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Use of Transcutaneous Application of CO_2 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 CO_2 as well as CO_2 water baths for therapeutic purpose. In the method used, gaseous CO_2 is applied transcutaneously using the PVR system®. CO_2 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 CO_2 into subcutaneous tissue, are non-invasiveness, the absence of pain and protection against infection. Compared to CO_2 balneotherapy this approach enables the use of higher CO_2 concentrations, application to chronic wound patients and, with appropriate precautionary measures, prevents the increase of CO_2 in the surrounding air. Finzgar et al. observed that the transcutaneous application of gaseous CO_2 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 CO_2 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 CO_2 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 CO_2 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 CO_2 as well as CO_2 water baths for therapeutic purposes. CO_2 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 CO_2 therapies on skin microcirculation have been studied in animal models. Duling BR [1] observed increased microvascular diameter and increased perivascular pO_2 at sites of exposure to a CO_2 aqueous solution. The increased diameter was due to the vasodilatory effect of topical CO_2, the phenomenon also known as active hyperaemia. The increased perivascular pO_2 was due to the effect of CO_2 on the oxyhemoglobin dissociation curve. Irie et al. [2] demonstrated that CO_2 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 CO_2 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 CO_2 in effective adjunctive treatment to prevent diabetic ulcer exacerbation.

Materials and methods

Gaseous CO_2 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 CO_2. CO_2 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 CO_2 to the body. The method of application is completely safe and prevents any inhalation of CO_2. The device also has an electronic sensor system which constantly monitors the air quality in the room.

Discussion

Brandi et al. [4] studied the effect of the subcutaneous application of gaseous CO_2 in the treatment of chronic lower limb lesions. Laser Doppler flux and transcutaneous pO_2 were measured in two groups. In one group, CO_2 therapy was used in addition to the standard methods of treatment for such lesions. The patients in the control group were

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treated using only standard methods. In the group that underwent subcutaneous treatment with CO_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_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_2 therapy. One lower limb of each subject was exposed to gaseous CO_2. The contralateral limb was the control, being exposed to air. The CO_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_2 molecules through the skin into microcirculation and a direct indicator of the vasodilatory effect of CO_2.

Favorable clinical and microcirculatory effects of gaseous CO_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_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_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_2 to the ulcerated area results in vasodilation 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_2 use in diabetic foot patients.

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