Phlebology (2000) 15:81–83
© 2000 The Venous Forum of the Royal Society of Medicine and Societas Phlebologica Scandinavica

PHLEBOLOGY

*Original Article*

# EMLA Anaesthetic Cream for Sharp Debridement of Venous Leg Ulcers: A Double-Masked, Placebo-Controlled Study

G. Agrifoglio[1], M. Domanin[1], E. Baggio[2], P. Cao[3], A. N. Alberti[4], F. Borin[5], A. R. Todini[6], G. Becchi[7] and M. Caserini[8]

[1]Institute of Vascular Surgery, University of Milan, Milan; [2]Department of Surgery, Borgoroma General Hospital, Verona; [3]Vascular Surgery Unit, Monteluce General Hospital, Perugia; [4]Department of Vascular Surgery, Melacrino Morelli Hospital, Reggio Calabria; [5]Department of Surgery, Fornaroli Hospital, Magenta; [6]Department of Angiology, San Camillo Hospital, Rome; [7]Department of Surgery, Sampierdarena Hospital, Genoa; and [8]Medical Department, AstraZeneca, Milan, Italy

## ABSTRACT

***Objective:*** The aim of this double-masked, placebo-controlled trial was to confirm the anaesthetic effect of EMLA cream compared with placebo when used for sharp debridement of venous leg ulcers and to test its feasibility with respect to the usual procedure.

***Methods:*** One hundred and ten patients with venous ulcers were randomised to EMLA or placebo cream treatment for 30–45 min. Pain from debridement was evaluated by the patient on a 100 mm visual analogue scale (VAS) and by the physician on a verbal scale.

***Results:*** The median VAS scores were 16.5 and 52 in EMLA- and placebo-treated patients, respectively ($p<0.00001$), a clinically relevant difference. On the verbal scale 61% of EMLA patients and 21% of placebo patients were placed in the category of no pain ($p<0.0001$). The physicians found debridement with EMLA easier to perform ($p<0.01$).

***Conclusion:*** Debridement of venous leg ulcers using topical anaesthesia is easy and safe, with adequate pain relief in both in- and outpatients.

**Keywords:** Analgesia; Debridement; EMLA cream; Pain; Venous leg ulcers

*Correspondence and offprint requests to:* Dr M. Domanin, Institute of Vascular Surgery, University of Milan, Via Commenda 12, Milan, Italy. Tel: +39 (0) 2 551 871 09; Fax: +39 (0) 2 5519 59 07.

## Introduction

There is an increasing demand worldwide for painless medical procedures. The sharp debridement of leg ulcers is very often painful, which sometimes necessitates interruption before the ulcer is satisfactorily cleaned, unless general anaesthesia is used. Holm et al. [1] and Lok et al. [12] have demonstrated in placebo-controlled studies effective topical anaesthesia with the lidocaine/prilocaine cream EMLA for the sharp debridement of leg ulcers. These studies included ulcers of both venous and mixed arteriovenous origin, and one study also included arterial ulcers [1]. In an open randomised study Hansson et al. [3] showed that EMLA significantly reduced sharp debridement pain in venous patients. The aim of the present study was to confirm the local anaesthetic efficacy of EMLA cream in patients with venous leg ulcers using a double-masked technique.

## Materials and Methods

The study was a randomised, double-masked, placebo-controlled trial, with the participation of seven centres of angiology and vascular surgery. It was approved by the ethics committee at each centre and performed in accordance with the principles stated in the Declaration of Helsinki. Signed or witnessed verbal informed consent was obtained from all patients before enrolment.

A total of 110 consecutive in- and outpatients with venous leg ulcers (ankle/brachial index $\geq 0.9$) who had been selected for sharp debridement were included.

Patients with signs of infection erysipelas were excluded as such patients often experience more pain. Diabetics were excluded in order to avoid patients with signs of neuropathy who could also confound the assessment of debridement pain. All treated ulcers had had a clinical history of 1–5 years prior to enrolment and had previously been debrided. Patients with an ulcer area exceeding 50 $cm^2$ were excluded to ensure the application of a thick layer of cream.

A thick layer of cream (2.5 g per 10 $cm^2$, max 10 g) was applied to the ulcer for 30–45 min, occluded with a plastic household dressing. Debridement was carried out by means of a curette or scissors, lancets and forceps.

After cleansing the patients were asked to rate the pain experienced during the procedure on a 100 mm horizontal ungraduated visual analogue scale (VAS). The end-points of the VAS were marked 'no pain' (0 mm) 'worst possible pain' (100 mm) [4]. Similarly the investigators rates their impression of the patients' pain on a four-point VRS (verbal rating scale) defined as no pain (no reaction), mild pain (slight reaction and minor movement), moderate pain (moderate reaction and verbal protest) and severe pain (marked distress).

The feasibility of the debridement procedure was recorded by the physicians on a three-point scale consisting of the following categories: more difficult, equally difficult and less difficult with respect to the usual procedure. Adverse effects were assessed during and after debridement.

## Statistics

The sample size was determined in order to enable the detection, with a power of 90%, of a mean difference in VAS score between the treatments of 20 mm. Based on previous studies, it was assumed that the standard deviation of the VAS score would be 30 mm. Sixty patients per group were planned for inclusion in the study, this sample size including a 20% increase to account for drop-outs.

The pain difference as measured by the VAS scale was tested with the Wilcoxon rank-sum test, stratified for centre (hospital). The corresponding Wilcoxon 95% confidence interval and Hodges–Lehmann point estimate of the difference in median VAS score between the groups were calculated. The difference in the feasibility of the debridement procedure and the difference in verbal pain scores between the two treatment groups were tested with the Wilcoxon rank-sum test.

## Results

Fifty-four patients were randomised to treatment with EMLA and 56 to placebo cream. The EMLA and placebo groups were similar with respect to age, sex and weight (Table 1). The application time was in the range 30–45 min, with a median of 40 min in both groups. The mean size of the ulcers was 8 $cm^2$ (range 1–36 $cm^2$) in the EMLA group and 5 $cm^2$ (range 1–50 $cm^2$) in the placebo group. The mean dose of cream was 3.0 g in the EMLA and 3.4 g in the placebo group.

Table 1. Demographic data

| Variable | EMLA group ($n$ = 54) | Placebo group ($n$ = 56) |
|---|---|---|
| Age (years); mean (range) | 67.0 (38–86) | 63.8 (41–80) |
| Sex (male/female) | 13/41 | 21/35 |
| Weight (kg); mean (range) | 76.9 (45–135) | 75.0 (50–105) |

The median VAS pain scores from ulcer debridement were 16.5 and 52 in the EMLA and placebo groups, respectively ($p<0.0000$), a 68% reduction in perceived pain in EMLA-treated patients (Fig. 1). The 95% confidence interval for the median difference in VAS score between the EMLA and placebo groups was (−37, −11) and the Hodges–Lehmann estimate of the treatment difference was −22.

According to the physicians' judgement, 61% of the patients in the EMLA group, compared with 21% of the patients in the placebo group, were classified in the category of no pain ($p<0.0001$; Table 2). The investigator rated the debridement as less difficult than usual in 59% of EMLA-treated patients as compared with 36% of placebo-treated patients ($p<0.01$; Table 3).

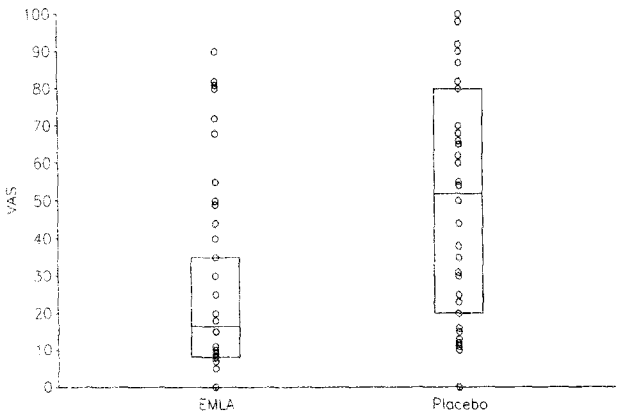


Fig. 1. Boxplot of VAS pain scores from sharp debridement ($p<0.00001$). The *bottom and top edges* of the boxes are the first (Q1) and third quartiles (Q3), while the centre *horizontal line* is the median. The *circles* represent the individual values.

Table 2. Vertebral pain scores from debridement assessed by the physician

| Verbal pain score | No. of patients | |
|---|---|---|
| | EMLA group | Placebo group |
| No pain | 33 (61.1%)* | 12 (21.4%) |
| Mild | 16 (29.6%) | 22 (39.3%) |
| Moderate | 2 (3.7%) | 12 (23.2%) |
| Severe | 3 (5.6%) | 9 (16.1%) |

*$p<0.0001$ versus placebo.

Table 3. Physicians' feasibility evaluation compared with the standard debridement procedure

| Feasibility evaluation | No. of patients | |
|---|---|---|
| | EMLA group | Placebo group |
| More difficult | 4 (7.4%) | 9 (16.1%) |
| Equally difficult | 18 (33.3%) | 27 (48.2%) |
| Less difficult | 32 (59.3%)* | 20 (35.7%) |

* $p<0.01$ versus placebo.

None of the 110 patients experienced any kind of systemic adverse event. Local skin reactions observed were few, mild and similar in both groups: mild itching was felt by 3 patients in each treatment group and mild burning by 3 EMLA-treated and one 1 placebo-treated patient. One patient in the EMLA group had slight local oedema.

## Discussion

In recent years the management of leg ulcers has shifted from simply changing dressings to become a multidisciplinary task, implying a higher frequency of correct diagnosis and up-to-date treatment which is often more active and effective. Financial constrains on costly medical procedures have increased. For example, the change from general to local anaesthesia and from in- to outpatient care is in line with this. Furthermore, the demand for pain-free procedures has increased.

Most leg ulcers are of venous origin. It has commonly been held that these ulcers are seldom painful, whereas other types of ulcers, such as arterial and vasculitic ulcers, have been considered to be much more painful. However, in a recent study the majority of patients with venous leg ulcers stated that pain was the worse part of having a leg ulcer [5].

The removal of dead tissue and slough from a leg ulcer is crucial for optimal healing [6–9], and sharp debridement is the most rapid method available [8,10]. Debridement also improves the results of skin grafting [11]. Venous leg ulcers may be particularly suitable for skin transplantation, which can easily be performed in primary care [12].

In the current trial the reduction in VAS pain scores from sharp debridement in the EMLA group compared with the placebo group was statistically highly significant. EMLA cream reduced the patients' pain experience by an average of 22 units on the VAS, a clinically significant difference. This can be compared with the physicians' evaluation, which showed that 90% of the EMLA-treated patients felt no or mild pain as opposed to 60% of the placebo-treated patients. Furthermore, the effective pain relief was the likely explanation for the facilitated debridement procedure. The application of the cream, using ordinary household Clingfilm for occlusion, was easy and feasible to incorporate into the clinical routine work. Local skin reactions were few, mild and transient.

The plasma levels of lidocaine and prilocaine recorded after doses of up to 10 g of EMLA cream are far below the levels associated with central nervous system toxicity. In a single-dose study Holm et al. [1] reported maximum plasma levels of 839 ng/ml of lidocaine and 81 ng/ml of prilocaine from a dose of 5–10 g EMLA. After repeated doses [2] of up to 10 g EMLA, 3–7 times a week over a period of 1 month, the maximum observed plasma levels of lidocaine and prilocaine were 410 and 80 ng/ml, respectively. There was no apparent accumulation in plasma of the local anaesthetics or their metabolites [2]. Initial signs of central nervous system toxicity can occur at plasma levels above 5000–6000 ng/ml of either anaesthetic [13].

In conclusion, our results confirm that EMLA anaesthetic cream provides effective pain relief for the debridement of venous leg ulcers and facilitates the debridement procedure in both in- and outpatients.

*Acknowledgements.* We are grateful to Gustavo Arraiz, AstraZeneca, Milan, Italy, for the statistical analysis.

## References

1. Holm J, Andrén B, Grafford K. Pain control in the surgical debridement of leg ulcers by the use of a topical lidocaine-prilocaine cream, EMLA. Acta Derm Venereol 1990;70:132–6.
2. Lok C, Paul C, Amblard P, Bessis D, Debure C, Faivre B, et al. EMLA cream as a topical anesthetic for the repeated mechanical debridement of venous leg ulcers: a double-blind, placebo-controlled study. J Am Acad Dermatol 1999;40:208–13.
3. Hansson C, Holm J, Lillieborg S, Syren A. Repeated treatment with lidocaine/prilocaine cream (EMLA) as a topical anaesthetic for the cleansing of venous leg ulcers: a controlled study. Acta Derm Venereol 1993;73:231–3.
4. Scott J, Huskisson EC. Graphic representation of pain. Pain 1976;2:177–84.
5. Hofman D, Ryan TJ, Arnold F, Cherry GW, Lindholm C, Bjellerup M, Glynn C. Pain in venous leg ulcers. J Wound Care 1997;6:222–4.
6. Ryan TJ. Current management of leg ulcers. Drugs 1985;30:461–8.
7. Holzegel K. The dry treatment of venous leg ulcers. In: Negus D, Jantet G, editors. Phlebology 1985. London: John Libbey, 1986:609–12.
8. Vowden KR, Vowden P. Wound debridement. 1. Non-sharp techniques. J Wound Care 1999;8:237–40.
9. Vowden KR, Vowden P. Wound debridement. 2. Sharp techniques. J Wound Care 1999;8:291–4.
10. Tong A. The identification and treatment of slough: a review of the problems encountered by clinicians in identifying slough in wounds and selecting debridement therapies for its removal. J Wound Care 1999;8:338–9.
11. Douglas WS, Simpson NB. British Association of Dermatologists workshop report. Guidelines for management of venous leg ulcers. Br J Dermatol 1995;132:446–52.
12. Öien RF, Hansen BU, Håkansson A. Pinch grafting of leg ulcers in primary care. Acta Derm Venereol 1998;78:438–9.
13. Covino BG, Wildsmith JAW. Clinical pharmacology of local anesthetic agents. In: Cousins MJ, Bridenbaugh PO, editors. Neural blockade in clinical anesthesia and management of pain. 3rd ed. New York: Lippincott-Raven, 1998.

*Received for publication 18 February 2000*
*Accepted in revised form 27 July 2000*