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NSAIDS in Dentistry: It's Principles in Practice

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Abstract:- Pain is one of the most common reason for the patients to visit the dentist. The pain may be due to diseases or conditions of dental, oral, facial, and related structures(1,6). It is the dentist's responsibility to diagnose the cause of pain. Pain during a dental procedure is well managed by sufficient local anaesthesia, while postoperative pain control is often insufficient due to inadequate pain relief or unacceptable side-effects(2). The most common and widely used drugs in management of pain in dentistry are NSAIDs for their analgesic, anti-inflammatory and anti-pyretic actions. This article intends to discuss the rationale in prescribing NSAIDs in dental practice in a concise way.(3)

Keywords:- *NSAIDS, pain, analgesic, cyclooxygenase, prostaglandin, acetaminophen, dentistry, dental pain*

I. INTRODUCTION

NSAIDs are a group of drugs that play an important role in relieving pain by anti-inflammatory, analgesic, and anti-pyretic effects(1). Their therapeutic effectiveness and toxicity are well-documented and provide evidence that NSAIDs generally provide satisfactory therapeutic ratio of pain relief with fewer adverse effects than the opioid- analgesic combination(2). The principle pharmacologic effects of NSAIDs are attributed to their ability to inhibit prostaglandin activity by blocking the activity of COX which exists in two forms i.e., COX-1 and COX-2. It is the gastrointestinal toxicity of long-term use of conventional non-selective NSAIDs that has led to the development of selective COX-2 inhibitors which are safer to the Gastrointestinal system. However, it has been evident that some COX-2 inhibitors increase cardiovascular risks. Other adverse effects are risk of unusual bleeding tendency due to anti-platelet action, renal toxicity due to decreased perfusion, premature closure of ductus arteriosus if prescribed in third trimester of pregnancy. Dentists should evaluate the risks and benefits of each medication, considering the medical history and analgesic requirement of each individual. Therefore, NSAIDs should be prescribed in applicable doses and intervals keeping in mind NSAID-associated complications.(2,6,7,9,12)

II. DENTAL PAIN

Dental pain/Odontogenic pain is a complex cascade process that results from dental tissue damage accompanied with heterogenous neuronal stimuli as a consequence of neurovascular, neuroinflammation and morphologic responses.

- *Pre-Requisites For Choosing NSAIDS:*

Odontogenic pain caused due to pulpal and periapical disease is most common in dental practice. According to clinical manifestation of pain, it can be classified as Acute and Chronic pain, according to intensity of pain, it can be

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classified as Mild, Moderate and Severe pain. Indications of an analgesic is related to treat acute, chronic, and postoperative pain. Once the clinician has quantified the intensity of pain, analgesics are prescribed accordingly. In case of mild pain, a single NSAID is used in its individual dose, for example, drug of choice in mild dental pain is Ibuprofen 200mg or Naproxen 250mg. In case of moderate pain, an NSAID should be used in pharmacologic full doses or in a combination with a weak opioid. In case of severe pain, a combination of strong opioid and NSAID can be considered. But, due to high abuse liability, opioids are not drug of choice for the treatment of odontogenic pain.(2)

➢ *Mechanism of Action of NSAIDS:*

Mechanism of action of NSAIDs is based on the inhibition of COX and therefore the inhibition of Prostaglandin synthesis.(9)

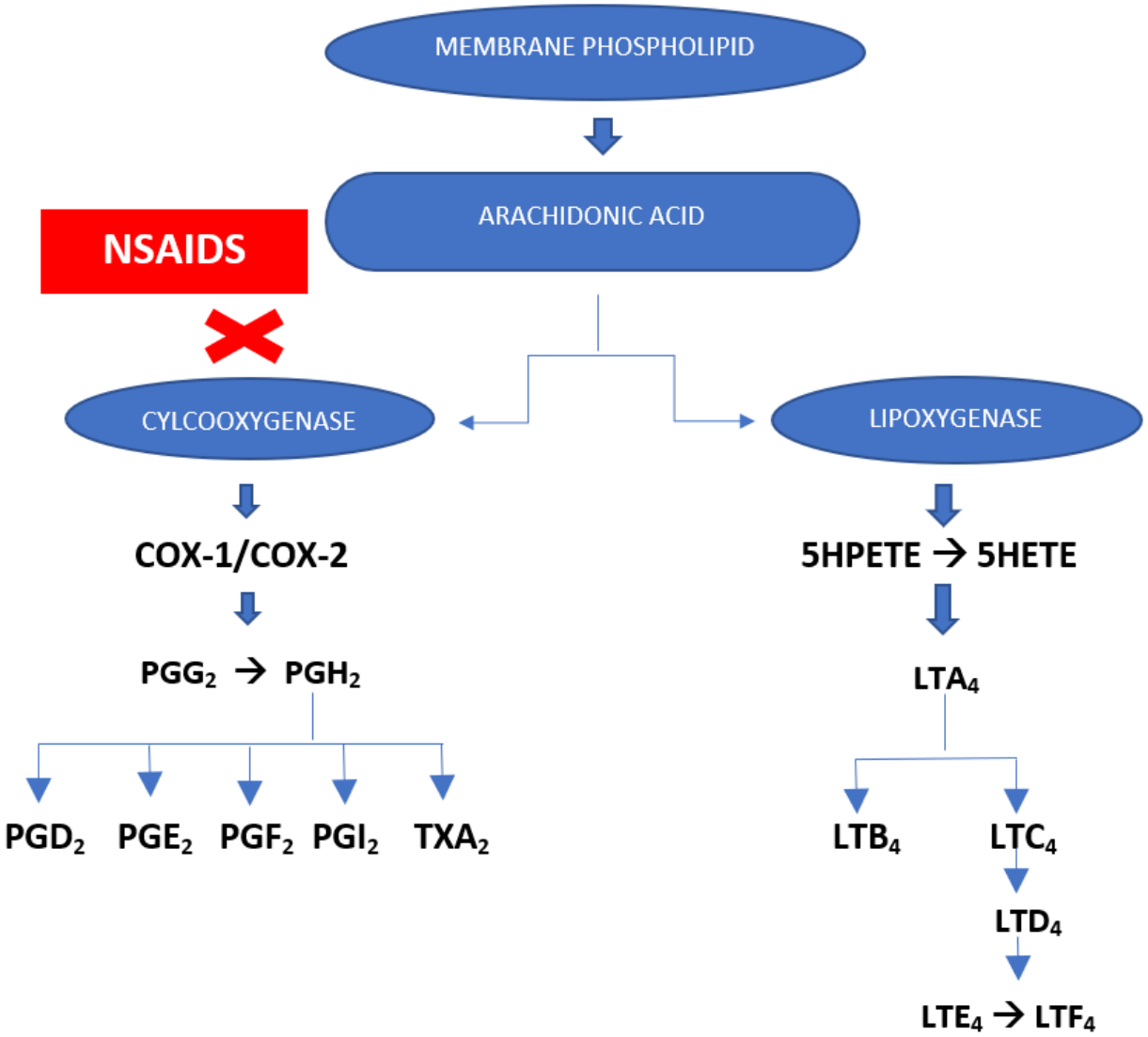
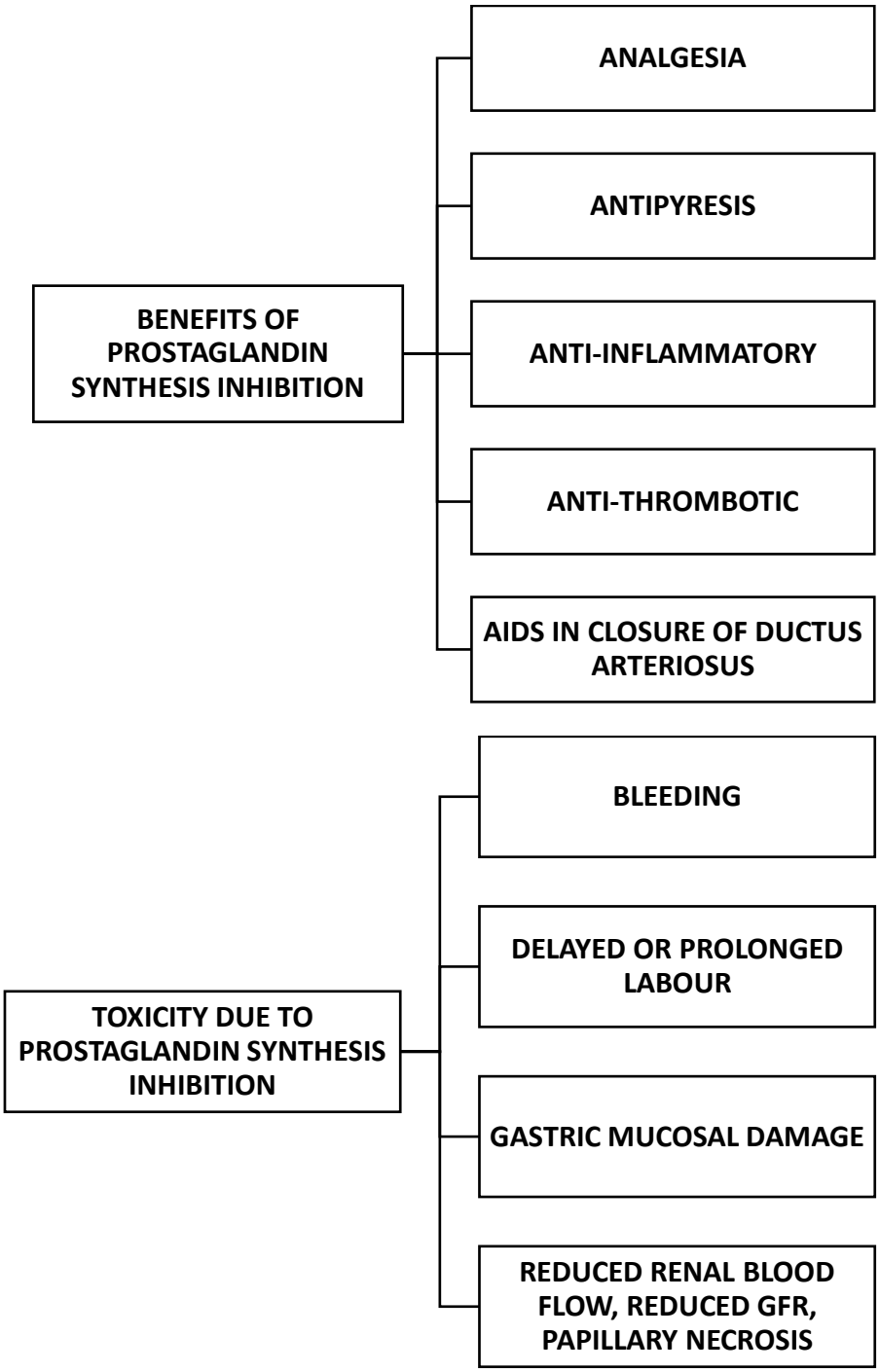


Fig 1:- A simple flowchart indicating the MOA of NSAIDs. COX-Cyclooxygenase; PG-Prostaglandin; TX- Thromboxane; HPETE- Hydroperoxyeicosatetraenoic acid; HETE- Hydroxy eicosatetraenoic acid; LT- Leukotriene



Flow chart 1 – Benefits of prostaglandin synthesis inhibition; Flow chart 2 – Toxicity due to prostaglandin synthesis inhibition

➢ *Sites Of Cox Receptors:*

COX-1: Blood vessels, interstitial cells, smooth muscle cells, platelets, and mesothelial cells.

COX-2: Fibroblasts, chondrocytes, endothelial cells, macrophages, and mesangial cells.

COX-1 regulates physiological functions of the body and is constitutively expressed in most tissues and cells in animal species, hence called Constitutive isoenzyme. Whereas COX-2 mediates inflammatory response. Hence, selective COX-2 inhibitors should decrease inflammation without disturbing normal physiology. COX-2 is induced by exposure to various stimuli like cytokines, mitogens, and endotoxin and hence called Inducible isoenzyme.(13)

➢ *Acetaminophen/Paracetamol:*

Aspirin, which is the prototype drug of NSAIDs, is a derivative of salicylate, whereas Acetaminophen is a derivative of para-aminophenol that has potent antipyretic and analgesic effects with poor anti-inflammatory activity. It does not produce gastric irritation; acid-base and electrolyte imbalance; and has got no antiplatelet action. Acetaminophen is the preferred analgesic and antipyretic in patients having peptic ulcer, bronchial asthma and in children. Excessive doses and long-term use can lead to liver damage and kidney toxicity respectively. In case of acute paracetamol poisoning, N-acetylcysteine is the antidote.(1)

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SAFE NSAID AND ACETAMINOPHEN DOSING REGIMEN FOR DENTAL PAIN:

DRUG	DOSAGE(ADULT)
DICLOFENAC	50mg TID
NAPROXEN	500mg followed by 250mg every 6-8h
IBUPROFEN	200-400mg every 6-8h
FLURBIPROFEN	50-100mg every 8h
KETOPROFEN	25-75mg every 6-8h
CELECOXIB	200mg BID
ACETAMINOPHEN/PARACETAMOL	500 -1000mg TID

DRUG	DOSAGE(CHILDREN)
ACETAMINOPHEN	10-15mg/kg every 4-6h
IBUPROFEN	AGE 2-12 – 10mg/kg
	AGE >12 – 200-400mg

Table 1:- Safe NSAID and Acetaminophen dosing regimen for dental pain in adults and children

GENERAL USE OF NSAIDS IN DIFFERENT DENTAL CONDITIONS:

TYPE OF DENTAL PAIN	NSAID	DOSING
Acute dental pain	Ibuprofen Ketoprofen Diclofenac Flurbiprofen Naproxen Acetaminophen Celecoxib	200-400mg every 6-8h 25-75mg every 6-8h 50mg TID 50-100mg every 8h 500mg, then 250mg every 6-8h 500-1000mg TID 200mg BID
Postoperative pain	Ibuprofen	200-400mg every 6-8h
Periodontal surgery	Ibuprofen/acetaminophen	400/1000mg every 6-8h
Orthodontic tooth movement	Acetaminophen	500mg every 12h
Impacted third molar surgery	Diclofenac/Acetaminophen	100/1000mg single dose
Root canal treatment	Ibuprofen/Acetaminophen	600/1000mg 30 minutes prior
TMD	Meloxicam	15mg OD

Table 2:- General use of NSAIDs in different dental conditions

➢ *NSAIDS In Pregnancy:*

The frequency of NSAID use during pregnancy is not easily enumerable, considering that some of these drugs are available over the counter (OTC) and thus can be easily bought without medical prescription. Evidence is available that NSAIDs cross placental barrier and reach foetal circulation and cause various adverse effects depending on the period of gestation. For example, congenital anomalies and miscarriage when NSAIDs are taken by pregnant mothers during early stages of gestation, renal and vascular effects when taken during third trimester. Choice of analgesic in any stage of pregnancy is Acetaminophen in lowest effective doses and short usage period.(9,10,11,17)

➢ *NSAIDS In Children:*

Use of aspirin in children suffering from chicken pox and influenza may result in a condition called Reye's syndrome. It is a triad consisting of encephalopathy, fatty liver degeneration, transaminase elevation. Acetaminophen and Ibuprofen may be considered the drug of choice in children within their recommended dosage.(5,7,17)

➢ *NSAIDS And Renal Disease:*

In patients with lessened kidney perfusion, the kidneys increase prostaglandin synthesis to raise the filtration rate and secure an adequate renal flow. Nevertheless, inhibition of

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prostaglandin synthesis by NSAIDS can trigger renal hypoperfusion, nephrotic syndrome or interstitial nephritis.

Forsaking the use of NSAIDs in patients with kidney disease may lead to consequences from other alternatives.

Attention has been drawn to the possibility of chronic interstitial nephropathy and chronic renal failure associated with the use of NSAIDs - including Acetaminophen.(7,9,10,11)

- *Nsaids In Hypertension:*

Evidence is available that consumption of more than 500 mg/day of Acetaminophen is associated with an increased risk of Atrial hypertension, conversely, use of aspirin has no association as such. Administration of Acetaminophen at a dose of 4 g/day during one month in hypertensive patients has seen to induce a 4mmHg rise in systolic pressure. It has also been found that NSAIDs could antagonize the effects of antihypertensive drugs.(7,9,10,11)

- *NSAIDS And Wound Healing:*

NSAIDs have shown to delay wound healing while simultaneously decreasing granulocytic inflammatory reaction. The reason behind this is NSAIDs have anti-proliferative effect on blood vessels, and tissues, thereby delaying healing. Nitrous Oxide(NO) produced in response to inflammatory cytokines during tissue injury helps in angiogenesis and inflammation mediation. Studies suggests that linking NO with Ibuprofen retains anti-inflammatory effects while preventing negative impact on healing.(4,15)

- *Drug Interactions With NSAIDS:*

- Aspirin displaces Warfarin, Sulfonylureas, Naproxen, Phenytoin, and methotrexate from binding sites on plasma proteins.
- Tubular secretion of uric acid and Methotrexate gets inhibited.
- Blunts diuretic action of Furosemide and potassium sparing action of Spironolactone.(7)

- *NSAID Hypersensitivity:*

When it comes to prescribing NSAIDs, one should also consider hypersensitivity reactions caused by them. NSAID hypersensitivity can be either skin reactions or respiratory symptoms. NSAID use can exacerbate underlying urticaria/angioedema and the condition is called NSAID exacerbated Cutaneous Disease(NECD), when there is no underlying disease but urticaria and angioedema are induced by use of NSAIDs, the condition is called NSAID Induced Urticaria/Angioedema(NIUA). Respiratory symptoms like rhinorrhoea, blocked nose, and bronchial asthma are classified under NSAID Exacerbated Respiratory Disease(NERD). Incidence of Adverse Drug Reactions to analgesics is 1.6%. Opioids can be recommended as safe alternatives for analgesia since their mode of action is completely different to that of NSAIDs. Although marked cross-interactions are to be expected, some patients tolerate NSAIDs that have a stronger COX-2 inhibition, such as oxicams, or, as an alternative, acetaminophen.(6)

III. ONGOING RESEARCH

Considering one of the common adverse effects of NSAIDs which is the gastric ulceration and bleeding when used chronically and frequently, research is under development in incorporating gaseous mediators like nitric oxide(NO), hydrogen sulphide(H_2S), and carbon monoxide(CO) which contribute to maintenance of gastric mucosal barrier integrity. Clinical and preclinical studies have been showing promising effects with respect to GI safety of these newer NSAIDs along with anti-inflammatory properties.(16)

IV. CONCLUSION

From a dentist's perspective, we are able to choose from a plethora of medications to provide patients with pain relief but, trying to judge the relative efficacy of analgesics is not easy. One must remember that the best means of managing pain is to remove the source of pain as quickly as possible. Each drug regimens have to be customized based on pain severity and the medical condition of the patient. Our goal should be to use these drugs optimally to treat dental pain most effective.

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