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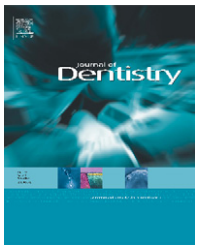

The effect of clove and benzocaine versus placebo as topical anesthetics

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ABSTRACT

Objectives: The purpose of this study was to examine whether the natural herb clove can replace benzocaine as a topical anesthetic.
Methods: Topical agents were applied to the maxillary canine buccal mucosa of 73 adult volunteers. Four substances were tested in the study: (1) homemade clove gel, (2) benzocaine 20% gel, (3) placebo that resembles clove and (4) a placebo that resembled benzocaine. After 5 min of material application in a randomized, subject-blinded manner, each participant received two needle sticks. Pain response was registered using a 100 mm visual analogue pain scale.
Results: Both clove and benzocaine gels had significantly lower mean pain scores than placebos ($p = 0.005$). No significant difference was observed between clove and benzocaine regarding pain scores.
Conclusion: Clove gel might posses a potential to replace benzocaine as a topical agent before needle insertion.

1. Introduction

Although local anesthetic injections are used to alleviate pain and reduce anxiety, they themselves are a source of pain and anxiety for many patients. Topical anesthesia has been described as reducing pain from needle stick.[1] It is widely used today in dental practice, especially for pediatric patients, with benzocaine (20%) being one of the most widely used agents. There is a substantial number of studies on benzocaine with varying designs and conflicting results.[2,3] Some studies reported a good effect,[1,4] whereas others have shown that benzocaine is not particularly efficacious.[2,5–7]

Traditionally, clove has been used as a spice in cooking, but it has also been used for the topical treatment of toothache because it contains eugenol, an oily liquid that is widely used in dentistry for analgesic and antiseptic properties.[8] Moreover, some studies have documented the antimicrobial effects of eugenol, vanillin and iso-eugenol, which are constituents of clove.[9] To our knowledge, there are no studies that have investigated clove as a topical anesthetic agent before needle sticks. The aims of this study were therefore to investigate the efficacy and compare the topical anesthetic effects of clove and benzocaine 20% gel in reducing pain from needle stick.

2. Participants, materials and methods

The study design was approved by the ethical committee of the Faculty of Dentistry, Kuwait University. The participants were healthy medical, dental or pharmacy students between

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the ages of 19 and 25 years. Participation was voluntary and informed consent was obtained. Participants having pain, ulceration or any other symptom that might affect the results of the trial were excluded. The trial was done on 73 volunteers (40 males, 33 females) grouped randomly into two groups as will be explained later in the article.

The materials used were (i) home made clove gel, (ii) benzocaine 20% gel (Topex™, Sultan Dental Products, Englewood, NJ, USA), (iii) placebo that resembled clove gel in texture and color (placebo C) and (iv) placebo that resembled benzocaine gel (placebo B). The clove gel was prepared by grinding commercially available clove to fine powder and then mixing it with liquid glycerin in a ratio of 2:3 (clove: glycerin) by volume. Placebo C was made from pumice mixed with glycerin to make it similar to clove gel in texture. Placebo B was made up of petroleum jelly (Vaseline™) so that it was similar to benzocaine in texture. All the materials used were sugar free and were stored in identical containers.

Each of the 73 participants was assigned to one of the two groups using predetermined data collection forms that were randomly arranged. Thirty-seven (37) volunteers received clove gel on one side and placebo on the other, while thirty-six (36) received benzocaine gel on one side and placebo on the other. Whither the placebo or the active drug was applied for the first needle stick and wither it is applied to the left or right side of the patient was randomly determined. The participants were asked if they have ever had dental local anesthesia before and whether they have had a good night's sleep before coming to the trial.

The participants were smell- and sight-blinded by using an eye cover over which a protective goggle was put. The protective goggle had a specially made projection on which a cotton roll was mounted. The cotton roll was covered with both materials (clove and benzocaine) before the trial began to blind the smell (Fig. 1).

After the blinding device was applied, the participants were laid comfortably on the dental chair. The first material, as indicated by the random data sheet, was applied generously on a cotton roll. Approximately 2 g of material were applied to the buccal mucosa superior to the gingiva over the canine prominence, covering an area of about 1.5 cm in diameter for 4 min and then was reapplied for another minute. The material was reapplied because the authors were concerned about material washout by saliva. The mucosa was not dried before material application. After the cotton roll and excess material were removed, the lip was lifted without squeezing and the needle stick was done 3 mm superior to the mucogingival border. A 25-gauge needle was inserted until bone contact was achieved and then withdrawn. The participants' eyes were then uncovered and they were then asked to rate pain on the pain scale. The participants were instructed in the use of a 100-mm visual analogue pain scale (VAS), where 0 indicated ''no pain at all'' and 100 indicated ''unbearable pain''. The participants rated two separated scales per trial. The score was then measured in millimeters using a ruler. The participants were allowed to rinse their mouth and rest for a short time. The trial was then completed using the second material on the left side with the same procedure. After the end of the trial, the participants were asked to report any changes or symptoms felt in the areas of material application over the next few days.

Fig. 1 – The picture depicts the set-up of the trial with the blinding device. In the frame is a pictures of the containers used (showing cloves and placebo C).

Statistical analysis was performed using SPSS (SPSS Inc., Chicago, IL, USA) and STATA programs. Analysis of variance (ANOVA) was done to test whether the differences between pain scores were significant as a function of material (clove versus benzocaine). Regression analysis was performed to check for the effect of gender, previous local anesthesia and good night's sleep on pain scores. Statistically significant differences were assumed when $p < 0.05$.

3. Results

All registrations were performed according to plan. In total, 146 registrations were performed in 73 participants. An overview of the pain scores registered is given in Table 1. Fig. 2 depicts mean pain scores as a function of the different agents.

When significance analysis was done the placebo observations were pooled together (there was no significant difference between the two placebos regarding pain score) and data was treated as if there were three groups. Both benzocaine and clove had significantly lower mean pain scores than placebo ($p = 0.05$), whereas no significant difference between clove and benzocaine on pain scores was noted. The regression analysis revealed that females had significantly higher mean pain scores than males in general ($p = 0.026$). However, there was no significant difference in pain scores on the variables a good night's sleep or previous local anesthesia ($p = 0.38$ and 0.19, respectively). The fact that two observations were obtained from each participant was taken into account in the analysis.

Four participants developed small aphthous-like ulcers in the area of clove gel application. Most of the participants reported a slight burning sensation during the application of both benzocaine and clove gels. One patient reported a ''pain-like'' feeling after the application of benzocaine; however, whether it was related to the material or to the needle stick is not clear.

Table 1 – The table shows a summary of the pain scores with means, standard deviations, standard errors, confidence intervals, and minimum and maximum scores for each material

Material	N	Mean	Standard deviation	Standard error	95% Confidence interval for mean		Minimum	Maximum
					Lower bound	Upper bound		
Placebo C	37	16.54	15.2	2.499	11.47	21.61	0	67
Placebo B	36	24.5	21.238	3.54	17.31	31.69	1	72
Cloves	37	10.51	8.431	1.386	7.70	13.32	0	27
Benzocaine	36	13.31	15.953	2.659	7.91	18.70	0	63
Total	146	16.18	16.516	1.367	13.48	18.88	0	72

4. Discussion

This study showed that both clove and benzocaine 20% gels are able to significantly reduce pain from needle sticks when compared with placebo. No significant difference in pain reduction was found between the two materials.

We aimed at making the experimental setting similar to the clinical environment. A needle stick is only one modality of pain; in clinical practice pain can also be felt from the deposition of the local anesthetic agent. Injections were avoided in this study because they are difficult to standardize. We regarded standardizing the needle stick more important. For practicality, the study was only single- and not double-blinded. However, this limitation should have no systematic influence because the participants themselves rate the pain.

We chose to test the effects of the buccal mucosa in the present study. In general, topical anesthetics seem to work if applied to either the maxillary or mandibular buccal fold as shown in several randomized clinical trials.[1,2,10,11] However, when it comes to palatal mucosa, topical anesthetics do not seem to produce the same effect as evidenced by several randomized trials with varying results.[2,12,13] We must therefore be careful not to draw any conclusions about the effects of the materials tested in this study at sites other than the buccal mucosa.

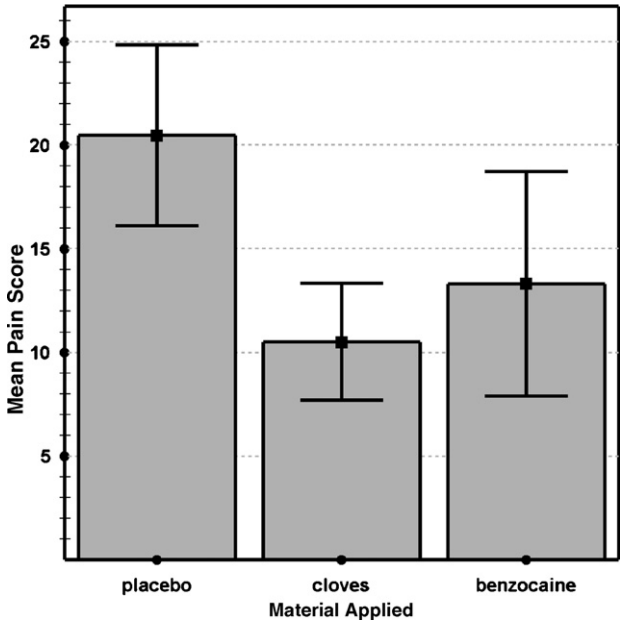

Fig. 2 – Bars represent mean pain scores according to the material applied and error bars represent 95% confidence intervals for means. The difference between placebo scores vs. clove; and placebo vs. benzocaine were significant ($p < 0.05$).

Studies that have employed 1–3-min application times have reported mixed results.[2,14,15] Thus, we chose a 5-min application time, which seems to be a safe choice in ensuring that topical anesthetics will have an effect in the buccal fold.[16]

In whatever concentration, topical anesthetics are drugs with toxicity and side effects. Several studies have shown that local anesthetic agents are detectible in plasma after intraoral use.[17–21] The fact that topical agents are related chemically to the local anesthetic injected makes systemic absorption of topical agents a source of worry. Some clinicians feel that the use of topical anesthetics would limit the amount of local anesthetic they can inject, especially in pediatric patients. Benzocaine has been reported to cause methemoglobinemia in some endoscopy cases when used in large amounts.[22–25] This brings us to the fact that a non-local anesthetic substitute for topical anesthetics would be very useful clinically.

Clove contains eugenol, a material known to cause tissue irritation.[26] This may help explain why four of our participants (5.4%) developed small ulcers. With a lower concentration, this side effect may possibly not occur; however, the optimal concentration with least side effects has to be evaluated in future studies. When the general effects of clove is considered, the literature suggests that clove posses an anti-platelet activity,[27–29] and that it inhibits lipid peroxidation.[30] When smoked in cigarettes or given intravenously, clove or its oil has been reported to cause pulmonary edema.[31,32] This serious problem might not be related to using it as a topical agent, but obviously requires further investigation. Contact dermatitis from eugenol has been reported in a physiotherapist with occupational use.[33]

The results of the study showed that clove gel is equally effective to benzocaine as a topical agent. This might mean that dentists can substitute clove for benzocaine in there daily practice. Clove gel is more than five times cheaper than other topical anesthetics; moreover, it is widely available even in rural areas. Thus, the natural herb clove has some advantages over other topical anesthetics, especially in poor countries where the use of topical anesthetics is restricted by cost and availability. The use of clove might give more people (and more children) the chance for needle stick pain reduction.

5. Conclusion

It is concluded that clove might replace the widely used topical anesthetic benzocaine, thereby reducing the dose of drugs the patient absorbs, lowering the cost on the dentist and allowing more patients throughout the world to benefit from a cheap and largely available topical anesthetic.

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