

## Articaine versus Lidocaine: The Author Responds

In the April issue of the *Journal of the California Dental Association*, a letter to the editor, written by Dr. James Dower, was published.<sup>1</sup> The major premise of this letter is that the paper “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.<sup>1,2</sup> I would like to address a number of his comments.<sup>3</sup>

In the first paragraph in the articaine section of the paper I stated: “Little to no evidence-based medicine exists demonstrating any superiority of articaine over other available local anesthetics. ... Included in these admittedly anecdotal reports are claims that articaine (1) works faster; (2) works “better”; (3) “I don’t miss as often”; and (4) “gets patients numb when other local anesthetics fail.” Dr. Dower interprets this as being “written to promote the use of articaine.” Let the reader judge. I disagree.

Dr. Dower continued by stating that I ignore the majority of clinical studies that demonstrate that the “efficacy of lidocaine for local anesthesia is unsurpassed” and “only listed a clinical trial where articaine had better results than lidocaine.”<sup>1</sup> The reality is somewhat different. I wrote: “Since its introduction in Germany in the early 1970s, articaine has been compared in double-blinded, randomized, controlled clinical trials to each of the other available local anesthetics. To date, only one clinical trial has demonstrated any superiority of articaine to any other local anesthetic.<sup>4</sup> I went on to describe the phase 3, double-blinded, randomized clinical trials mandated by the U.S. Food and Drug Administration requiring that a new drug be evaluated for its safety and efficacy.<sup>5,6</sup> Twenty-nine

dental schools in two countries, the United States and the United Kingdom, were involved. Articaine, the new drug, was compared to the “standard of comparison” lidocaine. Results of the studies, in which 1,325 patients were treated, found that “there were no clinically significant differences between articaine and lidocaine, and concluded

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that articaine was a ‘safe and effective local anesthetic’ for dentistry.”<sup>5,6</sup>

Lidocaine represented the first amide local anesthetic used in medicine and dentistry, entering the dental market in 1948. It still represents the most used local anesthetic in medicine and dentistry worldwide. Articaine, introduced in Germany in 1973 and the United States in 2000, has rapidly become either the most-used local anesthetic (e.g., Germany, Canada, and Denmark) or second most popular (United States).<sup>7</sup>

These are the scientific facts about the clinical trials regarding articaine and its subsequent use in dentistry.

The second, and major, theme of Dr. Dower’s letter is his claim that “the author(s) endeavors to nullify the global findings that the drug is associated with

very significant increases in paresthesias with mandibular block injections.”<sup>1</sup>

There is absolutely no scientific evidence available to support the claim that articaine is associated with a greater incidence of paresthesia (or stated more correctly, is more neurotoxic) than other local anesthetics.

This claim is addressed in considerable depth in the original paper.<sup>2</sup> The interested reader is also referred to the available statistical analysis of articaine found in the new drug application, NDA, which was reviewed and approved by the FDA.<sup>8</sup>

Yes, there is “buzz” in our profession today about the possibility of 4 percent drugs, specifically articaine, being associated with increased incidences of paresthesia. But as previously stated, there exists absolutely no scientific evidence demonstrating that this may be true. All reports and papers are anecdotal in nature, yet have taken on a life of their own with several insurance carriers and other organizations suggesting that 4 percent local anesthetics be avoided in the mandibular nerve block.”<sup>9,10</sup>

An example of the hysteria being generated by some is illustrated by the “Letter of Concern” sent to thousands of U.S. dentists in September 2006 by Emery & Webb, Inc., in which it was stated: “We at Emery & Webb/Ace USA have had a recent increase in anesthetic-related malpractice incidents. They are essentially related to the administration of articaine (Septocaine) as an anesthetic ... we have noticed an increase in reversible and, in some cases, nonreversible paresthesias. These have been mostly limited to the accomplishment of a mandibular inferior alveolar nerve block. ... We are writing you to alert you to these events in hopes that you will not fall victim to one of these incidents.”<sup>11</sup>

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The letter goes on to recommend: "Limit the use of articaine to infiltration and PDL anesthesia."

Concerned and informed dentists and dental educators across the United States communicated their concerns about the veracity of these statements with Emery & Webb resulting in a "Notice of Retraction" (Oct. 31, 2006) reading, in part: "Unfortunately, we at Emery & Webb discovered upon further review, and subsequent to the mailings, that both documents contained certain inaccuracies and an alarmist tone, which was not warranted."<sup>12</sup> "Emery & Webb has not noted an increase in malpractice claims or lawsuits in connection with articaine as referred to in the e-mails and further, it is not aware of any increase in claims at ACE USA. It should be made clear that Emery & Webb has not conducted any scientific investigation, sampling, testing, or other investigation of the articaine anesthetic, and has no independent knowledge or data which would restrict the use of the product."

In a paper published in the *International Journal of Oral and Maxillofacial Surgery* in 2006, Hillerup and Jensen reported on 52 cases of paresthesia reported in Denmark.<sup>13</sup> Of these, 42 involved only the lingual nerve, yet, the authors concluded by stating "Until factual information is available, a preference of other formulations to articaine 4 percent may be justified, especially for mandibular block analgesia" despite having made this important comment, "Thus, there is an urgent need for further studies focused on the problem of neurotoxicity of local analgesics with specific focus on articaine 4 percent."

Responding to an inquiry concerning the Danish paresthesia paper, the European Union's Pharmacovigilance Working Party re-evaluated the incidence of adverse effects, especially the hypothesis

that nerve injuries (paresthesias, sensory impairment) may be caused by local anesthetics used in relation with dental care and, specifically, that articaine was responsible for an increased risk of nerve injuries compared with other local anesthetics.<sup>14</sup> Their report included international experiences from 57 countries, estimating the annual number of patients treated with articaine at approximately 100 million.<sup>14</sup> The

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European Union's investigation reviewed experimental studies and clinical trials with healthy volunteers and patients, and included all local anesthetics used in dentistry, not only articaine.

The report concluded that the "safety profile of the drug (articaine) has not significantly evolved since its initial launch (1998). Thus, no medical evidence exists to prohibit the use of articaine according to the current guidelines listed in the summary of product characteristics" (the drug package insert).

This report from the European Union's Pharmacovigilance Working Party represents the most careful scientific analysis of the perceived "problem" of articaine-related paresthesia to date.

In a recent review of local anesthetic associated paresthesia, Missika and Khoury stated that "a clear causal relationship has not been established in the literature between the anesthetic agent and neurological complications such as paresthesia."<sup>15</sup>

In the April *Journal of the California Dental Association*, coincidentally, the same issue in which Dr. Dower's letter appeared, Dr. Pogrel reported on the first well-documented review of local anesthetic associated paresthesia.<sup>16</sup> His review included examination of all patients (n = 57), questioning of their dentists, and a review of their medical records. He concluded that "we do not see a disproportionate nerve involvement for articaine."

Thus, I remain firmly of the opinion that given the present level of scientific evidence or, more accurately, the lack thereof, linking 4 percent local anesthetics with an increased risk of neurotoxicity, it seems that advisories to dentists from agencies suggesting it might be prudent to avoid the use of articaine in mandibular nerve blocks is unjustified at this time.

To further debunk the statement that the primary focus of my paper was "to promote the use of articaine and nullify the reports of paresthesia rates up to 20x that of lidocaine," I offer the concluding statement in my paper: "However, as in all dental treatments and therapies, it is you, the doctor, who must make the ultimate decision as to whether or not to use a 4 percent local anesthetic, such as articaine, in mandibular block anesthesia. This decision should follow assessment of the benefits to be accrued from use of the drug versus the potential risks associated with its administration. Only when, in the mind of the doctor, the benefit clearly outweighs the risk should the drug be administered."

“Remember, that prior to the introduction of articaine into the United States in 2000, local anesthesia in dentistry was not a problem. Successful pain control can be achieved with other drugs.”<sup>2</sup>

To the readers of the *Journal* I would recommend that you carefully evaluate the quality of science presented in publications, including peer-reviewed journals such as the *Journal*, or in statements made by continuing education “gurus” before making decisions on whether or not to use a drug, or any other dental material or procedure.

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