



## 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

<sup>1</sup>Amin S Milani, <sup>2</sup>Vahid Zand, <sup>3</sup>Amir A Abdollahi, <sup>4</sup>Mohammad Froughreyhani, <sup>5</sup>Parvin Zakeri-Milani  
<sup>6</sup>Mohammad A Jafarabadi

### 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.

**How to cite this article:** Milani AS, Zand V, Abdollahi AA, Froughreyhani M, Zakeri-Milani P, Jafarabadi MA. 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. *J Contemp Dent Pract* 2016;17(7):592-596.

**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,<sup>1-3</sup> 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.<sup>4</sup> 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.<sup>5</sup>

<sup>1,2,4</sup>Dental and Periodontal Research Center, Faculty of Dentistry Tabriz University of Medical Sciences, Tabriz, Islamic Republic of Iran

<sup>3</sup>Dental and Periodontal Research Center, Department of Endodontics, Student Research Committee, Faculty of Dentistry, Tabriz University of Medical Sciences, Tabriz, Islamic Republic of Iran

<sup>5</sup>Department of Pharmaceutics, Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Islamic Republic of Iran

<sup>6</sup>Department of Biostatistics, Department of Statistics and Epidemiology, Faculty of Health and Nutrition, Tabriz University of Medical Sciences, Tabriz, Islamic Republic of Iran

**Corresponding Author:** Amir Ardan Abdollahi, Postgraduate Student, Dental and Periodontal Research Center, Department of Endodontics, Student Research Committee, Faculty of Dentistry, Tabriz University of Medical Sciences, Tabriz Islamic Republic of Iran, Phone: +989144091317, e-mail: ardan\_2000a@yahoo.com

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.<sup>6,7</sup> Lidocaine-prilocaine was first reported for dermal use in 1980.<sup>8</sup> In addition, its mucosal application was first presented by Holst and Evers.<sup>9</sup> Lidocaine-prilocaine has been investigated in dental procedures, including anesthesia of buccal mucosa for restorative procedures,<sup>10</sup> periodontal anesthesia before procedures, such as periodontal probing,<sup>11</sup> scaling and root planning,<sup>12</sup> oral mucosa anesthesia before removing maxillary and mandibular appliances,<sup>13</sup> and reduction of pain and discomfort during rubber dam placement.<sup>14</sup> Studies have reported some concerns about the toxic effects of this topical anesthetic agent on oral mucosa.<sup>13,15</sup> Also, low viscosity and high pH are other disadvantages of EMLA.<sup>10</sup>

Studies have reported conflicting results about the mucosal use of EMLA.<sup>5,15-25</sup> Nayak and Sudha<sup>26</sup> concluded that 5% EMLA cream was superior in pain reduction during buccal infiltration compared to benzocaine and lignocaine. However, Tulga and Mutlu<sup>15</sup> 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.<sup>15,27</sup>

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,<sup>28</sup> 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.<sup>28,29</sup>

The aim of this split-mouth 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 (PARKELL, 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](http://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 ge (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.<sup>26</sup> 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 pharmaceuticals. 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 (Darupakhsh, 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.<sup>30</sup>

**Statistical Analysis**

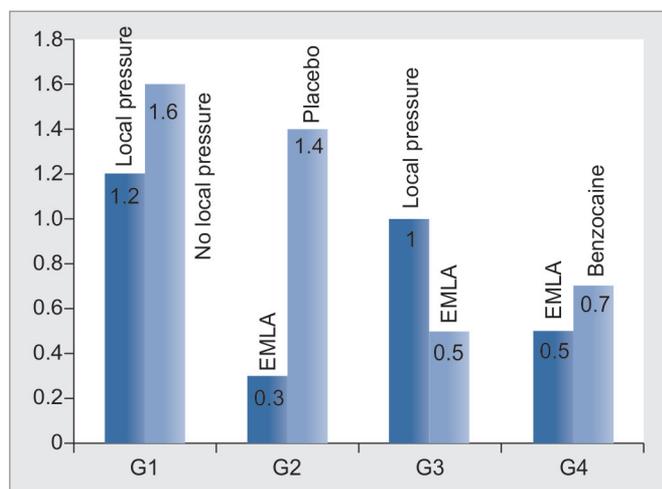
Statistical analysis was performed using statistical packages for the Social Science (SPSS) 20 (IBM, USA). Wilcoxon test was used for the analysis of data. Pairwise comparisons were made using the McNemar test. Statistical significance was set at  $p < 0.05$ .

**RESULTS**

A total of 140 volunteers, 68 males and 72 females, with an average age of  $33 \pm 2.6$  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

Groups	Gender		Mean age
	Male	Female	
1	19	16	$34 \pm 2.4$
2	18	17	$33 \pm 4.3$
3	15	17	$32 \pm 9.4$
4	16	22	$34 \pm 6.2$



**Graph 1:** The pain of the study groups (G1, G2, G3, and G4) based on median values

**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.<sup>7</sup> In addition, a number of investigations have studied EMLA intraorally with promising results.<sup>10-14</sup>

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.<sup>29,31</sup>

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 dentistry<sup>32</sup> and has been evaluated in several studies.<sup>17,29,33,34</sup>

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.<sup>9,16,20,35</sup> 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.<sup>29,30,33,34,36</sup>

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.<sup>27,37</sup> Furthermore, it was possible to conduct bilateral injections because of lack of nerve anastomosis with the other side in this region.<sup>38</sup>

This study was carried out in a split-mouth manner in order to eliminate confounding factors. A study by Lesaffre et al<sup>39</sup> 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.<sup>39</sup>

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 Sudha<sup>26</sup> and Al-Melh and Andersson.<sup>40</sup> Tulga and Mutlu<sup>15</sup> 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.<sup>5</sup> Other studies indicating the superiority of EMLA over placebo in reducing pain during infiltration evaluated the effect of topical anesthesia in the palatal region.<sup>18,23</sup>

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 studies by Hutchins et al<sup>29</sup> and Wiswall et al.<sup>31</sup> 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<sup>26</sup> also reported the same handling problems of EMLA cream. To overcome this problem, Svensson and Petersen<sup>18</sup> recommended the use of orahesive bandages. However, Tulga and Mutlu<sup>15</sup> 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,<sup>13,15</sup> which could be attributed to large areas of nonkeratinized and the rich blood supply of underlying tissues in the oral mucosa.<sup>13</sup> However, Vickers et al<sup>10</sup> 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<sup>41</sup> 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.<sup>42</sup> 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.

## ACKNOWLEDGMENTS

Authors would like to thank the Research Vice Chancellor and Dental and Periodontal Research Center of Tabriz University of Medical Sciences, Tabriz, Islamic Republic of Iran.

## REFERENCES

1. Milgrom P, Coldwell SE, Getz T, Weinstein P, Ramsay DS. Four dimensions of fear of dental injections. *J Am Dent Assoc* 1997 Jun;128(6):756-766.
2. Milgrom P, Fiset L, Melnick S, Weinstein P. The prevalence and practice management consequences of dental fear in a major US city. *J Am Dent Assoc* 1988 May;116(6):641-647.
3. Ram D, Hermida LB, Peretz B. A comparison of warmed and room-temperature anesthetic for local anesthesia in children. *Pediatr Dent* 2002 Jul-Aug;24(4):333-336.
4. Meechan JG, Howlett PC, Smith BD. Factors influencing the discomfort of intraoral needle penetration. *Anesth Prog* 2005 Fall;52(3):91-94.
5. Vickers ER, Punnia-Moorthy A. A clinical evaluation of three topical anaesthetic agents. *Aust Dent J* 1992 Aug;37(4):267-270.
6. Eidelman A, Weiss JM, Lau J, Carr DB. Topical anesthetics for dermal instrumentation: a systematic review of randomized, controlled trials. *Ann Emerg Med* 2005 Oct;46(4):343-351.
7. Friedman PM, Mafong EA, Friedman ES, Geronemus RG. Topical anesthetics update: EMLA and beyond. *Dermatol Surg* 2001 Dec;27(12):1019-1026.
8. Juhlin L, Evers H, Broberg F. A lidocaine-prilocaine cream for superficial skin surgery and painful lesions. *Acta Derm Venereol* 1980;60(6):544-546.
9. Holst A, Evers H. Experimental studies of new topical anaesthetics on the oral mucosa. *Swed Dent J* 1985;9(5):185-191.
10. Vickers ER, Marzbani N, Gerzina TM, McLean C, Punnia-Moorthy A, Mather L. Pharmacokinetics of EMLA cream 5% application to oral mucosa. *Anesth Prog* 1997 Winter;44(1):32-37.
11. Donaldson D, Meechan JG. A comparison of the effects of EMLA cream and topical 5% lidocaine on discomfort during gingival probing. *Anesth Prog* 1995;42(1):7-10.
12. Pandit N, Gupta R, Chandoke U, Gugnani S. Comparative evaluation of topical and electronic anesthesia during scaling and root planing. *J Periodontol* 2010 Jul;81(7):1035-1040.
13. Bernardi M, Secco F, Benech A. Anesthetic efficacy of an eutectic mixture of lidocaine and prilocaine (EMLA) on the oral mucosa: prospective double-blind study with a placebo. *Minerva Stomatol* 1999 Jan-Feb;48(1-2):39-43.
14. Lim S, Julliard K. Evaluating the efficacy of EMLA topical anesthetic in sealant placement with rubber dam. *Pediatr Dent* 2004 Nov-Dec;26(6):497-500.
15. Tulga F, Mutlu Z. Four types of topical anaesthetic agents: evaluation of clinical effectiveness. *J Clin Pediatr Dent* 1999 Spring;23(3):217-220.
16. Haasio J, Jokinen T, Numminen M, Rosenberg PH. Topical anaesthesia of gingival mucosa by 5% eutectic mixture of lignocaine and prilocaine or by 10% lignocaine spray. *Br J Oral Maxillofac Surg* 1990 Apr;28(2):99-101.
17. Rosivack RG, Koenigsberg SR, Maxwell KC. An analysis of the effectiveness of two topical anesthetics. *Anesth Prog* 1990 Nov-Dec;37(6):290-292.

18. Svensson P, Petersen JK. Anesthetic effect of EMLA occluded with Orahesive oral bandages on oral mucosa. A placebo-controlled study. *Anesth Prog* 1992;39(3):79-82.
19. Pere P, Iizuka T, Rosenberg PH, Lindqvist C. Topical application of 5% eutectic mixture of lignocaine and prilocaine (EMLA) before removal of arch bars. *Br J Oral Maxillofac Surg* 1992 Jun;30(3):153-156.
20. Vickers ER, Punnia-Moorthy A. Pulpal anesthesia from an application of a eutectic topical anesthetic. *Quintessence Int* 1993 Aug;24(8):547-551.
21. Meechan JG, Donaldson D. The intraoral use of EMLA cream in children: a clinical investigation. *ASDC J Dent Child* 1994 Jul-Aug;61(4):260-262.
22. Svensson P, Petersen JK, Svensson H. Efficacy of a topical anesthetic on pain and unpleasantness during scaling of gingival pockets. *Anesth Prog* 1994;41(2):35-39.
23. Meechan JG, Winter RA. A comparison of topical anaesthesia and electronic nerve stimulation for reducing the pain of intra-oral injections. *Br Dent J* 1996 Nov 9;181(9):333-335.
24. Meechan JG, Thomason JM. A comparison of 2 topical anesthetics on the discomfort of intraligamentary injections: a double-blind, split-mouth volunteer clinical trial. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1999 Mar;87(3):362-365.
25. Roghani S, Duperon DF, Barcohana N. Evaluating the efficacy of commonly used topical anesthetics. *Pediatr Dent* 1999 May-Jun;21(3):197-200.
26. Nayak R, Sudha P. Evaluation of three topical anaesthetic agents against pain: a clinical study. *Indian J Dent Res* 2006 Oct-Dec;17(4):155-160.
27. Nusstein JM, Beck M. Effectiveness of 20% benzocaine as a topical anesthetic for intraoral injections. *Anesth Prog* 2003;50(4):159-163.
28. Melzack R, Wall PD. Pain mechanisms: a new theory. *Science* 1965 Nov 19;150(3699):971-979.
29. Hutchins HS Jr, Young FA, Lackland DT, Fishburne CP. The effectiveness of topical anesthesia and vibration in alleviating the pain of oral injections. *Anesth Prog* 1997 Summer;44(3):87-89.
30. Parirokh M, Sadeghi AS, Nakhaee N, Pardakhty A, Abbott PV, Yosefi MH. Effect of topical anesthesia on pain during infiltration injection and success of anesthesia for maxillary central incisors. *J Endod* 2012 Dec;38(12):1553-1556.
31. Wiswall AT, Bowles WR, Lunos S, McClanahan SB, Harris S. Palatal anesthesia: comparison of four techniques for decreasing injection discomfort. *Northwest Dent* 2014 Jul-Aug;93(4):25-29.
32. Meechan JG. Intraoral topical anesthesia. *Periodontol* 2000 2008;46:56-79.
33. Drum M, Reader A, Beck M. Long buccal nerve block injection pain in patients with irreversible pulpitis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2011 Jul;112(1):e51-e54.
34. Fukayama H, Suzuki N, Umino M. Comparison of topical anesthesia of 20% benzocaine and 60% lidocaine gel. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2002 Aug;94(2):157-161.
35. Meechan JG, Welbury RR. Oral surgery for children: 2. Anaesthesia and sedation. *Dent Update* 1993 Jun;20(5):206-207, 209-212.
36. Rosa AL, Sverzut CE, Xavier SP, Lavrador MA. Clinical effectiveness of lidocaine and benzocaine for topical anesthesia. *Anesth Prog* 1999 Summer;46(3):97-99.
37. Gill CJ, Orr DL 2nd. A double-blind crossover comparison of topical anesthetics. *J Am Dent Assoc* 1979 Feb;98(2):213-214.
38. Yonchak T, Reader A, Beck M, Clark K, Meyers WJ. Anesthetic efficacy of infiltrations in mandibular anterior teeth. *Anesth Prog* 2001 Spring;48(2):55-60.
39. Lesaffre E, Philstrom B, Needleman I, Worthington H. The design and analysis of split-mouth studies: what statisticians and clinicians should know. *Stat Med* 2009 Dec 10;28(28):3470-3482.
40. Al-Melh MA, Andersson L. Comparison of topical anesthetics (EMLA/Oraqix vs. benzocaine) on pain experienced during palatal needle injection. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2007 May;103(5):e16-e20.
41. Setnikar I. Ionization of bases with limited solubility. Investigation of substances with local anesthetic activity. *J Pharm Sci* 1966 Nov;55(11):1190-1195.
42. Adriani J, Arens J, Authement E, Zepernick R. Clinical effectiveness and usefulness of topical anesthetics. *Postgrad Med* 1963 Mar;33:269-276.