

# Is it safe to use Articaine?

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**There is no national science just as there is no national multiplication table; what is national is no longer science.**  
Anton Chekhov

**C**an the use of articaine cause paraesthesia? Should dentists refrain from using it for mandibular blocks? How did these allegations start, what are the true risks and what is the science behind this controversy?

Over three decades ago, in 1976, articaine hydrochloride was introduced to the German market as the newest amide-type anesthetic. This new drug, originally known as carticaine, had a different molecular structure containing a thiophene ring instead of the usual benzene ring present in the other amide anesthetic drugs. It became available in North America (Canada) in 1983.

In 1995, an article by Haas and Lennon<sup>1</sup> analyzed the data from non-surgically induced paresthesia cases reported to the Professional Liability Program (PLP), which administers a group policy of malpractice insurance that covers all dentists licensed by the Dental College in Ontario, Canada.

This paper, which seems to have become the cornerstone in the discussion of the alleged relation between articaine and paresthesia, analyzed 143 cases reported in Ontario over a 21-year period. The authors

concluded that "...the overall incidence of paraesthesia following local anaesthetic administration for non-surgical procedures in dentistry in Ontario is very low, with only 14 cases being reported out of an estimated 11,000,000 injections in 1993. However if paraesthesia does occur, the results of this study are consistent with the suggestion that it is significantly more likely to do so if either articaine or prilocaine is used."

In another paper, the same authors reviewed<sup>2</sup> 19 reported paresthesia cases in Ontario for 1994, concluding that the incidence of paraesthesia was 2.05 per million injections of 4% anesthetic drugs.

A follow up study published in 2000<sup>3</sup>, concluded that the incidence of paresthesia from either prilocaine or articaine was close to 1:500,000 injections.

These studies implied a direct relationship between the higher concentration of prilocaine and articaine solutions, in possibly causing paresthesia after their injection.

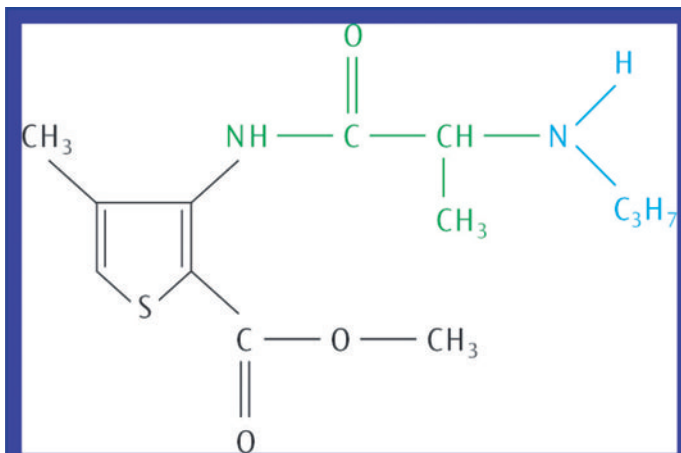
It is important to keep in mind these three papers were not true controlled scientific studies. They were strictly reviews of the voluntary reports received by the RCDSO. As a side note, the PLP switched insurance underwriters. In anticipation of the change, dentists were asked to report any potential claims, which could have increased the number of reported cases in the first paper.

Nonetheless, the conclusions from these papers are subjective, since the data used to make these claims has a number of inconsistencies which need to be pondered. For example:

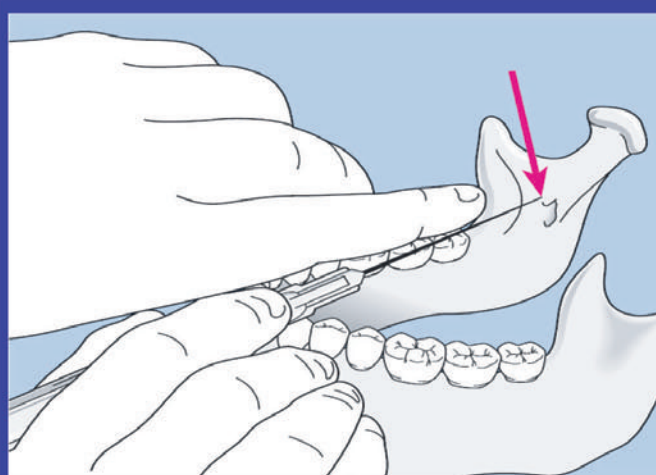
- **The total duration of the paresthesia episodes was not documented.** Paresthesia was defined as a prolonged numbness, tingling sensation, loss of taste, etc. There was no clear evidence of permanency, or of a total loss of movement or sensation in the affected areas.
- **The anesthetic used in over 30% of the incidents reported was not identified.** This missing information from such a high percentage of the cases assessed, could have shifted the results completely. It is also a good example of the inconsistency of the data used for these studies.
- **The size and caliber of the needle used was only documented in about 26% of the cases reviewed in the 21-year retrospective<sup>1</sup>.** This introduces another inconsistency in these reports.
- **The injection technique used in each incident was not described.** This is a key missing element when reviewing a multi-centre report. Even though there were reports of 31 patients feeling a “stabbing or electric shock type” pain during injection, no distinction was made when tallying the results for each drug. This sensation is often an indication of needle trauma to the nerve, and potentially a cause for the neuropathies reviewed<sup>4</sup>. The traditional Inferior Alveolar Block technique has a higher potential of direct nerve trauma than other techniques such as the A.R.T. mandibular block<sup>5</sup>, Gow-Gates<sup>6</sup> or Vazirani-Akinosi,<sup>7</sup> due to the change of direction of the needle at the approximate depth of the lingual nerve<sup>4</sup>. The question arises as to the number of cases that were due to traumatic injury, as opposed to those caused, or compounded, by the anesthetic solution.

Assuming the results of their analysis are accurate, and a proof that these paresthesia events are strictly concentration-dependent, we have to fully understand the magnitude of the numbers presented in them.

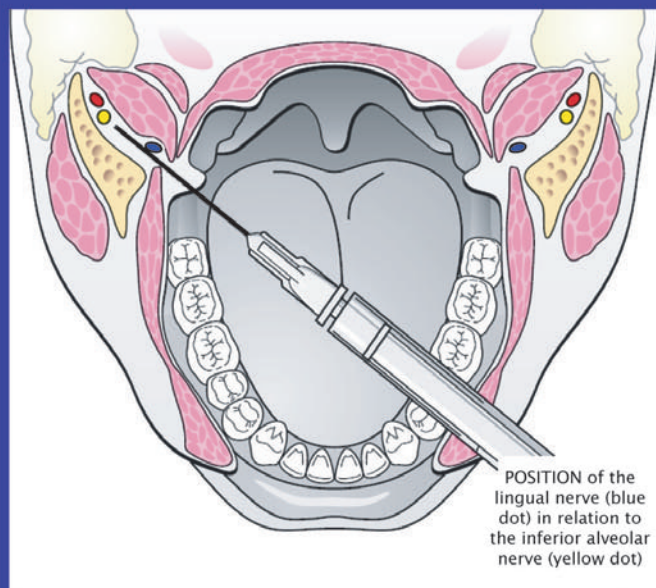
These articles, which are the foundations for this discussion, show that 4% anesthetic drugs have a paresthesia incidence of approximately 1 in 500,000 injections, and 1 in 785,000 for any other solution. If we consider the average Dentist in Ontario gives around 1,800 injections every year<sup>8</sup>, statistically, he or she could expect to cause an anesthetic-induced paresthesia in one of their patients every 277 years using 4% drugs, or every 436 with the 2-3% solutions. Fortunately, no one practices that long.



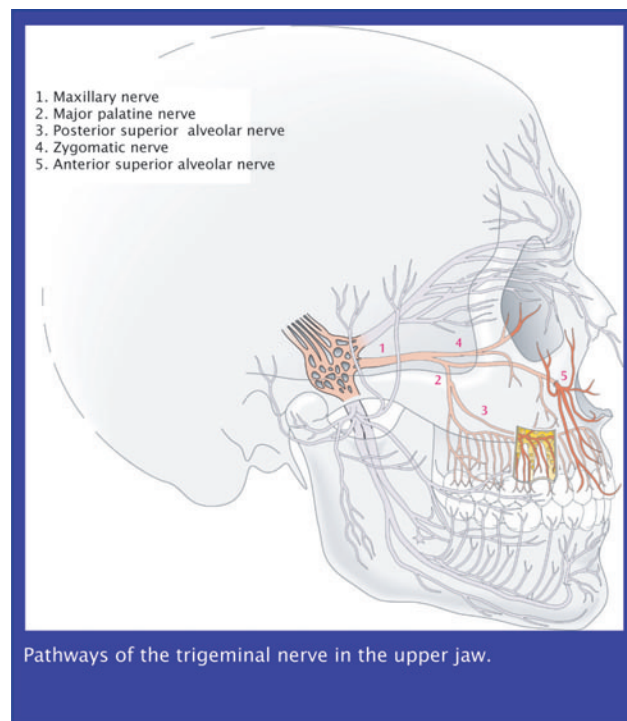
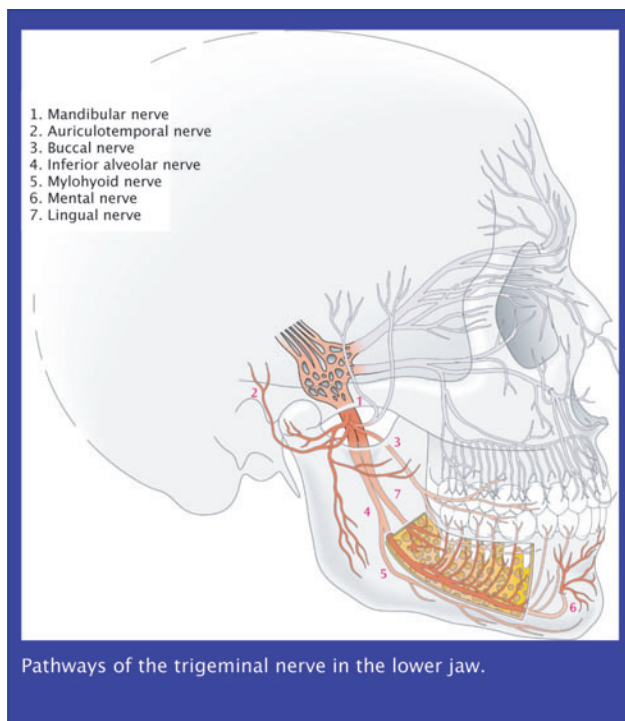
Chemical structure of articaine.



Target area for the traditional Inferior Alveolar Nerve block.



Path of a needle in the traditional Inferior Alveolar Nerve block.



Again, to clearly understand these odds, we have to compare them to other risks present in our daily lives. Then, we can see that one is two times more likely to die as a result of being struck by lightning (1 in 250,000)<sup>9</sup> than to experience a paresthesia event; and also illustrate that a patient is actually significantly more likely to die in a car accident on the way to his dental appointment (1 in 11, 236<sup>10</sup>), or of being murdered (1 in 50, 000<sup>11</sup>), than to experience this adverse reaction.

Other studies, such as one published by Hoffmeister<sup>12</sup>, indicate that 4% solutions are not capable of damaging the nerve, even when injected directly into it. His experiments demonstrated that, after direct injection of 4% articaine to the nerve, no morphologically detectable toxic lesions were observed under the microscope. He used a volume of articaine in proportion to the minute size of the animal nerves employed in his study, and concluded these neurosensory disturbances are the result of intraneural haematomas with consecutive fibrosis.

There are various studies, such as those by Krafft and Hickel<sup>13</sup> or Harn and Durham<sup>14</sup>, supporting his findings. They show an incidence of direct needle trauma to the nerve during traditional inferior alveolar blocks of 7.7% and 3.62% respectively. They demonstrate that the actual injection has a significantly higher risk of causing neural damage than the anesthetic solution itself, especially because, in the traditional IAN block, the lingual nerve lies directly in the path of the needle.

This evidence supports the use of alternative techniques to the traditional Inferior alveolar block, but not the need

to switch anesthetics. There are no reports of paresthesia in the scientific literature when using alternative mandibular block techniques. Why isn't this, then, an integral part of the debate?

This argumentation against articaine was brought back to the forefront when, in the summer 2005 issue of the Dispatch, the Royal College of Dental Surgeons of Ontario (RCDSO) published an article<sup>15</sup> under the heading of "Practice Alert" questioning the safety of articaine for local dental anesthesia due to the risk of paresthesia. Although the article didn't bring forward any specific evidence or new scientific data that would warrant such a warning, some dental professionals in Ontario felt compelled to rethink their anesthetic selection, feeling at risk of compromising their licences by going against the College's recommendation.

Direct damage to the nerve caused by 4% drugs has never been scientifically proven. As expressed above, some research suggests that these solutions can cause paresthesia more frequently than other anesthetics, or that needle trauma to the nerve when these substances are injected can have more negative consequences. Nonetheless, as Stanley F. Malamed, who is arguably one of the highest authorities in dental anesthesia in the world, has stated that "there is absolutely no scientific evidence to demonstrate there is a greater risk of paresthesia associated with the administration of a 4 percent local anesthetic"<sup>16</sup>.

Since Canada has been ground zero for this discussion, it's also important to ponder that anesthetic-induced

paresthesia has never become a concern for Canadian tribunals and health authorities.

As a matter of fact, the Ontario courts<sup>17</sup> established based on testimony, that the risk of a paresthesia caused by simple injection is extremely low, and not a common enough complication that would require obtaining consents from patients before administering an anesthetic drug<sup>18</sup>.

A search in the Health Canada Adverse Reaction Reports (1983-2008) in the CADRMP Adverse Reaction Database<sup>19</sup> reveals about 4% and 2% local anesthetics that, in almost 25 years, there are only 6 cases labeled as a "Paresthesia", and 14 more where the file shows symptoms that could be associated to a paresthesia, but is not labeled as such. None of them indicate the exact duration of these events, and 7 of these 20 are labeled as "recovered without sequelae".

In a country like Canada, where approximately 30 million dental local anesthetic injections are given per year, 20 Adverse Reaction Reports over 25 years are negligible, to say the least.

This also highlights the discrepancies between the PLP reports and the ones received by Health Canada. Besides, the information from Health Canada is readily accessible online to anyone interested in analyzing it. The PLP reports, on the other hand, are labeled as confidential, and not accessible for third parties to review.

In the United Kingdom, where some allegations about paresthesia in the presence of articaine were also made through letters to the editor of a journal<sup>20 21 22</sup>, a search of the reports made through the Yellow Card Scheme<sup>23</sup> of the Medicines and Healthcare Products Regulating Agency of the Ministry of Health, shows zero reports for adverse reactions caused by articaine.

In the USA, articaine became available in early 2000. During the approval process, clinical studies were submitted to the FDA. One of these research projects, conducted by Malamed et al<sup>24</sup>, is the only "three identical, single-dosed, randomized, double blind, parallel group, active-control, multicenter" study on this subject to date. He concluded that articaine and lidocaine were comparable in many ways, including their paresthesia incidence. In their trial, lidocaine 2% and articaine 4% had an identical incidence of paresthesia events 7 days after the injection: 1% for both groups. Despite the fact that the FDA approved articaine based on the findings of the above-mentioned study, there has been an ongoing discussion on the subject of paresthesia allegedly caused by Septocaine in the USA. A lawsuit-happy society has become a breeding ground for all sorts of rumors on the subject.

Recent reports, such as one by the C.R.A.<sup>25</sup>, offer conflicting numbers of paresthesia incidents in the presence of this drug. These reports originated from a group of 110

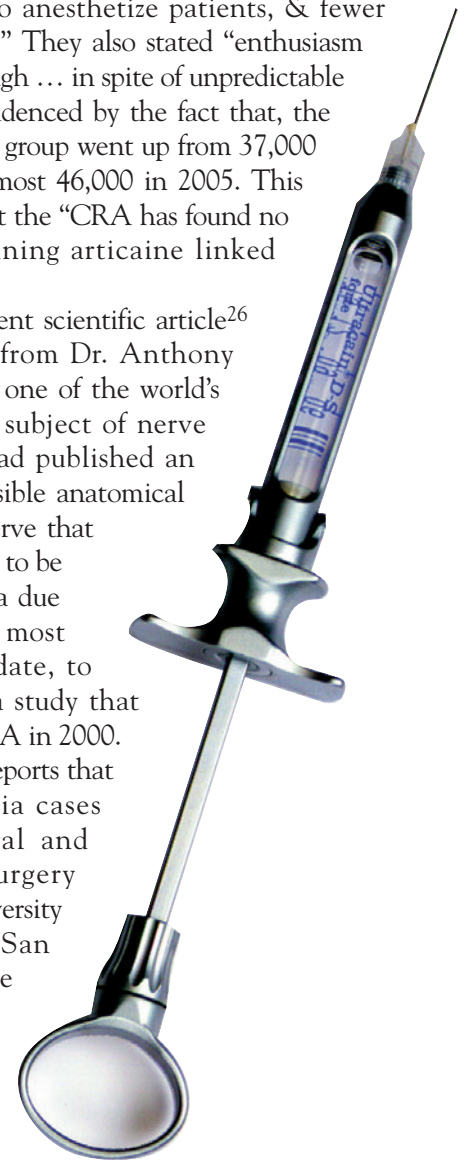
dentists (Permanente Dental Associates) who service the members of an American HMO (Kaiser Permanente). They state that the dentists in the group in question had 7 paresthesia reports on the first year they used articaine both for blocks and infiltration (2002). That same year, they had another 5 reports from the use of lidocaine, bupivacaine and mepivacaine.

The following year, this group of dentists decided to stop using articaine for mandibular blocks, and the reports about paresthesias caused by articaine went down to 4. Nonetheless, the events for other anesthetic solutions, including prilocaine (1 case), went up to a total of 5 incidents. In 2004, they only had 1 incident reported for articaine, but had a total of 3 for all the other anesthetic drugs.

Another interesting item in the CRA report were the comments from these dentists which "reported fast onset, success with difficult to anesthetize patients, & fewer unsuccessful anesthetics." They also stated "enthusiasm with articaine remains high ... in spite of unpredictable paresthesias." This is evidenced by the fact that, the usage of articaine in this group went up from 37,000 cartridges in 2002 to almost 46,000 in 2005. This paper also concludes that the "CRA has found no common factor explaining articaine linked paresthesias."

Notably, the most recent scientific article<sup>26</sup> on the subject comes from Dr. Anthony Pogrel, who is arguably one of the world's leading experts in the subject of nerve trauma. In 2003, he had published an article explaining a possible anatomical feature of the lingual nerve that can render it more prone to be affected by a paresthesia due to needle trauma. His most recent paper is an update, to include articaine, for a study that came to light in the JADA in 2000.

In this new study he reports that 35% of the paresthesia cases evaluated by the Oral and Maxillofacial Surgery Department of the University of California at San Francisco, involved the use of lidocaine. Articaine had only been used in 30% of the cases reviewed. He states "nerve blocks can



cause permanent damage to the nerves, independent of the local anesthetic used.” Also mentions “...we do not see any disproportionate nerve involvement from articaine.” He also concludes “articaine is associated to this phenomenon in proportion to its usage.”

It is quite remarkable that most, if not all, of the paresthesia incidents reported seem to be associated to mandibular blocks, and especially affecting the lingual nerve. If these anesthetic solutions were indeed chemically toxic, wouldn't it be expected that this type of nerve injury would appear in regions other than the mandible?

Why is it that, if articaine is also widely used around the world for ophthalmologic, orthopedic, and even for spinal anesthesia, there are no paresthesia reports in scientific literature for these surgical fields?

Since its introduction to the dental world more than 30 years ago, dentists around the world have claimed they have better anesthetic results with articaine. These claims had been considered only anecdotal, up until recently, when an increasing number of articles<sup>27 28 29 30 31 32 33</sup>, as recent as

January of 2009<sup>34</sup>, have surfaced corroborating the clinical perception of the superiority of articaine as a local anesthetic.

The fact is that thousands of dentists in over 135 countries have been using articaine with great success in their clinical practices for many years. In Germany, articaine is used in 90% of all dental anesthetics<sup>35</sup>. In less than a decade, this drug has captured roughly a third of the anesthetic market in the United States, with over 65 million cartridges sold every year<sup>26</sup>. In Canada, articaine has an even higher percentage of market share.

The author speculates that, if dentists couldn't see any clinical advantages in using articaine, or had experienced a significant number of paresthesias that might be attributed solely to the chemistry of this drug, they would have discontinued the use years ago.

More importantly, as Malamed has expressed: “Allegations that 4 percent local anesthetics are associated with a greater risk of paresthesia are based solely on anecdotal reports and have no scientific justification.”<sup>36</sup>

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