Articaine (4%) with epinephrine (1:100,000 or 1:200,000) in intraosseous injections in symptomatic irreversible pulpitis of mandibular molars: anesthetic efficacy and cardiovascular effects

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Objective. The aim of this study was to compare the cardiovascular effects and the anesthetic efficacy of intraosseous injections of 4% articaine with 1:100,000 epinephrine (EPI100) or 4% articaine with 1:200,000 epinephrine (EPI200).
Study Design. In this prospective, randomized, double-blind study, 0.9 mL EPI100 and EPI200 solutions were administered for endodontic treatment of mandibular molars with symptomatic irreversible pulpitis in 60 patients. The anesthetic success and pain during anesthesia were evaluated by visual analog scale. The cardiovascular parameters evaluated were heart rate, diastolic/systolic blood pressure, pulse oximetry, and electrocardiogram changes.
Results. Both solutions provided high anesthetic efficacy (96.8% and 93.1% for EPI100 and EPI200, respectively; $P > .05$), and the cardiovascular parameters showed minimal incidences of significant differences throughout the clinical procedure.
Conclusions. The epinephrine concentration did not affect the efficacy of 4% articaine, and both solutions produced a high success level of pulpal anesthesia. Intraosseous delivery by slow speed of injection did not induce significant clinical changes in cardiovascular parameters. (Oral Surg Oral Med Oral Pathol Oral Radiol 2012;xx:xxx)

Effective pain control during endodontic procedures is very important to improve patient care.[1] Pain increases patient stress[2] and can lead to release of endogenous catecholamines that may cause unwanted cardiovascular responses.[3] In addition, anxiety may alter the functional activity of neurons changing the central nervous system's pain process.[1]

The inferior alveolar nerve block (IANB) injection is the most popular technique used to block pain stimulus from mandibular molars. This technique has a high (15%-58%) rate of failure in noninflamed pulps,[4-7] increasing to 44%-81% in symptomatic irreversible pulpitis.[8,9-15]

Several methods have been used to improve the effectiveness of anesthesia in mandibular molars, such as intraosseous (IO) anesthesia (Table I). The use of IO anesthesia bypasses the thick mandibular buccal cortical bone, especially of mandibular molars, enabling the

deposition of the local anesthetic directly into cancellous bone adjacent to the root apices. The success rate of the IO technique has been reported to be 87% compared with 60% for IANB when using 2% lidocaine with 1:100,000 epinephrine.[16] This suggests that IO anesthesia is a useful supplemental technique in symptomatic irreversible pulpitis in mandibular molars.[17] The mandibular cancellous bone is well vascularized and any injected vasoconstrictor could be rapidly absorbed, providing a transitory but reversible increase in heart rate.[18-20] Some studies report that ~80% of patients receiving 2% lidocaine with 1:100,000 epinephrine for IO anesthesia experience heart rate increase.[5,21]

Anesthetic solutions of 4% articaine with lower concentrations of epinephrine (1:200,000) for IO injection have not been fully studied. To the best of our knowledge, no study has compared the anesthetic efficacy and cardiovascular effects of 4% articaine with 2 epinephrine concentrations (1:100,000 or 1:200,000) delivered by IO anesthesia in a patient population. The aim of the present study was to evaluate the anesthetic efficacy

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Statement of Clinical Relevance

To evaluate the anesthetic efficacy of intraosseous injections (IO) of 4% articaine associated with different concentrations of epinephrine and their influence in cardiovascular parameters.

Table I. Characteristics of earlier intraosseous anesthesia studies

Author	n	IO anesthesia	Anesthetic solution	Volume (mL)	Injection speed	Success rate
Lilienthal and Reynolds, 1975	*	Primary	2% lidocaine with 1:80,000 epinephrine	0.9	30-45 s	Not cited
Lilienthal, 1976	9	Primary	4% prilocaine with 1:200,000 epinephrine	0.9	30 s	Not cited
Cannell and Cannon, 1976	2	Primary	2% lidocaine with 1:80,000 epinephrine	1.0	30 s (bolus)	Not cited
Coggins et al., 1996	40	Primary	2% lidocaine with 1:100,000 epinephrine	1.8	Not cited	75% mandibular first molar
Dunbar et al., 1997	40	Supplemental	2% lidocaine with 1:100,000 epinephrine	1.8	<30 s	90%
Nusstein et al., 1998	33	Supplemental	2% lidocaine with 1:100,000 epinephrine	1.8	>1 min	82%
Replogle et al., 1999	42	Primary	2% lidocaine with 1:100,000 epinephrine	1.8	>2 min	74%
			3% mepivacaine	1.8	>2 min	45%
Guglielmo et al., 1999	40	Supplemental	2% mepivacaine with 1:20,000 levonordefrin	1.8	>2 min	100% mandibular first molars, 100% mandibular second molar
			2% lidocaine with 1:100,000 epinephrine	1.8	>2 min	100% mandibular first molars, 100% mandibular second molar
Gallatin et al., 2000	48	Supplemental	3% mepivacaine	1.8	>1 min	100% mandibular first molars
Stabile et al., 2000	48	Supplemental	1.5% etidocaine with 1:200,000 epinephrine	1.8	Not cited	100%
Gallatin et al., 2003	41	Primary	2% lidocaine with 1:100,000 epinephrine	1.8	>1 min	93% mandibular first molars, 95% mandibular second molars
Nusstein et al., 2005	40	Primary	2% lidocaine with 1:100,000 epinephrine	1.8	>2 min	98%
Bigby et al., 2006	37	Supplemental	4% articaine with 1:100,000 epinephrine	1.8	>1 min	86% mandibular molars
Remmers et al., 2008	15	Primary	2% lidocaine with 1:100,000 epinephrine	1.8	60 s	87%
Sixou et al., 2008	107	Primary	2% articaine with 1:200,000 epinephrine	0.8	Not cited	87.9%
Susi et al., 2008	61	Primary	2% lidocaine with 1:100,000 epinephrine	1.4	45 s, 4.75 min	Not cited
Jensen et al., 2008	55	Primary	2% lidocaine with 1:100,000 epinephrine	1.4	4.75 min	100% mandibular first molars, 94% mandibular second molar

*Description of the principles, armamentarium, and technique.

and the cardiovascular parameters of IO injections of 4% articaine with 1:100,000 or 1:200,000 epinephrine in patients with symptomatic irreversible pulpitis in a mandibular molar.

MATERIALS AND METHODS
This study was approved by the Ethical Committee of the School of Medical Science at the University of Campinas (no. 531/2008). Written informed consent was obtained from every subject.

Sixty adult patients (n = 60) participated in this prospective, randomized, double-blind clinical study. Inclusion criteria included: presence of ≥1 mandibular molar with symptomatic irreversible pulpitis respon-

sive to an electronic pulp tester (Sybron Endo; Elements Diagnostic, Orange, CA, USA), age 18-55 years, and presenting with good health (ASA I and II). Exclusion criteria included pregnancy, history of allergy to the components of the local anesthetic solutions, and local anesthesia in the region ≤2 weeks before the experiment. An individual not involved with the study, removed the cartridge labels and coded the solutions (A or B) before the beginning of the trial. The same person randomized the anesthetic sequence. The sequence of patient care was done according to the demand for endodontic urgent care.

This controlled, double-blind, randomized study was performed with 2 groups: one group received IO anesthe-

sia with 0.9 mL 4% articaine with 1:100,000 epinephrine (EPI100; Septanest with 1:100,000 epinephrine; Septodont, France); and the other group received IO anesthesia with 0.9 mL of 4% articaine with 1:200,000 epinephrine (EPI200; Septanest with 1:200,000 epinephrine).

Ten minutes before the IO anesthesia, 2 cardiovascular monitoring systems were connected to the subject. A multiparametric monitor system (DX 2021; Dixtal Biomedica, Brazil) automatically measured and recorded heart rate (HR), noninvasive diastolic blood pressure (DBP), systolic blood pressure (SBP), and oxygen saturation (SpO_2). These initial recordings were considered to be baseline. After intraosseous anesthesia, HR and SpO_2 were registered every minute after injection for 5 minutes and then every 5 minutes until the end of endodontic treatment. A digital system (Digital CardioFlash System; Cardios Systems, São Paulo, Brazil) recorded electrocardiogram (ECG) during the whole procedure. Three scales were used to assess the patient's anxiety before initiating treatment: a visual analog scale (VAS), a faces pain scale (FPS), and the Corah anxiety scale. Pulpal response was determined by electronic pulp tester before the anesthetic injection. The baseline sensitivity was considered to be the average of 3 consecutive measures (with 2-minute intervals).

The anesthetic procedure began with a topical application of 20% benzocaine gel for 1.5 minutes at the point of perforation. An injection of 0.45 mL (one-fourth of a cartridge) of the same anesthetic solution designed for the IO anesthesia (following the sequence previously determined) was made into the mandibular molar buccal mucosa with a Carpule syringe. A 27-gauge needle was inserted perpendicularly to the mucosa, with the flat part of the bevel facing the mucosal surface, 1-3 mm below the distal septum and adjacent to the tooth to be anesthetized. After 2 minutes, the cortical perforation was performed using the intraosseous technique.[18] Briefly, 2 lines crossing at a 90° angle were considered: one horizontal, running along the buccal gingival margins of teeth, and one vertical, bisecting the distal interdental papilla of the tooth to be anesthetized. The point of penetration was 2 mm in the apical direction from the intersection of vertical and horizontal lines.

The X-Tip system (X-Tip Technologies, Lakewood, NJ, USA) was used to perforate the cortical bone and deliver the anesthetic. The X-Tip system perforator/guide sleeve was placed in a handpiece. The perforator was pushed through the gingiva until the X-tip contacted the bone. Holding the drill at a 90° angle to the bone, the slow-speed handpiece was activated in a series of short bursts, using light pressure, until a breakthrough was felt or until 2-5 seconds elapsed. The handpiece was continuously activated while the perforator was within bone to prevent lodging or breakage that can occur if the perforator stops its rotation. After perforation, the drill was withdrawn from the guide sleeve, leaving this guide in place.

A 0.9 mL quantity of the anesthetic solution was slowly (~0.45 mL/min) injected into cancellous bone using a dental syringe (SS White Duflex, Rio de Janeiro, Brazil) and an X-Tip 27-gauge needle. If minor leakage of anesthetic solution was observed, the needle was repositioned.

After the IO injections, the pulp tester was applied every 2 minutes until the maximum reading (80) was achieved without sensation, allowing the clinical procedure to begin. The onset of pulpal anesthesia was considered to be the time from the end of injection to the first of 2 consecutive readings of 80 without response. Anesthetic success was considered to be when endodontic treatment was finished without pain or supplemental anesthesia. Teeth presenting an anesthetic onset time of >10 minutes or a patient reporting pain during treatment were considered to be anesthetic failures.

Volunteers were asked to record the pain associated with IO injection (needle insertion and anesthetic solution deposition) on a 100-mm VAS, ranging from 0 = "no pain" to 100 = "unbearable pain." VAS was completed immediately after the anesthesia, before the beginning of endodontic treatment. Both endodontic treatment and IO anesthesia were performed by a single experienced endodontist. All endodontic treatments were performed in a single visit.

The Bartlett test was used to assess variance homogeneity, and the Kolmogorov and Smirnov test to assess data distribution. Mann-Whitney test was used to assess the differences on time to complete the endodontic treatment, onset of pulpal anesthesia, and pain during cortical bone perforation. The anesthesia success rate was assessed by Fisher exact test.

Data of heart hate, SpO_2, and blood pressure were submitted to Shapiro-Wilk tests to verify similarity of variances and normal distribution. Two-factor analysis of variance (ANOVA) and Tukey tests were used to observe intra- and intergroup differences regarding heart hate, SpO_2 and blood pressure. All analysis was carried out using Systat 12/2/00. The level of significance was also set at 5%.

RESULTS

Table II shows age, sex, health, and anxiety profiles of the subjects for both treatments. There were no statistically significant differences ($P > .05$) between groups for sex or anxiety. However, subjects were older in the EPI200 group. This group also showed a

Table II. Distribution of age, sex, health, and anxiety profiles of the subjects according to the groups

| Profile	EPI 100	EPI 200	P value	Statistical test
n	31	29	—	—
Age, y	33.4 ± 2.1	41.0 ± 2.0	.0093	Mann-Whitney
Sex	Male = 19 (61.3%)	Male = 17 (58.8%)	.6955	chi-square
	Female = 12 (38.7%)	Female = 12 (41.4%)		
Health	ASA I = 30 (96.8%)	ASA I = 23 (79.3%)	.0490	Fisher exact
	ASA II = 1 (3.2%)	ASA II = 6 (20.7%)		
VAS, cm [median (first-third quartiles)]	3 (2-6)	4 (3-6)	.5104	Mann-Whitney
FPS [median (first-third quartiles)]	2 (1-3)	2 (1-2)	.5944	Mann-Whitney
Corah anxiety scale [median (first-third quartiles)]	9 (6.5-12.5)	9 (7-12)	.9764	Mann-Whitney
Pain (previously treatment)	4 (2.5-6)	4 (3-7)	.6307	Mann-Whitney
VAS during perforation	1 (0—1)	1 (0—1)	.7673	Mann-Whitney
Latency period (min)	2^{2-2}	2^{2-2}	.8072	Mann-Whitney
Anesthesia success	30/31 (96.8%)	27/29 (93.1%)	.6059	Fisher exact
Time of treatment (min)	85 (75-90)	90 (80-110)	.0771	Mann-Whitney

VAS, visual analog scale; *FPS,* faces pain scale.
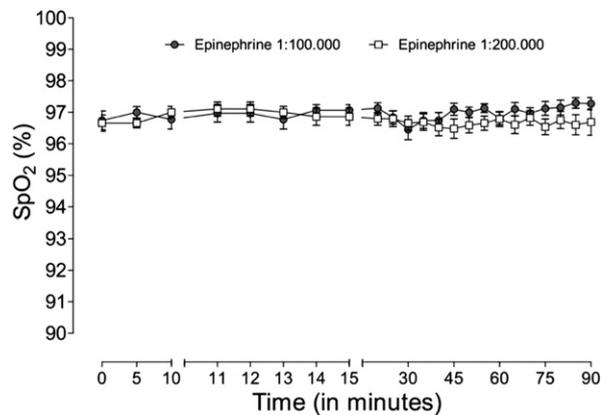
Fig. 1. Mean (±SD) of the percentage of partial oxygen saturation (SpO_2) according to the groups.

Fig. 2. Mean (±SD) heart rate according to the groups. *Statistically significant differences ($P < .05$) between groups.

higher number of ASA II subjects than the EPI100 group.

The average time to complete the whole procedure was 90.4 (±18.6) minutes, and no statistically significant differences ($P = .0771$; Mann-Whitney test) were found between the groups. The median onset of pulpal anesthesia was 2 minutes for both groups ($P = .8072$; Mann-Whitney test). Both groups showed a median score of 1 for pain during cortical bone perforation ($P = .7673$; Mann-Whitney test; Table II).

The success of the IO technique did not differ between groups ($P = .6059$; Fisher exact test). Articaine with 1:100,000 epinephrine was effective in 96.8% of the subjects (30/31) and articaine with 1:200,000 epinephrine produced successful pulpal anesthesia in 93.1% of the subjects (27/29; Table II).

Postoperative discomfort included 1 case of mucosa abscess at the perforation site 3 days after EPI100 anesthesia and 1 case of broken X-Tip guide, which was easily removed.
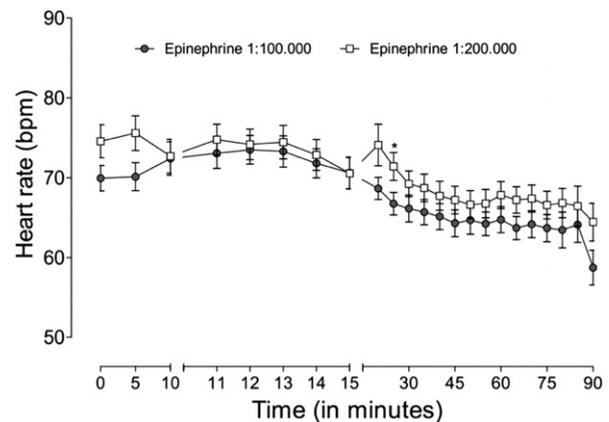
Figures 1-3 show the results of the SpO_2, HR, and blood pressure recordings. Considering SpO_2, no statistically significant differences ($P > .05$) were observed between groups or with time. Heart rate differences between groups occurred only within 20 minutes (ANOVA: $P < .05$). There were no statistically significant differences ($P > .05$) within treatments for both SBP and DBP. The 1:100,000 epinephrine group showed lower ($P < .001$) SBP at 30 minutes. For DBP, there were statistically significant differences between groups at 15, 20, 25, and 30 minutes ($P < .001$).

The ECG changes recorded were 3 and 2 ventricular ectopic episodes for the EPI100 and EPI200, respectively ($P > .05$; Mann-Whitney) and 2 supraventricular ectopic episodes, 1 episode in each group ($P > .05$; Mann-Whitney).

DISCUSSION
Some alternative techniques, such as Gow-Gates and Vazirani-Akinosi, have been associated with a higher success rate than the conventional IANB.[22-24] Although
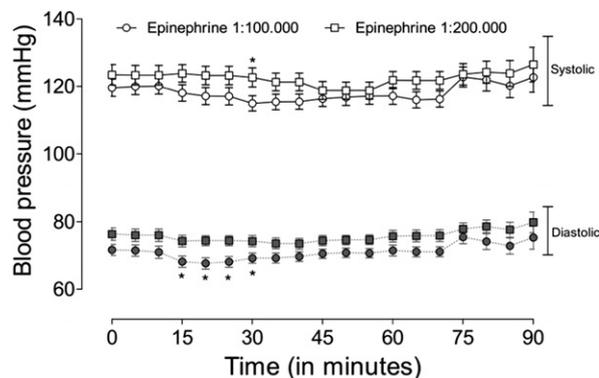
Fig. 3. Mean (±SD) of noninvasive systolic/diastolic blood pressure. *Statistically significant differences ($P < .05$) between groups.

Aggarwal et al. (2010)[25] showed that Gow-Gates technique may increase the success rates in patients with irreversible pulpitis compared with conventional IANB, none of these 2 techniques provided acceptable success rates. In addition, Gow-Gates and Vazirani-Akinosi IANB techniques did not show better results than traditional IANB in vital and asymptomatic teeth.[26] These techniques can also cause more complications in important anatomic structures owing to the needle deep penetration.[27]

Intraligamentary anesthesia (IA) is one of the most used supplementary technique when IANB fails. According to Childers et al.,[6] although the association of IANB with IA could improve the pulpal anesthesia in mandibular first molar, it was effective only for a short period of time (23 minutes) after injection.

Although articaine has been described as a safe local anesthetic in the dental armamentarium, there have been reports suggesting that articaine use is associated with higher rates of paresthesia. Haas and Lennon[28] conducted a 21-year retrospective study of paresthesia of the lingual and inferior alveolar nerves after mandibular block injections and restorative procedures. They authors concluded that the use of articaine and prilocaine was associated with an elevated risk of paresthesia. However, when considering the IO administration of articaine, earlier studies did not show the occurrence of paresthesia in the patients evaluated.[29,30] In the present study also, we did not observe paresthesia.

Teeth with irreversible pulpitis, especially mandibular molars, are more difficult to be anesthetize.[8,9,12,15,18,31,32] The inclusion criteria for both groups in the present study included the presence of ≥1 mandibular molar with irreversible pulpitis and a positive response to the pulp tester. Thus, groups did not differ regarding pulpal diagnosis, despite randomization to the EPI200 group showing a higher age and number of ASA II patients than the EPI100 group, and

thus the groups were not perfectly matched regarding these parameters.

The efficacy of IO anesthesia reported in the present study is similar to that reported by other authors, as presented in Table II,[5,9,16,19,21,33] which confirms the high success rate of this anesthetic technique. The onset of pulpal anesthesia observed for both groups in the present study was also similar to previous reports,[33] which used the same IO system, despite the use of other local anesthetic solutions.

Some studies[5,19,20,34] have reported that the IO injection of epinephrine-containing solutions produces a transient but perceptible heart rate increase. In the present study, the cardiovascular parameters did not change significantly (clinically or statistically) during the intraosseous injections, regardless of the vasoconstrictor dose (9 or 4.5 μg). Another report[35] showed no significant changes in the heart rate after a slow IO injection (1.4 mL 2% lidocaine with 1:100,000 epinephrine injected over 4.75 minutes). In the present study, the combination of a small amount of local anesthetic solution (0.9 mL) and the slow speed of injection (0.45 mL/min) could be responsible for absence of clinically significant cardiovascular effects.

The American Heart Association considers an HR of 60-80 beats/min to be physiologically normal under resting conditions for an adult. Because of the presence of more ASA II patients in EPI200, the basal HR was slightly higher than EPI100. However, this difference had no statistical or clinical significance, because they were within the normal physiologic range.

A significant difference in HR between groups was noted at 30 minutes. Nevertheless, in both studied groups, the HR never exceeded 80 beats/min at any measured time, which means that no clinically significant increase in HR occurred. Susi et al.[35] related similar findings, which they attributed to the slow rate of anesthetic solution administration (1.4 mL over 4 minutes 45 s of 2% lidocaine with 1:100,000 epinephrine).

Although no statistically differences occurred during and immediately after IO injection, the EPI100 group presented an ascendant curve on the HR graph during IO anesthesia and 3 minutes after with a very small increase in heart rate. The EPI200 showed more stability of HR.

Sympathetic stimulation influences HR. This is mediated by endogenous release of epinephrine/norepinephrine and its activity on β-adrenergic receptors accelerating the slow diastolic depolarization. Pain and stress, such as endodontic treatment, releases endogenous catecholamines, causing undesirable cardiovascular activity and, in some cases, leading to a medical emergency.[3] All scales indicated that the level of anx-

iety of the subjects in the present study was mild to moderate, and this was reflected in the initial cardiovascular parameters.

After 20 minutes, both groups showed a decrease in HR. At this time of treatment, the anesthesia, the use of a high-speed handpiece, and endodontic access, which are the worst stimulus of the endodontic treatment, were completed. The high level of pain control achieved with the IO anesthesia produced comfortable treatment.

Both endogenous and exogenous epinephrine affects not only the HR but also the blood pressure. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure has defined hypertension as SBP >140 mm Hg and DBP >90 mm Hg. A number of studies have reported that blood pressure is usually stable after administration of anesthetic solutions with epinephrine during nerve blocks or infiltrations.[36-39] Other authors[40,41] have noted increases in blood pressure after administration of 2% lidocaine with 1:80,000 epinephrine during both blocks or infiltrations. Rapid intraosseous injections (0.9 mL) with 2% lidocaine with 1:80,000 epinephrine have been shown to increase blood pressure.[19]

Arterial blood pressure remained stable during all treatment times, and none of the subjects showed blood pressure >140/90 mm Hg at any time. However, some significant differences between groups were noted in both SBP and DBP. These differences were not clinically relevant, because at all time the values remained within the normotensive limits defined above.

Ventricular ectopic beats (VEBs) are common and usually benign.[42] VEBs are detected by standard ECG in 1% of asymptomatic people and in 40%-75% of apparently healthy subjects submitted to 24-48-hour ambulatory ECG recording.[43] The VEBs' significance has been controversial.[44]

In the present study, VEBs corresponded to <1% of total QRS segments: 3 subjects (34 episodes in 21,879 QRS segments) in the EPI100 group and 2 subjects (3 episodes in 10,150 QRS segments) in the EPI200 group. Some of these VEBs (2 subjects in EPI100 and 1 in EPI200) occurred before the start of IO injection. They cannot be attributable to an effect of the anesthetic solution. One EPI100 subject presented VEB episodes 53 minutes after IO. One EPI200 patient group presented just 1 VEB episode 10 minutes after IO. The postanesthesia VEB episodes on both groups occurred a long time after anesthesia and can not be related to effects of the infiltration or IO injections.

Excessive supraventricular ectopic beats (ESVEBs) may increase the risk of atrial fibrillation and stroke. The number of ESVEBs corresponded to <1% of total QRS segments (119 from 12,162 episodes), being observed only before both buccal and IO injections in 2 subjects (1 per group). Because these episodes were <30 per hour, they had no clinically significance.[45]

CONCLUSION

The epinephrine concentration did not affect the efficacy of IO anesthesia with 4% articaine in mandibular molars with symptomatic irreversible pulpitis. Both anesthetic solutions tested promoted a high success level of pulpal anesthesia, allowing the accomplishment of painless endodontic treatment in 95% of the cases (57/60). IO anesthesia with a small amount (0.9 mL) of 4% articaine, with either 1:100,000 or 1:200,000 epinephrine, delivered by slow speed of injection (0.45 mL/min), did not induce clinically significant changes in HR, SBP, DBP, SpO$_2$, and ECG parameters.

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