EDITORIAL

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Role of Hyperbaric Oxygen Therapy on Microvascular Diabetic Complications and Metabolic Profile among Patients with Type 2 Diabetes Mellitus

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Hyperbaric oxygen therapy (HBOT) has been suggested as a valuable addition to conventional treatment for a variety of indications, including delayed radiation injury, necrotizing soft tissue infections, and chronic wounds.[1,2] By increasing the blood oxygen content, HBOT creates a favorable gradient for the diffusion of oxygen into the tissues. In hypoxic tissues, the enhanced oxygen supply has multiple effects that may benefit wound healing.[3] By increasing the expression of vascular endothelial growth factor and fibroblast growth factor, HBOT may enhance angiogenesis and fibroblast proliferation. In addition, the resulting hyperoxia may cause vasoconstriction, thereby decreasing tissue edema. By reducing the expression of pro-inflammatory cytokines, HBOT reduces inflammation, while simultaneously enhancing the bacterial killing activity of leukocytes.[3–5]

Type 2 diabetes mellitus (T2DM) is a common disease worldwide, with many macrovascular complications, including cardiovascular diseases, and microvascular complications such as diabetic nephropathy and retinopathy. Among patients with T2DM, HBOT is mostly used for the treatment of chronic diabetic ulcers, which involves intermittent administration of 100% oxygen, usually in daily sessions of 90 minutes each, at pressures of 1.5–3.0 ata in an airtight cabin.[1,3] Although the effect of HBOT in reducing limb amputation rates is still controversial,[6–8] old and current evidence shows the effectiveness of HBOT in improving the healing of diabetic leg ulcers in patients with concomitant ischemia.[2,8]

HBOT is considered one of the safest medical treatments when applied with the indicated operational protocols, including pre-HBO2 therapy evaluations and in-chamber monitoring.[9,10] In general, side effects of HBOT are rare.[11] These include middle ear barotraumas (ears, sinuses, and lungs), which has been noted only in 2% of treated patients, and can be prevented or minimized by teaching auto-inflation techniques, or by inserting tympanostomy tubes.[11] Another frequent complaint is claustrophobia, requiring reassurance and coaching. Infrequent side effects include oxygen toxicity to lungs and central nervous system, and progressive myopia, which is usually transient and reversible after stopping HBOT sessions.[11]

However, the role of HBOT in the treatment of microvascular complications of T2DM (nephropathy and retinopathy) and its effect on the metabolic profile is still not well-explored. In relation to diabetic nephropathy, findings from animal (rat) studies indicate that the periodic HBOT exposure limits some of the damage associated with the chronic high blood glucose levels, particularly those mediated through oxidative pathways.[12] These findings are consistent with studies conducted to assess the protection of human microvascular endothelial cells grown in culture from oxidants,[13] and protection of mouse skin from UV-damage using HBOT.[14] In addition, HBOT reduces intra-renal lactate production among mice without affecting either lactate dehydrogenase mRNA expression or activity.[15]

A similar lower renal lactate production has recently been demonstrated in response to

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antioxidant treatment.[16] This may indicate that HBOT is a clinically useful adjuvant therapy in patients with diabetes at risk of developing renal disease. However, clinical studies on humans are limited in this area.

To date, the role of HBOT in diabetic retinopathy is thought theoretically to be unfavorable due to the revascularization effect of HBOT and the high retinal consumption of oxygen, and it has potential to cause/worsen the condition.[17] However, clinical studies are very scanty on this topic. An observational study showed that the progression of non-proliferative retinopathy to the proliferative type due to HBOT is rare.[18] On the other hand, other animal studies have reported that HBOT may suppress the extent of the blood-retinal barrier breakdown in diabetic animals, indicating a protective effect.[19] In this regard, a recent small observational study observed that patients treated with HBOT showed a regression or stabilization of diabetic retinopathy lesions and a decrease in central macular thickness.[20] Another small cohort study showed no change in diabetic retinopathy after HBOT treatment despite the thinning effect on the choroid layer and thickening effect on the macula.[21]

Regarding the effect of HBOT on metabolic profile among diabetic patients, HBOT seems connected with improved glycemic control and anti-atherogenic metabolic changes. In this regard, HBOT was shown to have beneficial effects on glycemic control in patients with diabetes (fasting blood glucose and glycated hemoglobin), insulin resistance and lipid profile in these patients.[22–24] In this context, HBOT was observed to ameliorate glucose tolerance in diabetic patients and suggested that it could be used as a therapeutic intervention for T2DM.[25] Furthermore, HBOT was observed to increase insulin sensitivity in overweight or obese males with and without T2DM.[26] In addition, HBOT decreased subfractions of very-low-density lipoprotein (LDL), intermediate-density lipoprotein (IDL), LDL1, LDL2, and LDL3–7 after HBOT. However, the IDL1 subfraction and the concentration of C-peptide, increased significantly with HBOT.[23] However, these conclusions were based on limited human studies with small sample size and/or short-duration HBOT.[22–24] In addition, animal models showed that HBOT has the advantage of improving obesity, with a disadvantage of causing liver damage by increasing oxidative stress.[27]

To date, it seems that human clinical studies addressing the effect of HBOT on various diabetic complications, including nephropathy and retinopathy, as well as the metabolic parameters, are still limited worldwide. Very limited literature is available in this regard, showing inconclusive controversial results. In addition, the available clinical literature is mostly based on small sample sizes. Furthermore, the safety of this modality on other vital organs is still not explored. Hence, further confirmatory studies are highly needed.

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