Lignocaine ointment and local anaesthesia in preterm infants

D P Barker, N Rutter

Abstract

The ability of topically applied lignocaine ointment to produce surface anaesthesia was examined in 45 preterm infants (gestational age 25 to 35 weeks) at a median age of 2 days. Two strengths of ointment, 5% and 30%, were tested at 30 and 60 minutes after application to the dorsum of the foot. Anaesthesia was assessed by comparing the response to skin stimulation at the test and control sites, using von Frey hairs. In 84% of cases responses indicated that there was no surface anaesthesia.

Topically applied lignocaine ointment is not an effective local anaesthetic in preterm infants, presumably due to poor absorption.

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Local anaesthesia is now recognised as an essential component in the management of childhood pain.¹ Topical local anaesthesia using EMLA is commonly prescribed to alleviate the pain of venepuncture and is effective and safe in infants above 3 months of age.² EMLA consists of lignocaine and prilocaine in an oil in water emulsion. It is applied under an occlusive dressing one hour before the procedure, to overcome the problem of poor local anaesthetic absorption through intact skin. It is not recommended for use in younger infants, due largely to concern over the risk of methaemoglobinaemia associated with prilocaine.³

Newborn infants, especially sick preterm infants, often undergo painful procedures involving skin puncture. There is a need for topical anaesthesia similar to that given to children. We have already investigated the permeation of aqueous lignocaine through abdominal skin obtained at necropsy in preterm infants, and estimated resulting plasma concentrations were below those associated with systemic toxicity.⁴ We therefore undertook a study to examine the clinical efficacy of topically applied lignocaine in preterm infants.

Methods

Forty five preterm infants (25 female) of median gestational age 31 weeks (range 25–35) and median birthweight 1.48 kg (0.62–3.40) were studied at a median postnatal age of 2 days (range 0–30). Most (40/45, 89%) were studied once only. All infants were clinically

stable when tested, and none was receiving sedative or analgesics. No infant had an intravenous cannula in the vicinity of the test or control foot.

Lignocaine ointment (0.1 ml of either a 5% or 30% concentration) was applied by syringe to the central area (1 cm in diameter) of an adhesive ring applied to the dorsum of one foot, a site chosen as one commonly used for venous cannulation. The ointment was left uncovered for a period of either 30 or 60 minutes and was then wiped clear, with the adhesive ring left in place to allow testing in the centre.

Sensation was assessed using graded von Frey hairs, comparing responses of the test and control (contralateral, untreated) foot. The hair was lowered perpendicularly on to the dorsum of the foot and gently pressed until it became bowed, resulting in a reproducible force dependent on the grade (stiffness) of hair chosen. A response was first elicited on the control foot by choosing a hair which, for an infant of a given postconceptional age, would be expected to produce a response.⁵

A positive response was considered to be a well defined and prompt movement of the foot, often combined with withdrawal of the leg, or flexion or extension of the toes without foot movement. If a reaction was not obtained with this hair then successively higher grade (stiffer) hairs were applied until a response was obtained. When the baby had settled the same hair was applied to the test foot and the response recorded. If no response was obtained on the test foot, testing was then repeated on the control side. A local anaesthetic effect was assumed if repeat testing of the control site again produced a response, where none had been obtained on the test side. Lack of local anaesthetic effect was assumed if a response was obtained to the same grade of hair at both test and control sites.

Ethical approval was obtained for the study, and written parental consent was obtained for each infant.

Results

Five per cent lignocaine ointment produced responses suggesting surface anaesthesia in only two of 24 (8%) tests (table). Using 30% ointment, this proportion increased to six of 26 (23%) tests, but the rise was not significant ($p=0.25$, Fisher's exact test). Prolonging the application time from 30 to 60 minutes did not result in increased efficacy with either concentration of ointment. Responders did not differ significantly from non-responders in their

Department of
Neonatal Medicine and
Surgery, Nottingham
City Hospital,
Hucknall Road,
Nottingham NG5 1PB
D P Barker
N Rutter

Correspondence to:
Dr Barker.

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Efficacy of topical lignocaine ointment in producing surface anaesthesia

Lignocaine concentrations (%)	Duration (minutes)	No of tests	Local anaesthetic effect	
			Yes	No
5	30	12	1	11
5	60	12	1	11
30	30	12	3	9
30	60	14	3	11

gestation, birthweight, or postnatal age at the time of study (Mann-Whitney U test).

Discussion

Topical anaesthesia of the skin before venous cannulation and venepuncture is recognised as a major advance in paediatric practice,⁶ but EMLA, the most widely used agent, is not licensed for use for infants below 1 year of age in the United Kingdom. This restriction has particular implications for infants requiring neonatal intensive care, in whom numbers of invasive procedures involving skin puncture can amount to several hundred during admission.⁷ Concern centres over the ability of local anaesthetics in general, and prilocaine in particular, to cause methaemoglobinaemia. This results from a combination of factors, which include reduced erythrocyte methaemoglobin reductase concentrations in infants under 3 months old, and the greater tendency of Hb F to oxidation than Hb A. Case reports of methaemoglobinaemia in the newborn have been associated with infiltration of local anaesthetic rather than topical application,^{8,9} but the reduced epidermal barrier of premature infants raises the possibility of toxicity from greatly enhanced absorption. Almost a quarter of reported cases of methaemoglobinaemia resulting from the absorption of aniline marker dye were in premature infants.¹⁰

The risk of methaemoglobinaemia with lignocaine is reduced, and lignocaine is commonly used to infiltrate around the insertion sites of chest drains in premature infants. Topical 5% lignocaine ointment has recently been reported to be ineffective in reducing the pain of heel lance in premature infants (Rushforth J A, presentation to the Neonatal Society, July 1994), but 30% lignocaine cream was successful in reducing postoperative circumcision pain.¹¹ In this study we have demonstrated that neither 5% nor 30% lignocaine ointment produce skin surface anaesthesia after application times of 30 or 60 minutes. Infants demonstrated their ability to perceive touch with stimuli often equivalent to a force of as little as 1 g. Given that lignocaine failed to abolish even this, it is not therefore

surprising that it does not prevent the pain of a heel lance. The success of 30% lignocaine cream in the circumcision study, where a larger volume of cream was applied for 20 minutes before surgery, may have been due to the use of an occlusive dressing. Only a few of our responses (16%) were consistent with local anaesthesia, and the degree of anaesthesia was not assessed. These responses were seen more frequently with the 30% than with the 5% ointment, but this increase was not significant, and prolonging the application time had no effect with either concentration.

Considering our *in vitro* work, which found an inverse correlation between gestational age and lignocaine permeation, the failure of topical lignocaine to produce surface anaesthesia is surprising, particularly in infants below 31 weeks' gestation, in whom the skin barrier is weak. Possible explanations are insufficient drug release from the ointment (an aqueous formulation was used *in vitro*), poor absorption, or ineffectiveness despite adequate absorption. Although the skin over the dorsum of the foot is of reduced thickness compared with that of the heel, and exhibits similar barrier properties to that of abdominal skin, failure of absorption seems most likely. Failure of lignocaine to act on local nerves once absorbed seems unlikely, given that neurological pathways for skin sensation are well developed by 25 weeks, and that subcutaneous infiltration seems to be effective. Further work examining urinary excretion of lignocaine and its metabolites following topical application is in progress to help resolve these questions.

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