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HYPERBARIC OXYGEN THERAPY (HBOT) IN PEDIATRICS

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ABSTRACT

Therapy with hyperbaric oxygen (HBOT) was first used in pediatrics in Russia in the 1920s (1927). At present, HBOT is used in children in similar indications as in adults, as well as in perinatal, neurologic and neuro-developmental conditions, even though there is only limited evidence of it offering any benefit for such conditions. The aim of this publication is to present current indications and risks of the use of HBOT in children.
Keywords: recomendations supportive treatment, alternative therapy, efficacy.

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INTRODUCTION

The influence of hyperbaric oxygen on bodily organs and tissues is multidirectional. In the conditions of high partial concentrations, oxygen becomes a drug inducing numerous significant phenomena in the body of a sick child, the most important of which is the effect on cellular metabolism [1,2,3,4,5,6]. The use of hyperbaric oxygen is known to: increase the antimicrobial activity of leukocytes; reduces the adhesion of neutrophils to the vascular walls thereby limiting endothelial damage; leads to vasocontriction in areas with a regular oxygen concentration without causing changes in circulation in the areas with an impaired flow; restores fibroblast growth and collagen production; stimulates generation of peroxide dismutase and ATP storage which reduces tissue oedema; limits some mechanisms of immunoogical response; stimulates osteoclast activity; promotes capillary proliferation; reduces the elasticity of the lens in the eye; inhibits the production of surfactant in the lungs; blocks lipid peroxidation during CO poisoning as well as accelerates the disposal of carbon monoxide [7,8,9,10].

Oxygen can be provided both by placing a child in an atmosphere of pure oxygen, and by using oxygen masks and hoods in the chambers where patients are kept in an air atmosphere. Both of these methods increase the partial pressure of oxygen in the lungs and significantly increase its concentrations in the plasma, mainly based on the principle of physical dissolution of oxygen in water which constitutes its main component [2,3,4]. At the pressure used in HBOT, oxygen dissolves in water in quantities of up to 20 times higher than those encountered in normobaric conditions where oxygen concentrations of 21% are found. Increasing the oxygen concentration in plasma contributes to a significant increase in the oxygen diffusion radius from the capillaries to the surrounding tissues. While breathing with 100% oxygen at the pressure of 3 ATA, its pressure in the plasma can be as high as 2000 mm Hg, which increases the diffusion of oxygen to tissues on the arterial side by approximately four times and twice on the venous side of the capillary circulation. The HBOT pressure range applied in paediatric patients usually amounts to 2 ATM [8,9,2,3,4].

The first experiments using hyperbaric oxygen therapy (HBOT) in children were carried out in Russia, during respiratory-circulatory resuscitation, in states of brain damage, as well as in haemolytic disease in new-borns. Initially, those children in a severe general condition were qualified for HBOT procedures for whom the remaining therapeutic options available at that time were exhausted. It was shown that in neonatal asphyxia, the application of HBOT up to three hours after the birth, led to saving the lives and subsequent recovery of 3/4 of children subjected to this therapy.

It was also observed that HBOT reduced the concentration of free bilirubin in the blood, thus preventing brain damage associated with kernicterus [4]. Over time, hyperbaric oxygen therapy has been used as supportive therapy in numerous childhood diseases [2,3,4,5]. The specificity of paediatrics are health problems related to developmental disorders, congenital malformations and perinatal trauma. HBOT is tested for paediatric usefulness primarily in relation to neurological consequences of the said abnormalities. The greatest interest is instigated by the use of HBOT in cognitive disorders and paralysis, thus raising hopes that, combined with rehabilitation, it will help relieve spastic symptoms, improve sight, hearing, speech and other mental functions [11,12,13,14]. In practice, as in adults, HBOT is mainly used in children with ischaemia or tissue hypoxia and / or difficult-to-heal wounds, in order to complement the traditional therapy and to help improve the outcome of that therapy. The simultaneous use of surgical debridement, antibiotic therapy and HBOT facilitates a synergy effect, which significantly accelerates wound healing [7,8,9,10,2].

Indications for the use of HBOT in Europe have recently been updated based on the EBM methodology at the 10th ECHM (European Committee of Hyperbaric Medicine) consensus conference in Lille on 15-16 April 2016 [15]. The strength of evidence of the beneficial effects of HBOT was divided into 4 levels: (level I - strong evidence of beneficial effect of HBOT, level II - evidence of beneficial effects of HBOT, level III - poor evidence of beneficial effects of HBOT, level IV - no evidence of beneficial effects of HBOT).

On the basis of assessment of the available evidence, the committee issued recommendations based on consensus, whose strength could take three grades (recommendation of grade I - strong, recommendation of grade II - moderate and recommendation of grade III - poor, optional). At the same time, the quality of evidence was assessed according to the GRADE system (A - high quality of evidence, B - moderate quality of evidence, C - low quality of evidence, D - very low quality of evidence) [15].

The approved indications for the use of HBOT in children include:

<u>Grade I recommendation (strong)</u>

- CO poisoning (B),
- open fractures with a crush injury (B),
- prophylaxis of osteonecrosis after tooth extraction in a patient undergoing irradiation,
- necrosis after irradiation and radiation ulcers (mandible, rectum, bladder) (B),
- decompression sickness (C),
- gas embolism (C),
- infections caused by anaerobe or mixed flora with anaerobic involvement, soft tissue necrosis, especially gas gangrene (C),
- sudden deafness (idiopathic neurosensory deafness within 2 weeks, up to a maximum of 6 months after the occurrence) (B).

<u>Grade II recommendation (moderate)</u>

- hard healing wounds: diabetic foot (B), ischaemic ulcers (C),
- necrosis of the femoral head (B),
- skin grafts and skin patches endangered with necrosis (C),
- crush injuries without bone fractures (C),
- third degree burns – 20% of the body surface (C),
- chronic osteomyelitis resistant to treatment (C),
- ccclusion of the central retinal artery (C),
- pneumatosis cystoides intestinalis (C),
- osteoradionecrosis of bones, excluding the mandible (C),

- radiation enteritis/proctitis (C),
- radiation-induced damage to soft tissues, excluding the rectum and bladder (C),
- preventive in surgical procedures, including implants in irradiated tissues – (C),
- ischaemic ulcers (C),
- neuroblastoma grade IV (C).

Grade III recommendation (poor)

- injuries of the brain (acute and chronic brain injuries, chronic stroke, hypoxia encephalopathy) (C),
- post-radiation damage to the CNS (C),
- post-radiation damage to the larynx or central nervous system (C),
- reimplantation of the limbs (C),
- burns > 20% of total body surface (C),
- acute ischaemic eye disease – (C),
- reperfusion syndrome following vascular surgeries (C),
- a breakthrough in sickle-cell anaemia (C),
- non-healing ulcers in sickle-cell anaemia (C),
- interstitial cystitis (C).

Due to the lack of clinical data, recommendations regarding the use of HBOT in the following diseases were not issued:

- inflammation of the mediastinum after dissection of the sternum (D),
- malignant medial otitis (D),
- acute myocardial infarction (D),
- retinal pigment degeneration (D),
- palsy of the facial nerve (D).

An analysis of the above-mentioned indications in terms of paediatric usefulness indicates that HBOT can be used in children in all cases [6]. The differences relate to the epidemiology of the diseases in which it is recommended to use HBOT - such conditions as diabetic foot, acute myocardial infarction, retinal pigment degeneration or sudden deafness, which are common among adults and constitute one of the most frequent indications for HBOT are rare in the developmental age population. In turn, the paediatric domain concentrates on neurological and neurodevelopmental disorders, where, unfortunately, the usefulness of HBOT is small. The authors of the recommendations took into consideration the fact that there is evidence for a lack of beneficial effects of HBOT in the following clinical conditions mainly concerning children [15]:

- Conditions from the autism spectrum (strong recommendation not to use HBOT, evidence B);
- Cerebral palsy (strong recommendation not to use HBOT, evidence B);
- Placental insufficiency (strong recommendation not to use HBOT, evidence B);
- Multiple sclerosis (strong recommendation not to use HBOT, evidence B);
- Tinnitus (strong recommendation not to use HBOT, evidence B);
- Acute phase of stroke (strong recommendation not to use HBOT, evidence B).

Despite the expectations of parents and paediatricians, previous experience with the use of HBOT in the treatment of children with autism spectrum or cerebral palsy is negative and HBOT should not be recommended in these conditions [11,14,16]. Autism or broader autism spectrum (ASDs - autism spectrum disorders) constitute a continuum of complex, congenital brain developmental disorders that manifest themselves in children with difficulties in verbal and non-verbal communication, disturbed social interactions and repeated limited stereotypes of movement or other behaviours.

It is true that there is much evidence that HBOT reduces the severity of encephalitis in children with autism and affects the concentration of neurotransmitters, however it has not been demonstrated that HBOT benefited the patients [12,13]. When analysing the indications for HBOT recommended by ECHM, it should be noted that there is a fundamental difference between "evidence from clinical studies of a lack of effect" available e.g. in relation to patients with autism spectrum, and the lack of evidence for a favourable effect, which concerns many, if not the majority of potential indications for HBOT in children. In this situation, the authors of the recommendations advise an individual risk-benefit analysis [15].

In situations where the use of HBOT does not involve a significant risk for a child and may potentially help, HBOT should be used. In turn, if the use of HBOT involves a significant risk for the child and the illness was not mentioned in the above list of indications, the HBO therapy should not be applied in concord with the principle formulated by Hippocrates "whenever a doctor cannot do good, he must be kept from doing harm."

An example of neurological disorders in children that may be considered as an indication for HBOT are migraine and cluster headaches often occurring in adolescents, neurological symptoms accompanying FAS or ADHD syndromes, and other nervous system disorders and symptoms in which there is no evidence for the beneficial effects of HBOT, however there also is no evidence of HBOT's lack of effectiveness, particularly when some beneficial effects have been observed in studies or published reports or when there are theoretical indications that HBOT may be beneficial [4].

For example, one of the RCT studies showed a beneficial effect of HBOT on FAS (Foetal Alcoholic Syndrome) in the form of an improved reaction time, better attention and image recognition, which raises hopes that HBOT can benefit children [17]. Similarly, in several studies on the use of HBOT in children with ADHD, encouraging results were obtained in the form of its calming effect, reduction of mood swings, improvement of digestive functions and peaceful sleep [18].

THE RISK OF HBOT THERAPY IN CHILDREN

The side effects of HBOT result from an occurrence of a pressure difference between particular closed spaces of the body and the hyperbaric oxygen toxicity, i.e. the very mechanism to which HBOT owes its effect. The main side effects of HBOT associated with pressure differences include rupture of the eardrum and pneumothorax, whereas oxygen toxicity may lead to myopia and epileptic seizures.

To summarise the current knowledge about HBOT in children, it can be concluded that the therapy can be used in relation to all indications mentioned in ECHM

recommendations, providing that a child, particularly a small one, is ensured comfortable conditions. This usually involves the presence of a carer in the hyperbaric chamber and requires the exclusion of contraindications on his/her part (qualification to undergo HBOT like a regular patient) [15].

However, in frequent paediatric situations where there is a lack of evidence for the beneficial effect of HBOT based on animal studies, case reports or a series of cases, the use of HBOT should be considered by an individual assessment of the risk of side effects. The condition for qualifying for HBOT consists in a low risk of a harmful impact of HBOT. It is necessary to conduct research on the use of HBOT in children, which will enable a more precise definition of indications and contraindications and dispel today's doubts of physicians resulting from the lack of data.

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