Effect of Topical Anesthesia with Lidocaine-prilocaine (EMLA) Cream and Local Pressure on Pain during Infiltration Injection for Maxillary Canines: A Randomized Double-blind Clinical Trial

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ABSTRACT

Objectives: This study compared the effect of local pressure and topical lidocaine-prilocaine (EMLA) cream on pain during infiltration injection for maxillary canine teeth.

Materials and methods: A total of 140 volunteer students participated in this split-mouth design randomized clinical trial. The subjects were randomly divided into four groups (n = 35). Before administration of anesthesia, in each group, one side was randomly selected as the experimental and the opposite side as the control. In group 1, finger pressure was applied on the alveolar mucosa on the experimental side and on the tooth crown on the control side. In group 2, 5% EMLA cream and placebo; in group 3, finger pressure and 5% EMLA cream; and in group 4, 5% EMLA cream and 20% benzocaine gel were applied. In all the groups, a buccal infiltration procedure was carried out. Pain during injection was recorded with visual analog scale (VAS). Wilcoxon and McNemar tests were used for statistical analysis of the results. Statistical significance was set at p < 0.05.

Results: The results showed that EMLA reduced the injection pain significantly more than benzocaine (p = 0.02). Also, injection pain was significantly lower with the use of EMLA in comparison to placebo (p = 0.00). Application of local pressure reduced the injection pain, but the difference from the control side was not significant (p = 0.05). Furthermore, the difference between application of local pressure and EMLA was not statistically significant (p = 0.08).

Conclusion: Topical anesthesia of 5% EMLA was more effective than 20% benzocaine in reducing pain severity during infiltration injection. However, it was not significantly different in comparison to the application of local pressure.

Keywords: Anesthesia, EMLA, Injection, Pain, Pressure, Topical, Visual analog scale.


Source of support: Dental and Periodontal Research Center of Tabriz University of Medical Sciences.

Conflict of interest: None

INTRODUCTION

Pain during injection of local anesthetic agents is one of the main problems during most dental procedures, which might be attributed to the mechanical trauma of needle pressure to injection site, rapid expansion of tissues due to the local anesthetic agent, or rapid discharge of syringe contents. Application of topical anesthesia is the main technique dentists use to reduce pain severity during injection. Although various agents are available for topical anesthesia, none of them have been able to completely eliminate pain during injection.
Lidocaine-prilocaine (EMLA) cream, a widely used topical anesthetic agent, is the eutectic mixture of lidocaine (2.5%) and prilocaine (2.5%), which is theoretically more effective than each of them separately in pain reduction during injection.\(^6\)\(^,\)\(^7\) Lidocaine-prilocaine was first reported for dermal use in 1980.\(^9\) In addition, its mucosal application was first presented by Holst and Evers.\(^9\)

Lidocaine-prilocaine has been investigated in dental procedures, including anesthesia of buccal mucosa for restorative procedures,\(^10\) periodontal anesthesia before procedures, such as periodontal probing,\(^11\) scaling and root planning,\(^12\) oral mucosa anesthesia before removing maxillary and mandibular appliances,\(^13\) and reduction of pain and discomfort during rubber dam placement.\(^14\)

Studies have reported some concerns about the toxic effects of this topical anesthetic agent on oral mucosa.\(^15\),\(^15\) Also, low viscosity and high pH are other disadvantages of EMLA.\(^10\)

Studies have reported conflicting results about the mucosal use of EMLA.\(^1,\)\(^5\)-\(^15\)\(^,\)\(^25\) Nayak and Sudha\(^26\) concluded that 5% EMLA cream was superior in pain reduction during buccal infiltration compared to benzocaine and lignocaine. However, Tulga and Mutlu\(^15\) reported low efficiency of EMLA in comparison to other topical anesthetic agents, including 20% Vision gel (benzocaine). Benzocaine is a commonly used topical anesthetic agent from the ester group, which has yielded favorable results in clinical studies.\(^15\),\(^27\)

In addition to topical anesthesia, there are some other simple methods to diminish pain during injection, for example, local pressure on the area before injection. According to the theory of gate control, which was first presented by Melzack and Wall,\(^28\) local pressure could reduce pain during injection. Stimulation of A beta fibers through pressure and vibration could regulate the medullary dorsal horn, resulting in a decrease in painful nerve inputs from peripheral tissues.\(^28\),\(^29\)

The aim of this split-moth clinical trial was to compare the effect of local pressure and topical anesthesia with lidocaine-prilocaine (5% EMLA) cream on pain during infiltration injection for maxillary canine teeth.

**MATERIALS AND METHODS**

This study was approved by the Research and Ethics Committee of Tabriz University of Medical Sciences (TBZMED.REC.1394.600). A sample size of 140 was calculated to provide 80% power (\(\alpha = 0.05\)) to detect a 25% decrease in self-rated pain by using power analysis and sample size software (PASS) for Windows (NCSS Statistical Software, Kaysville, UT, USA).

In this split-mouth double-blind randomized controlled clinical trial, 140 volunteer dental students were evaluated. The inclusion criteria consisted of ASA I or II category, maxillary canine teeth with minimal caries and restorations, no abnormal findings in periapical radiography, and normal probing depth. Clinical diagnosis of intact tooth was confirmed by positive response to electric pulp tester (PARKE LL, PT-20, USA). Exclusion criteria consisted of known allergy or contraindications to use anesthetic materials (lidocaine and prilocaine), patients taking sedatives, use of analgesics and anxiety medications for 2 weeks before the study, or any other drugs that could have affected pain perception.

All the clinical procedures were carried out in the Department of Endodontic, Tabriz Faculty of Dentistry, Iran, from June to December 2015. All the subjects completed informed consent forms after full explanations we provided in relation to the nature of the procedures and the possible discomforts and risks. Volunteers who agreed to participate in this study were randomly assigned to four groups (n = 35) using an online random number generator (www.randomization.com). Before administration of anesthesia in each group, one side was randomly selected as experimental and the opposite side as control. In group 1, firm finger pressure was applied on the alveolar mucosa at injection site on one side (the experimental side) and on the tooth crown on the opposite side (the control side). In group 2, 5% EMLA cream (Astra Pharma Inc., Ontario) was applied on the injection site (the experimental side). Placebo was applied on the opposite side (the control side). In group 3, finger pressure was applied on the alveolar mucosa at injection site on one side and 5% EMLA cream was used on the opposite side. In group 4, 5% EMLA cream was applied on the injection site, while 20% benzocaine gel (Premier, Philadelphia, PA, USA) was used on the opposite side.

As a placebo for the topical anesthetic, a topical gel with the same appearance, smell and color was produced by one of the coauthors. The topical anesthetic agents, 5% EMLA cream (Astra Pharma Inc., Ontario) and 20% benzocaine (Premier, Philadelphia, PA, USA), were applied on the injection site using a cotton applicator for 1 minute as recommended by American Dental Association, US Food and Drug Administration, and Nayak and Sudha.\(^26\)

Also, finger pressure was applied on the alveolar mucosa by the operator carrying out the injections for 1 minute.

Both the commercial topical anesthetic agents, 5% EMLA and placebo creams, were kept in tubes with similar appearances labeled by the coauthor who is a specialist in pharmaceutics. Thus, both the patients and operator were blinded to the topical gels and placebo.

In all the groups, buccal infiltration of 1.8 mL of 2% lidocaine with 1:80,000 epinephrine (Darupaksh, Tehran, Iran) was carried out. All the injections were performed by a 3rd-year postgraduate student.
Immediately after the injection, the volunteers were asked to rate their pain during needle penetration and injection on the 10 mm VAS forms. In this scale, 0 was considered as no pain, 1 to 3 as mild pain, 4 to 6 as moderate pain, and 7 to 9 as severe pain.30

Statistical Analysis
Statistical analysis was performed using statistical packages for the Social Science (SPSS) 20 (IBM, USA). Wilcoxon test was used for the analysis of data. Pairwise comparisons were made using the McNemar test. Statistical significance was set at p < 0.05.

RESULTS
A total of 140 volunteers, 68 males and 72 females, with an average age of 33 ± 2.6 years, ranging from 18 to 59 years, participated in this study. Table 1 presents the baseline characteristics of the study groups. Analysis of data showed that use of EMLA topical anesthetic agent reduced pain of injection significantly compared to benzocaine (p = 0.02). Also, the results showed that injection pain was significantly lower with the use of EMLA in comparison to placebo (p = 0.00). Moreover, application of local pressure on the buccal mucosa before infiltration reduced the injection pain, but the difference was not significant (p = 0.05). Furthermore, the difference between application of local pressure and EMLA topical anesthetic agent was not statistically significant (p = 0.08) (Graph 1).

Table 1: Basic characteristics of the study groups

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<tr>
<th>Groups</th>
<th>Gender</th>
<th>Mean age</th>
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DISCUSSION
In this randomized clinical trial, we compared the effect of local pressure and 5% EMLA cream as a topical anesthetic agent on pain during infiltration injection for maxillary canine teeth. In this study, we evaluated the efficacy of EMLA in pain reduction during infiltration injection since it is one of the most commonly used topical anesthetic agents in dermatological practice.7 In addition, a number of investigations have studied EMLA intraorally with promising results.10-14

The rationale behind investigating the effect of local pressure on pain during infiltration injection in this study was that it could be effective in reducing pain during injection, according to the gate control theory. Furthermore, the effects of vibration and local pressure have been evaluated.29,31

In the present study, the topical anesthetic agent benzocaine was compared with EMLA because it is one of the commonly used topical anesthetic agents in dentistry32 and has been evaluated in several studies.17,29,33,34

Based on the application time of topical anesthetic agent EMLA, different studies have shown various results and recommended 1 to 8 minutes of application time.9,16,20,35 In the present study, 1 minute of application time was selected to obtain an appropriate and adequate topical anesthesia as suggested by ADA, FDA, and previous studies.29,30,33,34,36

In this study, the labial side of maxillary canines was selected for administration of local anesthesia since this site is one of the most painful injection sites.27,37 Furthermore, it was possible to conduct bilateral injections because of lack of nerve anastomosis with the other side in this region.38

This study was carried out in a split-mouth manner in order to eliminate confounding factors. A study by Lesaffre et al39 confirmed the advantages and importance of split-mouth design studies in oral health research. The split-mouth design is a popular design in oral health research. In the most common split-mouth study, each of the two treatments are randomly assigned to either the right or left halves of the dentition. The main benefit of the design is that it eliminates a lot of interindividual variability from the estimates of the treatment effect.39

Based on the results of present study, use of 5% EMLA cream as a topical anesthetic agent reduced the pain of injection significantly, which was higher than that achieved with 20% benzocaine. Similar results were reported by Nayak and Sudha29 and Al-Melh and Andersson.40 Tulga and Mutlu15 reported conflicting results, which might be attributed to different types of injection and age groups.

In this study, comparison between EMLA and placebo demonstrated that pain during injection was significantly
lower with the use of EMLA in comparison to placebo, consistent with the results reported by Vickers and Punnia-Moorthy.\textsuperscript{5} Other studies indicating the superiority of EMLA over placebo in reducing pain during infiltration evaluated the effect of topical anesthesia in the palatal region.\textsuperscript{18,23}

The results of the present study showed that application of local pressure to the buccal mucosa before administration of anesthesia reduced pain during injection, but the difference from the controls was not significant. The results were consistent with those of a study by Hutchins et al\textsuperscript{30} and Wiswall et al.\textsuperscript{31} In addition, the results showed no significant differences between the application of local pressure and topical use of EMLA.

One of the limitations of this study was the difficulty of topical application of EMLA cream, which might be attributed to its low viscosity and high pH, resulting in difficulty in its localization at the injection site. Nayak and Sudha\textsuperscript{26} also reported the same handling problems of EMLA cream. To overcome this problem, Svensson and Petersen\textsuperscript{18} recommended the use of orahesive bandages. However, Tulga and Mutlu\textsuperscript{15} reported some problems with sticking these bandages on to the mucosa.

Another point is that some authors reported concerns about the toxic effects of EMLA when used on oral mucosa,\textsuperscript{13,15} which could be attributed to large areas of nonkeratinized and the rich blood supply of underlying tissues in the oral mucosa.\textsuperscript{13} However, Vickers et al\textsuperscript{10} showed that 30 minutes of application of 5% EMLA cream did not induce any adverse reactions.

Despite the technical problems and limitations of this study, the superiority of EMLA over placebo and benzocaine in this study might be attributed to high pH of EMLA. Setnikar\textsuperscript{41} reported that increasing the pH increases the potency of the topical anesthetic agent. Moreover, a combination of two drugs in a single agent might have resulted in the increased efficacy.\textsuperscript{42} In addition, we concluded that application of local pressure, a simple method with no need for any materials or equipments, yielded no significantly different results in comparison to topical EMLA.

Future studies are suggested to evaluate and compare the effect of other topical anesthetic agents and other methods, such as precooling the injection site on pain during infiltration injection.

**CONCLUSION**

Based on the results of this randomized clinical trial, 5% EMLA cream as a topical anesthetic agent was more effective than 20% benzocaine in reducing pain during infiltration injection for maxillary canine teeth. However, it was not significantly different from the application of local pressure.

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**REFERENCES**


