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The effect of inferior alveolar nerve block anesthesia of 4% articaine and epinephrine 1:100,000 on blood flow and anesthesia of human mandibular teeth



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KEYWORDS Inferior alveolar nerve block; Laser-Doppler flow meter; Mandible; Pulpal blood flow	Abstract <i>Background/purpose:</i> Local anesthetics and anesthetic techniques affect the patterns of pulpal blood flow (PBF) and pulpal anesthesia in human teeth. This study aimed to determine PBF changes and pulpal anesthesia of intact mandibular first molars and canines after administration of 4% articaine with epinephrine 1:100,000 using inferior alveolar nerve block (IANB). <i>Materials and methods:</i> Ten healthy subjects received IANB of 4% articaine with epinephrine 1:100,000. Laser Doppler flowmetry and electrical pulp testing were combined to assess PBF changes and pulpal anesthesia of intact mandibular first molars and canines. The data were analyzed using one-way repeated-measures analysis of variance and Student–Newman–Keuls test. <i>Results:</i> IANB with 4% articaine and epinephrine 1:100,000 did not have any significant change in PBF for the first 20 min post injection in mandibular first molars, and for 45 min post injection in the canines ($P > 0.05$). However, a hyperemic response occurred during 25–60 min post injection in the molars, and between 60 and 75 min post injection in the canines ($P < 0.05$). Thereafter, the PBF in both teeth returned to the baseline. Onset of pulpal anesthesia was 8 60 + 2 12 min in the molars, and 9 + 1 94 min in the canines.
	8.60 ± 2.12 min in the molars, and 9 ± 1.94 min in the canines. Duration of pulpal anesthesia was 82.40 ± 41.56 min in the molars, and 84 ± 47.40 min in the canines.

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Conclusion: In case of successful IANB, 4% articaine and epinephrine 1:100,000 caused insignificant changes in PBF up to 30 min but a hyperemic response at later time points. Thereafter, the PBF returned to the baseline.

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Introduction

The inferior alveolar nerve block (IANB) is the gold standard anesthetic technique for inducing anesthesia in mandible.¹ Odor et al.² evaluated the effect of IANB with 2% lidocaine and epinephrine 1:100,000 on pulpal blood flow (PBF) and pulpal anesthesia in mandibular teeth. They found PBF reduction by 42% in mandibular canine and by 24% in mandibular molar, and duration of pulpal anesthesia was 76 min in the canine and 58 min in the molar.² In addition to 2% lidocaine, 4% articaine is frequently used due to its faster onset and longer duration of pulpal anesthesia.³ Like other amide local anesthetics, both 2% lidocaine and 4% articaine possess vasodilatation properties;⁴ therefore, they should be used together with epinephrine as vasoconstrictive adjunct to extend their anesthetic efficacy.^{5,6} However, the vasoconstrictive effect of epinephrine may limit the blood supply to the dental pulp which is enclosed within the rigid tooth structure.⁷ Prolonged reduction in PBF may increase the risk of pulpal ischemia and it may be not safe for pulpal health.⁸ In the study of Sukapattee et al.⁹ who observed the PBF changes in teeth with full coverage crown preparation, they found IANB administration of 4% articaine with epinephrine 1:100,000 did not produce PBF change at 5 min post injection; however, after that the PBF signals were recorded from exposed dentine. not enamel.

To complete explication of the clinical effect of IANB with 4% articaine and epinephrine 1:100,000, both electric pulp testing (EPT) and laser Doppler techniques were used to study the effect of local anesthesia on pulpal anesthesia and pulpal blood flow of mandibular teeth.^{2,7} Hence, the objective of the present study was to determine PBF changes and pulpal anesthesia of mandibular first molars and canines after IANB administration of 4% articaine and epinephrine 1:100,000 in 10 adult human subjects.

Materials and methods

Subjects

The study was approved by the Ethical committee of the Faculty of Dentistry, Mahidol university (COA.No.MU-DT-IRB 2016/029.0606 version 2), and complied with the principles of the Declaration of Helsinki. The study was explained to each subject and each subject gave a written informed consent prior to inclusion in the study. Ten human subjects (5 men and 5 women) with American Society of Anesthesiologists classification 1 (ASA I) physical status, age range 22-37 yr (mean 29.20, S.D. 5.55), intact mandibular teeth

and healthy gingiva were included in the study. The subjects with dental caries, periodontal disease, allergy to 4% articaine or amide type drugs, or being pregnant were excluded from the study.

In case of IANB failure (when an IANB failed to provide pulpal anesthesia), a new subject was recruited for replacement. In this study, all subjects had lip numbness with the IANB, but one subject was excluded and replaced with a new one because of no pulpal anesthesia in the experimental teeth.

Experimental procedures

Following the protocol of Vongsavan et al.⁷ PBF of the mandibular first molars and canines were measured prior to IANB injection as the baseline recordings. Thereafter, PBF changes were monitored at 1, 5, 10, 15, 20, 25, 30 min post injection, and afterwards at 15-min intervals until PBF returned to the baseline. To assess pulpal anesthesia in both teeth, EPT readings were made before IANB injection, at 2, 4, 6, 8, 10 min post injection, and afterwards at 10-min intervals until the tooth sensitivity returned to baseline. Systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) were also monitored by the cardiovascular monitoring device (DASH 4000; GE medical systems, Milwaukee, WI, USA) before injection, at 2, 10 min post injection and subsequently at 20-min intervals until the completion of the study.

Inferior alveolar nerve block anesthesia

After topical anesthesia with 20% benzocaine gel (Precain® B; Pascal, Bellevue, WA, USA) for 1 min, IANB injections of 4% articaine and epinephrine 1:100,000 (Ubistesin™ Forte; 3 M ESPE, Seefeld, Germany) were given using the direct technique (Halstead approach) with standard dental aspirating syringes (Hu-Friedy, Leimen, Germany) and 27-G, 21 mm dental needles (Terumo®, Tokyo, Japan). To avoid undesirable systemic effects of inadvertent intravascular injection,^{10,11} Aspiration was done prior to delivering 1.7 mL of anesthetic solution slowly over 60 s.¹²

Pulpal blood flow assessment

PBF recordings were obtained using a laser Doppler flowmeter (Periflux System 5000; Perimed AB, Järfälla, Sweden) and infrared laser light (wavelength 780 nm) throughout the study. According to the protocol of Vongsavan et al.⁷ the laser probe (type 415–159; external diameter 1.0 mm; optical fiber diameter 0.125 mm, fiber separation 0.25 mm) was inserted into the probe holder (type PH 07–5), incorporated into removable acrylic splint which attached to the opaque black rubber dam (Four D Rubber Co. Ltd., Heanor, England). The probe holder was positioned to ensure that the probe was perpendicular to the buccal-enamel surface of the tooth, with its tip over the central long axis of the crown, and its center at 2 mm above the gingival margin.¹³ After calibration of the probe,¹⁴ the blood flow signals were recorded from the digital output of the LDF machine using a computer running the Perisoft software program version 2.50.⁷

After each experiment, white card measurements were also made to calculate the offset due to noise in the detection system.¹⁴ For each blood flow recording at each test period, the mean and standard deviation values of blood flow were calculated in perfusion unit (P.U.), and the offset was subtracted from the mean.¹³

In 2 subjects, PBF recordings of healthy mandibular contralateral first molars and canines were also made as the controls to confirm no PBF change in un-anesthetized teeth throughout the test period.⁷ This additional PBF recordings verified that the well control procedures were performed such as the subjects were in the same position and the same operating environment throughout the test periods.^{7,13,14}

Electrical pulp testing

An electric pulp tester (SybronEndo; Elements Diagnostic, Orange, CA, USA) was used to assess tooth sensitivity and pulpal anesthesia during the experiment by placing the probe on the middle 1/3 of the buccal surface of the test tooth with fluoride toothpaste as a conducting medium. When the subject felt no response to the maximum signaling (80) of the electrical stimulus, pulpal anesthesia was occurred.^{15,16}

Healthy mandibular contralateral first molars and canines were used as the un-anesthetized controls to ensure that the pulp tester was operating properly and each subject was responding accurately during the study.⁷

Statistical analysis

The data of pulpal anesthesia, pulpal blood flow recordings, systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) were reported as means \pm S.D. (standard deviation). Differences between the means under the different time periods were analyzed using one-way, repeated-measures analysis of variance (one-way RM ANOVA). Where this showed significant differences between



Figure 1 Means and standard deviations (S.D.) of pulpal blood flow values with time in mandibular canines and first molars following inferior alveolar nerve block at time 0. Statistically significant increases (P < 0.05) in *canine and **molar pulpal blood flow compared with baseline value.

the means, the Student-Newman-Keuls test was used to make comparisons between them. *P* values less than 0.05 were considered to be statistically significant.

Results

Pulpal blood flow

After the IANB administration, the PBF in the molars slightly increased from 4.82 ± 1.93 perfusion units (P.U.) before injection to 5.48 ± 1.86 P.U., 5 min post injection. However, this change was not statistically significant (P = 0.537, n = 10). No significant PBF change was recorded in the mandibular first molars of all subjects during the first 20 min post injection (P = 0.080). However, a hyperemia response — a significant rise in blood flow from the baseline level was observed between 25 and 60 min after injection (P < 0.05). The molar blood flow reached the highest values with a peak of 7.65 ± 3.45 P.U. (increased by 58% compared to the baseline values) at 45 min after injection. Thereafter, the blood flow gradually decreased to the baseline.

The canine blood flow decreased from 5.90 ± 4.34 P.U. before injection to 4.69 ± 3.19 P.U., 5 min after injection in every subject, but this change was not statistically significant (P = 0.307). Following that, a gradual increase in the canine blood flow was observed, increasing from

 5.85 ± 4.36 P.U. at 10 min after injection to 7.95 ± 4.99 P.U. at 45 min after injection; however, no significant change was recorded (P = 0.056). A significant rise in PBF in the canines was observed between 60 and 75 min after injection (P < 0.05). The maximum PBF in the canines was 8.35 ± 3.91 P.U. (increased by 41% compared to the baseline values) at 60 min after injection. The blood flow then returned to the baseline. The mean PBF values following the IANB injections are presented in Fig. 1.

Pulpal anesthesia

All un-anesthetized control teeth responded normally to electrical pulp testing throughout the experiments. In anesthetized side of mandibular arch, mean changes in EPT readings in mandibular molars and canines are shown in Fig. 2. Complete pulpal anesthesia was achieved successfully in both mandibular first molars and canines after IANB administration. From 10-min intervals to 40-min intervals, all the subjects had complete pulpal anesthesia in both mandibular first molars and canines (mean EPT reading score = 80, S.D. = 0). The mean onset of pulpal anesthesia in the molars was $8.60 \pm 2.12 \text{ min}$ (n = 10). The mean duration of pulpal anesthesia in the molars was $82.40 \pm 41.56 \text{ min}$. In the canines, the mean onset of pulpal anesthesia was 9.00 ± 1.94) min, and the mean duration of pulpal anesthesia was 84.00 ± 47.40) min.



Figure 2 Means and S.D. of EPT readings with time in mandibular canines and first molars following inferior alveolar nerve block at time 0 * and ** denote significant differences from baseline value (P < 0.001) in mandibular canines and first molars, respectively.



Figure 3 Mean and S.D. values of (a) systolic/diastolic blood pressure (b) Heart rate, recorded at each time interval.

Cardiovascular parameters

The mean \pm S.D. of SBP, DBP and HR recordings are shown in Fig. 3. There were no statistically significant differences with time for SBP (P = 0.957), DBP (P = 0.256), and HR (P = 0.150).

Discussion

The present study demonstrated the effect of IANB of 4% articaine and epinephrine 1:100,000 on blood flow and

anesthesia of mandibular teeth in 10 human healthy subjects. The mandibular molar was chosen as the representative of posterior teeth, and the mandibular canine was used as the representative of anterior teeth in this study.² This study did not perform the long buccal nerve block because the long buccal nerve block can probably mask the effect of inaccurate IANB anesthesia.¹⁷ The results of this study found IANB with 4% articaine and epinephrine 1:100,000 did not induce any significant change in PBF for the first 20 min post injection in mandibular first molar, and for 45 min after injection in the canine. This was then followed by a hyperemic response between 25 and 60 min after injection in the molar, whereas a significant increase in PBF was observed between 60 and 75 min after injection in the canine. Thereafter, the PBF in both teeth returned to the baseline.

In contrast to the study of Odor et al.² they found IANB with 2% lidocaine and epinephrine 1:100,000 caused a reduction in PBF in the ipsilateral mandibular molars and canines. These varying results may be due to the concentration difference in the local anesthetics. Both 2% lidocaine and 4% articaine have almost identical vasodilator properties,⁴ but the doubled concentration in the case of articaine (4%) may enhance more vasodilating action and the local resorption of epinephrine may be facilitated.¹⁸ In the present study, the subjects received IANB, but did not receive the long buccal supplement. Thus, the buccal gingiva lateral to the mandibular molar was not anesthetized,¹ and could have possibly helped to provide normal peripheral blood supply to the dental pulp. This may be another reason why the PBF did not fall.

The results of this study is also in contrast to the results of Vongsavan et al.⁷ who found intraosseous injection with 4% articaine and epinephrine 1:100,000 at distal site of mandibular first molar caused a successful pulpal anesthesia in the first molar with a duration of 38 min and produced a decrease in molar blood flow of 60% with the duration of 31 min, but not in the ipsilateral mandibular canine. Variation in anesthetic techniques may affect the different patterns of PBF and pulpal anesthesia because the anesthetic solutions were placed in different neurovascular relationships. For intraosseous anesthesia, anesthetic solution acts locally on the networks of dental and alveolar nerve plexus, and the epinephrine acts directly on the arterioles supplying the dental pulp.^{1,7} Whereas, in human inferior alveolar nerve block, anesthetic solution is placed in the ptergomandibular space and acts on the neurovascular relationship of inferior alveolar nerve, lingual nerve and inferior alveolar vessels.^{19,20} Thus, IANB anesthesia is able to produce regional block anesthesia of the inferior alveolar and lingual nerves, bringing about a prolonged anesthetic effect in the subjective teeth as well as the ipsilateral mandibular teeth, even though the local anesthetic is placed at far away from the teeth.¹ Although IANB with 4% articaine and epinephrine 1:100,000 did not cause a decrease in the blood flow of mandibular teeth due to the vasodilatation properties of 4% articaine overwhelming the vasoconstrictor effect of epinephrine,^{16,21} but the effect of epinephrine on the inferior alveolar artery likely led to a delayed clearance of the epinephrine and the local anesthetic solution from the affected tissues.^{6,22} Sequentially, this resulted in a prolonged effect of the local anesthetic solution, hampering nervous sensations of the tooth.

A hyperemic response at a later time was observed in mandibular first molars and canines. This transient hyperemic reaction may be due to a pulpal regulatory response, allowing the increase of pulpal blood flow to affected tissues through pulpal vasodilation.²³ This might promote a clearance of local anesthetics. Thereafter, the PBF in both teeth returned to the baseline.

Regarding the onset and the duration of pulpal anesthesia, our results indicate that the onset periods were 8.6 min in the molars and 9 min in the canines, which were almost identical to the results found by Tofoli et al.²⁴ (7 min) and those found by Tortamano et al.³ (7.4 min). Our duration periods were 82 min in the molars and 84 min in the canines, which were higher than those found by Tofoli et al.²⁴ (66 min), but were lower than those found by Tortamano et al.³ (106.6 min). In addition, our study confirmed that a slow IANB injection (60 s) to deposit one cartridge of 4% articaine and epinephrine 1:100,000 did not produce significant changes in blood pressure and heart rate of a healthy subject, due to the low dosage of epinephrine in the anesthetic solution.^{1,25}

In summary, IANB with 4% articaine and epinephrine 1:100,000 produced successful pulpal anesthesia which lasted for 85 min, and caused insignificant changes in PBF up to 30 min but a hyperemic response at a later time was observed in mandibular first molars and canines. Thereafter, the PBF in both teeth returned to the baseline. Thus, this technique of anesthesia can be deemed safe to anesthetize mandibular teeth with normal pulp.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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References

- 1. Malamed SF. *Handbook of local anesthesia*, 6th ed. St Louis: Mosby, 2013.
- Odor TM, Pitt Ford TR, McDonald F. Adrenaline in local anaesthesia: the effect of concentration on dental pulpal circulation and anaesthesia. *Endod Dent Traumatol* 1994;10: 167–73.
- Tortamano IP, Siviero M, Lee S, Sampaio RM, Simone JL, Rocha RG. Onset and duration period of pulpal anesthesia of articaine and lidocaine in inferior alveolar nerve block. *Braz Dent J* 2013;24:371–4.
- 4. Winther JE, Nathalang B. Effectivity of a new local analgesic Hoe 40 045. Scand J Dent Res 1972;80:272-8.
- Paterakis K, Schmitter M, Said Yekta-Michael S. Efficacy of epinephrine-free articaine compared to articaine with epinephrine (1:100 000) for maxillary infiltration, a randomized clinical trial. J Oral Rehabil 2018;45:467–75.
- 6. Sisk AL. Vasoconstrictors in local anesthesia for dentistry. Anesth Prog 1992;39:187–93.
- Vongsavan K, Samdrup T, Kijsamanmith K, Rirattanapong P, Vongsavan N. The effect of intraosseous local anesthesia of 4% articaine with 1:100,000 epinephrine on pulpal blood flow and pulpal anesthesia of mandibular molars and canines. *Clin Oral Invest* 2019;23:673–80.
- 8. Ahn J, Pogrel MA. The effects of 2% lidocaine with 1:100,000 epinephrine on pulpal and gingival blood flow. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1998;85:197–202.

- 9. Sukapattee M, Wanachantararak S, Sirimaharaj V, Vongsavan N, Matthews B. Effect of full crown preparation on pulpal blood flow in man. *Arch Oral Biol* 2016;70:111–6.
- Frangiskos F, Stavrou E, Merenditis N, Tsitsogianis H, Vardas D, Antonopoulou I. Incidence of penetration of a blood vessel during inferior alveolar nerve block. *Br J Oral Maxillofac Surg* 2003;41:188–9.
- Vasconcelos BC, Freitas K, Canuto M. Frequency of positive aspirations in anesthesia of the inferior alveolar nerve by the direct technique. *Med Oral Pathol Oral Cir Bucal* 2008;13:E371–4.
- 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;32:919–23.
- 13. Kijsamanmith K, Timpawat S, Vongsavan N, Matthews B. Pulpal blood flow recorded from human premolar teeth with a laser Doppler flow meter using either red or infrared light. *Arch Oral Biol* 2011;56:629–33.
- Vongsavan N, Matthews B. Some aspects of the use of laser Doppler flowmeters for recording tissue blood flow. *Exp Physiol* 1993;78:1–14.
- **15.** Dreven L, Reader A, Beck M, Meyers WJ, Weaver J. An evaluation of an electric pulp tester as a measure of analgesia in human vital teeth. *J Endod* 1987;13:233–8. 1987.
- Certosimo A, Archer R. A clinical evaluation of the electric pulp tester as an indicator of local anesthesia. *Operat Dent* 1996;21: 25–30.
- 17. Cowan A. Clinical assessment of a new local anesthetic agentcarticaine. Oral Surg 1977;43:174–80.
- **18.** Sack U, Kleemann PP. Intraoral conduction anesthesia with epinephrine-containing local anesthetics and arterial

epinephrine plasma concentration. *Anesth Pain Contr Dent* 1992;1:77-80.

- Khoury JN, Mihailidis S, Ghabriel M, Townsend G. Applied anatomy of the pterygomandibular space: improving the success of inferior alveolar nerve blocks. *Aust Dent J* 2011;56: 112–21.
- Balasubramanian S, Paneerselvam E, Guruprasad T, Pathumai M, Abraham S, Krishnakumar RVB. Efficacy of exclusive lingual nerve block versus conventional inferior alveolar nerve block in achieving lingual soft-tissue anesthesia. *Ann Maxillofac Surg* 2017;7:250–5.
- Willatts DG, Reynolds F. Comparison of the vasoactivity of amide and ester local anaethetics. An intradermal study. Br J Anaesth 1985;57:1006–11.
- 22. Hague C, Gonzalez-cabrera PJ, Jeffries WB, Abel PW. Relationship between $\alpha_{1.}$ adrenergic receptor induced contraction and extracellular signal-regulated kinase activation in the bovine inferior alveolar artery. *J Pharmacol Exp Therapeut* 2002;303:403–14.
- Okabe E, Todoki K, Ito H. Microcirculation: function and regulation in microvasculature. In: *Dynamic aspects of dental pulp*. Dordrecht: Springer, 1990:151–66.
- Tofoli GR, Ramacciato JC, Oliveira PC, Volpato MC, Groppo FC, Ranali J. Comparison of effectiveness of 4% articaine associated with 1:100,000 or 1:200,000 epinephrine in inferior alveolar nerve block. *Anesth Prog* 2003;50:164–8.
- **25.** Throullos ES, Goldstein DS, Hargreaves KM, Dianne RA. Plasma epinephrine levels and cardiovascular response to high administered doses of epinephrine in local anesthesia. *Anesth Prog* 1987;34:10–3.