Topical anaesthesia of intact skin: liposome-encapsulated tetracaine vs EMLA

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Summary
In this randomized, double-blind study, we have compared the ability of 5% liposome-encapsulated tetracaine (amethocaine) (LET) vs 5% eutectic mixture of local anaesthetics (EMLA) to produce local anaesthesia of intact skin in 40 healthy volunteers. Volunteers had both preparations applied to their forearms under an occlusive dressing for 1 h. Superficial anaesthesia was measured by a total of nine 1-mm pinpricks, the 3-mm insertion was not performed. Results showed that the number of pinpricks perceived was significantly less (P<0.01) for LET (median 1.0; range 0–9) vs EMLA (1.5; 0–9). In volunteers who had deeper anaesthesia assessed, there was no significant difference (P=0.065) in VAS scores for LET (mean 1.5 (sd 1.4); n=34) vs EMLA (2.4 (2.1); n=28). Overall anaesthetic effect, as ranked by all of the subjects, was significantly better for LET compared with EMLA (P=0.024). We have demonstrated that when applied in equal volumes, 5% LET produced better superficial local anaesthesia than EMLA. (Br. J. Anaesth. 1998; 81: 972–973).

Methods and results
In this randomized, double-blind study, we have compared the efficacy of 5% LET with 5% EMLA for providing superficial and deep anaesthesia in 40 healthy volunteers. The study was approved by the Research Review Committee of the Victoria General Hospital, Dalhousie University, Halifax, NS, Canada. LET was prepared at the College of Pharmacy, Dalhousie University, Halifax, NS, Canada, based on a well-established and patented method.4 EMLA was obtained from Astra Pharmaceuticals Products Inc. (Westborough, MA, USA). The colour and consistency of the LET cream was adjusted to appear identical to that of EMLA.

After obtaining written informed consent, the surface of both forearms was swabbed with 70% isopropyl alcohol solution to remove excess skin oils. Then, 1 ml of either 5% LET or 5% EMLA was applied randomly (tossing of a coin) to a 4x4 cm area on each arm. These areas were covered with an occlusive dressing (Tegaderm, 3M, London, Ontario, Canada). After 1 h, the occlusive dressings were removed and the creams wiped off in the same order in which they had been applied. All subjects were scored immediately for the presence of erythema or blanching at the application site.

Both arms were tested for degree of superficial and deep anaesthesia. Superficial anaesthesia was assessed using a sterile 20-gauge needle (Becton Dickinson, Franklin Lanes, NJ, USA) inserted via a small cork so that the needle protruded 2 mm. Subjects were pricked a total of nine times over a 3 x 3 cm grid superimposed over the application site. An initial pinprick in a non-anaesthetized portion of the forearm was used for comparison. Results were recorded as the number of painful stimuli out of nine.

The study design stipulated that if a subject felt greater than four of the nine pinpricks, deeper anaesthesia would not be tested in that arm. If the subject felt four or less of the nine pinpricks, a 22-gauge needle was inserted randomly in the area of application to a depth of 3 mm and the subject’s response was recorded on a 0–10 visual analogue scale (VAS).

Finally, we asked subjects to rate their impression of both creams in terms of overall anaesthetic effect.

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Responses were recorded as no effect, some effect or good effect. Subjects were also asked to state which cream they preferred. Responses were recorded as “no difference”, “prefer A” or “prefer B”.

Superficial pinprick data were compared using McNemar’s test. VAS scores were compared using a Wilcoxon non-parametric test. Chi-square analysis was used to compare the number of sites tested for deeper anaesthesia for LET vs EMLA. Overall anaesthetic effect was compared using a Wilcoxon signed rank test. The assigned rankings were: 0 = no effect, 1 = some effect, 2 = good effect, 3 = best effect. Data are expressed as mean (SD). P < 0.05 was considered significant.

We studied 40 volunteers (26 females) aged 22–64yr (mean 34.7yr). Mean application time was 60.9 (1.0) min for both preparations. In the assessment of superficial anaesthesia, the number of pinpricks perceived was significantly less (P < 0.01) for LET (median 1.0; range 0–9) compared with EMLA (1.5; 0–9). Significantly fewer (P < 0.01) of the volunteers in the LET (n = 6) group felt greater than four of the nine superficial pinpricks compared with the EMLA group (n = 12). Assessment of deeper anaesthesia demonstrated a trend towards lower VAS scores for LET (1.5 (1.4); n = 34) vs EMLA (2.4 (2.1); n = 28), but this difference was not statistically significant (P = 0.065).

Overall anaesthetic effect was significantly better for LET than for EMLA (P = 0.024). Twenty-four (62.5%) volunteers preferred LET while nine (20%) preferred EMLA. Both preparations were judged to have good anaesthetic effects in all 33 of the volunteers. Certain individuals may require an extended period of application in order to achieve adequate local anaesthesia.

Side effects included mild erythema in 32 (80%) LET subjects. EMLA produced blanching in 23 (58%) subjects. The occlusive dressing produced mild localized itching in the area of skin contact in two volunteers.

Comment

We have demonstrated that 5% LET produced better superficial local anaesthesia than EMLA. This finding was likely the result of increased absorption of the liposomal preparation through the stratum corneum. In the assessment of deeper anaesthetic effect, there was a trend towards lower VAS scores for the LET group compared with the EMLA group, but this difference was not statistically significant. Testing a larger number of subjects or testing all volunteers regardless of superficial anaesthesia may have revealed a significant difference between the two preparations.

In the assessment of overall anaesthetic effect, the majority of subjects preferred LET (62.5%). However, it is interesting that 20% preferred EMLA while 12.5% found no difference; 5% had no anaesthesia with either preparation. These differences are probably related to individual differences in skin composition and thickness which alter the absorption of both preparations.

Erythema seen with LET is probably secondary to the vasodilating action of tetracaine, as application of empty liposomes to intact skin produces no erythema. If a local anaesthetic cream is being used before i.v. insertion, vasodilatation would be beneficial. Future studies are planned to compare the efficacy of LET vs EMLA to produce local anaesthesia of intact skin before i.v. insertion.

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References