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Effects of the iontophoresis of lignocaine with epinephrine into exposed dentine on the sensitivity of the dentine in man

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ABSTRACT

Objective: To determine the effects of the iontophoretic application of lignocaine and epinephrine to exposed dentine on the sensitivity of the dentine in human subjects.

Design: The experiments were carried out on 13 healthy premolars (13 subjects) that were scheduled for extraction. Dentine was exposed at the tip of the buccal cusp by cutting a cavity which was etched with 35% phosphoric acid. The sensitivity of the dentine was tested with probing and air blast stimuli. The subject indicated the intensity of any pain produced with a score of 0–100. In 7 teeth, the cavity was filled with a solution containing 20% (w/v) lignocaine HCl and 0.1% (w/v) epinephrine HCl, and an iontophoretic current of 120 μ A was passed for 90 s. The sensitivity of the dentine was tested before and immediately after the treatment and then at 10 min. intervals for 40 min. Pulpal blood flow was recorded at each stage. Control experiments were carried out on 6 teeth using a solution containing only the epinephrine.

Results: The lignocaine plus epinephrine solution completely blocked the pain produced by both forms of stimulus immediately, and this continued for at least 40 min. It also produced an immediate fall in pulpal blood flow that also lasted for at least 40 min. The epinephrine solution had the same effect on pulpal blood flow but no effect on dentine sensitivity.

Conclusions: The topical application of 20% lignocaine and 0.1% epinephrine, with an iontophoretic current of 120 μ A for 90 s, will anaesthetize exposed, normal, dentine.

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1. Introduction

The possibility of delivering local anaesthetic to the dental pulp through the dentinal tubules has been investigated, but generally this has met with little success. Anderson et al.,¹ applied 2% lignocaine to dentine that had been exposed by drilling in human premolars, and found no decrease in the intensity of pain produced when glucose syrup was applied to the same dentine. Brännström² obtained a similar result with the application of a solution of Citanest (8% prilocaine hydrochloride) to fractured human dentine. These results indicated that the local anaesthetic agents could not diffuse through the dentinal tubules in sufficient amounts to block conduction in nerve terminals in the dentine or underlying pulp. It was later shown that this was likely to be due to an outward flow of dentinal fluid opposing the diffusion of the anaesthetic towards the pulp rather than to the size of the pores in the dentine acting as a barrier to diffusion.^{3,4} If this were the case, one possible method of achieving successful topical anaesthesia would be to increase the concentration gradient of the anaesthetic. This was confirmed by Amess and Matthews⁵ who found that the topical application of 10% lignocaine to exposed dentine in cats for 3 min at atmospheric pressure blocked reversibly the response of intradental nerves to mechanical stimulation of the dentine, whereas a 2% solution applied in the same way had no effect. Amess and Matthews⁶ also showed that the application of 50% lignocaine HCl to human dentine for 10 min blocked the pain produced by air blast stimuli. More recently, Rirattanapong et al.,⁷ demonstrated that 50% lignocaine HCl could anaesthetize dentine to air-blast and probing stimuli but this effect required an application of up to 30 min, which is too long for routine clinical use.

An alternative way of increasing the rate of transfer of an anaesthetic into the dentinal tubules would be to apply the solution at a raised hydrostatic pressure to slow or even reverse the outward flow of dentinal fluid.^{3,8} This would have the effect of increasing the rate of inward diffusion and, if the outward flow of dentinal fluid was reversed, of transferring the anaesthetic solution by bulk flow. But there are practical problems in doing this in a decayed or fractured human tooth because of difficulties in making a seal with the tooth to enable the solution to be applied at a raised pressure.

A further method of facilitating the diffusion of a local anaesthetic into dentine is to use iontophoresis. In 1900, Gysi⁹ showed that this method could be used to anaesthetize dentine with cocaine, and several other studies have shown that the rate of diffusion of local anaesthetics into tissues can be influenced by the passage of an electric current.^{10–14}

In the present study, the combined effects of the iontophoresis of lignocaine and epinephrine into dentine were investigated. The reason for including the epinephrine was to produce pulpal vasoconstriction and thereby a fall in pulpal interstitial fluid pressure and a reduction in the rate of outward flow of dentinal fluid, to further facilitate the inward diffusion of the lignocaine.¹⁵ Since lignocaine and epinephrine ions are both positively charged, they can be iontophored together into dentine by an anodal current.^{12,16} Thus, in the

present experiments we attempted to anaesthetize dentine by producing optimal conditions for the inward diffusion of lignocaine by creating a steep concentration gradient with a solution of 20% lignocaine, including epinephrine to produce pulpal vasoconstriction and reduce the rate of outward flow of dentinal fluid, and by passing an anodal current between the solution and the dentine to enhance the inward movement of both the lignocaine and epinephrine ions towards the pulp.

2. Materials and methods

2.1. Brief outline of experiments

A cavity was cut at the tip of the buccal cusp of a premolar and the sensitivity of the exposed dentine was tested with mechanical stimulation and with an air-blast stimulus. A solution of 20% (w/v) lignocaine (synonym: lidocaine) with 1:1000 epinephrine was then applied to the cavity and an iontophoretic current of 120 μ A passed between the solution and the underlying dentine for 90 s. Immediately after this, the sensitivity of the dentine was tested again. The testing was repeated at 10 min. intervals for a further 40 min. Pulpal blood flow was recorded after each of these tests. In control experiments, the same procedure was followed except the solution contained only the epinephrine and data were recorded for only 20 min after the treatment.

2.2. Subjects and teeth

The experiments were carried out on 13, non-carious premolar teeth that were scheduled for extraction as part of orthodontic treatment in 13 healthy subjects (age: 16–24 years, mean 19.4). All teeth were healthy and had completely formed roots, as determined by clinical and radiographic examination. The study was approved by the Ethics Committee on Human Rights Related to Human Experimentation of Mahidol University, and complied with the principles of the Declaration of Helsinki. The experiment procedures were clearly explained to each subject and informed consent was obtained from the subject, or for those under 18 years, a parent or guardian. The privacy rights of the subjects were observed at all times.

2.3. Tooth preparation

An acrylic, clip-on splint was made on a plaster model to cover the crowns of the test tooth and the two adjacent teeth. A socket was incorporated into the splint to support a laser Doppler blood flow probe over the cervical area of the test tooth (see below). A hole was cut in the splint to expose the occlusal surface of the test tooth. The teeth were isolated with an opaque black rubber dam (Four D Rubber Co., Ltd., Hleanor, DE75 7SJ, England; S type, thickness: 0.33 mm) to minimize the contamination of the signal from the pulp by blood flow in adjacent tissues.¹⁷ The dam was held in place by the splint. After the splint had been clipped in place, the joint between it and the occlusal enamel of the test tooth was sealed with light-curing composite resin.

A cylindrical cavity (diameter, 3 mm; depth, 3 mm) was cut without anaesthetic at the tip of the buccal cusp using

diamond burs in an air-rotor with water coolant. The cavity was etched with 35% phosphoric acid for 30 s to remove the dentine smear layer. The volume of the cavity plus the overlying hole in the splint was approx. 25 μl .

2.4. Dentine sensitivity tests

After it had been blotted dry with cotton pellets, the sensitivity of the exposed, etched dentine was tested with two forms of stimulus: gently stroking the middle of the floor of the cavity with an explorer (tip diameter 0.15 mm, force approximately 20 g), and by directing a 3 s blast of air at room temperature onto the exposed dentine from a triple syringe (reservoir pressure = 41 Pa; distance from syringe tip to mouth of cavity: 1–2 mm). The stimuli were always applied in this order. After each stimulus, the subject was asked to rate the intensity of any pain experienced on a scale of 0–100. This was chosen to correspond with the visual analogue scale (VAS) used in other studies, in which 0 indicates no pain and 100, the most severe pain that can be imagined.¹⁸ The subject was asked to specify a numerical rating rather than place a mark on scale, as in the usual form in which the score is reported, as this was not convenient when the subject was lying in a dental chair. Also, the subjects were asked to give values that incremented in steps of 10, rather than use a continuous scale. Thus, in scoring the severity of the pain, the subject was asked to select from eleven possible values. Since this score is neither visual nor analogue it will be referred to as a pain score rather than a VAS score.

2.5. Solutions and iontophoresis

The test solution contained 20% (w/v) (0.69 mol/l) lignocaine HCl monohydrate (Sigma-Aldrich, Dorset, England) in sterile, distilled water to which was added 0.1% (w/v) (1:1000) epinephrine hydrochloride (GPO, The Government Pharmaceutical Organization, Thailand). This concentration of epinephrine was selected after trials in preliminary experiments in both normal and carious dentine (Vongsavan N, unpublished observations). A solution containing only the epinephrine was used in control experiments. Without iontophoresis, the

application of this solution to exposed dentine would not be expected to produce a change in pulpal blood flow.

In each tooth, 25 μl of either the test (7 teeth) or the epinephrine (6 teeth) solution was placed in the cavity and a direct current of 120 μA was passed for 90 s between an electrode (anode) that was inserted into the solution and another electrode (cathode) that was held in the subject's hand (Fig. 1). The current was applied from a battery-operated device (Dentaphore-II, model 611 D; Life-tech, Inc., Houston, TX, USA). In some cases, the current was increased gradually over a period of approx. 5 s and in others, 120 μA was applied from the start. The accuracy of the calibration of this device was confirmed by recording the current passed in a model system. The operator was aware which solution was applied to the cavity but the subject was not.

2.6. Pulpal blood flow recording

Pulpal blood flow was recorded with a laser Doppler blood flow monitor (Periflux 4001; Perimed AB, Järfälla, Sweden) which was equipped with an infrared laser (wavelength 780–820 nm). The probe (Perimed type 407: ext. diam. 1.0 mm; optical fibre diam. 0.125 mm, fibre separation 0.25 mm) was supported in a mini probe holder (type PH 07-5) that was incorporated into the removable acrylic splint (see above). The probe holder was positioned so that the probe was perpendicular to the labial enamel surface on the labial surface of the tooth, with its tip over the central long axis of the crown, and with its centre 2 mm from the gingival margin.

Pulpal blood flow was recorded after each of the sensitivity tests, before and after the iontophoretic treatment with either the test or the epinephrine solution. Data were recorded from the digital output of the flow metre with a computer running the PeriSoft (version 1.13) software program. The probe was calibrated according the manufacturer's instructions and the results are expressed in arbitrary perfusion units (PU).

2.7. Remaining dentine thickness

After extraction, each tooth was sectioned longitudinally through the cavity with a diamond disc and the minimum

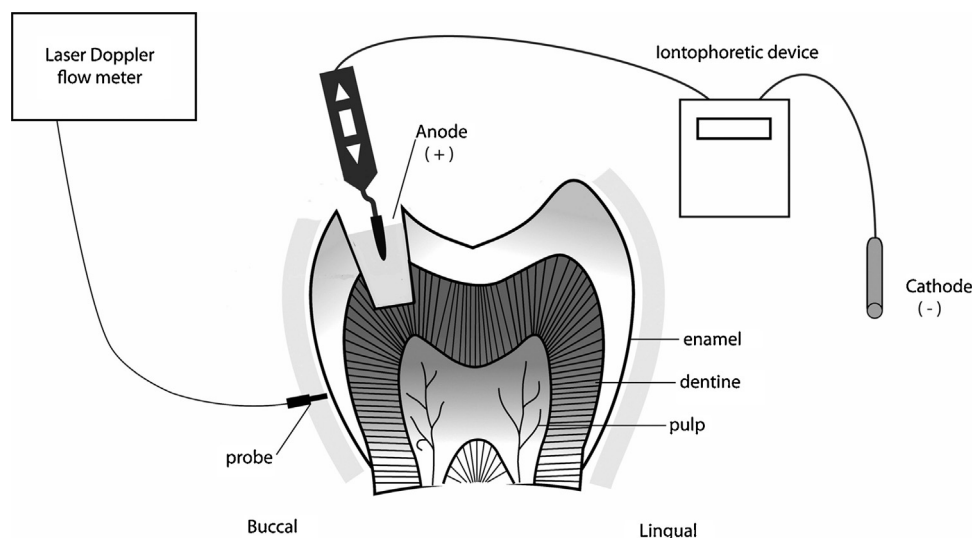


Fig. 1 – Diagram of the experimental set up for treatment with the test solution (not to scale).

length of the dentinal tubules between the cavity floor and the pulp horn was measured with callipers.

2.8. Statistical analysis

Non-parametric statistical methods were used to compare pain scores and blood-flow data. The median and the 25th and 75th percentile values were calculated for each set of data.

Comparisons between the median values of several groups were made with Friedman's Repeated Measures Analysis of Variance on Ranks (RMAVR) and where this indicated there was a significant difference within the groups of data, multiple paired comparisons were made between the control and each of the other groups using Dunn's Test. A *P* value of less than 0.05 was considered significant. The values of remaining dentine thickness were normally distributed and group mean

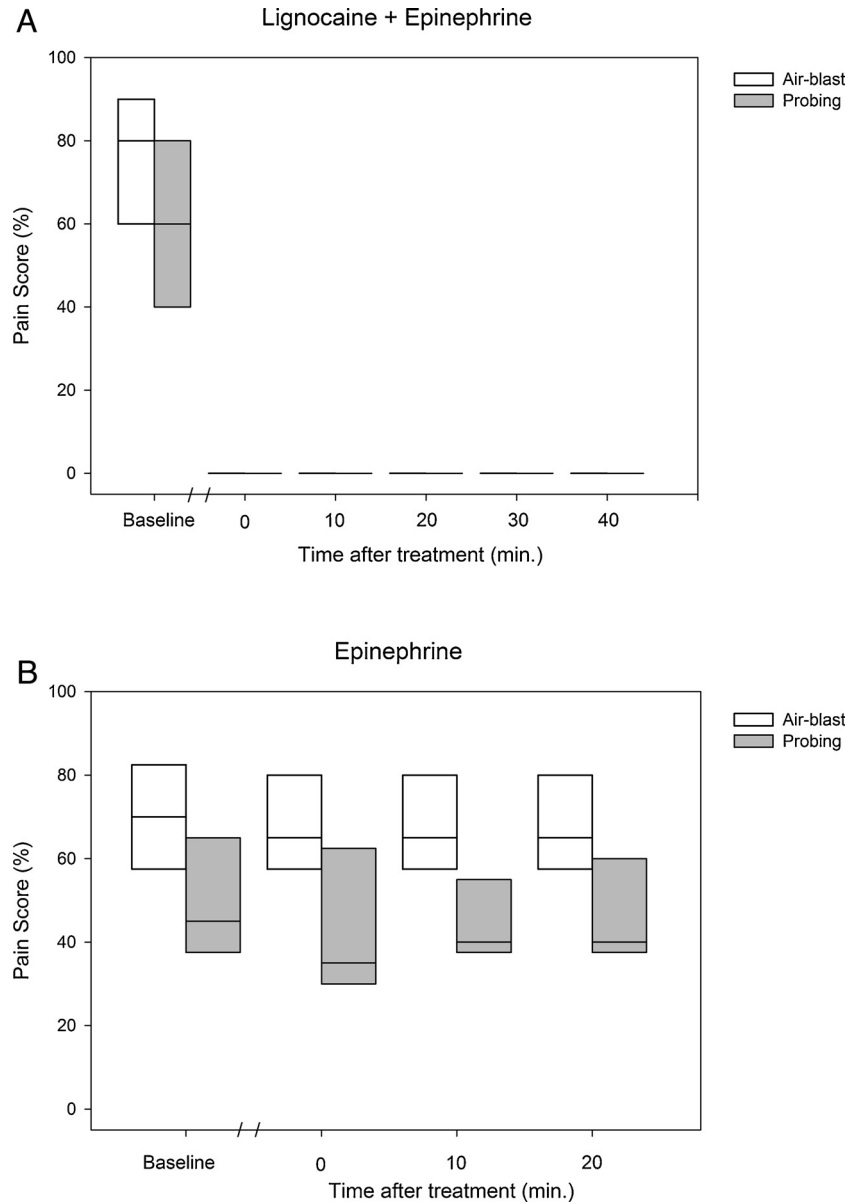


Fig. 2 – (A) The effect of the iontophoresis of 20% (w/v) lignocaine HCl with 0.1% (w/v) epinephrine HCl to exposed, etched dentine on the intensity of pain (pain score) evoked in 7 teeth by air-blast (open boxes) and by probing (grey boxes) stimulation of the dentine. The data were collected before (baseline) and immediately after (0 min) treatment, then at 10 min intervals for the next 40 min. The line through each of the baseline boxes indicates the median pain score and the lower and upper limits of the box, the 25th and 75th percentiles respectively. After treatment, the pain scores were all 0. **(B)** The effect of the iontophoresis of 0.1% (w/v) epinephrine HCl to exposed, etched dentine on the intensity of pain (pain score) evoked in 6 teeth by air-blast (open boxes) and by probing (grey boxes) stimulation of the dentine. The data were collected before (baseline) and immediately after (0 min) treatment, then at 10 min intervals for the next 20 min. The line through each box indicates the median VAS score and the lower and upper limits of the box, the 25th and 75th percentiles respectively.

values were compared with Student's *t*-test. The statistical analyses were carried out with Sigmaplot[®] (version 12) software.

3. Results

Treatment with the test solution produced a very clear effect: it reduced the median pain score with probing from 60 (range 20–80, *N* = 7) to 0 (range 0–0), and that with air-blast from 80 (range 50–100, *N* = 7) to 0 (range 0–0). These effects were recorded when the sensitivity of the dentine was first tested immediately after the 90 s iontophoretic treatment, and in every tooth they persisted throughout the subsequent 40 min period of observation (Fig. 2A). Two of the teeth were tested again after more than 60 min, when the sensitivity of the dentine was found to be recovering. In contrast, treatment with epinephrine alone produced no significant change in the median pain score with either probing or air-blast stimuli ($P > 0.05$, RMAVR) (Fig. 2B).

Applying the 120 μ A iontophoretic current caused no pain if the current was increased from zero over 5 s, but if it the full intensity was applied from the start, some patients felt pain for a few seconds.

The iontophoresis of lignocaine with epinephrine produced a decrease in pulpal blood flow from a median baseline value of 0.92 PU (range 0.25–2.36) to 0.61 PU (0.13–1.85) immediately after the treatment and to 0.47 (0.12–2.10), 0.27 (0.07–2.11), 0.28 (0.10–2.16), and 0.50 (0.50–1.98) at successive 10 min. intervals after this (Fig. 3). Compared with the median baseline value, all the changes in median blood flow after time 0 were significant

($P < 0.05$, RMAVR and Dunn's Test). Treatment with epinephrine alone produced a similar effect (Fig. 3).

The mean remaining dentine thickness of the teeth used for the test solution was 0.74 (s.d. 0.30, *n* = 7) and for the epinephrine solution, 0.95 (s.d. 0.35, *n* = 6). These mean values are not statistically different ($P > 0.05$, Student's *t*-test).

4. Discussion

The present experiments demonstrate that dentine can be anaesthetized by the topical application of a solution containing 20% (w/v) lignocaine HCl monohydrate and 0.1% (w/v) epinephrine HCl when diffusion of these substances into the dentine is facilitated by the application of an iontophoretic current of 120 μ A for 90 s. This is a simple procedure, which provides an alternative to the administration of the anaesthetic by injection that could find application clinically.

The possibility that the lignocaine had a toxic effect on the nerves was considered, but this seems unlikely. The design of the experiment did not provide for monitoring recovery for more than 40 min, but in 2 subjects testing could be continued for up to 1 h and in each case there were signs of recovery.

In the control experiments, the epinephrine alone produced the same fall in pulpal blood flow but no anaesthesia. This shows that the anaesthesia produced by lignocaine plus epinephrine was not just due to ischaemia. In preliminary experiments (Vongsavan, unpublished observations) it was found that the iontophoresis of 20% lignocaine without epinephrine produced anaesthesia lasting less than 10 min. The inclusion of epinephrine in the test solution had the effect

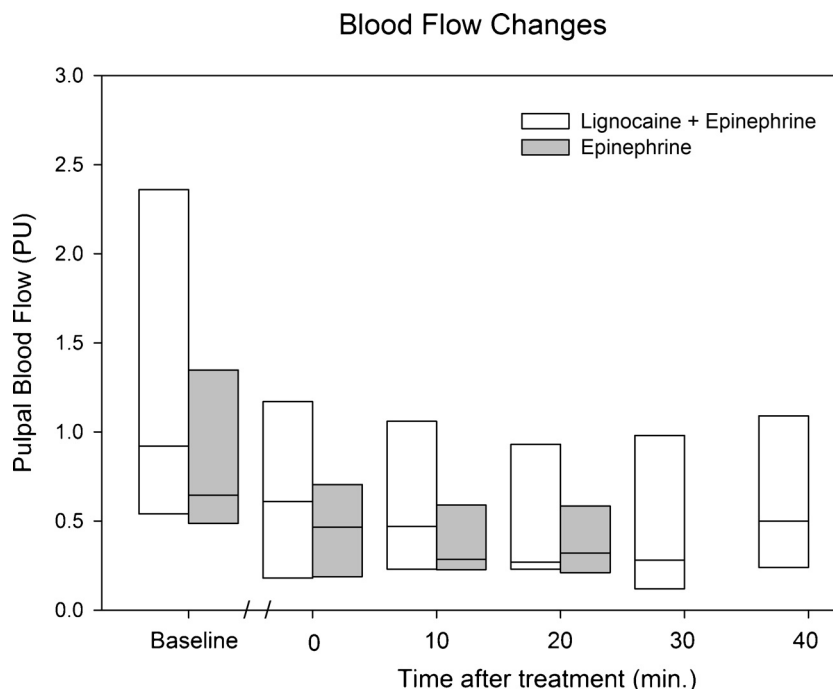


Fig. 3 – Pulpal blood flow values recorded before (baseline) and immediately after (0 min) treatment, then at 10 min intervals for up to 40 min subsequently, Data recorded from 7 teeth treated with 20% (w/v) lignocaine HCl and 0.1% (w/v) epinephrine HCl are represented by the open boxes, and those from 6 teeth treated with 0.1% (w/v) epinephrine only are represented by the grey boxes. The line through each box indicates the median value and the lower and upper limits of the box, the 25th and 75th percentiles respectively.

of increasing the duration of the anaesthesia to a value that would be adequate for most clinical procedures. Without iontophoresis, even a 50% solution of lignocaine applied topically produced anaesthesia for a maximum of 10 min, and after a latent period of up to 30 min.⁷ The duration of the anaesthesia produced by the iontophoresis of lignocaine with epinephrine appeared to be similar to that of the reduction in blood flow, when the rate of diffusion of the lignocaine towards the pulp would have been enhanced and the rate of its washout by the circulating blood, reduced. Further experiments are required to determine the optimal concentration of epinephrine to use.

These conclusions apply to normal dentine; further experiments are required to determine if they also apply to carious dentine and to dentine overlying inflamed pulp.

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Competing interests

We confirm that there were no actual or potential conflicts of interest (including any financial, personal or other relationships with other people or organizations) within three years of beginning the submitted work that could inappropriately influence, or be perceived to influence, the work.

Ethical approval

The work described in this manuscript was approved by The Ethics Committee on Human Rights Related to Human Experimentation of Mahidol University. A copy of the document granting this approval (No. 79/2004) is enclosed.

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