The Effect of Sonophoresis on Topical Anesthesia: A Pilot Project

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The dental anesthesia sonophoresis device (DASD) is a novel device that is intended to reduce the discomfort associated with intraoral mucosa needle puncture. The DASD produces ultrasonic energy that provides a sonophoretic effect on the oral mucosa, generating microchannels through the lipids between the keratinized cells that make up the stratum corneum. Once the topical anesthetic has permeated the stratum corneum, it quickly diffuses through the soft tissue, desensitizing the nerve endings and reducing the perception of pain caused by needle penetration. The aim of this study is to evaluate whether topical anesthesia applied using the DASD will reduce the discomfort of the needle puncture when compared to the control device. A split-mouth model, using 50 healthy subjects with puncture site at the maxillary canine vestibule, was used for this study. Subjects received a needle puncture on both sides of the mouth. Prior to the needle puncture, there was randomized application of 5% lidocaine with the DASD and a control device. Subjects rated their discomfort after needle punctures utilizing the visual analog scale pain scoring system. There was no statistically significant difference in the pain perception using the DASD versus the control device.

Key Words: Dental anesthesia sonophoresis device; Sonophoresis.

Sonophoresis, which is low-frequency ultrasound, has been shown to enhance transdermal transport of various drugs, including macromolecules. Enhancement from sonophoresis occurs by disordering the structured lipids in the stratum corneum. Although sonophoresis has been shown to be effective on the skin, its effect has not been studied intraorally. The development of the dental anesthesia sonophoresis device (DASD), a device whose design was specially developed for the application of sonophoresis in the oral cavity, has opened the door for exploration in the benefits and effectiveness of sonophoresis application in the dental field. Fear of

intraoral local anesthetic injection is one of the main reasons people avoid dental treatment.¹ Many investigators, using a variety of different techniques, have explored reducing the pain and discomfort of the dental injection. The majority of research has focused on the application of topical anesthesia.

The results are inconsistent with regard to the effectiveness of topically applied anesthetic. Some studies show that there are no significant differences when compared to the placebo.^{2–5} On the other hand, there are several studies that support the efficacy of topical anesthetic.^{3,6–9}

Duration of application has been isolated as an important factor to achieve adequate topical anesthesia. Meechan¹⁰ summarizes that the degree of topical anesthesia penetration and its effectiveness are governed by the duration of application. It has been suggested that

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success of topical anesthesia is guaranteed when used in the buccal fold of either jaw after a 5-minute application.¹¹ Due to the lack of consistency in the literature regarding the effectiveness of topical anesthesia, there is need for continued research and improvement.

Topical anesthetic must cross the physical barrier of the intraoral mucosa to reach the underlying nerve receptors. The free nerve endings are located close to the basal surface of the oral epithelium.¹² The location of these free nerve endings only reinforces the importance of the topical anesthetic passing through the oral mucosa barrier. The intraoral mucosa, like the skin, consists of stratified squamous epithelium with different layers of cells. The most superficial layer is the stratum corneum, which is filled with short stacks of lipid lamellae.¹³ This lipid layer makes it difficult for substances to cross the stratum corneum. To demonstrate this, Squier¹⁴ showed that horseradish peroxidase could not penetrate the top 3 layers of the oral mucosa of 3 mammals when applied topically.

Attempts have been made to improve the penetration of topical anesthetics across this anatomic barrier. Hutchins et al⁷ studied the effect of vibration with a placebo and vibration with 20% benzocaine on pain of intraoral injections, and found vibration had no effect on reducing pain. Others have studied the use of iontophoresis and phonophoresis for application of anesthesia.^{15,16} Research suggests that skin anesthesia by application of a topical anesthetic can be expedited through iontophoresis; however, this still requires a minimum of 10 minutes at relatively high voltage.¹⁷

Ultrasound has been shown to enhance transdermal transport of various drugs, including macromolecules. This type of enhancement is termed sonophoresis, indicating the enhanced transport of molecules under the influence of ultrasound.¹⁸

The DASD is a novel device intended to expedite penetration of topical anesthetic with a faster onset of clinical effectiveness. The DASD is a portable, battery-powered device that simultaneously generates ultrasonic energy and sonic vibration in a small applicator head that can easily reach and adapt to injection sites in the oral cavity. The ultrasonic energy is in small bursts of 300–350 kHz that provide a sonophoretic effect on the oral mucosa. The manufacturer claims the DASD works by generating microchannels through the lipids in the stratum corneum. The sonic vibration is provided simultaneously with the ultrasonic energy in the form of sinusoidal motion ranging from 200–300 Hz. This vibration helps to randomize and distribute the sensation associated with the ultrasonic energy. Once the topical anesthetic has permeated the stratum corneum, it quickly diffuses through the soft tissue, desensitizing the nerve endings. The purpose of this study is to evaluate whether

topical anesthesia applied using the DASD will reduce the discomfort of the needle puncture when compared to the control device. The null hypothesis is that there is no difference of perceived discomfort between the DASD and the control device (CD).

METHODS

Fifty ASA I and II volunteers between the ages of 22 and 50 participated in this clinical trial. Exclusion criteria were as follows: tobacco use, soft or hard tissue tumor of the oral cavity, advanced periodontal disease, pregnancy or breast-feeding, diabetes or allergies to local anesthetic, and previous dental treatment in tested area within 30 days. The anatomic site used was the maxillary mucobuccal fold above the canine eminence. One side of the subjects' mucosa was dried with a 2 × 2 sponge gauze, and 0.3 mL of 5% lidocaine was dispensed using a TB syringe onto the DASD (Figure 1). The DASD was applied to the site for 1 minute. The site was punctured using a short 27-gauge needle inserted to a depth of 3 mm (Figure 2). A rubber endodontic stopper was placed on the needle to standardize needle insertion depth. Immediately after the removal of the needle, the patients rated their pain according to the visual analog scale model. The same protocol was followed on the contralateral side using a CD, which was a modified battery-operated toothbrush applied with 0.3 mL of 5% lidocaine. The 2 needle punctures were performed at the same session. A single investigator performed the application of topical anesthetic utilizing the DASD and CD, randomly alternating the order of administration. Administration of needle punctures was divided randomly among 5 separate clinicians. The device application was blinded to both the clinician and the patient.

Figure 1. Picture demonstrating 0.3 mL of 5% lidocaine applied to the control device using a TB syringe.

Figure 2. A 27-gauge needle with a rubber endodontic stopper measured at 3 mm.

RESULTS

Ten of the 50 subjects (20%) reported no pain for either needle puncture. Twenty-two of the 50 subjects or 44% reported less pain after the DASD application. Sixteen or 32% of subjects reported more pain after the DASD administration. Two (4%) of the subjects reported the same pain score. There was no statistically significant difference in pain scores among the 5 investigators administering the needle puncture. There was no significant difference between the pain perceived according to the Wilcoxon signed rank test *P* value of .541 after application of topical anesthetic with the DASD versus the CD (Figures 3 and 4).

DISCUSSION

Prior to the present paper there was no published research on the application of sonophoresis intraorally; however, sonophoresis has had notable success in other medical applications in aiding the absorption of a topical application of medication. In 1950, Fellingner and

Hypothesis Test Summary

1	The Median of differences between DASD and CD equals 0.	Related-Samples Wilcoxon Signed Ranks Test	.541	Retain the null hypothesis
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Asymptotic significances are displayed. The Significance level is .05.

Figure 3. Statistical summary showing results according to Wilcoxon signed rank test.

Figure 4. Scatterplot showing the differences in perceived pain. Values are expressed as millimeters on the visual analog scoring system (0–100 mm). ◇ represents pain scores with the dental anesthesia sonophoresis device, and ● represents pain scores with the control device.

Schmidt reported the first successful use of sonophoresis for the treatment of polyarthritis of the joints of the hand with hydrocortisone ointment.¹⁸ Benson et al,¹⁹ in 1991, demonstrated the enhanced absorption of methyl and ethyl nicotinate by disordering the structured lipids in the stratum corneum using sonophoresis. Ultrasound was shown to enhance the effect of topically applied aqueous lidocaine to hairless mice by Tachibana and Tachibana²⁰ in 1993. Mitragotri et al²¹ used studies from cadaver skin to report that low-frequency ultrasound increases the permeability of human skin to many drugs, including high-molecular-weight proteins, by several orders of magnitude.

The development of the DASD, a device specially developed for the application of sonophoresis in the oral cavity, has opened the door for exploration of the benefits and effectiveness of its application in the dental field. The initial study goal was to create a baseline for further research of the effect of sonophoresis on topical anesthesia. In a preliminary trial application of the

Figure 5. Schematic drawing of the head of the dental anesthesia sonophoresis device as it is now.

Figure 6. Schematic drawing of the proposed dental anesthesia sonophoresis device head with a silicon cup to hold anesthetic.

DASD, subjects reported rapid anesthetic effect after application, leading to the hypothesis that the DASD reduces the time needed for onset of topical anesthesia (Figure 5).

The results indicate that there was not a significant enough difference to reject the null hypothesis. A larger sample size might show more significant results; however, this was outside the time and budget constraints of this study. One successful aspect of this study was creating a baseline for further research.

There were several limitations to this study. The first was our inability to separate sonic and subsonic factors. The CD emitted sonic frequencies, while the DASD device emitted both sonic and ultrasonic frequencies. A true baseline would have been created if the application of the DASD were compared directly with the application of the topical anesthetic alone.

Another limitation was that the puncture site selected for this study was not ideal for establishing the DASD's effectiveness. In comparison to the buccal mucosa, dense, keratinized palatal tissue is difficult to anesthetize. Topical anesthetic has been shown to be relatively ineffective for use on the palate. The DASD might show significant efficacy in comparison with the traditional means of topical application in this area. However, the DASD device is in the design phase for application on the hard palate and not currently available. The development of a cup-shaped applicator to hold the topical anesthetic in place will allow for DASD application on palatal tissues (Figure 6).

Further research should include establishing a true baseline with a direct comparison between the application of the DASD and topical anesthetic alone. Once a cup to hold the topical anesthetic has been developed, the effectiveness of the DASD in hard palate application can be explored. The variable of perceived pain is also a significant factor that should be considered in further research with longitudinal evaluation of a patient over

multiple visits in which they are subjected to both the application of DASD and topical anesthesia alone. If a patient consistently rated the DASD as reducing pain during injection, it would account for how individuals perceive and rate pain.

Based on the results, we conclude that within the limitations of this study the application of topical anesthetic with the DASD does not enhance the efficacy of 5% lidocaine when compared to the CD.

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