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

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The purpose of this prospective, randomized, double-blind crossover study was to compare the anesthetic efficacy of 2% mepivacaine with 1 : 20,000 levonordefrin versus 2% lidocaine with 1 : 100,000 epinephrine in maxillary central incisors and first molars. Sixty subjects randomly received, in a double-blind manner, maxillary central incisor and first molar infiltrations of 1.8 mL of 2% mepivacaine with 1 : 20,000 levonordefrin and 1.8 mL of 2% lidocaine with 1 : 100,000 epinephrine at 2 separate appointments spaced at least 1 week apart. The teeth were electric pulp tested in 2-minute cycles for a total of 60 minutes. Anesthetic success (obtaining 2 consecutive 80 readings with the electric pulp tester within 10 minutes) was not significantly different between 2% mepivacaine with 1 : 20,000 levonordefrin and 2% lidocaine with 1 : 100,000 epinephrine for the central incisor and first molar. However, neither anesthetic agent provided an hour of pulpal anesthesia.

Key Words: Lidocaine; Epinephrine; Mepivacaine; Levonordefrin; Infiltration; Maxillary.

Maxillary infiltration anesthesia is a common method to anesthetize maxillary teeth. A number of studies¹⁻⁵ have evaluated mepivacaine with epinephrine or levonordefrin in operative dentistry and for surgical procedures. However, electric pulp testing was not performed to evaluate pulpal anesthesia. Hinkley et al,⁶ in an experimental study of pulpal anesthesia, have shown that 2% mepivacaine with 1 : 20,000 levonordefrin is equivalent to 2% lidocaine with 1 : 100,000 epinephrine for an inferior alveolar nerve block. Because anesthesia may vary between

the maxilla and mandible, further research needs to be done to ensure the appropriate clinical use of 2% mepivacaine with 1 : 20,000 levonordefrin in maxillary teeth.

The purpose of this prospective, randomized, double-blind crossover study was to compare the anesthetic efficacy of 2% mepivacaine with 1 : 20,000 levonordefrin versus 2% lidocaine with 1 : 100,000 epinephrine in maxillary central incisors and first molars.

METHODS

Sixty adult subjects participated in this study. All subjects were in good health and were not taking any medication that would alter pain perception, as determined by a written health history and oral questioning.

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Exclusion criteria were as follows: younger than 18 or older than 65 years of age; allergies to local anesthetics or sulfites; pregnancy; history of significant medical conditions (American Society of Anesthesiologists classification II or higher); taking any medications that may affect anesthetic assessment (over-the-counter pain-relieving medications, narcotics, sedatives, or anti-anxiety or antidepressant medications); active sites of pathosis in area of injection; and inability to give informed consent. The Ohio State University Review Committee approved the study, and written informed consent was obtained from each subject.

Using a crossover design, 30 subjects received 2 maxillary central incisor infiltrations and 30 subjects received 2 maxillary first molar infiltrations at 2 separate appointments spaced at least 1 week apart. For each central incisor or first molar, the 2 infiltrations consisted of 1.8 mL of 2% mepivacaine with 1 : 20,000 levonordefrin and 1.8 mL of 2% lidocaine with 1 : 100,000 epinephrine.

With the crossover design, 60 infiltrations were administered for the central incisor and 60 infiltrations were administered for the first molar. Each subject served as his or her own control. Fifteen maxillary right central incisors and 15 maxillary left central incisors were used. Fifteen maxillary right first molars and 15 maxillary left first molars were used. The same side chosen for the first infiltration was used again for the second infiltration. The same tooth was used at the 2 visits for each anesthetic solution. The contralateral mandibular canine was used as the control to ensure that the pulp tester was operating properly and that the subject was responding appropriately. A visual and clinical examination was conducted to ensure that all teeth were free of caries, large restorations, crowns, and periodontal disease, and that none had a history of trauma or sensitivity.

Before the injections at both appointments, the experimental tooth and the contralateral canine (control) were tested 3 times with the electric pulp tester (Analytic Technology Corp, Redmond, Wash) to obtain baseline information. The teeth were isolated with cotton rolls and dried with an air syringe. Toothpaste was applied to the probe tip, which was placed in the middle third of the facial or buccal surface of the tooth being tested. The value at the initial sensation was recorded. The current rate was set at 25 seconds to increase from no output (0) to the maximum output (80). Trained personnel, who were blinded to the anesthetic solutions, administered all preinjection and postinjection tests.

Before the experiment, the 2 anesthetic solutions were randomly assigned 4-digit numbers from a random number table. Each subject was randomly assigned

to the right or left side infiltration grouping. The order of the anesthetic solutions was also randomly assigned to determine which solutions were to be administered at each appointment. Only the random numbers were recorded on the data collection sheets to help blind the experiment.

Under sterile conditions, the 2% mepivacaine cartridges with 1 : 20,000 levonordefrin (2% Carbocaine with Neo-Cobefrin, Cooke-Waite, Kodak, Rochester, NY) and the 2% lidocaine cartridges with 1 : 100,000 epinephrine (Xylocaine, Astra Pharmaceuticals Products Inc, Worcester, Mass) were masked with opaque labels. The corresponding 4-digit codes were written on each cartridge label. All anesthetic solutions were checked to ensure that the anesthetic solution had not expired.

A standard maxillary infiltration injection was administered with an aspirating syringe and a 27-gauge 1-in needle (Sherwood Medical Co, St Louis, Mo). The target site was centered over the root apex of the maxillary central incisor or between the mesiobuccal and distobuccal root apices of the maxillary first molar. The needle was gently placed into the alveolar mucosa with the bevel toward bone and advanced until the needle was estimated to be at or just superior to the apex of the central incisor or the apices of the first molar. The anesthetic formulation was deposited over a period of 1 minute. All infiltrations were given by the senior author (I.L.).

The depth of anesthesia was monitored with the electric pulp tester. At 1 minute after the infiltration injection, pulp test readings were obtained for the experimental tooth (first molar or central incisor) and the contralateral mandibular canine. The testing continued in 2-minute cycles for a total of 60 minutes. At every third cycle the control tooth was tested by an inactivated electric pulp tester to test the reliability of the subject. If a subject responded positively to an inactivated pulp tester then the subject was not reliable and could not be used in the study.

No response from the subject at the maximum output (80 reading) of the pulp tester was used as the criterion for pulpal anesthesia. Anesthesia was considered successful when 2 consecutive 80 readings were obtained with the pulp tester. With a nondirectional α risk of .05 and assuming a success rate of 50%, a sample size of 30 subjects was required to demonstrate a difference in anesthetic success of ± 30 percentage points with a power of 0.90. Anesthesia of short duration was defined as when the subject achieved 2 consecutive 80 readings, lost the 80 reading, and never regained it within the 60-minute period.

The data were analyzed statistically. Group comparisons between the mepivacaine and lidocaine formula-

Percentages and Number of Subjects Who Experienced Anesthetic Success and Short Duration of Anesthesia†

	2% Mepivacaine With 1 : 20,000 Levonordefrin	2% Lidocaine With 1 : 100,000 Epinephrine
Anesthetic success		
Central incisor*	87% (26/30)	87% (26/30)
First molar*	90% (27/30)	87% (26/30)
Short duration of anesthesia		
Central incisor*	38% (10/26)	42% (11/26)
First molar*	56% (15/27)	50% (13/26)

* There was no significant difference ($P > .05$) between the solutions.

† Failures were excluded from the calculation of short duration of anesthesia.

tions for anesthetic success, incidence of pulpal anesthesia (80 readings), and short duration of anesthesia were analyzed using multiple McNemar tests with P values adjusted using the step-down method of Holm. Comparisons were considered significant at $P < .05$.

RESULTS

For the central incisor, 15 men and 15 women ranging in age from 22 to 31 years, with an average age of 25 years, participated. For the first molar, 15 men and 15 women ranging in age from 21 to 29 years, with an average age of 24 years, participated.

The Table demonstrates the percentages of successful pulpal anesthesia for the test teeth and anesthetic solutions. The success rates ranged from 87 to 90%.

Figure 1. Incidence of maxillary central incisor pulpal anesthesia as determined by lack of response to electrical pulp testing at the maximum setting (percentage of 80 readings), at each postinjection time interval, for the 2 anesthetic formulations. There were no significant differences ($P < .05$) between the solutions.

Figure 2. Incidence of maxillary first molar pulpal anesthesia as determined by lack of response to electrical pulp testing at the maximum setting (percentage of 80 readings), at each postinjection time interval, for the 2 anesthetic formulations. There were no significant differences ($P < .05$) between the solutions.

There was no significant difference between the anesthetic formulations.

Anesthesia of short duration is presented in the Table. There was no significant difference between 2% mepivacaine with 1 : 20,000 levonordefrin and 2% lidocaine with 1 : 100,000 epinephrine for the central incisor and first molar.

The incidence of pulpal anesthesia (80 readings across time) for the 2 anesthetic solutions are presented in Figures 1 and 2. There were no significant differences between the anesthetic formulations.

DISCUSSION

We based our use of the electric pulp test reading of 80—signaling maximum output—as a criterion for pulpal anesthesia on the studies of Dreven et al⁷ and Certosimo and Archer.⁸ These studies^{7,8} showed that no patient response to an 80 reading ensured pulpal anesthesia in vital, asymptomatic teeth. Additionally, Certosimo and Archer⁸ demonstrated that electric pulp test readings of less than 80 resulted in pain during operative procedures in asymptomatic teeth. Therefore, using the electric pulp tester prior to beginning dental procedures on asymptomatic, vital teeth will provide the clinician a reliable indicator of pulpal anesthesia.

The success of the infiltration of 2% lidocaine with 1 : 100,000 epinephrine was 87% for the central incisor (Table). Various authors^{9–26} have evaluated success of maxillary infiltrations using the electric pulp tester. Generally, the results of these studies demonstrated successful anesthesia ranging from 62 to 100%. It is very difficult to compare the results of the previous studies to the current

study because the authors used different dosages of anesthetic agents and vasoconstrictors and evaluated different teeth. Nusstein et al,¹⁹ Gross et al,²¹ Mikesell et al,²² Evans et al,²³ Scott et al,²⁵ and Mason et al²⁶ used a similar methodology to the current study and demonstrated success rates of 85, 97, 97, 62, 95–100, and 100%, respectively, for the lateral incisor with an infiltration of 1.8 mL of 2% lidocaine with 1 : 100,000 epinephrine. Although we used a central incisor as the experimental tooth, the success rate was similar to that of the studies using the lateral incisor. A study comparing the anesthetic success rates of the central and lateral incisor would answer the question with regard to differences between the teeth.

The success rate for the first molar was 87% with 2% lidocaine with 1 : 100,000 epinephrine (Table). Gross et al,²¹ Mikesell et al,²² Evans et al,²³ and Mason et al²⁶ used a similar methodology to the current study and demonstrated an 82, 100, 72, and 97% success rate, respectively, for the first molar with an infiltration of 1.8 mL of 2% lidocaine with 1 : 100,000 epinephrine. The success rates for both the lateral incisor and the first molar in these studies^{21–23,26} show some variation, which may relate to population or operator differences. In general, the infiltration injection of 1.8 mL of 2% lidocaine with 1 : 100,000 epinephrine may not always be 100% successful because of the individual variations in response to the drug administered, operator differences, tooth position, and variations of anatomy.

The success of the infiltration of 2% mepivacaine with 1 : 20,000 levonordefrin was 87% in the central incisor and 90% in the first molar (Table). There was no significant difference between the lidocaine and mepivacaine formulations. Therefore, the 2 anesthetic formulations were similar for pulpal anesthesia in the central incisor and first molar. Because we studied a young adult population, the results of this study may not apply to children or the elderly.

Figure 1 demonstrates the decline of pulpal anesthesia over 60 minutes for the central incisor. For the 2% lidocaine with 1 : 100,000 epinephrine formulation, approximately 87% of the subjects had pulpal anesthesia at 30 minutes, 67% at 45 minutes, and 53% at 60 minutes. Nusstein et al,¹⁹ Gross et al,²¹ Mikesell et al,²² Evans et al,²³ Scott et al,²⁵ and Mason et al²⁶ also showed similar declining rates of pulpal anesthesia when using 1.8 mL of 2% lidocaine with 1 : 100,000 epinephrine. The 2% mepivacaine with 1 : 20,000 levonordefrin showed a similar pattern of pulpal anesthesia as the lidocaine formulation, with approximately 87% of the subjects having pulpal anesthesia at 30 minutes, 67% at 45 minutes, and only 43% at 60 minutes (Figure 1). Anesthesia of short duration occurred in 38–42% of the central incisors, with no

significant difference between the lidocaine and mepivacaine formulations. Therefore, the 2 formulations were similar for pulpal anesthesia in the central incisor. Mikesell et al²² demonstrated a statistically slower decline of pulpal anesthesia with a 3.6-mL volume of 2% lidocaine with 1 : 100,000 epinephrine over 60 minutes for the lateral incisor when compared to the 1.8-mL volume. Therefore, using a 3.6-mL volume of 2% lidocaine with 1 : 100,000 epinephrine will increase the duration of pulpal anesthesia but will not provide complete pulpal anesthesia for an hour. Mason et al²⁶ found that 1.8 mL of 2% lidocaine with 1 : 50,000 epinephrine maintained a significantly higher percentage of pulpal anesthesia from minute 37 through the 60th minute than 1.8 mL of 2% lidocaine with 1 : 100,000 epinephrine. The approximate percentage of subjects with pulpal anesthesia was 97% at 45 minutes and almost 80% at 60 minutes. Scott et al²⁵ found a repeated infiltration of 1.8 mL of 2% lidocaine with 1 : 100,000 epinephrine 30 minutes after an initial infiltration of the same dose of anesthetic significantly improved the duration of pulpal anesthesia from 37 minutes through 90 minutes in the maxillary lateral incisor. They found 90% of the subjects had pulpal anesthesia at 60 minutes for the repeated infiltration. If pulpal anesthesia is required for 60 minutes in the central incisor, an initial dose of 1.8 mL of 2% lidocaine with 1 : 50,000 epinephrine or a repeat infiltration at 30 minutes using 1.8 mL of 2% lidocaine with 1 : 100,000 epinephrine should both be reasonably effective. A future study could determine if duration would be prolonged using an initial infiltration of a 3.6-mL volume of 2% mepivacaine with 1 : 20,000 levonordefrin or by giving an additional 1.8 mL of 2% mepivacaine with 1 : 20,000 levonordefrin at 30 minutes.

For the first molar, pulpal anesthesia declined for both 2% lidocaine with 1 : 100,000 epinephrine and 2% mepivacaine with 1 : 20,000 levonordefrin (Figure 2). Gross et al,²¹ Mikesell et al,²² Evans et al,²³ and Mason et al²⁶ also showed a similar pattern of pulpal anesthesia of the first molar when using 1.8 mL of 2% lidocaine with 1 : 100,000 epinephrine. There was no significant difference in the incidence of pulpal anesthesia or anesthesia of short duration (incidence 50–56%) between the lidocaine and mepivacaine formulations (Figure 2, Table). Therefore, the 2 formulations are similar for pulpal anesthesia in the first molar. Anesthesia of short duration occurred between 50 and 56% of the time. Mikesell et al²² found an incidence of 50% using 1.8 mL of 2% lidocaine with 1 : 100,000 epinephrine. Mikesell et al²² also demonstrated that increasing the amount of lidocaine from 1.8 mL to 3.6 mL provided a longer duration of pulpal anesthesia after approximately 49 minutes for the first molar.

However, complete pulpal anesthesia was not obtained for 60 minutes. In the current study, pulpal anesthesia started to decline for the lidocaine and mepivacaine formulations after approximately 30 minutes (Figure 2). It is important to realize that if an hour of pulpal anesthesia is required for the first molar, 1.8 mL of 2% lidocaine with 1 : 100,000 epinephrine or 2% mepivacaine with 1 : 20,000 levonordefrin may not provide the necessary duration of pulpal anesthesia.

Concerning the vasoconstrictor agents, levonordefrin has 75% α activity and only 25% β activity, making it seemingly more attractive than epinephrine (50% α activity and 50% β activity)²⁷ because the pharmacology of the drug would indicate that it may produce less cardiac and central nervous system stimulation than epinephrine.²⁷ However, levonordefrin is marketed as a 1 : 20,000 concentration in dental cartridges,²⁷ which is 5 times the concentration of 1 : 100,000. Clinically, the higher concentration of levonordefrin makes it equipotent to epinephrine in clinical and systemic effects.^{6,28} Guglielmo et al²⁸ measured the heart rate (pulse rate) after the intraosseous injection of 1.8 mL of 2% mepivacaine with 1 : 20,000 levonordefrin and 1.8 mL of 2% lidocaine with 1 : 100,000 epinephrine. They demonstrated that both anesthetic formulations increased heart rate (mean increase of approximately 23–24 beats per minute from baseline) in 80% of the subjects, with no significant difference between the 2 anesthetic formulations. Because the Guglielmo et al²⁸ study found no difference in heart rate and the current study found no difference in anesthetic success, it would appear that 1 : 20,000 levonordefrin offers no clinical advantage over 1 : 100,000 epinephrine.

CONCLUSION

We concluded that anesthetic success was not significantly different between 2% mepivacaine with 1 : 20,000 levonordefrin and 2% lidocaine with 1 : 100,000 epinephrine for the maxillary central incisor and first molar. However, neither anesthetic agent provided an hour of pulpal anesthesia.

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