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SHORT REPORT

Pain, Quality of Life, and Functional Capacity With Topical Sevoflurane Application for Chronic Venous Ulcers: A Retrospective Clinical Study

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Introduction: Chronic venous ulcers (CVU) commonly have poorly controlled pain.
Report: Thirty patients older than 65 years of age with painful CVU were reviewed. At the initial visit, cleaning without sevoflurane was performed. Cleaning visits with sevoflurane every 2 days for 1 month were scheduled. The results of subsequent treatment with sevoflurane at the first, second, seventh, and twelfth cleanings were analysed. Pain was measured using a visual analog scale (VAS), quality of life by the Charing Cross Venous Leg Ulcer Questionnaire, and functional capacity by the Barthel Index.
Discussion: Initial VAS was 8.8 $\pm$ 1.3 points and at the twelfth cleaning VAS was 0.8 $\pm$ 1 points ($p = .001$). Latency time ranged between 2 and 7 m and duration ranged between 8 and 18 h. It improved quality of life (83 $\pm$ 14 points before treatment vs. 50 $\pm$ 14 at the twelfth cleaning) and functional capacity (82 $\pm$ 13.3 before treatment vs. 91 $\pm$ 11.6 points at the twelfth cleaning) ($p = .001$). The safety profile was favourable with mild and self limited local cutaneous adverse effects, including pruritus, erythema, and heat. No systemic toxicity was detected. Topical sevoflurane may be a therapeutic alternative for painful CVU with a fast, intense, and long-lasting analgesic effect.

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INTRODUCTION

Pain in chronic venous ulcers (CVUs) commonly increases with usual cleaning, surgical debridement, and dressing changes.[1—3] Approximately, 85% of CVUs have pain with a median visual analog scale (VAS) score of 4.6.[1] CVU usually causes diminished physical activity and quality of life.[4,5] Adequate analgesic control is essential. In spite of several systemic analgesic treatments pain is usually poorly controlled.[1—5]

Sevoflurane is an inhaled halogenated anaesthetic agent with an adequate safety profile, used for induction and maintenance of general anaesthesia.[6] There have been a few case reports of its efficacy as a topical anaesthetic in leg ulcers.[7—16]

MATERIAL AND METHODS

A retrospective pilot study of a series of 30 patients over 65 years of age with painful CVU is presented. VAS was $\geq$ 4 points. Written informed consent was obtained from all patients for the off label use of topical sevoflurane. The drug and study protocol were approved by a pharmacy committee and the hospital ethics committee, respectively. Hospitalised patients, patients with ulceration of any other cause, patients with generalised arteriosclerosis, patients with cognitive impairment, or patients with pain of another cause were excluded.

During an initial visit, VAS score, Charing Cross Venous Leg Ulcer Questionnaire (CCVUQ),[17] and Barthel Index[18] were registered, corresponding to the previous cleanings without sevoflurane. During the initial visit, a cleaning without sevoflurane was performed. Cleaning visits with sevoflurane every 2 days for a period of 1 month were scheduled. VAS, CCVUQ, and Barthel Index results of the previous and initial cleanings without sevoflurane and the subsequent treatments with sevoflurane at the first, second, seventh, and twelfth cleanings were compared.

Treatment consisted of irrigating the ulcer with 1 mL liquid sevoflurane per cm^2 wound size without covering the

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healthy skin edges; sterile gauze was used to protect the perilesional skin. Next the wound was quickly covered with a sterile hydrophilic braided cotton pad, soaked in physiological saline. Later, usual routine cleaning was performed.

RESULTS

Analgesic effect

Initial mean VAS was 8.8 ± 1.3 points in the previous and the initial cleanings without sevoflurane. Pain diminished from the first cleaning with sevoflurane. By the twelfth cleaning mean VAS was 0.8 ± 1 points ($p = .001$) (Figs. 1 and 2). Latency time varied between 2 and 7 minutes (mean 3.9 ± 1.5 minutes). Duration ranged between 8 and 18 hours (mean 12 ± 2.9 hours).

Quality of life

Initial mean CCVUQ score was 83 ± 14 points. There was a statistically significant improvement in quality of life from the second cleaning with sevoflurane. At the twelfth cleaning with sevoflurane mean CCVUQ score was 50 ± 14 points ($p = .001$) (Fig. 3).

Functional capacity

Initial median Barthel index was 82 ± 13.3 points. There was a significant increase in Barthel Index at the twelfth cleaning compared with the first, with a median Barthel index of 91 ± 11.6 points ($p = .001$) (Fig. 4).

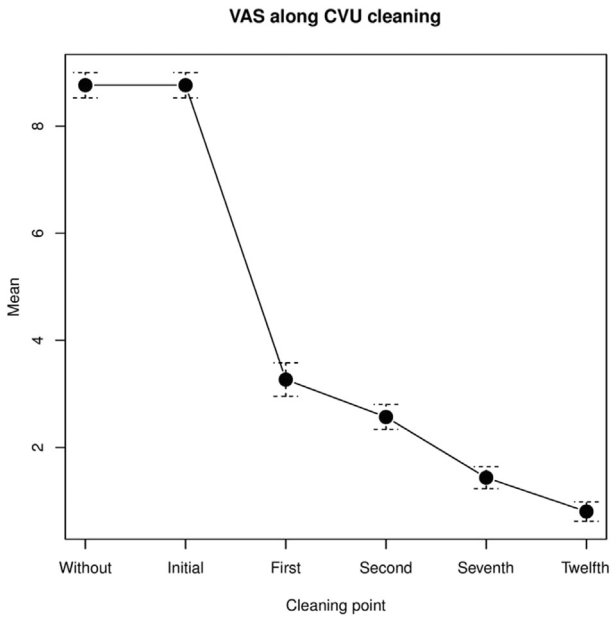

Figure 2. Visual analog scale along cleaning. *Note*. CVU = chronic venous ulcers.

Adverse effects

The main local adverse effects were mild and transient, including pruritus in five patients (16.7%), erythema in two (6.7%), heat in three (10%), and irritative dermatitis in one (3.3%). No systemic adverse effects or sensitisation were detected.

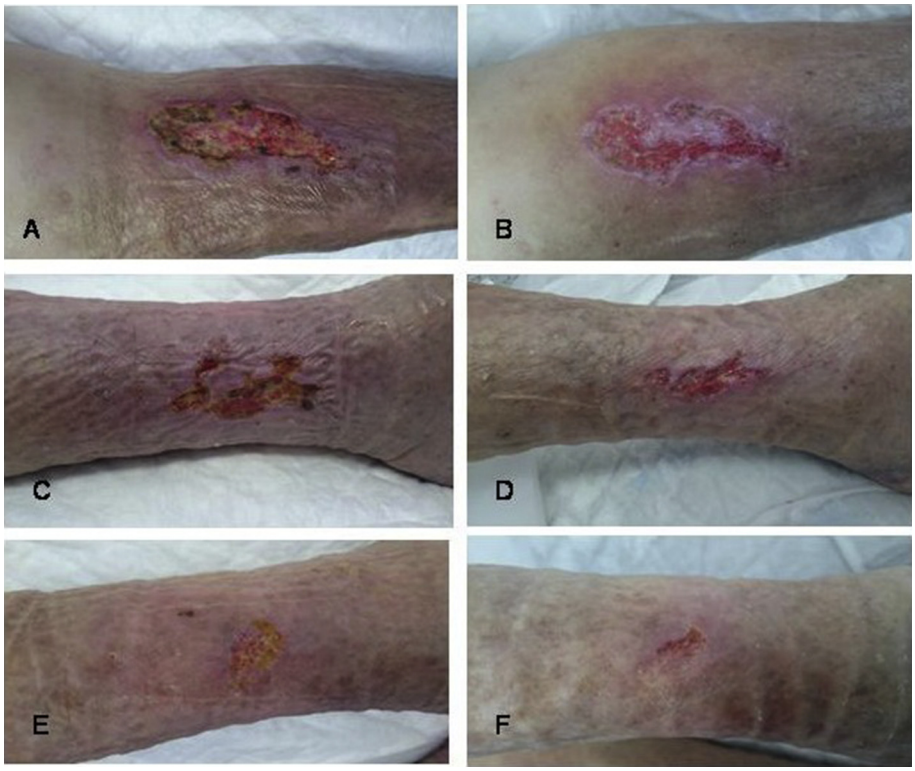

Figure 1. Chronic venous ulcers (A, C, E) before and (B, D, F) after sevoflurane treatment.

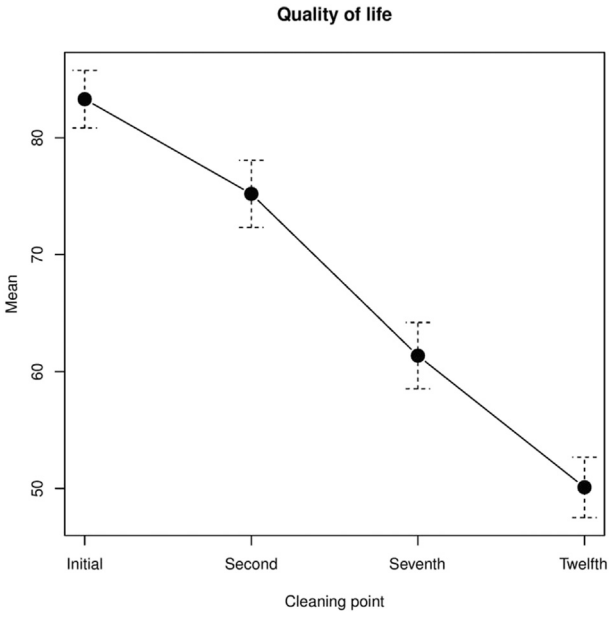

Figure 3. Quality of life with Charing Cross Venous Leg Ulcer Questionnaire.

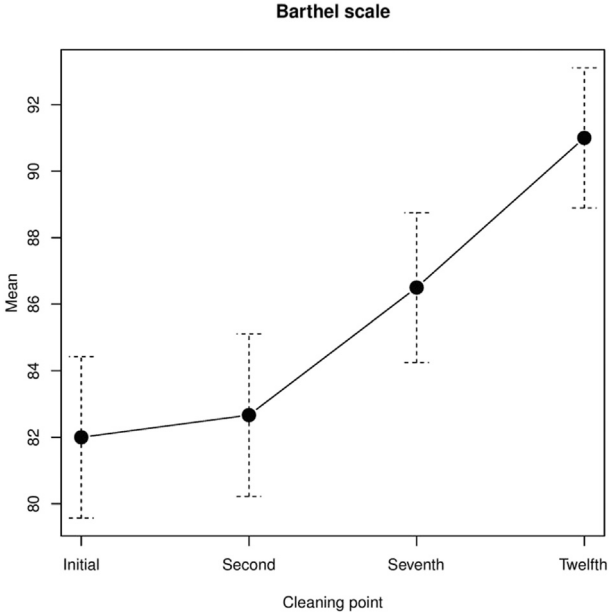

Figure 4. Barthel index.

DISCUSSION

An intense analgesic effect of topical sevoflurane has been reported in a few chronic vascular leg ulcer, surgical wound, malignant leg ulcer, and epidural abscess with cutaneous fistulisation case reports.[7–14] There were no VAS results. The latency period varied between 1 and 10 minutes and the duration ranged between 7 and 24 hours.

Dámaso Fernández-Ginés et al. reported 34 of 36 (94.4%) patients treated with topical sevoflurane for a mean of 10.5 months (range 3–24 months).[15] Excellent control of basal pain with rapid, intense, and lasting relief (2–48 hours) was found. An improvement in quality of life and a significant reduction in the consumption of analgesics were seen, but there were no results to report.

A prospective observational study assessed the efficacy and safety of topical sevoflurane for a period of 90 days.[16] Patients were randomly assigned to two groups: standard wound care with ($n = 10$) or without ($n = 5$) sevoflurane. In the sevoflurane group the mean VAS score was 7.36 ± 1.56 points at baseline and 0.59 ± 0.48 points at 90 days. At the start, patients were taking 102.7 ± 36.8 mg/day morphine which was reduced to 20.0 ± 5.4 mg/day after treatment with sevoflurane. The mean ulcer area was 12.5 ± 2.2 cm^2 at baseline and 6.1 ± 2.67 cm^2 at 90 days. The mean latency time was 3.2 ± 1.2 minutes and the mean duration was 9.6 ± 4.7 hours. In four patients a mild localised reddening and pruritus in the area surrounding ulcers occurred.

Sevoflurane improves the quality of life when it is used in the subsequent cleanings. The results showed that topical sevoflurane may cause a favourable change in functional capacity as the pain relief made ambulation easier.

Sevoflurane's mechanism of action is unknown. It is suggested that a vasodilatory effect increases vascular flow, improving the microcirculation. Topical sevoflurane may have a direct inhibitory effect on vascular smooth muscle independently of endothelium.[19] A central but not peripheral effect of inhaled sevoflurane has been clinically demonstrated. It is also suggested that a reversible peripheral concentration-dependent analgesic effect is probably caused by sufficient partial pressure in the peripheral nociceptors, which blocks the transmission of the pain stimulus.[20–24] The absence of harmful effects is probably due to no or negligible slow and incomplete systemic absorption.

Limitations include the retrospective nature of the study, the lack of randomisation and blindness, and the relatively small number of patients. Randomised clinical trials and larger prospective studies with longer follow-up are needed to better assess the efficacy and safety of topical sevoflurane.

CONFLICT OF INTEREST

None.

FUNDING

None.

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