The pulpal anesthetic efficacy of articaine versus lidocaine in dentistry

A meta-analysis

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Recognizing the importance of providing profound anesthesia for patients undergoing invasive dental procedures, clinicians continually seek to identify an anesthetic solution that provides the highest success rate at an affordable cost. Dentists in the United States have a variety of anesthetic solutions at their disposal (Table 1). Although these solutions are considered to be generally effective in providing patients with a pain-free oral environment for dental treatment, local anesthetic failure remains a common problem in certain instances. Clinicians constantly have sought an anesthetic solution with a better success rate than that of available anesthetics, which has been demonstrated to be well below 100 percent, particularly in procedures affecting the posterior mandible.1-4

Although for some time anesthetic solutions containing lidocaine have been used more widely in the United States than have solutions containing other anesthetics, the U.S. Food and Drug Administration’s approval of articaine for local anes-

ABSTRACT

Background. The authors evaluated published evidence from controlled clinical trials regarding the efficacy of two local anesthetic solutions in providing successful pulpal anesthesia.

Methods. The authors searched MEDLINE and Embase databases to identify peer-reviewed randomized controlled trials in which researchers directly compared articaine and lidocaine local anesthetic solutions in adult participants. They extracted study characteristics and outcomes data as a basis for meta-analysis. They completed subgroup analyses for both infiltration and mandibular inferior alveolar block anesthetic techniques.

Results. Articaine solutions had a probability of achieving anesthetic success superior to that of lidocaine, with an odds ratio of 2.44 (95 percent confidence interval [CI], 1.59-3.76; P < .0001). The greater odds ratio for articaine increased to 3.81 (95 percent CI, 2.71-5.36; P < .00001) when the authors analyzed only infiltration data. There was weaker, but still significant, evidence of articaine’s being superior to lidocaine for mandibular block anesthesia, with an odds ratio of 1.57 (95 percent CI, 1.12-2.21; P = .009), and no difference when the authors considered only symptomatic teeth.

Clinical Implications. Research evidence supports using articaine versus lidocaine for achieving pulpal anesthesia when the infiltration mode of administration is used. It is premature to recommend articaine for mandibular block anesthesia in cases involving irreversible pulpsitis.

Key Words. Systematic review; anesthesia; articaine; lidocaine.

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thetic use has given clinicians another choice. Lidocaine has been available in the United States for more than 60 years, whereas articaine was approved for use in the United States in

### TABLE 1
Available local anesthetic solutions.

<table>
<thead>
<tr>
<th>DURATION OF ACTION</th>
<th>SOLUTION</th>
<th>TRADE NAME</th>
<th>INFILTRATION (PULPAL)</th>
<th>NERVE BLOCK (PULPAL)</th>
<th>DURATION OF EFFECT IN SOFT TISSUE</th>
<th>MILLIGRAMS PER CARTRIDGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short Duration, Plain</td>
<td>Lidocaine hydrochloride (HCl) 2 percent</td>
<td>Xylocaine (Dentsply Pharmaceutical, York, Pa.)</td>
<td>5 minutes</td>
<td>Not indicated</td>
<td>2 hours</td>
<td>36</td>
</tr>
<tr>
<td>Mepivacaine HCl 3 percent</td>
<td>Carbocaine (Eastman Kodak, Rochester, N.Y.), Isocaine (Septodont, New Castle, Del.), Mepivacaine (Hospira, Lake Forest, Ill.; Henry Schein, Melville, N.Y.), Polocaine (Dentsply Pharmaceutical), Scandanest (Novocol Pharmaceutical, Cambridge, Ontario, Canada)</td>
<td>20 to 30 minutes</td>
<td>45 to 65 minutes</td>
<td>2 to 3 hours</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>Prilocaine HCl 4 percent</td>
<td>Citanest Plain (Dentsply Pharmaceutical)</td>
<td>10 to 15 minutes</td>
<td>45 to 65 minutes</td>
<td>3 to 4 hours</td>
<td>72</td>
<td></td>
</tr>
<tr>
<td>Normal Duration, With Vasoconstrictor</td>
<td>Articaine HCl 4 percent with epinephrine 1:100,000</td>
<td>Articadent (Dentsply Pharmaceutical), Septocaine (Septodont), Zorcaine (Eastman Kodak)</td>
<td>60 to 75 minutes</td>
<td>Up to 120 minutes</td>
<td>3 to 5 hours</td>
<td>68</td>
</tr>
<tr>
<td>Articaine HCl 4 percent with epinephrine 1:200,000</td>
<td>Articadent (Dentsply Pharmaceutical), Septocaine (Septodont)</td>
<td>60 to 75 minutes</td>
<td>Up to 120 minutes</td>
<td>3 to 5 hours</td>
<td>68</td>
<td></td>
</tr>
<tr>
<td>Lidocaine HCl 2 percent with epinephrine 1:50,000</td>
<td>Lidocaine (Carestream Health, Rochester, N.Y.; Hospira; Henry Schein), Lignospan Forte (Novocol Pharmaceutical), Octocaine 50 (Septodont), Xylocaine (Dentsply)</td>
<td>55 to 65 minutes</td>
<td>80 to 90 minutes</td>
<td>3 to 5 hours</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>Lidocaine HCl 2 percent with epinephrine 1:100,000</td>
<td>Lidocaine (Carestream Health; Hospira; Henry Schein), Lignospan Standard (Novocol Pharmaceutical), Octocaine 100 (Septodont), Xylocaine (Dentsply)</td>
<td>55 to 65 minutes</td>
<td>80 to 90 minutes</td>
<td>3 to 5 hours</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>Mepivacaine HCl 2 percent with levonordefrin 1:20,000</td>
<td>Carbocaine (Eastman Kodak), Isocaine (Septodont), Mepivacaine (Henry Schein), Polocaine (Dentsply), Scandanest (Novocol Pharmaceutical)</td>
<td>40 to 60 minutes</td>
<td>60 to 90 minutes</td>
<td>3 to 5 hours</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>Prilocaine HCl 4 percent with epinephrine 1:200,000</td>
<td>Citanest Forte (Dentsply)</td>
<td>35 to 45 minutes</td>
<td>50 to 70 minutes</td>
<td>3 to 6 hours</td>
<td>72</td>
<td></td>
</tr>
<tr>
<td>Long Duration</td>
<td>Bupivacaine HCl 0.5 percent with epinephrine 1:200,000</td>
<td>Bupivacaine (Hospira), Marcaine (Carestream Health), Vivacaine (Novocol Pharmaceutical)</td>
<td>Up to 7 hours</td>
<td>Up to 7 hours</td>
<td>Up to 12 hours</td>
<td>9</td>
</tr>
</tbody>
</table>

**ABBREVIATION KEY.** EPT: Electric pulp testing. HCl: Hydrochloride. IAN: Inferior alveolar nerve. RCT: Randomized controlled trial. VAS: Visual analog scale.
April 2000. Articaine is available as a 4 percent solution, and lidocaine is available as a 2 percent solution. Both can be combined with various concentrations of vasoconstrictors. Articaine contains a thiophene ring, instead of the benzene ring found in lidocaine and other amide local anesthetics; this allows the molecule to diffuse more readily through the nerve membrane owing to increased lipid solubility. A second molecular difference is the ester linkage incorporated into the articaine molecule, which results in hydrolysis of articaine by plasma esterases. Ninety to 95 percent of articaine is metabolized in the blood by plasma esterases, with the remainder being broken down in the liver, whereas approximately 90 percent of lidocaine is metabolized by the liver. The articaine solution’s plasma half-life has been reported to be as short as 20 minutes, versus lidocaine’s half-life of approximately 108 minutes in healthy patients. Adverse reactions to articaine are characteristic of those associated with other amide-type anesthetics. For a healthy adult weighing 70 kilograms, the maximum dose for a local anesthetic solution equates to seven carpules (1.7 milliliters) of 4 percent articaine or 13 carpules (1.8 mL each) of 2 percent lidocaine.

Since its introduction at the turn of the century, this relatively new solution rapidly has become popular with clinicians because of the hope that it may provide increased efficacy. In fact, articaine accounted for approximately 25 percent of total sales of dental anesthetics in the United States in 2007, second only to lidocaine at 54 percent. Although investigators have designed various clinical trials to compare articaine with a variety of other available anesthetic solutions, published data do not support a clear superiority of articaine in terms of anesthetic efficacy. Thus, clinicians still may wonder which anesthetic solution will afford them the best chance of success for a given procedure, particularly in cases of irreversible pulpitis.

Evidence-based medicine is based on assessment of the quality of evidence relevant to the risks and benefits of treatments. The Centre for Evidence-Based Medicine in Oxford, England, defined “evidence-based medicine” as “the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients.” The authors of systematic reviews can condense the results of many studies into valid and unbiased summaries of the best available evidence for a specific clinical problem. This type of overview may help clinicians stay current while the literature greatly expands. Systematic reviews can provide an objective summary of the best available evidence so as to help dentists and their patients make informed choices. To date, only one meta-analysis has been published in which investigators compared the anesthetic success rates of articaine and lidocaine. The author of this recent review, however, included only data originating from studies that were published in English and involved the use of a specific type of pain rating scale. In our review, we aim to offer a more broad comparison regarding the efficacy of articaine and lidocaine solutions when used to achieve profound pulpal anesthesia in adults.

METHODS

Literature search. We prepared a protocol and followed it throughout the review. In December 2009, we identified eligible studies through an electronic search of MEDLINE and Embase databases. We also identified National Library of Medicine Medical Subject Heading terms that would help us locate the potential studies for review. The detailed search strategies for each database were as follows:

- MEDLINE: “((exp Anesthesia, Dental/ (9655)) OR “(exp Anesthesia/ AND (exp Dentistry/ OR exp Stomatognathic system/ OR exp Stomatognathic diseases/)))” AND “(exp Carticaine/” OR “septocaine.mp.” OR “ultracaine.mp.” OR “articaine.mp.” OR “carticaine.mp.” OR “Thiophenes/))”
- Embase: “((‘articaine’/exp OR articaine)” OR “(carticaine/)” OR “carticaine)” OR > “(ultracaine’/exp” OR “ultracaine)” OR “septocaine” OR “ thiophene > derivative/de)” AND “(dentistry’/exp OR “(mouth’/exp OR mouth))”

Selection criteria. We selected an article for inclusion in the review if it met the following criteria:
- the investigators evaluated the pulpal anesthetic effect of local anesthetic solutions of articaine comparatively with lidocaine, using volumes of at least 1.0 mL per administration and in combination with a vasoconstrictor;
- the review concerned clinical trials that involved adult human participants;
- the review was published in a peer-reviewed journal in the period from January 1970 through December 2009;
- it provided original data generated by means of a comparative design.

We excluded an article if it did not satisfy the above criteria, if it did not describe or define the methods for evaluating anesthetic success or if it did not describe in detail the techniques for administering the anesthetic solution.

Initially, we reviewed only the titles of the
articles generated by the electronic search, eliminating a possible source of bias by masking ourselves as to knowledge of the author or the journal. We first excluded all obviously irrelevant records (judging only from titles). Next, we reviewed the abstracts of the potential studies identified from the title search for appropriateness, and we attempted to include as many studies as possible even if we found the methodology to be unclear after we reviewed the abstract. At this point, we obtained full-text copies of all relevant and potentially relevant studies that appeared to meet the inclusion criteria, or for which there were insufficient data in the title and abstract to facilitate a clear decision. We fully assessed these articles.

To locate relevant articles that were not identified by means of the electronic search, we conducted a hand search and a table-of-contents search. In our hand search, we reviewed the reference lists of all articles that met the inclusion criteria in an attempt to identify any additional studies. In our table-of-contents search, after we reviewed the journal of origin for each study we had not excluded after abstract review, we targeted the journals that accounted for 80 percent of the included studies. We then reviewed the table of contents for every issue of these journals for the most recent two years of their publication. Additional efforts to supplement the search results included searching of books and conference proceedings and the solicitation of recommendations from experts in the field.

**Data extraction.** Using full-text articles, we extracted for analysis detailed information that included, but was not limited to, study type (such as randomized clinical trial, controlled clinical trial, case-control study), population characteristics (for example, participants’ ages), local anesthetic solution and technique investigated, means of analyzing anesthetic success (such as electric pulp testing [EPT] or visual analog scale [VAS] of pain measurement), preoperative status of specific teeth tested (vital, irreversibly inflamed or unspecified), missing data and adverse outcomes. With respect to local anesthetic solutions and techniques investigated, we extracted the following details: type and dose in milligrams of anesthetic used, concentration of vasoconstrictor, location of administration (arch, specific tooth and aspect [buccal/lingual]) and technique used (infiltration or nerve block). The outcomes of interest were anesthetic success or failure, as defined by each comparative trial.

**Quality assessment.** We recorded on the data abstraction form the methodological quality of included trials and the indicators of quality we used. These included proper randomized allocation of participants to their respective study groups, as well as masking of participants and evaluators.

We considered a clinical trial “randomized” if it involved the generation of random sequences by means of random numbers or tables, a tossed coin or any other means. If the authors merely used the term “randomized” or “randomly allocated” but did not provide detailed information regarding the exact method of randomization, we deemed the trial to be “unclear” as regards to the randomization and sought clarification from the original authors. We considered allocation “concealed” if the article described measures of allocation concealment such as the use of opaque sealed and sequentially numbered envelopes, or if anesthetic cartridges were individually indistinguishable and numbered sequentially. We deemed the examiners of each trial to be properly masked if the outcome assessor could not determine the group to which a participant had been assigned randomly. We recorded reporting of adverse events as being present if the authors provided information on such events or noted it as “not mentioned” if the authors did not include a description of any adverse effects in the results. We considered the “intent to treat” adequate in studies for which treatment effects had been observed and evaluated on the same day of intervention. For the trials in which investigators had used a crossover design, we noted whether no losses occurred and whether outcome data were available for all randomly assigned participants. Thus, in our “intent to treat” analysis, we included all participants in these trials. We assessed analysis appropriateness and reviewed funding sources for included trials to evaluate any potential funding bias.

**Data analysis.** We conducted all statistical analysis of the extracted data by using software (Review Manager [RevMan] Version 5.0.25, The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark). We included in the final analyses only data regarding 4 percent articaine and 2 percent lidocaine, both with 1:100,000 vasoconstrictor. We calculated the Q statistic value according to the method of Cochran Q test to test for heterogeneity among the studies. We estimated treatment difference and expressed it graphically in a forest plot.

**RESULTS**

**Search results.** Our original electronic searches of MEDLINE and Embase databases
identified 165 and 174 potentially eligible articles, respectively. We removed duplicate records, and after our initial screening of first titles and then abstracts, we identified 35 potentially relevant clinical trials for full review. The various languages of the publications were English, German, Croatian and Russian. We secured translations of non-English articles to facilitate proper appraisal. We excluded two articles about studies involving partially or strictly pediatric populations. One article described an investigation of anesthesia in relation to surgical interventions that did not include any form of assessment of pulpal anesthesia; therefore, we excluded it. We excluded nine articles on the basis of their specific methodologies, such as absence of randomization, lack of control participants or nonstandardized assessment of pulpal anesthesia. In addition, we excluded articles in which investigators only assessed injection pain, cardiovascular effects or other systemic effects. We excluded three trials because the solutions being compared were confounded by the preadministration of additional anesthetic before the comparison. Two trials did not meet the minimum volume requirements as stated in the inclusion criteria.

The remaining 13 studies, all of which we included in our review, had been published in seven journals: British Dental Journal; The Journal of the American Dental Association; Journal of Endodontics; Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology; Quintessence International; Scandinavian Journal of Dental Research; and Schweizerische Monatsschrift für Zahnmedizin. Neither the tables of contents search of these journals nor the other search efforts located any additional trials that had not already been identified in the previous electronic search. At the end of the search process, then, we considered a total of 13 articles eligible. Their data form the basis of this review (Figure 1).

General study characteristics. We categorized each of the 13 included studies as randomized, controlled clinical trials in which researchers investigated pulpal anesthesia in adult participants (Table 2).

Study outcomes. Investigators in three of the included studies used the VAS to assess anesthetic efficacy, defining success as the participant’s rating pain as being no greater than that considered mild on the pain scale. Nine studies used electric methods as a measure of anesthetic success. Researchers in one study used both techniques in their investigation.

OUTCOMES OF DATA ANALYSES

Four of the 13 included studies provided data from independent samples. Lacking reporting of data in crossover studies necessary to calculate the dependent odds ratio, we included both designs in the overall analysis and forest plot (Figure 2, page 500).

We found strong evidence of heterogeneity among the estimated treatment effects of these 13 studies. For all studies combined, the $\chi^2$ value associated with the test of heterogeneity was 23.46, $P = .005$. The Cochrane Collaboration recommended using a $P$ value < .10, rather than the conventional cut-point of $P = .05$. Additiona-
sons, we used a random-effects model of statistical analysis, as fixed-effects models are used in cases with no evidence of heterogeneity.

Figure 21-3,36-45 presents a forest plot of odds ratios of treatment differences between the two anesthetic solutions. The combined effect of articaine was 2.44 times more likely to produce anesthetic success than was that of lidocaine, and the results were statistically significant (95 percent confidence interval [CI], 1.59-3.76).

### Table 2: Characteristics of included studies.

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Methods</th>
<th>No. of Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Srinivasan and Colleagues,* 2009</td>
<td>Compared articaine with lidocaine when delivered via buccal infiltration for maxillary posterior teeth diagnosed with irreversible pulpitis</td>
<td>40</td>
</tr>
<tr>
<td>Tortamane and Colleagues,** 2009</td>
<td>Compared articaine with lidocaine during pulpectomy in patients with irreversible pulpitis in mandibular posterior teeth, subsequent to IAN† block</td>
<td>40</td>
</tr>
<tr>
<td>Evans and Colleagues,* 2008</td>
<td>Compared articaine with lidocaine in maxillary infiltrations of first molars and lateral incisors</td>
<td>80</td>
</tr>
<tr>
<td>Sherman and Colleagues,** 2008</td>
<td>Compared articaine with lidocaine in patients with irreversible pulpitis in either maxillary or mandibular posterior teeth</td>
<td>40</td>
</tr>
<tr>
<td>Robertson and Colleagues,1 2007</td>
<td>Compared articaine with lidocaine when given via buccal infiltration in mandibular posterior teeth, testing from first premolar to second molar</td>
<td>60</td>
</tr>
<tr>
<td>Kanaa and Colleagues,** 2006</td>
<td>Compared articaine with lidocaine in mandibular buccal infiltrations of first molars</td>
<td>31</td>
</tr>
<tr>
<td>Berlin and Colleagues,** 2005</td>
<td>Compared articaine with lidocaine when administered via computer-controlled intraligamentary injections in mandibular posterior teeth</td>
<td>51</td>
</tr>
<tr>
<td>Costa and Colleagues,** 2005</td>
<td>Compared articaine with lidocaine for maxillary infiltration of posterior teeth</td>
<td>20</td>
</tr>
<tr>
<td>Mikesell and Colleagues,* 2005</td>
<td>Compared articaine with lidocaine when administered via IAN block, testing molars, premolars and incisors</td>
<td>57</td>
</tr>
<tr>
<td>Claffey and Colleagues,* 2004</td>
<td>Compared articaine with lidocaine when administered via IAN block in patients experiencing irreversible pulpitis</td>
<td>72</td>
</tr>
<tr>
<td>Oliviera and Colleagues,** 2004</td>
<td>Compared a standard 2.15-milliliter volume of articaine with the same amount of lidocaine for buccal and lingual infiltration of maxillary canine teeth</td>
<td>20</td>
</tr>
<tr>
<td>Ruprecht and Knoll-Köhler,** 1991</td>
<td>Compared infiltrations of articaine and lidocaine for maxillary central incisors</td>
<td>10</td>
</tr>
<tr>
<td>Winther and Nathalang,** 1972</td>
<td>Compared the anesthetic efficacy of maxillary infiltrations of 1.0-mL articaine for lateral incisors with the same volumes of lidocaine and mepivacaine</td>
<td>39</td>
</tr>
</tbody>
</table>

* VAS: Visual analog scale.
† IAN: Inferior alveolar nerve.
‡ EPT: Electric pulp testing.
When we calculated weighted odds ratios from data regarding infiltration anesthesia only (Figure 3),\textsuperscript{1,36,38-40,42-45} the value increased to 3.81 in favor of articaine, indicating an obvious superiority of articaine to lidocaine.

Subgroup analysis according to RCT design (that is, RCT with independent groups versus crossover design) showed that the overall finding for infiltration anesthesia did not change owing to the study design (data not shown). Articaine was shown to be clearly superior.

To enable comparison of the outcomes of the four mandibular block studies, we included in the analysis only data for premolars and molars from these studies. When we isolated data regarding mandibular block analysis (Figure 4A, page 501),\textsuperscript{2,3,37,39} the weighted odds ratio decreased to 1.57, and articaine showed a statistically significant better performance (95 percent CI, 1.12-2.21).

When we included only the results of independent-sample studies in the mandibular block analysis (Figure 4B, page 501),\textsuperscript{2,37,39} the odds ratio was 1.61 (95 percent CI, 0.74-3.53) and thus we determined that the results no longer were significantly different.

**DISCUSSION**

In this systematic review, we examined the literature regarding the use of the local anesthetic solutions articaine and lidocaine, with the goal of evaluating differences in providing anesthetic success. We targeted and identified well-designed clinical trials in which investigators compared these two solutions directly. Thirteen studies fulfilled the inclusion criteria, and data from them that related to 4 percent articaine and 2 percent lidocaine both with 1:100,000 vasoconstrictor served as the basis for a meta-analysis of the extracted data. Meta-analysis is the statistical pooling of data across studies to generate pooled estimates of effects.\textsuperscript{47} Benefits of meta-analysis include the ability to improve the power of small studies to answer questions, and meta-analysis also can help detect biases and deficiencies in the design, analysis and interpretation of research.\textsuperscript{48} These methods can highlight needed improvements in

<table>
<thead>
<tr>
<th>EVALUATION SCALE USED</th>
<th>CONCLUSIONS</th>
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<tbody>
<tr>
<td>VAS*</td>
<td>Articaine’s success rates were 100 percent for both the first molar and the first premolar, and lidocaine’s success rates were 30 percent in the first premolar and 80 percent in the first molar; there was a highly statistically significant difference</td>
</tr>
<tr>
<td>EPT, VAS</td>
<td>For patients reporting no pain or mild pain during pulpectomy, the success rate of articaine (65 percent) was higher than that of lidocaine (45 percent); however, differences were not statistically significant</td>
</tr>
<tr>
<td>EPT</td>
<td>In maxillary lateral incisors, articaine exhibited a statistically significantly higher success rate (88 percent) when compared with lidocaine (62 percent); differences were not significant for first molars (78 percent versus 73 percent)</td>
</tr>
<tr>
<td>VAS</td>
<td>Overall anesthetic success was 87.5 percent in both arches; articaine was as effective as, but not statistically superior to, lidocaine</td>
</tr>
<tr>
<td>EPT</td>
<td>Lidocaine resulted in anesthetic success ranging from 45 to 67 percent, whereas articaine resulted in a success rate ranging from 73 to 92 percent; articaine resulted in a statistically significant higher success rate for mandibular buccal infiltrations</td>
</tr>
<tr>
<td>EPT</td>
<td>Success rates were 65 percent for articaine and 39 percent for lidocaine, resulting in a statistically significantly greater chance for anesthetic success with articaine</td>
</tr>
<tr>
<td>EPT</td>
<td>Success rates were 74 percent for lidocaine and 86 percent for articaine solutions; there was no statistical difference between the two solutions</td>
</tr>
<tr>
<td>EPT</td>
<td>There were no statistical differences between articaine and lidocaine in terms of anesthetic success</td>
</tr>
<tr>
<td>EPT</td>
<td>Lidocaine resulted in anesthetic success ranging from 2 to 48 percent, whereas articaine resulted in a range of 4 to 54 percent; there was no statistical difference between the articaine and lidocaine solutions</td>
</tr>
<tr>
<td>VAS</td>
<td>The success rates of lidocaine (23 percent) and articaine (24 percent) revealed no statistical difference; neither solution resulted in an acceptable rate of success for patients with irreversible pulpitis</td>
</tr>
<tr>
<td>EPT</td>
<td>All administrations resulted in pulpal anesthetic success; onset and duration of anesthesia were not statistically different between the two groups</td>
</tr>
<tr>
<td>EPT</td>
<td>No statistically significant differences were observed in terms of anesthetic success, although articaine offered a longer duration of anesthesia</td>
</tr>
<tr>
<td>EPT</td>
<td>Articaine compared well with the other solutions, with the 2 percent solution providing a frequency of anesthesia close to 100 percent</td>
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the quality of the data to achieve optimal evidence-based clinical practice. In this way, meta-analysis can be a useful tool in planning a new clinical trial in clinical situations for which the evidence is sparse.

The results of this meta-analysis showed that in a clinical situation, articaine was more likely to produce anesthetic success than was lidocaine. This higher overall odds ratio of achieving anesthetic success with articaine indicates that there is an advantage to using this local anesthetic. This investigation provided a high level of evidence in support of articaine’s having greater success than other anesthetic solutions when used for pulpal anesthesia in dental applications. These results corroborate the findings of a recent meta-analysis that also favored articaine over lidocaine in terms of anesthetic success.\textsuperscript{13}

This review certainly is not without limitations. The quality of the underlying studies, the consistency of results across studies and the precision of the pooled data affect the strength of inference from systematic reviews considerably.\textsuperscript{12} Another limitation is the methodological heterogeneity of the trials included in this review, including variability of masking procedures, evaluation and definition of anesthetic success, sample size, experience of operator and...
preoperative pulpal status. Clinical practitioners should recognize these inherent limitations, understand the results and apply them judiciously to patient care.

One major challenge posed by this meta-analysis was the difference in the methods used by the investigators in the included trials in terms of assessing the success of pulpal anesthesia. Achieving the soft-tissue signs of local anesthesia is a poor predictor for the presence of profound pulpal anesthesia.49 Thus, our investigation focused on trials in which researchers evaluated the presence or absence of pulpal anesthesia by using electric testing or VAS. Researchers have used EPT to correlate a maximum reading of 80 on the device to indicate profound pulpal anesthesia.50,51 Additionally, research has demonstrated that EPT readings of lower than 80 were associated with pain during operative procedures in asymptomatic teeth.51 Most investigators interested in determining pulpal anesthesia use the EPT method. In this method, anesthetic success often is defined as the percentage of participants who achieve two consecutive EPT readings of 80 within 15 minutes of anesthetic administration and sustain this lack of responsiveness continuously for 60 minutes. These criteria help remove some of the subjectivity in assessing pulpal anesthesia, although the evaluation still relies on a patient’s response. The behavior of the patient and the responses seen in control teeth also require the clinician’s careful attention.52

Using electric testing as a more objective means of determining pulpal anesthesia has been useful in improving the clarity of research outcomes in the area of local anesthesia in dentistry. The investigators in 10 of the 13 studies included in this review used an electric device to determine anesthetic success, and those in the other three used solely the VAS (Table 2).

Evaluation of the efficacy of local anesthetics in dentistry is more difficult in symptomatic teeth. One of the most difficult situations that dentists face routinely is effectively anesthetizing a tooth that contains an acutely inflamed vital pulp. In such instances, success rates for traditional anesthetic methods may drop to unacceptable levels.53 Compounding the problem is the lack of reliability in determining

Figure 4. Forest plots of articaine versus lidocaine: mandibular block treatment effects (posterior teeth only). A. Analysis including both crossover and independent-sample studies (four trials), indicating a slight advantage of articaine (1.57 times) over lidocaine. B. Analysis of independent-sample studies only (inflamed teeth) indicated that there was no difference in treatment effect between the anesthetic solutions used.
pulpal anesthesia by means of electric testing. Even a lack of response to EPT may not guarantee that a tooth is experiencing profound pulpal anesthesia. Several explanations for the failure of anesthetic solutions in patients with such teeth appear in the literature. Nerves arising from inflamed tissues have altered resting potentials and decreased excitability thresholds. It also is known that certain classes of sodium channels are resistant to the action of local anesthetics. A class of tetrodotoxin-resistant sodium channels have been shown to be resistant to the measures of local anesthetics. These channels have been demonstrated to be upregulated during the inflammatory process and are thought to contribute to instances of orofacial hyperalgesia. Additionally, pulps that have been diagnosed with irreversible pulpitis may have an increased expression of sodium channels. These findings help explain why dental patients who seek treatment of pain arising from pulpal pathosis may have difficulty experiencing profound pulpal anesthesia.

The authors of four of the included studies (two studies that involved infiltration and three that involved mandibular block) investigated local anesthetic success in patients who required dental treatment in teeth that had a preoperative diagnosis of irreversible pulpitis. Because of the aforementioned difficulty in using EPT in such teeth, the investigators in these four studies used the VAS to define the outcome after local anesthetic administration. This psychometric response scale has been used as a measurement instrument for subjective characteristics such as dental pain, and it has been used successfully in dentistry primarily for patients who are symptomatic preoperatively. Although the number of studies and each study’s sample size were small, the data for symptomatic teeth showed that both infiltration and block administration had a treatment effect in favor of articaine, which in cases involving the use of mandibular block was not significant (Figure 4B).

One likely reason that the use of articaine has grown among dentists in the United States is the hope that it may become the agent of choice for the inferior alveolar nerve (IAN) block. Corbett and colleagues reported that the efficacy of 4 percent articaine infiltration (1:100,000 epinephrine) compared with that of 2 percent lidocaine IAN block (1:80,000 epinephrine) was not significantly different for anesthetic success in mandibular first molars. Additionally, Jung and colleagues found that the success rate of a standard volume of articaine was not different when used in either buccal infiltration or IAN block. However, successful anesthesia after buccal infiltration in mandibular posterior teeth appears to be not as likely when a lidocaine solution is used. Indeed, researchers in two clinical investigations have stated that articaine resulted in a significantly higher success rate for mandibular buccal infiltration when compared with lidocaine.

All of the studies cited in this paragraph were accounted for in our systematic review and contributed to the final outcome of our review. Several authors have raised concern that the administration of articaine solutions could be associated with an increased risk of inciting adverse events such as paresthesia. Evaluating such associations is outside the scope of this review. However, among the 1,022 independent administrations of articaine, the various authors reported no presence of short-term or long-term paresthesia. Reporting of adverse events among the included trials was not standardized, with several of the authors making no mention of the presence or absence of complications associated with the administration of articaine or lidocaine. Investigators in future trials should report clearly the presence of adverse events or state explicitly if none occurred.

**CONCLUSIONS**

When comparing the newer articaine solution with the gold standard of lidocaine, we identified an emerging trend in our review of published research. The results of these studies often have demonstrated that articaine has a superior anesthetic efficacy, even though proper statistical scrutiny frequently revealed that such differences were not always statistically significant. The findings of our meta-analysis summarize the unbiased direct comparison of articaine and lidocaine and support the argument that articaine does provide a higher rate of anesthetic success. This evidence-based review is aimed to aid clinicians in making informed, judicious decisions when selecting a local anesthetic solution.

In this meta-analysis of the data from 13 selected clinical trials, we found that the administration of an articaine solution for local anesthesia in dentistry has an advantage over lidocaine in respect to achieving pulpal anesthetic success. When we further stratified injection types, we found that the evidence more strongly supported articaine’s superiority to lidocaine with infiltration anesthesia; we found weak evidence for such differences in mandibular block anesthesia. When we took into account various
RCT designs, we found the difference in success rates between articaine and lidocaine to be statistically significant when the method of administration was infiltration or mandibular block in healthy teeth, but we found no statistically significant difference between the two when a mandibular nerve block was used in symptomatic teeth.

**Implications for research.** Well-designed and properly executed RCTs provide the best evidence regarding the efficacy of health care interventions, whereas trials with inadequate methodological approaches may be associated with overestimation of treatment effects. Additional well-designed and fully reported comparative effectiveness trials investigating the difference in anesthetic success between articaine and lidocaine may further strengthen the evidence that formed the basis for this review.

**Implications for practice.** Clinicians may expect a solution of 4 percent articaine (with 1:100,000 epinephrine) to provide a greater probability of anesthetic success than a solution of 2 percent lidocaine (with 1:100,000 epinephrine). The superiority of articaine is most significant when used during local infiltration anesthesia. Regarding the relative strength of treatment effects among multiple quantitative studies, we can state that within a 95 percent CI, the true odds ratio of articaine (2.44) indicates that this anesthetic is 1.59 to 3.76 times more likely to produce anesthetic success than is lidocaine. When we considered infiltration data only, we found that the results of our meta-analysis indicated that articaine is an estimated 3.81 times more likely to produce anesthetic success than is a similar volume of lidocaine. There is weak evidence that the use of articaine allows for a higher percentage of anesthetic success when administered via a mandibular block, and thus it is premature to recommend articaine as a substitute for lidocaine in achieving a successful mandibular block.

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