

Hyperbaric Oxygen Therapy in Thai Autistic Children

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Background: Autism is a developmental and behavioral pattern, the triad of impairments, 1. social interaction, 2. social communication, 3. imagination. Their memories are seemingly in picture or photo records. Difficulties in the treatment, management, and handling of autistic children are the main problems. Hyperbaric oxygen therapy (HBOT) is a modern treatment in Thailand for nitrogen imbalance (Decompression sickness syndrome or Caisson disease). HBOT can increase plasma oxygen to the tissues including the brain.

Objective: To determine whether Hyperbaric Oxygen Therapy is safe to use in children with autism, and has a statistically significant effect on autistic symptoms. This is the first study in Thailand.

Material and Method: Thai Autistic children (n = 7) received HBOT (1.3 atm., 10 sessions) treatment. Assessment was done before and after treatment in five domains: Social development, Fine motor and Eye - hand coordination, Language development, Gross motor development, Self - help skills.

Results: Improvement was shown in five domains with a significant level. Seventy-five percent of children shown improvement while 25% did not seem to respond to the treatment.

Conclusion: HBOT is a new treatment for Thai autistic children. Many scientific studies recently have shown that HBOT could be an effective treatment for autistic children. It could improve the major autistic symptoms.

Keywords: HBOT (hyperbaric oxygen therapy), Autistic (autism), Oxidative stress (free radicals), Oxygen (O₂)

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Hypotheses: 1. Hyperbaric Oxygen Therapy (HBOT) will be safe to use in children with autism, 2. Hyperbaric Oxygen Therapy will have a statistically significant effect on autistic symptoms.

Directed goals: 1. Is Autism able to be a new indication for HBOT? 2. Is HBOT able to be a new treatment for Autism? 3. Educational purposed aspects: family, social, and professional.

HBOT is a new way in the treatment for decompression sickness syndrome (Caisson disease) and it can be applied to intervene or concomitant treatments with some symptoms such as diabetic wounds, and burn wounds. This HBOT center is the only one stand-alone center of provincial hospitals in Thailand. If HBOT can be an effective method in alternative

therapies, the authors can help numerous autistic children. Generally many studies were done, but only one author's report can be found in PubMed (Rossignol, DA and LW Rossignol, 2006). Practically many HBOT were well-known used in autistic, treatment, but little knowledge was publicized in this field. There is no definite conclusion.

Early identification of autistic spectrum disorders in children and intervention is extremely important. Can autism be treatable and preventable in the early stage of the symptoms? According to many studies, they had shown brain injury could be caused by heavy metal effects, chemical poisoning, infection, autoimmune response, poor blood flow, and lack of oxygen.

There are many alternative therapies that were claimed to have some effects to make better results in autistic symptoms, but no definite one which

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could absolutely cure autism. In the authors' proceeding study, it was found that HBOT was the least interesting method of alternative therapies for autism in parental opinions (Fig. 1). The researchers think that the parents' knowledge about each therapy affected to their choosing. Vachira Phuket Hospital has a Hyperbaric Chamber, which is the new therapy for Autistic children. But the parents don't have the knowledge about it.

Whatever, it is our opportunities to prove how effective of HBOT in the treatment for autism and represent autistic pathological mechanisms in preceding hypotheses.

What is HBOT?

Hyperbaric Oxygen Therapy, "hyper" means more and "baric" means pressure. It uses pressure to allow more oxygen into blood cells, blood plasma, and cerebrospinal fluid. Under pressure, the lungs breathe in more oxygen per breath. Also, more gas is dissolved in fluid under pressure. This is how more oxygen is delivered to body tissues, including the brain.

How does HBOT work?

Oxygen exists in the blood in two forms, combined with hemoglobin (Hb) and dissolved in plasma (0.3 ml/100 ml). More oxygen is transported by Hb. Best oxygen is delivered to the tissue in dissolved form by the liquid portion of blood.

Neuropathology of the autism spectrum disorders

Reduced number of Purkinje cells in the cerebellum, and small tightly placed nuclei of the

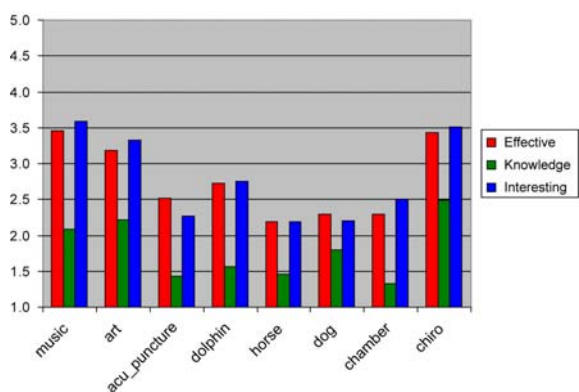


Fig. 1 Autistic parental attitude surveys in effective, knowledge and interesting in various therapies at Vachira Phuket Hospital, July 2007

amygdala (Courchesne, 1991, 1995; Kemper and Bauman, 1993; Ritvo et al, 1986; Bailey et al, 1998; Welsh et al, 2002; Kern, 2003). A significant neuronal loss was observed in the cerebral cortex of the youngest autistic patients. The neuronal and glial density was very different in control and autism in the adolescence. Neurons showing lipofuscin intracytoplasmic deposits increased with age both in controls and autistic patients, but the latter had significantly more such cells at all aged studies. According to their lipofuscin content, a residual sign of an excessive oxidative stress, the surviving neurons show signs of an accelerated process of aging (E. López-Hurtado, J. De Felipe and J. J. Prieto, 2002).

Heavy metals and oxidative stress

There is a particularly negative correlation between glutathione (GSH) levels and oxidative stress associated with toxic metal exposure. GSH is found in almost every cell of the body and is responsible for the removal of toxic metals. A study by Lenzi et al (1994) found that glutathione not only reduced lipid peroxidation and oxidative stress (Roy et al, 2000), but also reversed some of the damage of the cell membranes (Lenzi et al, 1994). Another more recent study had shown that glutathione exerted neuroprotective properties and reduced neuropathy (Cascinu et al, 1995).

Neurochemistry

The environment chemicals exert toxic effects not only to dopaminergic neurons but also to multiple kinds of neurons, such as noradrenergic and serotonergic (New technology to Identify Environmental Chemicals Causing Mental Disorders Assessment of Psychotropic Chemical with Experimental Animals, Translation of The AIST press released on August 25, 2004).

Similarities between symptoms produced by N-methyl-D-aspartate (NMDA) antagonists in healthy subjects and those seen in autism, it is proposed that infantile autism is a hypoglutamatergic disorder. The possible benefit of treatment may be glutamate agonists, as well as the potential usefulness of a selective 5-HT_{2A} receptor antagonist (Lam et al, 2006).

Cholinergic neurons in the basal forebrain, an area of the brain known to be involved in attention, have been found to be abnormally plentiful, and abnormally large, in children with autism.

Chemicals known to influence the development and function of cholinergic neurons in the basal



Table 1. Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
1. Both sexes	1. Uncontrolled severe explosive behavior
2. All aged-group	2. Uncontrolled organic or physical symptoms such as seizure, ear infection
3. All educated group	3. Severe phobic or fearful symptoms
4. Diagnosis - autistic disorder, autistic spectrums	4. No parent or caretaker
5. Major symptoms - delayed development, speech	

Table 2. Pre- and post-treatment assessment in five domains: social development, fine motor and eye-hand coordination, language development, gross motor development, self-help skills

	Pre treatment	Post treatment
Social score t =	5.17	15.00-9.13
Fine motor score t =	6.83	14.67-9.40
Language score t =	2.83	5.83-11.62
Gross score t =	1.67	9.17-17.52
Self help score t =	13.67	19.67-16.43

forebrain area - brain-derived neurotrophic factor - abnormally high levels of it had been found in the bloodstreams of newborns with autism: Joan Arehart-Treichel (*Psychiatric News*, July 20, 2001).

An important relationship between brain opioid systems and social attachment were found in infant animals (Chamberlain and Herman, 1991). Administrations of low doses of morphine decreased the separation anxiety of infant dogs, guinea pigs, and chickens. When Naloxone, a specific opiate antagonist, was administered, the frequency of distress vocalizations increased. The present study suggests that the lack of socialization behaviors in autism is possibly related to an increased circulation of brain opioids (Herman and Panksepp, 1984).

GABAergic receptor system is significantly reduced in high binding regions in brain of the autism (Blatt et al, 2001).

Material and Method

Experimental design: Reviewed literatures, Proposal drafting, Vachira Pkuket Hospital Ethics committee approval, Volunteers' preparation, Education and informed consent, Study Type: Interventional, Study Design: Treatment, Non-Randomized, Open Label, Single Group Assignment, Safety/Efficacy Study.

Population: Sample size: seven (5 male and 2 female), age: 5-9 years old, education: preschool to primary school, diagnosis: (DSM III-R, DSMIV) Autistic disorder, Autistic spectrums, material: development and skill training assessment, Rajanukul Hospital, 5th Edition, five domains assessment: Pre and Post Treatment evaluated in 1. Social development 2. Fine motor and Eye-hand coordination 3. Language development 4. Gross motor development 5. Self - help skills, Equipment: HBOT 1.3 atm., 100% oxygen concentration, Duration: 1 time per week, 10 sessions with evaluation, Statistic: percents, t-test, p-value and descriptive study in subjective findings.

Results

Data analysis: There were improvements in five domains with significant level $p < 0.001$. Positive finding was seventy-five percent of the children shown improvement and negative finding was 25% of children did not seem to respond. Most beneficial results were 33.34% of children show well sleeping, better improvement in cognitive abilities, social skills, more flexibility and more proper problem and solving and this data was confirmed by subjective findings from their parents. There was no serious adverse effect in any case and tinnitus was a mild side effect in one case and it disappeared in one week.

Discussion

Important finding was objective and subjective improvements. Problems and difficulties were duration and experiences. It was quite safe to use HBOT.

Comparative study of Rossignol, DA and LW Rossignol, 2006, represented that it had shown the improvement at 31.6% of cases by HBOT 1.3 atm. and 28-30% of oxygen concentration with 40 sessions. Comparison to the present study, it was shown that the improvement at 75% of cases by HBOT 1.3 atm.



and 100% of oxygen concentration with 10 sessions. Differences were found in oxygen concentration and duration of HBOT that may influence the results.

Benefits in educational and practical knowledge may need to have a guideline to this field. Hopefully a lesson learnt for the future.

Role of oxidative stress in the pathology of neuropsychiatric disorders. There is evidence supporting the role of oxidative stress involvement in autism (Zoroglu et al, 2004; Chauhan et al, 2004, 2006; Ming et al, 2005; Yao et al, 2006; Sogut et al, 2003; Sweeten et al, 2004; Golse et al, 1978; Yorbik et al, 2002; James et al, 2004, 2006; McGinnis, WR, 2004; Kern et al, 2006; Pasca et al, 2006; Vargas, et al, 2005; Rossignol, DA and LW Rossignol, 2006).

1. Increased lipoxidation markers in blood
2. Increased lipoxidation markers in urine
3. Increased nitric oxide (NO)
4. Increased thiobarbituric acid-reacting substances
5. Lower levels of plasma glutathione levels
6. Lower levels of two major serum antioxidant metalloproteins ceruloplasmin (copper-binding protein) and transferrin (iron-binding protein)
7. Lower levels of naturally occurring free radical scavengers
8. Impaired methionine metabolism in autism and associated with glutathione levels
9. There is a correlation between antioxidant proteins and loss of previously acquired skills in a subset of children with autism
10. High levels of circulating prooxidant organic toxins, heavy metals, xanthine oxidase and cytokines have also been observed in autism
11. A strong oxidant, homocysteine, is increased in plasma from children with autism
12. An increase in inflammatory cytokines has been reported in autistic brain tissue
13. Hypoperfusion, promoting oxidative stress, has been documented in several regions of autistic brains by both SPECT and PET scans

Antioxidant status in autism

Decreased Selenium (Se) levels in the red blood cells have been reported in autism (Audhya et al, 2004). It has been suggested that supra-nutritional levels of Se may be needed to prevent degenerative disease (Rayman MP, 2002). Se is an essential component of various enzymes, such as glutathione peroxidase (GSPHx). Lower levels of Se and GSPHx in autistic children may favor lipid peroxidation.

Se is also a component of enzymes involved in conversion of T4 to T3 (Foster, H.D, 1993), which is critical for normal brain development. It is of interest that hypothyroidism has been reported in autistic children (Gillberg et al, 1992). Another less known function of Se is its ability to counteract the neurotoxicity of heavy metals, such as Hg (Whagner, PD, 2001).

Mitochondria do not only produce less ATP, but they also increase the production of reactive oxygen species (ROS) as by-products of aerobic metabolism in the aging tissues of humans and animals (Yau-Huei Wei and Hsin-Chen Lee, 2002).

It is now generally accepted that aging-associated respiratory function decline can result in enhanced production of ROS in mitochondria (Yau-Huei Wei and Hsin-Chen Lee, 2002).

Debate

“There is no evidence in any brain problem that a hyperbaric chamber helps” (Dr. Gary W. Goldstein, president and CEO of the Kennedy Krieger Institute in Baltimore, which specializes in children’s development problems, Oxygen therapy for kids with autism debated, baltimoresun.com, April 27, 2007 by Kirsten Scharnberg). It is not a good idea to rely on “may be”. “We don’t know what the cause of autism is.” “There is little or no evidence that hyperbaric oxygen is helpful for established brain injury.” “It can cause seizures and oxygen toxicity in a limited number of patients.” “Doctor question benefit of hyperbaric oxygen therapy for autistic children.” (NorthJersey.com Jan 17, 2006 by Jessica Adler, Herald news).

The reality

The authors’ preliminary study has shown subjective responses from children with autism and subjective findings from their parents in beneficial results, such as attention, communication, hearing, emotions, postures, and manners. They had improved in their study from child chiropractic therapy and child developmental therapy. Whatever, the authors could not conclude which one was more effective than the other. Furthermore, the authors did not have the other alternative therapies in our experiences, such as music therapy, art therapy, animal therapy, acupuncture; so the authors could not know in other viewpoints.

Multidisciplinary approaches are as a holistic

Many alternative therapies were known that they could have some beneficial effects for the children with autism. There is no one-answer for many questions



but there are many answers for one question. Multiple factors are the possible causes of the autism. The curative factors may be from multidisciplinary approaches. A holistic approach includes different techniques, combines them altogether.

Conclusion

Abnormalities had been found in the limbic system, association of cortex and cerebellum. Defects in all of these structures correlated with some symptoms in autism. Therefore, it was very difficult to tell what abnormalities influenced which symptoms.

Future their goals: Is early identification able to have a benefit? Interaction with other factors, the pathophysiology, the side effects, the other beneficial effects, and the long-lasting healing effects. Further planning is: Long-term study, Follow-up phase.

Eligible outcome, HBOT is a new treatment for Thai autistic children. Many scientific studies recently have shown that HBOT could be an effective treatment for autistic children. It could ameliorate major autistic symptoms.

Suggestion

Multidisciplinary approaches are the most important for autism. The authors' hopefully expectation, HBOT can be unless for a new approach but also discloses the mystery of mechanisms and pathology in the autism.

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การรักษาด้วยออกซิเจนความดันสูง สำหรับเด็กออทิสติกในประเทศไทย

เจษฎา จงไพบูลย์พัฒนนะ, ทวีปณ สัมปทณรักษ์, นพพล ธาดากุล, ชาญสิน จันทรรัตน์, เมธินี ก้อนแก้ว, เมธิรา อรุณลิมสวัสดิ์

ภูมิหลัง: ออทิสติกเป็นภาวะผิดปกติทางพัฒนาการและพฤติกรรมที่สำคัญ 3 ประการ คือ 1. ทักษะทางสังคม 2. การสื่อสาร 3. จินตนาการ ความจำมักเป็นรูปหรือภาพ การรักษา, การจัดการและการแก้ปัญหายังเป็นเรื่องยาก การรักษาด้วยออกซิเจนความดันสูงนับเป็นเรื่องใหม่สำหรับประเทศไทยโดยเฉพาะการนำมาใช้ดูแลช่วยเหลือเด็กออทิสติกนอกเหนือจากการใช้หลักคือภาวะโรคน้ำหนึบจากการดำน้ำลึกที่มีภาวะไนโตรเจนในร่างกายนสูง การรักษาโดยใช้ออกซิเจนความดันสูงทำให้ออกซิเจนไปสู่เนื้อเยื่อโดยเฉพาะสมองมีเพิ่มมากขึ้น

วัตถุประสงค์: เพื่อทดสอบความปลอดภัยในการนำมาใช้ และพิสูจน์ผลที่ได้ต่ออาการสำคัญของเด็กออทิสติกว่ามีนัยสำคัญทางสถิติหรือไม่อีกทั้งยังไม่มีการศึกษามาก่อนในประเทศไทย

วิธีการศึกษา: ทำในเด็กออทิสติกไทย (จำนวน 7 ราย) รักษาด้วย เครื่องปรับออกซิเจน ความดันสูง (1.3 เท่าของความดันบรรยากาศ, 10 ครั้ง) ประเมินก่อนและหลังการรักษา 5 ด้านได้แก่ พัฒนาการด้านสังคม, กล้ามเนื้อมัดเล็ก และการทำงานประสานกัน, ด้านภาษา, กล้ามเนื้อมัดใหญ่, ทักษะการช่วยเหลือตนเอง ผลที่ได้พบว่ามีอาการดีขึ้นทั้ง 5 ด้านอย่างมีนัยสำคัญทางสถิติ โดยมีร้อยละ 75 ดีขึ้นชัดเจน อีกร้อยละ 25 ได้ผลไม่ชัดเจน

สรุป: การรักษาด้วยเครื่องปรับออกซิเจนความดันสูงนับว่าเป็นการรักษาชนิดใหม่ในการรักษาเด็กออทิสติกของไทย การศึกษาทางวิทยาศาสตร์หลายผลงาน สนับสนุนแนวคิดในการนำมาใช้ และมีประโยชน์ในการช่วยเหลือบรรเทาอาการที่สำคัญในเด็กออทิสติกได้

