
Articaine and mepivacaine efficacy in postoperative analgesia for lower third molar removal: a double-blind, randomized, crossover study

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Objective. Comparison of the clinical efficacy of 4% articaine in relation to 2% mepivacaine, both with 1:100,000 epinephrine, in the prevention of postoperative pain after lower third molar removal.

Study design. Twenty patients underwent removal of bilateral lower third molars under local anesthesia (articaine or mepivacaine) in 2 separate appointments, in a double-blind, randomized, and crossed manner. Objective and subjective parameters were recorded for paired comparison of postoperative courses.

Results. Duration of analgesia provided by articaine and mepivacaine was 198.00 ± 25.86 , and 125.40 ± 13.96 min, respectively ($P = .02$), whereas the duration of anesthesia was 273.80 ± 15.94 and 216.85 ± 20.15 min, respectively ($P = .06$). Both solutions exerted no important effects upon arterial pressure, heart rate, or oxygen saturation ($P > .05$).

Conclusions. Articaine provides a longer period of analgesic effect and a tendency for a longer period of anesthesia as compared to mepivacaine. The presence of a vasoconstrictor agent in local anesthetic solutions does not seem to influence hemodynamic parameters during lower third molar removal in healthy subjects.

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The management of postoperative pain and inflammation is a critical component of patient care.^{1,2} Postoperative pain control in patients who undergo oral and maxillofacial surgeries is frequently performed with the administration of short-acting local anesthetics and oral analgesics. With the surgical removal of lower third molars, the maximum intensity of pain occurs in the first hours after the end of the surgery, when the local anesthetic has worn off.^{3,4} Theoretically, postoperative pain control can be increased by using a local anesthetic with a more prolonged action.^{3,5-8}

The improvements in agents and techniques for local anesthesia are probably the most important advances in dental science to have occurred in the past 100 years. The agents currently available in dentistry have most of the characteristics of an ideal local anesthetic. Today's

anesthetics can be administered with minimal irritation and little concern for stimulating allergic reactions. A variety of agents are available that provide a rapid onset of surgical anesthesia with adequate duration.⁹

Various local anesthetic agents have been used in lower third molar surgeries. Mepivacaine, an amide local anesthetic, has been widely studied.^{2,10-12} In contrast, there are few studies in dental literature concerning the use of articaine, a relatively new amide local anesthetic.¹²⁻¹⁸ Therefore, the aim of this work was to assess the clinical efficacy of these 2 local anesthetic agents in impacted lower third molar removal, measuring the following parameters: total volume of anesthetic solution used during the surgery; onset of anesthetic action; duration of surgery; duration of postoperative analgesia and anesthesia; incidence, type, and severity of adverse reactions; postoperative mouth opening; subjective postoperative pain evaluation; total amount of rescue analgesic medication; and systolic, diastolic, and mean arterial pressure, heart rate, and oxygen saturation (before and during surgery and after suturing).

MATERIALS AND METHODS

All patients provided written informed consent during the pretreatment screening period before any study procedures were performed. The protocol of this study was approved by the Ethics Committee of Bauru

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The study population comprised 20 patients aged 18 years or over, with symmetrically positioned full bony impacted lower third molars,¹⁹ as observed in panoramic radiographs. Eligibility criteria included absence of systemic illness and no signs of inflammation or infection at the extraction sites. Exclusion criteria included medical history of cardiovascular and kidney diseases, gastrointestinal bleeding or ulceration, allergic reaction to local anesthetic, allergy to aspirin, ibuprofen, or any similar drugs, and pregnancy or current lactation.^{2,20} Instructions for not using antidepressants, diuretics, or aspirin in the days prior to the surgeries were given to the patients, because these drugs could cause hemorrhage or other blood problems, thus interfering with the results of this investigation. Patients were also given instructions not to take any other pain medication prior to the removal of the third molars.

This was a double-blind study; neither the surgeon nor the patients were aware of the local anesthetic being tested at the 2 different appointments. Each patient required similar surgical treatment on opposite sides of the mandible, which was performed in 2 visits, 1 to 2 months apart.^{16-18,21} For local anesthesia, in the first appointment the patients were randomly selected to receive either 2% mepivacaine or 4% articaine (both with 1:100,000 epinephrine). In the second appointment, the local anesthetic not used previously was then administered in a crossed manner. All surgeries and postoperative controls were performed by the same surgeon.

Initially, extraoral antisepsis with 0.2% chlorhexidine gluconate and intraoral antisepsis with 0.12% chlorhexidine gluconate were performed.²² Then the patient received a regional anesthetic blockade of buccal, lingual, and inferior alveolar nerves with 1.8 mL of the anesthetic solution. After 5 minutes, 0.9 mL of the same anesthetic was infiltrated in the mucosa in order to guarantee hemostasis and anesthesia of the site. Additional amounts of this solution would be infiltrated if the patient complained of pain during the surgery. The removal of third molars followed a standard surgical technique. Upon completion of the surgeries, the surgical sites were thoroughly irrigated, suctioned, and sutured.² Patients remained in the clinic for the first postoperative hour.

For postoperative pain control, all patients received 20 mg piroxicam,²³ which was administered once daily for 4 days. Rescue analgesic medication was available to any patient as needed throughout the study; for this purpose, 750 mg paracetamol was provided to all patients.²⁴⁻²⁶ Patients recorded the date and time at which rescue medication was taken. Because bone tissue re-

moval was necessary in all surgeries, 500 mg amoxicillin was prescribed every 8 hours (tid) for 7 days to prevent infection.

The following parameters were assessed:

Total volume of anesthetic solution used during the surgery (in mL).

Onset of anesthetic agent action (in seconds), determined by the loss of sensibility of the inferior lip, the corresponding half of the tongue, and the mucosa.

Duration of the surgery after anesthetic administration (in minutes), which corresponded to the period between the first incision and the last suture.²⁷

Duration of postoperative anesthesia, represented by the lack of sensibility of the mucosa, tongue, and inferior lip. Patients recorded the moment that the anesthetic had worn off.

Duration of postoperative analgesia (in minutes), which was determined by the difference between the end of the surgery and the ingestion of the first piroxicam tablet for pain relief.

Incidence, type, and severity of adverse reactions (nervousness, dizziness, tremors, blurred eyes, or any indication of effects on cardiovascular and central nervous systems) during the surgery and during the first postoperative hour.

Mouth opening (distance, in mm, between the mesial-incisal corners of the upper and lower right central incisors at maximum opening of the jaws) before the surgery and at the moment of suture removal (5 days postoperatively). The postoperative ability to open the mouth was expressed as a percentage of preoperative measure.²⁷

Subjective pain evaluation, with the aid of a 100-mm-length visual analog scale (VAS), with 0 anchored by "no pain" and 100 anchored by "worst pain imaginable."^{11,16} Subjects recorded the intensity of postoperative pain at 15-minute intervals for the first 60 postoperative minutes.

Total amount of rescue analgesic medication (paracetamol) needed during the postoperative period.

Systolic, diastolic, and mean arterial pressure, heart rate, and oxygen saturation before and during the surgery and after suturing. During the surgery, 2 measurements were made: one immediately after the regional anesthetic blockade and another 5 minutes later. All the measurements were automated and noninvasive, performed with the aid of equipment for monitoring hemodynamic param-

Table I. Duration (in min) of postoperative anesthesia and analgesia provided by 4% articaine or 2% mepivacaine (both with 1:100,000 epinephrine) in patients who underwent surgical removal of impacted lower third molars in 2 separate appointments. Local anesthetics were used in a double-blind, randomized, and crossed manner. Data are mean \pm SEM (n = 20).

Local anesthetic	Duration of anesthesia (min)	Duration of analgesia (min)
Articaine	273.80 \pm 15.94	198.00 \pm 25.86*
Mepivacaine	216.85 \pm 20.15	125.40 \pm 13.96

* $P = .02$.

eters (DX2010 Monitoring System; Dixtal Biomédica, São Paulo, Brazil).

Paired *t* test was used to compare both anesthetic drugs (4% articaine and 2% mepivacaine). The parameters “rescue analgesic medication” and “postoperative pain” were evaluated by nonparametric Wilcoxon test. All the other data were statistically analyzed by Kolmogorov-Smirnov normality test. Statistical significance was established at 5%. Data are presented as the mean \pm standard error of mean (SEM).

RESULTS

The study comprised 13 males and 7 females, with a mean age of 23.1 years (range 18-37).

The mean total volume of 4% articaine used during the surgery was similar to that of 2% mepivacaine (2.70 \pm 0.00 mL and 2.74 \pm 0.04 mL, respectively; $P > .05$). This was consistent with no perceived pain during the surgical procedures, because besides the 2.7 mL of local anesthetic solution to guarantee anesthesia and hemostasis of the site, the infiltration of additional 0.9 mL of mepivacaine for intraoperative pain control was necessary in only 1 surgery. No significant difference between the onset of articaine (149.50 \pm 14.29 s) and mepivacaine (149.50 \pm 7.61 s) actions was found ($P > .05$). However, there was a tendency for a longer period of anesthesia provided by articaine in comparison with mepivacaine ($P = .06$; Table I).

The mean duration of the surgeries from the time of administration of articaine until the completion of surgical wound suturing was 12.67 \pm 2.08 min, which was not statistically different from that observed after mepivacaine administration: 12.90 \pm 1.66 min ($P > .05$). However, patients who had received articaine experienced a significantly longer period of analgesia as compared to those who had received mepivacaine ($P = .02$; Table I).

No adverse reactions due to the use of either anes-

thetic solution were reported by the patients during the surgery and during the first postoperative hour. The mouth opening at the suture removal was 83.20% \pm 3.82% and 93.87% \pm 4.72% of the preoperative measure for articaine and mepivacaine groups, respectively ($P > .05$), indicating a similar reduction in mouth opening at the suture removal compared to the preoperative measures for each patient in both treatment groups.

With regard to the course of pain, according to the patients' evaluation on VAS at each determined time point, there was no significant difference between the scores of pain reported by patients treated with articaine or with mepivacaine. In the first postoperative hour, all patients reported low scores of pain (under 10 mm, on a 100-mm length scale) regardless of the local anesthetic employed ($P > .05$). Furthermore, there was no statistically significant difference concerning the total amount of rescue analgesic medication (paracetamol) ingested by the patients who underwent oral surgery with articaine or with mepivacaine (975.00 \pm 361.33 mg and 1162.50 \pm 405.25 mg, respectively; $P > .05$).

With respect to the hemodynamics parameters, there was no statistically significant difference in blood pressure, heart rate, or oxygen saturation before and during the surgery and after the suture for both groups (Figs. 1-3, respectively; $P > .05$).

DISCUSSION

In order to investigate the therapeutic efficacy of an anesthetic drug, every effort should be made to standardize the procedure. A crossover study design is useful to eliminate the variations in inflammatory response resulting from individual differences. The surgical technique and team should be the same in all of the procedures, and the patients should be meticulously selected to ensure that the similarity of the trauma caused in both surgeries is of the same magnitude.²⁷ Thus, the experimental model of bilateral surgical removal of impacted lower third molar teeth was used for anesthetic agent evaluation in this study.^{19,28} To the best of our knowledge, this is the first study focusing on postoperative analgesic efficacy of articaine in this model, so that comparison with other reports may become difficult.

Our results demonstrated that 4% articaine with 1:100,000 epinephrine provided a longer period of postoperative analgesia in comparison with 2% mepivacaine with 1:100,000 epinephrine (Table I). Our findings with articaine are in agreement with those of Tofoli et al.²⁹ (264 \pm 37 min).

The difference observed in analgesia duration evoked by the anesthetic solution during the first surgeries was more than 1 hour greater than that during the

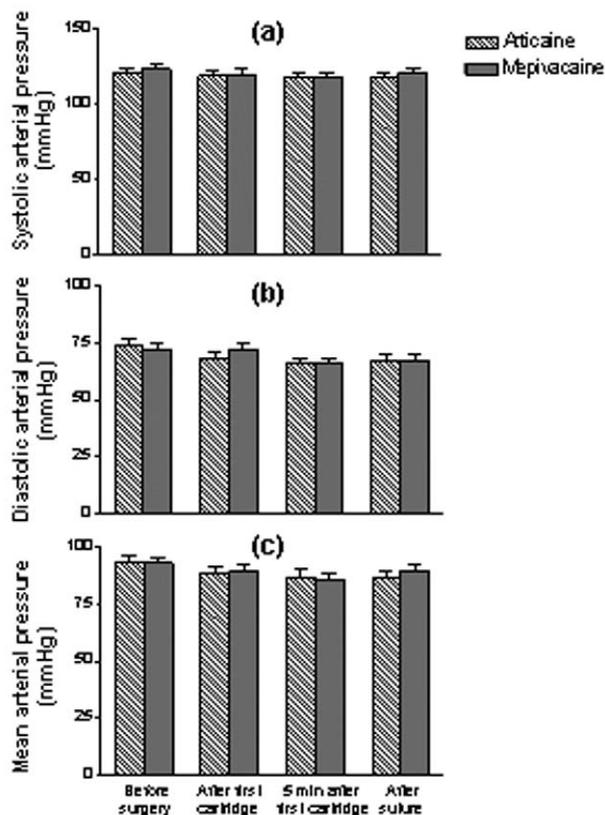


Fig. 1. Measurements of systolic (a), diastolic (b), and mean (c) arterial pressure (in mm Hg) in different times (before and during the surgery and after suturing) in patients who underwent surgical removal of impacted lower third molars with 4% articaine or 2% mepivacaine (both with 1:100,000 epinephrine) in 2 different appointments. Local anesthetics were used in a double-blind, randomized, and crossed manner. Data are mean \pm SEM (n = 20).

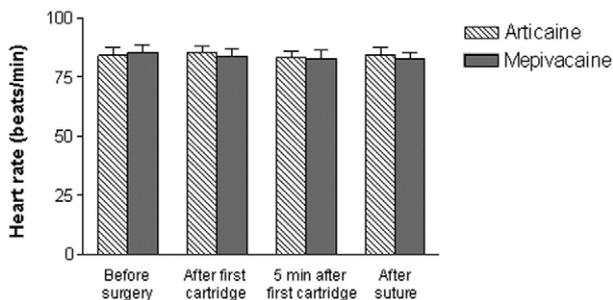


Fig. 2. Measurements of heart rate (in beats/min) in different times (before and during the surgery and after suturing) in patients who underwent surgical removal of impacted lower third molars with 4% articaine or 2% mepivacaine (both with 1:100,000 epinephrine) in 2 different appointments. Local anesthetics were used in a double-blind, randomized, and crossed manner. Data are mean \pm SEM (n = 20).

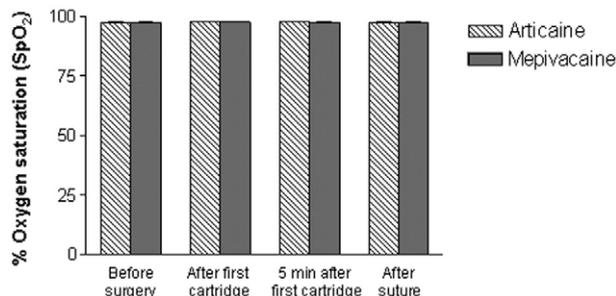


Fig. 3. Measurements of percentage oxygen saturation (SpO₂) in different times (before and during the surgery and after suture placement) in patients who underwent surgical removal of impacted lower third molars with 4% articaine or 2% mepivacaine (both with 1:100,000 epinephrine) in 2 different appointments. Local anesthetics were used in a double-blind, randomized, and crossed manner. Data are mean \pm SEM (n = 20).

second (Table I). This could contribute to an increase in postoperative pain control.^{3,5-8}

In the present study both agents had the same onset of action (2 min 30 s). In this respect, our results with articaine are in disagreement with those of Tofoli et al.,²⁹ who reported the onset of anesthetic action of around 7 min. However, this comparison is problematic because those authors tested the first premolars with a pulp tester to verify the anesthesia induced by the inferior alveolar nerve blockade, whereas we considered the loss of sensibility of the inferior lip, the corresponding half of the tongue, and the mucosa.

Our results also showed that there was no statistically significant difference between the values of mouth opening in both preoperative periods (44.50 ± 1.38 mm and 43.35 ± 1.68 mm; data not shown; $P > .05$), which demonstrates that all patients recovered totally after the first surgery, regardless of the local anesthetic employed. Additionally, there was no significant difference between the pre- and postoperative values of mouth opening for articaine and mepivacaine ($P > .05$), suggesting a lack of anesthetic substance influence on the function of masticatory muscles.

Patients ingested a very small amount of rescue analgesic medication (paracetamol), irrespective of the anesthetic agent used in the surgery. Actually, these data do not express the analgesic power of articaine or mepivacaine anesthetics, but that of the nonsteroidal antiinflammatory drug (piroxicam) provided to the patients.²³

No adverse reactions were observed either during the surgeries or 1 hour later. Other authors have reported some adverse events after the use of articaine with epinephrine, such as headache, edema of lips, face, and

eyelids, trismus, soreness, swelling, and paresthesia.^{14,18,30}

Monitoring of vital constants is required to rapidly correct possible hypoxia in patients subjected to oral surgery.^{15,31,32} Minor fluctuations in vital signs are common during administration of local anesthetic.¹⁴ In our study, the cardiovascular parameters analyzed were arterial pressure levels (systolic, diastolic, and mean), heart rate, and oxygen saturation before and during the surgery and after the suturing. There were no consistent changes in vital signs observed at baseline, right after the injection of the first anesthetic cartridge, 5 minutes later, or at the end of the surgical procedure for both treatment groups (Figs 1-3). Transient increases and decreases in blood pressure, heart rate, and oxygen saturation were observed, but they were not clinically significant, nor were the changes statistically significant between treatment groups. Our results are in agreement with others in the literature. In the study of Mestre Aspa et al.¹² with the same local anesthetics used in this investigation, no statistical differences in the values of blood pressure, heart rate, and oxygen saturation attributable to the type of local anesthetic were observed. It is important to note that our results were obtained when identical volumes of both anesthetic agents were used (2.7 mL). These volumes were less than those used by Mestre Aspa et al.,¹² in which a volume of anesthetic solution of 3.6 mL or less was used in 17 of the 45 patients, and in the remaining 28 cases the volume was in the range of 3.6-5.4 mL. Moreover, Gortzak et al.¹³ reported that in patients treated with articaine, no significant mean blood pressure changes during dental treatment could be established.

It is worth mentioning that none of our results was influenced by the type or concentration of vasoconstrictor substance associated to the local anesthetics employed, because both agents contained 1:100,000 epinephrine. Many authors state that the amount of epinephrine administered with the local anesthetic formulation exerts a summative effect with the plasma catecholamine levels, though this phenomenon would not suffice to induce hemodynamic changes in young and healthy individuals as those of our study. However, in patients with cardiovascular disease the risk of complications attributable to this mechanism increases. Systematic monitoring of such patients is thus advisable.¹²

CONCLUSIONS

The results of this study suggest that the use of 4% articaine with 1:100,000 epinephrine can improve postoperative pain control in impacted lower third molar removal as compared to the use of 2% mepivacaine with 1:100,000 epinephrine. Also, hemodynamic pa-

rameters in healthy subjects do not seem to be affected by the presence of a vasoconstrictor agent in combination with a local anesthetic.

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