A Prospective, Randomized, Double-Blind Study of the Anesthetic Efficacy of Sodium Bicarbonate Buffered 2% Lidocaine With 1 : 100,000 Epinephrine in Inferior Alveolar Nerve Blocks

Michael Whitcomb, DDS, MS,* Melissa Drum, DDS, MS,† Al Reader, DDS, MS,‡
John Nusstein, DDS, MS,§ and Mike Beck, DDS, MA||

*Private Practice, Endodontics, Worthington, Ohio, †Assistant Professor, Division of Endodontics, ‡Professor and Program Director of Graduate Endodontics, Division of Endodontics, §Associate Professor and Chair, Division of Endodontics, ||Associate Emeritus Professor, Division of Oral Biology, Ohio State University, Columbus, Ohio

The authors, using a crossover design, randomly administered, in a double-blind manner, inferior alveolar nerve (IAN) blocks using a buffered 2% lidocaine with 1 : 100,000 epinephrine/sodium bicarbonate formulation and an unbuffered 2% lidocaine with 1 : 100,000 epinephrine formulation at 2 separate appointments spaced at least 1 week apart. An electric pulp tester was used in 4-minute cycles for 60 minutes to test for anesthesia of the first and second molars, premolars, and lateral and central incisors. Anesthesia was considered successful when 2 consecutive 80 readings were obtained within 15 minutes, and the 80 reading was continuously sustained for 60 minutes. For the buffered 2% lidocaine with 1 : 100,000 epinephrine/sodium bicarbonate formulation, successful pulpal anesthesia ranged from 10–71%. For the unbuffered 2% lidocaine with 1 : 100,000 epinephrine formulation, successful pulpal anesthesia ranged from 10–72%. No significant differences between the 2 anesthetic formulations were noted. The buffered lidocaine formulation did not statistically result in faster onset of pulpal anesthesia or less pain during injection than did the unbuffered lidocaine formulation. We concluded that buffering a 2% lidocaine with 1 : 100,000 epinephrine with sodium bicarbonate, as was formulated in the current study, did not statistically increase anesthetic success, provide faster onset, or result in less pain of injection when compared with unbuffered 2% lidocaine with 1 : 100,000 epinephrine for an IAN block.

Key Words: Buffered lidocaine; Sodium bicarbonate; Inferior alveolar nerve block; Lidocaine.

The inferior alveolar nerve (IAN) block is the most frequently used injection technique for achieving local anesthesia for mandibular restorative and surgical procedures. However, the IAN block does not always result in successful pulpal anesthesia.^{1–14} Failure rates of 7–75% have been reported in experimental studies.^{1–14} Therefore, it would be advantageous to

improve the success rate of the IAN block, perhaps by buffering the local anesthetic.

Galindo et al¹⁵ used pH-adjusted local anesthetic solutions (pH of 7.4) in epidurals, peripheral nerve blocks, and regional anesthesia. They found that higher-pH solutions established anesthesia of better quality. A number of authors^{16–19} have reported faster onset with pH-adjusted anesthetic solutions. Davies²⁰ reviewed the literature on buffering local anesthetics to decrease the pain of injection and found that buffering local anesthetics with sodium bicarbonate significantly reduced injection pain.

Received September 21, 2009; accepted December 21, 2009.

Address correspondence to Dr Melissa Drum, Assistant Professor, Division of Endodontics, Ohio State University; drum.13@osu.edu.

Anesth Prog 57:59–66 2010

© 2010 by the American Dental Society of Anesthesiology

ISSN 0003-3006/10

SSDI 0003-3006(10)

No studies have used a sodium bicarbonate–buffered lidocaine formulation for IAN blocks. The authors wished to determine whether a buffered lidocaine formulation would produce less pain during injection, provide faster onset of anesthesia, and produce more profound numbness.

The purpose of this prospective, randomized, double-blind, crossover study was to compare the degree of pulpal anesthesia obtained with 2% lidocaine with 1 : 100,000 epinephrine/sodium bicarbonate versus 2% lidocaine with 1 : 100,000 epinephrine in an IAN block. Investigators also studied the pain of injection.

MATERIALS AND METHODS

Forty adult subjects participated in this study. Subjects were in good health and were not taking any medications that would alter their perception of pain. 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, taking any medications that may affect anesthetic assessment, active sites of pathology in areas of injection, and inability to give informed consent. The Ohio State University Human Subjects Review Committee approved the study, and written informed consent was obtained from each subject.

The 40 blinded subjects randomly received 2 IAN blocks using 2% lidocaine with 1 : 100,000 epinephrine and 2% lidocaine with 1 : 100,000 epinephrine/0.17 mEq/mL sodium bicarbonate at 2 separate appointments spaced at least 1 week apart, in a crossover design. With the crossover design, 80 total IAN blocks were administered, and each subject served as his or her own control. Forty IAN blocks were administered on the right side, and 40 blocks were administered on the left side. The senior author (M.W.) performed all injections. The same side randomly chosen for the first IAN block was used again for the second IAN block. Test teeth chosen for this experiment were first and second molars, first and second premolars, and lateral and central incisors. The contralateral canine was used as the unanesthetized control to ensure that the pulp tester was operating properly, and that the subject was responding appropriately during each experimental portion of the study. Clinical examinations indicated that all teeth were free of caries, large restorations, and periodontal disease; none had histories of trauma or sensitivity.

Before the experiment was begun, the 2 anesthetic formulations were randomly assigned 5-digit numbers from a random number table. Each subject was randomly assigned to each of the 2 anesthetic formula-

tions to determine which anesthetic formulation was to be administered at each appointment. Only the random numbers were recorded on the data collection sheets to blind the experiment.

Under sterile conditions, the 2% lidocaine solution with 1 : 100,000 epinephrine was prepared by adding 0.1 mL of 1 : 1000 (1 mg/mL) epinephrine (American Reagents Laboratories, Shirley, NY), using a tuberculin syringe, to a 10-mL ampule of 2% lidocaine (Abbott Laboratories, North Chicago, Ill). This produced a concentration of 1 : 100,000 epinephrine. The ampule was inverted 20 times to mix the solution. With a sterile 5-mL Luer-Lok syringe (Sherwood Medical Co, St Louis, Mo), 3.6 mL of the 2% lidocaine with 1 : 100,000 epinephrine solution was drawn into the syringe. The lidocaine formulation with sodium bicarbonate was prepared as follows: 0.6 mL was drawn from a 50-mL vial of sodium bicarbonate (8.4% weight/volume, 50 mEq/50 mL, Abbott Laboratories), using a tuberculin syringe, and this amount was added to 3.0 mL of the 2% lidocaine with 1 : 100,000 epinephrine solution in a sterile 5-mL Luer-Lok syringe. This produced a final concentration of 0.17 mEq/mL of sodium bicarbonate. The syringe was inverted 5 times to mix the solution. No precipitate was present. Peterfreund et al²¹ found that no precipitate formed when a lidocaine solution was alkalized with sodium bicarbonate. Each syringe for both anesthetic formulations was covered with opaque tape, and the 5-digit random number was written on each syringe. All formulations were prepared within 1 hour of the appointment. All components and final solutions of the anesthetic formulations had their pH values determined with the use of a pH/millivolt meter (Orion Research Inc, Boston, Mass).

At the beginning of each appointment and before any injections were given, experimental teeth and control contralateral canine were tested 3 times with the pulp tester (Kerr; Analytic Technology Corp, Redmond, Wash) to record baseline vitality. After the tooth to be tested was isolated with cotton rolls and dried with gauze, toothpaste was applied to the probe tip, which then was placed midway between the gingival margin and the incisal or occlusal edge of the tooth. The current rate was set at 25 seconds to increase from no output (0) to maximum output (80). The number associated with the initial sensation was recorded. Trained research personnel performed all preinjection and postinjection tests.

Before nerve blocks were administered, each subject was instructed on how to rate the pain of needle insertion, needle placement, and solution deposition. The pain scale ranged from 0 to 3. Zero indicated no pain; 1 indicated mild pain—pain that was recognizable but

not discomforting; 2 indicated moderate pain—pain that was discomforting but bearable; and 3 indicated severe pain—pain that caused considerable discomfort and was difficult to bear.

A standard IAN block²² was administered with a 27-gauge 1 ¼-inch needle (Monoject; Sherwood Services, Mansfield, Mass) attached to the 5-mL Luer-Lok syringe equipped with an aspirating handle (Becton-Dickinson & Co, Rutherford, NJ). The needle was inserted 2–3 mm into the alveolar mucosa, and the subject was asked to rate the pain of needle insertion. The needle was slowly advanced, and 0.2 mL of the anesthetic formulation was deposited until the target site was reached. The subject then rated needle placement pain. After negative aspiration, the anesthetic solution was deposited over a period of 2 minutes. The subject rated the pain of solution deposition after needle withdrawal.

At 1 minute after completion of the IAN block, first and second molars were pulp tested; at 2 minutes, first and second premolars were tested; at 3 minutes, central and lateral incisors were tested; and at 4 minutes, the control canine was tested. This cycle of testing was repeated every 4 minutes for 60 minutes. At every fourth cycle, the control tooth—the contralateral canine—was tested by a pulp tester without batteries to test the reliability of the subject, that is, if subjects responded positively to an inactivated pulp tester, then they were not reliable and could not be used in the study. Every 5 minutes, subjects were questioned regarding subjective lip numbness. If the subject did not obtain any signs of subjective anesthesia within 15 minutes, the block was considered a failure, and the subject was dismissed and reappointed for 1 week later. Three of 80 injections (4%) resulted in missed blocks, and subjects were reappointed.

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 within 15 minutes and this reading was continuously sustained for 60 minutes. The onset of pulpal anesthesia was defined as the time of the first of 2 consecutive 80 readings.

Comparisons of anesthetic success, onset of pulpal anesthesia, and incidences of pulpal anesthesia (percentage of 80 readings across time) between the anesthetic formulations were analyzed with the use of Exact McNemar tests, which were adjusted using the step-down Bonferroni method of Holm. With a nondirectional alpha risk of 0.05 and an assumed anesthetic success rate of 55%, a sample size of 40 subjects was required to demonstrate a difference in anesthetic success of ± 25 percentage points with a power of 0.88.

Table 1. Percentages and Numbers of Subjects Who Experienced Anesthetic Success

Anesthetic Success	Anesthetic Formulation	
	2% Lidocaine With 1 : 100,000 Epinephrine	2% Lidocaine With 1 : 100,000 Epinephrine/Sodium Bicarbonate
Second molar	65% (26/40)	72% (29/40)*
First molar	58% (23/40)	48% (19/40)*
Second premolar	68% (27/40)	60% (24/40)*
First premolar†	71% (25/35)	66% (23/35)*
Lateral incisor	35% (14/40)	28% (11/40)*
Central incisor	10% (4/40)	10% (4/40)*

* No significant differences ($P > .05$) between the anesthetic formulations were noted.

† Some teeth were missing from 40 subjects as the result of extractions for orthodontic treatment.

Comparisons of injection pain were analyzed using the Wilcoxon matched-pairs signed ranks test, with P values adjusted using the step-down Bonferroni method of Holm. Comparisons were considered significant at $P < .05$.

RESULTS

Forty adult subjects—12 women and 28 men, aged 18 to 38 years, with an average age of 26 years—participated.

One hundred percent of the subjects used for data analysis had profound lip anesthesia with all IAN block injections. Rates of anesthetic success are presented in Table 1. For the 2% lidocaine with 1 : 100,000 epinephrine formulation, successful pulpal anesthesia ranged from 10–71%. The success rate for the 2% lidocaine with 1 : 100,000 epinephrine/sodium bicarbonate formulation ranged from 10–72%. No significant differences between the 2 anesthetic formulations were noted. Figures 1–6 present the incidence of pulpal anesthesia (80 readings). No significant differences between the 2 anesthetic formulations were noted.

Pain ratings for each injection phase are presented in Table 2. No significant differences between the 2 anesthetic formulations were noted. Onset of pulpal anesthesia is presented in Table 3. No significant differences between the 2 anesthetic formulations were noted. Only matched pairs of teeth that demonstrated anesthetic success were analyzed statistically for onset of pulpal anesthesia.

The pH values of components and final anesthetic formulations are presented in Table 4.

Figure 1. Incidence of second molar anesthesia as determined by lack of response to electric pulp testing at the maximum setting (percentage of 80/80s), at each postinjection time interval, for the 2 anesthetic formulations. No significant differences ($P > .05$) between the 2 anesthetic formulations were noted.

DISCUSSION

We based our use of the pulp test reading of 80—signaling maximum output—as a criterion for pulpal anesthesia on the studies of Dreven and colleagues²³ and Certosimo and Archer.²⁴ These studies^{23,24} showed that no patient response to an 80 reading ensured pulpal anesthesia in vital asymptomatic teeth. Additionally, Certosimo and Archer²⁴ showed that electric pulp test readings less than 80 resulted in pain during operative procedures in asymptomatic teeth. Therefore, using the electric pulp tester before beginning dental procedures on asymptomatic vital teeth will provide the clinician with a reliable indicator of

Figure 2. Incidence of first molar anesthesia as determined by lack of response to electric pulp testing at the maximum setting (percentage of 80/80s), at each postinjection time interval, for the 2 anesthetic formulations. No significant differences ($P > .05$) between the 2 anesthetic formulations were noted.

Figure 3. Incidence of second premolar anesthesia as determined by lack of response to electric pulp testing at the maximum setting (percentage of 80/80s), at each postinjection time interval, for the 2 anesthetic formulations. No significant differences ($P > .05$) between the 2 anesthetic formulations were noted.

pulpal anesthesia. Because all subjects felt profound lip numbness, but pulp testing revealed that subjects did not always have pulpal anesthesia (80 readings), asking the patient whether the lip is numb indicates soft tissue anesthesia but does not guarantee successful pulpal anesthesia.

Even when 3.6 mL of 2% lidocaine was used with 1 : 100,000 epinephrine, the IAN block was not successful in providing complete pulpal anesthesia (Table 1). The IAN block in the current study had similar rates of anesthetic success as in other studies of the IAN block.²⁵ For example, Nusstein et al,²⁵ using 1.8–3.6 mL of 2% lidocaine with 1 : 100,000 epinephrine, found that success rates ranged from 44–

Figure 4. Incidence of first premolar anesthesia as determined by lack of response to electric pulp testing at the maximum setting (percentage of 80/80s), at each postinjection time interval, for the 2 anesthetic formulations. No significant differences ($P > .05$) between the 2 anesthetic formulations were noted.

Figure 5. Incidence of lateral incisor anesthesia as determined by lack of response to electric pulp testing at the maximum setting (percentage of 80/80s), at each postinjection time interval, for the 2 anesthetic formulations. No significant differences ($P > .05$) between the 2 anesthetic formulations were noted.

53% for the first molar, from 61–67% for the first premolar, and from 32–35% for the lateral incisor. These rates are similar to the success rates of 58% for the first molar, 71% for the first premolar, and 35% for the lateral incisor reported in the current study (Table 1). Although commercial formulations of 2% lidocaine with 1 : 100,000 epinephrine are more acidic (pH of 4–5) than the formulation used in the current study (pH of 6.4), success rates were similar to the success rates derived when commercial formulations were used.²⁵ The IAN block did not provide complete pulpal anesthesia for the mandibular teeth (Figures 1–6), which could present meaningful clinical problems in that the teeth may not be numb for procedures requiring complete pulpal anesthesia. Practitioners should consider supplemental techniques, such as intraosseous,^{26–29} periodontal ligament injections,³⁰ or buccal infiltration of 4% articaine with 1 : 100,000 epinephrine,³¹ when an IAN block fails to provide pulpal anesthesia for an asymptomatic tooth. Because we studied a young adult population, the results of this study may not apply to children or to the elderly.

We had considered raising the pH of the anesthetic formulation to 7.9, which is the acid dissociation constant (pKa) of lidocaine,¹³ thereby producing equal amounts of the cation and the base form. However, a pilot study of various formulations demonstrated irritating effects (cellulitis and tissue injury). We found that a concentration of 0.17 mEq/mL of sodium bicarbonate raised the pH of the lidocaine formulation to 7.5 (Table 4) without causing an irritating effect. We used a total volume of 3.6 mL of the lidocaine/sodium bicarbonate formulation to allow more sodium bicarbonate to be used, by volume, than a 1.8-mL volume would have allowed.

Figure 6. Incidence of central incisor anesthesia as determined by lack of response to electric pulp testing at the maximum setting (percentage of 80/80s), at each postinjection time interval, for the 2 anesthetic formulations. No significant differences ($P > .05$) between the 2 anesthetic formulations were noted.

For nonbuffered lidocaine, 72 mg of lidocaine was administered to each subject, and for buffered lidocaine, only 60 mg of lidocaine was administered. So, 17% less lidocaine was given to subjects in the buffered group. Even though less lidocaine was administered in the buffered formulation, the same anesthetic success rate was achieved as with the unbuffered lidocaine formulation.

For all teeth, anesthetic success (Table 1) and incidence of pulpal anesthesia (Figures 1–6) were not significantly different between the 2 anesthetic formulations. Although Galindo et al¹⁵ described better quality of anesthesia when a buffered lidocaine formulation was used with sodium bicarbonate, Sinnott et al¹⁹ did not. We could not confirm improvement in IAN block success. Therefore, the addition of sodium bicarbonate to a solution of 2% lidocaine with 1 : 100,000 epinephrine, as was formulated in this study, did not increase success of the IAN block.

Onset of pulpal anesthesia for the 2% lidocaine with 1 : 100,000 epinephrine formulation is presented in Table 3. Previous authors^{4,32,33} have found pulpal onset times for the IAN block, using 2% lidocaine with 1 : 100,000 epinephrine, to be 4–5 minutes for the second molar, 8–9 minutes for the first molar, 10 minutes for the second premolar, 7–11 minutes for the first premolar, 12–17 minutes for the lateral incisor, and 19 minutes for the central incisor. The values in the current study are lower for first molars, premolars, and incisors (Table 3), which may be related to differences in patient populations. Waiting approximately 10–15 minutes should ensure the onset of pulpal anesthesia in molars and premolars. Lateral and central incisors may require a longer waiting time for pulpal

Table 2. Pain Ratings for Each Injection Phase for the 2 Anesthetic Formulations†

Injection Phase	None	Mild	Moderate	Severe	Mean
Needle insertion*					
Lidocaine	40% (16/40)	55% (22/40)	5% (2/40)	0% (0/40)	0.65
Lidocaine/Sodium bicarbonate	38% (15/40)	50% (20/40)	12% (5/40)	0% (0/40)	0.75
Needle placement*					
Lidocaine	28% (11/40)	50% (20/40)	20% (8/40)	2% (1/40)	0.98
Lidocaine/Sodium bicarbonate	20% (8/40)	60% (24/40)	20% (8/40)	0% (0/40)	1.00
Solution deposition*					
Lidocaine	58% (23/40)	35% (14/40)	8% (3/40)	0% (0/40)	0.50
Lidocaine/Sodium bicarbonate	72% (29/40)	25% (10/40)	2% (1/40)	0% (0/40)	0.30

* No significant difference ($P > .05$) was noted between the 2 techniques.

† $n = 40$.

anesthesia than do posterior teeth. Pulp testing the tooth with an electric pulp tester or a cold refrigerant will give the clinician a reliable indicator of onset of pulpal anesthesia.

No significant differences in onset times were noted between the 2 anesthetic formulations (Table 3). DiFazio et al,¹⁶ Zahl et al,¹⁷ Benson et al,¹⁸ and Sinnott et al¹⁹ found that anesthetic formulations with higher pH values had a faster onset. However, Galindo et al¹⁵ and Christoph et al³⁴ did not find pH-adjusted agents to have a faster onset. It would seem that the higher pH-adjusted anesthetic formulations would have more of the uncharged base available initially. Therefore, a faster onset would theoretically result. However, we could not confirm a statistically faster onset with the lidocaine-sodium bicarbonate formulation (Table 3).

Needle insertion pain resulted in a 5–12% incidence of moderate pain with no reports of severe pain. No significant difference between the anesthetic formulations was noted. This would be expected because

needle insertion was the same for both anesthetics. For the needle insertion phase, Nusstein et al,³⁵ in a retrospective study of IAN blocks using 2% lidocaine with 1 : 100,000 epinephrine, reported an incidence of moderate to severe pain ranging from 14–22%, which is higher than the incidence in the current study. Needle placement resulted in a 20–22% incidence of moderate to severe pain, even though 0.2 mL of anesthetic solution was deposited ahead of the needle, with no significant difference between anesthetic formulations. For needle placement to the target site, Nusstein et al³⁶ reported that 22–56% of subjects reported moderate to severe pain. Solution deposition resulted in a 2–8% incidence of moderate pain, with no significant difference between anesthetic formulations. For deposition of the anesthetic solution at the target site for the IAN block, various authors^{2–4,6,10} have reported that the incidence of moderate to severe pain ranged from 20–40%. Generally, we recorded lower incidences of moderate to severe pain than previous authors^{2–4,6,10}—a fact that may be related to differences in operator or subject populations or in rates of solution deposition.

Using an intradermal injection model, Christoph et al³⁴ and McKay et al³⁷ found that buffered anesthetic solutions with sodium bicarbonate significantly decreased the pain of injection. However, Gershon et al³⁸ and Burns et al³⁹ found no significant pain reduc-

Table 3. Comparison of Pulpal Anesthesia Onset Times for the 2 Anesthetic Formulations (in minutes)

Onset of Pulpal Anesthesia†	Anesthetic Formulation	
	2% Lidocaine With 1 : 100,000 Epinephrine	2% Lidocaine With 1 : 100,000 Epinephrine/Sodium Bicarbonate
Second molar ($n = 35$)	5 ± 6.6	5 ± 8.9*
First molar ($n = 29$)	5 ± 6.0	10 ± 11.4*
Second premolar ($n = 30$)	7 ± 7.3	10 ± 12.8*
First premolar ($n = 29$)	7 ± 6.7	6 ± 6.3*
Lateral incisor ($n = 23$)	11 ± 6.3	10 ± 11.8*
Central incisor ($n = 11$)	12 ± 9.3	15 ± 15.9*

* No significant differences ($P > .05$) between the anesthetic formulations were noted.

† Teeth with failures were excluded from the onset of pulpal anesthesia.

Table 4. pH Values for Components of the Anesthetic Formulations and the Final 2 Anesthetic Formulations

Formulation Components	pH Values
2% lidocaine	6.59
1 : 1000 epinephrine	3.37
Sodium bicarbonate	8.29
2% lidocaine with 1 : 100,000 epinephrine	6.40
2% lidocaine with 1 : 100,000 epinephrine/sodium bicarbonate	7.50

tion with buffered anesthetic solutions for intradermal anesthesia. Younis and Bhutiani⁴⁰ and Ruegg et al⁴¹ reported less pain with buffered lidocaine compared with unbuffered lidocaine in medical-surgical procedures. In a dental model using maxillary infiltrations, Bowles et al⁴² found less pain with buffered lidocaine, but Primosch and Robinson⁴³ found no pain reduction. Because we used an IAN block, it is difficult to compare our results with those of previous studies. We can conclude that buffering a lidocaine solution with sodium bicarbonate, as it was formulated in the current study, did not significantly decrease the pain of injection.

In conclusion, buffering a 2% lidocaine with 1 : 100,000 epinephrine with sodium bicarbonate, as was formulated in the current study, did not statistically decrease the pain of injection, provide faster onset, or improve the profundity of anesthesia when compared with unbuffered 2% lidocaine with 1 : 100,000 epinephrine for an IAN block.

ACKNOWLEDGMENT

This study was supported by Graduate Endodontic Research Funds.

REFERENCES

1. Ågren E, Danielsson K. Conduction block analgesia in the mandible. *Swed Dent J*. 1981;5:81–89.
2. Vreeland D, Reader A, Beck M, Meyers W, Weaver J. An evaluation of volumes and concentrations of lidocaine in human inferior alveolar nerve block. *J Endod*. 1989;15:6–12.
3. Hinkley S, Reader A, Beck M, Meyers W. An evaluation of 4% prilocaine with 1 : 200,000 epinephrine and 2% mepivacaine with levonordefrin compared to 2% lidocaine with 1 : 100,000 epinephrine for inferior alveolar nerve block. *Anesth Prog*. 1991;38:84–89.
4. Chaney MA, Kerby R, Reader A, Beck FM, Meyers WJ, Weaver J. An evaluation of lidocaine hydrocarbonate compared with lidocaine hydrochloride for inferior alveolar nerve block. *Anesth Prog*. 1991;38:212–216.
5. Nist R, Reader A, Beck M, Meyers W. An evaluation of the incisive nerve block and combination inferior alveolar and incisive nerve blocks in mandibular anesthesia. *J Endod*. 1992;18:455–459.
6. McLean C, Reader A, Beck M, Meyers WJ. An evaluation of 4% prilocaine and 3% mepivacaine compared to 2% lidocaine (1 : 100,000 epinephrine) for inferior alveolar nerve block. *J Endod*. 1993;19:146–150.
7. Dagher BF, Yared GM, Machtou P. The anesthetic efficacy of volumes of lidocaine in inferior alveolar nerve blocks. *J Endod*. 1997;23:178–180.
8. Clark S, Reader A, Beck M, Meyers WJ. Anesthetic efficacy of the mylohyoid nerve block and combination inferior alveolar nerve block/mylohyoid nerve block. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1999;87:557–563.
9. Hannan L, Reader A, Nist R, Beck M, Meyers WJ. The use of ultrasound for guiding needle placement for inferior alveolar nerve blocks. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1999;87:658–665.
10. Ridenour S, Reader A, Beck M, Weaver J. Anesthetic efficacy of a combination of hyaluronidase and lidocaine with epinephrine in inferior alveolar nerve blocks. *Anesth Prog*. 2001;48:9–15.
11. Yonchak T, Reader A, Beck M, Meyers WJ. Anesthetic efficacy of unilateral and bilateral inferior alveolar nerve blocks to determine cross innervation in anterior teeth. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2001;92:132–135.
12. Mikesell P, Nusstein J, Reader A, Beck M, Weaver J. A comparison of articaine and lidocaine for inferior alveolar nerve blocks. *J Endod*. 2005;31:265–270.
13. Goodman A, Reader A, Nusstein J, Beck M, Weaver J. Anesthetic efficacy of lidocaine/meperidine for inferior alveolar nerve blocks. *Anesth Prog*. 2006;53:131–139.
14. Kanaa MD, Meechan JG, Corbett IP, Whitworth JM. Speed of injection influences efficacy of inferior alveolar nerve blocks: a double-blind randomized controlled trial in volunteers. *J Endod*. 2006;32:919–923.
15. Galindo A. pH-adjusted local anesthetics: clinical experience. *Reg Anesth*. 1983;8:35–36.
16. DiFazio CA, Carron H, Grosslight KR, Moscicki J, Bolding WR, Johns RA. Comparison of pH-adjusted lidocaine solutions for epidural anesthesia. *Anesth Analg*. 1986;65:760–764.
17. Zahl K, Jordan A, McGroarty J, Sorensen B, Gotta AW. Peribulbar anesthesia—effect of bicarbonate on mixtures of lidocaine, bupivacaine, and hyaluronidase with or without epinephrine. *Ophthalmology*. 1991;98:239–242.
18. Benson HT, Toleikis JR, Dixit P, Goodman I, Hill JA. Onset, intensity of blockade and somatosensory evoked potential changes of the lumbosacral dermatomes after epidural anesthesia with alkalinized lidocaine. *Anesth Analg*. 1993;76:328–332.
19. Sinnott CJ, Garfield JM, Thalhammer JG, Strichartz GR. Addition of sodium bicarbonate to lidocaine decreases the duration of peripheral nerve block in the rat. *Anesthesiology*. 2000;93:1045–1052.
20. Davies RJ. Buffering the pain of local anesthetics: a systematic review. *Emerg Med (Fremantle)*. 2003;15:81–88.
21. Peterfreund RA, Datta S, Ostheimer G. pH adjustment of local anesthetic solutions with sodium bicarbonate: laboratory evaluation of alkalization and precipitation. *Reg Anesth*. 1989;14:265–270.
22. Jorgensen NB, Hayden J Jr. *Local and General Anesthesia in Dentistry*. 2nd ed. Philadelphia, Pa: Lea & Febiger, 1967: 69–72.
23. Dreven L, Reader A, Beck M, Meyers W, Weaver J. An evaluation of the electric pulp tester as a measure of analgesia in human vital teeth. *J Endod*. 1987;13:233–238.

24. Certosimo A, Archer R. A clinical evaluation of the electric pulp tester as an indicator of local anesthesia. *Oper Dent*. 1996;21:25–30.
25. Nusstein J, Reader A, Beck M. Anesthetic efficacy of different volumes of lidocaine with epinephrine for inferior alveolar nerve blocks. *Gen Dent*. 2002;50:372–375.
26. Reisman D, Reader A, Nist R, Beck M, Weaver J. Anesthetic efficacy of the supplemental intraosseous injection of 3% mepivacaine in irreversible pulpitis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1997;84:676–682.
27. Nusstein J, Reader A, Nist R, Beck M, Meyers WJ. Anesthetic efficacy of the supplemental intraosseous injection of 2% lidocaine with 1 : 100,000 epinephrine in irreversible pulpitis. *J Endod*. 1998;24:487–491.
28. Parente SA, Anderson RW, Herman WW, Kimbrough WF, Weller RN. Anesthetic efficacy of the supplemental intraosseous injection for teeth with irreversible pulpitis. *J Endod*. 1998;24:826–828.
29. Nusstein J, Kennedy S, Reader A, Beck M, Weaver J. Anesthetic efficacy of the supplemental X-tip intraosseous injection in patients with irreversible pulpitis. *J Endod*. 2003;29:724–728.
30. Cohen HP, Cha BY, Spangberg LSW. Endodontic anesthesia in mandibular molars: a clinical study. *J Endod*. 1993;19:370–373.
31. Haase A, Reader A, Nusstein J, Beck M, Drum M. Comparing anesthetic efficacy of articaine versus lidocaine as a supplemental buccal infiltration of the mandibular first molar after an inferior alveolar nerve block. *J Am Dent Assoc*. 2008;139:1228–1235.
32. Goldberg S, Reader A, Drum M, Nusstein J, Beck M. Comparison of the anesthetic efficacy of the conventional inferior alveolar, Gow-Gates, and Vazirani-Akinosi techniques. *J Endod*. 2008;34:1306–1311.
33. Steinkruger G, Nusstein J, Reader A, Beck M, Weaver J. The significance of needle bevel orientation in achieving a successful inferior alveolar nerve block. *J Am Dent Assoc*. 2006;137:1685–1691.
34. Christoph RA, Buchanan L, Begalla K, Schwartz S. Pain reduction in local anesthetic administration through pH buffering. *Ann Emerg Med*. 1988;17:117–120.
35. Nusstein JM, Beck M. Effectiveness of 20% benzocaine as a topical anesthetic for intraoral injections. *Anesth Prog*. 2003;50:159–163.
36. Nusstein J, Steinkruger G, Reader A, Beck M, Weaver J. The effects of a 2-stage injection technique on inferior alveolar nerve block injection pain. *Anesth Prog*. 2006;53:126–130.
37. McKay W, Morris R, Mushlin P. Sodium bicarbonate attenuates pain on skin infiltration with lidocaine, with or without epinephrine. *Anesth Analg*. 1987;66:572–574.
38. Gershon RY, Mokriski BK, Matjasko MJ. Intradermal anesthesia and comparison of intravenous catheter gauge. *Anesth Analg*. 1991;73:469–470.
39. Burns CA, Ferris G, Feng C, Cooper JZ, Brown MD. Decreasing the pain of local anesthesia: a prospective, double-blind comparison of buffered, premixed 1% lidocaine with epinephrine versus 1% lidocaine freshly mixed with epinephrine. *J Am Acad Dermatol*. 2006;54:128–131.
40. Younis I, Bhutiani RP. Taking the 'ouch' out—effect of buffering commercial Xylocaine on infiltration and procedure pain—a prospective, randomised, double-blind, controlled trial. *Ann R Coll Surg Engl*. 2004;86:213–217.
41. Ruegg TA, Curran CR, Lamb T. Use of buffered lidocaine in bone marrow biopsies: a randomized, controlled trial. *Oncol Nurs Forum*. 2009;36:52–60.
42. Bowles WH, Frysh H, Emmons R. Clinical evaluation of buffered local anesthetic. *Gen Dent*. 1995;43:182–184.
43. Primosch RE, Robinson L. Pain elicited during intraoral infiltration with buffered lidocaine. *Am J Dent*. 1996;9:5–10.