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Review Article

Hyperbaric oxygen therapy heals diabetic wounds

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ABSTRACT

With the increasing prevalence of diabetes in the community, morbidity and mortality as a result of diabetic feet has been increasing. Foot complications are one of the most serious and yet preventable complications of diabetes mellitus having an economic impact to the individual and adding the burden to the already inadequate healthcare resources. Complications associated with diabetes are often expensive to treat, and commonly include foot ulceration. While most diabetic foot ulcers heal with standard treatment, when standard treatment measures fail, adjunctive therapies must be considered. Use of systemic Hyperbaric Oxygen Therapy (HBOT) as an adjunctive treatment for chronic lower extremity diabetic ulceration is safe, reasonable and cost effective modality.

HBOT in diabetic wounds has confirmed its role in promoting oxygenation; enhance immune mechanisms, neovascular formation, fibroblast proliferation and other beneficial actions. It is now accepted as a useful adjunctive treatment in a select group of diabetic patients with severe or limb threatening wounds. HBOT has been demonstrated to be an effective treatment when combined with careful attention to underlying diseases and wound care including debridement, grafting, and control of infection. This article discusses the role of oxygen in wound healing, and place of HBOT in the modern multidisciplinary approach to the treatment of diabetic foot wounds.

1. Introduction

Diabetes has become a global epidemic and is rapidly increasing at an alarming rate. Developing countries like India harbor the majority of diabetic people and by the year 2030 AD India will have the largest number of diabetic patients. As the prevalence of diabetes has increased, so has the burden on the healthcare system to provide treatment for the complications associated with the disease. The loss of a limb or foot is one of the most feared complications of diabetes and yet foot problems remain the commonest reason for diabetic patients to be hospitalized. In India, the prevalence of diabetic foot ulcers in the clinic population is 3.6% of which patients with foot problem had to spend 32.3% of the total income towards treatment.[1]

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Diabetic ulcers are chronic, complex, or problem wounds in people with diabetes, which fail to heal in three months and are usually considered chronic. Some take years to heal or never do.[2–5] Diabetic ulcers and other chronic wounds can be classified using the Wagner Grade Scale (Table 1).

Ulcers may develop over time as patients apply constant micro-trauma to the skin. Tissue ischemia, uncontrolled hyperglycemia, infection, poor nutrition, and improper shoe gear also contribute to chronic, on healing nature of diabetic ulcers (Fig. 1).

Diabetic ulcers require a healthy, oxygenated wound bed to heal. A lack of sufficient oxygen in the wound bed slows or stops the normal healing process[6–8] and is further complicated by poor blood circulation in the feet and legs.[6,7] Nerve disease may also cause a loss of sensation in the feet and legs, causing unnoticed small cuts, sore, or pressure ulcer.

Hyperbaric oxygen therapy is an effective adjunct to other wound care therapies, including topical cleaning; surgical removal (debridement) of dead skin and tissue; application of dressings, ointments, and biologics; and use of compression boots or stockings, vacuum or negative pressure wound therapy (NPWT) pumps, ultrasound, laser, and other emerging technologies.[4,5,9–11]

2. Physiological basis of HBO therapy

When we normally breathe air at sea level pressure, hemoglobin is 95% saturated with oxygen (O_2) and 100 ml blood carries 19 ml O_2 combined with Hb and 0.32 ml dissolved in plasma. At this same pressure if 100% O_2 is inspired, O_2 combined with Hb increases to a maximum of 20 ml and that dissolved in plasma to 2.09 ml. Most tissue needs of oxygen are met from the O_2 combined to Hb (Fig. 2).

This additional oxygen in solution is almost sufficient to meet tissue needs without contribution from oxygen bound to hemoglobin and is responsible for most of the beneficial effects of HBO therapy.

3. Role of oxygen in the healing process of diabetic foot wounds

Hyperbaric oxygenation is an important therapeutic adjunct in the management of wounds that exist in chronic oxygen deficiency and where the local oxygen tension is below that optimal for healing.[3,4,6–8] Measurements of tissue oxygen tensions in non-healing diabetic wounds have shown values far below those where healing could be expected. HBO therapy has been shown to increase tissue or transcutaneous oxygen tensions in diabetic patients with chronic wounds. The greatest benefit of HBO therapy is achieved in situations where the nutritive flow and oxygen supply to repair tissue are compromised, but in which the regional vascular network, a prerequisite for oxygen to reach tissues, is only partially impaired. HBOT delivers oxygen to the wound, allowing it to 'kick start' the healing process by promoting the development of new small blood vessels.[10] The main effects of HBO therapy on the healing of diabetic foot ulcers include:

- Enhanced periwound tissue oxygenation
- Decreased edema
- Enhanced oxidative killing of bacteria
- Enhanced cellular energy (ATP) production
- Potentiation of antibiotics
- Promotion of neoangiogensis
- Enhanced epithelial migration
- Enhanced collagen production, deposition

Table 1 – Wagner classification system for dysvascular foot lesions.

Grade 0	No ulcer in a high-risk foot
Grade 1	Superficial ulcer involving the full skin thickness but not underlying tissues
Grade 2	Deep ulcer, penetrating down to ligaments and muscle, but no bone involvement or abscess formation
Grade 3	Deep ulcer with cellulitis or abscess formation, often with osteomyelitis
Grade 4	Localized gangrene
Grade 5	Extensive gangrene involving the whole foot

Wagner, F., Levin, M., & O'Neal, L., 1983. Supplement: algorithms of foot care.

4. Systemic administration of HBOT

HBO is administered in either Multiplace or Monoplace hyperbaric chambers. The Multiplace chamber is pressurized with air and the patient breathes oxygen through a mask or head tent. The Monoplace chamber is pressurized with oxygen and the patient breathes pure oxygen directly. Normally, pressures of 2–2.5 atm absolute (ATA) are used (Fig. 3).[12]

5. Transcutaneous Oximetry for evidence based use of HBO therapy

Transcutaneous oxygen value ($TcPO_2$) is recognized as one of the most reliable and useful non-invasive method for evaluation of perfusion and selecting patients for HBOT. This helps by establishing the presence of tissue hypoxia and more importantly to demonstrate the reversal from hypoxic tissue oxygen levels to normoxic or hyperoxic levels with the administration of higher oxygen partial pressures.[13] Patients with Transcutaneous periwound $TcPO_2$ values greater than 40 mmHg on room air may heal without intervention while those with values less than 20 mmHg have poor prognosis. $TcPO_2$ values less than 10 mmHg indicate amputation will be unavoidable. An increase to 40 mmHg or greater while breathing 100% O_2 at room pressure (1ATA) or >200 mmHg inside a hyperbaric chamber indicates that HBOT will benefit the patient (Fig. 4).

6. Literature review

Duzgun et al (2008) compared HBOT ($n = 50$) with standard therapy without hyperbaric oxygen ($n = 50$) in individuals with diabetes and lower-extremity wounds. Participants in the HBOT group engaged in an average of 30–45 treatments; there

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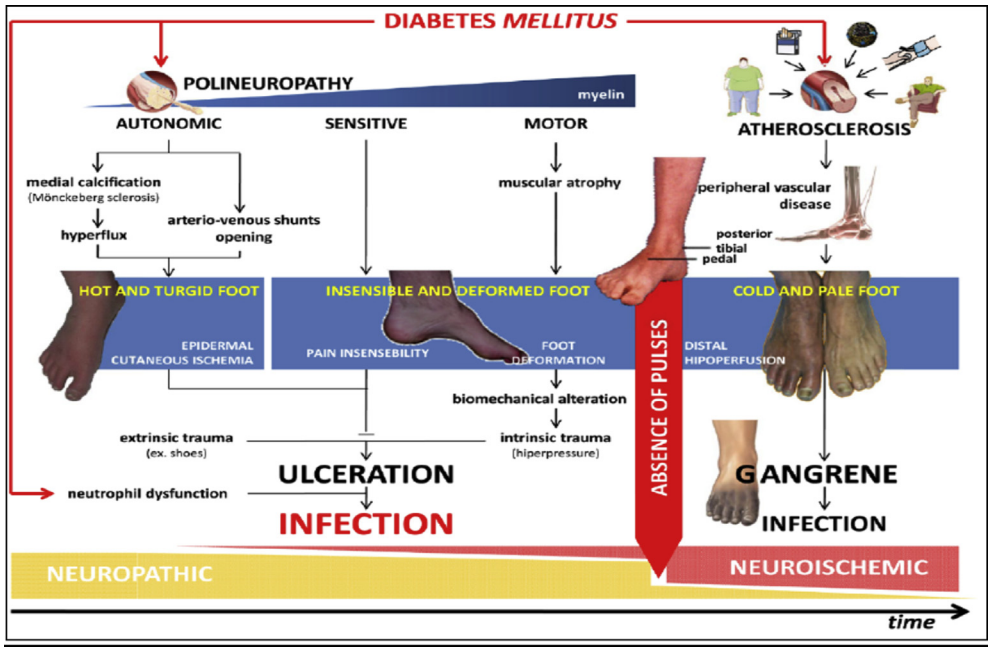

Fig. 1 – Etiology of diabetic wounds.

was no clear stoppage of treatment if wounds did not improve. The authors found that individuals in the HBOT group had foot ulcers that were more likely to heal and had to undergo less severe amputations compared with those receiving standard therapy.[12] Fife et al (2007) reviewed 971 records of individuals with diabetes receiving HBOT; overall, 73.8% showed improvement in their lower-extremity wounds. Individuals who benefited from HBOT received a mean of 34 treatments. Those with a wound not showing signs of improvement with HBOT had a mean of 24 treatments; a reduction in the number of sessions was related to the practitioner stopping the treatment if the wound was not healing.[13]

The authors found that the greatest benefit of HBOT occurred within the first 15 treatments. Zgonis et al (2005) looked at the effect of HBOT on 35 people with diabetes who had lower-extremity wounds from partial foot amputations; 27 individuals in the sample received revascularisation before their surgery to improve oxygen perfusion to the wound. Patients had a mean of 20 treatments of HBOT.

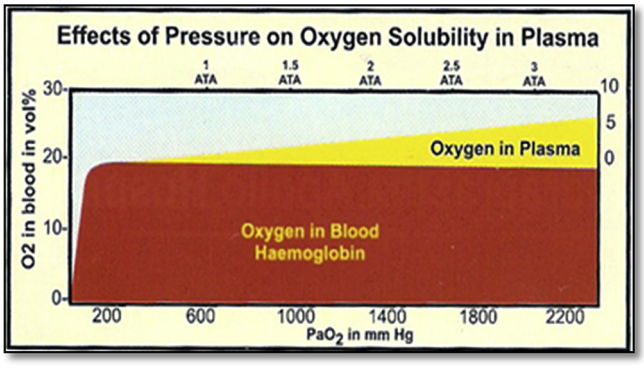

Fig. 2 – Physiological basis of hyperbaric oxygen therapy.

Seventy per cent of the sample had a successful course of treatment, meaning that their wound completely healed and their further amputation risk decreased. Each of the studies resulted in improved wound healing with HBOT in conjunction with standard wound care therapy, such as dressings and ointments. Each study also concluded that the use of HBOT saves overall cost by reducing the need for further medical treatments to improve or eliminate the wound, such as surgical incision and drainage, debridement or amputation.[14]

6.1. *Side effects*

HBOT is a safe treatment with several potential side effects such as pressure related traumas (barotraumatic otitis, pneumothorax) and adverse effects due to oxygen toxicity (seizures, pulmonary toxicity). Some patients may experience claustrophobia due to the confined space of the treatment chambers. However, pulmonary oxygen toxicity occurs very rarely. Hypoglycemia is also a complication of HBOT. However, the mechanism underlying this phenomenon is not completely understood. To minimize chances of side effects, patients should be screened thoroughly and monitored during their treatment to achieve maximum beneficial effects.[10]

6.2. *Contraindications*

The only absolute contraindication is untreated pneumothorax. Relative contraindications include pulmonary conditions – COPD, Asthma, URI etc, uncontrollable seizures, pregnancy, high grade fever >102 °F, some medications e.g. Cisplatin, doxorubicin, bleomycin, disulfiram, not approved implanted pacemaker and claustrophobia.

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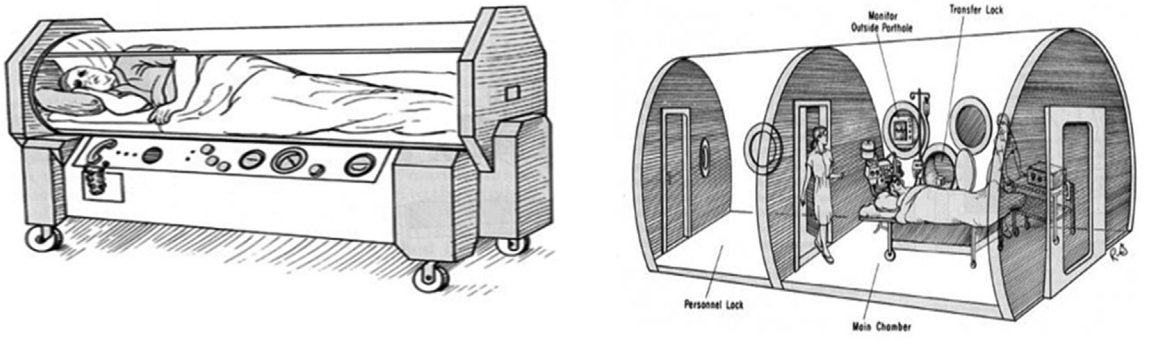

Fig. 3 – Method of administration of Hyperbaric oxygen therapy.

7. Utilization review and cost benefit analysis

The initial treatment schedule is dictated by severity of disease process. The presence of limb threatening infection after debridement or peripheral arterial occlusive disease, patient may require twice daily treatments. Once stabilized, treatment frequency may decrease to once daily. Measurement with Tcpo2 predicts the response to HBOT.

Addition of hyperbaric oxygen to conventional treatment leads to significant reduction in overall costs of treatment due to lesser stay in hospital and shorter course of illness. HBO helps preserve a functional extremity and reduce high cost of disability from amputation.

8. Discussion

As the number of people with diabetes rises worldwide, there can be little doubt that the burden of diabetes-related foot problems will increase in future years, particularly given that at least one in 10 people at the time of diagnosis of type 2 diabetes has risk factors for foot damage. Today, nearly 246 million people worldwide are diagnosed with diabetes, with India accounting for almost 45 million of those diagnoses. This number is expected to increase to 73 million by the year 2025 and India was deemed the diabetic capital of the world at the International Diabetes Federation Conference in Copenhagen in November 2006.[1] Diabetes is associated with a plethora of complications with foot ulcerations being the most common. An estimated 15% of all patients suffering with diabetes will develop foot ulcers and about half of these ulcers will become infected resulting in 20% of patients left to face some form of a lower extremity amputation.[1]

Fig. 4 – Transcutaneous oximetry.

The physiology that results in ulceration in the diabetic foot has been extensively reviewed. A non-healing diabetic foot ulcer is a result of multiple systemic and local factors, which contribute to inhibition of tissue repair like loss of nociceptive and autonomic nerves results in a dry, hyperkeratotic surface that is subject to mechanical cracking, infection, and tissue destruction. Local ischemia, age, and tissue reinjury result in chronic, non-healing wounds that remain a portal of entry for deep-tissue infection.

The basic mechanism is interplay between hypoperfusion and infection leading to decreased fibroblast proliferation, collagen production, and capillary angiogenesis and also impairs bacterial killing by polymorphs. Tissue oxygen tensions of such wounds usually measure as low as 20 mmHg. Modest improvements like HBOT restores these values to normal or higher values enhancing epithelialisation, fibroplasia, collagen deposition, angiogenesis, and bacterial and therefore substantially impacting costs, largely because of the avoidance of major amputation.[2–4]

In tertiary care, primary care physicians are the principal managers of the healthcare of patients with diabetes and, along with surgeons, are responsible for more than 70% of referrals for HBOT. Yet only 10% of the physicians exhibit good knowledge of HBOT, which can be limb salvaging therapy for some patients. Improved knowledge of HBOT could encourage physicians to consider HBOT as a treatment option for their patients.

The diabetic foot is a major healthcare concern on a worldwide scale. The implementation of a multi-disciplinary team and interventions like HBOT brings us one step closer in treating and preventing the deleterious effects of this arduous disease.

Other wounds where HBOT can be useful

- Problem wounds
- Vascular insufficiency ulcers
- Clostridial myositis & myonecrosis (Gas gangrene)
- Refractory osteomyelitis

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- Necrotizing soft tissue infections
- Crush injury
- Acute traumatic ischemia
- Compartment syndrome
- Skin grafts and flaps (Compromised)
- Thermal burns

9. Conclusion

Adequate tissue oxygen tension is an essential factor in wound healing. Diabetic foot wounds are ischemic frequently and adequate oxygen levels can be reached only through adjunctive HBOT. Oxygenation fuels the cellular function essential to the tissue repair process. HBOT shortens healing time, and helps in preserving limbs thereby reducing overall costs. Employing advanced wound care technologies in a directed and appropriate way can significantly enhance diabetic wound healing efforts. As part of a multidisciplinary program of wound care, HBOT is cost effective and durable.

Conflicts of interest

All authors have none to declare.

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The team work and the multidisciplinary approach in tackling Diabetic Foot has helped us to understand this problem better resulting in excellent outcomes for the patients.

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