Clinical study of hemodynamic changes comparing 4% articaine hydrochloride with 1:100,000 and 1:200,000 epinephrine

Hécio Henrique Araújo de Morais, DDS, Msc,[a,b] Ricardo José Holanda Vasconcellos, DDS, MSc, PhD,[a]
Thiago de Santana Santos, DDS, MSc,[c] Nelson Studart Rocha, DDS, MSc,[a]
Fábio Andrey da Costa Araújo, DDS,[a] and Ricardo Wathson Feitosa de Carvalho, DDS[a]
Faculdade de Odontologia, University of Pernambuco, Pernambuco; Faculdade de Odontologia de Ribeirão Preto, University of São Paulo, São Paulo; and Universidade Estadual do Rio Grande do Norte, Rio Grande do Norte, Brazil

Objective. To evaluate hemodynamic changes with the use of 4% articaine and 2 different concentrations of epinephrine (1:100,000 and 1:200,000) in the surgical removal of symmetrically positioned lower third molars.
Study Design. A prospective, randomized, double-blind clinical trial was carried out involving 42 patients each undergoing 2 surgeries on separate occasions under local anesthesia with 4% articaine and either epinephrine 1:100,000 or 1:200,000. The following parameters were assessed at 4 different moments: systolic, diastolic, and mean blood pressure; heart rate; oxygen saturation; rate pressure product (RPP); and pressure rate quotient (PRQ).
Results. The concentration of epinephrine did not affect diastolic blood pressure or oxygen saturation during the surgeries. Significant differences between were detected for heart rate, RPP, and PRQ ($P < .05$).
Conclusions. The epinephrine concentration (1:100,000 or 1:200,000) in a 4% articaine solution influences hemodynamic parameters without perceptible clinical changes in healthy patients undergoing lower third molar removal. (Oral Surg Oral Med Oral Pathol Oral Radiol 2013;116:e14-e22)

Pain control through a truncal block of the inferior alveolar nerve is one of the most widely used locoregional anesthetic techniques in oral surgery, affording comfort and safety to both the patient and operator when used correctly.[1] The choice of anesthetic solution should be based on 3 main clinical considerations: anesthetic potency, latency (time to the onset of anesthesia), and duration of the anesthetic effect.[2]

A number of local anesthetic agents provide the rapid onset of surgical anesthesia and adequate duration of the anesthetic effect.[3] Vasoconstrictors are added to local anesthetic solutions to increase the quality and duration of the anesthesia, avoid excessive intraoperative bleeding and decrease systemic toxicity. Epinephrine has been widely used for this purpose in several countries.[1,4,5]

Sung et al.[6] found that the administration of progressive doses of epinephrine at concentrations lower than those used in dental practice gives rise to increases in myocardial yield and oxygen consumption. On the other hand, it is known that pain during dental treatment can trigger the release of endogenous catecholamines, which, in turn, can give rise to hemodynamic changes, such as an increase in blood pressure and heart rate, and may even produce arrhythmia.[7] A significant increase (5-12 mm Hg) in systolic blood pressure has been reported in patients subjected to root scaling and planing when using anesthesia with a vasoconstrictor.[8] There is controversy regarding the use of epinephrine with local anesthetic solutions in patients with a history of cardiovascular problems, although the administration of a local anesthetic with a vasoconstrictor for the avoidance of patient pain and discomfort during dental treatment appears to be safe.[9,10]

Articaine was synthesized by Rusching et al. in 1969 under the name carticaine and first marketed in Germany in 1976. By 1983, the drug was available in practically all of Europe and Canada; it was not approved in the USA until March 2000 and only in its presentation as a 4% solution with 1:100,000 epinephrine.[1] Its pharmacologic characteristics are the main advantages over other local anesthetics and include the substitution of the aromatic ring with a

Statement of Clinical Relevance

Even though the epinephrine concentration influences hemodynamic parameters with a 4% articaine solution, no clinical changes are noted during third molar extraction in healthy patients.

[a]Faculdade de Odontologia de Pernambuco, University of Pernambuco.
[b]Universidade Estadual do Rio Grande do Norte.
[c]Faculdade de Odontologia de Ribeirão Preto, University of São Paulo.
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thiophenic ring, which increases the liposolubility and potency (1.5-fold greater than that of lidocaine) of the drug. Moreover, articaine is the only amide local anesthetic containing an ester group in its molecular structure, which allows the metabolism of the drug by both plasma esterases and liver microsomal enzymes.[11] The clinical advantages of articaine include the duration of its anesthetic effect—surpassed only by ultralong-acting anesthetics, such as bupivacaine, ethidocaine, and ropivacaine—and its superior diffusion through bone tissue.[12,13]

There are a large number of studies on the most commonly used local anesthetics in lower third molar surgeries (e.g., lidocaine, mepivacaine, bupivacaine).[1,14-19] However, the dental literature on the use of articaine for this kind of surgery is limited.[20-25] One study found that 4% articaine with 1:100,000 epinephrine provides a longer period of analgesia and a tendency toward a longer period of anesthesia on soft tissues compared with 2% mepivacaine with 1:100,000 epinephrine. Moreover, neither agent exerted an influence over hemodynamic parameters (blood pressure, heart rate, and oxygen saturation) during surgery.[21]

It has recently been shown that a 4% articaine solution with 1:200,000 adrenaline provides a degree of pulp anesthesia similar to that of 4% articaine with 1:100,000 adrenaline.[26] Although most information on the cardiovascular response to dental local anesthesia with articaine is limited to healthy patients,[22,27-29] these data may still be of value to cardiologists, primary care physicians, surgeons, and dentists regarding the selection of a preferred local anesthetic for patients with cardiovascular conditions. On the other hand, no significant hemodynamic changes in patients with controlled hypertension have been attributed to 4% articaine with 1:200,000 adrenaline when <3 local anesthetic carpules are administered.[7] Few studies have compared 4% articaine with 1:100,000 adrenaline and 1:200,000 epinephrine,[22-26,29-32] particularly in terms of controlling postoperative pain and intraoperative bleeding.

The present study was undertaken to evaluate hemodynamic changes with the use of 4% articaine and 2 different concentrations of epinephrine (1:100,000 and 1:200,000) in the surgical removal of symmetrically positioned lower third molars.

MATERIALS AND METHODS

The protocol of the present study received approval from the Institutional Ethics Committee (CEP/UPE: 001.0.097.000-08). The subjects were selected from a pool of patients admitted for regular dental treatment from January 2009 to December 2010. All participants signed a term of informed consent.

A prospective, randomized, double-blind clinical trial was carried out. The split-mouth design was employed, with the right and left quadrants of the mouth constituting the experimental units and randomly assigned to 2 treatment groups. The fact that each patient served as his or her own control (crossover design) enhanced the statistical power of the study.[33,34]

The sample size was estimated with the use of the PC-Size program (version 1.01), with data for independent samples used for comparison purposes. The difference in heart rate reported for different evaluation periods in the study carried out by Frabetti et al.[35] was used as the parameter, because the results were statistically significant ($P < .05$). With an alpha value of 5% and a beta value of 80%, it was determined that 42 patients would be needed for the study.

Forty-two healthy nonsmoking patients (33 men and 11 women aged 18-31 years; mean age 21.83 ± SD 5.57 years) scheduled for the surgical removal of bilateral symmetrically positioned impacted lower third molars were enrolled in the study. The subjects had no known immune impairment or contraindications for oral surgery and were not taking any medication. The eligibility criteria included absence of systemic illness and no signs of inflammation or infection at the extraction sites. Exclusion criteria included a medical history of cardiovascular or kidney disease, gastrointestinal bleeding or ulceration, allergic reaction to local anesthetic, allergy to aspirin, ibuprofen, or any similar drugs, and pregnancy or current lactation.[14,36] Instructions for not using antidepressants, diuretics, or aspirin in the days before the surgeries were given to the patients, because these drugs could cause hemorrhaging or other blood problems and would therefore interfere with the results of the present investigation. Patients were also given instructions not to take any other pain medication before the removal of the third molars. Orthopantomographic radiograms were taken to ensure the similarity of the tooth inclinations based on the Winter classification[37] and the Pell and Gregory classification.[38]

The randomization process was carried out based on items 8-10 of the CONSORT statement 2001 checklist for randomized controlled clinical trials (Cochrane Collaboration, Manchester, U.K.).[39] Allocation to the 2 groups was performed by selecting from a set of sequentially numbered opaque sealed envelopes containing either of the 2 interventions: 4% articaine with 1:100,000 epinephrine (A100) or 4% articaine with 1:200,000 epinephrine (A200). Each impacted lower third molar (right and left sides) had an equal chance of being assigned to 1 of the 2 groups. The randomization process also determined which side would undergo the first surgery and which would undergo the second sur-