Pharmacotherapy in Root Canal Treatment.

Sri Shoban Raaj Sri Ramulu and Prasanna Neelakantan*

Saveetha Dental College and Hospitals, Saveetha University, Chennai, Tamil Nadu, India

ABSTRACT

Management of pain, and complete elimination of infection preceding an endodontic treatment has always been a challenge to practitioners. The best of an endodontic treatment is achieved by means of successful management of pre- and post- endodontic treatment pain and eradication of any possible infection. This article reviews the pharmacodynamics comparison of non-steroidal and steroidal drugs, as a potentially successful analgesic, and efficiency of antibiotics based on recent bacterial susceptibility tests, for an effective endodontic treatment with minimal side-effect liability.

Keywords: pain, inflammation, analgesics, anti-inflammatory, endodontics

*Corresponding author
INTRODUCTION

Root canal treatment [endodontic treatment] involves removal of the diseased or infected pulp, disinfection of the root canal space followed by filling with an inert material. Root canal treatment is often perceived as one of the most painful procedures by patients. Nearly 41,000 root canal treatments are performed daily in the USA and a similar number or even higher is performed in the Indian subcontinent. Root canal treatment is routinely done under local anesthesia, however to achieve an effective control, a need arises for prescribing pre-operative and post-operative analgesics to patients. In isolated circumstances, the need for antibiotics also arises, either prophylactically or therapeutically. The objective of this review is to provide a comprehensive review of the literature regarding pharmacotherapy in endodontics.

Pain in Endodontics

Endodontic pain is often linked to pulpal or periodontal origin which initiates inflammatory process and results from stimulation of nociceptors as well as additional central mechanism [1][2]. During early stages of inflammation, mediators such as prostaglandins [PGs] and bradykinin [BK] change the sensitivity of receptors and reduce activation threshold for conducting ion channels. Prostaglandin, prevalently E2 have been associated to initiate the inflammatory process. They are generated from arachidonate by the action of cyclooxygenase [COX] isoenzymes. High levels of arachidonic acid metabolites have been reported in inflamed pulps and periapical tissues of humans and animals [3-7]. The significance of these elevated levels of metabolites are associated with the presence of pain.

An effective pain management, in this context should focus on reduction of chemical inflammatory mediators that mediates peripheral nociceptors. This is usually managed by the administration of analgesics which exhibits anti-inflammatory and analgesic properties. Analgesics are divided mainly into three main domain, namely non-steroidal anti inflammatory drugs [NSAIDs], non-narcotic analgesics and opioid analgesics, where NSAIDs are the most commonly prescribed drugs for the management of pain in endodontics.

Pain Management in Endodontics

Pre-operative Analgesics

Effective local anesthesia, is the key to painless root canal treatment, however in specific cases of chronic inflammation of the pulp adequate anesthesia may not be achieved. Such a tooth is termed as a hot tooth. Endodontic research has focused on this issue for a long time and several papers have been published on the use of analgesics pre operatively to enhance the success of local anesthesia. Although most studies did not demonstrate a significantly a higher success rate for this approach, few drugs have been shown to be effective. Premedication with ibuprofen [200-600mg], indomethacin, tenoxicam [20mg], lornoxicam [8mg], diclofenac potassium [5mg] and ketorolac have been shown to be able to achieve this goal. A pre-operative analgesic in endodontics focuses on pain management before beginning
with endodontic treatment. This works by alternating threshold, by increasing sensitivity towards peripheral nociceptive input [8, 9].

Penniston et al. recommended administration of periapical injection of ketorolac as an effective adjunct to local anesthesia in management of pain during root canal treatment [9]. Further research is required in this direction prior to routine clinical use of this approach. Studies have indicated that obtaining anesthesia with satisfactory results on a mandibular molar with irreversible pulpitis is rather harder compared to healthy pulps, and various investigations have been performed to overcome pulp pain even after administration of inferior alveolar nerve block [IANB] [10-14]. A study carried out with pre medication with ibuprofen and indomethacin indicated a higher success rate following administration of IANB on mandibular molar teeth with irreversible pulpitis, with reports of no side effects up to 48 hours after the procedure [15]. The study also proposed no significant difference between both the NSAIDs but superiority comparable to the placebo.

Degree of pain relief varies according to dosage of administration of ibuprofen, with higher relief recorded on 600mg by an investigation done by Seymour and Ward [17]. A single dosage of 200 mg ibuprofen, given prior treatment has been recorded to have successfully reduce the pain post treatment [16]. Newer NSAID such as tenoxicam, in a single dose of 20 mg administered before treatment, significantly reduced the pain after the treatment preceded, with reduced adverse effects with this drug [16].

Post-operative Analgesics

Post operative pain management in endodontics has always remained a subject of debate to practitioners, with reports of 25-40% of patients with pulpitis complaining of pain after endodontic pain after endodontic treatment [19]. Endodontic treatment relieves the pain significantly, but not definitely with pain ranging from mild to moderate, continuing for several days [20]. The potential risk of chemical agents used during the endodontic procedure gives rise to inflammation of the periapical tissue which is the common reason for post endodontic pain [18]. Post operative pain management should cardinal focus on peripheral and central mechanism of hyperalgesia which regulates pain threshold, where reports of insufficient pain control leads to development of greater pain during development of hyperalgesia [19].

Post operative pain is usually managed with oral administration of NSAIDs which suggests mixed reviews of success rate, and some reports of persistent presence of mild pain. The popularity of the usage of ibuprofen as an effective NSAID has been shown by studies to significantly reduce pain in a dosage of 600 mg, [20, 21] and others suggesting that combination of other drugs to ibuprofen increases its superiority. A combination of flurbiprofen/tramadol combination and pre-operative flurbiprofen/post-operative flurbiprofen were recorded to be the most effective in treatment of pain in endodontics. This review focuses on the most commonly used NSAIDs following endodontic treatment, based on abstracts and research publications.
Post Operative Analgesics with Non-steroidal Anti Inflammatory Drugs [NSAID]s

Ibuprofen is the most commonly used and available ‘over the counter’ [OTC] analgesic. The profound usage of ibuprofen is based on its effectiveness with very minimal to negligible side effects on controlled dosage. Ibuprofen is commonly prescribed for management of fever, pain and inflammatory diseases such as osteoarthritis and rheumatoid arthritis [26]. The effectiveness of this drug has gained its popularity among practitioners as an analgesic in endodontic therapy, with studies suggesting no difference in response between male and female and other studies suggesting of its analgesic property as dose dependent [22]. Ibuprofen 800 mg has been shown to be the most effective NSAID in endodontic pain management.

Ibuprofen, being a non-selective cyclooxygenase [COX] inhibitor, inhibits both COX-1 and COX-2 enzyme and subsequently converts arachidonic acid to prostaglandin H2 [PGH2]. The analgesic effect in post endodontic treatment is achieved mainly through the inhibition of COX-2. Ibuprofen is available as tablet and gel capsule formulation, with faster onset of analgesic delivery on gel capsule formulation [23]. Additionally, a wide spectrum of combination of drugs to ibuprofen has increased the pharmacodynamic of ibuprofen acting on its own. A few studies includes the combination of paracetamol [1000mg]/ ibuprofen [600mg], ibuprofen/acetaminophen which was reported to have surpass the effectiveness on post endodontic pain management over administration of ibuprofen[600mg] alone [24].

Relatively, the inhibition of COX-1, infrequently leads to gastric problems reported only on high doses of ibuprofen [25]. Recent research also found that patients with CYP-2C8 and CYP-2C9 polymorphism have reduced ability to methobolize ibuprofen once ingested, suggesting its interaction with genetic polymorphism of the liver enzyme cytochrome P450, where retention of this drug leads to certain degree of adverse effects [26]. Table 1 lists the commonly used NSAIDs and the recommended dosages for effective post operative pain control.

Table 1: Commonly used NSAIDs and recommended dosages for postoperative pain control

<table>
<thead>
<tr>
<th>Analgesic</th>
<th>Concentration (mg)</th>
</tr>
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<tbody>
<tr>
<td>Ibuprofen</td>
<td>800</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>600</td>
</tr>
<tr>
<td>Ketorolac</td>
<td>60</td>
</tr>
<tr>
<td>Ketorolac</td>
<td>20</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>100</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>400</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>200</td>
</tr>
<tr>
<td>Tramadol</td>
<td>150</td>
</tr>
<tr>
<td>Tenoxicam</td>
<td>15</td>
</tr>
<tr>
<td>Flurbiprofen + Tramadol</td>
<td>50 + 100</td>
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</tbody>
</table>
Ketorolac is a NSAID from the heterocyclic acetic acid derivative, used for its analgesic property with slightly delayed onset, but persistent effect which acts longer than other opioid drugs [27]. It was the first NSAID available for intramuscular injection and the study of ketorolac as an analgesic has been extended because of its efficacy [10]. Ketorolac acts on periphery by inhibition of prostaglandin, with recent studies indicating it to be active centrally as well [27]. According to Oxford League table of Analgesic Efficacy, ketorolac 20mg and ketorolac 60mg were listed to be the 2nd and 3rd most effective analgesia in management of pain control.

Diclofenac is a NSAID with anti-inflammatory and analgesic property. It is not widely used in management of post endodontic pain, but it exhibits good bacteriostatic property by inhibiting the DNA synthesis of the bacteria [28]. The drawback of this drug is observed by the side effects which is usually mild, but in most cases patients complains of gastrointestinal problem.

**Steroids in Endodontics**

Steroids in endodontic has been used for its potent anti-inflammatory and is used either by combination of antihistamine or antibiotics in means of intracanal medicaments or a direct administration of this drug systemically for management of pain [31]. Glucocorticoids, an example of steroids predominantly acts by binding to the glucocorticoid receptor [GR]. This in turn, regulates the expression of anti-inflammatory proteins of the nucleus and suppresses pro-inflammatory proteins in the cytosol.

Steroids are generally administered via intraoral IM, intraosseous IM and extraoral IM injection, but intraoral and intraosseous IM is more preferable mode of administration [30]. Based on a study, oral administration of dexamethasone 0.75mg/tablet after an endodontic treatment, reduced pain significantly 8 hours and 24 hours compared to their placebo study [31]. In other study to compare the efficacy of steroids and NSAIDs, it was suggested that prophylactic intra-oral infiltration dexamethasone reduced pain significantly comparable to oral administration of piroxicam [NSAID] [32].

Intraoral injection of corticosteroids which is not a new approach in dentistry has been reported to reduce post operative swelling and trismus after a surgical removal of impacted third molar [35]. Studies have indicated that management of pain in necrosed pulp with corticosteroids is more efficacious than administration of it in irreversible pulpitis [30].

The administration of steroids for the management of post endodontic pain maybe be hindered by its potency of causing adrenal suppression, and also report of post-operative infection in a single case, but studies have indicated that a single and short term use at high dose was proved to be significantly tolerable [33, 34]. In a recent study it was suggested that prophylactic periapical infiltration of 0.2ml of 4mg/ml dexamethasone [total 0.8mg] diluted with 1.6ml local anesthetic solution prior to endodontic treatment was significantly effective for relieving the post endodontic pain without further complications in healthy patients in contrast
to oral administration of piroxicam, unless it was followed with regular oral dose of the drug for 3 days postoperatively [32].

**Microbiology of Endodontic Pathosis**

Pulpal and periapical diseases are primarily initiated by pathogens which infects the predentin, before penetrating the calcified dentinal tubules. This condition is usually managed depending on the degree of and the extend of the pulpal disease, and in cases of irreversible pulpitis, it is most commonly managed by drilling the tooth and removal of the inflamed pulp in contrast of customary removal of the tooth. Thus, the primary goal of endodontic treatment is a successful eradication of pathogens which is infected within the pulp, and this has always remained a challenge to practitioners, since instrumentation and irrigation by itself could not completely eliminate pathogens. A combination of both results in a satisfactory desirable outcome, but not to a definite margin of elimination [35].

To achieve a satisfactory elimination of bacterial activity within the dentinal tubules, practitioners usually prescribe systemic antibiotics to combat the pathogens. However, practitioners more often fail to realize on the side effects and the unnecessity of prescribing these drugs, with reports of prescription by almost 17% of the members of the American Association of Endodontists [AAE] being unnecessary [36].

**Systemic Antibiotics in Endodontics**

Once an individual is susceptible to a pulpal and periapical disease, the host defense response would be activated to prevent and eliminate further susceptibility. This response is usually dependent on the extent of the disease progression and the host defense ability. The extent of the disease progression largely determines the necessity of prescribing a systemic antibiotic to control the rate of progression of the pathogenesis.

Systemic antibiotics, which includes Penicillin VK [Penicillin V Potassium], Amoxicillin, and Clindamycin which are most commonly prescribed, acts by re-establishment of the host’s defense mechanism and prevents further progression but does not totally eradicate the pathogenesis which has been activated. The lack of this understanding often leads to practitioners prescribing systemic antibiotics which are uneventful, in hope to totally remove the underlying causes. This in large scale, results in bacterial mutation developing resistant strains, against few over prescribed systemic antibiotics [37, 38].

**Prophylactic Antibiotics for Medically Compromised Patients**

Patients in this group could be categorized into either minimal risk of infection exposure or impaired host-defense mechanism, which has higher risk of infection exposure [39]. Patients who are medically compromised have higher degree of infection exposure. This suggests that these patients should be given a higher degree of consideration on prophylactic against infection. This is not an exception for patients who are medically compromised and going
through endodontic treatment. In a study conducted, it was suggested that antibiotic prophylaxis to only be used in 3 out of 8 medical condition experienced by patients, which is native heart disease, prosthetic heart valves and prosthetic joints [40]. These studies suggest that antibiotic prophylaxis should only be indicated for patients who are medically compromised, given a single high dose pre treatment. Based on systematic reviews and research, a formulation is proposed for the management of pulpal and periapical diseases [Figure 1].

*Proposed Systemic Antibiotic Prescription for Management of Pulpal Pather*

![Proposed Systemic Antibiotic Prescription for Management of Pulpal Pather](image)

*Figure 1*

REFERENCES