Comparison of Injection Pain, Heart Rate Increase, and Postinjection Pain of Articaine and Lidocaine in a Primary Intraligamentary Injection Administered With a Computer-Controlled Local Anesthetic Delivery System

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The purpose of this prospective, randomized, double-blind study was to compare the pain of injection, heart rate increase, and postinjection pain of the intraligamentary injection of 4% articaine with 1:100,000 epinephrine and 2% lidocaine with 1:100,000 epinephrine administered with a computer-controlled local anesthetic delivery system. Using a crossover design, intraligamentary injections of 1.4 mL of 4% articaine with 1:100,000 epinephrine and 1.4 mL of 2% lidocaine with 1:100,000 epinephrine were randomly administered on the mesial and distal aspects of the mandibular first molar with a computer-controlled local anesthetic delivery system in a double-blind manner at 2 separate appointments to 51 subjects. The results demonstrated the incidence of moderate pain was 14%–27% with needle insertion, with 0%–4% reporting severe pain. For solution deposition, moderate pain was reported 8%–18% of the time, with no reports of severe pain. There were no significant differences between the articaine and lidocaine solutions. Regarding heart rate changes, neither anesthetic solution resulted in a significant increase in heart rate over baseline readings. On day 1 postinjection, there was a 31% incidence of moderate/severe pain with the articaine solution and 20% incidence of moderate/severe pain with the lidocaine solution. The moderate/severe pain ratings decreased over the next 2 days. There were no significant differences between the articaine and lidocaine solutions. We concluded that the intraligamentary injection of 4% articaine with 1:100,000 epinephrine was similar to 2% lidocaine with 1:100,000 epinephrine for injection pain and postinjection pain in the mandibular first molar when administered with a computer-controlled local anesthetic delivery system. For both anesthetic solutions, heart rate did not significantly increase with the intraligamentary injection using the computer-controlled local anesthetic system.

Key Words: Articaine; Lidocaine; Intraligament injection; Heart rate; Wand.

Articaine has a reputation of providing an improved local anesthetic effect.[1] Articaine was approved for use in the United States in April 2000.[2] The formulation is known as Septocaine (Septodont, Inc., New Castle, Del) and is available as a 4% solution with 1:100,000 epinephrine. Articaine is classified as an amide and contains a thiophene ring instead of a benzene ring like other amide local anesthetics.[2] A second mo-

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lecular difference between articaine and other amide local anesthetics is the extra ester linkage incorporated into the articaine molecule,[2] which results in hydrolysis of articaine by plasma esterases. It has been reported that 90%–95% of articaine is metabolized in the blood, whereas only 5%–10% is broken down in the liver.[3,4] The plasma half-life has been reported to be as low as 20 minutes.[5,6]

A number of studies[2,7–13] have evaluated articaine and have concluded that it is safe when used in appropriate doses. Both lidocaine and articaine have the same maximum milligram dose of 500 mg (recommended dose of 6.6–7.0 mg/kg) for the healthy adult patient.[4] Because articaine is marketed as a 4% solution, the maximum manufacturer's recommended dose for a healthy 70-kg adult would be slightly less than 7 cartridges of an articaine solution compared with 13 ½ cartridges of a 2% lidocaine solution.[4]

Articaine, like prilocaine, has the potential to cause methemoglobinemia and neuropathies.[2] Although the incidence of methemoglobinemia is rare, dentists should be aware of this complication in patients who are at an increased risk of developing this condition.[14] Haas and Lennon[15] and Miller and Lennon[16] investigated the incidence of local anesthetic-induced neuropathies. The incidence of neuropathies (which involved the lip and/or tongue) associated with articaine and prilocaine was approximately 5 times that found with either lidocaine or mepivacaine.[16] Malamed et al[2] found, in a total of 1325 patients, that the incidence of paresthesia was the same for articaine (1%) as for lidocaine (1%). In all cases, the paresthesias resolved. In the Haas and Lennon retrospective study,[15] the incidence of paresthesia was only 14 cases out of 11 million injections, or approximately 1 in 785,000 injections. Therefore, although the incidence of paresthesia is higher for articaine and prilocaine, it is still a clinically rare event.

The intraligamentary injection (periodontal ligament injection) allows placement of a local anesthetic solution directly into the cancellous bone adjacent to the tooth to be anesthetized.[17] Traditionally, intraligamentary injections have been administered with a conventional syringe or high-pressure syringe.[17–34] The Wand Plus (CompuDent, Milestone Scientific, Deerfield, Ill) local anesthesia system was developed to deliver a controlled amount of anesthetic solution at a precise and continuous flow rate.[35] The Wand Plus has been advocated for infiltration injections, nerve block injections, and intraligamentary injections.[35]

Intraligamentary injection pain and postinjection pain has been reported using conventional and high-pressure syringes.[26–28,34,36] One study[37] has recorded intraligamentary injection pain using a computer-controlled local anesthetic delivery system in children. Additionally, articaine has not been compared with lidocaine in intraligamentary injections regarding injection and postinjection pain. Smith and Pashley[38] found intraligamentary injections of epinephrine-containing solutions, using a high-pressure syringe in dogs, caused cardiovascular responses similar to an intravenous injection. Cannell et al,[39] using a high-pressure syringe in human volunteers, found that the intraligamentary injections of epinephrine-containing anesthetic solutions did not significantly change heart rate, rhythm, amplitude, or blood pressure. No study has evaluated heart rate increases using intraligamentary injections delivered with a computer-controlled local anesthetic delivery system. The Wand Plus is potentially capable of delivering approximately 1.4 mL of anesthetic solution compared with only 0.4 mL routinely given for intraligamentary injections.[4] Therefore, it may be worthwhile to evaluate injection pain and postinjection pain when an intraligamentary injection is administered with a computer-controlled local anesthetic delivery system.

The purpose of this prospective, randomized, double-blind study was to compare the pain of injection, heart rate increase, and postinjection pain of the intraligamentary injection of 4% articaine with 1:100,000 epinephrine and 2% lidocaine with 1:100,000 epinephrine administered with a computer-controlled local anesthetic delivery system.

MATERIALS AND METHODS

Fifty-one adult subjects participated in this study. All subjects were in good health and were not taking any medication that would alter pain perception as determined by a written health history and oral questioning. The Ohio State University Human Subjects Review Committee approved the study, and written informed consent was obtained from each subject.

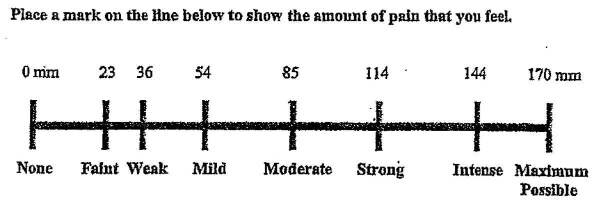
Subjects randomly received 2 intraligamentary injections at 2 separate appointments spaced at least 1 week apart in a crossover design. The 51 subjects received intraligamentary injections of 1.4 mL of 4% articaine (56 mg) with 1:100,000 epinephrine (14 µg; Septocaine; Septodont) at 1 appointment and 1.4 mL of 2% lidocaine (28 mg) with 1:100,000 epinephrine (14 µg; Xylocaine; Dentsply Pharmaceutical, York, Penn) at the other appointment (both being delivered as two 0.7-mL injections per appointment) using the Wand Plus local anesthesia system (Milestone Scientific). With the crossover design, there were 102 sets of intraligamentary injections administered, and each subject served as his or her own control. Twenty-six sets of intraligamentary injections were administered on the right side, and 25 sets of intraligamentary injections were administered on the left side. The same side randomly chosen for the first injection was used again for the second injection. One author (J.B.) gave all injections.

Before the experiment, the 2 anesthetic solutions were randomly assigned 6-digit numbers from a random number table. The random numbers were assigned to a subject to designate which anesthetic solution was to be administered at each appointment. The cartridges of anesthetic solutions administered were blinded by completely masking the aluminum caps with permanent black marker and masking the appropriate cartridges with opaque labels, which were labeled with the 6-digit numbers. The expiration dates on the cartridges were checked before they were masked. Two blinded cartridges of the same anesthetic solution were placed in letter-sized envelopes labeled with the 6-digit code. Two blinded cartridges were placed in the envelope so the code would not need to be broken in the event of a broken or dropped cartridge. Only the random numbers were recorded on the data collection sheets to further blind the experiment.

The experimental teeth, the mandibular first and second molars and the second premolar, were evaluated with an explorer and periodontal probe. Those teeth with large restorations, previous endodontic therapy, caries, full crowns, periodontal disease, or restorations with poor margins were eliminated from the study. Also, teeth with a history of trauma or sensitivity were eliminated. Preinjection vitality of the experimental teeth was confirmed with a Kerr electric pulp tester (Analytic Technology Corp, Redmond, Wash).

Before administering the intraligamentary injection, each subject was connected to a pulse oximeter (Criticare Systems, Inc, Waukesha, Wis) by means of a sensor attached to the nail of a forefinger. Five time periods were monitored: (a) Period 1, baseline readings were recorded at 1-minute intervals during the 8-minute preinjection resting period (8 readings);(b) Period 2, readings were recorded at 15-second intervals during anesthetic solution deposition on the mesial aspect of the mandibular first molar (10 readings); (c) Period 3, readings were recorded at 15-second intervals during anesthetic solution deposition on the distal aspect of the first molar (10 readings); (d) Period 4, readings were recorded at 15-second intervals for 2 minutes immediately after anesthetic solution deposition for each mesial and distal injection (8 readings per mesial or distal site); and (e) Period 5, readings recorded at 2-minute intervals for 28 minutes following completion of the intraligamentary injections (14 readings).

The computer-assisted local anesthesia system is a microprocessor-driven device that delivers a controlled infusion of anesthetic solution.[35] The device accepts standard 1.8-mL dental anesthetic glass cartridges. The microprocessor monitors and varies the infusion pressure while maintaining a constant flow rate. An electronically driven plunger contacts the rubber plunger in the cartridge and expels the anesthetic solution at a precisely regulated rate. Sterile tubing connects the cartridge receptor to a pen-like, hand-held plastic wand that is attached to a Luer-Lok needle (Becton Dickinson and Co, Franklin Lakes, NJ), together forming a disposable syringe assembly. A small portion of solution from a standard cartridge is lost during the purge cycle, and some of the solution remains in the cartridge and tubing; thus only 1.4 mL of anesthetic solution from a standard cartridge is delivered. Flow rate, initiation and cessation of flow, and aspiration are controlled with a foot pedal. To prevent cross-contamination, the handpiece, microtubing, and anesthetic cartridge are designed for single use only.



Heft-Parker visual analogue scale (VAS) used for assessment of pain. The millimeter demarcations were not shown on the patients' VAS.

One blinded cartridge was removed from the envelope, placed into the plastic barrel of the computer-assisted hand piece assembly, and placed into the cartridge holder socket with a quarter turn in a counter clockwise direction. The cap was removed from the needle and the foot pedal depressed once to activate the purge cycle to remove air from the plastic tubing and fill the line with anesthetic solution.

The patients were instructed to definitively rate any discomfort during needle insertion/placement and deposition of the anesthetic solution using a Heft-Parker visual analogue scale (VAS; Figure).[40] The VAS scale was divided into 4 categories. No pain corresponded to 0 mm. Mild pain was defined as >0 mm and ≤54 mm. Mild pain included the descriptors of faint, weak, and mild pain. Moderate pain was defined as >54 mm and <114 mm. Severe pain was defined as ≥114 mm. Severe pain included the descriptors of strong, intense, and maximum possible.

The intraligamentary injection, using the Wand Plus, was administered with a 27-gauge 0.5-inch Luer-Lok needle attached to the disposable tubing and hand piece assembly (Milestone Scientific). The subjects were informed that the injection would take almost 5 minutes and that they would hear chimes during the injection. The subject was placed in a supine position. The injection was performed by inserting the needle in the gingival sulcus at the mesio-buccal line angle of the tooth with the needle directed at an approximately 30° angle to the long axis of the tooth in the buccal-lingual plane. The needle was placed into the sulcus with the bevel facing away from the tooth and toward the alveolar bone. The needle was advanced with firm pressure until it could be advanced no farther. The Wand Plus unit was activated at a slow rate (by partially depressing the foot pedal) for 8 seconds; by removing the foot from the foot pedal, the anesthesia delivery unit was then activated on cruise control (continuous flow of anesthetic solution at the slow rate). Audible chimes from the machine and indicator lights on the front of the unit allowed monitoring of volume of anesthetic solution delivered. Approximately 1 drop of anesthetic solution was delivered every other second on the slow setting. Once 0.7 mL of the anesthetic solution had been delivered as shown by the indicator lights, the injection was stopped by lightly tapping the foot pedal once. The time to administer 0.7 mL of anesthetic solution was approximately 2 minutes and 22 seconds. The author waited 10 seconds before slowly removing the needle from the injection site. This step supposedly allows the anesthetic solution to dissipate within the tissue and reduces the amount of solution dripping from the site before needle withdrawal. However, in almost all cases, some anesthetic solution escaped upon removal of the needle from the sulcus. A pilot study determined the amount to be approximately 0.05 mL. The injection was then repeated on the distal aspect of the first molar using the same technique and sequence of steps listed above. The amount of anesthetic solution delivered was 0.7 mL.

The patient, using the VAS, rated the pain of needle insertion and solution deposition with mesial intraligamentary injection. Following the injection on the distal aspect of the first molar, the subject rated the pain of needle insertion and solution deposition.

No operative or restorative dental procedures were performed. Additionally, no probing or needle sticks of the soft tissues were performed. The first and second molars and second premolars were pulp tested in 2-minute cycles for 60 minutes. The results have been reported elsewhere.[41] Pulp testing the teeth would not result in postinjection pain or sequelae.[42]

All subjects completed postinjection surveys after each intraligamentary injection was administered. The subjects rated pain in the injection area, using the previous VAS, upon waking in the morning for 3 days following the appointment. Patients were also instructed to describe and record any problems, other than pain, that they experienced.

The data were statistically analyzed. Between anesthetic solution differences in pain of injection, postinjection pain, and pulse rate were analyzed using repeated-measures, factorial analyses of variance (ANOVA). Post hoc testing was done using the Tukey-Kramer procedure. With a nondirectional alpha risk of 0.05 and a power of greater than 80%, a sample size of 51 subjects was required to demonstrate a difference of ±15 mm in the VAS pain assessment and ±2 beats per minute (bpm) for pulse rate changes. Comparisons were considered significant at $P < .05$.

RESULTS

Fifty-one adult patients, 25 men and 26 women, from age 20 to 53 years with an average age of 26 years, participated in the study.

The discomfort ratings for the intraligamentary injection are presented in Table 1. The incidence of moderate pain was 14%–27% with needle insertion, with 0%–4% reporting severe pain. For solution deposition, moderate pain was reported 8%–18% of the time, with no reports of severe pain. There were no significant differences between the articaine and lidocaine solutions.

The mean pulse rates for the 5 time periods are presented in Table 2. There were no significant differences between the articaine and lidocaine solutions. There were no significant differences between Period 1 (baseline) and time Periods 2–5.

Postinjection pain ratings are presented in Table 3. On day 1, there was a 31% incidence of moderate/severe pain with the articaine solution, and a 20% incidence of moderate/severe pain with the lidocaine solution. The moderate/severe pain ratings decreased over the next 2 days. There were no significant differences between the articaine and lidocaine solutions. Thirty-five percent (18 of 51) of the subjects reported soreness or swelling of the injection site. Twenty-seven percent (14 of 51) reported sensitivity to chewing, and 8% (4 of 51) had ulcer formation.

DISCUSSION

The finding that there were no significant differences in pulse rate between Period 1 (baseline) and Periods 2–5 for both anesthetic solutions would indicate that the intraligamentary injection did not cause a significant or clinically meaningful increase in heart rate. That is, the readings during and after the intraligamentary injection were statistically the same as at baseline. Smith and Pashley[38] found intraligamentary injections of epinephrine-containing solutions, using a high-pressure syringe in dogs, caused cardiovascular responses similar to an intravenous injection. Cannell et al,[39] using a high-pressure syringe in human volunteers, found that the intra-

Table 1. Discomfort Ratings for Patients Receiving the Intraligamentary Technique (n = 102 Injections, 51 Mesial, 51 Distal)

Phase	*None (0 mm) % (No.)*	*Mild (1–54 mm) % (No.)*	*Moderate (55–113 mm) % (No.)*	*Severe (≥114 mm)† % (No.)*	*Mean (SD)*	P *value*
Needle insertion						
Mesial						
articaine	2 (1/51)	69 (35/51)	27 (14/51)	2 (1/51)	49 ± 3.6	.399*
lidocaine	4 (2/51)	65 (33/51)	27 (14/51)	4 (2/51)	45 ± 3.6	
Distal						
articaine	6 (3/51)	78 (40/51)	16 (8/51)	0 (0/51)	34 ± 3.6	.233*
lidocaine	18 (9/51)	67 (34/51)	14 (7/51)	2 (1/51)	28 ± 3.6	
Solution deposition						
Mesial						
articaine	14 (7/51)	74 (38/51)	12 (6/51)	0 (0/51)	26 ± 3.6	.899*
lidocaine	16 (8/51)	67 (34/51)	18 (9/51)	0 (0/51)	27 ± 3.6	
Distal						
articaine	22 (11/51)	67 (34/51)	12 (6/51)	0 (0/51)	22 ± 3.6	.573*
lidocaine	31 (16/51)	61 (31/51)	8 (4/51)	0 (0/51)	19 ± 3.6	

† Heft Parker visual analogue scale (VAS) ratings.
* There were no significant differences between the solutions.

ligamentary injections of epinephrine-containing anesthetic solutions did not significantly change heart rate, rhythm, amplitude, or blood pressure. Why there is such a contrast in results of the 2 studies cannot be explained. However, our current study would support the human study by Cannell et al[39] that intraligamentary injections do not cause significant changes in heart rate. Although we used a computer-controlled delivery of anesthetic solution at a slow rate compared with the use of a high-pressure syringe in previous studies, it is unknown if the lack of heart rate increase is related to the lack of response to the intraligamentary injection or rather to the slow rate of anesthetic solution deposition.

When used as a primary intraligamentary technique, List et al,[36] D'Souza et al,[26] and Meechan[34] reported low pain ratings with the injection. Schleder et al[28] and White et al[27] reported an incidence of approximately 25% moderate pain with needle insertion and solution deposition when using the intraligamentary technique in mandibular posterior teeth in asymptomatic subjects. There were very few reports of severe pain. All of these studies used a high-pressure or conventional syringe for the intraligamentary injection. Using the Wand (CompuDent), Ran and Peretz[37] found children displayed better behavior when they received intraligamentary injections with the Wand versus a conventional infiltration. In the current study, for needle insertion and placement, 14%–27% of the patients reported moderate pain and 0%–4% reported severe pain (Table 1). Deposition of the anesthetic solution resulted in 8%–18% of the patients reporting moderate pain and 0% reporting severe pain (Table 1). The injection on the distal aspect of the molar resulted in less pain for both needle insertion and solution deposition (Table 1). Similar results have been reported by White et al.[27] We feel the lower pain ratings may be due to the patients' acceptance of the procedure or anesthesia of the soft tissues from the mesial injection. Generally, the clinician should be aware that moderate/severe pain may be experienced when using the intraligamentary injection, delivered with a computer-controlled anesthetic delivery system, in asymptomatic patients.

Table 2. Mean Pulse Rates for the Articaine and Lidocaine Solutions for the 5 Time Periods (n = 51)

Time Period	*Articaine (±SD)*	*Lidocaine (±SD)*	P *value**
Period 1**	73.7 ± 1.5	73.1 ± 1.3	.960
Period 2	72.0 ± 0.4	72.7 ± 0.4	1.000
Period 3	73.6 ± 0.4	73.2 ± 0.4	.606
Period 4	74.2 ± 0.4	73.5 ± 0.4	.240
Period 5	71.9 ± 0.4	72.2 ± 0.4	1.000

* There were no significant differences between the articaine and lidocaine solutions.
** There were no significant differences between Period 1 (baseline) and time Periods 2–5 for the articaine and lidocaine solutions.

When used as a primary intraligamentary technique, postinjection pain has been reported in the majority of subjects.[26–28] D'Souza et al[26] found only a few subjects reported moderate pain, whereas Scheleder et al[28] and White et al[27] reported a 42%–53% incidence of moderate/severe pain. In the current study, 20%–31% of the subjects reported moderate/severe pain (Table 3). On day 1, there was a 31% incidence of moderate/

Table 3. Summary of Pain Ratings for Postinjection Survey With the Intraligamentary Injection (n = 51)

	Pain Ratings					
	None (0 mm) % (No.)	*Mild (1–54 mm) % (No.)*	*Moderate (55–113 mm) % (No.)*	*Severe (≥114 mm)† % (No.)*	*Mean (SD)*	*P value*
Day 1						
Articaine	20 (10/51)	49 (25/51)	29 (15/51)	2 (1/51)	35 ± 31	.958*
Lidocaine	20 (10/51)	61 (31/51)	16 (8/51)	4 (2/51)	31 ± 30	
Day 2						
Articaine	39 (20/51)	53 (27/51)	8 (4/51)	0 (0/51)	15 ± 19	.999*
Lidocaine	39 (20/51)	53 (27/51)	6 (3/51)	2 (1/51)	16 ± 25	
Day 3						
Articaine	59 (30/51)	39 (20/51)	2 (1/51)	0 (0/51)	6 ± 12	.999*
Lidocaine	57 (29/51)	41 (21/51)	0 (0/51)	2 (1/51)	7 ± 19	

† Heft Parker visual analogue scale (VAS) ratings.
* There were no statistically significant differences between the 2 solutions.

severe pain with the articaine solution and 20% incidence of moderate/severe pain with the lidocaine solution. The moderate/severe pain ratings decreased over the next 2 days. Because there was no statistical difference between the anesthetic solutions, articaine and lidocaine were similar regarding postinjection pain. In general, we can conclude that moderate/severe pain may be experienced a day after the intraligamentary injection, and the pain subsides over the next few days.

Thirty-five percent (18 of 51) of the subjects reported soreness or swelling of the injection site. Twenty-seven percent (14 of 51) reported sensitivity to chewing, and 8% (4 of 51) had ulcer formation. Previous studies of the primary intraligamentary injection[23,26–28] have found similar postinjection complications. The sequelae were evenly distributed between the articaine and lidocaine solutions, thus indicating both solutions were similar. There were no reports of paresthesia.

Generally, damage to the periodontium using conventional and high-pressure syringes has been reported to be minimal.[27,28,43–48] However, 2 studies[27,31] have reported periodontal abscesses and deep pocket formation after intraligamentary injections. Froum et al[49] evaluated the histologic response to intraligamentary injections in miniswine using a computer-controlled anesthetic delivery system. They found limited inflammatory responses within the first 24 hours, which abated by 7 days postinjection. Although it is not known how the computer-controlled delivery system compares with a conventional or high-pressure syringe in humans in this regard, we can speculate that they would be similar because the damage to the periodontium is most likely due to needle insertion rather than the pressure of depositing the anesthetic solution.[26] Therefore, clinically, there is a very small risk of periodontal abscess formation and bone loss when using the intraligamentary technique; although rare, the clinician should be aware of it.

We concluded that the intraligamentary injection of 4% articaine with 1 : 100,000 epinephrine was similar to 2% lidocaine with 1 : 100,000 epinephrine for injection pain and postinjection pain in the mandibular first molar when administered with a computer-controlled local anesthetic delivery system. For both anesthetic solutions, heart rate did not significantly increase with the intraligamentary injection using the computer-controlled local anesthetic delivery system.

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