American Journal of
Biomedical Science & Research

www.biomedgrid.com
ISSN: 2642-1747

Mini Review

Hyperbaric Oxygen Therapy for Vascular Dementia

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To Cite This Article: *Shuwen Ge, Chengyun Tang, Kuo Chen, Cuiping Zhao, Vladimir N Nikolenko, Jin Zhang. Hyperbaric Oxygen Therapy for Vascular Dementia. Am J Biomed Sci & Res. 2021 - 14(4). AJBSR.MS.ID.002006.* DOI: 10.34297/AJBSR.2021.14.002006.

Received: June 23, 2021; **Published:** October 20, 2021

Introduction

Diabetic vascular complications are a combination of specific abnormalities and vascular disease found in people with diabetes. Chronic and long-term metabolic and hormone imbalances are the pathogenesis of diabetic vascular disease [1]. Studies have shown that cerebrovascular diseases may cause Mild Cognitive Impairment (MCI) or vascular dementia (Vascular dementia, VD). In addition, in the elderly with normal cognition, it is also found that due to vascular risk factors and changes in cerebral blood flow (vascular disorders), there is a risk of subjective (self-perceived) cognitive decline. Therefore, improving cerebral blood perfusion, reducing intracranial pressure, alleviating brain edema, increasing tissue oxygen partial pressure, promoting brain tissue healing and neovascularization are important methods for the treatment of patients with MCI or VD. Due to the limitations and side effects of conventional therapies, studies have proposed a complementary therapy that can significantly improve this disease-Hyperbaric Oxygen Therapy (HBOT).

This article will discuss the additional effects, limitations, or side effects of HBOT by increasing cerebral blood flow to assist in the treatment of cognitive impairment. Due to decreased cerebral blood flow (cerebrovascular dysfunction), type 2 diabetes has a risk of mild cognitive impairment and dementia. Dementia is a disease characterized by memory loss, confusion, language and comprehension, personality and behavior changes, and increased dependence on others in daily activities. Vascular dementia is the second most common form of dementia, and its clinical manifestations are mainly cognitive impairment, cerebrovascular disease, and progressive memory decline. The risk factors are hypertension, obesity, diabetes, hyperlipidemia, metabolic syndrome, etc. [2]. Stroke or acute cerebral infarction caused by transient ischemic attack and large-scale cerebral vascular damage are the main pathogenic factors of VD [3]. Vascular dementia not only reduces the quality of life of patients, and suffers psychological and physical damage, but also causes significant medical and economic burdens on the family and society.

Therefore, research on effective treatment of VD has important social and clinical significance. The brain depends on the normal function of the vascular neural network to maintain cognitive function. This network includes neurovascular units (endothelial cells, pericytes, glial cells and neurons), upstream arteries and arterioles, which provide nutrients for the microcirculation of the brain. Studies have shown that vascular neural network dysfunction can lead to neuronal damage and degeneration of Cerebral Blood Flow (CBF). The rate at which arterial blood is transported to the capillary bed of a specific tissue is a functional measure of the vascular neural network and is related to normal aging and

cognitive decline. During normal and pathological aging, there is a reliable correlation between cerebral blood flow and cognitive ability. Studies have shown that in patients with no decline in subjective function, higher CBF supports memory function, but in patients with reduced subjective cognitive ability, higher CBF no longer supports memory function, which reflects the cognitive dysfunction. The patient has neurovascular disorders [4].

In addition, in patients with type 2 diabetes who may develop cognitive impairment, lower CBF is associated with poor memory, executive function, and processing speed. When adjusting for diabetes, a significant association between lower regional CBF and poor executive function and processing speed still exists. At present, the Conventional Treatment of VD (CT), including anticoagulant drugs, dilation of cerebrovascular, reducing blood viscosity, correcting electrolyte disturbances, controlling cerebral edema, etc., mostly focuses on symptomatic management and reducing potential risk factors for cerebrovascular diseases [5]. Cholinesterase inhibitors (donepezil, ristamine, and galantamine) and non-cholinergic drugs (memantine, nimodipine, and hydrobase) have been considered effective drugs for the treatment of VD [6]. However, due to its many contraindications, many side effects and unclear pathological mechanisms, the role of CT is still limited. At present, studies have proposed a complementary therapy that can significantly improve this disease-Hyperbaric Oxygen Therapy (HBOT).

Regarding The Improvement of Aerobic Exercise on Cerebral Blood Flow

For the elderly with a sedentary lifestyle, Cerebral Blood Flow (CBF) is a sensitive physiological marker of cerebrovascular function. Physical activity can improve cerebrovascular function and reduce age-related cognitive decline. A randomized controlled crossover trial of 17 apparently healthy men aged 60-70 years with BMI between 25 and 35kg/m^2. Study participants were randomly assigned to an 8-week period of fully supervised, progressive, aerobic exercise or no exercise control, with a 12-week clearance period in between. Measurements at the end of each period include aerobic fitness assessed using peak oxygen consumption during incremental exercise (VO2peak), CBF measured using pseudo-continuous arterial spin-labeled magnetic resonance imaging, and Oral Glucose Tolerance Test (OGTT) Glucose response after a determined load). In addition, cognitive performance in areas such as executive function, memory, and psychomotor speed were also evaluated.

Experimental results show that compared with non-exercise control, VO2peak after aerobic exercise training increased significantly by 262±236mL (P<0.001). The CBF of the bilateral frontal lobes increased by 27%, especially in the subcallosal area and the anterior cingulate gyrus (cluster volume: 1008mm3; P<0.05), while the CBF of the right medial temporal lobe decreased by 19%, mainly in the fusiform temporalis (Cluster volume: 408mm^3; P<0.05). After the average load determined by OGTT, the glucose concentration decreased by 0.33±0.63mmol/L (P=0.049). In addition, as the response delay was reduced by 5% (P=0.034), executive function was improved, but no changes were observed in memory or psychomotor speed [7]. This experiment shows that oxygen can increase the cerebral blood flow in the brain, thereby improving cognitive ability.

About The Efficacy of HBOT For Brain-Related Diseases

As an auxiliary treatment method, HBOT has been widely used in the treatment of brain injury and has shown great effects in reducing the disability rate and improving the cure rate. HBOT is to inhale 97% to 100% oxygen at a pressure greater than one Atmosphere (ATA). It has been reported that the use of 100% oxygen in a high-pressure environment higher than 1.4 atmospheres has achieved a certain effect in the treatment of VD [8]. According to the results of previous studies, the possible mechanisms of HBOT in the treatment of VD mainly include: increasing oxygen supply, increasing tissue oxygen partial pressure, relieving cerebral edema, reducing intracranial pressure, promoting tissue healing and angiogenesis, improving metabolic abnormalities, reducing blood oxygen saturation, and Balance cell apoptosis, reduce oxidative stress, increase mitochondrial function, and promote cell differentiation and regeneration [9-11].

Animal studies have shown that at the cellular level, HBOT reduces COX-2 mRNA and protein levels and inhibits COX-2 overexpression in cerebral ischemic animals [12]. In addition, HBOT has neuroprotective effects, antioxidant effects, and is related to the reduction of apoptosis related to the reduction of caspase-3 expression and activity [13,14]. A study in an animal model of hypoperfusion dementia showed that HBOT can improve the blood supply of the piriform cortex, promote neurogenesis, increase the number of hippocampal cholinergic neurons, and enhance learning and memory. These observations indicate the possibility that HBOT is beneficial to VD. An early animal experiment showed that HBOT significantly improved the learning, memory, and blood perfusion recovery of VD rats by increasing piriform cortex neurogenesis and cerebral blood flow [15]. Another meta-analysis related to Cerebral Hemorrhage (ICH) animal models also showed that the HBOT group significantly reduced Brain Water Content (BWC) and improved Neurobehavioral Outcomes (NO) [16].

About Other Functions of HBOT

Animal studies have proven that hyperbaric oxygen therapy has anti-inflammatory and analgesic properties. However, human

physiological data is scarce. In a recent experimental study, the authors used a burn model to observe that compared with the control group, the area of secondary hyperalgesia was reduced in the HBOT group. Surprisingly, a lasting neuroplasticity effect was observed in the HBOT pretreatment group to reduce the regional response of secondary hyperalgesia induced by burns [18,19]. In addition, HBOT also plays a role in delaying cellular senescence. Aging is characterized by the gradual loss of physiological capacity. At the cellular level, two key signs of the aging process include shortened Telomere Length (TL) and cellular senescence. The use of HBOT for repeated intermittent hyperoxia exposure during hypoxia can induce a regenerative effect. A study evaluated whether HBOT affects the concentration of TL and senescent cells in normal, non-pathological, and aging adults. The final study confirmed that HBOT may delay the effects of aging, including a significant increase in telomere length and the elimination of senescent cells in the aging population [20].

Conclusion

The available evidence in this review shows that adding HBOT to the standard conventional treatment of VD significantly improves mental status scales, activities of daily living, hemorheology, and clinical efficacy. In view of the effectiveness and safety of HBOT, it is reasonable to recommend HBOT as an adjuvant therapy for the treatment of VD.

Acknowledgement

None.

Conflict of Interest

No conflict of interest.

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