J Periodontal Implant Sci. 2020 Apr;50(2):68-73
https://doi.org/10.5051/jpis.2020.50.2.68
pISSN 2093-2278·eISSN 2093-2286

JPIS
Journal of Periodontal & Implant Science

Review
Periodontal Science

Check for updates

Selection of analgesics for the management of acute and postoperative dental pain: a mini-review

Sung-Jin Kim [1,2], **Jeong Taeg Seo** [1,*]

[1]Department of Oral Biology, Yonsei University College of Dentistry, Seoul, Korea
[2]Department of Oral Biology, BK21 PLUS Project, Yonsei University College of Dentistry, Seoul, Korea

OPEN ACCESS

Received: Oct 14, 2019
Revised: Jan 5, 2020
Accepted: Feb 12, 2020

***Correspondence:**
Jeong Taeg Seo
Department of Oral Biology, Yonsei University College of Dentistry, Yonsei-ro 50-1, Seodaemun-gu, Seoul 03722, Korea.
E-mail: jeong@yuhs.ac
Tel: +82-2-2228-3054

ORCID iDs
Sung-Jin Kim
https://orcid.org/0000-0003-4115-0403
Jeong Taeg Seo
https://orcid.org/0000-0003-2697-0251

Author Contributions
Conceptualization: Jeong Taeg Seo; Formal analysis: Sung-Jin Kim, Jeong Taeg Seo; Investigation: Sung-Jin Kim, Jeong Taeg Seo; Methodology: Sung-Jin Kim, Jeong Taeg Seo; Project administration: Jeong Taeg Seo; Writing - original draft: Jeong Taeg Seo; Writing - review & editing: Sung-Jin Kim.

Conflict of Interest
No potential conflict of interest relevant to this article was reported.

ABSTRACT

Pain management is an important part of dental practice, and dentists frequently prescribe analgesics to improve clinical outcomes. Dentists should be aware of the pharmacological characteristics of the analgesics commonly used in dentistry and should choose appropriate analgesics to treat and prevent pain associated with inflammation or surgery. In this article, we review the potential benefits and risks of the analgesics frequently used in dental practice and provide a stepwise approach for pain management.

Keywords: Acetaminophen; Analgesics; Ibuprofen; Naproxen; Non-steroidal anti-inflammatory drugs

INTRODUCTION

Effective and safe pain management is a primary goal in dental practice. Control of pain associated with dental or periodontal disease is a main reason that patients seek care from dentists. In addition, many dental procedures are painful, and postoperative pain may persist for days. Therefore, dentists should use appropriate analgesics to treat and prevent pain associated with inflammation or surgery.

A variety of analgesics are currently available. Analgesics can be classified into opioid and non-opioid analgesics. Non-opioid analgesics include non-steroidal anti-inflammatory drugs (NSAIDs) and acetaminophen; NSAIDs are further divided into nonselective traditional non-steroidal anti-inflammatory drugs (tNSAIDs) and selective cyclooxygenase (COX)-2 inhibitors (Table 1). The aim of this review was to describe considerations for selecting among those analgesics for the management of acute and postoperative dental pain. Drugs such as antidepressants and antiepileptics can also be used to manage the symptoms of some chronic pain conditions, but these medications will not be discussed in this article (for details, see Colloca et al. [1]).

JPIS Journal of Periodontal & Implant Science

Table 1. Classification of analgesics used in dental practice

Classification of analgesics
Opioid analgesics
Hydrocodone, oxycodone, codeine, tramadol[a]
Non-opioid analgesics
NSAIDs
tNSAIDs
Diflunisal, ibuprofen, naproxen, ketoprofen, loxoprofen, flurbiprofen, indomethacin, sulindac, etodolac, diclofenac, ketorolac, piroxicam, meloxicam, mefenamic acid, nabumetone
COX-2 inhibitors (COX-2-selective NSAIDs)
Celecoxib, etoricoxib, polmacoxib
Acetaminophen
Drugs used for neuropathic pain
Pregabalin, gabapentin, duloxetine

NSAIDs: non-steroidal anti-inflammatory drugs, tNSAIDs: traditional non-steroidal anti-inflammatory drugs, COX-2: cyclooxygenase-2.
[a]In Korea, tramadol is approved as a non-narcotic analgesic.

OPIOID ANALGESICS

Dentists often prescribe opioid analgesics, such as hydrocodone, codeine, oxycodone, and tramadol, for the management of dental pain. However, opioids may cause various adverse effects, such as nausea and vomiting, constipation, urinary retention, respiratory depression, sedation, sleep disturbance, dependence, and addiction. In contrast, non-opioid analgesics generally have less serious adverse effects than opioid analgesics at therapeutic doses. Although historically, the potency and efficacy of non-opioid analgesics have been thought to be lower than those of opioids, clinical studies have repeatedly shown that non-opioid analgesics, such as ibuprofen, are more effective than opioids in suppressing postoperative dental pain [2]. However, if non-opioid analgesics fail to relieve pain, an opioid may be administered in conjunction with non-opioid analgesics to provide synergistic analgesia. Therefore, in dental practice, rather than being prescribed alone, opioid analgesics are often prescribed in combination with acetaminophen or NSAIDs to increase the analgesic effect [3].

NSAIDS

NSAIDs decrease the production of prostaglandins, an effect that is attributed to the inhibition of COX. tNSAIDs inhibit both COX-1 and COX-2 to different degrees. These drugs have common therapeutic actions, including anti-inflammatory, analgesic, and antipyretic actions that are mainly due to the inhibition of COX-2, the expression of which is induced by inflammation. In contrast, the inhibition of COX-1 is generally responsible for NSAID-induced gastropathy, nephropathy, and prolonged bleeding time. Acetaminophen similarly has analgesic and antipyretic activities via the inhibition of COX enzymes, but it is technically not classified as an NSAID because it has only minimal anti-inflammatory activity, although its exact mechanism of action is still unclear [4].

Acetaminophen and tNSAIDs

The tNSAIDs currently available on the market include aspirin, diflunisal, ibuprofen, naproxen, ketoprofen, flurbiprofen, indomethacin, sulindac, etodolac, diclofenac, ketorolac, piroxicam, mefenamic acid, and nabumetone. To choose the most appropriate analgesics for pain relief, dentists should consider both the potential benefits and the risks. From the

https://doi.org/10.5051/jpis.2020.50.2.68

JPIS Journal of Periodontal & Implant Science

perspective of benefit-risk analysis, the primary drugs of choice for the relief of dental pain are acetaminophen and ibuprofen [5].

Acetaminophen (also known as paracetamol) is one of the most widely used analgesic antipyretic drugs and has minimal anti-inflammatory activity. Despite its long history as a painkiller, the mechanism of action of acetaminophen is still not completely understood. The current understanding is that while tNSAIDs inhibit the COX activity of the COX enzyme, acetaminophen inhibits the peroxidase activity of COX at low peroxide levels; this peroxide-dependent inhibition of COX allows acetaminophen to act preferentially within the central nervous system without peripheral anti-inflammatory activity, as the peroxide level is much higher at peripheral inflammatory sites than in the brain [4]. Due to its lack of inhibitory effect on the peripheral COX activity, acetaminophen is less likely than tNSAIDs to induce gastrointestinal and cardiovascular adverse effects and does not prolong bleeding time. Unlike aspirin, acetaminophen does not increase the risk of Reye syndrome, which causes brain and liver damage in children recovering from viral infection. Acetaminophen has no noteworthy limitations for use in pregnant women. Acetaminophen is therefore especially suitable for patients who do not tolerate tNSAIDs due to their adverse effects, such as the increased risk of gastrointestinal ulcer disease. However, acetaminophen may cause serious liver damage if excessive quantities of its toxic metabolite are generated through the phase I biotransformation induced by the hepatic cytochrome P450 system. Therefore, this drug should not be taken in excess of 4 g per day (the United States Food and Drug Administration recently suggested a maximum daily dose of 3 g), and those with serious liver disease or who regularly and continuously consume large volumes of alcohol should exercise extra caution. Since patients may unknowingly take acetaminophen combination products, dentists should ensure that the patient will not consume too much acetaminophen when prescribing the drug. Acetaminophen is used for mild pain and can be combined with tNSAIDs and/or opioid analgesics to increase effectiveness.

Ibuprofen is very effective for relieving mild or moderate pain and is one of the most frequently prescribed analgesics by dentists. Generally, the analgesic effect of 200 mg of ibuprofen is similar to or stronger than that of 500–1,000 mg of acetaminophen. For mild dental pain, 200 mg to 400 mg of ibuprofen every 4 to 6 hours is recommended [3,5]. Within this dose range, the potential of ibuprofen to cause adverse gastrointestinal, liver, or cardiovascular effects is relatively low compared with other tNSAIDs [6]. However, if this regimen does not provide sufficient analgesia, the dose may be increased to 400 mg to 600 mg to provide greater pain relief, and such a dosage increase is accompanied by increased gastrointestinal and cardiovascular risks.

Naproxen has a longer duration and a stronger anti-inflammatory effect than ibuprofen. However, despite its advantages over ibuprofen, naproxen has a higher risk of adverse effects such as gastrointestinal toxicity [7]. Thus, naproxen should be reserved for pain that is not relieved by ibuprofen. The gastrointestinal and cardiovascular risks associated with acetaminophen, ibuprofen, and naproxen are compared in Table 2.

Table 2. Gastrointestinal and cardiovascular risks of acetaminophen, ibuprofen, naproxen, and COX-2 inhibitors

Drugs	Gastrointestinal risk	Cardiovascular risk
Acetaminophen	Low	Low
Ibuprofen	Low to moderate	Moderate to high
Naproxen	Moderate to high	Low to moderate
COX-2 inhibitors	Low	High

COX-2: cyclooxygenase-2.

https://doi.org/10.5051/jpis.2020.50.2.68

JPIS Journal of Periodontal & Implant Science

Table 3. Drug interactions associated with NSAIDs

Drugs interacting with NSAIDs	Effects
Oral antidiabetic drugs	Hypoglycemia may occur.
Low-dose aspirin	The cardiovascular protective effects of aspirin may be compromised.
ACE inhibitors, β-blockers, and diuretics	Blood pressure may increase.
Antiplatelets or anticoagulants	Bleeding tendency may increase.
Other NSAIDs	NSAID-related adverse effects may increase.
Corticosteroids	Adverse gastrointestinal effects may increase.
Methotrexate, lithium, phenytoin, and calcium channel blockers	Toxicity may increase due to elevated blood level of these drugs.
Nephrotoxic agents, such as adefovir, aminoglycosides, cisplatin, and foscarnet	Risk of renal damage may increase.

NSAIDs: non-steroidal anti-inflammatory drugs, ACE: angiotensin-converting enzyme.

Other tNSAIDs, such as diclofenac, ketoprofen, and etodolac, may have analgesic effects similar to or stronger than those of ibuprofen or naproxen, but dentists should bear in mind that these drugs may also have more adverse gastrointestinal or cardiovascular effects, especially when used at high dosages.

Although tNSAIDs are safe if used for a short period of time, they may cause heartburn, nausea, vomiting, diarrhea, and in some cases potentially serious adverse effects such as gastric ulcer and gastric perforation. This is primarily due to their inhibition of prostaglandin production in the gastric mucosa, leading to decreased mucus and bicarbonate generation and increased gastric acid secretion. In patients at high risk of gastrointestinal disease, therefore, tNSAIDs may be prescribed in combination with mucosal protective agents or gastric acid secretion inhibitors, such as proton pump inhibitors. Alternatively, acetaminophen or COX-2 inhibitors can be prescribed.

Aspirin irreversibly inhibits COX and thus is distinguished from non-aspirin tNSAIDs, which are competitive reversible inhibitors. The irreversible mode of action of aspirin prevents thromboxane A2 synthesis by platelets for their circulating lifetime; thus, the antithrombotic effect of aspirin may last for 5 to 7 days [8]. Other tNSAIDs reversibly inhibit COX, such that the antiplatelet effect of these drugs declines as their plasma concentrations decrease via metabolism and excretion. Apart from their antithrombotic effect, tNSAIDs may cause renal toxicity because prostaglandins also play a role in the maintenance of renal function; thus, dentists should take care when prescribing tNSAIDs to patients with compromised renal function [9].

NSAIDs are associated with various drug interactions. For example, tNSAIDs such as ibuprofen and naproxen have been reported to interact with aspirin [10]. Many patients with cardiovascular diseases take low dose of aspirin regularly (often 81 mg daily) to decrease the risk of ischemic heart disease and stroke. If ibuprofen or naproxen is prescribed to patients taking aspirin, it will interfere with the antiplatelet effect of aspirin by antagonizing the acetylation of COX-1 and will thus reduce aspirin's cardioprotective effects [11,12]. If these tNSAIDs are deemed necessary, patients should be informed about this drug interaction and should be advised to take aspirin at least 30 minutes prior to taking such tNSAIDs. Drug interactions associated with NSAIDs are summarized in Table 3.

Selective COX-2 inhibitors

Inhibition of COX-1 by tNSAIDs is responsible for NSAID-induced gastropathy, nephropathy, and prolonged bleeding time. Selective COX-2 inhibitors were developed to avoid the

https://doi.org/10.5051/jpis.2020.50.2.68

Table 4. A stepwise approach for pain management in dental practice

Severity of pain	Recommended drugs
Mild	Acetaminophen 325–650 mg every 6 hours or ibuprofen 200–400 mg every 4 to 6 hours
Moderate	Ibuprofen 400–600 mg every 4 to 6 hours or naproxen 500 mg (or naproxen sodium 550 mg) every 12 hours
Severe	Ibuprofen 400–600 mg + acetaminophen 500 mg every 6 hours or ibuprofen 400–600 mg + acetaminophen 500 mg + opioids, such as hydrocodone 10 mg, every 6 hours

Specific considerations: 1) Maximum daily dose of acetaminophen: 3–4 g for healthy adults. The daily limit should be lower for those who regularly drink alcohol. 2) Patients should be warned to avoid the concomitant use of other acetaminophen-containing medicines. 3) Maximum daily dose of ibuprofen: 3.2 g. 4) Maximum daily dose of naproxen: 1.0 g. 5) Ibuprofen and naproxen may suppress the antiplatelet effect of aspirin. 6) For patients at high risk of gastrointestinal disease, gastric mucosa-protective agents may be administered in conjunction with ibuprofen or naproxen. Alternatively, acetaminophen or COX-2 inhibitors can be prescribed to these patients. 7) Use of analgesics before surgery is more effective than use after surgery in producing analgesia when postoperative pain is anticipated [14].

adverse gastrointestinal and bleeding-associated effects caused by COX-1 inhibition [13]. However, these drugs increase the risk of thrombosis and have been reported to have serious cardiovascular adverse effects, such as ischemic heart disease, heart failure, hypertension, and stroke. Therefore, COX-2 inhibitors should be used carefully, and dentists are advised to avoid these drugs in patients at high risk of cardiovascular disease [9]. Various COX-2 inhibitors (known as coxibs) have been developed; however, due to such cardiovascular side effects, some drugs, such as rofecoxib, have been withdrawn from the market. In Korea, celecoxib, etoricoxib, and polmacoxib are currently available. The anti-inflammatory, analgesic, and antipyretic effects of COX-2 inhibitors are reported to be similar to those of tNSAIDs.

CONCLUSION

When dentists prescribe analgesics in dental clinics, they should consider the severity of the patient's pain, the pharmacological properties of the drug, the patient's history of systemic disease, and potential interactions with drugs the patient is taking. Non-opioid analgesics have been shown to exhibit a safe profile when used for acute dental pain, and the overall risk of these drugs as they are used in dentistry is low. Considering the evidence regarding gastrointestinal and cardiovascular safety, acetaminophen, ibuprofen and naproxen appear to be the safest non-opioid drugs. A stepwise approach for the management of pain in dental practice is summarized in Table 4.

REFERENCES

1. Colloca L, Ludman T, Bouhassira D, Baron R, Dickenson AH, Yarnitsky D, et al. Neuropathic pain. Nat Rev Dis Primers 2017;3:17002.
PUBMED | CROSSREF
2. Moore PA, Hersh EV. Analgesic therapy in dentistry: from a letter to the editor to an evidence-base review. Dent Clin North Am 2019;63:35-44.
PUBMED | CROSSREF
3. Ong CK, Seymour RA. An evidence-based update of the use of analgesics in dentistry. Periodontol 2000 2008;46:143-64.
PUBMED | CROSSREF
4. Ghanem CI, Pérez MJ, Manautou JE, Mottino AD. Acetaminophen from liver to brain: new insights into drug pharmacological action and toxicity. Pharmacol Res 2016;109:119-31.
PUBMED | CROSSREF
5. Moore PA, Hersh EV. Combining ibuprofen and acetaminophen for acute pain management after third-molar extractions: translating clinical research to dental practice. J Am Dent Assoc 2013;144:898-908.
PUBMED | CROSSREF
6. Pozzi A, Gallelli L. Pain management for dentists: the role of ibuprofen. Ann Stomatol (Roma) 2011;2:3-24.
PUBMED

https://doi.org/10.5051/jpis.2020.50.2.68

7. Coxib and traditional NSAID Trialists' (CNT) Collaboration, Bhala N, Emberson J, Merhi A, Abramson S, Arber N, et al. Vascular and upper gastrointestinal effects of non-steroidal anti-inflammatory drugs: meta-analyses of individual participant data from randomised trials. Lancet 2013;382:769-79.
PUBMED | CROSSREF
8. Brennan MT, Wynn RL, Miller CS. Aspirin and bleeding in dentistry: an update and recommendations. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007;104:316-23.
PUBMED | CROSSREF
9. Becker DE. Pain management: part 1: managing acute and postoperative dental pain. Anesth Prog 2010;57:67-79.
PUBMED | CROSSREF
10. Tacconelli S, Bruno A, Grande R, Ballerini P, Patrignani P. Nonsteroidal anti-inflammatory drugs and cardiovascular safety - translating pharmacological data into clinical readouts. Expert Opin Drug Saf 2017;16:791-807.
PUBMED | CROSSREF
11. Catella-Lawson F, Reilly MP, Kapoor SC, Cucchiara AJ, DeMarco S, Tournier B, et al. Cyclooxygenase inhibitors and the antiplatelet effects of aspirin. N Engl J Med 2001;345:1809-17.
PUBMED | CROSSREF
12. MacDonald TM, Wei L. Effect of ibuprofen on cardioprotective effect of aspirin. Lancet 2003;361:573-4.
PUBMED | CROSSREF
13. Marnett LJ. The COXIB experience: a look in the rearview mirror. Annu Rev Pharmacol Toxicol 2009;49:265-90.
PUBMED | CROSSREF
14. Fletcher MC, Spera JF. Management of acute postoperative pain after oral surgery. Dent Clin North Am 2012;56:95-111.
PUBMED | CROSSREF

https://doi.org/10.5051/jpis.2020.50.2.68