

Pain Control in the Surgical Debridement of Leg Ulcers by the Use of a Topical Lidocaine-Prilocaine Cream, EMLA®

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The analgesic effect of EMLA 5% cream for surgical cleansing of leg ulcers was investigated in an open study and in a double-blind comparison with placebo. Eighty patients with ulcers of venous or arterial origin participated. The cream was applied under occlusion and removed before cleansing. Plasma concentrations of lidocaine and prilocaine were assessed. The maximum individual concentrations were 0.8 µg/ml for lidocaine and 0.08 µg/ml for prilocaine. Pain was assessed according to a verbal rating scale and on a 100 mm visual analogue scale. The median VAS pain scores for EMLA and placebo were 18.5 and 84 mm ($p < 0.01$). There were no severe adverse reactions. The results show that there is a need for pain control in surgical debridement of leg ulcers and that EMLA cream gives satisfactory analgesia for this procedure. **Key words:** Analgesic effect; Surface anesthesia; Arterial and venous ulcers.

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Thorough cleansing is essential in the treatment of leg ulcers (1, 2). Necrosis or devitalized tissues can act as foreign bodies and retard the healing. A clean leg ulcer can sometimes be achieved by enzyme preparations or repeated wet dressings or hydrocolloids (3, 4) etc., but in many instances mechanical surgical cleansing is necessary. Due to pain, the cleansing may not always be as radical as would be preferred. No doubt, an effective local anesthetic formulation applied topically, which would permit less painful cleansing, would be an advantage.

EMLA 5% cream is a water-based formulation of a mixture of lidocaine and prilocaine. It has been shown to produce anesthesia of intact skin mainly for the purpose of reducing needle puncture pain (5, 6) and for skin surgery, e.g. cutting split-skin grafts (7). It was therefore of interest to investigate if EMLA

would be effective also for reducing pain in connection with the debridement of leg ulcers.

The aims of the present investigation were

- a) to study the analgesic effect and the local and systemic tolerance of EMLA cream in the surgical debridement of leg ulcers, and
- b) to determine how painful a thorough surgical cleansing of leg ulcers is.

MATERIAL AND METHODS

The study was performed in two consecutive parts, first an open part and then a double-blind placebo controlled.

Ethics

The study protocols were reviewed by the ethical committee of the hospital (Sahlgrenska Sjukhuset, Göteborg). Before entry, the patients were informed about the purpose and procedures of the trial before giving their oral consent to participate.

Patients

Fifty patients participated in the open part and 30 in the double-blind.

Forty-four patients were women and 36 men. Their ages ranged from 32 to 95 years. In the double-blind part the mean age in the EMLA group was 70 ± 9.1 years and in the placebo group 62 ± 12.2 years (n.s.). The male/female ratios were 10/6 and 10/4 (n.s.).

Definitions

Venous ulcer: clinical signs of varicose veins, normal ankle pressure. Arterial ulcer: no clinical signs of varicose veins. Ankle pressure below 80 mmHg.

Design of study

In the open part all patients were treated with EMLA 5% cream.

In the double-blind part, patients were treated with either EMLA cream or placebo. The creams were cosmetically and visually identical and packed in identical aluminium tubes. The treatments were randomized and stratified for type of ulcer (venous or arterial) but not for concomitant diabetes. If, during the cleansing of the ulcer, the patient reported that the pain was intolerable, the procedure was interrupted. EMLA

cream was then applied and a second attempt at cleansing was made. This treatment was recorded by using the same variables as the first time.

Practical procedure

In the outpatient department, while the patient was resting on a couch, the existing bandage was removed. The size of ulcer was then determined by measuring the length and width, and a thick layer of test cream was applied and covered by an occlusive dressing (Glad®). Maximum 5 g of cream was used in all but 3 patients, where 10 g was used. The application times were 10, 20 or 30 min in the first 9 patients in the open part and then 30 min throughout the whole study. The ulcer was debrided by use of tweezers, scissors and a curette. The debridement was considered to be completed when the ulcer was free from necrotic tissue, fibrin deposits and pus.

Plasma concentrations

From the first 12 patients in the open study, blood samples were collected for determinations of the plasma concentrations of lidocaine and prilocaine. Some 5–7 5-ml blood samples were collected before the cream application and at intervals of maximum 30 min up to 1, 2, or 3 h. The blood was separated immediately and the plasma was kept at -20°C until assayed. The determination of lidocaine and prilocaine were made by massfragmentography at the Bioanalytical Laboratory at Astra Läkemedel, Sweden.

Local reactions

While the cream was being applied, the patient was asked about any local irritation such as burning or itching. After removal of the dressing and the remaining cream, the ulcer was examined for local reactions.

Analgesic effect

The patient was instructed to assess the degree of pain during the debridement, both according to a four-point verbal rating scale as 'None', 'Slight', 'Moderate' or 'Severe' and on a 100 mm visual analogue scale (end-points 'No pain' and 'Intolerable pain').

For each patient the investigator assessed whether subjectively the cleansing was satisfactory or not. In addition in the double-blind part of the study, the need for supplementary EMLA cream was recorded.

Statistics

Differences between EMLA and placebo were analysed by the Mann-Whitney U-test, the Wilcoxon matched pairs signed rank test or Fisher's exact test. Correlations between duration of symptoms and pain were tested by linear regression.

RESULTS

Ulcer

Sixty-eight per cent of the patients had ulcers of venous origin and the remaining ulcers were arterial. The most common locations of the ulcers were lower leg, ankle and malleolus as in 73% of the patients (Table I). The size of the ulcers varied between 0.24

Table I. Location, age and size of treated leg ulcers

	Open study EMLA (n=50)	Double-blind study	
		EMLA (n=16)	Placebo (n=14)
<i>Locations</i>			
Lower leg	20	4	2
Ankle/ malleolus	14	9	9
Foot	7	—	1
Heel	4	1	—
Toe	4	2	2
Thigh	1	—	—
<i>Duration of ulcer symptoms (months)</i>			
Median		14*	6
Mean	21	50.2	9.6
SD	—	110.58	12.76
Min	1	2	1
Max	14 (years)	38 (years)	39 (months)
		U=165, p<0.05	
<i>Size of ulcer</i>			
Median	5	8.5	6
Mean	—	14.25	8.27
SD	—	14.80	7.13
Min	0.24	1	2
Max	64	55	30
		NS	

and 64 cm². In the double-blind part there was no difference between the EMLA and placebo groups with regard to location of ulcer or size of ulcer. The duration of ulcer symptoms varied between 1 month and 38 years. The duration in the EMLA group was significantly longer than in the placebo group (Table I).

Plasma concentrations

The individual peak concentrations following 5 g and 10 g EMLA and the time for obtaining these concentrations are given in Table II. In no case did the plasma concentrations reach anywhere near those levels connected with toxic symptoms (5–6 µg/ml).

Analgesic effect

Open study. Among the 50 patients treated with EMLA, 41 reported either no or slight pain (Table III). The individual recordings on the visual analogue scale are shown in Fig. 1. The median score was 13.5 mm (min. 1, max. 98). The debridement was judged as satisfactory in 49 of the patients (98%).

Table II. Maximum individual concentrations of lidocaine and prilocaine following the application of EMLA cream

n.d. = not determined

Patient no.	Application			Lidocaine		Prilocaine		Time for last blood sample (min)
	Ulcer area (cm ²)	Amount of cream (g)	Time (min)	ng/ml	Sampling time (min)	ng/ml	Sampling time (min)	
1	18.5	5	10	n.d.		n.d.		60
2	24	5	11	36	30	25	30	60
3	3	5	10	41	45	26	60	60
4	20	5	20	357	120	24	30	120
5	20	5	20	77	120	n.d.		120
6	15	5	20	46	30	n.d.		120
7	15	5	30	53	90	17	90	120
8	19	5	30	231	120	29	120	120
9	24	5	30	839	90	23	60	120
10	60	10	30	243	150	81	60	180
11	64	10	30	165	90	73	120	180
12	25	10	30	101	90	56	90	180

Double-blind study. Eleven patients in the EMLA group and 4 in the placebo group reported either no or slight pain ($\chi^2=4.82$, $p<0.05$; all grades: $U=173$, $p<0.01$ one-tail test, Table III). The median scores on the VAS were 18.5 mm (min. 3, max. 87) for the EMLA group and 84 mm (min. 12, max. 95) for the placebo group ($U=173$, $p<0.01$, Fig. 1). The score from one patient in the placebo group was not obtained. Among patients with venous ulcers, the median scores were 17 mm for EMLA ($n=10$) and 89 mm for placebo ($n=9$; $U=79.5$, $p<0.01$). Corresponding scores for the arterial ulcers were 21.5 ($n=6$, 2 diabetics) and 33.5 ($n=4$, 4 diabetics; $U=15$ n.s.). There was no correlation between pain assessments and age of patient, sex or duration of ulcer symptoms.

When diabetics were excluded, then median VAS score for the EMLA group was 18.5, $n=14$ vis-à-vis 91, $n=7$, $p<0.01$, in the placebo group.

The debridement was judged satisfactory in 14 patients in the EMLA group and 6 in the placebo group ($p=0.01$). Ten patients who reported severe pain (2 EMLA and 8 placebo) were treated with supplementary EMLA cream. All reported less pain after the second treatment, i.e. no pain in one patient, slight pain in 7 patients and moderate pain in 2 patients. The median score on the visual analogue scale for the patients who were initially treated with placebo ($n=7$, one value missing) was reduced from 91 to 15 mm with EMLA ($T=0$, $p<0.01$). The degree of pain

relief did not seem to be influenced by the severity of the pain during the first attempt.

Local reactions

A transient burning sensation was reported by 10/66 patients who were treated with EMLA. A further 3 cases of burning were reported among the patients who were treated a second time. Other reactions which were described by altogether 6 patients were: itch, a creepy feeling, a feeling of warmth, a tingling sensation and intermittent pricking or stinging. Slight redness at the edges of the wound was observed in 2 cases and paleness was observed in one patient.

In the placebo group there were 2 cases of transient burning sensations.

Table III. Assessment of pain during debridement

	Open study	Double-blind study		Supplementary EMLA ^a ($n=10$)
		EMLA ($n=16$)	Placebo ($n=14$)	
<i>Pain during debridement</i>				
None	22	3	0	1
Slight	19	8	4	7
Moderate	7	3	2	2
Severe	2	2	8	0

$p<0.05$. ^a All patients had severe pain during first attempt.

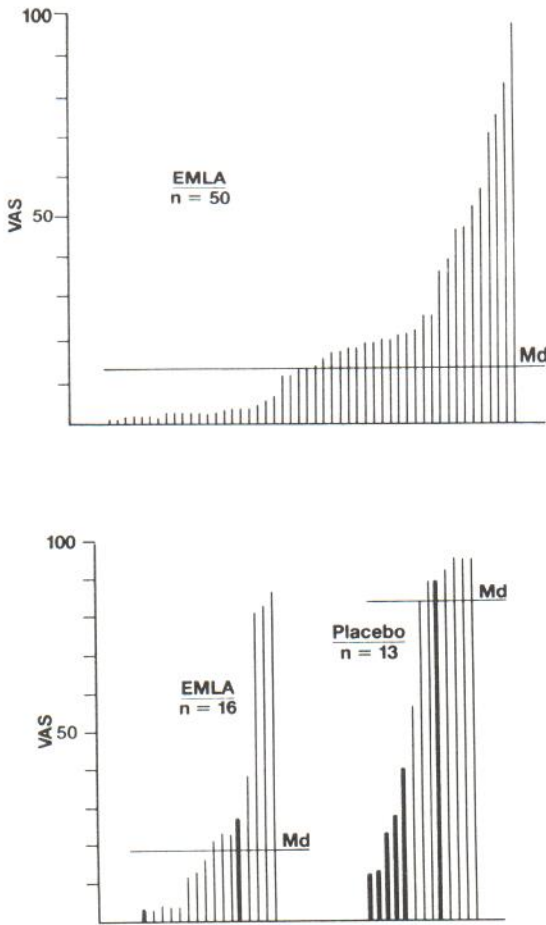


Fig. 1. Individual VAS pain scores arranged from lowest to highest, and median value; open study (top) and double-blind study (bottom). Thick bars indicate diabetics.

The reactions were of either mild or moderate intensity and did not necessitate any form of intervention.

DISCUSSION

According to Callam et al. (8) there are in Great Britain roughly 100 000 patients with active leg ulcers in a population of 400 000 leg ulcer patients. Prevalence surveys in Switzerland (9) and Sweden (10) have found similar proportions. The treatment of patients with leg ulcers is thus a medical problem of huge proportions.

One important part in the treatment of these patients is to eliminate factors which interfere with the healing of the ulcer. An essential part of this is the

mechanical removal of necrotic tissue which, if left, promotes bacterial in-growth and retards epithelialization. This procedure often has to be repeated many times during the treatment of a leg ulcer.

The results from the present investigation show that thorough cleansing of leg ulcers is a very painful procedure in non-diabetic patients, as demonstrated by the high pain scores in the placebo group. Local analgesia with topically applied EMLA cream offers the majority of patients good pain relief and is thus important for the achievement of satisfactory debridement. In this study, fewer than half of the patients could be treated satisfactorily (6/14) without surface anesthesia, while the majority of patients (14/16) with EMLA cream could. The duration of the leg ulcer did not have any influence upon the degree of pain, nor did the initial pain reaction to debridement influence the analgesic response to topically applied EMLA.

In this study the randomization protocol did not take account of diabetics. This resulted in an imbalance of patients with diabetes in the arterial ulcer group with the majority of diabetics in the placebo group. This is probably the explanation why we could not find any significant effect of EMLA in the arterial ulcer group, since all in the placebo group happened to be diabetics. Nevertheless, it is obvious that diabetic patients with leg ulcers feel less pain during debridement than non-diabetics do. In a comparison of pain score between EMLA and placebo, where all diabetics are excluded, the differences between EMLA and placebo are thus even more pronounced.

We are not aware of any studies on pain problems connected with the treatment of leg ulcers. Our findings with pain scores on the VAS scale up to 80–90 indicates that pain during cleansing of leg ulcers is a serious problem that should be taken into consideration in the treatment.

In the course of treatment of leg ulcers, repeated debridements are usually necessary and since the patients are often elderly, other forms of anesthesia such as general anesthesia or epidural anesthesia are not suitable methods for pain control. Resorption of EMLA through the ulcer does not seem to be a problem, since in no case did we see signs of systemic manifestation and in all cases serum levels of lidocaine and prilocaine were far from toxic levels. We could not detect any untoward effects on ulcer healing due to the application of EMLA. A randomized study is now being undertaken to see whether repeated application of EMLA affects ulcer healing.

REFERENCES

1. Burnand KG. Surgery of the veins and lymphatics. In: Kirk RM, Williamson RCN, eds. *General Surgical Operations*. Edinburgh, London, Melbourne, New York: Churchill Livingstone, 1987: 406–407.
2. Holzegel K. The dry treatment of venous ulcers. In: Negus D, Jantet G, eds. *Phlebology '85*. London, Paris: John Libbey, 1986: 609–612.
3. Amery MJ, Ryan TJ, Cherry GW. Successful treatment of venous ulcers with a new hydrocolloid dressing—passive or active in wound healing? In: Negus D, Jantet G, eds. *Phlebology '85*. London, Paris: John Libbey, 1986: 597–600.
4. Russ GM. Wet dressings in the treatment of venous leg ulcers. In: Negus D, Jantet G, eds. *Phlebology '85*. London, Paris: John Libbey, 1986: 592–596.
5. Evers H, von Dardel O, Juhlin L, Ohlsén L, Vinnars E. Dermal effects of compositions based on the eutectic mixture of lignocaine and prilocaine (EMLA). Studies in volunteers. *Br J Anaesth* 1985; 57: 997–1005.
6. Hallén B, Uppfeldt A. Does lidocaine–prilocaine cream permit painfree insertion of IV catheters in children? *Anesthesiology* 1982; 57: 340–342.
7. Juhlin L, Evers H, Broberg F. A lidocaine–prilocaine cream for superficial skin surgery and painful lesions. *Acta Derm Venereol (Stockh)* 1980; 60: 544–546.
8. Callam MJ, Ruckley CV, Harper DR, Dale JJ. Chronic ulceration of the leg: extent of the problem and provision of care. *Br Med J* 1985; 290: 1855–1856.
9. Widmer LK. Peripheral venous disorders. Prevalence and sociomedical importance. Observations in 4 529 apparently healthy persons. Basle Study III. Bern: Hans Huber Publishers, 1978.
10. Andersson E, Hansson C, Swanbeck G. Leg and foot ulcers. An epidemiological survey. *Acta Derm Venereol (Stockh)* 1984; 64: 227–232.