Articaine: Efficacy and Paresthesia in Dental Local Anesthesia

A Peer-Reviewed Publication
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Educational Objectives
The overall goal of this article is to provide information on local anesthetics.
Upon completion of this course, the clinician will be able to do the following:
1. Know the types of local anesthetics available for use in the dental office
2. Understand the chemistry and pharmacokinetics of articaine
3. Describe the data supporting the efficacy and safety of local anesthetics, and specifically articaine
4. Describe the factors influencing dysesthesia and paresthesia.

Abstract
This review analyzes the current reports and publications involving the performance and clinical effectiveness of local anesthetics (efficacy) and the rare occurrence of post-operative prolonged numbness or tissue hypersensitivity (paresthesia, dysesthesia). No particular local anesthetic is scientifically singled out as causing this effect. Historically, scientific data on superior performance of one local anesthetic compared to another was lacking. One recently published report, however, showed the statistically significant and superior effectiveness of articaine in obtaining anesthesia of first permanent molars by infiltration when compared to lidocaine. The paresthesia debate regarding the potential of a 4% local anesthetic solution to be allegedly more neurotoxic than other currently administered local anesthetic solutions of lesser concentrations is examined. There is a lack of conclusive and experimentally reproducible evidence, of the cause and effect of specific local anesthetics to chemically result in post-operative sequelae such as paresthesia. An examination of the potential causative factors associated with paresthesia suggests mechanical and/or neurotoxic phenomena. Further evidence and scientific study are required to conclusively determine the significant role, or lack thereof, of each factor.

The Evolution of Articaine
The synthesis of articaine (originally named carticaine) in 1969 created a new clinical and investigative enthusiasm in a market that had otherwise been dormant since the mid-1950s. Articaine was synthesized in Germany and then introduced for clinical use in Europe in 1976 (Ultracaine®, Hoechst Pharmaceuticals) and in Canada in 1982.1 It was reported to have superb diffusion capabilities, adequate onset and a highly efficacious drug. Just as lipid solubility is crucial for a drug’s rapid metabolism, articaine is distinguished from other amides. The thiophene portion of the molecule gives articaine a high lipid solubility.1,4,5

This chemical displays the following properties and behavior:
1. An amide group local anesthetic
2. A highly lipid-soluble thiophene aromatic ring
3. An ester hydrolysis component (90%) that contributes to the drug’s rapid metabolism

Figure 1. Structural formula and physico-chemical data for articaine.

Articaine HCl is recognized by the chemical name 4-methyl-3(2-[propylamino] propionamido)-2-thiophenecarboxilic acid, methyl ester hydrochloride.2 This chemical displays the following properties and behavior:
1. An amide group local anesthetic
2. A highly lipid-soluble thiophene aromatic ring
3. An ester hydrolysis component (90%) that contributes to the drug’s rapid metabolism

Articaine is distinguished from other amides. The thiophene portion of the molecule gives articaine a high lipid solubility.1,4,5 This fact is critical, as the higher the lipid solubility, the higher the potency and the better the diffusion through the medium into which it is injected, and, therefore, the greater its ability to cross the lipid membranes of the epineurium. Relative values or indices assigned to the lipid solubility of various local anesthetics are shown in Table 1. Though no definite scientific conclusions can be reached from this fact, theoretically, articaine would be a fast-onset and a highly efficacious drug. Just as lipid solubility is crucial
to the action of any drug, protein binding must also be considered with respect to increased duration (especially in block techniques), delayed systemic absorption, lowered risk of toxicity and whether or not a vasoconstrictor should be placed into a local anesthetic solution at all. The approved concentrations of epinephrine for use in dental anesthetic cartridges worldwide are epinephrine HCl 1:100,000 and epinephrine HCl 1:200,000.

Protein Binding

Although the term protein binding is generally conceptualized to occur at sites on circulating plasma proteins and colloids, local anesthesia protein binding refers specifically to the phenomenon occurring inside the neuron, notably in the sodium channels. The prolonged duration and slowed release of the agent into the systemic circulation result from protein binding at the cellular level. Table 1 illustrates, for example, that lidocaine is 65% bound to intracellular proteins in the sodium channels, compared to articaine, which is 95% protein bound. This has a more significant influence in block scenarios, whereas epinephrine concentration may play the dominant role in infiltration techniques.1

A significantly lower risk of rapid uptake of the local anesthetic solution into the systemic circulation is seen with the more concentrated 1:100,000 epinephrine compound. This increases the safety margin for the upper dose limits of the drug, yet also increases the potential of palpitations and related cardiotropic β1 episodes. In fact, Daublander et al. studied 2731 patients and found that 4% articaine 1:100,000 epinephrine caused more sympathomimetic effects than did 4% articaine 1:200,000 epinephrine.6 These effects included chest discomfort, tachycardia, diaphoresis and increased apprehension.

In a retrospective study on local anesthetic use by dentists in the province of Ontario, Canada, articaine had captured 38% of the market share of all dental local anesthetics by 1995, with usage almost equally divided between the 1:100,000 epinephrine and 1:200,000 epinephrine containing solutions.7 This represents a significant choice advantage for a dentist pondering the maximum dose of a vasoconstrictor to be used in a patient.1

Metabolism

A significant molecular difference exists between articaine and the other amides. Articaine possesses an additional ester linkage on the thiophene ring. This molecular configuration is subject to rapid hydrolysis by plasma cholinesterases after it is absorbed into the systemic circulation. Almost 95% of the drug is broken down this way into inactive metabolites. Only the remaining 5-10% is subject to the slower, traditional hepatic metabolism. This has important implications toward understanding maximum doses and potential systemic toxicity. Bouchard et al. showed that a lower amount of a thiophene derivative in a product may be required to block the sodium and potassium channels in the endoneurium.8 The fact that a sulfur atom exists in the articaine molecular structure is allergenetically immaterial, in spite of occasional citings in the literature to the contrary.9

Table 1. Chemical/physical properties of local anesthetics. – Moore PA 1996 – Eastman – Kodak; Local Anesthesia Marketing Handbook, 1996.

<table>
<thead>
<tr>
<th>Agent</th>
<th>Internal Linkage</th>
<th>Effective Concentration</th>
<th>Duration</th>
<th>Lipid Solubility</th>
<th>% Base (RN) at pH 7.4</th>
<th>Ionization (pkA)*</th>
<th>Protein Binding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lidocaine</td>
<td>Amide</td>
<td>2%</td>
<td>Medium</td>
<td>2.9</td>
<td>25</td>
<td>7.9</td>
<td>65%</td>
</tr>
<tr>
<td>Mepivacaine</td>
<td>Amide</td>
<td>2%</td>
<td>Medium</td>
<td>1</td>
<td>40</td>
<td>7.6</td>
<td>75%</td>
</tr>
<tr>
<td>Mepivacaine</td>
<td>Amide</td>
<td>3%</td>
<td>Medium</td>
<td>1</td>
<td>40</td>
<td>7.6</td>
<td>75%</td>
</tr>
<tr>
<td>Prilocaine</td>
<td>Amide</td>
<td>4%</td>
<td>Medium</td>
<td>1.5</td>
<td>25</td>
<td>7.9</td>
<td>55%</td>
</tr>
<tr>
<td>Bupivacaine</td>
<td>Amide</td>
<td>0.50%</td>
<td>Medium</td>
<td>30</td>
<td>18</td>
<td>8.1</td>
<td>95%</td>
</tr>
<tr>
<td>Endocaine</td>
<td>Amide</td>
<td>1.50%</td>
<td>Long</td>
<td>141</td>
<td>33</td>
<td>7.7</td>
<td>94%</td>
</tr>
<tr>
<td>Articaine</td>
<td>Amide</td>
<td>4%</td>
<td>Medium</td>
<td>49.5</td>
<td>29</td>
<td>7.8</td>
<td>95%</td>
</tr>
</tbody>
</table>

* pkA is a dissociation constant

Half-Life

The duration of clinical effect of a drug is not related to what is termed the half-life of the drug. Half-life is a serum phenomenon and a function of elimination, although it may be incorrectly perceived as a function of duration.10 Half-life is defined as the time it takes a plasma concentration of a drug to decrease by 50%, for potentially toxic levels to accumulate and potentially have an adverse affect on the cardiovascular, respiratory and central nervous systems. A short half-life implies that the drug is metabolized and eliminated in a period of time that is irrelevant to the local anesthetic continuing to perform effectively at the operative site. Amides tend to demonstrate a half-life of 90 minutes, whereas the half-life of articaine is 20-30 minutes.11,12 Correspondingly, at higher doses of 476 mg of articaine (6.61 cartridges or approximately 11.2 ml), the elimination half-life lengthens to 43.8 minutes and 44.4 minutes for articaine solution containing 1:100,000 and 1:200,000 epinephrine, respectively.11 Articaine is excreted primarily through urine, with 53-57% of the administered dose eliminated in 24 hours.13 Reports of systemic toxic effects following the use of articaine for dental anesthesia are extremely difficult to find. Although marketed as a 4% solution, the rapid inactivation in the plasma may explain the apparent lack of overdose reactions following its administration.5 This results in articaine possessing a wide ED 50:LD 50 safety index, a vital clinical consideration when analyzing its serum levels, and resulting safety for use in children.14 This wide safety index also allows for earlier re-injection during a dental appointment, with fewer concerns of reaching toxic levels.15

Efficacy of Articaine

Efficacy is defined as the capability of a substance to produce an intended result. It is derived from the Latin efficax, meaning powerful or efficient.16 Pharmacologically, the word is used as a comparative term to describe a drug’s potential performance when compared to other medications, usually of the same class.
In dentistry, it has commonly been used to describe the relative performance of available local anesthetics for regional infiltration and nerve block. Early publications by Haas et al. stated that articaine had a lack of differential effect (n=20) when compared to prilocaine (Citanest®, Astra Pharmaceuticals, Inc.). However, in a recent randomized crossover double-blind trial comparing the efficacy of buccal infiltration with 4% articaine and 2% lidocaine (both with 1:100,000 epinephrine), articaine infiltration produced statistically and significantly more episodes of no response to maximum (80 µA) stimulation from electronic pulp testing in first molars than with lidocaine (n=31). A publication by Robertson et al. further supported these findings. It has been reported that articaine may have superior clinical properties, including more success in achieving anesthesia, the ability to achieve more profound anesthesia and, in the case of buccal infiltration in the maxilla, occasional success in achieving palatal anesthesia without a palatal injection. This latter claim, however, has been refuted by Haas et al. The success of mandibular infiltration to replace inferior alveolar block anesthesia – if proper case selection is performed, and provided that buccal infiltrations are supplemented with lingual infiltration – appears to be a currently viable and increasingly popular technique.

In 2000, a majority of the 94 dentists participating in a multicenter study stated that anesthesia using articaine was more profound than “routinely used anesthetics.” Onset was faster and the anesthesia achieved greater success among the difficult-to-anesthetize patients. A majority of the dentists in one study cited a reduction in the number of missed blocks and noted that the effectiveness of articaine in mandibular infiltration facilitated treatment of pediatric and apprehensive patients. Haas and Lennon recognized that articaine is effective when used in mandibular infiltration. Articaine has also been proven to be effective in children for infiltration of primary molars. According to Dudkiewicz et al., articaine was able to diffuse through bone to the lingual side of each tooth. This higher diffusion characteristic could result from articaine’s higher lipid solubility compared to lidocaine, prilocaine and bupivacaine.

Safety and Efficacy in Pediatrics
In clinical trials, 61 pediatric patients between the ages of 4-16 received Septocaine® with epinephrine 1:100,000. Among these pediatric patients, doses from 0.76-5.65 mg/kg (0.9-5.1 mL) were administered safely to 51 patients for simple procedures, and doses from 0.37-7.48 mg/kg (0.7-3.9 mL) were administered safely to 10 patients for complex procedures. In these studies, however, there was insufficient exposure to Septocaine® with epinephrine 1:100,000 at doses greater than 7.00 mg/kg to assess its safety in pediatric patients. No unusual adverse effects were noted in these patients, while approximately 13% required additional injections of anesthetic for complete anesthesia. Safety and effectiveness in pediatric patients under the age of four years have not been established, and its use of is not recommended for patients younger than this age. Doses in pediatric patients should be reduced commensurate with age, body weight and general physical condition.

Safety and Efficacy in Geriatrics
In clinical trials, 54 patients between the ages of 65-75 years and 11 patients 75 or over received Septocaine® with epinephrine 1:100,000. Among all patients between 65-75, doses from 0.43-4.76 mg/kg (0.9-11.9 mL) were administered safely to 35 patients for simple procedures, and doses from 1.05-4.27 mg/kg (1.3-6.8 mL) were administered to 19 patients for complex procedures. Among the patients 75 or older, doses from 0.78-4.76 mg/kg (1.3-11.9 mL) were administered to seven patients for simple procedures, and doses of 1.12-2.17 mg/kg were safely administered to four patients for complex procedures.

Approximately 6% of patients between 65-75 years and none of the patients 75 or older required additional injections of anesthetic for complete anesthesia, compared with 11% of patients between 17-65 who required additional injections.

No overall differences in safety or effectiveness were observed between elderly subjects and pediatric subjects.

For normal, healthy adults, the maximum dose of articaine HCl administered by submucosal and/or nerve block should not exceed 7mg/kg (0.175 mL/kg) or 3.2 mg/lb (0.0795 mL/lb) of body weight (7 cartridges, or 11.9 mL) for a 150 lb. patient. For children under 10 years of age who have a normal lean body mass and normal body development, the maximum dosage may be determined by the application of one of the standard pediatric drug formulas. The maximum dose should not exceed the equivalent of 7 mg/kg (0.175 mL/kg) or 3.2 mg/lb (0.0795 mL/lb) of body weight.

Paresthesia and Dysesthesia
The term paresthesia is defined as an abnormal or inappropriate sensation of an organ, part or area of the skin characterized by a burning, prickling or tingling sensation. It is derived from the Greek anaisthesia, defined as an absence of feeling or sensation, and the Latin para, meaning beside or beyond, as in parameter.

In dentistry, paresthesia most commonly presents as a prolonged numbness in the circumoral or intraoral hard and/or soft tissue structures. Dysesthesia, a related condition, is defined from the Latin prefix dys-, meaning diseased, abnormal or faulty. It is a term used most often to describe a heightened, uncomfortable or painful sensation.

In dentistry, it occasionally presents as a post-operative sequela to regional administration of local anesthesia.

Incidence of Paresthesia
Recent reports suggest that the incidence of permanent paresthesia after inferior alveolar or lingual nerve block ranges from 1:20,000 to 1:850,000. Although retrospective surveys and publications (as opposed to scientific data) state that there is a correlation between 4% local anesthetic administration and a higher incidence of paresthesia, no individual anesthetic solution has been singled out as responsible. Pogrel elaborates on permanent nerve damage from blocks and recorded post-operative paresthesia associated with the administration of lidocaine versus articaine. Lidocaine was associated in 35%, and articaine in 30%, of the reported paresthesia cases. Nerve blocks can cause permanent damage independent of the brand of local anesthetic.
used. Furthermore, local anesthetic products may be implicated in this phenomenon in proportion to their usage.25

One published viewpoint by Dower, however, gives the opinion that “it appears that informed consent is merited in performing mandibular block and lingual block injections with articaine and prilocaine,” and asks, “Does the risk of paresthesia warrant use of articaine and prilocaine for lingual nerve, inferior alveolar nerve and other mandibular block injections?”22 The package insert for articaine states that the patient should be informed in advance of the possibility of temporary loss of sensation and muscle function following infiltration and nerve block injections.23 However, a precedent judgment (DeFerrari v. Neville, Ontario Court of Justice) was passed down in 2005 in an Ontario, Canada, court stating, in part, that “paraesthesia following local anesthesia used in non-surgical cases is so rare that dentists are not legally required to warn patients of the possibility of temporary or permanent paraesthesia as part of informed consent”.24 It is also important to distinguish between the terms inferior alveolar block and mandibular block. These are two distinct entities aimed at anesthetizing a branch of a nerve (the former) or a core nerve (the latter). As such, these definitions should not implicate each geographically different injection target zone in the same sentence.2

In 2000, Pogrel and Thamby evaluated 83 individuals with permanent nerve involvement and determined that only on rare occasions does an inferior nerve block permanently alter the sensation of the lingual nerve, inferior alveolar nerve or both.21 The lingual nerve was affected 79% of the time, while the inferior alveolar nerve was affected 21% of the time. When a nerve is affected by a local anesthetic, 85-94% of cases resolve within an eight-week period. If recovery does not occur fairly quickly, approximately two-thirds of remaining cases suffer permanent damage.20,21 Of the 68 cases in which the local anesthetic was known, 33 (49%) received lidocaine 2.0% with epinephrine 1:100,000, 32 (47%) received prilocaine 4.0% with epinephrine 1:200,000, and 3 (4%) received mepivacaine 3.0%. Some patients received multiple agents.20,23

Malamed et al. analyzed the occurrence of post-injection numbness or tingling both 24 hours and 7 days following a patient’s procedure, utilizing either 4% articaine 1:100,000 epinephrine (n=882) or 2% lidocaine 1:100,000 epinephrine (n=443). The total number of subjects who reported these symptoms four to eight days after the procedure was eight (1%) for the articaine group and five (1%) for the lidocaine group. Although more articaine patients were believed by investigators to have drug-related (local anesthetic) symptoms, these symptoms did not begin on the day of administration, suggesting that they were caused by the injection procedure rather than by the anesthetic product. In cases for which resolution dates were available, the researchers determined that the duration of these events was less than 1 to 18 days following the dental procedure. In all cases, the paresthesias ultimately resolved.2

Factors Influencing Data on Paresthesia and Dysesthesia

Three major categories essential to assessing the validity of existing published reports influence the data:

1. Neuronal factors
2. Research and reporting variables
3. Anatomical location of local anesthetic injection

1. Neuronal factors

Nerve morphology and needle positioning are critical. In Pogrel and Thamby’s study, the lingual nerve was affected 79% of the time compared to the inferior alveolar nerve, which was affected 21% of the time, even though anatomically these nerves are of approximately the same diameter.

This is not surprising since the pathway of needle entrance through – and exit from – the pterygomandibular triangle has two opportunities of mechanically encountering the lingual nerve. Furthermore, physical needle trauma is not unexpected when considering that the inferior branches of the mandibular nerve are sometimes inescapable from relatively stationary and firm structures, such as the medial surface of the ramus (I.A.N.) and the lateral surface of the medial pterygoid muscle (L.N.). This has a very important implication. There is no reported paresthesia of the core mandibular nerve. The third division of the trigeminal nerve is the largest of the 12 cranial nerves before it trifurcates into the lower terminal pterygomandibular branches of the inferior alveolar, lingual and buccal nerves. The question arises as to whether or not the core nerve, V3, is subject to mechanical or theoretical chemical assault, potentially resulting in post-operative complications such as prolonged numbness. An in vitro study using a dissecting microscope to assess the effects of injecting 20 µl and 10 µl of 4% articaine into rat sciatic and cat sciatic nerves observed that after 30 days, the average axonal cross-section areas were unchanged when compared to the non-injected opposite side.29

The author’s experience suggests there is an increased resistance to injury of this large diameter mandibular nerve (third division of the trigeminal nerve, V3) traversing the superior region of the triangle. This is illustrated in the estimated administration of more than 12,000 Gow-Gates mandibular blocks by this author, using articaine almost exclusively since it first became available in Canada in 1983. The author was personally trained by Dr. George Gow-Gates at the Astra Pharmaceutical Annual Symposium in Worcester, Mass., in 1978.

Figure 2. Dissection, medial view, left pterygomandibular triangle showing mandibular n. (MN), buccal n. (BN), condyle (C), lateral pterygoid m. (LPM), lingual n. (LN), inferior alveolar n. (IAN) and temporalis tendon (TT).

2. Research and reporting variables

Inconsistencies during repeated anesthetic block administration, including human variations in operator technique, introduce discrepancies to retrospective survey results. Another report indicates paresthesia with use of local anesthetics in a multicenter group of 110 dentists. A controlled in vitro or in vivo research study using a saline control protocol has yet to prove that a 4% local anesthetic solution is more neurotoxic than the chemistry or concentration of other local anesthetic products. Further scientific study and research is essential before any definitive cause-and-effect link can be drawn.

3. Mandibular block technique selection

The dental literature suggests several advantages to the administration of local anesthesia in the superior regions of the pterygomandibular triangle compared to the lower conventional anatomical disadvantages inherent with the inferior alveolar block. These techniques include the closed-mouth approach or Akinosi mandibular block, and the condylar neck approach or the Gow-Gates mandibular block.

Figure 3. Medial view of right ramus illustrating the average vertical height of the Akinosi mandibular block, superior to the horizontally parallel conventional IAN block.

Figure 6. Medial view, hard tissue left ramus.

Hard Tissue

1) The vascular and connective tissue is dense with a correspondingly sparse lipid cell concentration at the anatomically horizontal level of the coronoid notch and the lingula, the traditional landmark for the initiation of inferior alveolar block administration. The horizontally parallel target zone is also defended by structural barriers to lateral diffusion of solution toward the ramus. The placement of the needle tip medial or inferior to the sphenomandibular ligament and its associated sagittal connective tissue fascia is one of the primary reasons for conventional block failure. This is due to the inability of the local anesthetic to diffuse laterally toward the mandibular sulcus and foramen. The histological tissue density decreases toward the superior aspect of the anatomical “space,” with an increase in lipid cell content in the condylar neck region of the ramus and just below the insertion of the lateral pterygoid muscle into the condylar capsule.

Since the lipid solubility of any drug is vital and proportional to its onset and duration, the diffusion of a highly lipid-soluble local anesthetic drug such as articaine results from the contributing properties of the thiophene, sulfur-atom-containing chemical ring. This results in relatively unimpeded superior diffusion through an inert lipid-based medium, and concurrently favors the penetration of the epineurium at the site of action by the local anesthetic molecules in the free base, uncharged ionic form. This may help explain the higher reported success rates with the Akinosi and Gow-Gates block techniques. Further, it also allows for more distant deposition of solution from the actual nerve, while still preserving the high efficacy of these techniques.

2) The prevalence of arterioles and capillaries is reduced superiorly. Slower systemic absorption occurs, resulting in longer tissue clearance time and reduced risk of systemic toxicity, and questions the need for the presence of a vasoconstrictor higher in concentration than 1:200,000 epinephrine or even the need to administer a solution containing a vasoconstrictor at all.

3) Connective tissue density decreases superiorly and, therefore, needle deflection is progressively reduced for the Akinosi and Gow-Gates mandibular block approaches. Although a long 1 ⅞ inch, 35mm needle is still advantageous for use in most adults, technique modifications such as bending or lumen/bevel orientation are not required. There is a resulting lowered resistance to needle advance.
ment. Diffusion barriers diverge superiorly too, resulting in a more predictable needle placement lateral (favorable) to the sphenomandibular ligament, its fascia and even the medial pterygoid muscle.

4) Landmark orientation is facilitated with reduced anatomical concerns. The height of the lingula, mandibular sulcus (foramen) and orthognathic classes are less influential.

Figure 7. Histology graphic of medial view of the left pterygomandibular triangle depicting the transition from dense connective tissue and high vascularity at the level of the conventional, inferior alveolar block superiorly toward low tissue density and increasing prevalence of lipid (fat) cells at the level of the Gow-Gates mandibular block.

The author has not experienced any paresthesia incidents in his patients after years of clinical administration of high blocks using predominantly 4% prilocaine and then 4% articaine from 1976-2003 and 1982-2003, respectively, in a four-day-a-week general practice. This lack of paresthesia incidents is also evident in more than 1,500 post-course participation surveys collected by the author after personally supervising dentists when injecting each other using the higher block techniques, including from courses throughout North America including the Thomas P. Hinman participation programs in 1996-2003; the Modular Curriculum in Conscious Sedation programs in Dayton, Ohio, in 1992-2004; a University of Toronto program and multiple courses in 1985-2003 given throughout Canada on behalf of the Ontario Dental Association.

The issue of paresthesia in dentistry linked specifically to 4% local anesthetic solutions requires careful scrutiny and further study. Malamed concludes that, “given the lack of scientific evidence linking 4% local anesthetics with an increased risk of neurotoxicity, advisories to dentists from agencies or dental publications suggesting that it might be prudent to avoid the use of articaine for the administration of nerve blocks in the mandible is unjustified at this time.”27,36,37,38 The administration of any drug must be based on the benefits accrued clearly outweighing the potential risks associated with its administration. As in all treatments and therapies, it is ultimately the doctor’s decision as to whether or not to use a 4% local anesthetic solution such as articaine in inferior alveolar or mandibular nerve block anesthesia.36

Future Potentials
The analysis of the truths and myths of any drug must consider effects, side effects and adverse effects. Some concepts have been introduced that require scientific assessment. In particular, the current literature needs to compare and contrast all local anesthetic product variables with respect to efficacy, tolerance, toxicity and paresthesia.

Some of the above observations involve survey-based, practice-based and unpublished data. Nonetheless, a trend of infrequent post-op sequelae emerges. A scientific, randomized, double-blind crossover study with controls would appear to be virtually impossible. Where would the volunteer patient base come from? What consent and liability issues would exist?

Conclusion
Although retrospective and prospective information suggest that articaine has a slightly greater or equal incidence of paresthesia compared with other local anesthetics, articaine administration would appear to have a risk-benefit ratio with the therapeutic efficacy and safety benefits outweighing the minimal risk.20

The perspectives and reports on paresthesia should continually be explored and reassessed. “Super” local anesthetics yet to be developed will direct and underline the ongoing pursuit of new and improved products for application in both medicine and dentistry.

References

Author Profile

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Dr. Mel Hawkins graduated from the University of Toronto, Faculty of Dentistry with his DDS degree in 1973 and returned for his formal training in Dental Anesthesiology at the same University from 1975-1976. He is the Director of the Intravenous Sedation, Continuing Education Program at the University of Alberta, Faculty of Medicine and Dentistry, Professor of Pharmacology and Department Chair at the Aurora Dental College and the Founding Director of the Intravenous Sedation Program at the University of Toronto, Faculty of Dentistry. He has 35 years private practice experience in Toronto, Canada, with special emphasis on pain control and pain management and unique local anesthesia requirements for the dental patient. Dr. Hawkins is Board Certified as a Diplomate of the American Dental Board of Anesthesiologists and is a Fellow of the American Dental Society of Anesthesiology. Dr. Hawkins holds fellowships with the International College of Dentists and with the Pierre Fouchard International Academy. He serves as a Consultant to the Council of the American Dental Association and is also a Consultant for the Canadian Dental Protective Association. Additionally, Dr. Hawkins is internationally recognized as an author, lecturer and clinician on topics concerning sedation and pain free management of the dental patient.

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1. Articaine HCl is in the amide group of local anesthetics.
   a. True  
   b. False

2. The thiophene aromatic ring in articaine is _________.
   a. soluble and highly alkaline  
   b. soluble and highly acidic  
   c. soluble and highly lipid  
   d. none of the above

3. Paraminobenzoic acid is a by-product of the hydrolysis phase of articaine.
   a. True  
   b. False

4. The approved concentrations of epinephrine for use in dental anesthetic cartridges worldwide are ________ and ________.
   a. epinephrine HCl 1:20,000 and epinephrine HCl 1:100,000  
   b. epinephrine HCl 1:50,000 and epinephrine HCl 1:100,000  
   c. epinephrine HCl 1:100,000 and epinephrine HCl 1:200,000  
   d. none of the above

5. Local anesthesia protein binding refers specifically to _________.
   a. the phenomenon occurring inside the plasma, in the potassium channels  
   b. the phenomenon occurring inside the neuron, in the sodium channels  
   c. the phenomenon occurring inside the neuron, in the potassium channels  
   d. none of the above

6. Lidocaine is _________ bound to intracellular proteins.
   a. 55%  
   b. 65%  
   c. 75%  
   d. 85%

7. Daublander et al. found that the concentration of epinephrine in articaine influenced sympathomimetic effects.
   a. True  
   b. False

8. The molecular configuration is subject to rapid hydrolysis by plasma cholinesterases after it is absorbed into the systemic circulation.
   a. True  
   b. False

9. The duration of clinical effect of a drug is related to what is termed the half-life of the drug.
   a. True  
   b. False

10. Efficacy is defined as the capability of a substance _________.
    a. to effect drug breakdown  
    b. to produce an intended result rapidly  
    c. to produce an intended effect  
    d. none of the above

11. Half-life is the time it takes a drug’s plasma concentration to decrease by _________.
    a. 30%  
    b. 50%  
    c. 70%  
    d. 90% when above body temperature

12. 0.5% bupivacaine produces long duration anesthesia.
    a. True  
    b. False

13. 2% lidocaine produces short duration anesthesia.
    a. True  
    b. False

14. In 2000, a majority of the 94 dentists participating in a multicenter study stated that anesthesia using articaine was _________.
    a. less profound than “routinely used anesthetics”  
    b. more profound than “routinely used anesthetics”  
    c. less desirable than “routinely used anesthetics”  
    d. none of the above

15. Doses of local anesthetics in pediatric patients should be reduced commensurate with age, body weight and general physical condition.
    a. True  
    b. False

16. For normal, healthy adults, the maximum dose of articaine HCl administered by submucosal and/or nerve block should not exceed ________ for a 150 lb. patient.
    a. 4 cartridges, or 8.9 mL  
    b. 6 cartridges, or 9.9 mL  
    c. 7 cartridges, or 11.9 mL  
    d. 9 cartridges, or 15.2 mL

17. Paresthesia is defined as a normal sensation characterized by a prickling or tingling sensation.
    a. True  
    b. False

18. Pogrel found that post-operative paresthesia associated with the administration of lidocaine was ________ versus ________ with articaine.
    a. 15%; 20%  
    b. 25%; 30%  
    c. 35%; 30%  
    d. 45%; 40%

19. An inferior alveolar block is aimed at anesthetizing a core nerve.
    a. True  
    b. False

20. In reality, dysesthesia is unrelated to paresthesia.
    a. True  
    b. False

21. When a nerve is affected by a local anesthetic, ________ of cases resolve within eight weeks.
    a. 65-74%  
    b. 75-84%  
    c. 85-94%  
    d. none of the above

22. Nerve morphology and needle positioning are critical factors in paresthesia and dysesthesia.
    a. True  
    b. False

23. The ________ is a technique used to administer local anesthesia in the superior regions of the pterygomandibular triangle.
    a. condylar neck approach  
    b. Gow-Gates mandibular block  
    c. Akinosi mandibular block  
    d. all of the above

24. Placement of a needle tip medial or inferior to the sphenomandibular ligament and its associated sagittal connective tissue fascia is the primary reason for conventional block success.
    a. True  
    b. False

25. Where the prevalence of arterioles and capillaries is reduced superiorly, ________.
    a. slower systemic absorption occurs  
    b. slower systemic adsorption occurs  
    c. slower systemic resorption occurs  
    d. none of the above

26. The administration of any drug must be based on knowledge that the benefits accrued clearly outweigh the potential risks associated with its administration.
    a. True  
    b. False

27. The vascular and connective tissue is dense with a correspondingly sparse lipid cell concentration at the anatomic level of the coronoid notch and the lingual.  
    a. True  
    b. False

28. The diffusion of a highly lipid-soluble local anesthetic drug results in ________.
    a. inferior diffusion through an inert protein-based medium  
    b. inferior diffusion through an inert lipid-based medium  
    c. superior diffusion through an inert protein-based medium  
    d. superior diffusion through an inert lipid-based medium

29. The third division of the trigeminal nerve is the largest cranial nerve before it trifurcates.
    a. True  
    b. False

30. Categories essential to assessing the validity of published reports on paresthesia include neuronal factors, research variables and the anatomical location of local anesthetic injection.
    a. True  
    b. False
**Articaine: Efficacy and Paresthesia in Dental Local Anesthesia**

**Evaluational Objectives**

1. Know the types of local anesthetics available for use in the dental office.
2. Understand the chemistry and pharmacokinetics of articaine.
3. Describe the data supporting the efficacy and safety of local anesthetics, and specifically articaine.
4. Describe the factors influencing dysesthesia and paresthesia.

**Course Evaluation**

Please evaluate this course by responding to the following statements, using a scale of Excellent = 5 to Poor = 0.

<table>
<thead>
<tr>
<th>Objective</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective #1: Were the individual course objectives met?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Objective #2: To what extent were the course objectives accomplished overall?</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Objective #3: Please rate your personal mastery of the course objectives.</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Objective #4: How would you rate the objectives and educational methods?</td>
<td>5</td>
<td>4</td>
</tr>
</tbody>
</table>

**Course Requirement**

Completing a single continuing education course does not provide enough information to give the participant the feeling that s/he is an expert in the field related to the course topic. It is a combination of many educational courses and clinical experience that allows the participant to develop skills and expertise.

**Additional Information**

- Requirements for successful completion of the course and to obtain dental continuing education credits: 1) Read the entire course. 2) Complete all information above. 3) Complete answer sheets in either pen or pencil. 4) Mark only one answer for each question. 5) A score of 70% on this test will earn you 4 CE credits. 6) Complete the Course Evaluation below. 7) Make check payable to PennWell Corp.

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