

[62.7%]; 90 mg [72.2%]), and 84% maintained a response that was equal to or greater than PASI 50.

Although it seems that there was no major decrease in response over time in the study population as a whole, it is important to identify this subgroup and prepare rescue strategies, such as reduction in the administration interval (eg, 12 to 8 weeks) or combination with other topical or systemic agents or phototherapy.

Several clinical studies have found that combination with narrowband UV-B phototherapy improves the efficacy of some tumor necrosis alfa (TNF- α) factor inhibitors such as etanercept^{4,5} and adalimumab.^{6,7} A recent study based on a small clinical series revealed similar findings in patients treated with ustekinumab,⁸ as in the 2 cases described above.

The clinical improvement in psoriasis treated with narrowband UV-B phototherapy is linked to suppression of the signaling pathways of type 17 helper T cells and types I and II interferons, which play a key role in pathogenesis.⁹ The modifying effects of phototherapy also have an effect on the antigen-presenting function and direct apoptosis of T lymphocytes.

Given that some experimental studies have shown how combination therapy with anti-TNF- α agents can increase the risk of photocarcinogenesis,¹⁰ the combination of biologic agents and phototherapy should be administered with caution and only in selected patients.

To conclude, narrowband UV-B phototherapy could be a good alternative for restoration of the response to ustekinumab in selected cases of moderate to severe psoriasis.

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P. Soro Martínez, I. Belinchón Romero,*
M.P. Arribas Granados

Servicio de Dermatología, Hospital General Universitario de Alicante, Alicante, Spain

* Corresponding author.

E-mail address: belinchon_isa@gva.es (I. Belinchón Romero).

Sevoflurane: A Valid Alternative for the Treatment of Vascular Ulcers?☆

Sevoflurano, ¿una alternativa en el tratamiento de las úlceras vasculares?

To the Editor:

Vascular ulcers are a major health problem because of their frequency, chronic nature, and high recurrence rate. The standard treatment, which consists of cleansing, debridement, and application of dressings, achieves cure rates of 65% to 85%.¹

The approaches used to accelerate scarring of these ulcers include dressings (biologic, synthetic, or biosynthetic), human amniotic membrane transplantation,¹ and autologous platelet-rich plasma.²

Options for analgesia to control the pain associated with vascular ulcers include topical anesthetics such as the creams Emla (lidocaine and prilocaine) and Lambdalina (lidocaine), oral analgesics, and even opiates. These products aid in the healing process and in pain control, although they can produce undesirable effects.

Sevoflurane is an inhaled general anesthetic from the halogenated ether family that is indicated for induction and maintenance of general anesthesia during hospital or outpatient surgery.³ Its analgesic effect is both central⁴ and peripheral,^{5–7} although it has traditionally been thought that halogenated anesthetics lack a peripheral analgesic effect.⁸

Topical sevoflurane has been reported to be effective in the treatment of long-standing venous ulcers⁹ and ischemic ulcers⁶ that are refractory to standard treatment; when irri-

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gated topically over the painful ulcer bed, it produces a rapid, intense, and lasting analgesic effect, with a suitable safety profile that is well accepted by patients. In addition, it significantly reduces the size of the ulcer and the time necessary for epithelialization.⁵⁻⁷ Its effect can be so intense that it is even possible to perform surgical debridement without the need for further analgesia.⁶

Similarly, it has been suggested that direct application of sevoflurane has an antimicrobial effect on ulcers that are superinfected by multiresistant *Pseudomonas aeruginosa*,⁶ and a bactericidal effect has been reported in vitro against *Staphylococcus aureus*, *P. aeruginosa*, and *Escherichia coli*.⁹

Sevoflurane (Sevorane) is marketed as a colorless volatile liquid with no additives or preservatives in a 250-mL amber-colored polyethylene naphthalate bottle with a safety cap and a filling adapter. Each milliliter of liquid contains 1 mL of sevoflurane (INN). It should be kept at room temperature and protected from sunlight.

Once the ulcer has been cleansed with saline solution, sevoflurane is applied directly on the ulcer bed, ensuring that the liquid is distributed throughout the tissue and taking care that it does not come into contact with the surrounding healthy skin. It is necessary to wait 2 minutes before applying standard wound care^{6,7} and placing the dressing. A compression bandage should also be applied when necessary.

To date, 12 patients have been treated with topical sevoflurane, and 2 of these cases have been published.^{5,6} The case of an immunodepressed patient with a postsurgical wound superinfected by multiresistant *P. aeruginosa* who was cured after several applications of sevoflurane is pending publication.⁷ At the 17th Annual Meeting of the European Society of Regional Anesthesia in Barcelona in October 2011, a series of 9 patients was presented (6 women and 3 men with diabetes). The patients had painful venous ulcers on the lower limbs that were refractory to regular analgesics and were treated with sevoflurane on an outpatient basis to control the pain.⁷ In all cases, the reduction in pain at rest was rapid (less than 2 minutes), intense (7.4 [0.5] to 2.1 [0.6] points with the first application and 7.2 [1.3] to 1.1 [0.6] points with all of the remaining 67 applications), and lasting (from 7 to 16 hours). The ulcers were cured in 4 cases.

The risk-benefit ratio of sevoflurane has proven very favorable to date.^{6,7} The only undesirable effects of topical application are pruritus at the borders of the wound and irritation of the surrounding skin with repeated applications.⁵ Sevoflurane has not been reported to have sensitizing potential. Similarly, local irrigation with sevoflurane was well tolerated in patients with heart disease.⁵⁻⁷ Systemic absorption of sevoflurane applied to an ulcer involving circulatory compromise is thought to be slow and incomplete,⁶ although blood levels have not been measured in patients treated with this procedure.

The mechanism underlying the analgesic, epithelializing, and antimicrobial effects of sevoflurane remains unknown.

Inhaled sevoflurane has no peripheral analgesic effect⁸; however, topical or subcutaneous administration does produce a peripheral effect.¹⁰ When a halogenated agent is inhaled, the partial pressure reached in the peripheral nociceptors may not be sufficient to block transmission of a painful stimulus; however, with direct application, the nociceptors are exposed to sufficient partial pressure to block transmission of painful stimuli.⁵

In conclusion, topical sevoflurane could prove to be a promising strategy for analgesia and epithelialization in the treatment of vascular ulcers.

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R.F. Lafuente-Urrez,^{a,*} Y. Gilaberte^b

^a *Servicio de Dermatología, Hospital Reina Sofía, Tudela, Spain*

^b *Servicio de Dermatología, Hospital San Jorge, Huesca, Spain*

*Corresponding author.

E-mail addresses: fati1997@gmail.com, rfz97@yahoo.com (R.F. Lafuente-Urrez).