Evaluation of the efficacy and safety of amethocaine gel applied topically before venous cannulation in adults

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Summary
We have assessed in a placebo-controlled, double-blind trial, the efficacy and safety of an amethocaine gel preparation for alleviating the pain of venous cannulation. Forty-two unpremedicated adult patients were allocated randomly to receive either amethocaine gel 1 g (4% w/w) or placebo gel 1 g applied to the dorsum of the hand for 40 min before venous cannulation. After removal of the gel, a 20-gauge cannula was inserted and the pain of cannulation assessed by a three-point rank score and a 100-mm visual analogue scale: 90% of patients who received amethocaine reported clinically acceptable topical anaesthesia. Both verbal rating scores and visual analogue scores for pain were significantly less with amethocaine. Slight erythema associated with amethocaine occurred in one patient and slight itching in two patients. No other adverse features were evident. (Br. J. Anaesth. 1995; 74:706-708)

Key words
Anaesthetics local, amethocaine.

Since the introduction of EMLA (eutectic mixture of local anaesthetics) cream, the use of topical anaesthesia has become commonplace for venepuncture and cannulation, particularly in children. This eutectic combination of 2.5% lignocaine base and 2.5% prilocaine base has to be in contact with the skin for a minimum of 60 min to be effective, and when removed produces topical anaesthesia for approximately 30-60 min [1].

The time between application and effective anaesthesia is related to the ability of an agent to inactivate cutaneous nociceptors by crossing the stratum corneum. This in turn depends on the physicochemical properties and anaesthetic potency of the agent, and the mode of delivery. The ester local anaesthetic, amethocaine, has been shown to provide promising topical anaesthesia to venepuncture for several hours after application times of 30 min as a gel [2], and to cannulation as a cream [3] and patch [4].

For reasons of accessibility, cannulae for induction of anaesthesia are usually inserted in the dorsum of the hand. This study aimed to assess the efficacy and adverse effects of an amethocaine gel preparation compared with placebo, in preventing pain from venous cannulation in the dorsum of the hand of adults.

Methods and results
After obtaining Ethics Committee approval and written patient consent, we studied 42 unpremedicated ASA I and II patients undergoing day-case procedures under general anaesthesia. Patients were excluded if they had known or suspected hypersensitivity to local anaesthetics, had broken skin, had used analgesic preparations within the previous 24 h, were females not using effective contraceptive protection or were less than 18 yr of age. Patients were allocated randomly to receive either amethocaine gel 1 g (4% w/w amethocaine) or a placebo gel 1 g identical in appearance and texture. Both were packed in identical 1.5-g tubes designed to deliver 1 g on squeezing. Neither patients nor investigators were aware of the contents. The cannulation site (dorsum of the non-dominant hand) was identified by the investigator and the gel applied by nursing staff, also blinded to its identity. The gel was applied as a "mound" and occluded with a 6 cm x 7 cm OpSite Flexigrid transparent dressing (Smith and Nephew Medical Ltd). The time of the completed application of gel and dressing was recorded.

The occluded gel remained in contact with the skin for 40 min. The dressing was then removed and the remaining gel wiped away. The time of gel removal was recorded. Heart rate and non-invasive arterial pressure were measured immediately before gel application and again immediately after gel removal but before cannulation. The area to which the gel was applied was assessed also for erythema, oedema and itching (none, slight, moderate or severe) immediately before gel application and after gel removal. After completion of these assessments, cannulation was performed using a 20-gauge (1.0-mm diameter) cannula and the time of cannulation recorded. All measurements and cannulations were performed by the same investigator (B.O'C).

At the time of cannulation, the patient was asked to grade the severity of pain (no sensation of pain = 0, some sensation of pain but no discomfort = 1, painful = 2). In addition, the patient was asked to complete a 100-mm visual analogue scale (VAS)

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Topical amethocaine gel

Table 1  Verbal rating score (VRS) and visual analogue scale score (VAS) (median (range)) between groups. 0 = No pain; 1 = some sensation of pain, no discomfort; 2 = painful.

<table>
<thead>
<tr>
<th>Group</th>
<th>VRS 0</th>
<th>VRS 1</th>
<th>VRS 2</th>
<th>VAS (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>5</td>
<td>6</td>
<td>10</td>
<td>27 (1-88)</td>
</tr>
<tr>
<td>Amethocaine</td>
<td>14*</td>
<td>5*</td>
<td>2</td>
<td>7 (0-62) *</td>
</tr>
</tbody>
</table>

*P < 0.05 for VRS = 0; †P < 0.05 for VRS = 0 + 1. ‡P = 0.01

Comment

To be of value in clinical anaesthesia, topical anaesthetic agents should have a short onset and a long duration of action. This would allow simultaneous application to several patients in whom topical anaesthesia was appropriate and so ease the workload of nursing staff. EMLA cream, the only topical anaesthetic in current practice, requires an application time of 60 min to produce clinically acceptable percutaneous anaesthesia. In addition, its effect may decline within 30 min of removal [1]. Amethocaine, an ester local anaesthetic, is more potent and lipophilic than either lignocaine or prilocaine and therefore is better suited for crossing the stratum corneum. In volunteer studies, amethocaine gel has been shown to exert superior anaesthesia to EMLA cream at 30 min, ceasing to be significant at 60 min, but with a significantly longer duration of action (4 h) [1]. Furthermore, increased lipophilicity may lead to absorption within the stratum corneum and action as a reservoir, prolonging duration of action by slow release [5].

The results of the present study indicate that application of 4% amethocaine gel for 40 min provides acceptable topical anaesthesia for cannulation in 90% of adults. This is in agreement with similar work involving cannulation in volunteers and children [2-4]. Side effects associated with topical amethocaine include erythema of the skin, itching and oedema. Erythema results from increased perfusion of the microcirculation and is a pharmacological property of the drug rather than a side effect. Although the numbers of subjects in the groups were too small for statistical analysis, we noted that the incidence of these effects in this study was lower than reported previously, with itching in 2 of 21 (9.5%), erythema in 1 of 21 (4.8%) subjects and oedema not observed at all.

As amethocaine is a potent local anaesthetic, the possibility of systemic absorption should be considered. Metabolism by tissue esterases within the dermis implies that plasma concentrations should be low [6]. No amethocaine or metabolites were detectable in the serum of 70% of volunteers who had 5% amethocaine cream applied for 4 h, and concentrations of up to 0.2 mg litre⁻¹ in the remaining 30% were not associated with clinical signs of toxicity [6], so it is unlikely that patients exposed to 4% gel for 40 min are at risk. Care must be taken to ensure that the gel is not ingested orally as rapid systemic absorption may then occur. Esters are more likely than amides to produce idiosyncratic reactions, although none has been reported in several thousand topical amethocaine applications to date [1-5].

Acknowledgement

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References

3. Molodecka J, Stenhouse C, Jones JM, Tomlinson A. Com-