DOUBLE-BLIND EVALUATION OF A LIGNOCAINE-PRILOCaine CREAM (EMLA) IN CHILDREN
Effect on the Pain Associated with Venous Cannulation

E.-L. MAUNUKSELA AND R. KORPELA

Fear and pain can make i.v. cannulation a traumatic experience for a child, and time consuming for the clinician or nurse. It is a special problem in children with chronic diseases such as leukaemia, who undergo repeated blood sampling or i.v. injection. A topical preparation applied to the skin without discomfort which alleviated the pain of the needle puncture would be helpful to both patients and staff.

The solid, pure bases of lignocaine and prilocaine, if mixed in equal amounts, form an oil at temperatures greater than 16 °C; that is, they constitute a eutectic mixture. An oil-in-water emulsion cream of that mixture, EMLA (Eutectic Mixture of Local Anaesthetics), has been tested previously in adults (Ehrenstrom Reiz, Reiz and Stockman, 1983; Wahlstedt et al., 1984; Hallén, Carlsson and Uppfeldt, 1985) and in older children (Hallén and Uppfeldt, 1982; Ehrenstrom Reiz and Reiz, 1982). Although our clinical experience with the preparation in the paediatric haematology/oncology ward has been promising, these children tend to be prejudiced against all kinds of procedure. Therefore, we decided to study the tolerance and efficacy of the local anaesthetic cream on young children scheduled for elective surgery under general anaesthesia.

PATIENTS AND METHODS

Sixty boys and girls (aged 4–10 yr; ASA groups I or II) participated in the study (table I). No child had to be excluded because of suspected allergy to local anaesthetics.

The study was performed in accordance with the principles of the 1975 Declaration of Helsinki and was approved by the Ethics Committee of the Children’s Hospital, University of Helsinki. All patients received premedication with diazepam (4–6 mg, orally) or flunitrazepam (0.05 mg/kg, orally). The children were divided into two groups: one received EMLA cream, the other placebo. The venous cannulation was performed during the preparation for general anaesthesia.

SUMMARY

The effect of the topical application of a lignocaine-prilocaine cream (EMLA) on the pain of venous cannulation was tested in a double-blind manner. Sixty boys and girls between the ages of 4 and 10 yr who were to undergo surgery participated in the study. No analgesic premedication was given and the venous cannulation was performed during the preparation for general anaesthesia. Pain was assessed by the anaesthetist and the patient using a verbal rating scale and two different pictorial scales. The effect of EMLA in the alleviation of the pain of venous cannulation was considered significantly better than placebo by both anaesthetist (P < 0.001) and patient (P < 0.05) (verbal scales). One conventional pictorial scale showed a statistically significant difference (P < 0.05), but the other, based on facial expressions, did not. Local reactions to the cream were minor and transient in both groups.

Table I. Distribution of sex, age, body weight and premedication in the study groups

<table>
<thead>
<tr>
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<th>EMLA (n = 30)</th>
<th>Placebo (n = 30)</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>Boys/girls</td>
<td>15/15</td>
<td>22/8</td>
<td>ns</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>6.4 ± 1.92</td>
<td>7.1 ± 1.86</td>
<td>ns</td>
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<td>(mean ± SD)</td>
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<tr>
<td>Weight (kg)</td>
<td>24.1 ± 9.42</td>
<td>22.8 ± 6.06</td>
<td>ns</td>
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<tr>
<td>(mean ± SD)</td>
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<tr>
<td>Premedication</td>
<td></td>
<td></td>
<td>ns</td>
</tr>
<tr>
<td>None</td>
<td>6</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Flunitrazepam</td>
<td>13</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Diazepam</td>
<td>11</td>
<td>8</td>
<td></td>
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EMLA CREAM IN CHILDREN

A

FIG. 1. Visual scales used for subjective evaluation of pain in The Children’s Hospital, University of Helsinki. Scale A is 50 x 10 cm, and coloured bright red and white (Tammisto, Tigerstedt and Wirtavuori, 1983). Scale B has been designed in our hospital for use in young children. The left extreme of scale A and face 1 in scale B are defined as “no pain”, the opposite ends of each scale as “pain as bad as it could possibly be”.

B

the patients or their parents, or both, gave informed consent to the study.

The children were allocated randomly to treatment with either EMLA or placebo, with 30 in each group. Each millilitre of the EMLA cream contained lignocaine 25 mg and prilocaine 25 mg and in the placebo cream the eutectic mixture of local anaesthetics was substituted by Miglyol R 812 oil. The formulations were visually and cosmetically identical and they were packed in identical, numbered 5-ml aluminium tubes.

The design of the study and the rating scales (see below) were explained during the pre-operative visit and examples were given to verify that the child could use the scales. Premedication, diazepam 0.5 mg kg⁻¹ by mouth or flunitrazepam 0.5-1.0 mg kg⁻¹ up to 2.0 mg (by mouth) was given to 24 children in the EMLA group and to 27 in the placebo group (table I).

At least 60 min before the anticipated time of cannulation, a thick layer (2 g) of cream from a numbered tube was applied over the selected vein. The cream was covered with a thin plastic sheet (Glad R, Union Carbide) to form an occlusive dressing. Immediately before the insertion of the cannula the bandage was removed, and the skin was wiped dry and inspected for any local reaction. The skin was then disinfected with 0.5% chlorhexidine in 70% alcohol and the vein was cannulated with a Venflon 0.8- or 1.0-mm cannula.

Pain on cannulation was assessed, first, by the anaesthetist and then by the patient using a verbal rating scale of none, slight, moderate or severe. The patient was then asked to assess the pain using two different pictorial scales (fig. 1).

Differences between EMLA and placebo groups were tested by the Mann–Whitney test with rank sums and variances corrected for ties when appropriate.

RESULTS

One child was withdrawn from the placebo group; venous cannulation was not performed because the child was very anxious and unco-operative. There were no differences between the groups in size of cannula used, site of cannulation and the time for which the cream was applied. Local reactions after EMLA and placebo comprised slight redness in two and no children, and slight blanching of the skin in 11 and nine children, respectively. One patient receiving EMLA developed moderate blanching. All reactions disappeared within 1 h, except slight blanching in one patient receiving EMLA, in whom it lasted for 2 h.

Verbal assessments of pain are shown in figures.
FIG. 2. Verbal rating of pain associated with cannulation as determined by the anaesthetist ($P < 0.001$).

FIG. 3. Verbal rating of pain on cannulation as indicated by the patient ($P < 0.05$).

2 and 3. Three patients in the EMLA group were unable to co-operate with the verbal rating of pain. The differences in pain on cannulation between the EMLA and the placebo groups, as evaluated by the anaesthetist and the patient, were significant ($P < 0.001$ and $P < 0.05$, respectively).

Assessments using the pictorial scales 1 and 2 (fig. 1) were carried out in 21 and 22 children in the EMLA group and 25 and 27 in the placebo group, respectively. The remaining children were unable or unwilling to co-operate. On the red and white, linear scale the mean (median) figures in the EMLA and placebo groups were 12.4 (4) and 23.5 (22.5), respectively. The differences were significant ($P < 0.05$). There was no difference between the two groups when the degree of pain was assessed using the facial expressions.

DISCUSSION

Children learn to be afraid of all kinds of injections at a very early age (Mather and Mackie, 1983). For children with chronic diseases this becomes a major problem. Extreme fear can make minor procedures very traumatic for the child and time consuming for the personnel involved (Jay, Ozolins and Eliot, 1983). It would be preferable to avoid this, but until recently there has been no effective remedy.

In the earlier studies of EMLA in paediatric patients (Ehrenström Reiz and Reiz, 1982; Hallén and Uppfeldt, 1982) the mean age of the children was between 10 and 11 yr. However, in our opinion children who are too young to accept reasoned explanations would benefit most from an effective topical preparation of local anaesthetic.
Additionally, we wished to have the child’s subjective evaluation of the degree of pain. Children between 4 and 10 years of age can localize and indicate the severity of pain (Eland, 1974) and, usually, understand the visual scales (own unpublished observations).

In the present series the efficacy of EMLA cream in alleviating the pain of venous cannulation was significantly better than placebo. The anaesthetist’s evaluation was slightly more in favour of EMLA than the patient’s (figs 2 and 3). From the technical point of view, a moderate or severe reaction to pain interferes with cannulation.

There were more young children in the EMLA group than in the placebo group; however, the difference in age was not significant (table I). Three of the four children in the EMLA group who considered the pain on cannulation severe were 4 yr and one 5 yr. When the patients’ verbal assessments of pain were analysed according to age, there was no difference between EMLA and placebo in children aged 4–6 yr (n = 28). On the other hand, all the 7–10 yr old children (n = 28) in the EMLA group, and 43% in the placebo group, reported no or slight pain (P < 0.001, Mann-Whitney U test). This result correlates well with the findings of Katz, Kellerman and Siegel (1980) and Jay, Ozolins and Eliot (1983). Children older than 7 yr can understand the meaning of medical procedures and display dramatically less overt distress than younger children, who have a strongly emotional attitude.

Although most of the children were premedicated, an analgesic was not used. While it might have been ideal to study the efficacy of the local anaesthetic without any premedication whatsoever, we felt that the preoperative situation was potentially distressing for young children and thought that a calm, premedicated child would concentrate more on the study than an anxious one. In some cases, premedication was too heavy and the child was unable to co-operate. However, there was no difference in the verbal rating of pain between the premedicated and un-premedicated children in the EMLA group.

Local reactions were insignificant and disappeared rapidly: one lasted for less than 2 h and all others disappeared within 1 h. The slight blanching seen with both EMLA and placebo creams was perhaps partially caused by the moisture under the occlusive bandage. The reactions did not correlate with the duration of application, which was at least 60 min, as recommended by Hallén, Olsson and Uppfeldt (1984). A shorter time would be advantageous in acute situations, but the 60-min application time was easy to arrange in conjunction with premedication. Our current clinical experience is that the local anaesthetic effect lasts several hours after the removal of the occlusive dressing and the cream.

The present study confirmed the local anaesthetic effect of EMLA cream in alleviating the pain of venous cannulation in young children. Local adverse effects were minimal.

ACKNOWLEDGEMENTS
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REFERENCES


