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Research Article

Hyperbaric oxygen therapy of diabetic foot ulcers: a pilot study

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Abstract

Introduction: Ulcers caused by a diabetic foot are among the most common and serious complications of diabetes mellitus and lead to severe medical and social consequences for individuals and society. Their treatment should be complex and individualized, given the complex etiology and pathogenesis of this type of lesion. One of the established complementary methods in therapy is the application of oxygen by inhalation under high pressure (above atmospheric) or the so-called hyperbaric oxygenation.

Aim: This study aims to evaluate the effect of hyperbaric oxygen therapy on the treatment of diabetic ulcers.

Materials and methods: This pilot study was conducted from October 2024 to January 2025. The study group comprised 15 patients (10 males and 5 females) diagnosed with diabetic foot ulcers. All participants underwent hyperbaric oxygen therapy as a complementary treatment. Blood sugar levels, wound area, Wagner score, and pain level were followed up before and after therapy.

Results and discussion: Regarding blood sugar levels, no definitive evidence was found to confirm or rule out the influence of hyperbaric oxygenation. A statistically significant difference was observed in the mean wound area values before therapy (20.46±16.12 cm^2) and after 10 HBO sessions (11.38±10.58 cm^2) (p=0.019). The mean Wagner score prior to therapy was 2.92, and after the 10th session it was 2.00, p=0.014. The difference in pain perception before and after hyperbaric oxygenation therapy was statistically significant (p<0.0001) with an effect size r=−0.99.

Conclusions: Hyperbaric oxygen has a positive effect as an adjuvant therapy in the treatment of patients with diabetic foot ulcers. Due to the small sample size and number of sessions, more in-depth and large-scale clinical studies are needed to confirm the results.

Keywords

hyperbaric oxygenation, diabetic wounds, pain, Wagner score

Introduction

Diabetes mellitus (DM) is a disease of significant social concern both nationally and globally, characterized by increasing morbidity and mortality rates. In Bulgaria, the latest data from the Diabetes Registry indicate that over half a million people live with this diagnosis, with approximately 3,500 people developing peripheral vascular complications.[1] Diabetic foot is a serious complication of DM, characterized by chronic ulcers, infections, and an

increased risk of amputations. This condition arises from a complex interaction of factors, including neuropathy, peripheral arterial disease, foot deformities, and infections. The treatment of these lesions poses significant challenges due to the presence of peripheral neuropathy, macro- and microangiopathy, and impaired immune response. Diabetic microangiopathy is a prerequisite for impaired capillary function and increased capillary distance.[2] Reduced immune function and elevated blood glucose levels increase the likelihood of infections, primarily caused by gram-positive and gram-negative aerobes, which are more likely in these types of wounds.[3] Peripheral neuropathy leads to decreased sensation, callus formation, reduced microcirculation, and other pathomorphological and pathophysiological changes that contribute to the formation of diabetic ulcers.

Diabetic lesions are intrinsically challenging to treat because of their multiple genesis, demanding both conventional and adjuvant therapies. Surgical procedures such as incisions, fasciotomies, and amputations are examples of conservative treatments. The use of various dressings and antiseptics, both conventional and modern, is required. Relieving pressure in the foot area through the use of appropriate shoes and aids, and maintaining good skin hygiene, is essential. Adjuvant therapies encompass local oxygen therapy, negative pressure treatment, platelet-rich plasma applications, growth factor utilization, copper dressings, ozone therapy, and hyperbaric oxygenation (HBO). HBO therapy involves intermittent inhalation of 100% oxygen in chambers under pressure above 1 absolute atmosphere (1 ATA). Pharmacologically, this therapy is characterized as a short-term intervention aimed at delivering high doses of oxygen.[4] In the context of diabetic foot treatment, hyperbaric oxygen therapy exerts beneficial effects in terms of hypoxia of ulcerated tissues by increasing fibroblast proliferation and collagen production, enhancing leukocyte activity (increasing phagocytic activity and synthesis of reactive oxygen species with a bactericidal effect), and accelerating the processes of epithelialization and neoangiogenesis (activating HIF 1α and VEGF).[5]

Aim

This study aims at investigating the impact of HBO therapy on patients suffering from diabetic ulcers.

Materials and methods

The study design is a clinical, quasi-experimental, and prospective investigation aimed at assessing the impact of HBO on the healing process of diabetic wounds.

Sample selection

The study included 15 patients (10 men and 5 women) with diabetic foot ulcers. They first underwent HBO therapy as a complementary treatment between October 2024 and January 2025. The inclusion criteria were age 18 years or older, no contraindications for HBO therapy, and a Wagner score for diabetic ulcers ranging from 2 to 4. Exclusion criteria included individuals under 18 years, those classified as Wagner score 0, 1, and 5 of diabetic foot, and patients with contraindications such as pneumothorax, mental illness, or severe decompensated heart and lung diseases. Conventional treatment included standard iodine dressings (86.6%) and hydrocolloid and absorbent dressings (13.4%). Half of the patients (53.3%) underwent surgical debridement with drainage, and one-third (33.3%) received antibiotic treatment according to the etiological agent.

Monitored signs (regarding therapy)

The parameters monitored throughout the treatment included pain levels, blood glucose levels, ulcer area, and the degree of chronic lesions.

Procedure

The technical specifications of the utilized hyperbaric chambers comprise an OxyOne chamber accommodating four individuals located in Pazardzhik (Hyperbaric Center), and another OxyOne chamber that accommodates eight individuals situated at St George University Hospital in Plovdiv. The working pressure for these chambers is set at 2.46 ATA with a permissible maximum pressure of 3.45 ATA. In the analyzed sessions, the operating pressure was 2.3 ATA. Patients undergo ten sessions, five days a week, with breaks on Saturday and Sunday. The operating mode is set at 2.3 ATA with a total duration of 80 minutes, of which 50 are allocated for breathing oxygen. Two 5-minute breaks are taken for breathing only air, in order to avoid oxygen intoxication. Ten minutes are allocated for compression and ten minutes for decompression. Patients inhale through an oxygen mask with a balloon reservoir.

Safety protocol

All study participants received oral safety training. This encompassed the permitted items in the hyperbaric chamber, how to behave in the event of an accident, and when to take medications and other substances. Patients were trained in pressure equalization techniques such as the Valsalva maneuver. All participants signed two informed consents: one for the hyperbaric chamber and one for the study. None of the patients were unconscious. During the sessions, drains were opened, peripheral venous cannulas were closed, and urethral catheters were clamped. No complications or incidents were reported during or after the sessions. The most commonly reported adverse reaction was tinnitus.

Statistical analysis

To evaluate the equality of mean blood glucose levels before and after each of the 10 HBO sessions, as well as the wound area (measured in cm^2), a *t*-test for related samples was employed, predicated on the normal distribution of values due to the limited sample size (N=15).[6] The normality of the data was confirmed using the Kolmogorov-Smirnov test. The Wagner score and the rank variables related to the verbal pain assessment scale, recorded before and after the tenth HBO session, were analyzed through the Wilcoxon signed-rank test for related samples. Pain levels were categorized as follows: 0 for no pain, 1 for weak pain, 2 for moderate pain, and 3 for severe pain. Cases of amputation were not included in the wound area and Wagner score analyses. Central tendencies were reported as the arithmetic mean ($\bar{X}$) and standard deviation (SD), while analysis of rank variables was depicted as mode (Mo) and median (Me). A significance level of α=0.05 was established for statistical tests. The IBM SPSS v. 23 statistical package was used for the statistical analyses.

Results

The study included 15 participants, comprising 10 men and 5 women, with a mean age of 65.67±8.93 years, ranging from 51 to 78 years old. During the study period, three participants underwent amputation, resulting in missing values for the Wagner score and wound area after supplemental HBO therapy.

All variables representing blood glucose measurements taken before and after each HBO session (a total of 10 sessions, yielding 20 variables) demonstrated a normal distribution, with *P* values greater than 0.05. The Wagner score and wound area measurements, both before and after HBO therapy, followed a normal distribution (p>0.05).

The average blood sugar levels are lower following therapy, with five out of ten sessions demonstrating a statistically significant difference **(Table 1)**. These significant sessions are not concentrated within a specific timeframe during the study period. Specifically, for the 2nd, 3rd, 5th, 6th, and 10th sessions, we have sufficient grounds to reject the null hypothesis and accept the alternative one, which suggests hyperbaric chamber sessions effectively lower blood sugar levels. Conversely, for the remaining sessions, we lack sufficient evidence to make a similar inference.

Table 1. Blood sugar values before and after each HBO session

HBO session	Before $\bar{X}$±SD, mmol/L	After $\bar{X}$±SD, mmol/L	*p*
1	11.85±4.33	11.05±3.52	0.053
2	11.61±3.51	10.26±2.29	**0.042**
3	10.82±3.66	9.57±2.99	**0.005**
4	10.61±3.56	9.70±3.62	0.159
5	10.36±2.07	8.92±1.75	**<0.0001**
6	9.78±2.98	9.21±3.06	**0.033**
7	9.49±3.82	8.99±2.32	0.393
8	11.17±3.06	10.31±2.67	0.052
9	9.79±1.99	9.33±1.83	0.143
10	10.64±2.24	9.11±1.45	**<0.0001**

A statistically significant difference was observed in the mean wound area values before therapy and after the 10th HBO session, with a *p*-value of 0.019. The mean wound area before therapy was measured at 20.46±16.12 cm^2 (N=12), while after the 10th HBO session, it decreased to 11.38±10.58 cm^2 (N=12). The effect size d=0.79[6] can be regarded as significant. A significant positive correlation was identified between the wound size before and after HBO therapy, with p=0.011.

The mean Wagner score prior to therapy was 2.92 (N=2), whereas after the 10th session, it decreased to 2.00 (N=12). Although no correlation was identified between the Wagner scores before and after therapy, the Wilcoxon signed-rank test for related samples showed a statistically significant difference (p=0.007) in the scores. The effect size r=−0.78[6] can be considered substantial.

Prior to the study, all patients reported experiencing pain, with seven individuals suffering from severe pain and eight from moderate pain. The median (Me) and mode (Mo) values were both 2 (moderate pain). Following the therapy, the median decreased to 1 (indicating weak pain), and the mode values were 1 (weak pain) and 2 (moderate pain). One patient reported no pain, while 7 reported weak pain and 7 reported moderate pain. Notably, no participants experienced severe pain after HBO therapy. The calculated effect size[6] was r=−0.99. The difference in pain perception before and after HBO therapy was statistically significant (p<0.0001) with an effect size much larger than usual.

Discussion

The European Committee for Hyperbaric Medicine (ECHM) recommends HBO for diabetic foot with Wagner classifications ≥3 when there is no improvement after 30 days of standard therapy.[7] The therapy is protocolized according to recommendations for a specific number of sessions under the appropriate pressure. The American Undersea and Hyperbaric Medical Society (UHMS) sets similar indications.[8] The results of these recommendations are supported by studies of various types, which focus on reducing wound area and Wagner score, as well as monitoring the healing process itself. When it comes to chronic lesions, the initial results of the therapy's effect can be precisely measured by these indicators. A systematic review of 14 studies published in 2024 showed that HBO doubles the probability of complete healing after 8 weeks or more and reduces the risk of major amputations by 69%.[9] Another pooled analysis of 20 randomized clinical trials confirmed a higher rate of healing and a shorter time to epithelialization.[10]

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The obtained results regarding the healing processes leading to a reduction in wound surface show similar findings to those reported in the studied literature. Hyperoxygenation leads to increased oxygen dissolution in the plasma, which enhances its diffusion to a depth of up to 400 μm beyond the capillaries, helping to overcome local ischemia.[11] A review of the literature, which focused solely on randomized trials, demonstrated the effectiveness of HBO in preventing major amputations.[12] In a randomized, prospective study involving 50 patients in the experimental group, 33 patients experienced healing without the need for surgical intervention, while the remaining patients underwent minor amputations after receiving more than 30 sessions of treatment.[13] Löndahl et al. reported comparable results from a study with a similar sample size and number of sessions conducted in a barochamber, and they also highlighted improvements in the patients' quality of life.[14]

HBO therapy has been shown to influence blood sugar levels in plasma, particularly in patients with diabetes mellitus. Several studies have investigated the effects of HBO on blood glucose levels, with varying results. A study by Zakiyah and Anggraini found that HBO significantly reduced blood glucose levels in diabetic patients, with average levels dropping from 229 mg/dL to 159 mg/dL after treatment.[15] Ekanayake and Doolette reported a significant decrease in blood sugar levels by 3.5±0.7 mmol/L during HBO in diabetic patients, although insulin dosages remained unchanged.[16] Peleg et al. noted a small but statistically significant decrease in blood glucose levels during HBO; however, this decrease was not significantly different from that observed during normobaric air sessions, suggesting that the hyperbaric environment itself may not be the primary cause of the reduction.[17] There is emerging evidence suggesting a reduction in glycaemia following hyperbaric oxygen treatment in patients with diabetes mellitus.[18] Our research suggested a potential causal relationship between the reduction in plasma glucose levels and hyperbaric chamber visits. Additional large-scale and comprehensive studies are essential to fully elucidate the strength of this relationship and the underlying mechanisms involved.

The findings from the verbal pain rating scale indicate a trend towards reduced pain intensity following HBO treatment. In a randomized trial, patients with Wagner score 3–4 diabetic wounds who underwent HBO therapy experienced a significant reduction in pain levels and an improvement in their overall quality of life.[10] Similar outcomes were reported by researchers in another randomized clinical trial, where 54 patients noted decreasing pain after treatment in a hyperbaric chamber.[19] A systematic review and meta-analysis encompassing 14 studies with over 700 patients confirmed that HBO significantly alleviates pain in individuals with diabetic wounds and accelerates the healing process.[20] The mechanisms underlying this decrease in pain intensity are attributed to the healing processes instigated by the treatment, as well as the avoidance of procedures that commonly induce pain, such as bandaging and amputations. Some studies investigate the effects of HBO on nociceptive and neuropathic pain in conditions like fibromyalgia, which would pave the way for additional research in this area.[21]

Limitations of the study

This pilot study has several limitations that should be acknowledged. The small sample size limits the statistical power and generalizability of the findings. The exploratory nature of the design also means that findings should be interpreted with caution and not as conclusive evidence. The study's limited scope focused primarily on essential indicators, leaving some variables underexplored. The absence of a control group makes it difficult to attribute observed effects solely to the intervention. Furthermore, the potential influence of confounding variables could not be fully accounted for. These limitations highlight the need for a more comprehensive follow-up study.

Conclusion

HBO is still a debated adjuvant therapy for difficult-to-heal diabetic wounds. Several studies report a positive effect, as HBO influences the healing process through different mechanisms. The reduced wound surface and the decrease in the Wagner classification score confirm the effect of only ten sessions in a hyperbaric chamber. There is no clear evidence that HBO has a direct hypoglycemic effect, due to the size of the sample and other confounding factors. HBO affects the degree of pain, not through analgesic action, but by improving tissue condition.

Ethical approval

This research was granted an approval by the Ethics Committee of the Medical University of Plovdiv (protocol No. 5/29.10.2024).

Ethical statements

The authors declared that no clinical trials were used in the present study.

The authors declared that no experiments on humans or human tissues were performed for the present study.

The authors declared that the participants signed two informed consent forms: one for the hyperbaric chamber and one for the study.

The authors declared that no experiments on animals were performed for the present study.

The authors declared that no commercially available immortalized human and animal cell lines were used in the present study.

Conflict of interest

The authors have declared that no competing interests exist.

Use of AI

No use of AI was reported.

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Author contributions

All authors have contributed equally.

Data availability

All data used are referenced or included in the article.

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