

INPLASY PROTOCOL

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None declared.

Effects of hyperbaric oxygen therapy on patients with diabetic foot ulcers: A protocol for systematic review and meta-analysis

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Review question / Objective: Diabetic foot ulcer (DFU) is a common complication of distal vascular and peripheral neuropathy caused by poorly controlled diabetes, which seriously threatens the life safety of diabetic patients. At present, the clinical efficacy of hyperbaric oxygen therapy (HPOT) for DFU is still controversial. The purpose of this study is to systematically review and meta-analyze the scientific basis of the effectiveness and clinical efficacy of hyperbaric oxygen in the treatment of diabetic foot ulcers, hoping to provide a reference for the future of this treatment, and hope to provide a reference for future research in this field.

Information sources: Comprehensive retrieval databases include the following databases: Pubmed, Cochrane Library, EMBASE, Scopus, Sinomed, Web of Science, Weipu, Wanfang Data, and China National Knowledge Infrastructure (CNKI). The retrieval time is from the establishment of the database to July 2022.

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INTRODUCTION

Review question / Objective: Diabetic foot ulcer (DFU) is a common complication of distal vascular and peripheral neuropathy caused by poorly controlled diabetes, which seriously threatens the life safety of diabetic patients. At present, the clinical efficacy of hyperbaric oxygen therapy

(HPOT) for DFU is still controversial. The purpose of this study is to systematically review and meta-analyze the scientific basis of the effectiveness and clinical efficacy of hyperbaric oxygen in the treatment of diabetic foot ulcers, hoping to provide a reference for the future of this treatment, and hope to provide a reference for future research in this field.

Condition being studied: Diabetic foot ulcer (DFU) is a common foot complication of poorly controlled diabetes mellitus (DM). Most DFU patients have similar ulcer pathways, which are caused by two or more risk factors, among which peripheral neuropathy plays a major role, followed by minor foot trauma. It can not be ignored that DM also leads to distal microvascular lesions. Insufficient blood supply due to hyperglycemia often leads to prolonged wound healing. In 2015, studies in Mainland China found that the annual incidence of DFU and amputation in DFU patients were 8.1% and 5.1% respectively. In 2019, Lin Chengwei announced that the annual prevalence of DFU in Taiwan province remained at 2%, but with the increase of DM patients, the absolute number of DFU increased by 33.4%. DFU treatment has a long duration, high cost, high mortality, and easy recurrence. After recovery, the new incidence rate of DFU patients reached 31.6% in 1 year. Untreated DFU can invade the bone below the ulcer and cause osteomyelitis, which leads to osteonecrosis and is the only choice for decaying bone or amputation, which is the majority cause of non-traumatic lower limb amputation (LEAs) worldwide. In 2010, a Chinese survey showed that diabetic feet accounted for 56.5% of non-traumatic amputations. A retrospective study in Australia found that DFU patients had a 5-year mortality rate of 24.6% and a 10-year mortality rate of 45.4%. Ashu Rastogi's multicentre cohort study revealed that one in three patients with neurological DFU had an amputation and one in six patients died early. According to statistics, more than 500 million people in the world are suffering from diabetes. In 2021, the total amount of global healthcare will be close to us \$1 trillion, and it is expected that the number of diabetes patients will reach more than 700 million globally in 2045. With the deepening aging degree, elderly patients will face higher risks of related complications.

At present, the treatment of DFU mainly includes drug therapy and physical therapy. Drug treatment is mainly for patients with a skin infection on the ulcer surface; Non-infected patients are mainly treated with

life management and wound nursing. Hyperbaric oxygen therapy (HPOT) refers to the use of pure oxygen at two to three atmospheres to raise oxygen levels in blood and tissues for antibacterial, immune regulation, and angiogenic wound healing. Currently, HPOT has approved indications for medical emergency hypoxia conditions, as well as accelerated wound healing and angiogenesis. All wound granulation requires oxygen and full exposure to pure oxygen accelerates wound healing. HPOT has been widely used in the clinical treatment of DFU. Many people believe that HPO can increase tissue oxygenation, oxygen partial pressure, local oxygen, etc. Can promote ulcer surface to heal, and prevent infection. Robert et al. 2020 clinical controlled trial surface HPTO have a good healing effect on DFU, especially in deeper ulcers. Wang Aiping et al. suggested the use of HPOT for adjuvant therapy when the DFU area did not improve after 4-6 weeks, but the recommendation was weak. On the contrary, IWGDF recommended not to use of any adjuvant therapy for DFU in 2016, and there is no definite evidence that HPOT has a therapeutic effect on DFU infection. 2019 IWGDF Guidelines update Systemic oxygen therapy as adjunctive therapy for ischemic ulcers.

Although HPTO has been used in the clinical treatment of DFU patients with good efficacy, the effect of HPOT on DFU treatment is still controversial and definitive evidence is needed.

METHODS

Participant or population: For all patients with Symptomatic or asymptomatic diabetic foot ulcers, no restrictions will be applied in terms of age, sex, race, country, and disease.

Intervention: Used basic nursing treatment plus hyperbaric oxygen treatment.

Comparator: For all patients with Symptomatic or asymptomatic diabetic foot ulcers, no restrictions will be applied in terms of age, sex, race, country, and disease.

Study designs to be included: We will include randomized controlled trials of the effect of hyperbaric oxygen therapy on patients with a diabetic foot ulcers.

Eligibility criteria: We will include randomized controlled trials of the effect of hyperbaric oxygen therapy on patients with a diabetic foot ulcers. For all patients with Symptomatic or asymptomatic diabetic foot ulcers, no restrictions will be applied in terms of age, sex, race, country, and disease. The experimental group used basic nursing treatment plus hyperbaric oxygen treatment, the control group used basic nursing treatment. The Primary Prognostic Indicators are VAS pain Scale, Wound area, Wound depth, Granulation growth, and Wound healing time. And the secondary prognostic WBC, ESR, CRP, Bacterial culture, Adverse reactions, and Efficacy evaluation.

Information sources: Comprehensive retrieval databases include the following databases: Pubmed, Cochrane Library, EMBASE, Scopus, Sinomed, Web of Science, Weipu, Wanfang Data, and China National Knowledge Infrastructure (CNKI). The retrieval time is from the establishment of the database to July 2022.

Main outcome(s): The Primary Prognostic Indicators are VAS pain Scale, Wound area, Wound depth, Granulation growth, and Wound healing time. And the secondary prognostic WBC, ESR, CRP, Bacterial culture, Adverse reactions, and Efficacy evaluation.

Quality assessment / Risk of bias analysis: Two authors (XJC and LZ) independently evaluated the risk of bias in the included studies and cross-checked the results. Disagreements were resolved by consulting a third reviewer (YCP). The quality of the included studies was assessed using the Cochrane Collaboration risk assessment tool for RCTs. The risk of bias (low, unclear, or high) was assessed based on random sequence generation, allocation concealment, blinding of

participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases.

Strategy of data synthesis: RevMan5.4 software will be used to integrate and analyze included studies. Dichotomous data will be reported as risk ratio (RR) with a 95% confidence interval (CI), whereas continuous data will be reported as mean difference (MD) or standard mean difference (SMD) with 95% CI. Results of the meta-analysis will be visualized by forest plots.

Subgroup analysis: If sufficient comparable studies are available, subgroup analysis will be conducted in terms of age, sex, intervention forms, treatment course, etc.

Sensitivity analysis: Sensitivity analysis will be performed according to sample size, study design, heterogeneous quality, methodological quality and statistical model, the trials with quality defects will be excluded to ensure the stability of the analysis results.

Country(ies) involved: Chengdu Sport University, 2 Tiyuan Road, Wuhou District, Chengdu, 610041, Sichuan Province, China.

Keywords: hyperbaric oxygen therapy; Diabetic foot ulcer; Meta-analysis; Protocol

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