

Analgesics for the Dental Pain Management: A Comprehensive Review

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Abstract

Analgesics are the drugs which relieve pain as a symptom, without affecting its cause. Analgesics are most commonly prescribed in dentistry for pain relief which include the non-steroidal anti-inflammatory drugs (NSAIDs) and various opioid-containing analgesic combinations. Selection of an analgesic for the management of dental pain should be judiciously planned. The literature was searched using "Pub Med" and electronic databases from 1981 to 2021. A total of 98 articles were retrieved from 1952 to 2021. Among the retrieved articles, most of them were case reports related to medical treatment procedures, seven were original research articles and five articles reviewed the use of NSAIDs in dentistry. Various medical therapies using NSAIDs are often prescribed by dentists. The literature review proves that the use of NSAIDs in the field of dentistry is very broad and is considered as safer drug. However, each drug has side effects and work power, each of which is adjusted to the needs and systemic conditions of patients who require administration of this drug. The present paper reviews the information currently available on NSAIDs, with special emphasis on those aspects related to dental practice. The dental practitioner has a wide range of drugs for analgesic/anti-inflammatory purposes. A rational prescription should be promoted, taking into account different aspects related to the drugs (pharmacodynamics and pharmacokinetics) and patients (medical history, type of procedure, and the like), leading to an individualized prescription for each patient. The accuracy of the use or administration of NSAIDs is supported by the knowledge and expertise of doctors or dentists.

Key words: Analgesics, Dental pain, Non-steroidal anti-inflammatory drugs in dentistry

INTRODUCTION

Most commonly non-steroidal anti-inflammatory drugs (NSAIDs) are the choice of drugs which are prescribed in dental practice to manage pain and swelling. Paracetamol and ibuprofen are the most widely used NSAIDs. Their mechanism of action is based on the inhibition of cyclooxygenase (COX), and therefore of prostaglandin synthesis. Side effects of all of these drugs are similar as they have similar mechanism of action. Symptoms vary from mild (e.g., nausea or vomiting) to serious gastric problems (such as gastric bleeding or perforation). Further side effects comprise of high risk of vascular accidents (specifically acute myocardial infarction), renal toxicity

secondary to a decrease in perfusion, and the antiplatelet effect of these drugs enhances the risk of abnormal bleeding tendency. These drugs induce a premature ductus arteriosus closure, hence, contraindicated during third trimester of pregnancy. Broadly speaking, NSAIDs are classified into aspirin and non-aspirin NSAIDs. The ADA delegation house adopted a statement in 2016, that said, "Dentists should consider NSAIDs as a first-line therapy for the management of acute pain."^[1]

DISCUSSION

Dental Indications for Analgesic Use

Odontogenic pain due to periapical and pulpal disease is considered as the most frequent in dental health settings^[2] and it is a warning sign and subjective perception of altered pulpodentinal tissue and periapical tissue. Differentiation between these two influences the proper selection of analgesic drugs. The dental pain can be classified as mild, moderate, and severe according to the anticipated pain intensity. This classification of dental pain intensity

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www.ijss-sn.com

Month of Submission : 04-2022
Month of Peer Review : 05-2022
Month of Acceptance : 05-2022
Month of Publishing : 06-2022

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influences the appropriate selection procedure of analgesic therapy for adequate pain relief.

NSAIDs are the first choice of drug in patients with mild dental pain. NSAIDs can be prescribed in amalgamation with other analgesics like paracetamol or it can be prescribed in over-the-counter doses.^[3]

Ibuprofen 200 mg or naproxen 200–225 mg individual dose is the options of drugs from NSAIDs group for the management of mild odontogenic pain. The amalgamation of ibuprofen or naproxen with paracetamol (NAPROSYN P) tablet is found to be the most effective than individual NSAID agents in patients suffering from persistent mild dental pain.

Paracetamol 500–1000 mg is the drug of choice in patients where NSAIDs are contraindicated. Acetyl salicylic acid (ASPIRIN) is not the recommended option of drug for the treatment of dental pain because of its intervention with platelet aggregation. Patients suffering from heart disease should be treated with precautions with aspirin.

NSAIDs can be administered solitary or in amalgamation with aniline derivatives, such as mefenamic acid and meclofenamic acid. NSAID in its pharmacological full doses is the appropriate option of analgesic in patients having moderate dental pain. A weak opioid analgesic can be administered in some cases where NSAIDs combined with paracetamol does not provide an adequate relief.

The discrete dose of naproxen is 500–550 mg and the individual dose of ibuprofen is 400 mg. In the addition of full dose of paracetamol is advised in patients where pain is not controlled successfully. If pain is still present, the supplementation of weak opioid agents in full doses is recommended, that is, codeine 30 mg and hydrocodone 5 mg.^[4]

The recommended pharmacological management of patients having severe dental pain is the combinations of strong opioid analgesics with high doses of NSAIDs with or without aniline derivatives. There is a higher probability of adverse drug reactions so these patients should be treated under close supervision of dental doctor.

Hydrocodone 10 mg, oxycodone 5 mg, codeine 60 mg, or tramadol 50–75 mg are the foremost options. Tramadol is not the drug of choice for the management of severe odontogenic pain because of the possibility of its misuse. The amalgamation of full dose opioid agents and NSAIDs is advised in patients having unsatisfactory level of pain control.

Utilization Pattern of Analgesic Use

The studies on consumption of drugs are empirical tools for the evaluation of analgesic usages and for recognizing the considerations of quality refinement of dental pain therapy. NSAIDs are the most desired analgesic drug group followed by acetaminophen. Opioid analgesics are earmarked for higher intensity dental pain. There is an increase in the prescribing of opioid analgesics or their combination with non-opioid analgesics in non-traumatic dental condition-related visits with more severe pain in the emergency departments.^[5,6]

Opioids such as hydrocodone (78%), followed by oxycodone (15.4%), propoxyphene (3.5%), and codeine (1.6%) were delineated as the most commonly recommended analgesics after surgical extraction of teeth entailing dental care as per the new published study with enormous cohort of patients. Although, latterly disparate studies outlined a decline by 5.6% in the prescribing of opioids.^[7,8] In this context, enormous studies should be done to stave off the opioid abuse and dentists perform a crucial role in this aspect, helping to slash the opioid abuse by vigilant patient education and significant prescribing practice.^[9]

Paracetamol and NSAIDs are the best choices in cases of mild-to-moderate acute dental pain. Patients having gastrointestinal diseases or taking blood thinners such as warfarin may be considered at risk for prescribing COX-2 inhibitors. Doctor should prescribe shorter duration of treatment and he/she must be aware to limit the use of maximum recommended doses.^[10]

Ibuprofen was found to dominate over other analgesics.^[11-14] This also applies to pediatric dentistry, whereby ibuprofen and paracetamol predominate in prescription rates.^[15]

Although there are tendentious studies which show that diclofenac or paracetamol may offer improved benefits. Nimesulide followed by diclofenac, ketoprofen, and ibuprofen was the most recommended NSAIDs in patients undergoing thirs molar surgery.

NSAIDs, Opioids, and their Mechanism of Action

Opioids show its effect in the central nervous system (CNS) through its depression while NSAIDs demonstrate its analgesic effects through inhibition of prostaglandin synthesis at the peripheral nerve endings.^[16] NSAIDs mechanism of action is through the suppression of prostaglandin and thromboxane (eicosanoids) biosynthesis by impediment of activity of COX-1 discovered by John Vane or COX-2 from Daniel Simmons in reversible or irreversible pattern and dose-dependent manner competition of arachidonic acid.

Newer drugs such as piroxicam, flurbiprofen, diclofenac, naproxen, ibuprofen, etoricoxib, and celecoxib were started based on their COX activity in the past four decades. Their mechanism of action determines on whether they impede COX-1, COX-2, or both. COX-1 and COX-2 are in charge of synthesis of distinct prostaglandins found in pathological situations (COX-2 is more expressed in inflammatory conditions).

Although, this suppression results in the loss of few protective effects of prostaglandins with respect to the gastrointestinal (COX-1), cardiovascular, platelet, and renal function.^[17] Taking this into contemplation, COX-1 inhibitors are more vulnerable to cause gastrointestinal bleeding. This can be intercepted by a switch to COX-2 inhibitors. Although, momentary use of the COX-2 inhibitors is advised based on their cardiovascular side effects which occurs due to disparity of PGI₂ as antithrombotic mediator and as one of the most crucial prostanoid in regulating homeostasis of the cardiovascular system and also TXA₂ as prothrombotic mediator.^[18-20]

Opioid activity is arbitrated through its affinity for μ , κ , δ , and opioid receptor like-1 which are G-protein-coupled opioid receptors acting on GABAergic neurotransmission as agonists, weak agonists, and partial agonists in CNS and throughout the body. The mediated consequence is the dwindling of intracellular cAMP, which helps in modulating the release of substance P, a nociceptive neurotransmitter.^[21]

Principles of Dental Pain Management

In adult patients

Dental doctors should give consideration to disease, patient, and to the available pharmacologically and non-pharmacologically effectual treatment modalities for effectual management of dental pain.

There are few researches that describe that premedication with NSAIDs such as ibuprofen and indomethacin remarkably rises the level of alveolar nerve block anesthesia in dental procedures (78 and 62%) compared to placebo (32%).^[22]

It is recommended that analgesic drugs should be administered preoperatively to dwindle the post-operative pain and to decrease the need for post-operative analgesic while performing dental operative procedure.

Moreover, there is an obtainable fallacious information that naproxen sodium has a higher analgesic efficacy in contrast with ibuprofen at post-dose interval from 1 to 12 h.^[23,24] Para-aminophenol derivative such as paracetamol (acetaminophen) is the most crucial analgesic agent for use

in dentistry. Paracetamol can be prescribed individually for the treatment of mild form of dental pain when NSAIDs are contraindicated.

Ibuprofen in doses 200–512 mg versus paracetamol 600–1000 mg provides higher relief in post-operative pain as per the clinical corroboration. The amalgamation of ibuprofen and paracetamol is the most appropriate approach for the treatment of pain. This amalgamation is more effectual than the outcome of individual analgesic when taken at 6 h after dental procedure.

The most common amalgamation of doses of respective analgesics advised in clinical practice are 400 mg for ibuprofen and 1000 mg for paracetamol as per the studies.^[25] Opioid and NSAIDs administration is advised for intense pain and when individual NSAID or combination of NSAID and paracetamol is not effective. The effect of this drug amalgamation is superior than doubling the dose of with analgesic prescribed individually.^[26]

There are various prospects of amalgamation of non-narcotic and narcotic analgesics, which might be very effectual in dental pain.

Acetaminophen-codeine (300 mg + 30 mg), oxycodone-ibuprofen (5 mg + 400 mg), or hydrocodone-acetaminophen (5 mg + 325 mg or 7.5 mg + 500 mg) are the most widely used combinations for effectual dental pain management.^[27]

The main prototype for the management of dental pain is the proper choice of effectual analgesic, at truncated doses with the lowest possibility for side effects.

ELDERLY PATIENTS

Paracetamol is the drug of choice for effectual pain relief in elderly patients. Paracetamol is contraindicated in patients with terminal hepatic insufficiency. Dosage modification is advised in patients with hepatic or renal functional disorders. These patients need close monitoring and NSAIDs are the preferred choice of drugs in these cases.

To decrease the chances of possible side effects of these analgesic drugs, NSAIDs should be administered in its lowest possible doses in short periods of time to elderly patients.

The use of opioid analgesic is advised in patients suffering from severe dental pain. Tramadol in its lowest possible dosage is recommended in these cases. The amalgamation of paracetamol and tramadol or codeine is prescribed to use the opioid analgesic drugs in the lowest doses.

The strongest opioid of choice in elderly cases with intense pain is MORPHINE.

CHILDREN

The progressive pain management approach depends on two main directions, comprehending the interventional pharmacological (incorporating the use of NSAIDs and other analgesics) and non-pharmacological strategy. Non-pharmacological strategy comprises of creating health awareness among children by educating them. Psychological approaches include emancipation of the perception of fear and other behavioral problems in children patients, breathing techniques, hypnosis, transcutaneous electrical nerve stimulation, guided imagery, acupuncture, relaxation, and other procedures for pain reduction.

There are various principles which are followed for the pain management in children patients, contemplating the difference between children and adult pain management. Prevention of pain should be focused which authenticates greater treatment outcomes before painful procedures. This is initiated by concocting the family and the child patient in advance, intending to ease fear and anxiety before procedure and enacting patient-controlled analgesia (PCA). Oral analgesics can be prescribed in cases of major surgical procedures according to the need of the patient.

Multimodal and multiapproach therapy is the cornerstone of pain management in children. These approaches utilize disparate analgesia and non-pharmacological supportive approaches intending to diminish the pain and drug-induced adverse effects. Coalescing non-opioid (NSAIDs, other analgesic agents, local anesthetics, alpha2-adrenergic agonists, and voltage-gated calcium channel alpha-2 delta-proteins) and opioid analgesics and other agents in lowest possible doses intending to halt the clinical manifestations of drugs side effects.^[28]

Analgesic dosages in children patients are formulated on the basis of mg/kg body weight. Intramuscular injections should be avoided in children patients. Pain management in severe cases by infusions, PCA, and other course of constant analgesic disburse is recommended.

The utilization of opioid analgesics is dodged in neonates and premature infants for the management of pain. Whenever there is no other choice left, in that case, opioid analgesics should be administered and monitored closely in intensive care units. Opioids are very vulnerable to cause dependency and depression of cardiorespiratory functions in this group of infants.

Prescribing the NSAIDs, paracetamol is the popular pharmacological pain management. In general, it is suggested to use paracetamol (infant dose is 10–15 mg/kg/dose every 6–8 h and pediatric oral dose 10–15 mg/kg/dose every 4 h), ibuprofen (10 mg/kg/dose every 6 h), and diclofenac (1 mg/kg/tds or 1.5 mg/kg/bd, maximum daily dose is 3 mg/kg). The utilization of naproxen (2 years or older: 5 mg/kg orally twice a day; 12 years or older: 220 mg orally every 8–12 h) is recommended more in inflammatory diseases. The dosages of individual analgesics are abated when it is amalgamated with other analgesics in treatment modalities. Opioids are advised for intense pain management. To enhance the effect of codeine (0.5–1 mg/kg every 4–6 h) (which is a weak opioid analgesic), it is amalgamated with paracetamol more often. The utilization of codeine in children should be closely monitored and should be used only in those cases where benefits exceed the risks as per the alert by FDA.^[29]

Tramadol (1–1.5 mg/kg) is the other opioid analgesic for the management of mild-to-severe dental pain in children. The use of morphine (0.2–0.5 mg/kg q4–6 h) is advised for intense pain. Fentanyl, hydromorphone, methadone, and other opioid agents are considered as other substitutes to morphine. The use of regional analgesia such as local anesthetic administration, wound anesthetic infiltration, topical regional analgesia (lignocaine gel), and peripheral nerve block is the other choices to manage dental pain in children patients. Treatment of dental pain in children is intricate and supplemental data are required to revamp the success and safety of pain management.

Oral Analgesics Dosage for Healthy Adults and Children^[30]

Drug Recommended Dose (Adult).

Mild-to-moderate Pain

- Acetamenophen 325 mg 2 tab.* q. 4 h #
- Aspirin 325 mg 2 tab.* q. 4 h #
- Ibuprofen 200 mg 1 tab. * q. 4 h#
- Naproxen Sodium 220 mg 1 tab. * q. 6-8 h”.

Moderate-to-severe Pain

- Diclofenac potassium 50 mg 1 tab. * t.i.d†
- Ibuprofen 200 mg 2 tab. * q. 4 h# or 3 tab. q. 6 h”
- Ibuprofen 400 mg 1 tab. * q. 4 h#
- Ibuprofen 600 mg 1 tab. * q. 6 h”
- Ketorolac 20 mg 1 tab. * q. 6 h”, not to exceed 5 days
- Rofecoxib 50 mg 1 tab. * q.d.¶

In Moderate-to-severe Pain, when NSAIDs are Contraindicated, Opioids are Prescribed

- Acetamenophen 325 mg + Codeine 30 mg 2 cap.^ q. 4 h#
- Acetamenophen 650 mg + Hydrocodone 10 mg 1 tab. * q. 4–6 h #

- Acetamenophen 650 mg + Oxycodone 10 mg 1 tab. * q. 4–6 h #
- Acetamenophen 325 mg + Tramadol 37.5 mg 2 tab. * q. 4–6 h #, maximum 8 tab/24 h.

Drug Recommended Dose (Children)

- Acetaminophen 10–15 mg/kg body weight 1 tab. * q. 4–6 h # (Also available in an elixir form)
- Ibuprofen Age 2 - 12–10 mg/kg body weight 1 tab. * q. 6–8 h” (Obtainable in an elixir form also)
- Over age of 12 - 200–400 mg 1 tab. * q. 4 h# (Also available in an elixir form)
 - * - Tablet
 - # - quaque quarta hora (every 4 h)
 - “- quaque sex- octa hora (every 6–8 h)
 - † - ter in die (a thrice-daily dosage)
 - ¶ - quaque die (every day)
 - ^ - Capsule.

CONCLUSION

Numerous studies have been done to determine the safest analgesic but every medication comes with its benefits and risks. The accuracy of the utilization or administration of NSAIDs is supported by the knowledge and expertise of the dentists.

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How to cite this article: Tekam D, Vaz V, Sahithi M, Ruchitha TG, Sruthi MK, Gahana GC. Analgesics for the Dental Pain Management: A Comprehensive Review. *Int J Sci Stud* 2022;10(3):18-22.

Source of Support: Nil, **Conflicts of Interest:** None declared.