

## Duration of Analgesia Following Application of Eutectic Mixture of Local Anaesthetics (EMLA) on Genital Mucosa

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The topical anaesthetic formulation EMLA cream (eutectic mixture of local anaesthetics) is increasingly used prior to minor painful procedures performed on genital mucosa. The aim of the present study was to gain knowledge about the correlation between duration of application of EMLA and duration of analgesia. Three different application times – 5, 10 and 20 min – were investigated in 12 healthy young women. Pin-prick pain thresholds to argon laser stimulation were measured before and after application of EMLA. Repeated measurements were performed until normal sensitivity returned. No significant difference in duration of analgesia was seen between the three application times. However, 10 min application time tended to produce the longest mean duration of analgesia (22.2 min). Surprisingly, a large inter-individual variation in duration of analgesia was seen. Thus, after 10 min application time the shortest duration of sufficient analgesia was 5 min, while the longest was 46 min. On the basis of this work, it seems advisable to start minor surgery on genital mucosa after about 10 min application time, and it is recommended to bear in mind that the duration of analgesia varies and may be very short in some patients. *Key words:* Argon laser; Experimental pain; Threshold; Topical analgesia.

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Application of analgesia to female genital mucosa has until recently mainly been limited to infiltration with local analgesics. This is a painful procedure with a theoretic risk of infection, bleeding and intravascular administration.

It has previously been shown that application of eutectic mixture of local anaesthetics (EMLA<sup>®</sup> cream) on female genital mucosa for 5–10 min provides an effective analgesia (visual analogue scale) for minor vaginal surgery, for example treatment of genital warts with cautery (1). Optimal application time of EMLA cream on genital mucosa with regard to depth of analgesia has also been thoroughly investigated by Rylander et al. (2), who applied EMLA cream for 1–75 min. The most effective analgesia was shown to be achieved after 5–15 min application time estimated by a visual analogue scale. If the application time was extended to more than 15–20 min, a decrease in analgesic effect was seen.

The introduction of lasers for experimental pain stimulation has made it possible to determine the pin-prick pain threshold (3) and thereby experimentally to study the effect of different analgesics. Laser stimulation has recently been used to evaluate the effect of EMLA cream on intact skin (4, 5). In the present study the laser stimulation method was used to deter-

mine the onset and duration of analgesia following application of EMLA on vaginal mucosa.

Three different application times – 5, 10, and 20 min – were compared in order to investigate a possible correlation between duration of application and duration of analgesia.

### MATERIAL AND METHODS

#### Subjects

Twelve healthy, female volunteers participated in this study (mean age 25.3 years  $\pm$  2.7 years (s.d.)).

All volunteers gave their written informed consent according to the Helsinki Declaration. The experiment was approved by the regional scientific-ethical committee and The National Board of Health.

#### Methods

The output from an argon laser (Model 168, Spectra Physics, USA) was transmitted to the mucous membrane of the inside of the labia minora via a quartz-fibre. An external laser power meter (Ophir, Israel) was used to measure the power applied to the mucosa. The output could be adjusted from 50 mW to 2.9 W. A continuous low energy beam was used to visualize the stimulation site. The pin-prick pain thresholds were determined by means of a laser stimulus with a duration of 200 ms and a beam diameter of 3 mm using a fixed distance between the fibre and the mucous membrane. The stimulation site was changed between every measurement to avoid receptor sensitization or fatigue in the areas tested. The pin-prick pain threshold was defined as the lowest energy output from the laser which produced a distinct, sharp pricking pain. The thresholds were found by starting at a low output. A gradual increase in output followed until the first pin-prick pain was felt by the volunteer. The thresholds were calculated as the mean of five ascending series of stimulation. The highest output level was limited to 1.5 W to avoid superficial burn lesions.

The 12 volunteers were tested with repeated laser stimulation after three different application times (5, 10 and 20 min). A minimum of 6 h was required between each test session. Every session started with determination of the pre-application pin-prick pain threshold. Two tubes of EMLA cream each containing 5 g were then applied to the inside of the labia minora. EMLA cream contains 25 mg lidocaine and 25 mg prilocaine per gram. The volunteers thus received 250 mg lidocaine and 250 mg prilocaine. No occlusion was used and the volunteers were permitted to rest sitting while waiting for the start of pin-prick pain threshold measurements.

After the end of the application time the cream was wiped off and the measurement of the pin-prick threshold was performed immediately. Measurements were performed after 5 and 10 min. Then repeated measurements followed every 2 min. When the pin-prick pain thresholds started to decrease, measurements were performed every minute until the preapplication thresholds were reached.

#### Statistical analysis

Statistical analysis was performed with non-parametric tests (Mann-Whitney test). Statistical significance was accepted at the 5% level. The results are expressed as a mean  $\pm$  s.d.

Table I. Duration of analgesia following application of EMLA cream

The maximal duration of efficient analgesia was observed after 10 min application of EMLA cream, at which point an argon laser stimulus of 1.5 W for 0.2 s could not be felt for a period of 22 min on average. The differences in duration of analgesia are not statistically significant. Standard deviations are given in brackets.

Duration of application	Average pre-application thresholds (W)	Average duration of analgesia (min)
5 min	0.38 (0.15)	16.2 (5.3)
10 min	0.42 (0.19)	22.2 (11.8)
20 min	0.46 (0.16)	18.3 (7.5)

## RESULTS

Analgesia was obtained with all three application times. Thus, the volunteers were unable to feel maximal (1.5 W) laser power immediately after the end of application time.

The maximal average duration of analgesia was reached after 10 min application time, after which a laser stimulus of 1.5 W could not be felt for 22 min (Table I). Compared to the 5 min application time, where analgesia lasted on an average 16.2 min, this represents an increase of 37%. The difference in duration of analgesia between the 20 min application time and the 10 min application time was 21%.

The differences, however, are not statistically significant. The duration of analgesia varied from 5 min to 46 min when EMLA cream was applied for 10 min.

None of the volunteers reported any discomfort related to the application of EMLA cream. No adverse reactions were noted in relation to this study.

## DISCUSSION

In this study, we applied EMLA cream to vaginal mucosa to demonstrate which application time produces the longest duration of analgesia. The method used was quantitative laser stimulation. Pain can be elicited by several different stimuli, e.g. electrical current, mechanical pin-prick and pressure. The use of electrical stimuli is often criticized, since the obtained pain is very different from any other natural pain experience. And mechanical pin-prick and pressure do not activate the nociceptive system specifically, since they stimulate more than one sensory component (e.g. touch and pressure at the same time). The laser method selectively stimulates with heat, and it has been used as an experimental model to evaluate the effect of various analgesics. Previously, the technique has thus been used to describe e.g. 1) the hypoalgesic profile of EMLA cream applied to skin (4); 2) the hypoalgesic profile of lidocaine infiltration in skin (5); and 3) the duration of analgesia obtained by lidocaine spray applied to the mucous membranes of the mouth (6).

In this study the maximal laser energy output was limited to 1.5 W. In previous studies with the argon laser the maximal energy output has been limited to 2.5 W (4, 5). However, in these studies the stimulation was performed on intact skin

where the resistance to laser stimulation is higher, due to a much higher reflection of the laser light from the surface compared to mucosa. The 1.5 W limit was chosen to avoid superficial burn lesions.

When considering the method used in the present study one should be aware that the laser stimulus is quite superficial. Thus, the recommendations from this study only apply to surgery of superficial layers, e.g. removal of condylomata acuminata, and the results cannot be extended to surgery performed on deeper layers of the genital mucosa.

Differences in average duration of analgesia were observed in the present study (Table 1). There was a non-significant trend indicating that 10 min is the optimal application time. However, the differences seen were not statistically significant.

More important is the inter-individual variation in duration of analgesia. After 10 min of EMLA application the shortest period of analgesia was 5 min and the longest 46 min. Thus, the duration of analgesia shows a great inter-individual variability, and in clinical work it is important to remember that a few patients will allow only a very short period for minor surgery in EMLA-induced analgesia. Cyclic changes in the genital mucosa with changes in vascularization might be responsible for this inter-individual variability in duration of analgesia.

## CONCLUSION

Application of EMLA cream on genital mucosa is a suitable method to obtain analgesia before minor surgery. In this study we found no statistically significant difference in duration of analgesia between application times of 5, 10 and 20 min. Average duration of effective analgesia was 19 min. However, a large variation in the duration of analgesia between patients should be expected, since the range of duration of effective analgesia was 5 to 45 min after a 10 min application time.

The application of EMLA was painless in all patients and no adverse reactions were noted.

On the basis of this work it is recommended to start minor surgery on genital mucosa after about 10 min application time and to bear in mind that the duration of analgesia may be very short in some patients.

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