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Reducing the pain of intradermal lignocaine injection by pH buffering

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SUMMARY

The effect of pH on the pain of administration and efficacy of 1% lignocaine was investigated in a prospective, double-blind, randomized study of 20 adult volunteers. Onset and spread of anaesthesia by intra-dermal injection were not altered, but there was a significant reduction in pain scores with a higher pH. Overall, pain scores appear to be more dependent on the speed of injection rather than alteration of pH.

INTRODUCTION

Lignocaine shares with all other local anaesthetics the undesirable side-effect of pain on injection. Recent work has shown that increasing the pH of the local anaesthetics can reduce this pain significantly (Christoph *et al.*, 1988).

Lignocaine is a weak organic base which comprises charged and uncharged fractions when in solution. The fraction of each is pH dependant with more of the uncharged fraction present at a higher pH. The pKa value of lignocaine is 7·9. It is thought that the uncharged form diffuses more rapidly through tissue and nerve membranes. Once within the nerve axoplasm the uncharged lignocaine dissociates according to axoplasmal pH to form a charged fraction (Hille, 1977). This charged fraction then blocks neurotransmission at the sodium channel.

There are three brands of plain 1% lignocaine currently available in this country, Phoenix (pH 5·0), Antigen (pH 5·5) and Astra (pH 6·7). The acidic pH of these products allows a shelf-life of 3 to 4 years. If the product's pH is increased then the percentage of the uncharged form, which is chemically unstable, also increases.

Our study was undertaken to confirm that increasing the pH of lignocaine 1% does have a beneficial effect. In particular, did the Astra brand with a higher pH have a clinical advantage over a brand with a lower pH?

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METHOD

Twenty healthy adult (18 to 50 years old) volunteers were recruited into the trial which was approved by the hospital medical ethics committee. None had a history of allergy to local anaesthetic drugs.

The solutions under test included; 0·9% saline (pH 5·5), lignocaine 1% (phoenix ph 5·0), lignocaine 1% (astra pH 6·7), lignocaine 1% (phoenix, adjusted to pH 7·35). The last solution was prepared by the addition of 1·3 ml 8·4% Sodium Bicarbonate to a 40 ml vial of Lignocaine 1% (phoenix). The pH of each solution was measured using a pH meter (E.I.L. model 7060). In view of the stability of lignocaine at pH 7·35 the solution was used within 24 h.

Disposable 1 ml insulin syringes (100 unit) with a 27 gauge needle were used to draw up 0·5 ml aliquots of each of the solutions. These were randomly labelled A to D by investigator 1. Injections were given intradermally by 'blind' investigator 2 over a period of 4 seconds timed by a metronome. A linear Visual Analogue Scale from 0 to 10 was made available to each subject in order to assign a numerical value to the pain of each injection.

The flexor surface of the non-dominant forearm of each subject was prepared with isopropyl alcohol and allowed to dry. The intradermal injections were initially made distally. Each subsequent injection was performed at least 5 cm proximal to the last on alternate sides of the flexor surface. At the completion of each injection a stopwatch was started.

Each subject was then asked to indicate on the visual analogue scale the degree of pain experienced. The pain scores for each of the four solutions were averaged and solutions were compared using the Student's T-test for paired samples.

Immediately following injection a strip of adhesive tape was applied to the skin over the intradermal injection site. The edge of the tape was located over the centre of the wheal, with the long axis at 90 degrees to the line of the injection. Pinprick sensation was assessed at 30, 60, 90, 120 and 180 seconds and marked by pen on the tape. The surface of anaesthetized skin was calculated assuming that the intradermal wheal created was a circle. The results at each time interval were compared using the Student's T-test for paired samples.

RESULTS

The pain scores of subjects were greater with lignocaine at lower pH (see Table 1) which confirms the work of Christoph *et al.*, (1988). Results were statistically significant when the modified Phoenix solution (pH 7·35) was compared against the standard Astra ($P<0·05$) and Phoenix ($P<0·01$) solutions. However, there was no significant difference between the two commercially available products. 0·9% saline has an acidic pH (5·5) and no local anaesthetic action and predictably produced high pain scores. Comparisons of the surface area of skin anaesthetized by the three types of local anaesthetic showed no significant trend towards increased interstitial spread with a higher pH.

Table 1 Visual analogue pain scores for intradermal injections

Test solution	pH	Mean	Median	Range
Astra	6·7	2·15	1·9	0–8·1
Phoenix	7·35	1·37	1·5	0–2·8
Phoenix	5·0	2·28	2·1	0–5·8
0·9% saline	5·5	4·12	3·6	0·2–8·1

Table 2 Mean (SD) surface area of skin ansesthetized to pinprick (cm squared)

Lignocaine	Time after injection (secs)				
	30	60	90	120	180
Astra	0·9 (0·5)	1·6 (0·9)	2·6 (1·4)	3·4 (1·8)	4·1 (2·3)
Phoenix	1·1 (0·8)	1·8 (1·2)	2·3 (1·7)	3·0 (2·6)	4·2 (3·5)
Phoenix pH 7·35	1·3 (0·9)	2·7 (2·0)	3·4 (2·6)	4·1 (3·5)	4·7 (3·6)

DISCUSSION

The reduction of pain associated with the use of local anaesthetic at a higher pH could be explained by two mechanisms. Firstly, there is less direct tissue irritation as the pH approaches physiological values. Secondly, concentration of local anaesthetic in the uncharged form is increased, so enhancing spread within the tissue and diffusion of lignocaine into neural tissues. Although subcutaneous infiltration of lignocaine is more usual in clinical practice it was decided to study intradermal injections in order to standardize injections within the study. Results should be applicable to subcutaneous injections.

Although the results did confirm the work of Christoph *et al.*, (1988) there was no 'dramatic' reduction in pain scores. In his study the average pain scores of unbuffered local anaesthetic were 5 whereas in our study they were 2·2. The depth of the intradermal injection might have affected the pain score however we tried to ensure that this was a constant factor by having one investigator do all the injections. All injections were performed on the non dominant arm as there may be differences in pain threshold between arms (O'Driscoll & Jayson, 1982). Apart from possible cultural differences in the perception of pain the most likely explanation is that our injections were done over 4 seconds as opposed to 2·5. In a pilot study we found it difficult to repeatably inject in less than 4 seconds. Our study used a smaller needle (27G) compared to Christoph's (25G). Although it might be a counsel of perfection to increase the pH of the local

anaesthetic prior to injection we would oppose this as a routine because of the danger of precipitation of lignocaine above a pH of 7·4. In addition, in the busy clinical situation the possibility of injection of sclerosant, undiluted sodium bicarbonate must exist. The degree of pain experienced by our A&E patients during local anaesthetic injection is likely to be more related to the patience of the doctor than the pH of the solution. The slower the injection the less pain!

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