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Local Anaesthesia with a Lidocaine/prilocaine Cream (EMLA®) for Cautery of Condylomata Acuminata on the Vulval Mucosa. The Effect of Timing of Application of the Cream

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The analgesic efficacy of a lidocaine/prilocaine cream (EMLA®) for the cautery of genital warts was evaluated in an open study. Fifty-two women aged 18 to 28 with at least two condylomata on the vulval mucosa took part. In a pilot study ($n=10$) the time of onset of anaesthesia after the application of EMLA to the mucosa was established by pinching with a forceps. All ten patients were anaesthetized within 5–7 min and cautery was performed with no or only slight pain in 9/10 patients. In the main study EMLA was applied to the mucosa of 42 women for 10, 15 or 20 min. The anaesthesia was satisfactory for the cautery of condylomata in 92% of the patients after the application of EMLA for 10 minutes. The analgesic efficacy decreased gradually with application times of 15 min or longer ($p<0.05$). In the case of insufficient anaesthesia, an additional application of EMLA for 2–5 min enabled the operations to be completed in 7/8 patients.

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A common treatment for genital warts is surgical removal by cautery. Cautery is painful and requires analgesia, which may be provided by infiltration of local anaesthetics. Injections in the genital area are, however, painful in most patients and cause bleeding. Hallén et al. (1) recently showed that a lidocaine/prilocaine cream (Eutectic Mixture of Local Anaesthetics, EMLA®) was effective when used as a topical anaesthetic for the cautery of condylomata in men, whereas this was the case in only 40% of the women investigated. The results suggested that the applica-

tion time to the mucosa should be studied further. The present study was performed to determine the time of onset of anaesthesia of EMLA cream and the effect of timing of application of the cream to the genital mucosa.

PATIENTS AND METHODS

The study was approved by the Ethics Committee of the University of Uppsala. Fifty-two female out-patients, 18 to 28 years old, with at least two condylomata on the vulval mucosa took part. Following the recommendations of the Declaration of Helsinki, the patients gave their informed consent to participate.

In a pilot study the minimum effective application time and the correlation between analgesia of the genital mucosa, as measured by a forceps pinch, and pain caused by cautery of warts was assessed in ten patients. The analgesic efficacy for cautery after 10, 15 or 20 min application of EMLA to the genital mucosa was subsequently investigated in 42 patients.

The patient was placed in the dorsosacral position and EMLA cream (Astra, Södertälje, Sweden) containing lidocaine 25 mg and prilocaine 25 mg per gram was applied. The patient remained in this position until the time of cautery. All patients were treated by the same investigator.

Pilot study

A dose of 5–10 g cream was spread evenly over the vulval mucosa, including the external part of the hymenal fold. A plastic film (Glad®, Union Carbide, USA) which was taped to the skin, was applied over the cream for the first five minutes. The pain from a forceps pinch in the genital mucosa was assessed before application of the cream, after five minutes, and then after every one or every two minutes until the patient did not feel the pinch. Each pinch was given at the side of any previously-tested site, and at the side of the condylomata to be cauterized. When analgesia was present, the cream was wiped off and the condylomata removed by thermocautery and curettage a few minutes later.

Main study

Each wart on the genital mucosa was covered with a thick layer of cream, at least one gram per lesion, up to a maximum of 10 g per patient. Plastic film was not used. When the warts were situated at the introitus vaginae, the cream was applied to the external part of the hymenal fold. In the first 25 women every odd patient received 10 and every even patient 15 min application of the cream. The following 10 patients were given 20 min and the remaining seven women 15 minutes' application. The surgical removal of the condylomata was performed as in the pilot study and the duration of the cautery was also recorded.

Two patients were excluded from the analysis of analgesic efficacy: One woman in the 10-min group was very nervous and distressed, causing the investigator to discontinue treatment. Another patient was to be treated for 15 min but had the cream applied for only 13 min.

Assessments

In the pilot study the patient rated the pain experienced from each pinch on a 100 mm horizontal visual analogue scale (VAS) where 0 mm indicated "no pain" and 100 mm "severe pain" (2). The patient rated the pain experienced from the cautery on a VAS and on a verbal scale as no pain, slight pain (= tolerable) or moderate pain (= almost tolerable). If the patient felt moderate pain, the treatment was stopped and additional analgesia was given by local infiltration of lidocaine (Xylocaine®) or by the further application of cream. The need for supplementary analgesia was recorded.

The patient was asked about local irritation, particularly any burning sensation, before the start of the cautery. The physician examined the mucosa for the presence of pallor, erythema, oedema or other reaction. The assessments were recorded on a verbal scale as none, mild, moderate or severe.

Statistics

In the main study the differences in verbal pain assessment, the need for additional analgesia and local reactions in relation to application time were tested in accordance with Mantel & Haenszel (3, 4, 5). The difference in VAS scores between the 10-, 15- and 20-minute groups was tested by analysis of variance and linear regression.

RESULTS

The treatment groups were comparable with regard to age, number of condylomata and location of the lesions. In the main study the groups were well-matched in respect of the dose of EMLA given (median 5 g) and the duration of the cautery (median 7–10 min).

Time of onset of anaesthesia (pilot study)

The pain ratings of the forceps pinch before EMLA was given ranged from 26 to 76 (median 53.5) on the visual analogue scale. After five minutes' application of EMLA the pain rating had decreased in all patients to between 0 and 12 (median 7). All ten patients were completely anaesthetized (score 0) within seven minutes (median 6 minutes).

Analgesic efficacy

The pain from the cautery was rated as either none or slight by nine out of ten patients in the pilot study. The corresponding figures were 92% in the 10-min group, 67% in the 15-minute group and 50% in the 20-minute group ($p<0.05$). The median pain scores (VAS) increased from 7 to 34.5 with increasing application time, but this trend did not reach statistical significance.

There was a significant increase in the need for additional analgesia with application time (Fig. 1).

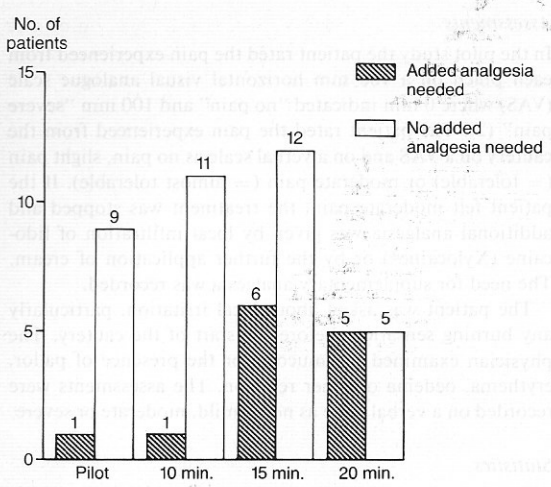

Fig. 1. Need for additional analgesia ($p<0.05$, main study).

The results in the 10-minute group were similar to those in the pilot study, where patients were treated with EMLA for 5–10 min. Five patients received additional infiltration of lidocaine. EMLA cream given as additional analgesia during 2–5 (median 5) minutes enabled the operation to be completed in 7/8 patients.

Adverse reactions

No sign of systemic reactions was seen in any of the patients. In all but two of the patients the local reactions were rated as mild. There was no significant change in the frequency of the local reactions with application time. Altogether, mild oedema was present in 33%, erythema in 67% and pallor in none of the patients. A mild burning sensation was reported by 13.5%. Two patients experienced pruritus.

DISCUSSION

A local anaesthetic cream offers several advantages compared to the conventional infiltration of local anaesthetics. The cream is easier to apply, especially to the vulval mucosa. Its application does not cause pain or bleeding and hematomas are avoided.

This study indicates that the time of onset of anaesthesia by EMLA cream of the genital mucosa is 5–7 min. As three patients in the pilot study did not feel the first pinch after five minutes, onset may have been even more rapid in these women. In clinical practice an application time of seven minutes has subsequently proved to constitute a suitable minimum. The analgesic efficacy decreased gradually with application times of 15 minutes or longer. A majority of the patients had condylomata on the introitus vaginae. When additional analgesia was required, this was usually necessary for warts situated under the hymenal folds in the introitus. Clinical experience after completion of the study suggests that anaesthesia in this region is more effective if EMLA is also applied to the inside of the hymenal fold, and not only to the outside, as was the case in the study.

The results are in agreement with those of Rylander et al. (6) who studied the local anaesthetic efficacy of EMLA when applied to the vulval mucosa between 1 and 75 min prior to carbon dioxide laser treatment of condylomata. They found that the most effective degree of anaesthesia was achieved after 5 to 15 min application of EMLA. The results may also in part explain why Hallén et al. (1) reported satisfactory analgesia in only 40% of women when EMLA cream was applied for 30–105 min prior to the thermocautery of condylomata. In the earlier study, however, genital warts situated on the perigenital skin were also treated (1). Juhlin et al. (7) removed genital warts in both men and women without pain after 15–30 min application of EMLA.

In the present study a thick layer of cream was applied. The cream stayed in place until it was wiped off prior to surgery. The reason for the decrease in analgesic efficacy with increasing application time of the anaesthetic cream may be that when the local anaesthetics in the cream layer closest to the mucosa have been absorbed, the transport rate of the local anaesthetics from the cream into the mucosa decreases. This is supported by the fact that additional cream gave satisfactory anaesthesia when applied for 2 to 5 min immediately after the cautery was interrupted. An additional possible explanation could be lidocaine-induced vasodilation (8) and subsequent increased systemic absorption of the local anaesthetics from the mucosa. The observed erythema may result from vasodilation.

The earlier investigators (1) found that additional local anaesthetic infiltration was less painful than injections generally are in the genital area without pretreatment with EMLA. This finding was supported since four out of six women described the pain from the injection of additional lidocaine into the mucosa as slight. In two further patients perineal and/or perianal injections were given without pain after 10–20 min application of EMLA.

In conclusion, the application of EMLA cream for

5–10 min produced satisfactory anaesthesia for the cautery of condylomata in more than 90% of patients. The analgesic efficacy decreased gradually with application times of 15 min or longer. In the case of insufficient anaesthesia, a further application of EMLA enabled the operations to be completed in most patients. The painless administration of the cream was appreciated by those patients who had earlier been given an injection of local anaesthetics. The method is also practical in clinical use, especially in the common situation where multiple warts are present.

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Cutaneous Cryptococcosis Resembling Molluscum Contagiosum: A First Manifestation of AIDS

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A 30-year-old homosexual man developed multiple skin umbilicated lesions resembling molluscum contagiosum. Initially the lesions were on his face but they rapidly spread. Histopathology and mycologic cultures of a skin biopsy revealed cryptococcus neoformans which was also identified in cerebrospinal fluid and in bronchoalveolar washings. The patient had fever, weight loss, generalized lymph node enlargement, depletion of the T helper subpopulation and positive HIV-1 serology. During treatment with flucytosine and amphotericin B, the skin lesions regressed in 3 months (cryptococcus neoformans disappeared in the cerebrospinal fluid and skin within one and five weeks, respectively). Our case demonstrates that molluscum contagiosum-like skin manifestations may be caused by cryptococcal infections. So it is necessary to perform skin biopsy in HIV seropositive patients with skin lesions resembling molluscum contagiosum, to diagnose mycotic infections, and especially cryptococcosis. Cutaneous cryptococcosis was, in this case, the first symptom of AIDS.

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Cutaneous lesions, in particular fungus infections, are frequently observed in the acquired immunodeficiency syndrome (AIDS). We report a case of cryptococcus neoformans (CN) cutaneous infection of an atypical presentation, which was the first manifestation of AIDS.

CASE REPORT

A 30-year-old homosexual male was hospitalized for multiple skin lesions (Fig. 1), fever and weight loss. A month earlier, he had first consulted due to the appearance of facial skin lesions. At that time, he had three facial lesions which spread on the trunk and which involved the trunk and extremities