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Non-Steroidal Anti-inflammatory Drugs to Improve the Success of Inferior Alveolar Nerve Block In Root Canal Treatment

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ABSTRACT

Inferior alveolar nerve block [IANB] is the most commonly used technique of local anaesthesia for root canal treatment of mandibular molar teeth. A high failure rate of the IANB has been reported owing to the inflammatory conditions that exist in the pulp and periapical tissues of the teeth - a condition termed "hot pulp". The endodontic literature suggests several methods of enhancing the success of the IANB in cases of hot pulp. The most clinically relevant and successful approach has been the use of pre-anaesthetic medication with specific Non-Steroidal Anti-inflammatory Drugs [NSAID]. The objective of this article is to thoroughly review the literature on preanaesthetic medication with NSAIDs to increase the success of IANB in root canal treatment.

Keywords: Hot tooth, local anaesthesia, NSAID, analgesics, root canal treatment, inferior alveolar nerve block

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INTRODUCTION

The inferior alveolar nerve block is the most frequently used injection technique for achieving local anesthesia in root canal treatment of mandibular teeth. During root canal treatment, profound pulpal anesthesia must be achieved for both patient benefit and making the procedure less stressful for the dentist. The inferior alveolar nerve block has been shown to fail in 44% to 81% of the time [1]. This failure could be attributed to several reasons, like anatomical variation of the nerve, decreased local pH, activation of nociceptors like tetrodotoxin, capsaicin-sensitive, transient receptor potential vanilloid type 1 channels [TRPV1].

Inflammatory changes within the pulp worsen as the carious lesion approximates the pulp. This leads to an influx of neutrophils and release of inflammatory mediators like prostaglandins, interleukins, substance P, bradykinin, and calcitonin gene-related peptide [2]. Although pulp inflammation produces a number of inflammatory mediators, prostaglandin is one of the most studied. Generally the mediators sensitize the peripheral nociceptors within the pulp of the affected tooth, which increases pain production and neuronal excitability [2]. Prostaglandin is an end-product of arachidonic acid metabolism which is produced via the cyclooxygenase [COX] pathway [3]. Prostaglandin leads to activation and sensitization of peripheral nociceptors which in turn leads to sprouting of nerve terminal in the pulp [4]. This then upregulates the expression of sodium channels in the nerve cells like tetrodotoxin [TTX] [4]. TTX is four times resistant to the blockade of lidocaine and moreover their expression is doubled in the presence of prostaglandins 4. Prostaglandins also act by sensitizing nerve endings to bradykinins and histamines which increases pain and tenderness during inflammation [3]. Hot tooth generally refers to a tooth which has been diagnosed as irreversible pulpitis, with spontaneous, moderate to severe pain, and does not respond to local anaesthesia [2]. IANB has a failure rate of 15% in patients with normal tissue [5] whereas it fails in 44-81% of teeth with irreversible pulpitis [6]. Essentially, it is not a failure of technique in these cases. The pulpal anaesthesia does not occur due to presence of inflammatory mediators as discussed earlier. Rate of failure in maxillary infiltration is also as high as 30% in teeth with irreversible pulpitis [5]. Therefore inability or difficulty to achieve anesthesia in patients with irreversible pulpitis remains as barrier for a successful endodontic treatment. This review discusses the role of preoperative non-steroidal anti-inflammatory drugs in increasing the success rate of inferior alveolar nerve block.

Drugs Used As Premedication

Several drugs of the NSAID class have been recommended as a premedication to enhance success of local anaesthesia in teeth with hot pulp. The aim of this review is to comprehensively discuss the pharmacology of these agents and the literature surrounding these NSAID's in bringing about success of local anesthetics.

Ibuprofen

Ibuprofen was the first propionic acid derivatives introduced in 1969 [7]. It is a non-selective inhibitor of cyclooxygenase-1 [COX-1] and Cyclooxygenase-2 [COX-2] [8]. It mainly

acts as an analgesic, an anti-inflammatory and an antipyretic agent [9]. Other function of NSAIDs can also be attributed to the inhibition of prostaglandins [PGs] or thromboxane synthesis, including alteration in platelet function [PGI₂ and Thromboxane], prolongation of gestation and labor [PGE₂, PGF_{2A}], gastrointestinal mucosal damage [PGI₂ and PGE₂], fluid and electrolyte imbalance [renal PGs], premature closure of ductus arteriosus [PGE₂] and bronchial asthma [PGs] [10]. Its anti-inflammatory property may be weaker compared to some other NSAIDs, but has a good analgesic and antipyretic role [11]. Ibuprofen is supplied as tablets with a potency of 200 to 800 mg. The usual dosage is 400 to 800 mg three times a day. It is well absorbed orally and the peak serum concentrations are attained in 1 to 2 hours after oral administration. A low dose ibuprofen is as effective as aspirin and paracetamol [12].

Efficacy in hot pulp

Wells et al in 2007 has demonstrated a study by using immunoreactivity. He found that, there is increase in Nav1.9 isoform in painful and inflamed teeth [13, 14]. There are presences of 4 types of prostaglandin receptors, of which only EP₂ and EP₃ subtypes are expressed in trigeminal sensory neurons. Due to activation of EP₂ and EP₃, there will be increase in PGE₂ which contributes to odontogenic pain [15,16]. Ibuprofen acts as an indirect analgesic by blocking the continued production of prostaglandins [15]. However Mark et al. showed that ibuprofen did not significantly increase the IAN block [13]. In contrast, Nusstein et al. comparing preoperative oral administration of ibuprofen, dexamethasone, or placebo [lactose]. It was found that, all the three agents were effective and improved the anesthetic success rate of an inferior alveolar nerve block in patients with irreversible pulpitis [17].

Maingret et al in 2008 reported a study demonstrating inflammatory mediators such as prostaglandin, serotonin and histamine were applied singly to neurons, up regulation of Nav1.9 isoform did not occurs, however when the inflammatory mediators are combined and applied to the neuron, up regulation of Nav1.9 isoform occurs. Therefore removal of single inflammatory mediator is not sufficient as the effects of other mediators are still involved [18]. Activation if TRPV4 does not occur by single inflammatory mediator, hence removal of single mediator again does not help to overcome the effect of other inflammatory mediators involved [19]. Although ibuprofen inhibits the prostaglandin production, the inflammatory damage previously created is still present, along with the action of other multiple inflammatory mediators [13]. Noguera-Gonzalez compared ibuprofen and placebo, and showed that preoperative oral administration of ibuprofen significantly improved the efficacy of inferior alveolar nerve block in patients with symptomatic irreversible pulpitis [20]. Simpson et al in contrast, showed that 800 mg ibuprofen showed a statistically significant increase in anesthetic success in patients with symptomatic irreversible pulpitis as compared to 1000 mg acetaminophen [21].

Acetaminophen

Acetaminophen is not considered a true non-steroidal anti-inflammatory drug [NSAID] because of its negligible anti-inflammatory properties therefore acetaminophen is an analgesic and antipyretic agent with insignificant anti-inflammatory properties [22]. It has

been clinically proven that, it is effective as a temporary relief for minor aches and pains associated with the common cold, headache, toothache, muscular aches, backache, for the minor pain of arthritis, for the pain of menstrual cramps, for the reduction of fever and also as an effective antipyretic in infants, children, and adults [23]. It acts as an anti pyretic by blocking the formation and release of prostaglandins in the central nervous system and inhibiting the action of endogenous pyrogens at the hypothalamic thermoregulatory centers leading to reduction of fever [24]. It also has analgesic property by inhibiting prostaglandin synthesis centrally and elevating the pain threshold [25]. Recent research suggests that acetaminophen has the ability to inhibit a specific site on the prostaglandin H2 synthase [PGHS] molecule, the 2 isoforms of which, PGHS1 and PGHS2, are also referred to as COX-1 and COX-2 [25].

Efficacy in hot pulp

Simpson et al. compared the efficacy of acetaminophen alone or with combination of 800mg ibuprofen and 1000mg acetaminophen given 45 minutes before administration of IAN block [21]. A higher rate of success was found with acetaminophen as a preoperative medication in patient with asymptomatic irreversible pulpitis [26]. It was stated that the varying results of several studies was probably because of the variation in the degree and duration of the pulpal inflammation influences the success of a premedication in achieving adequate pulpal anaesthesia.

Lornoxicam

Lornoxicam [LNX], a congener of tenoxicam, is a NSAID which belongs to the oxicam group. Compared to other NSAIDs, lornoxicam has a strong analgesic and anti-inflammatory property. Its analgesic property is comparable to that of opioids. It is available in oral and parenteral formulations. Its oral dose is 4mg thrice daily or 8mg twice daily [27]. Studies have been reported that it is more effective than 10 mg morphine when used at doses ≥ 8 mg to control pain after oral surgery [27]. It produces dose related analgesia like, 16 mg and 32 mg were significantly superior to 4 mg with respect to pain relief. The total pain relief score after 6 hours of intake, are highest at 32 mg [28]. Clinical investigations have established it as a potent analgesic with excellent anti-inflammatory properties in a range of painful or inflammatory conditions like postoperative pain and road accidents. It also acts by inhibiting the metabolites of COX branch of arachidonic acid pathway like all other NSAIDs. It inhibits both isoforms in the same concentration range i.e. COX-1/ COX-2 = 1. Thus, a perfectly balanced inhibition of COX- 1 and COX-2 is achieved [29].

Efficacy in hot pulp

Prasanna et al. showed that premedication using 8mg LNX but not 50mg of DP resulted in higher rate of successful IANB in patients with irreversible pulpitis compared to PLAC when used as premedication. This is because LNX inhibited the conduction of C fibres which are more resistant to LA compared to A-delta fibres and also opening of K⁺ channels which produces anti-nociceptor. Activation of GMP pathway also induces opening of K²⁺ channels. This in turn leads LNX to produce a peripheral analgesic effect and increase the success rate of IANB [30]. Besides LNX can also be more effective as a premedication

because LNX may have the ability to inhibit TRPV channels which have been indicated in pain signaling and thermoreception more effectively than diclofenac [31].

Ketorolac

Ketorolac is a nonsteroidal anti-inflammatory drug [NSAID]. Its analgesic property is considered to be more compared to anti-inflammatory activity [32]. It inhibits synthesis of prostaglandins and may be considered a peripherally-acting analgesic therefore it is a potent analgesic. It is indicated for the short-term [up to 5 days] management of moderately severe, acute pain that requires analgesia at the opioid level [33].

Efficacy of hot pulp

Premedication using ketorolac and ibuprofen has no significant effect on success rate on IANB in patients with irreversible pulpitis. Reasons being, the inflammatory mediators had already activated the nociceptors. NSAIDs only inhibit the formation of prostaglandins but not the already activated nociceptors [3]. Jena et al. compared ketorolac, ibuprofen, combination of aceclofenac with paracetamol, combination of etodolac with paracetamol and a placebo group and found that the use of preoperative medication did improve the anesthetic success rate of an inferior alveolar nerve block in patients with irreversible pulpitis.

Indomethacin

Indomethacin is non-steroidal anti-inflammatory drug which acts as an anti-inflammatory and as well as an antipyretic drug. It is mainly used for symptomatic relief of pain and stiffness in rheumatic diseases. Following oral administration the absorption of the drug is rapid and complete but it varies from patient to patient with peak plasma concentrations of 2 to 3 mg/ml which is achieved within 1 to 2 hours [34].

Efficacy on hot pulp

Parirokh et al in the year 2010, has reported a study showing indomethacin and ibuprofen as an effective adjunct analgesic for pain during endodontic treatment of teeth with irreversible pulpitis [26]. Based on the result of this study and also previous investigations suggest that, premedication in emergency patient is not effective. This is because previously released prostaglandin has already result in the formation of TTx resistant receptors, therefore there is no significant effect on IANB, however, usage of premedication in patients who have prolong pain and no spontaneous pain improves the effectiveness of IANB anesthesia for it inhibits the formation of prostaglandins [35,36]. Although effective anesthesia was obtained with NSAIDs as a premedication, neither drug gave complete anesthesia during endodontic treatment in irreversible pulpitis [26].

Diclofenac

Diclofenac sodium is a nonsteroidal anti-inflammatory drug. Diclofenac sodium acts by potent cyclo-oxygenase inhibition, reduction of arachidonic acid release, and

enhancement of arachidonic acid uptake. It thereby results in a dual inhibitory effect on both the cyclo-oxygenase and lipoxygenase pathways therefore it is an effective drug in acute and subchronic inflammation, and has gives good analgesic effect [37]. It has been used to achieve pain relief in several musculoskeletal conditions including arthritis, rheumatoid arthritis, polymyositis, dermatomyositis, osteoarthritis, dental pain, spondylarthritis, ankylosing spondylitis, temporomandibular joint problems, gout attacks and pain management of kidney stones, gall stones as well as migraine. Besides that, it also appears to exhibit bacteriostatic activity by inhibiting bacterial DNA synthesis [38].

Efficacy in hot pulp

Wali et al in 2012 has proved in a clinical trial stating that Diclofenac potassium brings about increase effectiveness as an IANB as a premedication. This study reported success rate was 75% [15 out of 20 patients] [39]. 50 mg of diclofenac potassium has been shown to increase the success rate of inferior alveolar nerve blocks by Prasanna et al. [31]

CONCLUSIONS

The use of several NSAIDs to improve the success of local anaesthesia in the case of a hot tooth was presented in this review. Research has shown controversial results in some papers, but the degree of inflammation and the inflammatory mediators present seem to play a pivotal role in causation of failure of the local anaesthetics. The need of the hour is to develop pharmacotherapeutic means to manage all cases of hot tooth immaterial of the degree of inflammation present. This will enable painless root canal treatment thereby enhancing patient compliance and dentist's confidence.

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