Chapter

Tackling Local Anesthetic Failure in Endodontics

Krishnamachari Janani, Kavalipurapu Venkata Teja, Harini K, Kaligotla Apoorva Vasundhara and Jerry Jose

Abstract

Achieving anesthesia in a hot tooth or tooth with inflamed pulp is challenging, especially during endodontic treatment. In the presence of symptomatic irreversible pulpitis, mainly in mandibular teeth, pose even more challenge to attain profound anesthesia. Tetradoxin resistant channel is a class of sodium channel that is found to be increased in such condition and is found to resist local anesthesia. The pH also determines the success of local anesthesia. In inflammatory conditions, the surrounding area's pH, which eventually decreases the amount of base form of local anesthetic penetration into the nerve membrane, thereby causing anesthetic failure. In such conditions, the excitability threshold is reduced, leading to failure in achieving anesthesia. This chapter highlights and discusses the cause of anesthetic failure and its management in obtaining profound anesthesia during endodontic treatment.

Keywords: Local Anesthesia, Endodontic Treatment, Pain, Irreversible Pulpitis Pulpal Inflammation

1. Introduction

Pain is an unpleasant sensation that can range from slight discomfort to excruciating agony and can be linked to actual or potential tissue damage [1]. It is a multimodal and biopsychosocial event with an individual objective and subjective occurrences, resulting in significantly diverse perceptions of pain between the individuals. One of the most common reasons for a patient to visit an endodontist is dental pain. Managing dental pain and anxiety during and after treatment is still a difficult task, which depends on the clinician's skill and knowledge [2].

2. Pulpal inflammation

In symptomatic pulp tissue diagnosed with irreversible pulpitis, extracellular levels of Substance P are elevated. When comparing pulp tissue diagnosed with irreversible pulpitis to clinically normal pulp tissue, an 8-fold rise in Substance P was found [3]. As a result, irreversible pulpitis is linked to high peptidergic system activation. It is generally known that root canal preparation causes inflammation in the periapical tissues, explaining why root canal therapy causes post-treatment pain (such as symptomatic apical periodontitis). SP is released in the periodontal

ligaments as a result of varied canal preparation approaches, which was found to be quite interesting. However, the amount of released SP differs among procedures. Inflammation in the periapical tissues could be triggered by an elevation in SP [4]. This might thus be considered a key mediator of neurogenic inflammation and related hyperalgesia, and hence a prospective target for therapeutics targeted at regulating pain and minimizing the harmful effects of tissue injury [5].

When a carious lesion gets close to the pulp, the pulp's inflammatory alterations get worse. An acute exacerbation of chronic inflammation occurs at this stage, with an influx of neutrophils and the release of inflammatory mediators (prostaglandins and interleukins), proinflammatory neuropeptides and mediators (substance P, Bradykinin, and calcitonin gene related peptide) [6]. These mediators can increase pain perception and neuronal excitability by stimulating peripheral nociceptors within the pulp of the affected tooth. This causes moderate-to-severe discomfort. Conventional procedures may not provide sufficient anesthesia. As a result, endodontists must achieve profound anesthesia in order to alleviate the pain [7].

3. Local anesthetics

The use of local anesthetic agents in pain management plays a vital role. It is the safest and most effective medications to prevent and manage pain during dental treatment [8]. Today's availability of a variety of local anesthetic agents allows dentists to choose an anesthetic with specific properties such as time of onset and duration, hemostatic control, and degree of cardiac side effects that are suited for each individual patient and dental operation [9]. 2 percent lignocaine (Xylotox, Adcock Ingram; Xylesthesin, 3 M) with 1:80000 adrenaline content, 3 percent mepivacaine (Carbocaine) without a vasoconstrictor and 4 percent articaine (Ubistesin 3 M) with either 1:100000 or 1:200000 adrenaline concentration is currently the most commonly used local anesthetic agents in general dentistry [10]. Each local anesthetic has its own maximum recommended dose (MDR) measured in mg/kg body weight. Unfortunately, the literature7 shows that the mg/kg MDR for each drug ranges from 4.4 mg/kg 8 to 6.6 mg/kg [11, 12].

4. Evaluate the anesthesia before treatment

When dealing with a tooth that has been diagnosed with irreversible pulpitis or "Hot" tooth, it's critical to determine whether enough local anesthetic has been attained. Subjective and objective testing has historically been used to validate successive inferior alveolar nerve block (IANB). Signs such as lip numbness, probing the gingiva surrounding the tooth to be treated, and so forth are examples of subjective tests [13]. Patients should not suffer discomfort throughout therapy if they respond favorably to the subjective results. These approaches, however, are not confirmatory test for detecting pulpal anesthesia.

5. Failure of local anesthesia

5.1 Anatomic factors

While it's possible that the operator's inability to deposit anesthetic solution close to the targeted nerve would result in an insufficient blockade in both normal

and non-inflamed states, it's also possible that a partial blockade would suffice in neurons that inflammatory mediators did not sensitize. It's crucial to understand the nerve supply to the anesthetized tissue and the anatomy of the injection site and any changes [14].

During a local infiltration at the root apex, however, the cortical bone of the body of the mandible can effectively block the anesthetic. The maxillary cortical bone is often thinner. Anesthetic diffusion is more easily achieved through this bone. Therefore, infiltration anesthesia, which is routinely used in the maxilla, would be less affected by anatomic variance. Block anesthesia is advised in the mandible because it is more predictable. Still, it demands a deeper awareness of the deep anatomy of the jaw and is more technique sensitive, which is why anesthetic failures in the mandible are more common. Inadequate local anesthetic has also been linked to accessory innervation of the mandibular teeth from various sources. The nerve to the mylohyoid muscle, in particular, has been linked to the transport of afferent fibers from the mandibular teeth [14]. The clinician has many alternatives for overcoming accessory innervations from the mylohyoid nerve, including using a blocking technique that deposits anesthetic solution higher in the pterygomandibular space.

5.2 Inflammation and tissue pH

The pH of the anesthetic solution determines the ratio of RN to RNH^+. According to the Henderson–Hasselbalch equation, there are equal amounts of half-charged and half-uncharged molecules when the acid dissociation constant Pka equals the pH of the solution. In a cartridge of local anesthetic solution, both charged (RNH^+) and uncharged (RN) molecules exist in equilibrium. The deionized lipid-soluble (RH) form penetrates the neuronal membrane and takes up H^+. RNH^+ within the nerve, resulting in RNH^+, which enters the sodium channel and blocks conduction. To produce anesthesia, the body buffers the pH-injected anesthetic solution to the physiological pH [15].

This becomes potentially critical since inflammation-induced tissue acidosis can cause local anesthetics to get "ion trapped." According to this theory, the low tissue pH causes a higher proportion of the local anesthetic to be held in the charged acid form of the molecule, preventing it from passing through cell membranes. This theory has been proposed as a primary cause of local anesthetic failures in situations like endodontic pain [16].

5.3 Central sensitization

Local anesthetic failures may be exacerbated by central sensitization. Increased sensitivity may enhance incoming sensory nerve impulses. There is a significant response to peripheral stimuli in central sensitization, and as a result, the IANB may allow adequate signaling to occur, leading to the experience of pain [16].

5.4 Central core theory

According to this hypothesis, the nerves on the exterior of the nerve bundle supply the molar teeth, while the nerves on the inside supply the anterior teeth. Even if the anesthetic solution is placed in the right location, it may not disperse enough into the nerve trunk to reach all nerves and cause a sufficient block. This concept may only apply to the increased failure rates associated with IANB in the anterior teeth, not the posterior teeth [17].

5.5 Tetrodoxin resistant channels (TTXr)

The Tetrodoxin resistant channels (TTXr) family of sodium channels have been demonstrated to be resistant to the effects of local anesthesia. Anesthetic failures in a hot tooth are caused by increased expression of sodium channels in the pulp. The TTXr channels are resistant to lidocaine, resulting in insufficient anesthetic [18]. TTXr channels are expressed on nociceptors, and their activation with Prostaglandin E2 is relatively resistant to lidocaine. Because they are less susceptible to lidocaine, sodium channels that are resistant to TTX. As the concentration of lidocaine rises, the sodium channels get blocked [19].

5.6 Altered membrane excitability of peripheral nociceptors

Inflamed tissue nerves have a lower excitability threshold and an altered resting potential. Lower excitability thresholds are responsible for impulse transmission [20].

5.7 Psychological factors

Anxiety in the patient may also play a role in the local anesthetic failure. Clinicians who have worked with anxious patients know that they have a lower pain threshold and are more likely to complain about an unpleasant dental experience. The sight of a needle and the sound of the dental handpiece are frequently reported as causes of anxiety in patients. Furthermore, patients may be particularly apprehensive about root canal therapy.

5.8 Effect of inflammation on blood flow

Inflammation has several additional consequences on the physiology of local tissues. Inflammatory mediators cause peripheral vasodilation, which increases the rate of systemic absorption, lowering the concentration of local anesthetics. Local anesthetics, in most circumstances, need formulation with vasoconstrictor drugs. Thus, this is a potentially relevant mechanism. Although regional variations in blood flow occur in inflamed dental pulp, little is known regarding inflammation-induced vascular alterations in periradicular tissue [21]. Furthermore, this vasodilation is likely to be confined and not seen at distant injection sites. As a result, compared to nerve block anesthesia, this concept may be more useful in understanding issues with infiltration anesthesia.

5.9 Effect of inflammation on nociceptors

Inflammation alters the production of many proteins in nociceptors, resulting in a rise in neuropeptides such substance P and calcitonin gene-related peptide. These neuropeptides have an essential role to perform have a role in regulating pulpal inflammation. Furthermore, tissue damage can change the composition, distribution, and activity of sodium channels expressed on the nociceptors. Inflammation's effect on these sodium channels might substantially impact local anesthetic failures [22].

5.10 Tachyphylaxis

Tachyphylaxis is a condition in which a receptor agonist medication causes a reduction in responsiveness to a subsequent dose of the drug. Because local

anesthetics are frequently used in conjunction with vasoconstrictors, the medication may remain in the tissue long enough to trigger tachyphylaxis at the sodium channel. This has been suggested as a factor in decreased anesthetic efficacy, particularly after many administrations [21].

6. Factors influence the efficiency of local anesthesia

6.1 Anesthetic agent

Contrary to popular belief, most moderate-duration anesthetics are equally efficient in inducing deep pulpal anesthetic for root canal treatment. Understanding the anatomical, local, and psychological aspects of each patient against the type of anesthetic utilized is critical to success. Most dentists prefer to employ a combination of anesthetics and a vasoconstrictor. When some types of anesthetic drugs are used, it is possible that the patients would experience more pain. Because of the acidic nature of local anesthetics, lower pH values are considered to produce a burning sensation during injection [23].

6.2 Site of injection

The injection location might influence injection discomfort. According to one study, maxillary buccal injections with plain 2% lidocaine Was found to be considerably less discomfort than 2% lidocaine with 1:80000 epinephrine. However, using the same anesthetic drugs, no difference in injection discomfort was recorded at the palatal location [12]. The type of anesthetic solution has little effect on injection discomfort when a location with less connective tissue (such as the palatal site in the maxilla) is injected. Faster injection speed leads to increased drug distribution. It has been proposed that a speed of injection exposes a larger portion of a nerve to the anesthetic solution, resulting in a higher rate of local anesthesia success. The rapid injections, on the other hand, produced more pain and discomfort during the procedure [23–25].

6.3 Preoperative pain

In individuals with symptomatic irreversible pulpitis, the degree of preoperative pain might impact anesthetic success. The activation of nociceptors during inflammation might be one reason for the lower success rate of inflamed pulp. The peripheral and central pain pathways are altered and modulated by the barrage of painful stimuli, as well as tissue destruction. Another reason for failure is that nerves from inflamed tissue have reduced excitability thresholds and altered resting potentials [26].

6.4 Pre emptive medication

Inflamed pulps may have more tetrodotoxin-resistant sodium channels, which are resistant to local anesthetics. Prostaglandins, which can influence tetrodotoxin-resistant receptors and reduce nerve responses to anesthetic drugs, have also risen considerably in inflamed pulps [27]. As a result, premedication with nonsteroidal anti-inflammatory medicines (NSAIDs) and corticosteroids to increase anesthetic success appear to be a viable option. However, the findings of such research do not agree on the effectiveness of premedication on anesthetic success [28, 29]. However, if the patient does not have spontaneous pain, pre-treatment with

particular types of NSAIDs may improve the effectiveness of anesthesia when treating irreversible pulpitis [30]. Premedication with corticosteroids before anesthesia with an inferior alveolar nerve block (IANB) injection resulted in a considerably better success rate.

6.5 Gender and genetic factor

Genetics may play a role in predisposing specific individuals to problems such as discomfort, delayed healing, and abscess development. A range of genetic variations influences pain perception and behavior. Pain becomes significantly more common in women, and various explanations have been proposed, including hormonal and genetically driven sex variations in brain neurochemistry [27].

7. Pain management

7.1 Supplementary anesthesia

7.1.1 Intraligamentary anesthesia

Intraligamentary anesthesia is a technique wherein local anesthetic solution administered via the periodontal ligament to reach the pulpal nerve supply. The use of conventional or customized syringes can be used for this technique. At the mesiobuccal aspect, the needle is placed as deeply between the root surface and alveolar bone at a 30° angle to the long axis of the tooth. The needle can be placed with the bevel pointing in either direction, and 0.2 ml of the solution should be injected per root using back pressure. For 5 to 10 seconds, the needle is held in place [31]. The anesthetic action begins almost immediately and lasts for around 15–20 minutes [32].

In comparison to other anesthetic techniques, Intraligamentary anesthesia allows for a substantial reduction in the overall volume of anesthetic solution and vasoconstrictor supplement. At the same time, the unintentional intravascular application is avoided [33]. Furthermore, the effectiveness of Intraligamentary anesthesia is limited in cases of severe marginal periodontitis or teeth with a sclerotic periodontal gap, and alternate anesthetic methods such as inferior alveolar nerve block can be advised [32].

7.1.2 Intraosseous anesthesia

Intraosseous Anesthesia is more invasive and necessitates the use of specialist equipment, such as a perforator (e.g., Stabident, X-Tip). The gingiva must first be sedated for the perforator to penetrate without discomfort. A slow-speed handpiece is used to move the perforator into the anesthetic gingiva and bone until the cancellous bone is felt like a sharp dip. The perforator is then withdrawn, and a small 27-gauge needle is introduced through the perforation, injecting approximately 1 mL of solution over 2 minutes. It's one of the most effective supplemental methods available [34]. The intraosseous injection permits the local anesthetic solution to be injected directly into the cancellous bone adjacent to the tooth that has to be sedated [35]. The intraosseous anesthetic onset of anesthesia is immediate and lasts for around 15 to 30 minutes, and was found to be more efficient than intraligamentary anesthesia [36].

7.1.3 Buccal infiltration

After a failed IANB, buccal infiltration has been utilized as a supplemental anesthetic for anesthetizing mandibular molar teeth, especially in symptomatic irreversible pulpitis. A mandibular buccal infiltration injection of 4% articaine with 1:100,000 epinephrine as an additional injection to improve the effectiveness of the IANB injection has recently been investigated. The usage of the articaine solution was shown to be better than the lidocaine solution in asymptomatic individuals (88 percent vs. 71 percent, respectively) [37]. Only 58% anesthesia was achievable with buccal infiltration injection when used as a supplement to the IANB in case of symptomatic irreversible pulpitis [38].

7.1.4 Intrapulpal anesthesia

Intrapulpal anesthesia is one of the supplementary anesthesia that is beneficial, especially in a hot tooth. The most crucial aspect of this technique is to pump the fluid into the pulp forcefully. If the physician does not feel pressure or resistance to injection, the solution is not reaching the pulp and is most likely running out of the pulp chamber and back into the access cavity [39]. However, this type of anesthesia is excruciating and should only be used as the last option during endodontic therapy. Intrapulpal anesthesia has the drawback of having a limited duration of effect. As a result, it's critical to remove the pulp from all of the root canals as soon as possible after injection to avoid repeated injection [40]. It is necessary that the patient should be informed that the type of anesthesia will cause moderate to severe discomfort in the beginning.

7.2 Buffered anesthesia

Buffered local anesthesia technique to one of the techniques to improve the efficiency of the local anesthetics. Alkalinization accelerates the dissociation of the LA molecule, increasing in the uncharged base form that penetrates the nerve membrane and acts in the intraneuronal location. The addition of sodium bicarbonate is the most frequent technique for buffering LAs. The addition of sodium bicarbonate to local anesthetics reacts to form sodium chloride water and carbon dioxide. Alkalinization with sodium bicarbonate raise the pH of the solution. Carbon dioxide produces an independent anesthetic effect by changing the local anesthetic inside the nerve direct depressant effect of carbon dioxide on the nerve axon [41]. 50 mEq is the maximum dose of sodium bicarbonate. 20 ml of 1 or 2% lignocaine is recommended to be added with 2 ml of 8.4 percent sodium bicarbonate. The ratio of lignocaine to bicarbonate should be between 5:1 and 10:1 for best effects. If the bicarbonate level exceeds this ratio, precipitation may occur. In individuals with metabolic acidosis and hypocalcemia, this method is contraindicated [15].

8. Conclusion

Pain being the most common symptom, every effort should be made to manage it during and after root canal treatment and should be informed priorly the type of anesthesia administered to the patient. Although various anesthetic agents and techniques are available, the choice of them is specific and customized to each patient and their preoperative status and clinical condition. So, ultimately, the clinician should critically decide on a specific agent or a technique for the clinical

condition of the patient. It is necessary to provide appropriate pulpal anesthesia when treating teeth with irreversible pulpitis.

Conflicts of interest

The authors declare no conflict of interest.

Author details

Krishnamachari Janani[1], Kavalipurapu Venkata Teja[2*], Harini K[3], Kaligotla Apoorva Vasundhara[4] and Jerry Jose[2]

1 Department of Conservative Dentistry and Endodontics SRM Dental College, Ramapuram, Chennai, Tamilnadu, India

2 Department of Conservative Dentistry and Endodontics, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, Tamilnadu, India

3 Centre for Food Technology, Anna University, Guindy, Chennai, Tamilnadu, India

4 Private Practitioner MDS, Prosthodontist and Oral Implantologist, Andhra Pradesh, India

*Address all correspondence to: venkatatejak.sdc@saveetha.com

References

[1] Sadaf D, Ahmad MZ. Factors associated with postoperative pain in endodontic therapy. Int J Biomed Sci IJBS. 2014;10(4):243-7.

[2] Perković I, Romić MK, Perić M, Krmek SJ. The level of anxiety and pain perception of endodontic patients. Acta Stomatol Croat. 2014;48(4):258-67. https://doi.org/10.15644/asc48/4/3

[3] Bowles WR, Withrow JC, Lepinski AM, Hargreaves KM. Tissue levels of immunoreactive substance P are increased in patients with irreversible pulpitis. J Endod. 2003;29(4):265-7. https://doi.org/10.1097/00004770-200304000-00009

[4] Bamini L, Sherwood IA, Abbott PV, Uthandakalaipandian R, Velu V. Influence of anti-inflammatory irrigant on substance P expression for single-visit root canal treatment of teeth with irreversible pulpitis. Aust Endod J. 2020;46(1):73-81. doi: 10.1111/aej.12353.

[5] Caviedes-Bucheli J, Azuero-Holguin MM, Gutierrez-Sanchez L, Higuerey-Bermudez F, Pereira-Nava V, Lombana N, et al. The effect of three different rotary instrumentation systems on substance P and calcitonin gene-related peptide expression in human periodontal ligament. J Endod. 2010;36(12):1938-42. doi: 10.1016/j.joen.2010.08.043.

[6] Abdulkhaleq LA, Assi MA, Abdullah R, Zamri-Saad M, Taufiq-Yap YH, Hezmee MNM. The crucial roles of inflammatory mediators in inflammation: A review. Vet World. 2018;11(5):627-35. doi: 10.14202/vetworld.2018.627-635.

[7] Byers MR, Närhi MV. Dental injury models: experimental tools for understanding neuroinflammatory interactions and polymodal nociceptor functions. Crit Rev Oral Biol Med Off Publ Am Assoc Oral Biol. 1999;10(1):4-39. doi: 10.1177/10454411990100010101.

[8] Zanjir M, Lighvan NL, Yarascavitch C, Beyene J, Shah PS, Azarpazhooh A. Efficacy and safety of pulpal anesthesia strategies during endodontic treatment of permanent mandibular molars with symptomatic irreversible pulpitis: A systematic review and network meta-analysis. J Endod. 2019;45(12):1435-1464.e10. doi: 10.1016/j.joen.2019.09.002.

[9] Vijayalakshmi B. Knowledge of students about local anaesthetics used during oral surgical procedures. J Pharm Sci. 2015;7:4.

[10] Moodley DS. Local anaesthetics in dentistry - Part 2: Choice of local anaesthetic agent. South Afr Dent J. 2017;72(3):128-30.

[11] Weaver JM. Calculating the maximum recommended dose of local anesthetic. J Calif Dent Assoc. 2007;35(1):61-3. PMID: 17269289

[12] Meechan JG. Why does local anaesthesia not work everytime? Dent Update. 2005;32(2):66-8, 70-2. doi: 10.12968/denu.2005.32.2.66.

[13] Claffey E, Reader A, Nusstein J, Beck M, Weaver J. Anesthetic efficacy of articaine for inferior alveolar nerve blocks in patients with irreversible pulpitis. J Endod. 2004;30(8):568-71. doi: 10.1097/01.don.0000125317.21892.8f.

[14] Hargreaves KM, Keiser K. Local anesthetic failure in endodontics: Endod Top. 2002;1(1):26-39. https://doi.org/10.1034/j.1601-1546.2002.10103.x

[15] Senthoor P, Janani K, Ravindran C. A prospective, randomized double-blinded study to evaluate the efficacy of

buffered local anesthetics in infected and inflamed pulp and periapical tissues. J Maxillofac Oral Surg. 2020 Jun;19(2):246-250. doi: 10.1007/s12663-019-01188-y. Epub 2019 Feb 1. PMID: 32346235; PMCID: PMC7176779.

[16] Boopathi T, Sebeena M, Sivakumar K, Harikaran J, Karthick K, Raj A. Supplemental pulpal anesthesia for mandibular teeth. J Pharm Bioallied Sci. 2013;5(Suppl 1):S103-8. doi: 10.4103/0975-7406.113307.

[17] Fernandez C, Reader A, Beck M, Nusstein J. A prospective, randomized, double-blind comparison of bupivacaine and lidocaine for inferior alveolar nerve blocks. J Endod. 2005;31(7):499-503. doi: 10.1097/01.don.0000167395.61075.38.

[18] Kistner K, Zimmermann K, Ehnert C, Reeh PW, Leffler A. The tetrodotoxin-resistant Na+ channel Na (v)1.8 reduces the potency of local anesthetics in blocking C-fiber nociceptors. Pflugers Arch. 2010;459(5):751-63. doi: 10.1007/s00424-010-0785-5

[19] Pinto V, Derkach VA, Safronov BV. Role of TTX-sensitive and TTX-resistant sodium channels in Adelta- and C-fiber conduction and synaptic transmission. J Neurophysiol. 2008;99(2):617-28. doi: 10.1152/jn.00944.2007

[20] Byers MR, Taylor PE, Khayat BG, Kimberly CL. Effects of injury and inflammation on pulpal and periapical nerves. J Endod. 1990;16(2):78-84. doi: 10.1016/S0099-2399(06)81568-2

[21] Vandermeulen E. [Pain perception, mechanisms of action of local anesthetics and possible causes of failure]. Rev Belge Med Dent. 2000;55(1):29-40.

[22] Coward K, Plumpton C, Facer P, Birch R, Carlstedt T, Tate S, et al. Immunolocalization of SNS/PN3 and NaN/SNS2 sodium channels in human pain states. Pain. 2000;85(1-2):41-50. doi: 10.1016/s0304-3959(99)00251-1

[23] Kanaa MD, Whitworth JM, Corbett IP, Meechan JG. Articaine and lidocaine mandibular buccal infiltration anesthesia: a prospective randomized double-blind cross-over study. J Endod. 2006;32(4):296-8. doi: 10.1016/j.joen.2005.09.016.

[24] Whitworth JM, Kanaa MD, Corbett IP, Meechan JG. Influence of injection speed on the effectiveness of incisive/mental nerve block: a randomized, controlled, double-blind study in adult volunteers. J Endod. 2007;33(10):1149-54. doi: 10.1016/j.joen.2007.07.016

[25] Aggarwal V, Singla M, Rizvi A, Miglani S. Comparative evaluation of local infiltration of articaine, articaine plus ketorolac, and dexamethasone on anesthetic efficacy of inferior alveolar nerve block with lidocaine in patients with irreversible pulpitis. J Endod. 2011;37(4):445-9. doi: 10.1016/j.joen.2011.01.016.

[26] Aggarwal V, Singla M, Subbiya A, Vivekanandhan P, Sharma V, Sharma R, et al. Effect of preoperative pain on inferior alveolar nerve block. Anesth Prog. 2015;62(4):135-9. doi: 10.2344/15-00019.1.

[27] Rosenberg PA. Clinical strategies for managing endodontic pain. Endodontic Topics. 2002;3(1):78-92. https://doi.org/10.1034/j.1601-1546.2002.30108.x

[28] Parirokh M, Ashouri R, Rekabi AR, Nakhaee N, Pardakhti A, Askarifard S, et al. The effect of premedication with ibuprofen and indomethacin on the success of inferior alveolar nerve block for teeth with irreversible pulpitis. J Endod. 2010;36(9):1450-4. doi: 10.1016/j.joen.2010.05.007.

[29] Jena A, Shashirekha G. Effect of preoperative medications on the efficacy

of inferior alveolar nerve block in patients with irreversible pulpitis: A placebo-controlled clinical study. J Conserv Dent JCD. 2013;16(2):171-4.doi: 10.4103/0972-0707.108209.

[30] Parirokh M, V. Abbott P. Various strategies for pain-free root canal treatment. Iran Endod J. 2014;9(1):1-14. doi:10.22037/IEJ.V9I1.5126

[31] Subbiya A, Pradeepkumar AR, Vivekanandhan P, Karthick A. Comparative efficacy evaluation of articaine as buccal infiltration and lignocaine as IANB in the mandibular first molar with irreversible pulpitis. Indian J Multidiscip Dent. 2011 1;2(1):370.

[32] Burtscher D, Dalla Torre D. Intraligamentary anesthesia–A brief review of an underestimated anesthetic technique. Oral Health. 2019;4:1-3. doi:10.15761/OHC.1000177

[33] Kämmerer PW, Adubae A, Buttchereit I, Thiem DGE, Daubländer M, Frerich B. Prospective clinical study comparing intraligamentary anesthesia and inferior alveolar nerve block for extraction of posterior mandibular teeth. Clin Oral Investig. 2018;22(3):1469-75. doi: 10.1007/s00784-017-2248-2

[34] Pradeepkumar AR. Pain management in endodontics. J Oper Dent Endod. 2016;1(2):76-81.

[35] Bigby J, Reader A, Nusstein J, Beck M, Weaver J. Articaine for supplemental intraosseous anesthesia in patients with irreversible pulpitis. J Endod. 2006;32(11):1044-7. doi: 10.1016/j.joen.2006.06.006.

[36] Idris M, Sakkir N, Naik KG, Jayaram NK. Intraosseous injection as an adjunct to conventional local anesthetic techniques: A clinical study. Journal of conservative dentistry: J Conserv Dent 2014;17(5):432. doi: 10.4103/0972-0707.139828.

[37] Haase A, Reader A, Nusstein J, Beck M, Drum M. Comparing anesthetic efficacy of articaine versus lidocaine as a supplemental buccal infiltration of the mandibular first molar after an inferior alveolar nerve block. J Am Dent Assoc 1939. 2008;139(9):1228-35. doi: 10.14219/jada.archive.2008.0338.

[38] Matthews R, Drum M, Reader A, Nusstein J, Beck M. Articaine for supplemental buccal mandibular infiltration anesthesia in patients with irreversible pulpitis when the inferior alveolar nerve block fails. J Endod. 2009;35(3):343-6. doi: 10.1016/j.joen.2008.11.025.

[39] VanGheluwe J, Walton R. Intrapulpal injection: factors related to effectiveness. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1997;83(1):38-40. doi: 10.1016/s1079-2104(97)90088-3.

[40] Evans G, Nusstein J, Drum M, Reader A, Beck M. A prospective, randomized, double-blind comparison of articaine and lidocaine for maxillary infiltrations. J Endod. 2008;34(4):389-93. doi: 10.1016/j.joen.2008.01.004.

[41] Saatchi M, Khademi A, Baghaei B, Noormohammadi H. Effect of sodium bicarbonate-buffered lidocaine on the success of inferior alveolar nerve block for teeth with symptomatic irreversible pulpitis: a prospective, randomized double-blind study. J Endod. 2015;41(1):33-5. doi: 10.1016/j.joen.2014.09.011.