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PAIN MANAGEMENT IN ENDODONTICS: A DETAILED REVIEW ON CAUSES AND MANAGEMENT OF PAIN IN IRREVERSIBLE PULPITIS AND APICAL PERIODONTITIS

Dr. A. Jeyavivili

ABSTRACT

Managing endodontic pain is one of the major challenges faced by dentist in clinical practice. Endodontic pain management consists of a wide range of treatment options ranging from local anesthesia modifications to irrigation and disinfection of the canal depending on the etiology. To find a proper protocol for pain management, through understanding and knowledge of pathophysiology of pain is mandatory. This article reviews the treatment strategies of both irreversible pulpitis and apical periodontitis in detail.

INTRODUCTION:

DC with irreversible pulpitis (IP) and/or apical periodontitis (AP) is an inflammatory response caused by bacterial infection of the pulp and periapical region. Its prevalence ranges from 16 to 86% and increases with age.

This inflammation is characterized by a complex interaction between microbial invasion and host defense. The defense mechanism holds the microbial infection in the root canal system, thereby inhibiting its spread beyond apical foramen, but the persistence of bacteria in the pulpal tissues leads to pulpal pathology and periapical inflammation [1].

It is quite difficult to anesthetize teeth with irreversible pulpitis. Successful local anesthesia is the prime factor of pain control in endodontics [2]. However altering the composition of LA and use of supplemental injections can be beneficial in such cases.

Endodontic therapy aims to remove bacteria, eliminate microbial biofilms and by-products of the root canal system, and prevent subsequent contamination of the intracanal spaces. In apical periodontitis, reduction of bacterial load to a level below the one required to assure healing is achieved by combining root canal preparation and disinfection [1].

Diagnostic Considerations:

The initial challenge for the dentist is to understand the biological process resulting in pain. The diagnostic questions that must be resolved preceding the treatment are:

- Is the pain of odontogenic or non-odontogenic origin?
- Is the tooth vital or non-vital?
- Is the pain primarily due to an inflammatory or infectious process?
- Is the pain of pulpal or periradicular origin or both?

Answers to these questions are obtained from a combination of the medical and dental histories as well as highly subjective clinical tests including electrical, thermal and percussion. From the results of these tests, radiographs and the history, the dentist determines which procedure or combination of procedures will most likely relieve pain [3].

Pathophysiology of Pulpal Pain:

Pulpal inflammation is mediated by a large number of endogenous factors including neurotrophic factors, proinflammatory cytokines, products of the arachidonic acid pathway, bradykinin and others. All of these factors are capable of sensitizing peripheral nociceptors (pain-sensing neurons). Neurotrophic factors such as nerve growth factor (NGF) are produced by mast cells, fibroblasts, and macrophages during inflammation. NGF also induces the liberation of proinflammatory cytokines such as tumor necrosis factor alpha and interleukin1. These cytokines have been implicated in a number of inflammatory conditions such as pulpitis and periodontitis. They are known to modulate nociceptors and play a vital role in central and peripheral sensitization.

Bradykinin is another potent mediator of inflammation. Other inflammatory mediators include products of the arachidonic acid pathway. The expression of the inducible isoform of cyclooxygenase, cyclooxygenase 2, is high in inflamed pulp which contributes to the production of prostaglandin (PGE2).

Pathophysiology of Periradicular Pain:

The main feature of chronic apical periodontitis is extensive sprouting of peripheral peptidergic nerve fibers into the periradicular tissue. This extensive neuronal arborization occurs during the onset of periapical lesions with the selective increase in SP and neuropeptide CGRP [4].

Causes Of Pain:

1. Local Anesthetic Failure:

When planning dental procedures on teeth with clinically normal pulps, effective local anesthesia is the bedrock of controlling dental pain. Local anesthetics administered by the infiltration route are more effective in producing clinical anesthesia in normal tissue. Although nerve-block injections are more difficult in technical aspects, clinical studies suggest success rates of about 75 to 90% or more in patients with clinically normal teeth.

However, local anesthetics are statistically less effective when administered to patients with inflamed pulp. This could be possibly due to failure in the blockade of sodium channels. Sodium channels are expressed by excitable cells, such as neurons, skeletal muscles and cardiac cells. These voltage-gated sodium channels are activated in the presence of an appropriate electrical field. Under normal physiological conditions, sodium channels are activated by the depolarization of peripheral neurons in the adjacent region. This ability to detect electrical fields serves as the fundamental factor for electrical pulp testers. And local anesthesia can block myelinated fibers preferentially over the unmyelinated fibers [5].

1.1 Anatomical causes for LA failures:

As anatomical variations would have less impact on infiltration anesthesia (in maxilla), this discussion focuses mainly on mandibular anesthesia. Traditionally, the pulps of mandibular teeth have been anesthetized by a blockade of the inferior alveolar nerve through an intraoral approach to deliver the solution in the pterygomandibular space. In the classic technique, the

needle is advanced to a point where a pool of anesthetic is deposited in the sulcus colli mandibulae which lies just below the lingula near the mandibular foramen. It is quite difficult to place the tip of the needle in the sulcus colli mandibulae because of the medial projection of bony lingula and it has been suggested that the bevel should be oriented towards the midline in order to take advantage of the lateral deflection. However, failure of the inferior alveolar nerve block occurs even when needle placement is optimized with ultrasound guidance, due to the erratic post-injection distribution of anesthetic solution in the pterygomandibular space over which the operator has no control [6]. Accessory innervation of the mandibular teeth from several sources (in particular, nerve to mylohyoid [7]) has also been suggested as the cause for inadequate anesthesia.

1.2 Acute Tachyphylaxis of LA:
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 vaso-constrictors, there is the possibility that the drug persists in the tissue for a sufficiently more 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 [5].

1.3 Effect of Inflammation On Local Tissue pH:
This is a potentially important issue as inflammation induced tissue acidosis causes 'ion trapping' of local anesthetics. And the low tissue pH will result in a greater proportion of the local anesthetic being trapped in the charged acid form of the molecule and therefore, incapable of crossing cell membranes. Thus, this hypothesis has been advanced as a major mechanism for local anesthetic failures in endodontic pain [5].

1.4 Effect of Inflammation On Blood Flow:
Inflammation has various other effects on local tissue physiology. For example, it has been proposed that peripheral vasodilation induced by inflammatory mediators would lower the concentration of local anesthetics by increasing the rate of systemic absorption. This is a potentially important mechanism, because local anesthetics are well-recognized vasodilators that, in most cases, require formulation with vasoconstrictor agents. 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 [5].

1.5 Effect of Inflammation On Nociceptors:
Substances released from inflamed tissue have two main effects on nociceptive ('pain detecting') neurons. Activation and sensitization are two major mechanisms by which inflammatory mediators change the activity of these normally quiescent neurons. Although local anesthetics display use-dependent blockading properties, peripheral sensitization and activation have been reported to produce an increase in the resistance of nerves to anesthetics [8].

1.6 Effect Of Inflammation On Central Sensitization:
Inflammation also causes changes in the central nervous system's pain processing system. Activation and sensitization of nociceptors in pulpal and periradicular tissue results in obstruction of impulses sent to the trigeminal nucleus and brain. This obstruction, in turn, produces central sensitization. Central sensitization is the increased excitability of central neurons and is thought to be a prime central mechanism of hyperalgesia [9]. Under conditions of central sensitization, there is an exaggerated CNS response to even very mild peripheral stimuli.

2. Role Of Endodontic Bacterium:
Primary root canal infections are polymicrobial, typically influenced by obligate anaerobic bacteria. The most frequently isolated microorganisms before root canal treatment include Gram-positive anaerobic cocci, Gram-negative anaerobic rods, Gram-positive anaerobic and facultative rods, Lactobacillus species, and Gram-positive facultative Streptococcus species. The obligate anaerobes are rather eradicated during root canal treatment. On the other hand, facultative bacteria such as non mutans Streptococci, Enterococci, and Lactobacilli, once established, are more likely to resist chemomechanical instrumentation and root canal medication [10]. In particular Enterococcus faecalis has gained attention in the endodontic literature, as it can frequently be isolated in failed root canal treatments [11].

3. Psychological Factors:
Investigators have suggested a close relationship between anxiety and pain. In a clinical study of children, it was found that anxiety is the strongest indicator of poor intraoperative pain control. Similarly, during heightened anxiety, the pain threshold is reduced for patients. Highly fearful patients are more sensitive to pain and those who are dentally anxious are likely to be more sensitive to dental pain. High levels of stress, anxiety or pessimism in preoperative patients predict poor outcomes (especially in terms of wound healing) [3].

Management of LA failure:
1. Altering the Composition of LA:
The first consideration could be to alter the local anesthetic agents. Research comparing various local anesthetic agents such as 3% mepivacaine plain, 2% mepivacaine with 1:20,000 levonordefrin and 4% articaine with 1:100,000 epinephrine to 2% lidocaine with 1:100,000 for the INAB in patients with normal pulps showed that there is no difference in success rates. Clinical studies involving patients diagnosed with irreversible pulpitis also failed to show any superiority of 4% articaine with 1:100,000 epinephrine or 3% mepivacaine over 2% lidocaine with 1:100,000 epinephrine for the INAB[12].

2. Altering The Injection Technique:
The second strategy would be to change the injection technique in attempting to block the inferior alveolar nerve. The Gow-Gates technique [13] has been reported to have a higher success rate than the conventional INAB, but controlled clinical studies have failed to prove its supremacy [51]. The Vazirani-Akinosi technique (closed mouth) also has not been shown to be superior to the conventional INAB technique [14]. Therefore, replacing the conventional INAB injection with these techniques will not improve success in attaining pulpal anesthesia in mandibular teeth.

3. Supplemental Injections:
Failure of the traditional INAB in asymptomatic and symptomatic patients requires that a clinician should develop alternative strategies to attain good pulpal anesthesia, especially in patients with irreversible pulpitis. There are several supplemental injection techniques available to help the endodontists. It should be remembered that these supplemental injections are best used only after attaining a clinically successful INAB (lip numbness) [12].

3.1 Intraligamentary (periodontal ligament) Injection:

Bangerter [15] and colleagues reported that the periodontal ligament supplemental injection is still one of the most widely used supplemental techniques. The success of supplemental PDL injections in achieving anesthesia for endodontic procedures has been reported to be 50% to 96%. Often reinjection is needed because of failure of the initial PDL injection. Walton and Abbott [16] reported an initial success rate of 71%, and when reinjection was used the overall success rate was 92%. The PDL injection works on the principle of back pressure theory.

3.2 Intraosseous Injection:

The use of the intraosseous injection allows the dentist to deliver local anesthetic solution directly into the cancellous bone surrounding the affected tooth. There are various IO systems available in the market, including the Stabident system, X-Tip system and intraflow handpiece [12].

One of the advantages of IO injection is immediate onset of anesthesia. The site of injection is recommended to be given distal to the tooth to be anesthetized. The exception to this rule would be the maxillary and mandibular second molars, for which a mesial site injection would be required [17]. The duration of anesthesia for a supplemental IO injection in patients with irreversible pulpitis has been reported to be 45 minutes.

One of the drawbacks when using the IO injection is reported to be transient increase in heart rate when injecting epinephrine and levonordefrin containing anesthetic solution.The increase in heart rate ranged from 12 to 32 beats per minute.The use of 3% mepivacaine has been reported not to cause any significant increase in the heart rate and may be the best alternative when a patient's medical history or drug therapies contraindicate the use of epinephrine or levonordefrin [18].

3.3 Mandibular Buccal Infiltration with Articaine:

Recent research has suggested the use of a mandibular buccal infiltration injection of 4% articaine with 1:100,000 epinephrine as a supplemental injection to increase the success of the IANB injection. Articaine is the only amide local anesthetic that contains a thiophene ring and an additional ester ring [19]. Lipid solubility is an intrinsic quality of local anesthetic potency. This quality permits the easier penetration of the anesthetic via the lipid nerve membrane and surrounding tissues [20]. The degree of anesthetic molecules binding to the nerve membrane indicates the duration of the anesthetic effect. The more secure a bond is, the slower the anesthetic is released from the receptor sites in the sodium channels, and greater the duration of the anesthesia. In asymptomatic patients, the use of the articaine solution was found to be better than the lidocaine solution. However , when the buccal infiltration injection was used as a supplement to the IANB in patients diagnosed with irreversible pulpitis , success was reported as only 58% which was less than that attained with the IO and PDL injections [12].

3.4 Intrapulpal Injection:

In approximately 5% to 10% of mandibular teeth diagnosed with irreversible pulpitis, supplemental injections (PDL and IO) do not produce effective anesthesia, even when repeated, to enter the pulp chamber painlessly. This is a major indication that an intrapulpal injection may be necessary. Intrapulpal injection functions well when it is given under back pressure. Onset of anesthesia is immediate. A disadvantage of the intrapulpal injection is its short duration of action (approximately 15 to 20 minutes). Once anesthesia is achieved, the practitioner must work immediately to remove all the tissues from the pulp chamber and the canals [12].

Management of Inflammation (by Premedications):

1. NSAIDs:

Ketorolac, a pyrrolo-pyrrole derivative, is as effective as morphine in pain management. Ketorolac inhibits the enzyme cyclooxygenase, thereby reducing inflammation and pain [21]. Oral ketorolac is absorbed completely, with a mean peak plasma concentration occurring at average of 44 minutes after a single dose of 10 mg dosage. Oral premedication can be given one hour before the procedure to allow ketorolac to achieve an adequate plasma concentration. Because NSAIDs reduce nociceptor activation by decreasing the level of inflammatory mediators (such as PGE2), it is hypothesized that premedication with NSAIDs would enhance the success rate of local anesthesia in patients with IP [22].

2. Steroidal Anti-inflammatory Drugs:

Prednisolone (derivative of cortisol) is a synthetic glucocorticoid. A steroid-induced protein, lipocortin, has anti phospholipase A2 activity, preventing the synthesis of arachidonic acid and thereby lowering the biosynthesis of both cyclooxygenase and lipoxygenase products. Glucocorticoids' better anti-inflammatory potential compared with NSAIDs might have an edge over the other drugs to reduce peripheral sensitization [23].

Management Of Therapy-resistant Strains (microbes):

The effectiveness of endodontic instrumentation and irrigating solutions to clean, shape, and disinfect root canals influences the success, longevity, and reliability of modern endodontic treatments [24]. Elimination of microbes from infected root canals is a complicated task. The chances of a favorable outcome with root canal treatment are significantly higher if infection is effectively eliminated before the root canal system is obturated.

Irrigation:

It is generally believed that mechanical enlargement of canals must be accompanied by adequate irrigation in order to facilitate maximum removal of microorganisms so that the prepared canal becomes as bacteria-free as possible [25].

Ideal Requirements of Root Canal Irrigants [26]:

(I) have a broad antimicrobial spectrum and high efficacy against anaerobic and facultative microorganisms organized in bio lms,
(ii) dissolve necrotic pulp tissue remnants,
(iii) inactivate endotoxin,
(iv) prevent the formation of a smear layer during instrumentation or dissolve the latter once it has formed,
(v) be systemically nontoxic,
(vi) be non caustic to periodontal tissues,
(vii)be less likely to cause an anaphylactic reaction.

1. Sodium Hypochlorite:

Sodium hypochlorite (NaOCl) is the most widely used irrigant because of its antimicrobial activity, ability to dissolve organic matter [26] and low cost. The disadvantages of NaOCl are its toxicity when accidentally injected into the periradicular tissue. Moreover, NaOCl significantly affects mechanical properties of dentine such as microhardness, roughness, elastic modulus flexural strength and organic-inorganic ratio [27]. Commonly used concentrations are 1.3% and 2.5%. But, NaOCl is ineffective in removing the inorganic components of the smear layer and the hard-tissue debris [28].

2. EDTA:
Even though sodium hypochlorite appears to be the most desirable single endodontic irrigant, it cannot dissolve inorganic dentin particles and thus prevent the formation of a smear layer during instrumentation. Hence, demineralizing agents such as ethylenediamine tetraacetic acid (EDTA) and citric acid have been recommended as adjuvants in root canal therapy [29]. These are highly biocompatible. Although citric acid appears to be slightly more potent at similar concentration than EDTA, both agents show high efficiency in eliminating the smear layer. In addition to their cleansing property, they may detach bio-films adhering to root canal walls. An alternating irrigating regimen of NaOCl and EDTA may be highly efficient in reducing bacterial loads in root canal systems than NaOCl alone [26].

3. Chlorhexidine:
Chlorhexidine was developed in the late 1940s in the research laboratories of Imperial Chemical Industries Ltd. (Macclesfield, England). Chlorhexidine is a potent antiseptic, which is commonly used for chemical plaque control in the oral cavity. Aqueous solutions of 0.1 to 0.2% are recommended for that purpose, while 2% is the concentration used for endodontic therapy [26]. It is commonly held that chlorhexidine would be less caustic than sodium hypochlorite.

Despite its usefulness as a final irrigant, chlorhexidine cannot be advocated as the main irrigant in standard endodontic cases, since
(a) chlorhexidine is incapable of dissolving necrotic tissue remnants, and
(b) chlorhexidine is relatively less effective on Gram-negative than on Gram-positive bacteria.

Recent Advancements:
All the irrigation solutions have their own range of limitations and the search for an ideal root canal irrigant still continues. Newer root canal irrigants in the horizon are as follows:
(1) MTAD,
(2) HEDP
(3) tetraclean,
(4) electrochemically activated solutions,
(5) ozonated water,
(6) photon-activated disinfection,
(7) herbal irrigants.

MTAD:
Bio Pure MTAD is a mixture of a tetracycline isomer, an acetic acid and Tween 80 detergent which was designed to be used as a final irrigant.

Tetracycline has many unique properties of low pH and thus can act as a calcium chelator and cause enamel and root surface demineralization. In addition, it has been reported that it is a substantive medication (becomes absorbed and gradually released from tooth structures such as dentin and cementum) [30]. Finally, studies have shown that tetracycline significantly enhances healing after surgical periodontal therapy.

The main advantage of MTAD is its effectiveness in removing the smear layer along the whole length of the root canal and in removing organic and inorganic debris. It does not significantly produce any signs of erosion or physical changes in dentin. In particular, MTAD mixture is effective against *E. faecalis* [31] and it is also less cytotoxic than other endodontic medications

HEDP:
The beneficial effects of HEDP are as follows:
- Prevention of smear layer
- Reduction of hard tissue debris accumulation [32]
- Reduction of torsional load on rotary instrumentation.

Tetraclean:
Tetraclean (like MTAD) is a mixture of an antibiotic, an acid and a detergent. However, the concentration of the antibiotic and the type of detergent (polypropylene glycol) differ from those of MTAD [33].

Electrochemically Activated Solutions:
Electrochemically Activated (ECA) solutions are synthesized from tap water and low-concentrated salt solutions.

The ECA technology is a new scientific paradigm developed by Russian scientists at the All-Russian Institute for Medical Engineering (Moscow, Russia, CIS). Principle of ECA is transferring liquids into a metastable state via an electrochemical unipolar (anode or cathode) action through the use of an element/reactor ("Flow-through Electrolytic Module " or FEM). The FEM is capable of producing solutions that have bactericidal and sporicidal activity with odorless and non-toxic nature [34].

The quality of debridement was much better in the coronal and middle parts of canal walls where only scattered debris was noted in contrast to the apical part that contained enormous debris. ECA is showing promising results due to the ease of removal of debris along with the smear layer. It is a potent root canal irrigant.

Ozonated Water:
Ozone is a highly powerful bactericide that can kill microorganisms effectively. It is an unstable gas, capable of oxidizing any biological organism. It was reported that ozone at low concentration, (0.1 ppm) is sufficient to destroy bacterial cells including their spores. Although ozonated water is a powerful antimicrobial agent against bacteria, fungi, protozoa, and viruses, less attention has been paid to the antibacterial activity of ozonated water against bacterial biofilm and hence in root canal infection. Therefore, there is need for further studies and modifications in ozonated water before it could be used as a root canal irrigant [35].

Photon-Activated Disinfection:
The use of photodynamic therapy (PDT) for the inactivation of microorganisms was first developed by Oscar Raab who reported the lethal effect of acridine hydrochloride on Paramecia caudatum. PDT is based on the concept that nontoxic photosensitizers can be preferentially localized in certain tissues and subsequently activated by light of a certain wavelength to generate singlet oxygen and free radicals that are cytotoxic to cells of the target tissue [36]. Methylene blue (MB) is a well-established photosensitizer that has been used in PDT for targeting various gram-positive and gram-negative oral bacteria and was previously used to study the effect of PDT on endodontic therapies. Several studies have shown incomplete destruction of oral bio-films using MB-mediated PDT due to inadequate penetration of the photosensitizer. PAD can currently be considered a useful adjunct to traditional root canal treatment.

Herbal Irrigants:
- Triphala (IMPCOPS Ltd, Chennai, India) is an Indian ayurvedic herbal formulation made of dried and powdered fruits of three medicinal plants, Terminalia bellerica, Terminalia chebula, and Emblica officinalis.
- Green tea polyphenols (GTPs; Essence and Flavours, Mysore, India) [37].

Dimethyl sulfoxide (DMSO) is used as a solvent for Triphala and GTP. It helps in bringing out the pure properties of all the components of the herb being dissolved [38]. Although Triphala and green tea polyphenols (GTPs) exhibited similar antibacterial sensitivity on E.faecalis planktonic cells, Triphala showed high efficacy on E. faecalis biofilm. This may be due to its formulation, which contains three different medicinal plants in equal proportions.

Triphala and GTPs are proven to be safe, containing active constituents that have beneficial physiologic effect apart from its curative property such as antioxidant, anti-inflammatory and radical scavenging activity and may have an additional advantage over the traditional root canal irrigants.

Activation Methods:

Two studies compared the effectiveness of ultrasonic activation methods in reducing bacteria compared to traditional needle irrigation. In both cases, ultrasonic irrigation showed statistically significant action in lowering the bacterial load. Based on recent studies, ultrasonic activation methods are fundamental to the effectiveness of irrigants [39]. They are based on the transmission of acoustic energy through the irrigant through a stainless steel wire or endodontic file. Acoustic energy is dissipated through the irrigant, leading to cavitation and microstreaming; this allows the irrigant to move dynamically within the root canal system. Acoustic waves produce a cavitation bubble; the energy released after bubble collapse is transmitted to the root canal walls, releasing the debris found. Microstreaming then carries the debris coronally to remove it from the canal completely [40].

Management of Psychological Factors:

Several methods have been suggested for managing anxious patients. First, the dentist should establish a positive and confident relationship and avoid exposing the patient to obvious fear-producing stimuli. Many dentists report that a sense of humor often helps to relax apprehensive patients. For highly fearful patients, cognitive behavior-based programs have shown significant long-term reduction in pre dental treatment anxiety.

Second, pharmacologic agents can be administered to control patient fear and anxiety. While these agents can be delivered through oral, inhalation (N2O) 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. Kaufman et al showed that oral triazolam 0.25mg was equally effective in comparison to intravenous diazepam in reducing anxiety in patients undergoing endodontic therapy [5].

CONCLUSION:

Hopefully the reader has found this review to be highly informative. Our objectives were to review various etiological factors and relevant remedial measures associated with pain in IP and AP respectively. In cases of pain with irreversible pulpitis, effective pain management can be achieved by supplemental injections and premedications. Whereas in AP, irrigation plays a crucial role and use of activation methods could be highly beneficial. Given the greater understanding of pain mechanisms that we currently enjoy and the ongoing research efforts in laboratories throughout the world, it is not difficult to imagine a time when endodontic therapies will be an absolute pain free procedure.

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