Hyperbaric oxygen therapy in the management of diabetic lower limb wounds

Ong M

ABSTRACT

Introduction: Hyperbaric oxygen therapy (HBOT) involves the inhalation of 100 percent oxygen at pressures greater than at sea level. One of the most common indications for HBOT is to aid healing of diabetic foot wounds.

Methods: All cases of diabetic foot wounds that were seen by the Hyperbaric Medicine Centre in Tan Tock Seng Hospital from May 2005 to March 2006 were analysed in terms of outcome (wound healing) after HBOT.

Results: A total of 45 cases of foot ulcers/wounds were analysed. 32 patients had a favourable outcome, giving a success rate of 71 percent. The remaining 13 (28 percent) did not have a favourable outcome to HBOT. The success rate was even more significant as a large number of these patients (34 [77 percent]) were told by their specialist that they were at high risk of a further amputation. No major complications were noted.

Conclusion: The experience of the Hyperbaric Medicine Centre in Singapore is consistent with that reported in other centres. With proper patient selection, HBOT, together with a multidisciplinary team of vascular and orthopaedic surgeons, podiatrists, infection disease physicians and endocrinologists, can help reduce the numbers and severity of amputations as well as downtime due to increased wound healing.

Keywords: amputations, diabetes mellitus, diabetic foot, hyperbaric oxygen therapy, non-healing wounds

INTRODUCTION

Hyperbaric oxygen therapy (HBOT) involves the inhalation of 100 percent oxygen in a chamber at pressures greater than at sea level. In addition to its use in treating decompression illness and gas embolism, there are 13 other clinical indications recognised by the Undersea and Hyperbaric Medicine Society (Table I). These indications have also been adopted by the Ministry of Health in Singapore. The Hyperbaric Medicine Centre in Tan Tock Seng Hospital was set up in 2002. This was followed by another hyperbaric centre in Camden Medical Centre in 2004. A third centre will be established in another local hospital soon. One of the most common indications for HBOT is diabetic foot wound healing and limb salvage. This article hopes to share some of the recent experiences of the Hyperbaric Medicine Centre in the treatment of diabetic foot wounds.

METHODS

A cross-sectional study was done for all cases of foot ulcer/wounds that were seen by the centre from May 2005 to March 2006. They were analysed in terms of outcome after commencement of HBOT. All cases of foot wounds in diabetic patients that were referred to the centre were included. The main source of referral was from Tan Tock Seng Hospital, and the other restructured hospitals in Singapore.

Cases were excluded from the outcome analysis if less than five treatments were completed, or if treatment was aborted. Of the cases that were analysed, they were divided into a favourable outcome group and treatment failure group. Favourable outcome was defined as either achieving 80% or more granulating tissue, or partial/complete epithelisation one week upon completion of the prescribed HBOT sessions. Treatment failures were defined as wounds with no signs of reduction of inflammation, wound contracture or any increase in granulation tissue after a course of treatment.

All patients were given 100% oxygen at 2.5 ATA for 90 minutes daily, five days a week, with a break over the weekend. Records of outcome were done by periodic measurement of the wound and by taking a photograph of the wound. Wound culture, appropriate antibiotics, appropriate dressing material, wound debridement, and pressure relief precautions were all concurrently instituted. Nutrition and diabetic control were optimised.

RESULTS

A total of 55 cases of foot ulcers/wounds were seen at the centre. Except for five patients who had long-standing
venous/vasculitic ulcers, all the patients had diabetic foot wounds. The mean age of the patients was 59 years, with the oldest being 78 years and the youngest being 26 years of age. The median number of treatments was 20, with a range of 7–30. The five cases with venous/vasculitic ulcers were excluded, as were another five cases with less than five treatments. Two died shortly after commencement of treatment, one proceeded to go for below knee amputation after only five treatments on order of the surgeon, while two received less than four treatments as a trial of hyperbaric oxygen.

The remaining 45 patients completed the prescribed course of treatment and their outcome were analysed. Of these patients, 25 (56%) had either a ray amputation, or a forefoot amputation with a non-healing wound, prior to the commencement of HBOT. Two (4%) patients had a below knee amputation prior to the treatment, and the remaining (40%) had a variety of problematic wounds, including heel ulcers, necrotising infections of the leg and wounds at the midfoot. Of the 45 patients who completed the course of treatment, 32 of them had a favourable outcome, giving a success rate of 71%. The remaining 13 (29%) did not have a favourable outcome to HBOT. The success rate was even more significant as a large number of these patients (34 [77%]) were told by their specialist that they were at a high risk of a further amputation (above/below knee) despite already having had one amputation.

Using the Statistical Package for Social Sciences version 6.0 (SPSS Inc, Chicago, IL, USA) to analyse the subgroups of patients with and without a palpable dorsalis pedis pulse, and their success rate, we found that although there was no statistical difference detected in the outcome between those that had a palpable dorsalis pedis pulse and those that did not, the trend was that a patient who had a dorsalis pedis pulse had two times the success rate compared to those without (Table II). There were no major complications recorded, such as oxygen toxicity, pulmonary barotrauma or pneumothorax. Some patients had some ear pain as a result of a mild (Teeds 1–2) middle ear barotraumas, which resolved spontaneously. One patient had a painless ruptured tympanic membrane in the left ear. None had their treatment terminated because of claustrophobia.

**DISCUSSION**

HBOT for the use of non-healing wounds in the lower extremity is well documented by numerous case series and at least 13 controlled trials, of which six were randomised controlled studies. Although the wounds encountered are largely diabetic/ischaemic, its usefulness has also been shown in other types of lower extremity non-healing wounds. In a non-healing wound, the tissue is often hypoxic. This hypoxia can be due to ischaemia as a result of macrovascular or microvascular disease, or other complications such as infection and oedema, causing reduction in the local oxygenation. The role of oxygen in wound healing has been elucidated by many in vivo and animal studies. The increase in the tissue oxygenation of the hypoperfused, infected wound induces significant positive changes in the wound repair process by enhancing fibroblastic replication, collagen synthesis and neovascularisation. It also increases leucocyte bacteriocidal activity and exerts a direct lethal effect on anaerobic organisms.

Our experience showed that the success rate after completion of a course of HBOT is 71%. In an earlier unpublished study report for cases seen in the same centre

---

**Table I. Clinical indications for hyperbaric oxygen therapy listed by the Undersea and Hyperbaric Medicine Society.**

<table>
<thead>
<tr>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air gas embolism</td>
</tr>
<tr>
<td>Carbon monoxide poisoning</td>
</tr>
<tr>
<td>Clostridial myonecrosis</td>
</tr>
<tr>
<td>Crush injury</td>
</tr>
<tr>
<td>Decompression sickness</td>
</tr>
<tr>
<td>Enhancement of healing in problematic wounds</td>
</tr>
<tr>
<td>Exceptional blood loss</td>
</tr>
<tr>
<td>Necrotising soft tissue infection</td>
</tr>
<tr>
<td>Osteomyelitis (refractory)</td>
</tr>
<tr>
<td>Radiation tissue damage (osteoradionecrosis)</td>
</tr>
<tr>
<td>Skin graft and flaps (compromised)</td>
</tr>
<tr>
<td>Thermal burns</td>
</tr>
<tr>
<td>Adjunctive hyperbaric therapy in intracranial abscess</td>
</tr>
</tbody>
</table>

**Table II. Subgroup of patients with and without dorsalis pedis pulse and their success rates.**

<table>
<thead>
<tr>
<th>Dorsalis pedis pulse</th>
<th>Favourable (%)</th>
<th>Non-favourable (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td>Absent</td>
<td>12</td>
<td>8</td>
</tr>
</tbody>
</table>

\( p = 0.14 \)
prior to May 2005, out of 32 patients who completed the prescribed course of treatment, 29 experienced a positive outcome, while three did not heal satisfactorily and subsequently had further amputations. Again, this success rate is especially significant as many of these patients have already been told that they would otherwise have required another amputation. These results are in agreement with those reported in other studies, which success rates range from 70% to 95%. In a prospective controlled clinical trial involving diabetic foot patients, Baroni et al showed that the wounds of 16 out of 18 patients (89%) treated with HBOT healed, compared to one out of ten control patients (10%).

Oriani et al showed that for patients with grade 3 and 4 diabetic feet, the HBOT group achieved a 96% healing rate, whereas the non-HBOT group achieved a 66% healing rate with a 33% amputation rate. Similarly, Oriani et al showed that in grade IV lesions (Wagner’s classification), the HBOT group had an amputation rate of 13.9%, versus 47% for the control group (p = 0.005). Similar results were achieved by Wattel et al and Zamboni et al. Randomised controlled trials by Hammarlund and Sundberg, Leslie et al, Abidia et al, Faglia et al, Doctor et al and Kessler et al also achieved similar results.

In a large retrospective case control study by Stone et al, 501 consecutive patients with diabetes mellitus and ischaemic wounds were grouped by treatment modality: HBOT (n = 119) versus conservative treatment alone (n = 382). The patients referred for HBOT were substantially sicker than those treated with standard care, with larger and more wounds per patient. Despite this, in the HBOT group, the rate of limb salvage was significantly better (72% vs. 53%, p < 0.002) (Table III). Our study also showed the same findings, 34 out of 45 were told that they were at risk of another amputation, or a higher initial amputation (below/above knee amputation). Infection can worsen pedal ischaemia by increasing tissue demand for oxygen, which can overwhelm a marginal blood supply, and even good blood flow on occasion. 55% of our cases had wounds that were infected and were deteriorating despite treatment with antibiotics and surgical debridement, and in spite of adequate foot pulses and circulation. Infection aggravates pedal ischaemia by increasing tissue demand for oxygen to as high as 20 times. This results in a relative reduction of oxygen transported in a marginal blood supply, causing the wound to become ischaemic and subsequently, turn gangrenous or necrotic. The immediate role of HBOT, in addition to ensuring survival of the at-risk tissue in the infected wound bed, increases the effect of antibiotics and the white blood cells.

Although not statistically significant, one point worth noting is that clinically, a patient with a relatively intact peripheral blood supply will respond better to HBOT. In our case series, patients with a palpable dorsalis pedis pulse were two times more likely to succeed than those without. A fair number of our cases that responded favourably (12 out of 32, 38%) had an absent dorsalis pedis pulse. Patients with correctable large vessel obstruction would benefit from angioplasty or a revascularisation surgery, wherever possible before HBOT is started. However, such procedures may not always be possible because of high operative risk, non-correctable diffuse peripheral vascular diseases or a comorbidity, such as end-stage renal failure. In spite of adequate pulses and large vessel perfusion, some diabetic patients still develop wounds that appear to be hypoxic/ischaemic and fail to heal. There are also functional abnormalities of the microcirculatory system in diabetic patients that may impair local blood flow and oxygen delivery, thus delaying wound healing. Associated mechanical trauma may also play a role. In such cases, the use of HBOT can be as an adjunct after vascular intervention to ensure wound healing, especially for some wounds that still heal poorly after vascular procedures.

The mean number of treatments was 20. One of the long-term effects of HBOT is neovascularisation of hypoxic wounds. In vivo as well as in vitro animal and human studies have shown that this takes place after 15 treatments. From the socioeconomic perspective, there was a fairly even mix of the different ward classes in our study. Part of the payment could be covered by Medisave and also through a 24-month interest-free installment period. The very poor patients were not deprived of any treatment, as the medical social worker provided assistance. On the other hand, the cost associated with a major amputation includes hospital admission fees, actual amputation procedures, repeated debridements, antibiotic treatment,
subsequent wound care, readmission, rehabilitation, prosthesis and after-care as well as intangible costs such as psychological depression. Although our study did not look at the cost-effectiveness of HBOT, compared to major lower limb amputations in our local context, studies conducted overseas suggest that HBOT and limb salvage may reduce the costs associated with a major amputation.  

HBOT is generally safe. The incidence of temporary oxygen-induced seizures is about one in 10,000. In our nine-month study period, we only experienced one case of oxygen seizures. The most common incident is aural barotrauma, but most cases were mild Teeds 1-2 grade type of middle ear barotrauma. One patient had a painful rupture of the tympanic membrane. In our centre, there was no case of claustrophobia that was severe enough to terminate the treatment. This can likely be attributed to the size of the hyperbaric chamber, which is big enough to accommodate three persons, as well as the transparent acrylic casing, which creates the impression of a more spacious chamber. (Fig. 1).

![Photograph shows a Perry Sigma II-3 Hyperbaric Chamber (USA) used in Tan Tock Seng Hospital.](image)

Diabetic foot wounds remain the main reason for non-traumatic amputation of the lower limb. Our experience, and those of other international studies, have shown that the success rate of HBOT in properly-selected patients can be as high as 70%-80%. With proper patient selection, HBOT, together with a multidisciplinary team of vascular surgeons, orthopaedic surgeons, podiatrists, infectious disease physicians, and endocrinologists, can help reduce the number and severity of amputations, as well as reduce downtime resulting from delayed wound healing and its complications, such as prolonged immobilisation and repeated infections. It may also be cost-effective when measured against outcomes such as cost of amputations, repeated debridement, hospital stay, after-care, and social and psychological disability. More studies will be needed in our local context to assess the economic impact of HBOT. It is hoped that this local experience will be of use in giving physicians a better appreciation of the use of HBOT for non-healing wounds and limb salvage.

**REFERENCES**


---

2008 SMJ Best Research Paper Awards

The Singapore Medical Association will be presenting awards for the Best Research Paper published in the Singapore Medical Journal (SMJ) in 2008. All original research papers that are published in the SMJ during the one year period from January 1, 2008 to December 31, 2008 will be considered for this award.

The following are the judging criteria:
- The paper with the most potential impact on clinical practice
- Most rigorous study design/research methodologies
- Comprehensive data analysis and balanced discussion
- Data interpretation

Distinguished members of the medical profession will be invited to serve on our panel of judges for selecting the winning papers.

The authors of the winning papers selected by our panel of judges will receive cash prizes for the first, second and third places. Prize winners will also receive a commemorative trophy and certificate.

We thank you for your support of the SMJ. The quality of our journal depends on the quality of your submissions.