Does Lidocaine-Prilocaine Cream Permit Painfree Insertion of IV Catheters in Children?

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Fear and pain can make injections and the introduction of iv catheters a traumatic experience for the child and a difficult and time-consuming task for the physician. A topical preparation that can be applied to the skin without discomfort and which alleviates pain from needle puncture would be helpful to both patients and staff.

The solid, pure bases of lidocaine and prilocaine, if mixed in equal amounts, form an oil above the temperature of 16° C, i.e., they constitute a eutectic mixture. This mixture, called EMLA (Eutectic Mixture of Local Anesthetics) has been formulated as an oil-in-water emulsion cream and tested in experimental and clinical studies in adults. The present study reports the results of tests performed in children with the objective to evaluate if the cream: 1) diminishes the pain from injection of promedication; 2) diminishes the pain from insertion of intravenous catheters; 3) facilitates injections and insertion of intravenous catheters; and 4) causes any adverse reactions.

Materials and Methods

The cream consists of an eutectic mixture of lidocaine base and prilocaine base together with an emulsifier (Arlatone®). A thickener (Carbopol®) is added to obtain a suitable consistency. The total concentration of the active ingredients is 107 mmol/l (25 mg/ml) of lidocaine and 113 mmol/l (25 mg/ml) of prilocaine. A placebo cream in which the active substances were substituted with Miglyol® oil was prepared so that both formulations were visually and cosmetically identical. The active and the placebo creams were packed in identical aluminum tubes marked with numbers according to a randomization list. The tubes were used in numerical order in a double-blind manner.

Patients between 4–15 years of age were selected consecutively for study as they appeared at the Department of Pediatric Anesthesia at the Karolinska Hospital. All patients and their parents were informed about the aim and nature of the study in accordance with a standard format to comply with the Helsinki declaration. Oral consent was obtained and the investigation was subjected to evaluation of the peer review committee of the hospital. Patients with known or suspected allergy to local anesthetics of the amide type were considered ineligible for the study.

In Series 1, 58 patients were studied who were scheduled for minor surgery requiring general anesthesia and received premedication drug. At least one hour before the injection, 1 ml of the cream was applied in a thick layer over the puncture site on the thigh. Blenderm® tape was used to cover the cream in order to form an occlusive dressing. When the injection was to be given, the tape was removed and the skin wiped dry and observed for any adverse reactions. After disinfection with 0.5% chlorhexidine in 70% ethanol, the injection was given as slowly as possible. The premedication consisted of oxycodon 1% and scopolamine 0.04% in a standardized volume according to the weight of the child (0.25–1.00 ml).

In Series 2, 53 patients were studied who were to receive an intravenous catheter or cannula, usually as preliminaries to general anesthesia. At least one hour before the planned insertion of the cannula, about 1 ml of the cream was applied to the skin and covered with tape as described previously. Two areas were selected in order to have one area as a reserve should the first insertion be a failure. The preferred areas of applications were in order of rank: the dorsum of the hand, the cubital fossa, and the forearm.

The patients’ pain reaction was evaluated by the nurse who performed the injection or the insertion of the cannula. Immediately after the procedure, she recorded her estimation according to a three-grade scale: no pain (no reaction to the needle prick, i.e., no whimpering, no grimacing, no reflex movements); slight pain (slight reaction to the needle, i.e., slight whimpering, grimacing, minor reflex movements); or severe pain (loud crying, intense reflex movements). In Series 2, the patients were also asked to evaluate the pain using the same scale.

The nurse also subjectively evaluated how easy it was.

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*‡ Blenderm® tape No 1525, 3M CORP.
to perform the procedure according to a three-graded scale: easier than usual, as usual, or more difficult than usual—especially considering anxiety of the child and reflex movements during the procedure.

Edema, redness, and paleness of the treated skin were recorded according to a four-graded scale: none, slight, moderate, or severe. Any spontaneously reported reactions were noted.

Differences between active and placebo groups were tested with the Mann-Whitney U-test, variance being corrected for ties when appropriate.

RESULTS

In the first series, the 58 patients were divided equally between active and placebo cream. In the placebo group, seven patients were excluded from analyses; six due to application times shorter than 60 minutes and one because no premedication was given. In the active group, two patients were excluded due to application times shorter than 60 minutes. The active group then consisted of 27 patients and the placebo group of 22 patients. The groups were comparable regarding sex, age, and weight (table 1) and there was no difference between the groups regarding application time and injected volume. In the second series, 53 patients participated—26 received active cream and 27 placebo cream. In the active group, four patients were excluded. Three of them did not receive an intravenous cannula because the operation was postponed, and one was excluded as being outside the age limits. The active group then consisted of 22 patients and the placebo group of 27 patients. The groups were comparable regarding age, sex, and weight (table 1). Application times were also comparable.

In both series there were statistically significant differences between the active and placebo groups (table 2). When the premedication was given, three patients in the placebo group and four in the active group mentioned discomfort from the tension induced by the injected volume. There was no correlation between age and pain score.

The subjective evaluation of the ease with which the
under the adhesive tape and not where the cream had been applied. “Goose pimples” were noted briefly in three cases. All reactions were transient and no traces could be detected an hour after the procedure.

**DISCUSSION**

Many attempts have been made to obtain a suitable formulation for effective topical anesthesia. Examples of preparations that have been tested are lidocaine, benzocaine combinations of local anesthetics with dimethylsulphoxide (DMSO) and ketocaine in alcoholic solutions (Pettersson: personal communication.). A main obstacle has been poor penetration of the local anesthetics through intact skin. Physical methods such as iontophoresis also have been tried to increase the penetration. No formulation has yet gained wide acceptance mainly due to either poor pain relieving effect, irritation, or toxic reactions.

In adults, the eutectic mixture of lidocaine base and prilocaine base has been shown to penetrate intact skin and abolish the pain response to pin-prick. It has even been possible to perform superficial skin surgery without any additional anesthesia. The eutectic mixture of 25 mg/ml lidocaine and 25 mg/ml prilocaine is more effective than 50 mg/ml of either base alone in a corresponding oil-in-water preparation. The reason for the greater effectiveness of the mixture, compared with the individual active components, is the higher concentration of the local anesthetic bases in the emulsion droplets. In the EMLA emulsion, 80% of each droplet consists of lidocaine and prilocaine, in contrast to only 20% active substance (base) in the single-component formulation.

There were considerably more males (83) than females (15) in the study. This reflects the sex distribution at the clinic due to a large number of male circumcisions and inguinal hernia repairs in males.

Children are often afraid of needles and syringes and the pain associated with injections. Our study shows that EMLA cream reduces the pain of needle puncture to a considerable extent in children. Results from delayed hypersensitivity tests and skin irritation tests have not revealed any negative effects of EMLA cream. The adverse reactions observed in our studies were mild and transient. It thus seems as if this preparation is both effective and well-tolerated.

The disadvantages of the applied technique are the comparatively long application time and the need for an occlusive dressing. However, application of the cream could easily be included in the preparatory procedures necessary for insertion of iv cannulae. The occlusive dressing causes some minor problems as the redness observed was mainly located under the tape and not under the cream itself. A thin plastic sheet wrapped around the hand or arm is now being tested as an alternative dressing.

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