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The iontophoresis of lignocaine with epinephrine into carious dentine for pain control during cavity preparation in human molars



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A B S T R A C T

Objective: To determine the effectiveness of the iontophoretic delivery of lignocaine with epinephrine through carious dentine for pain control during cavity preparation.

Design: The experiments were carried out on 56 carious molars that required class I restorations in 42 subjects (aged 15–20 years). The overhanging enamel and soft caries were removed then the sensitivity of the exposed dentine was tested with drilling, probing and air blast stimuli. The subject indicated the intensity of any pain produced by marking a visual analogue scale (VAS). The cavity was then filled with 20% w/v lidocaine with 0.1% w/v epinephrine and a 200 μ A iontophoretic current applied for 2 min after which the sensitivity of the dentine was re-tested. If the dentine was not anaesthetized, the treatment and testing were repeated up to 6 times.

Results: The total duration (min) of iontophoresis required to anaesthetize the dentine was: 2 in 7 teeth, 4 in 17 teeth, 6 in 14 teeth, 8 in 4 teeth, and 10 in 7 teeth. The remaining 7 teeth were not anaesthetized even after 14 min of iontophoresis.

Conclusions: The iontophoretic delivery of lignocaine with epinephrine anaesthetized dentine for cavity preparation in 49 of 56 (87.5%) of carious molars.

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1. Introduction

It has been shown recently that dentine can be anaesthetised rapidly by the topical application of a solution containing 20% w/v lignocaine HCl and 0.1% w/v epinephrine HCl if an

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iontophoretic, anodal current of $120 \,\mu\text{A}$ is passed for 90 s between the solution and the dentine.¹ These experiments were carried out on freshly exposed, healthy dentine; if the technique could be used for cavity preparation in carious teeth, it would avoid the need for the administration of local anaesthetics by injection, which causes patients pain and

anxiety. Injections are one of the most anxiety-provoking procedures in dental treatment for both children and adults.^{2–5}

In the present experiments, the possibility of anaesthetising carious molars for cavity preparation using a technique similar to that described by Thongkukiatkun et al.¹ was investigated. Preliminary experiments indicated that the original technique did not provide adequate anaesthesia for the treatment of carious teeth and for this reason the iontophoretic current was increased from 120 to 200 μ A and it was applied for 2 min rather than 90 s. In every other respect, the method of treatment was as described by Thongkukiatkun et al.¹

2. Materials and methods

2.1. Brief outline of experiments

Molar teeth were selected that required a class I cavity to remove caries. The cavity was cut by first removing the overhanging enamel with an air-rotor, and then removing the soft caries with a spoon excavator. The sensitivity of the dentine in the floor of the cavity was then tested with a 3 s period of drilling with a diamond bur, with a 3 s blast of air from a triple syringe, and by gently stroking the centre of the cavity floor with an explorer. After this, a solution of 20% w/v lignocaine (synonym: lidocaine) with 0.1% w/v epinephrine was applied to the cavity and an anodic iontophoretic current of 200 μ A passed for 2 min. Immediately after this, the sensitivity of the dentine was tested again. If the patient felt no pain during these tests, the cavity preparation was completed and the cavity was filled with composite resin.

If, after the first treatment, the patient felt pain during any of the three dentine sensitivity tests, the treatment was repeated and the sensitivity of the dentine tested again. This procedure of treatment and testing was repeated up to 7 times until the patient felt no pain. If the dentine was anaesthetised, cavity preparation was completed as described above. If the dentine was not anaesthetised by seven treatments, the tooth was anaesthetised by injection of local anaesthetic and the cavity preparation completed.

2.2. Subjects and teeth

The experiments were carried out on 56 carious, asymptomatic molar teeth that required class I restorations, in 42 healthy subjects (age: 15–20 years, mean 16.7). The experiments were carried out either in the Department of Paediatric Dentistry of the Faculty of Dentistry of Mahidol University or in the Dental Surgery of a local school. In all the teeth, the caries extended into the dentine, and in some the caries was of moderate depth. Teeth with deep caries, under which the pulp might have been exposed, were excluded. The teeth were not X-rayed.

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

The enamel over-hanging the caries was drilled away with a diamond bur in an air-rotor hand-piece with water-spray and the soft caries was removed with a spoon excavator. To prevent the spread of the local anaesthetic solution a temporary wall of composite resin was built up on the enamel around the cavity (height approx. 2 mm) and rubber dam was applied to the tooth. The cavity was not etched.

After the tooth had been anaesthetised, the final stage of cavity preparation was completed with diamond and steel burs in an air-rotor hand-piece with water-spray. The cavity was filled with composite resin (FiltexTM, 3M Dental Products, USA).

2.4. Dentine sensitivity tests

After it had been blotted dry with cotton pellets, the sensitivity of the dentine in the floor of the cavity was tested in three ways: by gently drilling for 3 s with a diamond bur (no. 204) in an air-rotor hand-piece with water-spray, by 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). After each stimulus, the subject was asked to rate the intensity of any pain experienced by placing a mark on a 100 mm visual analogue scale (VAS), in which 0 indicated no pain and 100, the most severe pain that could be imagined.⁶

2.5. Anaesthetic solution and iontophoresis

The anaesthetic solution contained 20% w/v (0.69 mol/l) lignocaine HCl monohydrate (Sigma-Aldrich, Dorset, England) and 0.1% w/v (1:1000) of epinephrine hydrochloride (GPO, The Government Pharmaceutical Organization, Thailand) in sterile, distilled water. In each tooth, 50 μ l of the this solution was placed in the cavity and a direct current of 200 μ A was passed for 2 min 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, Texas, USA). To prevent the current causing pain by stimulating intradental nerves, its intensity was increased gradually from 0 over a period of approx. 10 s.

2.6. Statistical analysis

The median and the 25th and 75th percentile values of the VAS scores were calculated for each set of data. In addition, the 10th and 90th percentiles were calculated for each set with more than 9 values. 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 with the Tukey test. A P value of less than 0.05 was considered significant.

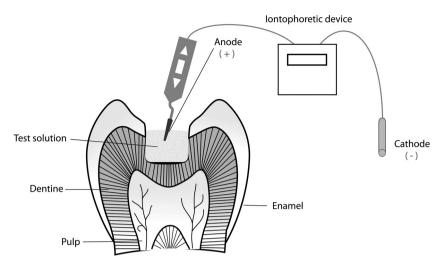


Fig. 1 - Diagram of the experimental set up (not to scale).

3. Results

The median VAS scores when the dentine was first tested after removal of the soft caries were 40 mm (range 5 to 75, n = 56) with the drilling stimulus, 10 mm (range 0 to 80, n = 56) with the air-blast stimulus, and 0 mm (range 0 to 30, n = 56) with probing. The value for drilling was significantly greater than those for air-blast and probing (P < 0.05; RMAP and Tukey test), but the values for air-blast and probing were not significantly different. All the teeth responded to at least one form of stimulus.

After the first treatment, the corresponding values for the 56 teeth were 20 (0 to 60); 0 (0 to 60); and 0 (0 to 30). The reduction in the median VAS score with drilling was significant, but the changes in the responses to the other stimuli were not. None of the three stimuli produced pain in 7 of the 56 teeth and the cavity preparation was completed in these without further iontophoresis.

A second anaesthetic treatment was carried out on the remaining 49 teeth and after this the median responses to the test stimuli were 20 (0 to 50) with drilling; 0 (0 to 50) with air-blast and 0 (0 to 30) with probing. Again, only the change in the response to drilling was significant. There was no response to any of the test stimuli in 17 teeth and the cavity preparation was completed in these without further iontophoresis.

The results obtained with up to 7 treatments (14 min total) are summarised in Fig. 2. The drilling stimulus consistently caused more pain than either air-blast or probing.

The numbers of teeth that required more than 4 min of iontophoresis were as follows: 14 required 6 min, 4 required 8 min, and 7 required 10 min. The remaining 7 teeth were not fully anaesthetised even after a further 2 treatments, and an injection of local anaesthetic was required for the cavity preparation to be completed in these teeth.

The cumulative proportions of the teeth that were successively anaesthetised with different periods of iontophoresis were 12.5% after 2 min, 42.9% after up to 4 min, 67.9% after up to 6 min, 75.0% after up to 8 min, and 87.5% after up to 10 min. The remaining 12.5% were not anaesthetised even after a total of 14 min iontophoresis.

Once the stage had been reached in a tooth at which none of the three forms of test stimulus caused pain, the cavity preparation could be completed without causing further pain.

The teeth were examined after 3 months and 1 year. On each occasion, all were symptomless and vital.

4. Discussion

These experiments have shown that it is possible to anaesthetise a high proportion of carious teeth, to permit cavity preparation to be carried out without pain, by the iontophoresis of a mixture of lignocaine and epinephrine into the dentine. The carious dentine in these teeth was however much more resistant to anaesthesia than the freshly exposed, normal dentine that was investigated using a similar procedure in a previous study.¹ The same solution was applied to the dentine in both studies (20% w/v lignocaine HCl with 0.1% w/v epinephrine HCl) but whereas the normal dentine was immediately anaesthetised when an anodal current of 120 μ A was passed from the solution into the dentine for 90 s, the carious dentine required a current of 200 μ A, and this had to be applied for much longer. Most teeth were anaesthetised after between 2 and 10 min, but even after a total of 14 min, 7 out of 56 teeth (12.5%) were not anaesthetised to the level that would permit dentine to be drilled without pain. Despite this relatively long period of induction of anaesthesia, most of the subjects preferred it to an injection.

The most likely explanation for the greater resistance to anaesthesia of carious dentine compared with normal dentine is that, as a result of inflammatory changes in the pulp associated with the caries, Na+ channels of a type that are not sensitive to lignocaine were expressed in the nerve terminals and that these continued to support the propagation of action potentials despite the presence of the anaesthetic.^{7–11} There are several other possible explanations: for example, the dentine under the caries is likely to have been less permeable to the lignocaine than the normal dentine due to

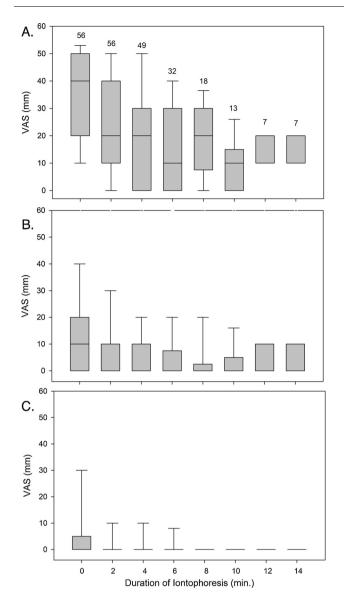


Fig. 2 – The effect of the iontophoresis of 20% w/v lignocaine HCl with 0.1% w/v epinephrine HCl to dentine in a carious cavity on the intensity of pain (VAS score) evoked by: (A) drilling, (B) air-blast, and (C) probing stimulation of the dentine. The data were collected before treatment (Duration 0) and after a variable number of 2 min periods of iontophoresis up to a maximum of 14 min. The data are represented by box plots in which the lower and upper limits of the box represent the 25th and 75th percentiles respectively of the data. The median VAS score is the horizontal line through the box or is the lower limit of the box. The bars below and above each box indicate the 10th and 90th percentiles. The number above each box in (A) shows the number of teeth treated with that duration of iontophoresis.

the presence of secondary and tertiary dentine. The hydraulic conductance of dentine under a carious lesion has been shown to be much lower than that of normal dentine.^{12,13} Also, if the pulp under the caries was inflamed and the pulpal interstitial fluid pressure was raised above normal, the rate of outward flow of dentinal fluid in the opened tubules may have been higher than in normal teeth and this would have reduced the rate of inward diffusion of the lignocaine.^{14–16}

The VAS scores recorded from the carious teeth when tested with air-blast and probing stimuli before treatment, were substantially lower than those obtained with the same stimuli under similar conditions from normal teeth.¹ This was probably because the dentine in the normal teeth had been etched, which would have both removed the smear layer left by drilling, unblocking the mouths of the tubules, and left the dentine surface more compliant than normal. These changes may have allowed the air-blast to cause more fluid to be lost from the tubules and the probing to cause a greater displacement of the tubule contents; both resulting in a greater excitation of the hydrodynamic receptors in the normal than in the carious teeth. There are no data to compare the sensitivity to drilling of normal dentine with that of dentine under caries, although, from our experience of cutting cavities in normal teeth, we believe that the dentine in these teeth is much less sensitive than dentine under caries.

It may be possible to improve the technique we have employed to anaesthetise dentine by for example using an alternative anaesthetic that blocks a wider range of ion channels. Even in its present form, the method could be useful for anaesthetising teeth for conservatory procedures in patients who should avoid injections, such as those suffering from haemophilia or other haemorrhagic conditions, and in those who very much dislike injections.

Conflict of interest statement

No conflict of interest declared.

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Competing interests

None declared.

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 document granting this approval (11/2005) is enclosed.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j. archoralbio.2015.04.005.

REFERENCES

- Thongkukiatkun W, Vongsavan K, Kraivaphan P, Rirattanapong P, Vongsavan N, Matthews B. Effects of the iontophoresis of lignocaine with epinephrine into exposed dentine on the sensitivity of the dentine in man. Arch Oral Biol 2015. <u>http://dx.doi.org/10.1016/j.archoralbio.2015.04.006</u>. [in press].
- 2. Corah NH. Dentist's management of patient fear and anxiety. J Am Dent Assoc 1985;110:724–6.
- 3. Giangrego E. Controlling anxiety in the dental office. J Am Dent Assoc 1986;113:728–38.
- Milgram P, Fiest L, Melmicle S, Wienstein P. The prevalence and practice management consequence of dental fear in a major US city. *Quintessence Int* 1988;166:641–7.
- 5. Weine AA. Current behavior modes of reducing dental anxiety. *Quintessence Int* 1982;9:981–5.
- **6**. Holland GR, Narhi MN, Addy M, Gangarosa L, Orchardson R. Guidelines for the design and conduct of clinical trials on dentine hypersensitivity. *J Clin Periodontol* 1997;**24**(11): 808–13.

- Renton T, Yiangou Y, Plumpton C, Tate S, Bountra C, Anand P. Sodium channel Nav1.8 immunoreactivity in painful human dental pulp. BMC Oral Health 2005;5(1):5.
- 8. Wells JE, Bingham V, Rowland KC, Hatton J. Expression of Nav1.9 channels in human dental pulp and trigeminal ganglion. J Endod 2007;**33**(10):1172–6.
- 9. Warren CA, Mok L, Gordon S, Fouad AF, Gold MS. Quantification of neural protein in extirpated tooth pulp. J Endod 2008;34(1):7–10.
- Kistner K, Zimmermann K, Ehnert C, Reeh PW, Leffler A. The tetrodotoxin-resistant Na+ channel Na (v)1.8 reduces the potency of local anesthetics in blocking C-fiber nociceptors. *Pflugers Arch* 2010;**459**(5):751–63.
- Suwanchai A, Theerapiboon U, Chattipakorn N, Chattipakorn SC. NaV 1.8, but not NaV 1.9, is upregulated in the inflamed dental pulp tissue of human primary teeth. Int Endod J 2012;45(4):372–8.
- Pashley EL, Talman R, Horner JA, Pashley DH. Permeability of normal versus carious dentin. *Endod Dent Traumatol* 1991;7(5):207–11.
- Elgalaid TO, Creanor SL, Creanor S, Hall AF. The permeability of natural dentine caries before and after restoration: an in vitro study. J Dent 2007;35(8):656–63.
- Pashley DH. Dentine permeability and its role in the pathobiology of dentine sensitivity. Arch Oral Biol 1994;39(Suppl.):73S–80S.
- Heyeraas KJ, Berggreen E. Interstitial fluid pressure in normal and inflamed pulp. Crit Rev Oral Biol Med 1999;10(3):328–36.
- Ajcharanukul O, Chidchuangchai W, Charoenlarp P, Vongsavan N, Matthews B. Sensory transduction in human teeth with inflamed pulps. J Dent Res 2011;90(5):678–82.