Success of Pulpal Anesthesia Following Buccal Infiltration of the Maxillary First Molar With 1.8 mL and 3.6 mL of 4% Articaine With 1:100,000 Epinephrine: A Prospective, Randomized Crossover Study

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Objective: The purpose of this prospective, randomized crossover study was to compare the peak incidence of success, onset, and incidence over time of pulpal anesthesia in maxillary first molars following a buccal infiltration of 1.8 mL or 3.6 mL of 4% articaine with 1:100 000 epinephrine.

Methods: A total of 118 adults received 1.8 mL or 3.6 mL of 4% articaine with 1:100 000 epinephrine via buccal infiltration of the maxillary first molar at 2 separate appointments. Electric pulp testing (EPT) of the maxillary first molar was performed over 68 minutes.

Results: There was no significant difference in the peak incidence of anesthetic success (85% and 92%, respectively) in the maxillary first molar between 1.8 mL and 3.6 mL. The difference in onset times (4.5 min for 1.8 mL vs 4.4 min for 3.6 mL) was not statistically significant. However, the 3.6-mL volume did produce a significantly higher incidence of pulpal anesthesia from minutes 48 to 68 compared with the 1.8-mL volume.

Conclusion: There was no significant difference in peak incidence or onset of pulpal anesthesia in the maxillary first molar between 1.8 mL and 3.6 mL of articaine with epinephrine. The incidence of pulpal anesthesia was significantly higher with 3.6 mL of articaine at 48 minutes and beyond, but neither volume provided complete pulpal anesthesia for all subjects that lasted at least 60 minutes.

Key Words: Maxillary anesthesia; Articaine; Lidocaine; Infiltration; Pulpal anesthesia.

Articaine differs from other amide local anesthetics because of a thiophene ring and an intramolecular hydrogen bond, which may enhance its diffusion through membranes and connective tissue.[1] Several studies have discussed the clinical increase in the success of articaine. Mandibular first molar buccal infiltrations of articaine were more successful than when lidocaine was used.[2,3] One study used 4% concentrations of articaine, lidocaine, and prilocaine for mandibular buccal infiltrations and found that 4% articaine performed the best for pulpal anesthesia.[4] The molecular structure of articaine is perhaps more important than the concentration,[4] although authors of additional studies may want to explore this association further.

Articaine has been compared to lidocaine in several studies.[2–20] In asymptomatic subjects, no significant difference in success was found between articaine and lidocaine in the maxillary first molar.[5,6] In 2 systematic reviews, Liew et al.[7] and Brandt et al.[8] found that articaine formulations achieved higher success when compared with lidocaine formulations for infiltrations.

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In patients presenting with irreversible pulpitis, equivalent success (no or mild pain upon access or instrumentation) was found between articaine and lidocaine formulations.[9–17] Although only a small number of patients were sampled, one study found that articaine was better than lidocaine.[18] Systematic reviews by Nagendrababu et al[19] and Miglani et al[20] found that articaine was better than lidocaine for patients presenting with irreversible pulpitis.

Studies of maxillary anesthesia have determined that some subjects do not achieve pulpal anesthesia (defined as electric pulp testing [EPT] readings of 80) in the maxillary first molar.[5,21–26] The incidence of failed pulpal anesthesia was approximately 13%. Specifically, Evans et al[5] found a 22% failure rate (no 80 EPT readings) using 1.8 mL of 4% articaine with 1:100 000 epinephrine for infiltration of the maxillary first molar. Because previous studies on articaine have demonstrated higher success rates, the current study evaluates whether a 3.6-mL volume of articaine would result in lower failure rates.

In addition, maxillary first molar anesthesia with 1.8 mL of 2% lidocaine or 4% articaine, each with 1:100 000 epinephrine, failed to provide pulpal anesthesia for 60 minutes.[5,21–26] Increasing the volume of articaine to 3.6 mL may increase the duration of pulpal anesthesia.

No study has been performed to compare the effects of using an increased volume (1.8 mL vs 3.6 mL) of articaine for maxillary first molar local anesthesia in asymptomatic subjects. Therefore, the purpose of this prospective, randomized crossover study was to compare the peak incidence of success, onset, and incidence of pulpal anesthesia from 2 to 68 minutes in maxillary first molars following a buccal infiltration of 1.8 mL or 3.6 mL of 4% articaine with 1:100 000 epinephrine.

METHODS AND MATERIALS

Asymptomatic adult subjects in good health as determined by a written health history and oral questioning were recruited for participation in this study. Criteria for inclusion were adults 18 to 65 years of age and good health (American Society of Anesthesiologists [ASA] physical status classification of I or II). Exclusion criteria consisted of allergy to local anesthetics or epinephrine, history of significant medical comorbidities (ASA physical status classification $\geq$III), recent use of central nervous system depressants (including alcohol or any analgesic medications, tranquilizers, sedatives, or hypnotics), pregnant or lactating patients, or the inability to give informed consent. The Human Subjects Review Committee approved this study. Written informed consent, HIPAA authorization, and medical history were obtained from each subject. All experimental procedures followed the Centers for Disease Control and Prevention.

Before the subjects were brought to the treatment area, a medical questionnaire regarding COVID-19 symptoms was completed. Subjects also had their temperatures checked, and only those reporting no symptoms and not demonstrating a fever participated at that testing appointment. Subjects who reported symptoms, demonstrated a fever, or reported a recent positive COVID-19 test were sent home and advised to contact their primary care physician for follow-up. This evaluation occurred prior to each testing appointment. Subjects who were sent home were rescheduled for future appointments once their negative COVID-19 status was confirmed.

Subjects randomly received 2 volumes of maxillary buccal infiltrations at 2 appointments spaced at least 2 weeks apart. Prior to the first study appointment, each subject was randomly assigned a 6-digit number from a random number table (www.random.org) which determined the order of the anesthetic volumes administered and the injection side (right or left). At the first appointment, each subject received a buccal maxillary infiltration of either 1.8 mL or 3.6 mL of 4% articaine (Septocaine; Septodont, Inc) with 1:100 000 epinephrine. Whichever volume was rendered at the first appointment, the subject was administered the other in the same site as the first injection during the second appointment at least 2 weeks later. All injections were administered by the principal investigator (A.W.). Clinical examination was performed first to ensure all test teeth were free of caries and periodontal disease, although single occlusal restorations were permitted. A dental history was also taken to ensure there was no history of orthodontic treatment or trauma to the test teeth.

Prior to each appointment, the volume of anesthetic was premeasured by the investigator to provide either a 1.8-mL or 3.6-mL volume. The appropriate volume was drawn from anesthetic cartridges into a sterile Luer-Loc 5-mL syringe. All cartridges were inspected to ensure the expiration dates had not been exceeded. The syringe was preloaded prior to the subject arriving and covered with a sterile napkin so that it was not visible to the subject.

Prior to the injection, pulp testing of the maxillary first molar and control contralateral canine was performed with an EPT device (Vitality Scanner 2006, Analytic Technology) at each appointment to ensure vitality of the test tooth and obtain baseline pulp test readings. The testing cycle was performed twice prior to any injection.

The injections were administered as follows. All patients were placed in a supine position. A 20%

benzocaine topical anesthetic (Patterson Brand Dental Supply, Inc) was placed for 1 minute at the injection site via cotton swab. Either 1.8 mL or 3.6 mL of 4% articaine with 1:100 000 epinephrine was administered as a standard buccal infiltration of the maxillary first molar using the sterile syringe and a 27-gauge short needle. The needle was gently inserted into the alveolar mucosa to a depth of 2 to 3 mm and then advanced to a depth approximating the apices maxillary buccal roots. The operator deposited the 1.8-mL volume over 60 seconds, and the needle was kept in the mucosa for an additional 30 seconds. For the 3.6-mL volume, the solution was deposited over 90 seconds. A computer timer (https://www.timeanddate.com/stopwatch/) was used to record the time of injection and the postinjection times.

All pulp testing was performed in the same manner. The teeth were isolated with cotton rolls and dried with 2- × 2-inch cotton gauze. A small amount of toothpaste (Crest Gel, Procter & Gamble Co) was placed on the EPT electrode tip to aid in electrical pulse conduction to the teeth. The patient held the ground wire in his or her hand during the pulp testing. The electrode was placed firmly on sound enamel in the middle third of the buccal surface and not on restorations, enamel supported by restorations, or exposed dentin. The testing of each tooth commenced upon contact of the electrode to the tooth and ended when the subject raised his or her hand to indicate an initial sensation in the tooth. The value on the EPT digital readout was recorded. If the subject did not feel a sensation and the maximum value of 80 was reached, the testing was stopped and a value of 80 was recorded.

At 2 minutes following completion of the infiltration, the first molar was pulp tested. At 3 minutes, the control canine was tested. This cycle of pulp testing was then repeated, and at every fourth cycle, the control tooth (the mandibular canine) was tested with the EPT ground wire disconnected to test subject reliability. All testing ended at 68 minutes postinjection. The EPT testing cycle was set to 25 seconds, increasing from a reading of 0 to 80 and allowing for testing to be completed for each tooth and isolation of the next tooth.

Pulpal anesthesia was considered successful when an 80 EPT reading was achieved. However, pulpal anesthesia varied over time, so we determined the peak incidence of anesthetic success (Figure). The onset time was recorded when the first of 2 consecutive 80/80 readings were obtained. These values were then averaged for the 118 subjects. We also evaluated the incidence of pulpal anesthesia from 2 to 68 minutes.

Statistical Analysis

Comparisons between the anesthetic volumes for the highest recorded anesthetic success rate, onset, and incidence of pulpal anesthesia (percentage of 80 readings) were analyzed nonparametrically using McNemar's chi-squared tests with continuity correction.

An a priori power analysis was performed to calculate the required number of subjects. With a nondirectional alpha risk of .05, a power of .80, and assuming a total proportion of discordant pairs of 0.5, a sample size of 118 subjects was calculated to demonstrate a difference of ±18 percentage points in anesthetic success.[22]

RESULTS

A total of 118 subjects participated in this study with an average age of 27 years, ranging from 20 to 44 years of age. Sixty-six subjects were female, and 52 were male.

The percentage of patients who demonstrated anesthetic success (EPT score of 80 indicating pulpal anesthesia of the maxillary first molar) is presented in the Figure. The highest incidence of anesthetic success occurred at 14 and 18 minutes (92%) for the 3.6-mL volume and at 14 minutes (85%) for the 1.8-mL volume (Figure). There was no significant difference between 1.8 mL and 3.6 mL regarding the highest anesthetic success rates observed.

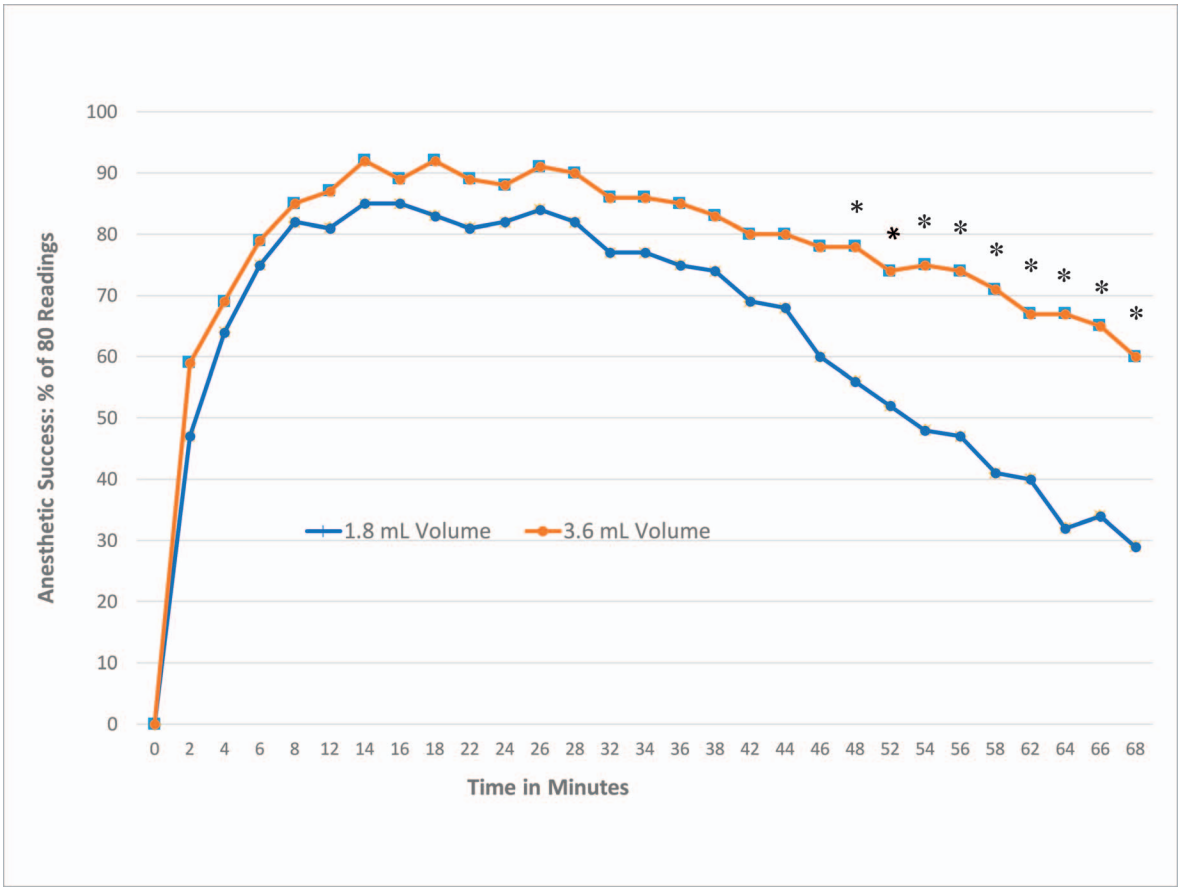
The difference in onset times (4.5 minutes for 1.8 mL and 4.4 minutes for 3.6 mL) for maxillary first molar pulpal anesthesia was not statistically significant ($P = .467$).

There was no statistically significant difference in the incidence of pulpal anesthesia between 1.8 mL and 3.6 mL until minute 48. The decline in the incidence of pulpal anesthesia was significantly greater for the 1.8-mL volume from minutes 48 to 68 ($P < .05$).

DISCUSSION

Dreven et al[27] and Certosimo and Archer[28] clinically demonstrated that a lack of a patient response to EPT ensured pulpal anesthesia in asymptomatic vital teeth. In other words, there was no pain during the clinical restorative procedure if an EPT reading of 80 out of 80 (the maximum reading) was achieved before the procedure. Certosimo and Archer[28] also demonstrated that patients who had less than the maximum EPT reading (<80/80) experienced pain during operative procedures. Therefore, testing a tooth with EPT prior to a dental procedure in asymptomatic vital teeth should provide a reliable indication of pulpal anesthesia.

Figure. Percentage of Subjects Obtaining Pulpal Anesthesia of the Maxillary First Molar for the 2 Anesthetic Volumes Over Time.



The incidence of successful pulpal anesthesia as determined by the lack of electric pulp testing response at the maximum setting (overall percentage of 80 readings) at each postinjection time interval for the maxillary first molar using 1.8 mL and 3.6 mL of articaine with epinephrine.
* Statistically significant differences were shown from minutes 48 to 68.

Success rates (highest percentage of 80 EPT readings) of articaine and lidocaine in the maxillary first molars of asymptomatic subjects ranges from 78% to 87%.[5,21–26] In the current study, the 1.8-mL and 3.6-mL volumes of articaine had the highest success rates of 85% and 92%, respectively, which was not statistically different. Factors associated with a lack of 100% success are related to the following: tooth position in the maxillary arch[5,21–26] as lower success rates were reported when there was a greater distance from the palatal root to the buccal alveolus of the first molar,[14,17] and individual variations in subjects.[5,21–26]

The approximate onset of pulpal anesthesia of the first molar was around 4 to 5 minutes with no significant difference between the 2 articaine volumes used. Other studies have shown similar results.[5,21–26] Onset before 2 minutes was not recorded. Testing was started 2 minutes after completing the injection because that was the time necessary for isolating the tooth with cotton rolls, drying the tooth surface, setting up the pulp tester, and applying toothpaste to the electrode tip. Previous studies of maxillary first molar anesthesia using 1.8 mL of 2% lidocaine or 4% articaine, each with 1:100 000 epinephrine, have reported onset times of approximately 4.5 minutes, which are similar to this study.[21–26]

The incidence in pulpal anesthesia over time began to decline around 30 minutes (Figure). However, the greatest decline occurred around 45 minutes for both volumes. Previous studies[21–26] have also demonstrated that the greatest decline in pulpal anesthesia for the maxillary first molar was around 45 minutes. The 3.6-mL volume in the current study provided a significantly higher incidence in pulpal anesthesia from minutes 48 to 68. At 48 minutes, approximately 78% of the subjects had pulpal anesthesia, which steadily declined to 71% at 58 minutes. While improved with the 3.6-mL volume, neither 1.8 mL nor 3.6 mL provided pulpal anesthesia for all subjects for a full 60 minutes.

If a clinical procedure requires at least 60 minutes of pulpal anesthesia or the patient experiences pain during the later stage of a restorative procedure, reinjection around 45 minutes may be needed to provide profound anesthesia for the remainder of the appointment.[29,30] Two studies found that if another injection is administered as soon as anesthesia begins to decline, augmentation (an enhanced anesthetic effect) occurs.[29,30] Therefore, reinjection could be a clinical strategy to ensure adequate anesthesia in the maxilla for procedures lasting 60 minutes or longer.

As far as we know, only 1 study has evaluated different volumes of local anesthetic infiltrations on anesthetic success in the first molar of asymptomatic subjects. Mikesell et al[22] compared the degree of anesthesia obtained with 1.8 mL and 3.6 mL of 2% lidocaine with 1:100 000 epinephrine. The authors found there was no statistically significant difference between the 2 anesthetic volumes in terms of pulpal anesthetic success. However, the 3.6-mL volume of lidocaine did provide a statistically longer duration of pulpal anesthesia than the 1.8-mL volume did for the first molar, but it did not consistently extend pulpal anesthesia to a full 60 minutes. The results are similar to the current study.

A limitation of the current study is that it evaluated pulpal anesthesia, which has the most relevance to restorative dentistry. Surgical procedures and local anesthesia for symptomatic teeth may have different anesthesia requirements.[31]

CONCLUSION

There was no significant difference between 1.8 mL and 3.6 mL of 4% articaine with 1:100 000 epinephrine on the peak incidence (85% and 92%, respectively) of successful pulpal anesthesia of the maxillary first molar. Pulpal anesthesia onset time was also not significantly different. The incidence of pulpal anesthesia was significantly higher from minutes 48 to 68 for the 3.6-mL volume of articaine; however, neither volume provided pulpal anesthesia for a full 60 minutes for all subjects.

REFERENCES

1. Skjevik AA, Haug BE, Lygre H, Teigen K. Intramolecular hydrogen bonding in articaine can be related to superior bone tissue penetration: a molecular dynamics study. *Biophys Chem*. 2011;154(1):18–25.

2. Claffey E, Reader A, Nussyein J, Beck M, Weaver J. Anesthetic efficacy of articaine for inferior alveolar nerve blocks in patients with irreversible pulpitis. *J Endod*. 2004;30:568–571.

3. Robertson D, Nusstein J, Reader A, Beck M, McCartney M. The anesthetic efficacy of articaine in buccal infiltration of mandibular teeth. *J Am Dent Assoc*. 2007;138:1104–1112.

4. Nydegger B, Nusstein J, Reader A, Drum M, Beck M. Anesthetic comparisons of 4% concentrations of articaine, lidocaine, and prilocaine as primary buccal infiltrations of the mandibular first molar: a prospective randomized, double-blind study. *J Endod*. 2014;40:1912–1916.

5. Evans G, Nusstein J, Drum M, Reader A, Beck M. A prospective, randomized, double-blind comparison of articaine and lidocaine for maxillary infiltrations. *J Endod*. 2008;34:389–393.

6. Soysa NS, Soysa IB, Alles N. Efficacy of articaine vs lignocaine in maxillary and mandibular infiltration and block anesthesia in the dental treatments of adults: a systematic review and meta-analysis. *Investig Clin Dent*. 2019;10:e12404.

7. Liew AKC, Yeh Y-C, Abdullah D, Tu Y-K. Anesthetic efficacy in vital asymptomatic teeth using different local anesthetics: a systematic review with network meta-analysis. *Restor Dent Endod*. 2021;21:e41.

8. Brandt RG, Anderson PF, McDonald NJ, Sohn W, Peters MC. The pulpal anesthetic efficacy of articaine versus lidocaine in dentistry: a meta-analysis. *J Am Dent Assoc*. 2011;142:493–504.

9. Tortamano IP, Siviero M, Costa CG, Buscariolo IA, Armonia PL. A comparison of the anesthetic efficacy of articaine and lidocaine in patients with irreversible pulpitis. *J Endod*. 2009;35:165–168.

10. Sherman MG, Flax M, Namerow K, Murray PE. Anesthetic efficacy of the Gow-Gates injection and maxillary infiltration with articaine and lidocaine for irreversible pulpitis. *J Endod*. 2008;34:656–659.

11. Kanaa MD, Whitworth JM, Corbett IP, Meechan JG. Articaine and lidocaine mandibular buccal infiltration anesthesia: a prospective randomized double-blind cross-over study. *J Endod*. 2006;32(4):296–298.

12. Atasoy UO, Alacam T. Efficacy of single buccal infiltrations for maxillary first molars in patients with irreversible pulpitis: a randomized controlled clinical trial. *Int Endod J*. 2014;47:222–227.

13. Kung J, McDonagh M, Sedgley CM. Does articaine provide an advantage over lidocaine in patients with symptomatic irreversible pulpitis? A systematic review and meta-analysis. *J Endod*. 2015;41:1784–1794.

14. Askari ME, Parirokh M, Nakhaee N, Hosseini HR, Abbott PV. The effect of maxillary first molar root length on the success rate of buccal infiltration anesthesia. *J Endod*. 2016;42:1462–1466.

15. Hosseini HR, Parirokh M, Nakhaee N, Abbott PV, Samani S. Efficacy of articaine and lidocaine for buccal infiltration of first maxillary molars with symptomatic irreversible pulpitis: a randomized double-blinded clinical trial. *Iran Endod J*. 2016;11:79–84.

16. Syed GA, Mulay SA. Comparative evaluation of anesthetic efficacy of 4% articaine and 2% lidocaine for buccal infiltration in adult patients with irreversible pulpitis of

maxillary first molar: a prospective randomized study. *Contemp Clin Dent*. 2022;13:61–68.

17. Parirokh M, Kakooei S, Nakhaee N, Manochehrifar H, Abbott P. The effect of the anatomic variables on the success rate of anesthesia in maxillary molars with irreversible pulpitis. *J Endod*. 2022;48:707–713.

18. Srinivasan N, Kavitha M, Loganathan CS, Padmini G. Comparison of anesthetic efficacy of 4% articaine and 2% lidocaine for maxillary buccal infiltration in patients with irreversible pulpitis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2009;107:133–136.

19. Nagendrababu V, Duncan HF, Whitworth J, et al. Is articaine more effective than lidocaine in patients with irreversible pulpitis? An umbrella review. *Int Endod J*. 2020; 53:200–213.

20. Miglani S, Ansari I, Patro S, et al. Efficacy of 4% articaine *vs* 2% lidocaine in mandibular and maxillary block and infiltration anaesthesia in patients with irreversible pulpitis: a systematic review and meta-analysis. *PeerJ*. 2021; 24:e12214.

21. Gross R, McCartney M, Reader A, Beck M. A prospective, randomized, double-blind comparison of bupivacaine and lidocaine for maxillary infiltrations. *J Endod*. 2007; 33:1021–1024.

22. Mikesell A, McCartney M, Reader A, Beck M. Anesthetic efficacy of 1.8 mL and 3.6 mL of 2% lidocaine with 1:100,000 epinephrine for maxillary infiltration. *J Endod*. 2008;34:121–125.

23. Mason R, Drum M, Reader A, Nusstein J, Beck M. A prospective, randomized, double-blind comparison of 2% lidocaine with 1:100,000 epinephrine and 1:50,000 epinephrine and 3% mepivacaine for maxillary infiltrations. *J Endod*. 2009; 35:1173–1177.

24. Katz S, Drum M, Reader A, Nusstein J, Beck M. A prospective, randomized, double-blind comparison of 2% lidocaine with 1:100,000 epinephrine, 4% prilocaine with 1: 200,00 epinephrine and 4% prilocaine for maxillary infiltrations. *Anesth Prog*. 2010;57:45–51.

25. Lawaty I, Drum M, Reader A, Nusstein J. A prospective, randomized, double-blind comparison of 2% mepivacaine with 1:20,000 levonordefrin versus 2% lidocaine with 1:100,000 epinephrine for maxillary infiltrations. *Anesth Prog*. 2010;57:139–144.

26. Fowler S, Drum M, Reader A, Nusstein J, Beck M. Pulpal anesthesia of adjacent teeth following infiltration of 2% lidocaine with 1:100,000 epinephrine in the maxillary lateral incisor and first molar. *Anesth Prog*. 2019;66:14–19.

27. Dreven LJ, Reader A, Beck M, Meyers WJ, Weaver J. An evaluation of the electric pulp tester as a measure of analgesia in human vital teeth. *J Endod*. 1987;13:233–238.

28. Certosimo A, Archer R. A clinical evaluation of the electric pulp tester as an indicator of local anesthesia. *Oper Dent*. 1996;21:25–30.

29. Scott J, Drum M, Reader A, Nusstein J, Beck M. The efficacy of a repeated infiltration in prolonging duration of pulpal anesthesia in maxillary lateral incisors. *J Am Dent Assoc*. 2009;140:318–324.

30. Pabst L, Nusstein J, Drum M, Reader A, Beck M. The efficacy of a repeated buccal infiltration of articaine in prolonging duration of pulpal anesthesia in the mandibular first molar. *Anesth Prog*. 2009;56:128–134.

31. Reader A, Nusstein J, Drum M. *Successful Local Anesthesia for Restorative Dentistry and Endodontics*. 2nd ed. Quintessence Publishing; 2017:7, 165–212.