Use of Transcutaneous Application of CO₂ in Diabetic Foot Pathology

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Abstract

In neuropathic foot ulcers, the most prominent finding is the loss of peripheral sensation and is typically seen in diabetic patients. In addition, vasculopathy may lead to foot ulcerations in diabetic patients. CO₂ therapy was found to improve chronic wound healing in patients with vascular impairment. It refers to the transcutaneous and subcutaneous application of CO₂ as well as CO₂ water baths for therapeutic purpose. In the method used, gaseous CO₂ is applied transcutaneously using the PVR system®. CO₂ is applied by means of a single-use, low-density polyethylene bag which is wrapped around the leg being treated and secured with an elastic strap. The advantages of this method, compared to injecting CO₂ into subcutaneous tissue, are non-invasiveness, the absence of pain and protection against infection. Compared to CO₂ balneotherapy this approach enables the use of higher CO₂ concentrations, application to chronic wound patients and, with appropriate precautionary measures, prevents the increase of CO₂ in the surrounding air. Finzgar et al. observed that the transcutaneous application of gaseous CO₂ caused a significant increase in the Laser Doppler (LD) flux in cutaneous microcirculation in vivo in humans. The favourable clinical and microcirculatory effects of gaseous CO₂ have further been observed in studies of patients with intermittent claudication as well as patients with primary and secondary Raynaud's phenomenon. The reviewed studies suggest that the increased delivery of CO₂ to the ulcerated area will cause vasodilation and an increase in blood flow. The improved angiogenesis and oxygenation will result in healing of the chronic wound. This principle may be applied in the treatment of diabetic foot ulceration. Moreover, the effect on blood flow may also be important in preventive and curative treatment of patients with impaired mobility due to organic or functional causes. Further work is needed for the development of therapeutic strategies to optimize CO₂ use in diabetic foot patients.

Keywords Carbon dioxide therapy; Microcirculation; Contralateral limb; Vasculopathy; Polyneuropathy

Introduction

Carbon dioxide therapy refers to the transcutaneous and subcutaneous application of CO₂ as well as CO₂ water baths for therapeutic purposes. CO₂ rich water bathing has been used since 1930 and was found to improve chronic wound healing in patients with vascular impairment. With neuropathic foot ulcers, the most prominent finding is the loss of peripheral sensation and is typically seen in diabetic patients. Repeated stress and lack of sensation lead to trauma, breakdown of overlying tissue and eventual ulceration. At pressure points, vascular impairment may additionally lead to ulceration.

One major goal of treatment is to improve microcirculation and thereby oxygen supply and the transport of metabolic pathway end-products. The effects of CO₂ therapies on skin microcirculation have been studied in animal models. Dulig BR [1] observed increased microvascular diameter and increased perivascular pO₂ at sites of exposure to a CO₂ aqueous solution. The increased diameter was due to the vasodilatory effect of topical CO₂, the phenomenon also known as active hyperaemia. The increased perivascular pO₂ was due to the effect of CO₂ on the oxyhemoglobin dissociation curve. Irie et al. [2] demonstrated that CO₂ immersion induced the production of plasma vascular endothelial growth factor (VEGF), resulting in no-dependent angiogenesis associated with the mobilization of endothelial progenitor cells. Hayashi et al. [3] showed that CO₂ immersion increased blood flow in feet to a much higher extent than plain water and it improved the limb salvage rate in critical limb ischemia patients without the option of revascularization. These results showed the potential role of topical CO₂ in effective adjunctive treatment to prevent diabetic ulcer exacerbation.

Materials and methods

Gaseous CO₂ with 99.995% purity (medical grade) was applied transcutaneously using the PVR system® (produced by DermaArt Ltd., Brezice, Slovenia). The PVR system consists of a compressor, a CO₂ level monitoring sensor and a conduit tube for CO₂. CO₂ was applied by means of a single-use, low-density, polyethylene bag which was wrapped around the leg being treated and tightened with an elastic strap. The 35-minute therapies are performed twice a week over a period of 5 weeks. The PVR system enables the safe and controlled application of a high concentration of CO₂ to the body. The method of application is completely safe and prevents any inhalation of CO₂. The device also has an electronic sensor system which constantly monitors the air quality in the room.

Discussion

Brandt et al. [4] studied the effect of the subcutaneous application of gaseous CO₂ in the treatment of chronic lower limb lesions. Laser Doppler flux and transcutaneous pO₂ were measured in two groups. In one group, CO₂ therapy was used in addition to the standard methods of treatment for such lesions. The patients in the control group were

treated using only standard methods. In the group that underwent subcutaneous treatment with CO\textsubscript{2}, a significant increase in tissue oxygenation values were observed. They showed progress in healing and a decrease in size of the injured area.

Finzgar et al. [5] conducted a study of the effect of the transcutaneous application of gaseous CO\textsubscript{2} on cutaneous blood flow in vivo in humans. The Laser Doppler (LD) flux in cutaneous microcirculation was measured simultaneously in a group of 33 healthy men during rest and a 35-minute CO\textsubscript{2} therapy. One lower limb of each subject was exposed to gaseous CO\textsubscript{2}. The contralateral limb was the control, being exposed to air. The CO\textsubscript{2} therapy caused a statistically significant increase in the LD flux of the studied extremity, whereas in the LD flux of the control extremity was not statistically significant. Aside from a minor decrease in heart rate, no systemic effects were found. The LD flux change is most likely an indirect sign of the successful diffusion of CO\textsubscript{2} molecules through the skin into microcirculation and a direct indicator of the vasodilatory effect of CO\textsubscript{2}.

Favorable clinical and microcirculatory effects of gaseous CO\textsubscript{2} were further observed in studies of patients with intermittent claudication [6] and patients with primary and secondary Raynaud’s phenomenon [7]. The same principle is applied in the treatment of diabetic foot ulceration. The reviewed studies suggest that CO\textsubscript{2} therapy can be a safe outpatient treatment option for patients with chronic wounds [8]. There are a number of other possible application for CO\textsubscript{2} therapy as well. Indications include intermittent claudication, peripheral artery disease and arteriolar blood flow occlusion/disorders, diabetic feet, diabetic vasculopathy and polyneuropathy, and bedsores. Contraindications include acute pyretic diseases, consumptive diseases and ulcers, severe hypertension, new cardiac infarctions, aortic and mitral valve stenosis, severe congenital heart failure, cor pulmonale, broncho pulmonary diseases accompanied by hypercapnia and acute inflammatory vascular diseases [9].

**Conclusion**

The reviewed studies suggest that the increased delivery of CO\textsubscript{2} to the ulcerated area results in vasodilatation and an increase in blood flow. The improved angiogenesis and oxygenation enhances the healing of chronic wounds. This principle may be applied in the treatment of diabetic foot ulcerations. The effect on blood flow may be important in the preventive and curative treatment of patients with impaired mobility due to organic or functional causes. Further work is needed for the development of therapeutic strategies to optimize CO\textsubscript{2} use in diabetic foot patients.

**References**