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Emla for Pain Relief During Arterial Cannulation

A double-blind, placebo-controlled study of a lidocaine-prilocaine cream

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ABSTRACT

The aim of the study was to evaluate the effect of a lidocaine-prilocaine cream (EMLA cream, Astra) in relieving pain during arterial cannulation. The study had a random, double-blind, placebo-controlled design and included altogether 90 patients. All the patients were premedicated with an opioid before cannulation. An EMLA application time of 60 minutes was used in 60 patients (30 EMLA/30 placebo) and there was no difference in the pain reaction measured on a visual analogue scale (VAS) or on an observer's verbal scale. The study was extended with a further 30 patients (15 EMLA/15 placebo) with an application time exceeding 90 minutes. Between these groups pain experience measured by VAS did not show any significant difference although the mean value was lower in the EMLA group. Observer ratings showed a significant ($p<0.01$) difference in distribution towards lower ratings in the EMLA group.

In conclusion EMLA was found to have a weak, but measurable effect when the application time exceeded 90 minutes but not after 60 minutes.

INTRODUCTION

Cannulation of the radial artery is a frequently performed procedure in clinical medicine. Its most common indications are repeated blood analysis and direct arterial pressure monitoring. Apart from the general comfort of the patient, pain relief during cannulation may also be indicated in patients with cerebral aneurysms, raised intracranial pressure etc. Usually this pain relief is achieved by infiltration of a small volume of local anaesthetics prior to cannulation or the procedure is performed after the induction of general anaesthesia.

EMLA is a lidocaine-prilocaine mixture for topical analgesia. After 60 minutes under an occlusive dressing the cream has penetrated the skin sufficiently to allow pain-free venipuncture, and after 120 minutes superficial operations (skin-grafting) can be performed (4,5). Its clinical use is now well-documented and widespread, especially in paediatrics (3).

Only one study has been published on the use of EMLA for the alleviation of pain during arterial cannulation (9). In this study EMLA was compared with the intradermal injection of local anaesthetics. Since arterial puncture is generally considered to differ from venipuncture as far as pain is concerned, there were grounds for a double-blind, placebo-controlled study.

PATIENTS AND METHODS

The study protocol was approved by the Ethics Committee of the Medical Faculty, University of Uppsala. A total of 90 patients participated in the study, which had a double-blind, placebo controlled design. They were all scheduled for major surgery where arterial cannulation for direct arterial pressure monitoring was indicated. Initially 60 patients were randomly allocated to two groups. EMLA 2.5 g or placebo (from identically marked tubes) was applied under an occlusive dressing (Tegaderm TM,3M) over each of the radial arteries at the wrist. All patients were premedicated with an opioid. After 60 minutes the dressings were removed and the skin was inspected for local skin reactions. A Venflon^{R} Arterial Cannula (outer diameter 1 mm) was then inserted. No other skin punctures or painful procedures were allowed before the arterial cannulation. The patients rated their pain experience on a visual analogue scale (VAS) (8). The pain reaction was graded on a verbal scale by one of the two observing nurses involved in the study (no pain, slight, moderate, severe pain).

The initial trial with an application time of 60 minutes did not reveal any statistically significant difference between EMLA and placebo in VAS or observer scores. Since the application time has an influence on the analgesic effect, it was decided to extend the study with a further 30 patients (15 placebo). The same protocol was used but the application time was extended to at least 90 minutes.

For the first part of the study, 30 patients in each group were estimated to be sufficient to allow the detection of a difference between the groups of 10 mm with a risk level of 5% and a power of 80% (assuming a standard deviation of 19.5) (values obtained from previous studies on venipuncture). For the second part 15 patients in each group were estimated to be sufficient.

Mean values and standard deviations were calculated according to standard formulas. For the comparison of mean values Student's t-test for unpaired data and for comparisons of proportions (i.e. observer scores) the Ansari-Bradley test was used (2).

RESULTS

For patient data see Table 1. In the patient groups with extended application time a total of thirteen patients in each group was evaluated since there were four drop-outs due either to failure to perform arterial cannulation or to cancellation of surgery.

Table 1. Patient characteristics, application times and interval between removal of dressing and puncture (mean ± sd).

60 minutes' application

	EMLA	PLACEBO
No of patients	30	30
Weight (kg)	74 ± 13	70 ± 12
Height (cm)	174 ± 10	171 ± 7
Actual application time (min)	78 ± 30	77 ± 25
Interval between removal and cannulation (min)	7 ±	9 ± 10

90 minutes' application

	EMLA	PLACEBO
No of patients	13	13
Weight (kg)	74 ± 12	74 ± 11
Height (cm)	171 ± 7	172 ± 11
Actual application time (min)	124 ± 9	122 ± 13
Interval between removal and cannulation (min)	8 ± 7	7 ± 6

As indicated above, no statistically significant difference in pain experience could be measured between EMLA and placebo after 60 minutes' application (Table 2, Fig. 1).

When the application time exceeded 90 minutes there was no statistical difference in pain experience measured in VAS scores (Table 2) but there was a statistically significant ($p<0.01$) difference in distribution of observer pain scores with lower values in the EMLA group (Fig. 2).

Apart from paleness or redness of the skin at the site of application no local side effects were noted. None of the reactions observed were considered of clinical importance. No general side effects were noted.

Table 2. VAS scores (mean ± sd)

60 minutes' application	EMLA	PLACEBO
VAS	29 ± 26	36 ± 27

90 minutes' application	EMLA	PLACEBO
VAS	17 ± 28	28 ± 31

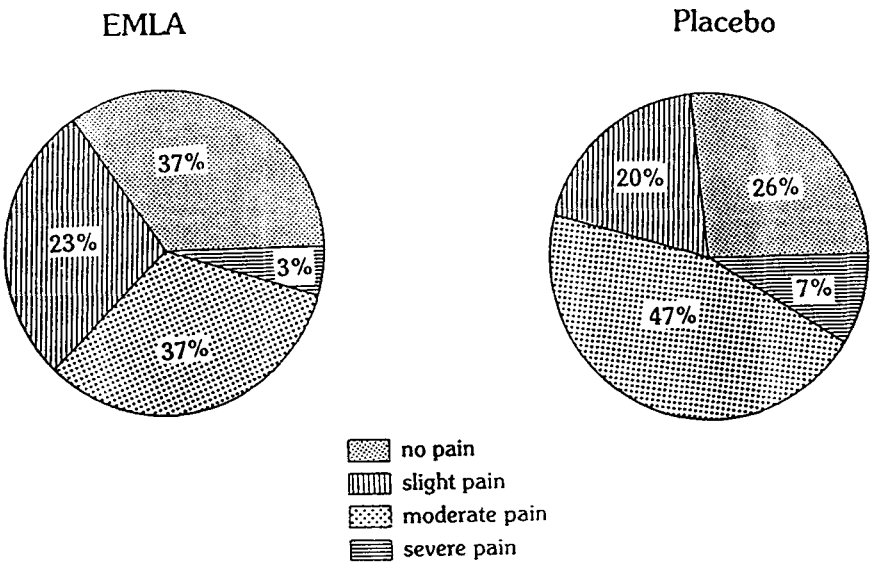

Fig. 1. Observer pain ratings after 60 minutes application

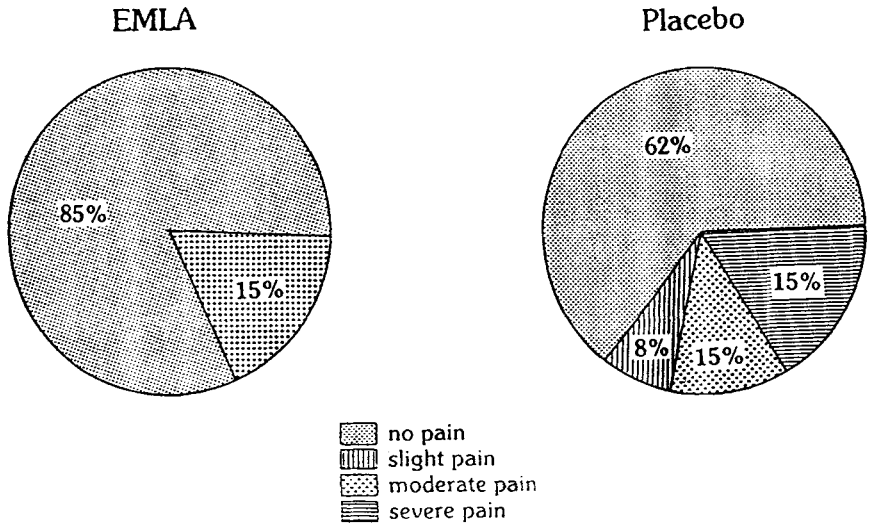

Fig. 2. Observer pain ratings after 90 minutes application

DISCUSSION

With the introduction of EMLA, pain-free venipuncture before the induction of anaesthesia, for blood-sampling etc. can be achieved with ease and this has contributed to an increase in comfort to patients, especially in paediatric care (6). In many clinical situations arterial cannulation is indicated and this should preferably be achieved without causing too much discomfort to the patient. Although EMLA permits pain-free venipuncture in most patients after an application time of 60 minutes, the results from these studies cannot be directly transferred to the technique of arterial puncture. It is a generally held view among anaesthetists that arterial puncture is more painful than venipuncture. Ray and Wolff (7) have studied the pain-sensitive structures of the head in patients undergoing neurosurgery. They found that extracranial arteries were more pain-sensitive than veins. The introduction of procaine hydrochloride into the adventitia of the artery produced immediate anaesthesia and the authors implied that sensory nerves originate nearby and travel along with the arteries. It has not been possible to find any comparable data concerning the perception of pain in peripheral arteries at the wrist. The slow penetration of the skin by local anaesthetics and the subcutaneous location combined with the higher blood flow in the artery may cause a reduced concentration of local anaesthetics in the surrounding tissues after dermal application and thus contribute to a difference in pain experience as compared to the veins.

In the present study, the actual application time in the 90-minute groups averaged just over 120 minutes. The effect of EMLA is at its maximum after application times of this length (1). In a study by Russel, Desmond and Fox (9) 90 minutes of EMLA application was found to produce better analgesia for arterial cannulation than local infiltration with lignocaine. Since the infiltration of the local anaesthetic may cause pain per se, it is interesting to compare their results with ours where EMLA was tested against placebo. In their study the majority of patients indicated mild or moderate pain when infiltration was used while the pain scores were none (65%) or mild (30%) after 90 minutes of EMLA application. In our study 11 out of 13 patients (85%) in the EMLA group scored no pain after this application time, whereas 8 out of 13 did so (61%) in the placebo group. In the study by Russel et al. diazepam was used as premedication, whereas opioid premedication was used in the present study. This is probably the reason why the placebo group in our study has surprisingly low pain ratings.

After a mean application time of 120 minutes there is a tendency towards lower VAS scores, but these figures do not reach statistical significance due to a large variation. Neither the actual application time or interval between removal of the dressing and the arterial puncture could be correlated to this variation. A longer application time might be effective and a comparative study without the influence of premedication may also reveal an increased difference between EMLA and placebo. However, the aim of the study was to evaluate the effectiveness of the drug in the clinical situation.

In conclusion, neither 60 nor 120 minutes of EMLA application significantly reduced subjective pain experience measured on a VAS scale. Observer scores of pain indicated an effect of EMLA after an application time exceeding 90 minutes (with 85% of the patients scored as no pain) but not after 60 minutes of application.

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