...1 2000; 7 (Edisi Khusus): 83-86
...erbitkan di Jakarta

Jurnal Kedokteran Gigi
Universitas Indonesia

ISSN 0854-364X

THE RATIONALE OF USING NON-STEROIDAL ANTI-INFLAMMATORY DRUGS IN DENTISTRY

Angky Soekanto

Department of Oral Biology, Faculty of Dentistry, University of Indonesia

Angky Soekanto: The Rationale of Using Non-Steroidal Anti-Inflammatory Drugs in Dentistry. Jurnal Kedokteran Gigi Universitas Indonesia. 2000; 7 (Edisi Khusus): 83-86

Abstract

Pain control is of great importance in dental practice. It is pain that brings the patient to the dental office. The use of non-steroidal anti-inflammatory drugs is one important component in dentistry. But the adverse reaction of these drugs cause serious problems. The adverse reaction effects are most frequently related to the gastrointestinal tract, such as simple dyspepsia or nausea, vomiting, or gastric bleeding. These adverse reaction effects result from direct gastric irritation or prostaglandin inhibition. Since prostaglandins are responsible for inhibition of gastric acid secretion and stimulation of the cytoprotective mucous in the stomach, most non-steroidal anti-inflammatory drugs can counteract these effects. Since 1971, the mechanism of action of non-steroidal anti-inflammatory drugs was known through their inhibition of prostaglandin biosynthesis. These drugs prevent the synthesis of prostaglandins through their inhibition effect on the cyclooxygenase enzyme (COX). The unwanted side-effects of these drugs are due to their inhibition of COX-1, while their anti-inflammatory effects are due to inhibition of COX-2. Several points need to be considered to use this drug safely and effectively in dentistry. Knowing the action of non-steroidal anti-inflammatory drugs and recognizing the possibility of drug interactions is an important step toward preventing problems in dental clinics.

Introduction

Everyone, regardless of age, status or economic level has experienced pain to some degree. Pain control is of great importance in dental practice. It is pain that brings the patient to the dental office.

Advances in medical research and the discovery of analgesic drugs have given us

---

Kem. Ilmiah KPPIKG XII

some answers to questions about the origins and persistence of pain. Recent advances have led to new depths of understanding and control. Acute pain can be a warning symptom. Persistent pain is now thought to be an aggressive disease in itself, producing changes in the brain that underlie the pathology of what we term chronic pain.

The use of non-steroidal anti-inflammatory drugs is one important component in dentistry. Aspirin is the archetypal non-steroidal anti-inflammatory drugs and was first used clinically in 1899. Since then numerous other non-steroidal anti-inflammatory drugs have been developed. The adverse reaction effects are most frequently related to the gastrointestinal tract, such as simple dyspepsia or nausea, vomiting, or gastric bleeding. These adverse reaction effects result from direct gastric irritation or prostaglandin inhibition. Since prostaglandins are responsible for inhibition of gastric acid secretion and stimulation of the cyto-protective mucous in the stomach, most non-steroidal anti-inflammatory drugs can counteract these effects. In the United States, approximately 20.000 cases of adverse reaction to this drug have been reported and around 2,600 proved to be fatal cases.[1]

This paper will discuss the mechanism of action and side effects of non-steroidal anti-inflammatory drugs, as well as several attempts to use this drug safely and effective in dentistry.

Therapeutic Uses in Dentistry

Non-steroidal anti-inflammatory drugs are useful in the management of dental pain. Acute pain can occur during tooth extraction, tooth and soft tissue injury, and with infection and inflammation. This pain can be modulated and removed by treating its cause and through combined strategies using analgesics to treat the pain and antibiotics to treat the infection.

There are numerous non-steroidal anti-inflammatory drugs and each can be used to treat mild to moderate pain with an inflammatory component:

- Mild to moderate pain with an inflammatory component (e.g. toothache, periodontitis, osteoarthritis, rheumatoid arthritis)
- The pain of cancer metastases, injury (e.g. surgical procedures, bone fractures).

Action of Non-steroidal Anti-inflammatory Drugs

These drugs have potent analgesic, antipyretic and anti-inflammatory properties. In 1971, Professor Sir John Vane and coworkers proposed that the mechanism of action of the aspirin-like drugs was through their inhibition of prostaglandin bio-synthesis.[2] These drugs prevent the synthesis of prostaglandins through their inhibition effect on the cyclooxygenase enzyme (COX).[3] Physiologic concentrations of prostaglandins do not cause pain, but other inflammatory mediators such as bradikinin are able to trigger a painful reaction and prostaglandin potentiate this reaction.[4]

All non-steroidal anti-inflammatory drugs inhibit COX activity and this effect underlies their analgesic activity. Two separate isoforms of COX have been identified:[5]

- COX-1 is a constitutive enzyme found in a wide variety of cells throughout the body; it maintains the formation of prostaglandins involved in "house-keeping" (i.e. control of vascular flow through individual organs).
- COX-2 is synthesized *de novo* in inflammatory cells such as neutrophils and mast cells following exposure to bacterial endotoxins and/or cytokines (e.g. TNF, IL-1). It is responsible for generating prostaglandins at the side of inflammation and/or tissue damage.

COX inhibition effectively blocks the conversion of arachidonic acid to prosta-glandins via the COX pathway of the arachidonic acid cascade. This inhibition of

prostaglandin synthesis explains both the therapeutic and the adverse effects of these agents. The therapeutic effects are achieved through the inhibition of pathological over-production of prostaglandins which contribute to the inflammatory process. The adverse effects result from the inhibition of physiological formation of prostanoids.

Pharmacokinetics

Most non-steroidal anti-inflammatory drugs peak in about 1-2 hours. The effect of food on absorption of these drugs approved to treat pain is to reduce the rate but not the extent of absorption of ibuprofen, the naproxens, and diflusinal. There is no effect on absorption of these drugs with oral antacids. They are metabolized in the liver and excreted by the kidney. They mostly bind to protein (90%), so interaction with other drugs can occur (e.g. oral anti-coagulant), and they increase intoxication.[6]

Adverse Reactions

- Gastrointestinal effects. Prostaglandin inhibitors, like non-steroidal anti-inflammatory drugs, can interfere with the normal protective mechanisms in the stomach and increase acid secretion, causing symptoms or even an ulceration or perforation.
- CNS effects. This includes sedation, dizziness, confusion, mental depression, headache, vertigo and convulsions. Patients taking them should be cautioned about driving a car.
- Blood clotting. These drugs reversibly inhibit platelet aggregation because they inhibit TXA2 production.
- Renal effects. This includes renal failure, cystitis, and an increased incidence of urinary tract infections. The non-steroidal anti-inflammatory drugs have little effect on patients with normal kidney function; however, with disease, decreases in both renal blood flow and glomerular filtration rate can occur.
- Other effects. Oral manifestations reported include ulcerative stomatitis, gingival ulcerative, and dry mouth.
- Hypersensitivity reaction. A wide range of sensitivity reactions, including itching, Steven-Johnson syndrome, anaphylactoid reaction have been reported.
- Pregnancy and nursing. The non-steroidal anti-inflammatory drugs given late in pregnancy can prolong gestation, delay parturition and cause premature closure of the ductus arteriosus The uterine prostaglandins are responsible for parturition and premature closure of the ductus arteriosus.
- Drug interactions. The drug interactions of the non-steroidal anti-inflammatory drugs are summarized in the table below:

Table-1

Drug Interaction of the non-steroidal anti-inflammatory drugs	
Medical drug	Potential outcome
ACE inhibitors-captopril ß-blockers Thiazide diuretics	Decreases antihypertensive effect
Oral anticoagulants Lithium	Increases effect of medical drug
Cyclosporin Methotrexate Salicylates or other NSAIDs	Nephrotoxicity Stomatitis, bone marrow toxicity Decreases NSAIDs level, increases toxicity
Corticosteroids	Increases ulcerogenik risk

How To Reduce the Adverse Reaction of These Drugs

The non-steroidal anti-inflammatory drugs play an important role in the management of dental pain. To use this drug safely and effectively in dentistry, the following points need to be considered:[7]

1. Paracetamol as the first choice of drug for simple dental cases with no or mild inflammation.
2. Give the smallest effective dose of these drugs
3. Give more attention to the elderly, cardiovascular patients, and patients with gastrointestinal history.
4. Choose non-steroidal anti-inflammatory drugs that selectively inhibit COX-2 to prevent gastrointestinal effects.
5. A combination of 2 or more non-steroidal anti-inflammatory drugs will not increase their effectiveness but can increase toxicity.
6. Recognize the possibility of drug interactions.

Summary

The rationale of using non-steroidal anti-inflammatory drugs is to treat mild to moderate pain with inflammation component. Because these drugs nowadays are easy to buy over the counter, we have to continuously reminding the patient about the side effect of these drugs.

The non-steroidal anti-inflammatory drugs play an important role in the management of dental pain, but the side effects can cause clinical problems. Knowing the action of non-steroidal anti-inflammatory drugs and recognizing the possibility of drug interactions is an important step toward preventing problems in dental clinics.

All the results so far published support the hypothesis that the unwanted side-effects of these drugs are due to their inhibition of COX-1, while their anti-inflammatory effects are due to inhibition of COX-2. The identification of selective inhibitors of COX-1 and COX-2 will lead to advances in the therapy of inflammation, especially dental inflammation pain.

References

1. Fries JF, Miller SR, Spitz PW, William CA, Hubert HB, et al. Toward an epidemiology of gastrophaty associated with nonsteroidal antiinflammatory drug use. *Gastroenterology* 1989; 96 (2 Pt 2 Suppl), 647-55.
2. Vane JR. Inhibition of prostaglandin synthesis as a mechanism of action for the aspirin-like drugs. *Nature* 1971;231:232-5.
3. Vane JR, Botting RM. New insight into the mode of action of anti-inflammatory drugs. *Inflamm. Res.*1995; 44: 1-10.
4. Page CP, Curtis MJ, Sutter MC, Walker MJA, Hoffman BB. *Integrated Pharmacology*. 1st ed. London, UK: Mosby International. 1997:385-7
5. Otto JC, Smith WL. Prostaglandin endoperoxide synthesis-1 and 2. *J. Lipid Mediators Cell Signalling* 1995;12:139-56.
6. Requa-Clark BS, Holroyd SV. *Applied Pharmacology for the Dental Hygienist*. 3rd edition. Missouri, USA Mosby –Year Book, Inc.; 1995.
7. Setiabudy R. Penggunaan Rasional Obat Anti-inflamasi Nonsteroid. *The Indonesian Journal of Pharmacology and Therapeutics*. 2000;13 (1): 29-33.