A Prospective, Randomized Single-blind Study of the Anesthetic Efficacy of Frequency-dependent Conduction Blockade of the Inferior Alveolar Nerve

Gregory Hutchison, DDS, MS, * *Todd Halcomb, DDS, MS,*[†] *Al Reader, DDS, MS,*[‡] *Melissa Drum, DDS, MS,*[‡] *John Nusstein, DDS, MS,*[‡] *and Mike Beck, DDS, MA*[§]

Abstract

Introduction: The purpose of this prospective, randomized single-blind study was to evaluate the degree of pulpal anesthesia obtained with frequency-dependent conduction blockade of the inferior alveolar nerve (IAN). **Methods:** Eighty adult volunteers randomly received two IAN blocks: an IAN block followed by continuous electrical stimulation for 3 minutes of the first molar or lateral incisor for six cycles over a time period of 64 minutes; an IAN block followed by mock electrical stimulation using the same cycles. The IAN blocks were administered at two separate appointments spaced at least 1 week apart in a crossover design. An electric pulp tester was used to test for anesthesia of the first molar and lateral incisor. Anesthesia was considered successful when two consecutive 80 readings were obtained within 15 minutes, and the 80 reading was recorded through the 60th minute. **Results:** The anesthetic success rate for the stimulated IAN block was 35% and 48% for the lateral incisor and first molar, respectively. For the mock stimulated IAN, success was 18% for the lateral incisor and 62% for the first molar. There was no significant difference between the two IAN block techniques. **Conclusions:** We concluded that the stimulation of nerves in the presence of local anesthesia (frequency-dependent nerve block) did not statistically increase the success rate of pulpal anesthesia for an IAN block. (J Endod 2011;37:938–942)

Key Words

Frequency-dependent nerve block, inferior alveolar nerve block, lidocaine, local anesthesia

From *Private Endodontic Practice, Findlay; [†]Formerly in Private Endodontic Practice, Hamilton; and Divisions of [‡]Endodontics and [§]Oral Biology, The Ohio State University, Columbus, Ohio.

Address requests for reprints to Dr Al Reader, Division of Endodontics, College of Dentistry, The Ohio State University, 305 West 12th Avenue, Columbus, OH 43210. E-mail address: reader.2@osu.edu

The inferior alveolar nerve (IAN) block does not always result in successful pulpal anesthesia (1). Failure rates of 10% to 39% have been reported in experimental studies (1). Clinical studies in endodontics (2–12) have found success with the IAN block occurring between 15% and 57% of the time. Therefore, it would be advantageous to improve the success rate of the inferior alveolar nerve block.

Local anesthetic action has been shown to be potentiated by the application of repetitive high-frequency electrical stimulation (13–16). This action is known as frequency-dependent, use-dependent, or phasic blockade (13–15). Higher frequencies (100 Hz) of stimulation have greater frequency-dependent inhibition than lower frequencies (40 Hz) (13, 15).

Despite this evidence, only a few *in vivo* studies of frequency-dependent blockade have been reported (17, 18). Stevens et al (17) found that nonnoxious electrical stimulation with high frequencies accelerated the onset of anesthesia and extended the spread of sensory block for the ulnar nerve. Watson et al (18) showed frequency-dependent conduction block of the median nerve in patients with carpal tunnel syndrome. However, it is unknown how other nerves are affected by frequency-dependent blockade. Differences in the nerve anatomy, physiology, conductivity, and application of the stimulation may affect the clinical efficacy of frequency-dependent blockade.

No studies of the IAN block have been performed using frequency-dependent conduction blockade. The purpose of this prospective, randomized single-blind study was to evaluate the degree of pulpal anesthesia obtained with frequency-dependent conduction blockade of the IAN.

Materials and Methods

Eighty adult subjects participated in this study. All of the subjects were in good health as determined by a written health history and oral questioning. Exclusion criteria were as follows: younger than 18 or older than 65 years of age, allergies to local anesthetics or sulfites, pregnancy, a history of significant medical conditions (American Society of Anesthesiologists II or higher), taking any medications that may affect anesthetic assessment (eg, over-the-counter analgesic medications, opioids, antidepressants, and alcohol), active sites of pathosis in area of injection, or 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 subjects randomly received two IAN blocks: an IAN block followed by electrical pulpal stimulation and an IAN block followed by mock electrical pulpal stimulation at two separate appointments spaced at least 1 week apart in a crossover design. With the crossover design, there were 160 total injections administered, and each subject served as his/her own control. Eighty blocks were administered to one group of 40 subjects, and the first molar was the test tooth. Another group of 40 subjects received 80 blocks, and the lateral incisor was the test tooth. An equal number of block injections was administered on the right and left sides to control for anatomic and operator variability during the IAN block. The same side randomly chosen for the first injection was used again for the second injection. The study was divided into two separate groups of first molars and lateral incisors because stimulation of the first molar may have had an

affect on the lateral incisor. Additionally, using the sequence of stimulation for a tooth would be prohibitive if both the first molar and lateral incisor were being tested. 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, the two nerve blocks, with stimulation or mock stimulation, were assigned random numbers. Each subject was randomly assigned to the right or left side. The order of assignment to the stimulation or mock stimulation group was also randomly determined.

All stimulation was administered with a modified electric pulp tester. We modified the electric pulp tester (Kerr; Analytic Technology Corp, Redmond, WA) by changing the circuitry and adding a two-position switch. One switch caused a gradual increase in voltage that could be halted by the subjects depressing a hand-held button (Fig. 1). However, once the level of stimulation was achieved, this level of stimulation was continually applied at this position. High-frequency (100 Hz) stimulation is more strongly supported for frequency-dependent conduction block (14, 15, 19, 20). Therefore, the frequency of stimulation was set at 100 Hz and verified using a Tektronix oscilloscope (Model 465; Tektronix, Beaverton, OR). The voltage and current were controlled in the current experiment because the Kerr Analytic Technology pulp tester has a voltage range of 0 to 350 V and a range of 0 to 50 mA. Only the Hertz (frequency of a current waveform) was modified with the pulp tester to alternate at 100 times each second (based on the experimental studies of frequency-dependent blockade). Therefore, Hertz is a measure of how quickly the voltage and current changes or vibrates (100 times a second). The previous clinical studies (17, 18) of frequency-dependent blockade did not use the same voltage, current, or Hertz as the current study because they applied the stimulus cutaneously. The modified pulp tester could also be used as a normal pulp tester when the second position of the switch was activated.

A pilot study using 10 additional subjects tested the ability of the nerve to adapt to stimulation and remain adapted after cessation of the stimulation. The right and left mandibular first molar and right and left lateral incisor were tested in 10 subjects using the modified pulp tester in the stimulation mode with the subject controlling stimulation level with the handheld button. The teeth were stimulated with 100 Hz for 3 minutes without anesthetic administration to determine if any changes in pulp test readings occurred because of the stimulation when compared with baseline values. After the first minute of stimulation the subject was questioned regarding any change in sensation (higher, same, or less). The subject was allowed to rest for 60 seconds, and three trials were performed at 2-minute intervals. This cycle of stimulation was repeated three times for each molar and lateral incisor.

At the beginning of each experimental appointment and before any injections were given, the experimental teeth and control canine were tested three times with the modified pulp tester in its normal mode of operation. After the tooth to be tested was isolated with cotton rolls and dried with gauze, toothpaste was applied to the probe tip, which was then placed midway between the gingival margin and the occlusal or incisal edge of the tooth. The current rate was set at 25 seconds to increase from no output (0) to the maximum output (80). The number at the initial sensation was recorded. Trained research personnel performed all preinjection and postinjection tests.

Subjects were administered a standard IAN block using 2% lidocaine with 1:100,000 epinephrine (Septodont, Deproco, Newcastle, DE) and a standard aspirating syringe by the two senior authors

Figure 1. The experimenter's box is shown in the middle. The modified electric pulp tester (right) is shown along with the hand-held push button device (left) used to control the current output of the pulp tester.

(G.H. and T.H.). Lidocaine was chosen because Scurlock et al (19) and Courtney (21) found that lidocaine was a more potent blocker of sensory nerves during frequency-dependent conduction block than other anesthetic agents tested. After negative aspiration, 1.8 mL of the anesthetic solution was deposited over a 1-minute time period. A sterile rubber stopper, previously placed on the 27-G needle, was adjusted to rest flush with the oral mucosa at the completion of the injection. Upon withdrawal of the needle, the distance from the needle tip to the rubber stopper was measured. The subject was asked every minute for 15 minutes if they were experiencing lip numbness. All subjects used for data analysis reported profound lip numbness.

To blind the subject to whether stimulation was used, a mock treatment was used. An experimenter's box with a red light, a standard voltmeter, and an on/off switch was constructed for this study (Fig. 1). Turning the on/off switch to the on position activated the red light and voltmeter (the power source was a 9-V battery and was independent of any voltage applied to the subject's teeth). The box was also wired to the modified pulp tester so that when the switch was activated there was no current output to the pulp tester. Subjects and the pulp testers were told that the voltmeter reading would determine the amount of current delivered to the tooth and they may feel pain. During this time, the subject actually received no stimulation. The experimenter's box was initially shown to the subject but was positioned out of view for the subject during the experimental phase of the study. The stimulation cycle was the same as for the experimental procedure.

At 5 minutes after each block was given, a pulp test reading was recorded. At 6 minutes, the pulp tester probe tip was applied to the test tooth, and the modified pulp tester (stimulation mode) became activated as seen by the advancing digital readout. Once a sensation in the tooth was experienced, the subject halted the advancement in stimulation by depressing the handheld button. Stimulation at the halted level continued for 3 minutes. If no sensation was recorded by the subject, the maximum current (80 reading) was applied for 3 minutes. For the mock stimulation, the switch on the experimenter's box was turned on, and the probe was placed on the tooth for 3 minutes. After the stimulation or mock stimulation, the subject was allowed to rest for 1 minute.

The modified pulp tester was switched to the normal mode of operation, and the experimental tooth (lateral incisor or first molar) was tested each minute for 3 minutes. The contralateral control canine was tested 1 minute later. The 3 minutes of continuous stimulation or mock stimulation cycles were then repeated as outlined previously.

http://endodontic.ws/

This cycle was repeated for 64 minutes. The same cycle of testing and subject questioning used for the experimental treatment was used for the mock treatment. At every third cycle, the control tooth, the contralateral canine, was tested by another pulp tester without batteries to test the reliability of the subject; that is, if the subject responded positively to an inactivated pulp tester, then they were not reliable and could not be used in the study. Subjective signs of lip anesthesia were evaluated every minute for 20 minutes and then at 2-minute intervals until the end of the session to ensure subjective anesthesia did not wear off. If profound lip numbness was not recorded within 20 minutes, the block was considered unsuccessful, and the subject was either reappointed or another subject was recruited. Of the 15 subjects who did not achieve lip numbness, 13 were reappointed and achieved lip numbness. The two subjects who were replaced were not used in the data analysis. Basically, reappointing or replacing subjects because of a lack of lip numbness is required in experimental studies. If these subjects were included in the data, none would achieve pulpal anesthesia (80 readings), and the results would be skewed. Achieving lip numbness is a sign that the needle and anesthetic solution were placed close enough to the nerve to at least achieve lip numbness. It is common to use this criterion clinically even though it does not guarantee pulpal anesthesia. All testing was stopped at 64 minutes after injection.

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 two consecutive 80 readings were obtained within 15 minutes and the 80 reading was recorded through the 60th minute; that is, for most restorative procedures, we would want the patient numb within 15 minutes and to remain numb through the 60th minute.

Data were analyzed statistically. All subjects used for data analysis had profound lip anesthesia. Comparisons of the two nerve blocks for anesthetic success were analyzed using the McNemar test. The incidence of pulpal anesthesia (80 readings) was analyzed using multiple McNemar tests with P values adjusted using the step-down Bonferroni method of Holm. Electric pulp test values for the pilot study were analyzed using a repeated-measures analysis of variance. Comparisons were considered significant at $P < .05$. With a nondirectional alpha risk of 0.05 and assuming a success rate of 40%, a sample size of 40 subjects per experimental tooth was required to show a difference in anesthetic success of ± 25 percentage points with a power of 0.85.

Results

A total of 80 adult subjects, 36 women and 44 men aged 18 to 38 years with an average age of 26 years, participated in the experimental portion of the study. Forty adult subjects, 21 women and 19 men aged 19 to 38 years with an average age of 25 years, participated in the first molar experiment. Forty adult subjects, 15 women and 25 men, aged 18 to 38 years with an average age of 27 years participated in the lateral incisor experiment. Ten adult males, aged 22 to 38 years with an average age of 26 years, participated in the pilot study.

The pilot study indicated no significant difference between pulp test readings before and after stimulation with 100 Hz for 3 minutes without anesthetic administration. Sensation during this stimulation for the first molars and lateral incisors stayed the same in 88% to 89% of the subjects, decreased in 4% to 9%, and increased in 3% to 5%.

Eight subjects in the lateral incisor group (8/88 injections) and seven subjects in the first molar group (7/87 injections) did not achieve lip numbness with the IAN block. Therefore, the incidence of missed blocks was 8.6% (15/175 total injections). None of the subjects achieved pulpal anesthesia. These 15 subjects were reappointed (13 subjects) or replaced with new subjects (two subjects).

One hundred percent of the 80 subjects used for data analysis had profound lip anesthesia. Anesthetic success is presented in Table 1. Figures 2 and 3 present the incidence of pulpal anesthesia (percentage of 80 readings) for the two nerve blocks. There were no significant differences between the two nerve blocks. The mean depth of needle placement to the target site for the IAN block was 18 mm for the stimulated session and 18 mm for the unstimulated session.

Discussion

The potency of sodium channel blocking of local anesthetics is dependent on the channel states (ie, resting, open, and inactive) (14). Open channel blocking (interpreted as drug binding) is greater than resting channel blocking (14). Inactive channel binding appears to be greater than resting channel binding. A more rapidly firing excitable membrane will spend more time in the higher affinity open and inactive channel states (14). Therefore, there is an increase in drug blocking potency. This action is called frequency-dependent blockade. The conditions necessary for frequency-dependent nerve blockade include a local anesthetic and a train of repetitive stimuli (15).

Expectations were that success would be improved by the nonnoxious electrical stimulation of specific nerves at high frequency (100 Hz) (14, 15, 19, 20) and in the presence of lidocaine (19, 21). Placing sodium channels in open-state anesthetic molecules should more readily block ion exchange, thereby improving blockade (16, 21). Although recordings in the current study would mimic other studies using pulp testing to evaluate anesthesia, constant electrical stimulation in 3-minute cycles was unique to this study. Based on previous studies (14, 15, 19–21), we believed that experimentally using stimulation in cycles of 3 minutes over the 64 minutes should have resulted in opening of the sodium channels because high levels of stimulation were used to ensure that impulses would be transmitted in partially or incompletely anesthetized nerves. Although no statistical differences in anesthetic success was shown in the current study (Table 1), the stimulated block did have higher incidences of 80 readings than the mock stimulated block for the lateral incisor (Fig. 2). According to Fink and Cairns (15), using an animal model, if too many axons are effectively blocked by a local anesthetic, a frequency-dependent blockade is difficult to show. Because the lateral incisor had a lower overall incidence of 80 readings than the first molar (Figs. 2 and 3), indicating less effective nerve blockade, perhaps the effects of frequency-dependent blockade would be more apparent in the lateral incisor. However, to be clinically meaningful, we would require a complete set of 80 readings across the 60 minutes so that the patient would feel no pain. Further study may be indicated using different stimulation times or anesthetic agents to exhibit frequency-dependent effects more effectively.

Although previous clinical studies (17, 18) showed an effect of frequency-dependent block, both studies used cutaneous stimulation at a maximum of 30 and 50 Hz, one study used only seven subjects (17), and the other study (18) used patients with an entrapment neuropathy. These studies are different than using normal subjects with noninflamed teeth and stimulating pulpal nerves at 100 Hz rather than cutaneous stimulation. The limitations of these two studies (17, 18) would indicate that further investigations are indicated to definitively prove the effect of frequency-dependent blockade in medicine.

The lateral incisor showed lower rates of anesthetic success than the first molar. Nusstein et al (1) found similar results and related the differences to the central core theory. The premise of the theory is that nerves on the outside of the nerve bundle supply molar teeth while nerves on the inside supply anterior teeth. The anesthetic solution

TABLE 1. Percentages and Number of Subjects Who Experienced Anesthetic Success with the Stimulated IAN Block and the Mock-stimulated IAN Block

	Nerve block	
	Stimulated IAN (%)	Mock-stimulated IAN (%)
Lateral incisor*	35 (14/40)	18 (7/40)
First molar*	48 (19/40)	62 (25/40)

n = 40 per group.

*There was no significant difference between the two nerve blocks.

may not diffuse into the nerve bundle to reach all nerves to produce an adequate block even if deposited at the correct site. Therefore, although small gains were noted when nerves were stimulated in the lateral incisor, the stimulation of teeth after local anesthetic administration cannot be recommended for routine clinical use. We believed it was important to first test the efficacy of the frequency-dependent nerve block on normal teeth. If it had clinical application in normal teeth, we could then apply the methods for teeth with irreversible pulpitis. Because it was only marginally efficient in the current study, the application to teeth with irreversible pulpitis would not be indicated at the present time.

The incidence of missed blocks was 8.6%, which is similar to the incidence found by Simon et al (22), a 9% incidence. Clinically, the presence of soft-tissue anesthesia does not adequately indicate pulpal anesthesia (1). However, the lack of soft-tissue anesthesia is a useful indicator that the block injection would not be clinically successful.

We based our use of the pulp test reading of 80 (signaling maximum current) as a criterion for pulpal anesthesia on the studies of Dreven et al (23) and Certosimo and Archer (24). These studies (23, 25) showed that no patient response to an 80 reading ensured pulpal anesthesia in vital, asymptomatic teeth. Additionally, Certosimo and Archer (24) showed that electric pulp test readings of less than 80 resulted in pain during operative procedures in asymptomatic teeth.

Because no significant differences were noted between pulp test readings before and after stimulation in the pilot study, adaptation (a gradual decrease in response to a repetitive stimulation) did not occur with the study design used. Additionally, the majority of the subjects (88%–89%) reported no change in sensation during stimulation. Therefore, differences in pulp test readings between the stimulated and mock stimulated blocks would likely be caused by frequency-dependent effects.

Needle depth was recorded in the current study to evaluate if they were similar in the two IAN blocks. The mean depth of needle penetra-tion was 18 mm for both IAN blocks. Simon et al (22) found needle depth for location of the IAN block with a peripheral nerve stimulator to be 19 mm. Hannan et al (25) compared depth of needle penetration for an IAN block using ultrasound location and a conventional technique. They found that the average depth of needle penetration was 19 mm for the conventional IAN and 17 mm for the IAN block using ultrasound. Malamed (26) recommends a depth of penetration of 20 to 25 mm. Bremer (27) found the mean needle depth to be 24 mm. Menke and Gowgiel (28) found a mean depth of 16 mm. Therefore, there is some variation on the recommendations for needle depth. The results obtained in the current study are closer to the findings of Simon et al (22) and Hannan et al (25).

Generally, the mock stimulated IAN block had higher rates of anesthetic success for the first molar but lower success rates for the lateral incisor (Table 1) than other studies of the IAN block (1). Nusstein et al (1) found success rates ranged from 44% to 53% for the first molar and 32% to 35% for the lateral incisor. The success rate of 62% for the first molar and 18% for the lateral incisor in the current study probably relates to differences in subject populations. The conventional IAN block did not provide complete pulpal anesthesia for the lateral incisor and first molar (Table 1 and Figs. 2 and 3), which could present meaningful clinical problems because the teeth may not be numb for procedures requiring complete pulpal anesthesia. Practitioners should consider supplemental techniques such as intraosseous (3, 4) or periodontal ligament injections (2) or an infiltration of 1.8 mL of 4% articaine with 1:100,000 epinephrine for the first molar (29) when a conventional IAN block fails to provide pulpal anesthesia for a particular asymptomatic tooth. Because we studied a young adult population, the results of this study may not apply to children or the elderly. We concluded that stimulation of nerves in the presence of local anesthesia (frequency-dependent nerve block) was not statistically superior to an IAN block without stimulation.
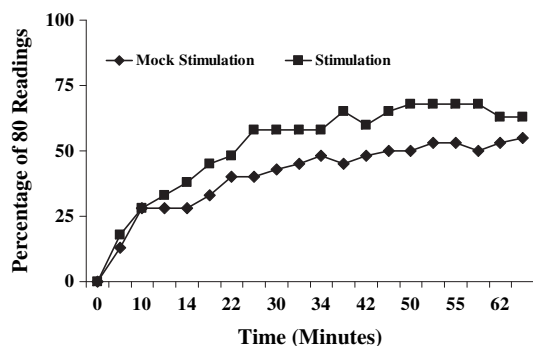
Figure 2. The incidence of lateral incisor anesthesia as determined by the lack of response to electrical pulp testing at the maximum setting (percentage of 80/80s) at each post-injection testing interval for the stimulated and mock stimulated IAN blocks.
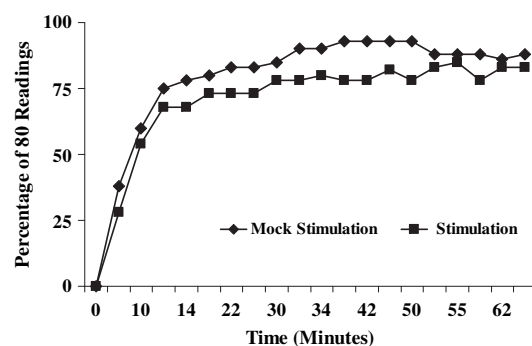
Figure 3. The incidence of first molar anesthesia as determined by the lack of response to electrical pulp testing at the maximum setting (percentage of 80/80s) at each post-injection testing interval for the stimulated and mock stimulated IAN blocks.

Clinical Research

References

1. Nusstein J, Reader A, Beck M. Anesthetic efficacy of different volumes of lidocaine with epinephrine for inferior alveolar nerve blocks. Gen Dent 2002;50:372–5.
2. Cohen HP, Cha BY, Spangberg LSW. Endodontic anesthesia in mandibular molars: a clinical study. J Endod 1993;19:370–3.
3. 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;84:676–82.
4. 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;24:487–91.
5. Kennedy S, Reader A, Nusstein J, Beck M, Weaver J. The significance of needle deflection in success of the inferior alveolar nerve block in patients with irreversible pulpitis. J Endod 2003;29:630–3.
6. Claffey E, Reader A, Nusstein J, Beck M, Weaver J. Anesthetic efficacy of articaine for inferior alveolar nerve blocks in patients with irreversible pulpitis. J Endod 2004;30:568–71.
7. Bigby J, Reader A, Nusstein J, Beck M. Anesthetic efficacy of lidocaine/meperidine for inferior alveolar nerve blocks in patients with irreversible pulpitis. J Endod 2007;33:7–10.
8. Matthews R, Drum M, Reader A, Nusstein J, Beck M. Articaine for supplemental buccal mandibular infiltration anesthesia in patients with irreversible pulpitis when the inferior alveolar nerve block fails. J Endod 2009;35:343–6.
9. Oleson M, Drum M, Reader A, Nusstein J, Beck M. Effect of preoperative ibuprofen on the success of the inferior alveolar nerve block in patients with irreversible pulpitis. J Endod 2010;36:379–82.
10. 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;35:165–8.
11. Aggarwal V, Jain A, Debipada K. Anesthetic efficacy of supplemental buccal and lingual infiltrations of articaine and lidocaine following an inferior alveolar nerve block in patients with irreversible pulpitis. J Endod 2009;35:925–9.
12. Aggarwal V, Singla M, Kabi D. Comparative evaluation of anesthetic efficacy of Gow-Gates mandibular conduction anesthesia, Vazirani-Akinosi technique, buccal-plus-lingual infiltrations, and conventional inferior alveolar nerve anesthesia in patients with irreversible pulpitis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2010;109:303–8.
13. Courtney KR, Kendig JJ, Cohen EN. Frequency-dependent conduction block: the role of nerve impulse pattern in local anesthetic potency. Anesthesiology 1978;48:111–7.
14. Courtney KR. Structure-activity relations for frequency-dependent sodium channel block in nerve by local anesthetics. J Pharm Exp Ther 1980;213:114–9.
15. Fink BR, Cairns AM. Differential use-dependent (frequency-dependent) effects in single mammalian axons: data and clinical considerations. Anesthesiology 1987;67:477–84.
16. Strichartz GR. The inhibition of sodium currents in myelinated nerve by quaternary derivatives of lidocaine. J Gen Physiol 1973;62:37–57.
17. Stevens MF, Klement W, Lipfert P. Conduction block in man is stimulation frequency dependent. Anaesthesist 1996;45:533–7.
18. Watson BV, Brown WF, Doherty TJ. Frequency-dependent conduction block in carpal tunnel syndrome. Muscle Nerve 2006;33:619–26.
19. Scurlock JE, Meymaris E, Gregus J. The clinical character of local anesthetics: a function of frequency-dependent conduction block. Acta Anaesthesiol Scand 1978;22:601–8.
20. Brodin P, Roed A. Inhibition by local anesthetic drugs at low and high stimulation frequencies. Neuropharmacology 1984;23:83–8.
21. Courtney KR. Mechanism of frequency-dependent inhibition of sodium currents in frog myelinated nerve by the lidocaine derivative GEA 968. J Pharm Exp Ther 1975;195:225–36.
22. Simon F, Reader A, Drum M, Nusstein J, Beck M. A prospective, randomized single-blind study of the anesthetic efficacy of the inferior alveolar nerve block administered with a peripheral nerve stimulator. J Endod 2010;36:429–33.
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;13:233–8.
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. 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;87:658–65.
26. Malamed SF. Handbook of Local Anesthesia. 5th ed. St Louis, MO: C.V. Mosby Co; 2004. 231.
27. Bremer G. Measurements of special significance in connection with anesthesia of the inferior alveolar nerve. Oral Surg 1952;5:966–88.
28. Menke RA, Gowgiel JM. Short-needle block anesthesia at the mandibular foramen. J Am Dent Assoc 1979;99:27–30.
29. 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;139:1228–35.