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REVIEW

Hyperbaric oxygen therapy for chronic diabetic wounds

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SUMMARY

We performed a systematic search for articles on the topic of hyperbaric oxygen (HBO_2) therapy and chronic diabetic wounds between Jan 2009 and Dec 2012. This was supplemented by other relevant articles known to the authors. There is growing evidence supporting HBO_2 therapy for this condition. Increased understanding of the mechanisms underlying HBO_2 therapy combined with refinements in patient selection will enhance the cost-effectiveness of this treatment.

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1. Introduction

The global prevalence of diabetes mellitus in adults is expected to rise from 6.4% (285 million adults) in 2010 to 7.7% (439 million adults) in 2030.[1] Although chronic diabetic wounds may not be a leading cause of death,[2] the associated morbidity places a huge burden on the healthcare system. The economic and social cost from complications such as high level amputations are a lot harder to measure but no less important.[3]

Hyperbaric oxygen (HBO_2) therapy has been used as an adjunct in the management of chronic diabetic wounds. In spite of the increasing evidence supporting its use and its cost-effectiveness,[4] there is still a lack of awareness about its benefits.[5] Access to HBO_2 therapy remains limited by the lack of facilities offering this treatment.[6] This review incorporates data from recent publications and summarises the role of HBO_2 therapy in this condition.

2. Methodology

We performed a PubMed, CINAHL and Scopus search using the MeSH/Index search terms: hyperbaric oxygen therapy, hyperbaric oxygenation, diabetes mellitus and wound healing. A filter was applied to restrict the search to articles published in the last five years (Jan 2009–Dec 2012). This generated 152 articles. These articles were screened and selected if they addressed the role of hyperbaric oxygen therapy in chronic diabetic wounds. Of these, 27 were original articles including animal and human studies; 84 were review articles, expert guidelines, case reports or letters to the editor. The remaining articles were not relevant. These articles were supplemented by relevant cross references as well as key articles known to the authors.

3. Mechanisms of action

The effects of hyperbaric oxygen can be explained using its two primary mechanisms. One is the mechanical effect of increased pressure on reducing bubble size, and the other is the increased partial pressure of oxygen in the blood and tissues.[7] The secondary effects of hyperoxygenation that may facilitate wound healing include an improvement in immune system activity,[8] enhancement of antibiotic effect,[9,10] neovascularization[11–16] and enhanced fibroblast activity and collagen synthesis.[17]

4. Complications and contraindications

HBO_2 is well-tolerated by most patients but complications may occur (Table 1).[18] There are also several contraindications which need to be taken into consideration (Table 2).[18] The clinical significance of some of these contraindications remain disputed[19] and there have been reports of HBO_2 therapy being used uneventfully when these contraindications exist.[20]

5. Patient selection

Although, the reported incidences of complications are generally low,[21,22] HBO_2 therapy remains expensive and time consuming. There are several factors which may aid patient selection. Wound healing is impaired by persistent infection, pressure damage, tissue ischaemia and hypoxia. Hyperoxygenation could reduce the effect

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Table 1
Complications of HBO_2 therapy.

Barotrauma of the ear
Round window blowout
Sinus squeeze
Visual refractive changes
Numb fingers
Dental problems
Anxiety in confined space
Seizures
Pulmonary oxygen toxicity
Pneumothorax
Hypoglycaemia
Congestive cardiac failure
Cataracts
Fire

Table 2
Contraindications for HBO_2 therapy.

Condition	Potential side effect
Doxorubicin	Cardiotoxicity
Bleomycin	Pulmonary fibrosis
Disulfiram	Increased oxygen toxicity
Cisplatin	Impaired wound healing
Mafenide acetate	Carbon dioxide buildup
Untreated pneumothorax	Tension pneumothorax
Known malignancies	Stimulation of tumour growth
Pregnancy	Retinopathy of the newborn
Pacemakers	Pacemaker malfunction
Upper respiratory infections and chronic sinusitis	Middle ear and sinus barotrauma
Seizure disorder	Seizures
Emphysema with carbon dioxide retention	Respiratory depression. Oxygen seizures
High fevers	Oxygen seizures
History of spontaneous pneumothorax	Pneumothorax
History of thoracic surgery	Pneumothorax
History of surgery for otosclerosis	Damage to the strut
Viral infections	Worsening of infection
Congenital spherocytosis	Severe haemolysis
History of optic neuritis	Blindness

of some of these factors. Confirmation of tissue ischaemia and hypoxia has been proposed as a means of identifying patients who may respond to HBO_2 therapy.[23] Noninvasive vascular studies (NIVS) such as the ankle-brachial index (ABI), toe-to-brachial index (TBI), pulse volume recording (PVR), segmental limb pressures, duplex ultrasound (DUS), transcutaneous oxygen tension ($TcPO_2$) and skin perfusion pressure (SPP) provide objective information about the circulation to the lower limbs.[24] Transcutaneous oximetry (TCOM) is the most widely used technique to stratify patients for HBO_2 therapy but it is still an imprecise test.[25] Combining clinical information (duration of diabetes, evidence of microangiopathy in other organs etc) and objective tests could improve our ability to identify patients who may benefit from HBO_2 therapy. The lack of response to alternative treatments is another indication for HBO_2 therapy. Medicare in the United States currently reimburses health care providers for HBO_2 therapy when it can be shown that advanced wound care has not worked after 30 days.[26] Although this duration is fairly arbitrary, it does allow for adequate time to treat concomitant infections, manage excessive exudates, optimise glucose control and nutrition. Instituting HBO_2 therapy as a rescue technique reduces its application in patients who may otherwise not need it. However this approach could also lead to a delay in a limb or life-saving intervention. Wound classification systems offer an objective way of stratifying wounds according to their severity. The most widely used and validated system is the Wagner system.[27,28] A Grade III or worse Wagner score has been used as a threshold to consider HBO_2 therapy as a treatment adjunct.[29] The key factors that influence patient selection for HBO_2 therapy are listed in Table 3.

6. Administration of HBO_2 therapy

HBO_2 therapy is delivered using monoplace or multiplace chambers. Monoplace chambers cost less to build and operate but they can only accommodate one adult at a time. The larger size of the multiplace chambers gives it more flexibility and allows additional healthcare personnel to be present inside the chamber. This enhances the capability of the chamber to treat patients who may require direct medical intervention. Examples include patients with severe carbon monoxide poisoning and necrotizing soft tissue infections. Due to the scarcity of data on what constitutes the optimal pressure or duration of treatment, there are variations in the treatment protocols used for chronic wounds. One example involves having the patients breathe 100% oxygen at 2.4 atm absolute (ATA) for 90 min once a day. Although 2.0 ATA has been shown to be effective, a pressure of 2.4 ATA was proposed to adjust for potential dilution of oxygen by entrainment of air through a loose-fitting mask.[33] This could occur in a multiplace chamber where the ambient oxygen concentration is kept low to minimise the risk of fire. This problem does not exist in a monoplace chamber which is completely filled with 100% oxygen or where fixed oxygen concentration interfaces e.g. oxygen hood are used in a multiplace chamber. Other protocols utilise a 2.0 ATA table which could reduce the risk of decompression illness in hyperbaric attendants in multiplace chambers.

7. Efficacy of HBO_2 therapy

There are several randomised controlled trials demonstrating the efficacy of HBO_2 therapy (Table 4). Improvements in outcomes include time to healing and number of high level amputations.

Table 3
Factors affecting selection of patients for HBO_2 therapy.

Factors favouring recommending HBO_2 therapy	Factors against recommending HBO_2 therapy
Wagner Grade III and IV[30]	Wagner Grade V[30]
Failure of response to advanced wound care[6]	
No contraindications for HBO_2 therapy	Contraindications for HBO_2 therapy
Good arterial supply[31]	Poor arterial supply[31]
Oxygen saturation >= 92%[25]	Oxygen saturation < 92%[25]
$TcPO_2$ (normobaric air) > 25mm Hg[32]	$TcPO_2$ (normobaric air) > 40 mm Hg[30,33]
$TcPO_2$ (normobaric air) <= 40 mm Hg[30,33]	$TcPO_2$ (normobaric air) < 15 mm Hg and $TcPO_2$ (hyperbaric oxygen) < 400 mm Hg[30]
$TcPO_2$ (normobaric oxygen) >= 35 mm Hg[30]	$TcPO_2$ (normobaric oxygen) increase < 10 mm Hg[32]
$TcPO_2$ (hyperbaric oxygen) > 200 mm Hg[30]	$TcPO_2$ (normobaric oxygen) < 35 mm Hg[30]

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