

Carbon dioxide hand baths for Raynaud's phenomenon in systemic sclerosis: from acute vascular responses to serial application

Sir,

Raynaud's phenomenon (RP) affects almost all patients with systemic sclerosis (SSc) and is a clinical manifestation of the interaction between environmental exposure and disease-specific vasculopathy. Cold exposure and emotional stress trigger digital vasospasm in vessels already affected by endothelial dysfunction, intimal proliferation, capillary loss and reduced vasodilatory reserve (1, 2). Despite guideline-based vasoactive pharmacotherapy, many patients continue to experience substantial RP-related symptoms, while treatment outcome is frequently limited by incomplete efficacy, adverse effects, contraindications or poor tolerability. At the same time, current non-pharmacological recommendations largely focus on protection from cold, self-management and rehabilitation rather than interventions directly targeting the microcirculation (3).

Carbon dioxide (CO₂)-enriched water has long been used in peripheral circulatory disorders and RP (4, 5). Proposed mechanisms include transcutaneous CO₂ uptake, local hypercapnia and acidosis, relaxation of vascular smooth muscle and pericytes, and ultimately enhanced oxygen unloading through a rightward shift of the oxyhaemoglobin dissociation curve (4, 6, 7). These mechanisms provide a strong rationale for testing whether CO₂ immersion elicits effects beyond warming alone, particularly because thermoregulatory vasodilation is impaired in SSc (8).

From 2019 onward our group has investigated CO₂ hand baths in SSc-associated RP through a structured series of studies using complementary hemodynamic, capillaroscopic and patient-reported outcomes. The first study examined the acute effects of a single CO₂ hand bath to establish physiological proof of concept. 24 patients with SSc-associated RP were randomised to either a single 15-minute CO₂ hand bath at 2 g/L and 35°C or a warm-water bath at 40–42°C (9). The Doppler-derived resistance index (RI) of the digital arteries decreased from 0.83 to 0.76 immediately after CO₂ immersion ($p < 0.01$), whereas warm water produced no significant change. Despite the lower bath temperature, the CO₂-associated RI reduction provided controlled evidence of an effect beyond warming alone.

A subsequent analysis of prospectively acquired nailfold capillaroscopy data from the same randomised trial provided complementary, segment-specific mechanistic



Fig. 1. Standardised carbon dioxide hand bath in systemic sclerosis-associated Raynaud's phenomenon. The hands are immersed for 15 minutes in water at 35°C. A CO₂ concentration of approximately 2 g/L is generated by dissolving 3.75 g/L sodium bicarbonate as the CO₂ carrier and 5.0 g/L aluminium sulphate hydrate as the activator. The intervention can be administered in hospital and outpatient settings or, after appropriate instruction, self-administered at home.

information (10). CO₂ increased the diameters of the afferent limb, capillary apex and efferent limb of the acral vessels, whereas immediate changes after warm water were negligible. Baseline-adjusted differences versus warm water were large for the afferent limb (Cohen's $d = 2.7$) and capillary apex ($d = 2.2$). Dilation of both segments remained longer than after warm water at 10 minutes. These segment-specific findings localised the acute response to the nailfold microcirculation and aligned with the digital-artery Doppler results. The concordant findings across both assessment methods, despite the lower temperature of the CO₂ bath, argue against warming alone as an explanation and support a specific vasodilatory contribution of CO₂.

The next study moved from acute vas-

cular physiology to repeated clinical application. In a controlled feasibility study, 14 patients with SSc and severe RP and 14 age-matched healthy controls received daily CO₂ hand baths for seven days (11). The RI decreased in both groups, with a larger absolute change in SSc (−0.17 versus −0.11, between-group Cohen's $d = 1.2$). After adjustment for baseline differences, day-7 RI values were statistically comparable between groups. In patients with SSc, the Raynaud Condition Score decreased progressively, exceeded its minimal clinically important difference from day 4 and reached a median change of −3.0 points by day 7 (11, 12). Median attack frequency decreased by three attacks per day and median daily attack duration by 68 minutes. Although the magnitude and progressive

time course of the objective and patient-reported changes are notable, the non-randomised design precludes definitive efficacy conclusions. Expectation effects, natural RP variability, ambient temperature and a residual acute response at the final Doppler assessment cannot be completely excluded (13, 14). Nevertheless, the findings extend beyond a transient single-bath response, with vascular and patient-reported outcomes changing consistently in a favourable direction.

CO₂ hand baths have also been incorporated into multimodal care for severe SSc-associated RP. In a randomized trial of adjunctive water-filtered infrared-A irradiation (wIRA), all participants received intravenous iloprost and daily CO₂ hand baths, while only the addition of wIRA was randomised (15). Several RP-related outcomes improved in both groups. Adjunctive wIRA resulted in greater reductions in pain and RP duration, while other between-group differences were non-significant. Because both groups received iloprost and CO₂ hand baths, the study cannot determine the independent contribution of CO₂. Nevertheless, it demonstrates that a standardised CO₂ protocol can be implemented alongside iloprost in patients with a history of digital ulcers. CO₂ hand baths are non-invasive, technically simple and inexpensive, costing approximately €5 per application in Germany. A standardised application is illustrated in Figure 1. After appropriate instruction and exclusion of contraindications, they can be administered by physiotherapists, used in outpatient settings or also self-administered at home. This accessibility is particularly relevant for a recurrent condition frequently triggered outside clinical encounters. Taken together, the available studies indicate that CO₂ hand baths modify digital vascular responses and that repeated treatment is associated with meaningful symptom improvement. The intervention was well tolerated, with no treatment-related adverse events observed across the studies. CO₂ hand baths may therefore represent a practical non-pharmacological addition to evidence-based vasoactive therapy, particu-

larly when symptoms remain inadequately controlled or pharmacological treatment is poorly tolerated. The key remaining question is whether these physiological and symptomatic effects translate into sustained benefit under routine treatment, which should be examined in larger trials with an active warm-water comparator and longer follow-up.

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