Review Article

Local anesthesia failure in endodontics

K. B. S. Anandadeeban, R. N. Balakrishna*

ABSTRACT

Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage local anesthesia is essential for successful completion of endodontic treatment. Although pain treatment is well managed in many endodontic patients, there exists a group of patients who do not receive adequate local anesthesia in spite of proper administration of local anesthesia. This article reviews about the reasons for the failure of local anesthesia during endodontic treatment.

KEY WORDS: Inflammation, Local anesthesia, Mandibular molars, Pain

INTRODUCTION

During dental procedure, local anesthesia plays a major role in controlling the pain. They are the safest and most effective drugs in all of medicine for the prevention and management of pain during the dental procedure. Extraction of teeth, root canal treatment, minor surgical procedures and periodontal procedures, and tooth preparation mandatorily need administration of a local anesthetic to minimize patient discomfort and make patient cooperative during dental treatment.[1] Fear of pain is the main issue which causes patients to refuse dental treatment. Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage. This discomfort signals actual or potential injury to the body.[2] The success of local anesthetic administration depends on various factors such as site of administration if local anesthesia, injection techniques, dosage, and allergic complications. Many studies say that local anesthetic failures are more likely to occur due to choosing improper site for injection and inappropriate techniques to administer it.[3]

It has been estimated that about 20% of patients experience moderate-to-severe pain after treatment.[4]

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Very few patients will experience a sudden "flare-up" of severe pain or swelling after endodontic treatment has been over. Thus, clinical management of endodontic patients is often problematic due to inadequate local anesthesia.

VARIOUS REASON FOR FAILURE OF LOCAL ANESTHESIA

Anatomical Factors

Few suggest that the inability of the operator to load the local anesthesia in close proximity to the corresponding nerve would lead to inadequate blockade in both normal and uninflamed states, it may be possible that a partial blockade would be adequate in neurons that were not sensitized by inflammatory mediators. Thus, it is important to know the nerve supply to the tissue to be anesthetized, as well as the anatomy of the injected site and its variations present. Anatomic variation would have a lesser impact on infiltration anesthesia which is commonly used in the maxilla.

Usually, the pulps of mandibular teeth will anesthetized by blocking of the inferior alveolar nerve (IAN) through an intraoral approach to deliver the local anesthetic to the pterygomandibular space. In the classic technique, the needle is advanced to a point where a pool of anestheticis deposited near the mandibular foramen, which lies below the lingula, and in the sulcus colli mandibulae.[5] As the bony prominence of the lingula

Department of Oral and Maxillofacial Surgery, Saveetha Dental College, Saveetha Institute of Medical and Technical Science, Saveetha University, Chennai, Tamil Nadu, India

***Corresponding author:** R. N. Balakrishna, Department of Oral and Maxillofacial Surgery, Saveetha Dental College, Saveetha Institute of Medical and Technical Sciences, Saveetha University, 162, Poonamallee High Road, Chennai - 600 077, Tamil Nadu, India. Phone: +91 8939896729. E-mail: balakrishdr8394@gmail.com

Received on: 02-07-2018; Revised on: 04-08-2018; Accepted on: 05-09-2018

projects medially, it is often difficult to place the tip of the needle in the sulcus colli, and it has been suggested that the bevel should be orientated toward the midline to take advantage of the lateral deflection that would be provide through tissue resistance. However, even when needle placement is given with proper technique there occur the failures of local anesthesia. This may be due to the erratic post-injection distribution of anesthetic solution in the pterygomandibular space over which the operator has no control.[6]

Accessory innervation to the mandibular teeth from several sources has also been known as the cause for inadequate local anesthesia. In particular, the nerve to the mylohyoid muscle has been implicated in carrying afferent fibers from the mandibular teeth. In a study of 37 cadavers, it has been found the point at which the mylohyoid nerve branched from the IAN to be an average of 14.7 mm above the foramen of mandible a distance which is sufficient to prevent a blockade of the mylohyoid nerve when the classic technique is used. To overcome accessory innervations from the mylohyoid nerve, the clinician has several options, including the use of a block technique that deposits anesthetic solution higher in the pterygomandibular space (i.e., Gow-Gates or Akinosi), infiltration on the lingual surface of the mandible adjacent to the tooth operated, or techniques that deposit anesthetic solution in the medullary space surrounding the operated tooth, such as the intraligamentary or intraosseous routes of injection. Lingual nerve, buccal nerve is the other nerves which give stimulus to the mandibular teeth. Regardless of the origin, the technique that would predictably block all sources of accessory innervation to the mandibular teeth would be one in which the anesthetic solution is deposited at the apices of the teeth in question (i.e., intraligamentary or intraosseous routes). Even though both of these techniques appear to increase the efficacy of inferior alveolar block anesthesia, research shows a greater duration of lower molar pulpal anesthesia (as determined by a reading of 80 on an electric pulp tester) to be provided by the intraosseous technique.[7]

Effect of Local Tissue Inflammation

Usually, local anesthetics diffuse through the cell membrane and then block the sodium channel by accessing the protein from the cell's cytoplasm. This action requires the shift of drug between its acid form (an ionized or charged molecule) and its base form (an uncharged molecule). The pH of most local anesthetics in cartridge form is purposefully low (pH = 3–4), because the charged, acid form of the molecule is more stable (as is the vasoconstrictor) at a low pH, and thus gives a longer shelf life.[8] Once injected, the local tissue pH and the drug's strength as an acid regulate the distribution of the local anesthetics between the acid and base forms according to the well-known Henderson–Hasselbalch equation. The proportion of the drug that exists in the uncharged base form is available to diffuse across the cell membrane. As it enters the cell, the drug repartitions into the acid and base forms, and it is the acid form of the drug that blocks the sodium channel.

This becomes an potentially important issue because inflammation-induced tissue acidosis may cause "ion trapping" of local anesthetics. According to this hypothesis, the low tissue pH will result in a greater proportion of the local anesthetics being trapped in the charged acid form of the molecule and, therefore, unable to cross cell membranes. This has been advanced as a major mechanism for failures of local anesthesia in conditions such as endodontic pain. The reduction in tissue pH results in a substantial proportion of the drug being trapped in the charged acid form. Thus, over the pH range of 7.4–6.6, in comparison to lidocaine or bupivacaine, mepivacaine is relatively resistant to ion trapping. To the extent that this hypothesis explains local anesthetics failure, mepivacaine represents a logical local anesthetics for use in patients with irreversible pulpitis.

The relationship between the proportions of local anesthetics in the cationic acid form of the drug as a function of tissue pH. Note that, the cationic acid form cannot diffuse across cell membranes and is referred to as the "ion trapped" proportion of the molecule. This proportion is derived from the Henderson–Hasselbalch equation and the pKa value for each drug.

However, there are considerations that may limit the local pH hypothesis. First, the acidosis may be minor in magnitude. Although severe forms of liquefaction necrosis may have pH levels as low as 4–5, the affected area is restricted to the actual abscess. Studies on cutaneous inflammation indicate that tissue pH may be only marginally reduced to pH values of about 5.8–7.2.[9] In addition, inflamed tissue possesses greater buffering capacity than normal tissue (possibly due to extravasation of protein or erythrocytes into the inflamed tissue). Thus, the actual pH change may not be large enough to produce substantial ion trapping of local anesthetics. In addition, a reduction in tissue pH is likely to be a localized event and, with the exception of mandibular second and third molars, most probably does not involve distinct facial space compartments that isolate the site for an IAN block from the mandibular teeth. Thus, even in severe forms of inflammation, local tissue pH may explain problems with infiltration anesthesia in maxillary teeth, but is unlikely to explain local anesthetics failures in nerve block anesthesia.

To the extent of its validity, the local pH hypothesis has at least two clinical implications. First, it suggests that local anesthetics with lower pKa values are likely

to be more effective in endodontic pain patients. This recommendation is based on the physical properties and available formulations of these drugs, and it should be evaluated in a prospective clinical trial. Second, the temporary adjustment of tissue pH may be used to augment clinical anesthetics. This strategy has been employed by anesthesiologists with sodium bicarbonate to alkalinize the local anesthetics and tissue pH and thereby enhance local anesthesia. Addition of sodium bicarbonate also raises the pCO_2 of the anesthetic solution bathing the nerve. When CO_2 crosses the nerve membrane and decreases the intracellular pH, the ionized form of the drug is favored, and as mentioned previously, it is this form that binds to the sodium channel to effect blockade.

Although alkalinization may have theoretical utility, there is a paucity of clinical trials in dental pain patients to support its use. In one study, compared with a standard lidocaine formulation, a buffered lidocaine formulation demonstrated no significant difference when given by infiltration injection into inflamed maxillary incisors.[10] Although other formulations may warrant testing in additional studies, there does not appear to be a preponderance of clinical evidence to support the use of alkalinization of local anesthetic solutions.

Effect of Inflammation on Central Sensitization

Inflammation also induces changes in the central nervous system's pain processing system. Activation and sensitization of nociceptors in pulpal and periradicular tissue results in a barrage of impulses sent to the trigeminal nucleus and brain. This barrage, in turn, produces central sensitization. Central sensitization is the increased excitability of central neurons and is thought to be a major central mechanism of hyperalgesia.[11] Under conditions of central sensitization, there is an exaggerated central nervous system response to even gentle peripheral stimuli. A common example to this is sunburn, where even the innocuous stimulation of wearing a t-shirt is considered painful. Similarly, percussing a tooth with an inflamed periodontal ligament (e.g., acute apical periodontitis) may produce an exaggerated pain response which is due, in part, to central sensitization.

Although we often consider central sensitization when discussing endodontic pain mechanisms (65), this same process may contribute to local anesthetic failures. Under normal conditions, many patients tolerate dental procedures, even though a slight or occasional sensation may still be felt. In other words, under normal conditions, a local anesthetic injection that blocks most of the fibers (say, 90%) may still be clinically successful. This has been reported in other clinical models (e.g., IV cannulation of the arm), where patients treated with a topical anesthetic reported that they did not experience pain, even though their visual analog pain scores were greater than zero.[12] However, under conditions of central sensitization, there is an exaggerated response to peripheral stimuli and, under these conditions, the same 90% block may permit sufficient signaling to occur to lead to the perception of pain. Thus, central sensitization may contribute to local anesthetic failures.

Unfortunately, there are no selective drugs for blocking central sensitization. The only clinical implication would be to reduce the afferent barrage and thereby reduce central sensitization. This is done routinely by clinicians through cleaning and shaping techniques, but this is a conundrum, as the endodontic treatment is performed after local anesthesia. One interesting study has demonstrated that intraosseous injection of steroid (methylprednisolone acetate 40 mg) reduces endodontic pain in 24 h. If confirmed, then this approach may reduce peripheral and central mechanisms sufficiently to obtain predictable local anesthesia.

Psychological Factors

Patient anxiety may also contribute to local anesthetic failure. Experienced clinicians understand that apprehensive patients have a reduced pain threshold and are more likely to report an unpleasant dental experience.[13] Fear of seeing and/or feeling the needle and the sound of the dental handpiece are routinely cited as causative agents in the creation of anxiety in the dental patient. Moreover, patients may be particularly anxious about impending root canal therapy. Investigators have also demonstrated that patient anxiety predicts a poor outcome for clinical procedures involving local anesthetics applied to the arm before IV cannulation. Thus, patient anxiety should be considered when managing the endodontic pain patient.

Several methods have been advocated for managing anxious emergency pain patients. First, the clinician should establish a positive and confident relationship and avoid exposing the patient to obvious fear-producing stimuli. Many clinicians report that a sense of humor often helps to relax apprehensive patients. For extremely fearful patients, cognitive behavior-based programs have shown a significant long-term reduction in predental treatment anxiety. Other studies have demonstrated that instructing patients to focus on sensory stimuli significantly reduces intraoperative endodontic pain. This effect was most evident in patients who were characterized as having a high desire for control and low perceived control over their clinical care.

Second, pharmacologic agents can be administered to control patient anxiety. While these agents can be

delivered via oral, inhalation (N_2O) or intravenous routes, a decreased likelihood of serious morbidity, reduced monitoring and demonstrated efficacy have made oral or a combination of oral and inhalation routes attractive.[14] Kaufman *et al.* showed that oral triazolam 0.25 mg was equally effective in comparison to intravenous diazepam in reducing anxiety in patients undergoing oral surgery.

One could certainly consider an integrated approach that involves both non-pharmacologic and pharmacologic techniques. Regardless of the technique utilized, providing some means of anxiety control should enhance the clinician's ability to provide adequate local anesthesia for endodontic pain patients.

Acute Tachyphylaxis of Local Anesthetics

It is well known in pharmacology that administration of receptor agonist drugs often leads to reduced responsiveness to a subsequent administration of the drug, an effect called tachyphylaxis. Since local anesthetics are often administered together with vasoconstrictors, there is the possibility that the drug persists in the tissue for a sufficient amount of time to produce tachyphylaxis at the sodium channel. It has been proposed that this contributes to reduced anesthetic effectiveness, especially after repeated injections. However, it is not clear that local anesthetics produce substantial, or in fact any, tachyphylaxis under clinical conditions. Several clinical trials have evaluated repeated or continuous local anesthetic administration to treat chronic pain patients. Despite continuous infusion or daily administration for periods of up to several years, these studies have not reported tachyphylaxis to local anesthetics.[15] Thus, this hypothesis may have comparatively little merit for explaining local anesthetic failures.

Effect of Nociceptors Inflammation

Substances released from inflamed tissue have two major effects on nociceptive ("pain detecting") neurons.[16] First, they change the functional activity of these neurons. As might be expected, nociceptors are thought to be quiescent throughout much of our lives and only discharge in the presence of stimuli strong enough to damage the tissue or chemicals that stimulate receptors on these neurons. Inflammatory mediators activate or sensitize these neurons by interacting with specific receptors. An example of a mediator that activates nociceptors are bradykinin (BK): Its administration causes a brisk firing of unmyelinated C nociceptors through activation of cell surface bradykinin receptors (BK1 or BK2). Prostaglandin E2 (PGE2) is an example of a mediator that sensitizes nociceptors: Administration of PGE2 reduces the threshold for firing to the point where gentle stimuli can now activate these neurons. For example, the throbbing nature of pulpal pain is thought to be due to pulpal nociceptors sensitized to the point where they discharge in response to the patient's heartbeat. Thus, activation and sensitization are two major mechanisms by which inflammatory mediators alter the activity of these normally quiescent neurons. Although local anesthetics display use-dependent blockading properties, peripheral sensitization and activation have been reported to cause an increase in the resistance of nerves to anesthetics.

In addition, inflammatory mediators, including certain growth factors, have profound effects on these neurons by altering their structural properties. In particular, the elegant studies by Byers and her colleagues have led to the realization that the terminals of peripheral nerves literally grow ("sprout") into areas of inflammation in dental pulp and periradicular tissue.[17] Clinical studies have confirmed that a similar sprouting occurs in inflamed human dental pulp. This increase in nerve terminals in inflamed tissue increases the size of their receptive field, indicating that pain neurons may now be more easily activated by a spatial summation of stimuli.

Inflammation also changes the synthesis of several proteins in nociceptors, leading to an increase in neuropeptides, such as substance P and calcitonin gene-related peptide. These neuropeptides play important roles in regulating pulpal inflammation. In addition, tissue injury may alter the composition, distribution or activity of sodium channels expressed on nociceptors. The effect of inflammation on these sodium channels may have profound implications in local anesthetic failures.

Several types of sodium channels have been discovered over the past decade. One particular group of channels is characterized as being resistant to the puffer fish toxin and tetrodotoxin (TTX). At least two channels are members of the TTX-resistant class, including the PN3 (also known as SNS, or NaV 1.8) and NaN (also known as the SNS2 or NaV 1.9) sodium channels. The TTX-resistant class of sodium channels is of interest since they are less sensitive to lidocaine.[18] The TTX-resistant class of sodium channels is expressed on nociceptors under normal conditions. In addition, their activity more than doubles after being exposed to PGE2. Thus, we hypothesize that the TTX-resistant class of sodium channels represents a logical mechanism for local anesthetic failures: The channels are relatively resistant to lidocaine, they are expressed on nociceptors, and their activity is increased with PGE2.

Effect of Inflammation on Blood Flow

Inflammation has several other effects on local tissue physiology. For example, it has been proposed that

peripheral vasodilation induced by inflammatory mediators would reduce the concentration of local anesthetics by increasing the rate of systemic absorption.[19] This is a potentially important mechanism because local anesthetics are well-recognized vasodilators that, in most cases, require formulation with vasoconstrictor agents. Although inflamed dental pulp experiences regional changes in blood flow, less is known about inflammation-induced vascular changes in periradicular tissue. Moreover, it is likely that this vasodilation may be localized and not evident at distant sites of injection (i.e., nerve block injection sites). Thus, this hypothesis may have greater utility in explaining difficulties with infiltration anesthesia when compared with nerve block anesthesia.

To the extent that this hypothesis predicts local anesthetic failure, there are clinical implications that may improve the success of local anesthesia. If vasodilation leads to increased drug absorption, then the use of higher concentrations of vasoconstrictors may produce more profound or longer duration anesthesia. Thus, in patients who can tolerate it, the use of 1:50,000 epinephrine may improve clinical success in anesthetizing patients with endodontic pain. However, to date, the results from clinical trials have been equivocal. The use of 1:50,000 epinephrine produces a greater degree of vasoconstriction in patients than 1:100,000 epinephrine[20] and yet, there is no difference in the magnitude or duration of clinical anesthesia in normal subjects. In this latter study, the clinical anesthesia for 2% lidocaine was the same, regardless of whether the epinephrine was present at 1:50,000, 1:80,000 or 1:100,000. Knoll-Kohler and Fortsch, however, showed a dose-dependent relationship between the onset and duration of anesthesia and the concentration of epinephrine (1:200,000, 1:100,000, 1:50,000) when used with 2% lidocaine for infiltration anesthesia.[21] It should be noted that these studies were conducted in normal subjects and, to date, no clinical trial has tested whether these higher concentrations of epinephrine alter anesthesia in endodontic pain patients in whom tissue vasodilation may be increased.

CONCLUSION

Analgesia is essential for successful completion of modern dental procedures. Difficulty experienced in obtaining satisfactory analgesia after proper administration especially of an acutely inflamed mandibular molar remains a common clinical problem. This article reviews about the various reason for failure of local anesthesia during the endodontic procedure.

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Source of support: Nil; Conflict of interest: None Declared