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Effect of normobaric hyperoxic therapy on tissue oxygenation in diabetic feet: A pilot study☆

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Summary Adequate tissue oxygenation is an essential factor in diabetic foot management. Hyperbaric oxygen (HBO) therapy has been successfully used as adjunctive treatment to improve the healing of diabetic foot ulcers. However, the clinical uses of HBO therapy are limited due to the low availability of HBO chambers, poor patient compliance, and high oxidative potential. Normobaric hyperoxic (NBO) therapy may be a potentially attractive alternative to HBO therapy because of its high availability, good patient compliance, and few technical requirements. Several studies on NBO therapy to attenuate infarct volume after stroke have provided compelling evidence. However, there have been no reports regarding the effect of NBO therapy in the field of wound healing. The purpose of this study was to evaluate the effect of NBO therapy on tissue oxygenation of diabetic feet. This study included 100 patients with diabetic foot ulcers (64 males and 36 females). Transcutaneous partial oxygen tension ($TcPO_2$) values of diabetic feet were measured before, during, and after NBO therapy. The mean $TcPO_2$ values before, during, and after therapy were 46.6 ± 21.5, 88.9 ± 48.0, and 49.9 ± 23.8 mmHg ($p < 0.001$), respectively. The lower the initial $TcPO_2$ level, the more $TcPO_2$ increased. The results reveal that NBO therapy significantly increases the tissue oxygenation level of diabetic feet.

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Introduction

Adequate tissue oxygenation is an essential factor during diabetic wound healing.[1] Improving tissue oxygenation with hyperbaric oxygen (HBO) therapy has been a reasonable therapeutic strategy with a relatively low risk of complications.[2–4] The current literature suggests that HBO therapy is effective for increasing blood and tissue oxygenation in the management of diabetic foot ulcers. Increasing oxygen levels in hypoxic tissues may help maintain cellular function and integrity, thereby contributing to wound healing.[5–8] Therefore, HBO therapy is used as an adjunctive therapy to treat several clinical conditions associated with tissue hypoxia such as severe soft tissue infections and ischemic diabetic foot ulcers.[9] However, clinical applications of HBO therapy are limited by high cost, low availability of HBO chambers, need for trained personnel to monitor patients, poor patient compliance because of headache and otalgia, and the possibility of high oxidative potential contributing to pulmonary edema and brain injury.[10] The occurrence of oxygen-toxic seizures after HBO therapy has also been reported.[11] Cardiopulmonary, nephrologic, and neurologic comorbidities may be more frequent in patients with diabetic foot ulcers, who commonly have a poor general health condition. In addition, many patients with diabetic feet have difficulty moving to a HBO chamber or may have claustrophobia. For these reasons, the use of HBO therapy has been limited in patients with diabetic feet.

Normobaric hyperoxic (NBO) therapy, which requires increasing the fractional inspired oxygen to almost 100% at normobaric pressure, has gained great interest in the treatment of cerebral ischemia.[12–16] Several animal and clinical studies on NBO therapy as adjuvant treatment to attenuate infarct volume after stroke and to improve functional outcomes after brain trauma have provided compelling evidence in the past years. NBO therapy is a potentially attractive alternative to HBO therapy because of its high availability, good patient compliance, cost-effectiveness, decreased complications, and few technical requirements.[17] However, no reports regarding the effect of NBO therapy on its potential to contribute to wound healing have been published. The purpose of the study was to evaluate the effect of NBO therapy on tissue oxygenation of diabetic feet.

Patients and methods

This study protocol was approved by the Institutional Review Board of Korea University Guro Hospital. Additional written informed consent was obtained from all patients included in the study. This study was performed in full accordance with the Declaration of Helsinki.

We included 100 patients with diabetic foot ulcers (64 males and 36 females), with a mean age of 63.2 ± 12.9 years (range, 27–90 years) and a duration of the diagnosis with diabetes of >5 years, who were admitted to the Diabetic Wound Center of Korea University Guro Hospital between June 2012 and May 2013.

Transcutaneous partial oxygen tension ($TcPO_2$) of the foot was measured before, during, and after NBO therapy to evaluate tissue oxygenation using a PF 5040 $TcPO_2$ (PeriFlux System 5040; Perimed AB, Stockholm, Sweden) and the PeriSoft program (Perisoft for Windows 2.50; Perimed AB). A $TcPO_2$ sensor was fixed on the dorsum of the foot adjacent to the ulcer with the patient in the supine position. Even if an ulcer was present on the plantar aspect, $TcPO_2$ was always measured on the dorsum of the foot in the area directly opposite the lesion. $TcPO_2$ levels were recorded at 44 °C after a 15-min equilibration period. The initial $TcPO_2$ level was measured with patients breathing room air (21% oxygen). As the effects of edema and hyperemia on $TcPO_2$ measurements remain controversial, patients with wound infections or cellulitis were excluded from this study.

NBO therapy was administered to the patients through a mask under a condition of 98% oxygen (oxygen flow was 13 L/min with gas overflow) supplied via a mechanical nebulizer (Respiflo®, Tyco Healthcare, Hampshire, UK) with constant monitoring of the $TcPO_2$ levels until the $TcPO_2$ level reached a stable plateau (Figure 1). After discontinuing inhalation of 98% oxygen, the patients breathed room air (21% oxygen) again until the $TcPO_2$ level reached a plateau. The $TcPO_2$ levels before, during, and after NBO therapy were compared. The times required to reach a plateau after the 98% oxygen inhalation and that after discontinuation of the therapy were measured.

In addition, patient data were divided into two subgroups according to their initial $TcPO_2$ values: ≥40 mmHg and <40 mmHg. The results were analyzed separately.

Repeated-measures analysis of variance was used to detect significant differences. All statistical analyses were performed using SPSS for Windows, ver. 12.0 (SPSS, Inc., Chicago, IL, USA).

Results

The NBO therapy augmented $TcPO_2$ levels in all patients. Of the 100 feet, 92 revealed marked improvements in $TcPO_2$ values (>10 mmHg) and eight feet showed a slight increase (0.7–10 mmHg). The average $TcPO_2$ value before NBO therapy was 46.6 ± 21.5 mmHg. The $TcPO_2$ value increased to 88.9 ± 48.0 mmHg during therapy, representing an increase of 190.8% ($p < 0.001$). The mean $TcPO_2$ value decreased to 49.9 ± 23.8 mmHg after discontinuing

Figure 1 Measurement of transcutaneous partial oxygen tension ($TcPO_2$) during normobaric hyperoxic (NBO) therapy.