion, HBOT is a harmless and possibly beneficial treatment for kids with autism. However, additional studies are necessary before it can become an internationally accepted treatment method. Future studies should be more specific and directed towards the specific physiological abnormalities within the various ASD subdivisions and should use control groups as well to promote efficiency and determine which people can gain from HBOT treatment. Furthermore, why don't the hospitals in Thailand publish anything regarding their routine HBOT usage? They value intellectual property not academic publications. If it were not more clinically effective than the use of HBOT would not be used regularly and its ineffectiveness would spread like wildfire. Based on the studies performed, overall, the use of hyperbaric oxygen therapy appears to be a promising treatment for children with ASD.

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