

Articaine vs. Lidocaine

An article in the December issue of the *Journal of the California Dental Association* by Stanley Malamed, DDS, "Local Anesthetics: Dentistry's Most Important Drugs, Clinical Update 2006" appears to be written to promote the use of articaine and nullify the reports of paresthesia rates up to 20x that of lidocaine. The word "articaine" appears 17 times, three times noted as "articaine is very popular," and once as "it is increasingly popular in the United States." The article uses the word "superiority" four times with the local anesthetic, "superior" once, and "advantage" once.

Dr. Malamed reports claims that articaine works faster, works better, is effective more often, gets the patient numb when other local anesthetics fail, and that endodontists have become "enamored" with the drug. Terms used for the other amide local anesthetics are "very effective in general," "darned good," and "more traditional." Although there are many studies, including Septodont's FDA study on Septocaine, that the efficacy of lidocaine for local anesthesia is unsurpassed, he only listed a clinical trial where articaine had better results than lidocaine. However, that study was for trying to achieve anesthesia of mandibular posterior teeth via a buccal infiltration. A testimony to the efficacy and safety of lidocaine compared to articaine are the data in Table 2 of the article where it can be seen that lidocaine is used nearly 50 percent of the time and nearly twice as much as articaine. Also supporting the efficacy and safety of lidocaine is its predominant use in dental schools in the United States.

Interestingly, Jeffrey Caputo, DDS, a 2005 graduate from University of Southern California and a resident in the University of Pacific, Arthur A. Dugoni School of Dentistry, Oral and Maxil-

lofacial Surgery Program at Highland Hospital, publicly stated that articaine is not used, or is seldom used, at University of Southern California. According to Dr. Caputo, Dr. Malamed said articaine was restricted for "political reasons."

While appearing to promote the use of articaine, the author endeavors to nullify the global findings that the drug is associated with very significant

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increases in paresthesias with mandibular block injections. Very few of the possible references reporting the increased paresthesias with articaine are included, and the article by Hillerup and Jensen on the 52 paresthesias in Denmark is mischaracterized.¹ Dr. Malamed stated on two occasions there is no scientific evidence that articaine is associated with increased paresthesia rates. He also stated that the advisories to dentists from TDIC and the Professional Liability Program of Toronto, Canada, suggesting that it might be prudent to avoid the use of articaine in mandibular nerve blocks is unjustified. Actually, there is substantial evidence of the very significant increase in paresthesias with the use of articaine. The concluding quote from the FDA statisticians on the Septocaine study was, "Regarding the adverse events, there is

evidence that the risks of paresthesia and nausea are higher with articaine than with lidocaine."²

At least three times the FDA has required changes in the product insert for articaine because of reports of adverse events to the FDA. One of the changes is listed as "Persistent paresthesias of the lips, tongue, and oral tissues have been reported with the use of articaine hydrochloride with slow, incomplete, or no recovery. These postmarketing events have been reported chiefly following nerve blocks in the mandible and have involved the trigeminal nerve and its branches."^{3,4} An article demonstrating articaine has up to a 20x higher paresthesia rate than lidocaine can be seen at dentistrytoday.com.⁵ Contrary to the portrayal by Dr. Malamed, Hillerup and Jensen concluded, "This indicates that during the two-year period mentioned, Articaine produced a more than 20-fold higher incidence of injection injury when applied for mandibular block analgesia."¹

The increased paresthesia rate with articaine has been noted by a large dental clinic, government agencies, and dental insurance carriers (SAFECO in 2001, Royal College of Dental Surgeons of Ontario, Canada in 2005, The Dentists Insurance Company in 2005).⁶⁻¹¹ Note that the European Union's Eudravigilance does not publish adverse events data.

The depth and breadth of the problem can also be seen by a literature search on "articaine AND paresthesias" as well as via search engines (google.com, yahoo.com, ask.com, answers.com and wikipedia.com) on the subject, and discussion boards on dentaltownusa.com and other dental Web sites.

Two of the references cited by Dr. Malamed are his papers on the safety and efficacy of articaine from the Septodont's

CONTINUES ON 242

LETTERS, CONTINUED FROM 240

FDA study on Septocaine, for which he was the principal investigator.^{12,13} Dr. Malamed quotes the conclusion of his research that articaine is a “safe and effective local anesthetic” for dentistry. Having more than 11 paresthesias in 882 treatments seen in the product insert could hardly be characterized as “safe.”^{3,4,14} I also found a number of irregularities in the Septocaine study and journal articles from the study. Listed below are what I believe to be some of the irregularities in these publications.

- The efficacy article on Septocaine (articaine) was reported nine months before the safety article on Septocaine (articaine) even though all data was available for reporting.^{12,13}

- The authors stated the drug was “well-tolerated” in the efficacy article, on articaine despite 21 paresthesias documented in 882 patient treatments.^{12,15}

- The references listed in the efficacy article did not include any with reported paresthesias.¹²

- Cases of paresthesia that did not begin on the day of the injection were attributed to the dental procedure and not the anesthetic even though there was no dental surgery that could have damaged the lingual or inferior alveolar nerves.^{13,15}

- Although Dr. Malamed’s textbook recommends patients should be seen clinically to determine the degree and extent of paresthesia and to record findings, this was not done in the study.¹⁶

- The lexicon for neuropathies was reported as being inconsistently used.¹⁵

- Data on paresthesias was reported as being inconsistently gathered.¹⁵

- Several cases of pain and burning were reported with the paresthesias.¹⁵

- Cases of paresthesias were listed as, and with, minor adverse events from local anesthesia.¹³

The number of mandibular block injections administered in the study is not noted.^{12,13}

- The authors reported that lidocaine had the same frequency of paresthesias as articaine.¹⁵

Even without reporting the number of mandibular block injections and apparently not reporting some paresthesias, the Septodont’s FDA application indi-

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cated there were 21 paresthesias in 882 patient treatments.¹⁵ This is reported as a 2 percent paresthesia rate. This number of paresthesias would be 1:42 treatments and does not select out the number of mandibular block injections where the paresthesias occurred.

The authors also did not consider some of the paresthesias to be due to the local anesthetic. On page 259 of the FDA application it was stated, “In many cases, symptoms did not begin on the same day as the administration of study drug, indicating that these symptoms were more likely to be due to the procedure than the anesthetic.”¹⁵ This indicates it was the study drug articaine that was connected with these paresthesias. Also, their conclusion that it was the dental procedure and not the articaine that was responsible for the paresthesias is preposterous since there were

no dental procedures adjacent to the lingual or inferior alveolar nerves. Also, “delayed” paresthesias are known in dentistry to be associated with the injected solutions, not the procedure. Evers and Haegerstam in “Introduction to Local Anesthesia” indicated injected solutions may cause edema that over time may induce a paresthesia some time after the treatment.¹⁷ It has also been reported that the highest concentrations of local anesthetics are associated with endoneurial edema.¹⁸ The issue of “delayed” paresthesias is also discussed on page 183 of the safety article on articaine.¹³ In the FDA study a table listed as, “Summary of patients with numbness/tingling at the second follow-up interview” shows 38 percent of the patients with pain or burning.¹⁵

There were serious self-reported flaws in the author’s data gathering. Page 256 of the FDA application states, “In some cases the numbness and tingling were recorded as adverse events (coded as paresthesia, hypesthesia, or circumoral paresthesia), but this was not consistent across all investigators.¹⁵ Therefore, the overall rate of paresthesia derived from telephone follow-up is higher than the rate of paresthesia recorded as adverse events.” It goes on to say, “Follow-up was continued for these reports of paresthesia; however, these additional phone contacts were not consistently recorded in the database.” The safety article on articaine indicates that the providers of dental treatment did not make the calls to the patients.¹³

Concerning the sampling and demographics, the efficacy article on articaine indicates, “Many factors were equally distributed by the authors in the study.”¹² Although the demographics of complexity of procedure and patient age, weight, gender, and race were distrib-

LETTERS, CONTINUED FROM 242

uted and listed, there is no listing of the number of maxillary and mandibular procedures or the number and type of injections administered. The distribution of arch and injection would be critical for reporting the frequency of paresthesias with mandibular block injections. Although the study submitted to the FDA indicated a 2 percent (21/882-actually 2.38 percent) paresthesia rate for articaine, if half of the patients received mandibular block anesthesia the paresthesia rate would be 4.76 percent (21/442) or 1 paresthesia per 21 mandibular block injections.

It appears the FDA approval of articaine was based on the Septocaine study reporting that articaine had the same safety and efficacy profile as lidocaine. Lidocaine was the control local anesthetic administered in 443 patient visits and articaine was administered in 882 patient visits. On page 256 of the Septodont study to the FDA reports 2 percent (21/882) of the patients who received Septocaine (articaine) and 2 percent (10/443) of the patients who received lidocaine had paresthesias.¹⁵ On page 259 it states, "Thus, there were no differences between treatment groups in the rate of or nature of prolonged numbness/tingling following anesthesia and a dental procedure." This would be very unusual considering the study done in Ontario, Canada, where there were only five confirmed lidocaine-linked paresthesias reported in 21 years.¹⁹ If the 10 paresthesias for lidocaine were accurate, and if half of the injections were for mandibular block injections, the paresthesia rate would be 10 paresthesias in 222 patients, or 1 in every 22 patients receiving a mandibular block injection.

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