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RESEARCH ARTICLE **Open Access**

Biomolecular Mechanism Of Hyperbaric Oxygen Therapy As An Alternative Treatment In Autism Spectrum Disorder

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Abstract

Introduction Many alternatives have appeared in the recent technology days for Autism Spectrum Disorder (ASD), many which may have higher risks and harder compliance especially for children. Hyperbaric oxygen therapy (HBOT) has been in a lot of talks as an alternative treatment for ASD lately and showed improvements in the recent cases. This paper aims to elaborate about biomolecular mechanism involved and how it affect the symptoms of ASD.

Methods This research was conducted using the electronic databases Pubmed, GoogleScholar, EBSCO, ScienceDirect, Ovid, Science, Springer, Scopus, Cochrane Database, Web of Science and Wiley Online Library for articles published between January 2020 and May 2025. Only peer-reviewed articles published in English were included.

Results HBOT works by reducing tissue hypoxia, increasing mitochondrial function, restoring impaired blood circulation, anti-inflammatory effects, and many more. These effects help relieve psychological and behavioral symptoms of ASD, especially the alleviating effects on mitochondrial biochemical dysfunction.

Conclusion Autism Spectrum Disorder (ASD) is a complex neurodevelopmental condition marked by difficulties in communication, social interaction, and repetitive behaviors. While its exact cause remains unclear, ASD cases in Indonesia are rising. Hyperbaric Oxygen Therapy (HBOT) shows potential in easing symptoms, particularly related to mitochondrial dysfunction, but its safety and efficacy need further study.

Keywords: ASD; HBOT; mitochondrial dysfunction; hyperbaric oxygen therapy; autism spectrum disorder

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Introduction

Autism Spectrum Disorder (ASD) is a neurological disorder characterized by a collection of symptoms such as impaired communication and social interaction as well as limited and repetitive behaviour (Floris et al., 2021). According to (Ministry of Health, 2024), the number of children with ASD in Indonesia has reached 2.4 million in 2024 with a prevalence of 1 in 160 children in Indonesia having ASD. The main cause of ASD is thought to originate from dysfunctional central nervous system (CNS). However, many recent medical studies state that ASD may involve systemic physiological abnormalities such as dysfunction of chemicals and mitochondria of body cells (Balachandar et al., 2020).

The hypothesis of the relationship between ASD and dysfunction of chemicals and mitochondria of body cells introduced hyperbaric hyperoxia therapy or therapy that uses oxygen levels and pressures higher than normal levels and pressures in the atmosphere. Hyperbaric Oxygen Therapy or Hyperbaric Oxygen Treatment (HBOT) is a treatment by inhaling high levels of oxygen in a special room (chamber) with a pressure of more than 1.4 ATA (Zwolinskiet al., 2020). Early attempts to use Hyperbaric Oxygen Therapy in ASD patients showed satisfactory results, but some recent uses have shown controversial results for the health world. With the development of technology and HBOT trials conducted on experimental animals, the effect of HBOT on ROS (Reactive Oxygen Species) is believed to influence the effects of HBOT treatment on ASD patients, especially children. This journal aims to collect information and explain the effects of alternative HBOT treatment on ASD biomolecularly.

Autism Spectrum Disorder (ASD)

ASD is a complex pervasive neurodevelopmental disorder characterized by three main symptoms, namely impaired communication and socialization, limited interests,

and repetitive behavior.(Meyer, 2020). Autism is a psychological and behavioral disorder that cannot be cured but its symptoms can be treated. This disorder can be diagnosed at any age with symptoms appearing in toddlers. Signs of ASD are symptoms and varying severity that can appear in any population and at any age. The symptoms of autism disorder have their own level of severity which often interferes with sufferers in carrying out daily activities such as aggression, irritability, hyperactivity, impaired focus, depression, and anxiety (Tsai et al., 2020).

Because of the wide variety of symptoms, no intervention is completely effective in treating ASD. However, early diagnosis and therapy can provide maximum effects such as reducing difficulties in learning activities and increasing special advantages from behavioral and psychological interventions involving everyone around the child, namely parents, teachers and doctors. These efforts to improve the quality of life of children sometimes cannot guarantee that they can be accepted in society with the disabilities they have. For that, the emergence of alternatives allows to increase the opportunity for children with ASD to improve their quality of life.(Beamish et al., 2021).

Hyperbaric Oxygen Therapy (HBOT)

Hyperbaric Oxygen Therapy is a treatment that uses the phenomenon of inhaling high levels of oxygen in a special chamber with a pressure of more than 1.4 ATA.(Zwolinskiet al., 2025). HBOT works by causing a hyperbaric hyperoxia environment that will increase oxygen levels in body tissues so that tissues lacking oxygen (hypoxia) will return to normal and function properly. In addition, HBOT also works with the mechanism of oxidative stress by increasing ROS and triggering the production of antioxidants and stimulating neovascularization or the formation of new blood vessels to provide blood flow to tissues whose blood flow is closed or blocked.

The relationship between ASD and HBOT

Pathophysiologically, HBOT works in mechanisms such as oxidative stress, cerebral hypoperfusion, inflammation, immune dysregulation, and mitochondrial dysfunction in ASD cases (Frye et al., 2021). HBOT reduces oxidative stress and brain inflammation and increases cerebral perfusion. According to (Frye et al., 2021), HBOT alleviates cerebral hypoperfusion which causes symptoms in ASD such as difficulty learning language, repetitive behavior, emotional disorders and facial expressions. HBOT plays a role in anti-inflammatory effects for ASD patients with symptoms characterized by neuroinflammation, immune dysregulation and gastrointestinal inflammation (Zarimeidani, 2025).

How HBOT Affects Mitochondrial Dysfunction in Austism Spectrum Disorder

Biochemically, HBOT affects mitochondria which play a major role in the oxidative products of body cells. Abnormal biomarkers were found in blood samples of ASD patients, namely mitochondrial deficiency in lymphocytes of ASD patients. In lymphoblast cells taken from children with ASD, changes in mitochondrial storage capacity were found which made them more susceptible to ROS which can be caused by immune activation or a pro-oxidant environment (Frye et al., 2021). Mitochondrial dysfunction is an abnormality that has been widely studied in ASD and is thought to be caused by various genetic factors. AMBRA1, a gene associated with mitochondrial autophagy, is thought to be mutated in ASD which causes autistic behavior usually in girls. Deficiency of tripartite motif protein 32 (TRIM32), a regulator of mTOR (a protein that plays a role in cell metabolism and proliferation), is known to cause increased autophagy and impaired generation of GABAergic neurons along with autistic behavior (Balachandar et al., 2020).

In animal experiments by (Podgorska-Bednarz and Perenc, 2021), HBOT causes increased mitochondrial formation and autophagy that destroys old and damaged mitochondria and leaves new and healthy mitochondria. This phenomenon is believed to occur due to the production of ROS that stimulates mitochondrial oxidative production. HBOT also causes increased levels of antioxidant enzymes that protect against the damaging effects of ROS (Bjørklund, 2020). These effects make HBOT an option for parents of ASD children as an alternative treatment at an early age despite the expensive cost of the procedure.

HBOT not only brings benefits to ASD patients, but HBOT can cause side effects and complications such as ear barotrauma, excessive fatigue, headaches and claustrophobia that need to be considered before implementing the treatment (Hooper, MR, 2020). Although after considering its advantages and disadvantages, HBOT is not recommended by ASD specialists at this time, further technological developments or the addition of combination therapies may increase the benefits of HBOT compared to the side effects and complications it causes.

In research conducted by(Abdel-Rahman et al., 2021), platelets in ASD patients cause damage to mitochondrial respiration due to defects in oxygen consumption in the OXPHOS-mediated complex. In addition, immune function abnormalities were also found in neutrophils of ASD patients due to deficits in NOX-dependent oxygen consumption, hydrogen peroxide, and superoxide production. The correlation between mitochondrial respiration and clinical psychometric parameters was also found using the AUTISM Treatment Evaluation Checklist (ATEC) and CARS (Childhood Autism Rating Scale) scales (Balachandar, 2020). However, HBOT treatment did not provide significant results on mitochondrial respiration parameters of platelets in ASD patients

or restore NOX-dependent oxygen consumption and hydrogen peroxide production in neutrophils in ASD patients(Abdel-Rahman et al., 2021).

Method

The research method used is the literature study method or Systemic Literature Review with a descriptive research design. Descriptive research is research that does not use hypothesis testing but rather describes and summarizes conditions, situations, or phenomena that occur in society and makes them the object of research (Prof. Dr. Sugiyono, 2017). Systemic Literature Review (SLR) is a systematic literature review that aims to identify, evaluate, and interpret previous studies to produce more acute and systematic data (Andriani et al., 2021)

The population of the study was scientific articles, publications, and journals about Autism or ASD (Autism Spectrum Disorder) and Hyperbaric Oxygen Therapy (HBOT) and the relationship between the two. The samples selected were national journals indexed by SINTA (Science and Technology Index) and international journals indexed by Pubmed, Google Scholar, and Elsevier.

Result and Discussion

Autism or ASD is a pervasive complex neurodevelopmental disorder characterized by three main symptoms; impaired communication and socialization, limited interest in things, and repetitive behavior. The cause is not clearly known, the symptoms are varied, and the lack of further technological developments make ASD a psychological and behavioral disorder that is difficult to control without structured treatment. In Indonesia, the number of ASD patients increases every year and treatment with other alternatives is needed to help the quality of life of ASD patients, especially children. One alternative that can be considered is Hyperbaric Oxygen Therapy (HBOT) (Podgorska-Bednarz and Perenc, 2021).

HBOT is a therapy using oxygen with levels and pressures above normal levels and pressures in the atmosphere. HBOT works by reducing tissue hypoxia, increasing mitochondrial function, restoring impaired blood circulation, anti-inflammatory effects, and many more. These effects help relieve psychological and behavioral symptoms of ASD, especially the alleviating effects on mitochondrial biochemical dysfunction.

Hyperbaric Oxygen Therapy (HBOT) addresses several pathophysiological mechanisms involved in Autism Spectrum Disorder (ASD), including oxidative stress, reduced blood flow to the brain, inflammation, immune system imbalance, and mitochondrial dysfunction. It helps lower oxidative stress and brain inflammation while improving cerebral blood flow. Frye et al. (2021) highlight that by enhancing brain perfusion, HBOT may relieve ASD-related symptoms such as language difficulties, repetitive behaviors, emotional disturbances, and impaired facial expressions. Additionally, HBOT has anti-inflammatory properties that may benefit individuals with ASD who experience neuroinflammation, immune irregularities, and gastrointestinal issues (Zarimeidani, 2025).HBOT influences mitochondrial function, which is often impaired in individuals with ASD. Studies show mitochondrial deficiencies in lymphocytes and lymphoblasts of ASD patients, making them more vulnerable to oxidative stress due to immune activation or pro-oxidant environments (Frye et al., 2021). Genetic factors like AMBRA1 and TRIM32 mutations are linked to mitochondrial dysfunction and autistic behaviors, particularly in females (Balachandar et al., 2020).

Animal studies demonstrate that HBOT promotes the formation of healthy mitochondria through increased autophagy and antioxidant enzyme activity (Podgorska-Bednarz & Perenc, 2021; Bjørklund, 2020). Despite its potential, HBOT carries risks such as ear barotrauma, fatigue, headaches, and claustrophobia (Hooper, 2020). Currently, it is not broadly recommended for ASD due to limited effectiveness and possible side effects. Research by Abdel-Rahman et al. (2021) found mitochondrial respiration defects in ASD patients' platelets and neutrophils, but HBOT showed no significant improvement in these parameters, despite clinical correlations with autism severity scales.

However, the use of HBOT for ASD patients still requires further research to ensure the safety and effectiveness of the treatment.(Abdel-Rahman et al., 2021).

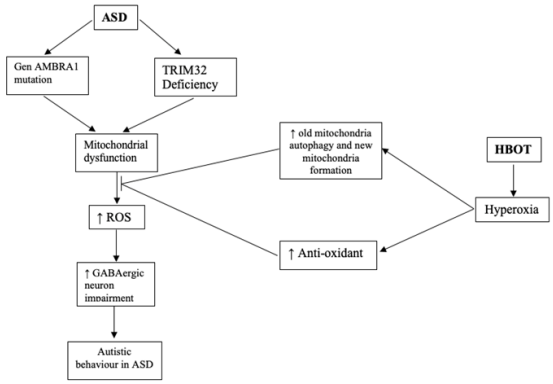

Figure 1. Biomolecular mechanism of HBOT in ASD

Conclusion

Autism or Autism Spectrum Disorder (ASD) is a complex neurodevelopmental disorder that is difficult to control without structured treatment, with the main symptoms being impaired communication, social interaction, and limited and repetitive behavior. Although the cause is not yet known for certain, the number of ASD cases in Indonesia continues to increase, especially in children. One promising alternative therapy is

Hyperbaric Oxygen Therapy (HBOT), which works through various biological mechanisms to relieve ASD symptoms, especially mitochondrial dysfunction. However, the effectiveness and safety of this therapy still require further research before it can be used widely.

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