DERMAL ANAESTHESIA: COMPARISON OF EMLA CREAM WITH IONTOPHORETIC LOCAL ANAESTHESIA

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SUMMARY
We have compared the efficacy of two non-invasive methods of transdermal anaesthesia: application of EMLA cream and iontophoresis of 5% lignocaine with adrenaline 1:50000 in six healthy subjects. We tested depth of tissue penetration (pinprick) and effect on pain evoked by i.v. injection. After iontophoresis, pain on i.v. injection was abolished in five of six volunteers, whereas EMLA had no effect. We conclude that local anaesthetics penetrate deeply enough to numb both veins and skin with iontophoresis only.

KEY WORDS
Anaesthesia, local; iontophoresis; EMLA.

Pain and discomfort associated with insertion of i.v. needles have been shown to be reduced significantly by EMLA (eutectic mixture of local anaesthetics) cream after topical application [1, 2]. However, there has been little attention paid to its ability to prevent pain on i.v. injection of several drugs used in anaesthesia [3]. Iontophoresis of local anaesthetics enhances transdermal ionic transport [4, 5]. Although effective in reducing the pain of needle insertion [6], it has never been compared with EMLA cream for either venepuncture or i.v. administration of pain evoking drugs. This is surprising, since iontophotically applied local anaesthetics are effective within 10 min [6-8], whereas EMLA cream requires a rather long application time of up to 1 h [9-11]. We have therefore compared the efficacy of EMLA cream with that of iontophotically applied local anaesthetic on pain during venepuncture and during i.v. injections.

SUBJECTS AND METHODS
After approval by the Ethics Committee of the University of Düsseldorf and informed consent had been obtained, we studied six healthy volunteers (five male; ages 27-30 yr). Experiments started at 15:00 with the subject sitting comfortably, semi-recumbent at an ambient temperature of 20-22 °C.

Experimental design
Effects of each method of application were tested simultaneously on the ventral surface of the forearms of each volunteer. Two areas of about 20 cm² were selected so that a large vein crossed the full length of the area (fig. 1).

Pain during venepuncture was induced by inserting a 27-gauge cannula. To assess drug evoked pain (i.e. to test sensory innervation of the vein) 2 ml of hyperosmolar saline (2500 mosmol kg⁻¹, pH 7.4, temperature 24 °C) was injected within 10 s while the vein was compressed proximally for 1 min; saline 2500 mosmol kg⁻¹ (an osmolality more than 8-fold that of blood) has been demonstrated always to evoke pain in isolated vein segments [3]. To determine depth of tissue penetration provided by each method of application, a 27-gauge cannula was inserted perpendicularly through the skin in five well-defined sites within the numbed area until pain or discomfort were felt (pinprick). The cannula was marked with a piece of paper so that depth of insertion could be measured easily [7].

EMLA cream is a eutectic mixture of lignocaine base 2.5 g dl⁻¹ and prilocaine base 2.5 g dl⁻¹ [12, 13]. The cream was applied under an occlusive dressing (Tegaderm) for 60 min as recommended by the manufacturer and others [13, 14]. Iontophoresis enhances transdermal ionic transport by direct electrical current [4, 15]. In the present experiments, blotting paper was impregnated with 5% lignocaine 0.5 ml with and without adrenaline 1:50000. Adrenaline was used to provide approximately equal durations of anaesthesia for EMLA cream and iontophotically applied local anaesthetic [7, 16]. The experiments without adrenaline were performed to study its influence on penetration of iontophotically applied lignocaine. As the positively charged drugs, lignocaine and adrenaline, travel from anode to cathode, the blotting paper was fixed on the test area under the anode, the cathode being placed on the dorsal side of the forearm. Constant direct current was adapted to the individual tolerance (appearance of stinging or burning sensations) of the volunteers, leading to a current density of 0.1-0.2 mA cm⁻² [4].

Experimental programme
The test areas on each forearm were swabbed with an alcohol solution for degreasing and disinfection. The chosen vein was punctured and 2 ml of...
Fig. 1. Schematic presentation of the experimental design. Test areas were of identical size for either application method. EMLA = 2.5% lignocaine + 2.5% prilocaine. Placement of the cathode was on the dorsal surface of the forearm. Anode: 0.1-0.2 mA cm\(^2\) d.c. for 10 min. Blotting paper was impregnated with 5% lignocaine plus adrenaline 1:50000.

Data analysis

Pain during injection of hyperosmolar saline (expressed as percent of maximum pain), depth (mm) of painless needle insertion (mean of five measurements at the test sites) and duration of anaesthesia (time (min) from removal of cream or electrodes until full sensitivity to pinprick) were measured for each volunteer or presented as medians and ranges, or both. Data were analysed using Wilcoxon's signed-rank test. Significance was assumed when \( P < 0.05 \).

RESULTS

In each volunteer, venepuncture was painful before but not after numbing the skin with EMLA cream or iontophoretically applied local anaesthetic. In contrast, pain on i.v. injection of hyperosmolar saline was significantly reduced only after iontophoresis of lignocaine with adrenaline \((P = 0.04)\), but not after EMLA cream \((P = 0.35)\). Pain on injection was abolished in five of six volunteers after iontophoresis, whereas pain decreased only slightly in three and increased in three volunteers after EMLA cream (fig. 2). In each subject, anaesthesia as tested by painless insertion of a 27-gauge cannula extended significantly deeper after iontophoresis than after...
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application of EMLA cream (fig. 3). Duration of anaesthesia did not differ between the methods (table I). Depth of painless needle penetration after iontophoretic application of lignocaine both with and without adrenaline did not differ significantly, whereas duration of anaesthesia was significantly prolonged by adrenaline (table I). Iontophoresis of plain lignocaine induced local hyperaemia, but iontophoretically applied lignocaine with adrenaline markedly blanched the anodal skin area.

DISCUSSION

We have found that transdermal local anaesthesia by iontophoresis, but not by EMLA, reduced pain on i.v. injection of hyperosmolar saline, whereas venepuncture was painless with both methods.

The experiments were designed to compare the efficacy of transdermal local anaesthesia by two methods, therefore iontophoresis of local anaesthetics and EMLA cream were applied as recommended in the literature for best effect. Covered with an occlusive dressing for 60 min, EMLA penetrates intact skin. Although application times up to 120 min were thought necessary in one study [16], EMLA has been shown to be effective after a period as short as 20 min [17]. In accordance with most investigators [9, 14, 18, 19], we exposed the skin for 60 min, as recommended by the manufacturer.

The effect of iontophoretically applied local anaesthetic depends on direct electrical current intensity [7]. In the present experiments, current was increased slowly until discomfort (stinging or burning sensations) was felt, usually at 0.1–0.2 mA cm⁻² [4]. Although 2–4% lignocaine is recommended for iontophoresis [7], a 5% solution was used in the present experiments to provide adequate local anaesthetic. Adrenaline was added to lignocaine in one series of experiments to provide a duration of action similar to that of EMLA cream. When testing iontophoretically applied lignocaine with or without adrenaline under otherwise identical conditions, we found that the depth of tissue penetration did not differ. Obviously, the addition of adrenaline influenced the duration of action, whereas depth of tissue penetration depended only on the electrical conditions used during iontophoresis. Other workers have found that the mean depth of penetration of lignocaine with and without noradrenaline into skin, as measured by radioactive tracers, was identical [20].

Peripheral veins are invested with polymodal nociceptors which, in common with cutaneous receptors, respond to hyperosmolar solutions [3]. As only the iontophoretically applied local anaesthetics reduced pain on i.v. injection, iontophoresis obviously forces the molecules deep enough into skin to block vein wall afferents. Depth of painless needle insertion in each volunteer was also greater with iontophoresis than with EMLA cream.

Although five volunteers did not feel any pain after iontophoretic application of lignocaine with adrenaline, pain intensity after i.v. injection of hyperosmolar saline was unchanged in one subject. This volunteer was very sensitive, as demonstrated by the low current (0.1 mA cm⁻²) necessary to induce stinging or burning sensations. As the effect of iontophoresis correlates with the current applied [4], penetration of lignocaine may have been limited in this volunteer; indeed, he had the least difference in depth of tissue penetration (subject No. 3 in figure 3: 4.4 mm EMLA, 4.8 mm iontophoresis). We believe that the use of a larger current (up to 0.6 mA cm⁻² as used and tolerated by volunteers in several studies [7, 8, 21]) would have increased depth of anaesthesia and made this particular subject analgesic to i.v. injection of hyperosmolar saline.

![Fig. 3. Depth of painless insertion of a 27-gauge cannula after application of EMLA cream (■) (mean 4.4 mm; range 3.2–4.8 mm) or iontophoresis of 5% lignocaine with adrenaline 1:50000 (□) (mean 6.0 mm; range 4.8–7.4 mm). Depth of tissue penetration was significantly greater after iontophoresis than after EMLA (P = 0.03).](https://academic.oup.com/bja/article-abstract/71/3/375/2782835/12/March/19)

| TABLE I. Depth and duration of transdermal anaesthesia (median (range)). * Significant difference (P < 0.05) compared with EMLA; ns compared with no adrenaline. † Significant difference (P < 0.05) compared with no adrenaline; ns compared with EMLA |
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| Iontophoresis: 5% lignocaine | Adrenaline | No adrenaline | EMLA cream |
| Depth of tissue penetration (mm) | 6.0 (4.8–7.4)* | 5.3 (2.4–8.4) | 4.4 (3.2–4.8) |
| Duration of anaesthesia (min) | 63 (53–83)† | 9.5 (6–15) | 63 (57–103) |
REFERENCES


