



# Clinical implications of prescribing nonsteroidal anti-inflammatory drugs in oral health care—a review

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Nonsteroidal anti-inflammatory drugs (NSAIDs), including both the traditional nonselective NSAIDs and the selective cyclooxygenase (COX)-2 inhibitors, are widely used for their anti-inflammatory and analgesic effects. They are routinely prescribed in dental practice for the management of pain and swelling. Their use in treating acute dental pain and chronic orofacial pain, as adjuncts to the treatment of periodontal disease, and to minimize edema following surgical procedures is well documented. However, long-term utilization of nonselective NSAIDs could increase the risk of gastrointestinal symptoms, ranging from mild (e.g., dyspepsia, nausea, or vomiting) to serious gastric problems (e.g., gastric bleeding or perforation). Therefore, selective COX-2 inhibitors have been developed with fewer GI side effects but the recently identified cardiovascular adverse reactions limit their routine use in dental practice. Another major concern for oral physicians is NSAID-induced mucosal lesions and prolongation of bleeding time during invasive dental procedures. This article reviews therapeutic and analgesic uses of NSAIDs in dentistry. The various issues surrounding NSAID-induced adverse reactions and their implications in dentistry are also discussed. (*Oral Surg Oral Med Oral Pathol Oral Radiol* 2015;119:264-271)

The primary goal of oral health care providers is to relieve dental pain for the optimal well-being of patients. Nonsteroidal anti-inflammatory drugs (NSAIDs) provide important analgesic and anti-inflammatory benefits to millions of patients. They are widely used therapeutic agents for the treatment of a wide spectrum of pathophysiologic conditions. Due to their effectiveness in reducing mild to moderate pain, they are commonly prescribed in dental practice.<sup>1</sup>

Vane discovered that aspirin and related drugs act by inhibiting prostaglandin (PG) biosynthesis.<sup>2</sup> The principal pharmacologic effects of NSAIDs are attributed to their ability to inhibit PG activity by blocking the activity of both cyclooxygenase 1 (COX-1) and COX-2.<sup>2,3</sup> Although NSAIDs relieve symptoms, they are not without potentially significant adverse effects. The most noteworthy adverse effect is upper gastrointestinal (GI) toxicity. Cardiovascular

(CV) safety is a major concern and has resulted in NSAID withdrawal in many patients. Therefore, dentists should assess the risk and benefits of each medication, taking into account the medical history and analgesic requirement of each individual. These drugs should be prescribed in appropriate doses and durations to reduce or avoid NSAID-associated complications.<sup>4</sup> This review discusses the mechanisms of action, therapeutic uses, and potential side effects associated with the use of NSAIDs in dental practice.

## MECHANISM OF ACTION

NSAIDs act as nonselective inhibitors of the tissue COX, which exists in two well-known subtypes: COX-1 and COX-2. COX catalyzes the formation of PGs and thromboxanes (TXA<sub>2</sub>) from arachidonic acid. COX-1 is constitutively expressed in various tissues, whereas COX-2 is a largely inducible form found predominantly in the kidneys and the central nervous system. COX-1 generates PGs for the body's housekeeping functions, such as gastric mucosal integrity, platelet homeostasis, and regulation of renal blood flow. TXA<sub>2</sub> generated initiates platelet aggregation. COX-2 synthesizes "proinflammatory PGs" that mediate pain and inflammation at the site of tissue damage, such as in pulpitis,

## Statement of Clinical Relevance

Acute pain is the most common complaint that causes patients to seek help from oral health care professionals. Nonsteroidal anti-inflammatory drugs are routinely prescribed but have been associated with adverse reactions. Therefore, consideration of the medical history and the analgesic requirement of patients are essential.

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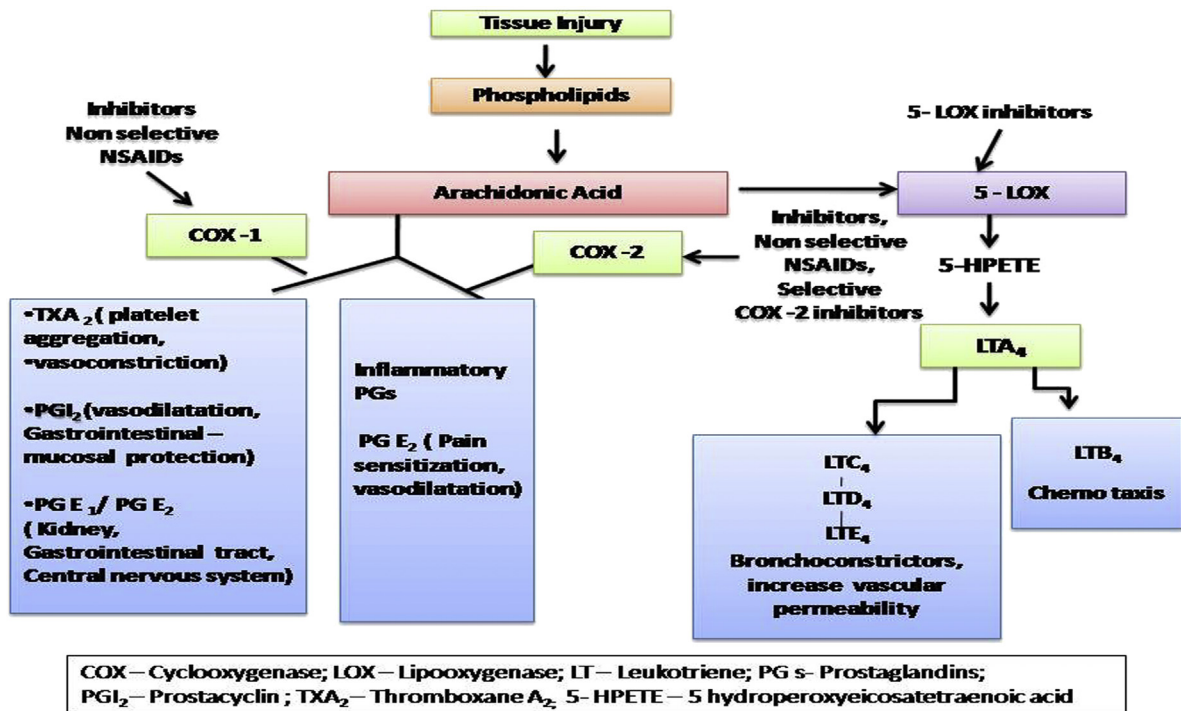


Fig. 1. Mechanism of action of nonsteroidal anti-inflammatory drugs (NSAIDs).

periodontitis, or pain from surgery. Thus, the therapeutic anti-inflammatory effects of NSAIDs are primarily due to COX-2 inhibition, whereas undesirable side effects are due to COX-1 inhibition.<sup>5</sup>

Commonly used nonselective or traditional NSAIDs block both COX-1 and COX-2, but serious GI effects have been reported with their long-term use. This has led to the development of selective COX-2 inhibitors (rofecoxib, celecoxib, valdecoxib), also known as the “coxibs,” which have an improved gastric safety profile. In addition, selective inhibitors of COX-2 depress prostacyclin (PGI<sub>2</sub>), an atheroprotective agent, but not COX-1–derived TXA<sub>2</sub>, a proaggregatory and vasoconstrictor mediator, which might predispose patients to heart attack and stroke<sup>6</sup> (Figure 1).

### ANALGESIC AND THERAPEUTIC USES OF NSAIDS IN DENTISTRY

The introduction of NSAIDs into clinical practice has dramatically improved pain management in dentistry.<sup>7</sup> Drugs available for pain management belong to two major groups: the non-narcotic analgesics (NSAIDs and acetaminophen) and the opioids (or narcotics). The most commonly used non-narcotic analgesics in dentistry are available as over-the-counter medications. Unlike opioid analgesics, NSAIDs exhibit the ceiling effect to analgesia, with no tolerance or physical dependence and possess both anti-inflammatory and analgesic actions.<sup>8</sup>

NSAIDs are the mainstay therapy for acute dental pain. They have also been evaluated for treatment of

chronic orofacial pain; as an adjunct in the treatment of periodontal disease; and to minimize postoperative edema, endodontic pain, and bone pain from oral cancer.<sup>9</sup> Ibuprofen is the prototypical nonselective NSAID and represents the gold standard against which new analgesic agents are evaluated. Shorter-acting (4-6 hours and 6-8 hours) nonselective NSAIDs are more appropriate for treating acute dental pain with fewer GI side effects when used on a short-term basis. Recently introduced selective COX-2 inhibitors are being widely prescribed by health care professionals to manage chronic pain in certain conditions, such as temporomandibular disorders (TMDs), due to their improved gastric tolerability in conjunction with the comparable efficacy of nonselective NSAIDs.<sup>10,11</sup> Table I lists the NSAIDs commonly used in dental practice.

### Prescribing considerations

NSAIDs have been established as the drugs of first choice for the management of mild-to-moderate dental and postoperative pain. They are usually more effective when prescribed in adequate doses before the synthesis of PGs at the site of inflammation (within 2 hours of tissue injury). Therefore, clinicians should consider an initial loading dose, such as double the maintenance dose, which will allow therapeutic levels to be reached more rapidly.<sup>12,13</sup>

Another consideration for the use of NSAIDs is reduction of pain after surgery; therefore, NSAIDs are prescribed on a regular basis for the first 1 to 2 days following a surgical procedure, such as every 4 hours,

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