Original Article

pISSN 2383-9309 ▮ eISSN 2383-9317
J Dent Anesth Pain Med 2015;15(4):201-205 ▮ http://dx.doi.org/10.17245/jdapm.2015.15.4.201

Articaine (4%) with epinephrine (1:100,000 or 1:200,000) in inferior alveolar nerve block: Effects on the vital signs and onset, and duration of anesthesia

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Background: This prospective, randomized, double-blind, clinical study was conducted to compare the effects of 4% articaine with 1:100,000 epinephrine (A100) and 4% articaine with 1:200,000 epinephrine (A200) on the vital signs and onset and duration of anesthesia in an inferior alveolar nerve block (IANB).
Methods: In the first appointment, an IANB was performed by injecting A100 or A200 in 1 side of the mouth (right or left) randomly in patients referred for extraction of both their first mandibular molars. In the second appointment, the protocol was repeated and the other anesthetic solution was injected in the side that had not received the block in the previous session. Systolic and diastolic blood pressures (SBP and DBP) and pulse rate were measured during and 5 min after the injection. The onset and duration of anesthesia were also evaluated. Data were analyzed using t-test and Mann-Whitney U-test, and p-value was set at 0.05.
Results: SBP and pulse rate changes were slightly more with A100; however, DBP changes were more with A200, although the differences were not significant ($P > 0.05$). There were no statistically significant differences in the parameters evaluated in this study. The onset and duration of anesthesia, and the changes in SBP, DBP, and pulse rate during and 5 min after the injection were the same in both the groups.
Conclusions: For an IANB, A200 and A100 were equally efficient and successful in producing the block. Epinephrine concentration did not influence the effects of 4% articaine.

Key Words: Alveolar nerve, inferior; Articaine; Epinephrine; Local anesthetics; Vital signs.

INTRODUCTION

Pain control with local anesthetics is important during dental surgeries [1]. A local anesthetic injection allows painless treatment in the oral cavity; however, it provokes anxiety and fear in the patients, which is one of the main reasons for dental anxiety [2]. Each dentist in Canada injects approximately 1,800 cartridges of local anesthetics yearly [1]. Successfully administered local anesthesia allows the dentist to build a relationship with the patient, proceed with the appointment, and successfully complete the therapeutic procedure [3]. An inferior alveolar nerve block (IANB) is the most popular technique used to block pain stimulus from the mandibular molars [4].

Articaine (Carticaine) is one of the most recently developed local anesthetic drug available to dentists worldwide [5]. Articaine hydrochloride was developed by Rusching et al. in 1969 [6] and approved for use in the United States in April 2000 [7,8]. Articaine accounted

Received: 2015. December. 7. • Revised: 2015. December. 19. • Accepted: 2015. December. 22.
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for about 25% of the total dental anesthetic sales in the United States in 2007 [9]. Considering the pharmacokinetics/pharmacodynamics, the duration of soft tissue anesthesia in a nerve block with 1.8 ml of 4% articaine was 4.3–5.3 h [10]. The plasma half-life of articaine is short, approximately 20 min. The maximum dose of 4% articaine as a local anesthetic solution in a healthy adult weighing 70 kg is 7 carpules (1.7 ml) [11].

Vasoconstrictors are beneficial in dentistry when used with local anesthetics. There are clear indications for their use, among which improving the depth and duration of anesthesia are most important. Without them, many local anesthetic solutions would have a short duration of intraoral action [12]. Adding a vasopressor also has other benefits such as retarding the absorption of articaine leading to prolonged maintenance of its active tissue concentration, minimizing the systemic absorption of both the active compounds (articaine and epinephrine) [6], reducing systemic toxic effects, and providing hemostasis [12].

The most common vasoconstrictor is epinephrine, which is available in formulations of 1:50,000, 1:100,000, and 1:200,000. However, its cardiovascular effects should be considered before its use [13]. Epinephrine can be used for most dental procedures; however, it may be necessary to minimize the dose for patients receiving specific medications and for those with cardiovascular disease [13,14]. Epinephrine causes vasoconstriction by stimulation of α1 receptors in the mucous membranes. However, it also stimulates the β1 receptor in the heart, increasing the heart rate and the oxygen consumption and strength of contraction of the myocardium, and the β2 receptors, which causes vasodilation in the skeletal muscle [12].

Many studies regarding the hemodynamic effects of dental anesthesia using epinephrine-containing local anesthetic solutions in young healthy patients have been conducted. The aim of this prospective, randomized, double-blind, clinical study was to compare the effects of 4% articaine with 1:100,000 epinephrine (A100) and 4% articaine with 1:200,000 epinephrine (A200) on the vital signs and onset and duration of anesthesia in an IANB.

MATERIALS AND METHODS

Twenty adult patients (10 men and 10 women), with a mean age of 38.3 ± 11.3 years (range, 18–50 years), participated in this prospective, randomized, double-blind, clinical study. These patients had been admitted to the Department of Oral and Maxillofacial Surgery, Dental Branch, Azad University, Tehran, Iran between 2014 and 2015 for the extraction of both the first mandibular molars. The study was approved by the Committee of the Ethics of Research on Human Beings of the Craniomaxillofacial Research Center, Azad Islamic University, Tehran, Iran. It was conducted in accordance with the guidelines of the Declaration of Helsinki. Informed consent was obtained from each patient. The exclusion criteria were as follows: systemic conditions in which injection of articaine with epinephrine is contraindicated [15], pregnancy, use of medications (over-the-counter pain-relieving medications, narcotics, sedatives, antianxiety, or antidepressants) that could affect anesthetic assessment, history of psychiatric illness, allergy to the components of the local anesthetic solutions, and local anesthesia in same region < 2 weeks before the experiment.

The procedures were performed during 2 separate appointments. In the first session, the side of the mouth for administering the IANB (right or left) and the type of anesthetic solution (A100 and A200) (Primacaine, Pierre Rolland, Bordeaux, France) were chosen randomly. This information was recorded. The surgeon and patient were blinded about the type of anesthetic solution administered. The injection was administered using an aspirating syringe (Aspirating Syringes, KAS A; Shanghai Kangqiao Dental Instruments Factory, Shanghai, China) with a long needle (27Gauge: 30 mm; Pierre Rolland, France). The timings of the onset (tingling or numbness of the lower lip indicated anesthesia of the inferior alveolar nerve) [15] and the end of anesthesia were recorded using a stop watch, and the duration of anesthesia was calculated. The SBP and DBP were

measured by means of an automatic digital manometer, Visomat (Zum Ottersberg, Wertheim, Germany), before the injection and 5 min later. In the second session, 7 days later, the protocol was repeated and the other anesthetic solution was injected in the other side, which had not received the injection in the previous session. Data were analyzed using the T-test and Mann–Whitney U-test. P-value was set at 0.05.

RESULTS

In a crossover design, 20 subjects received 2 sets of IANB during 2 separate appointments spaced 1 week apart. The SBP, DBP, pulse rate, and the onset and duration of anesthesia were evaluated for each patient during and 5 min after the injection. Table 1 shows the values of the parameters.

1. SBP

Changes in the SBP during and 5 min after the injection were a slightly more with A100; however, the difference between the 2 groups, A100 and A200, was not statistically significant (P = 0.4).

2. DBP

Changes in the DBP were slightly more with A200 than with A100. Changes of DBP during and 5 min after the injection were the same in each group of A100 and A200 (P = 0.8).

3. Pulse rate

Pulse rate with A100 was a slightly more than with A200. Changes of this parameter were the same in both groups and there was no difference between them (P = 0.6).

4. Onset of anesthesia

It was in approximately 2 min and 1.4 min for A200 and A100, respectively. The difference was not statistically significant (P = 0.9).

5. Duration of anesthesia

It was approximately 4 h with both, A100 and A200, with no statistically significant difference (P = 0.8).

DISCUSSION

Administration of a local anesthetic with a vasoconstrictor is a known method in decreasing the systemic toxicity, increasing the duration of anesthesia, and providing hemostasis during surgery [15]. Articaine with epinephrine is one of the most commonly used anesthetic worldwide [5]; however, epinephrine containing anesthetics may cause unwanted effects on the blood pressure, pulse rate, and hemodynamic condition of the patient; these effects were evaluated in this study. This study had a crossover design, which was advantageous because each patient acted as his own control. Thus, the individual characteristics of each patient did not influence the results of the study.

Hersh et al. compared the pharmacokinetic and cardiovascular effects of 11.9 ml A100 with the effects of 11.9 ml A200. They found that the short-term cardiovascular effects (increase in heart rate and SBP) were significant with A100 than with A200 [16]. These results demonstrated the effects of a larger volume of the local

Table 1. The vital parameters and changes in on them with different anesthetic drugs

	SBP (mmHg)		DBP (mmHg)		Pulse rate (beats/min)		Onset of anesthesia (min)	Duration of anesthesia (min)
	during injection	after 5 min	during injection	after 5 min	during injection	after 5 min		
A100	−1.9 (8.21)	−2.75 (9.08)	0.25 (4.75)	−1.2 (5.14)	2.35 (7.76)	1.75 (7.46)	1.4 (0.42)	235.5 (13.32)
A200	−1.2 (6.33)	−0.45 (8.40)	−0.35 (5.63)	−1.35 (5.91)	−0.7 (9.40)	−1.5 (5.59)	2 (0.45)	230 (14.10)
P-value	P = 0.9	P = 0.4	P = 0.9	P = 0.8	P = 0.6	P = 0.8	P = 0.9	P = 0.8

SBP: systolic blood pressure; DBP: diastolic blood pressure; A100: 4% articaine with 1:100,000 epinephrine; A200: 4% articaine with 1:200,000 epinephrine.

anesthetic.

Troullos et al. also reported a greater increase in the heart rate with larger volumes of epinephrine containing anesthetic formulations (8 cartridges of A100) [17]. Therefore, it can be concluded that increasing the amount of epinephrine in a nerve block injection increases the differences in the effects of A100 and A200. Hence, the likelihood of an increase in the heart rate or blood pressure (hemodynamic changes) with articaine containing epinephrine is dose-dependent. Regarding vasoconstriction with epinephrine, in low dosages, its absorption in the blood is slow but its hydrolysis is fast; therefore, the hemodynamic changes caused by it are not significant in these dosages that are used in routine dental procedures [15].

Few studies have reported that the blood pressure is usually stable after administration of anesthetic solutions containing epinephrine during nerve blocks or infiltrations [18-20]. Our current study supports the results of previous human studies. Knoll-Köhler reported no differences in the effects of A100 and A200 (containing 4 ml [160 mg] of 4% articaine hydrochloride) on the heart rate or blood pressure of patients undergoing extraction of an impacted lower third molar [21]. Tofoli et al. [22] and Santos et al. [23] found that the efficacy of A100 was equivalent to that of A200 in inferior alveolar nerve blocks. Moore et al. found no differences in the cardiovascular effects of A100 and A200 on using 1 cartridge volume for IANB [24]. It can be concluded that there were no significant hemodynamic changes on administration of 1 cartridge of the local anesthetic for IANB with negative aspiration in healthy patients.

In our study, the time taken for the onset of anesthesia was 1.4 and 2 min with A100 and A200, respectively. In previous studies, the time taken for onset was approximately 2–2.5 min with A100 and 2.5–3 min with A200 [15]. The duration of soft tissue anesthesia in a nerve block with 1.8 ml of 4% articaine was reported to be 4.3–5.3 h [10]. These results of the onset and duration of anesthesia are similar to the results of our study.

In conclusion, there was no significant difference in the onset and duration of anesthesia between 1 cartridge volume of A100 and A200. Therefore, in operations requiring a larger amount of anesthetic solutions, A200 should be preferred in healthy patients; however, it may be necessary to minimize the dose for patients receiving specific medications and for those with cardiovascular disease. Thus, A200 might be preferable in patients with cardiovascular disease and in those taking drugs that enhance the systemic effects of epinephrine.

Declaration of interests: The authors deny any conflicts of interest related to this study.

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