# ANALGESIC & ANTI INFLAMMATORY DRUGS

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Fb/Nurse-Info

## CLASSIFICATION

#### Divided into 2 groups:

 Opioid Analgesics -Narcotics/Morphine like analgesics

Non Opioid Analgesics -NSAIDs/Non narcotic/aspirin like analgesics

## **OPIOID ANALGESICS**

#### Natural Opium alkaloids Morphine & Codeine.

### Semi synthetic opiates

Diacetylmorphine oxymorphone Pholcodeine

#### Synthetic opioids

Pethidine Fentanyl Methadone Dextropropoxyphene Ethoheptazine Tramadol

#### B. Preferential COX-2 inhibitors

- Nimesulide
- Meloxicam
- Nabumetone

#### C. Selective COX-2 inhibitors

- Valdecoxib
- Celecoxib
- Rofecoxib

#### D. Analgesics with poor Anti inflammatory action-

- Paraminophenol derivative
  - Paracetamol (Acetaminophen)
- Pyrazolone derivative
  - Metamizol, Propiphenazone
- Benzoxazocine derivative
  - Nefopam

# Adverse effects

Analgesics doses are usually well tolerated but antiinflammatory doses are usually associated with adverse effects whed used for a long period.

- G.I tract:- Epigastric distress, nausea, vomiting, erosive gastritis, peptic ulcer, increase occult blood loss in stools are common
- Allergic reactions are not common and may be manifested as rashes, photo sensitivity..etc
- Haemolysis
- Nephrotoxicity
- Reye's syndrome
- Salicylism
- Acute salicylate intoxication

# Functions of NSAIDs

#### Analgesia –

PGs induce hyperalgesia by affecting the transducing property of free nerve endings – stimuli that normally do not elicit pain are able to do so. NSAIDs do not affect the tenderness induces by direct application of PGs but block the pain sensitization mechanism induced by bradykinin.

#### Antipyresis –

NSAIDs reduce body temperature in fever, but do not cause hypothermia in normothermic individuals. NSAIDs block the action of pyrogens but not that of PGE2 injected into the hypothalamus.

Ductus arteriosus closure- Administration of NSAIDs in late pregnancy has been found to promote premature closure of ductus in some cases.

Parturation – Sudden spurt of PG synthesis by uterus probably triggers labor and facilitates its progression .NSAIDs has the capacity to retard and delay labor . Gastric mucosal damage –

Gastric pain , mucosal damage are produced by all NSAIDs .Inhibition of synthesis of PG { PGE2, PGI2 } is clearly involved. Deficiency of PGs reduces mucus and HCO3- secretions, tends to enhance acid secretion and may promote mucosal ischaemia. Thus, NSAIDs enhance aggressive factors and contain defencive factors in gastric mucosa - which are ulcerogenic. PCM, a very weak inhibitor of COX is practically free of gastric toxicity and selective COX - 2 inhibitor are safer...

Anaphylactoid reaction –

Aspirin PPts asthma , angioneuretic swellings , urticaria or rhinitis in certain susceptible individual . These subjects react similarly to chemically diverse NSAIDs ,ruling out immunological basis for the reaction .

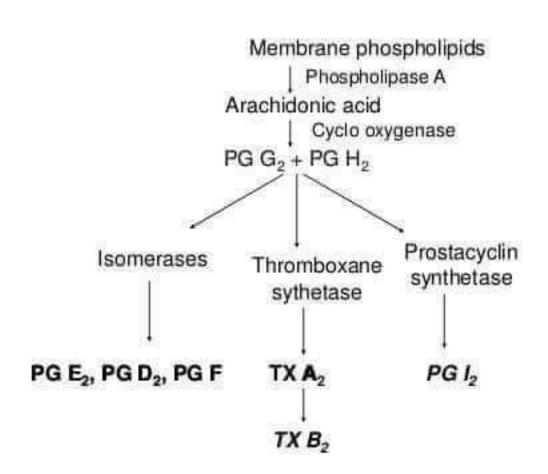
#### Uses

Acute or chronic conditions where pain and inflammation are present.

(Rossi, 2006)

- Rheumatoid arthritis
- Osteoarthritis
- Inflammatory arthropathies (e.g. ankylosing spondylitis, )
- Acute gout
- Dysmenorrhoea
- Metastatic bone pain
- Headache and migraine
- Postoperative pain
- Mild-to-moderate pain due to inflammation and tissue injury
- Pyrexia
- Renal colic
- They are also given to just born infants whose ductus arteriosus is not closed within 24 hours of birth

# Prostaglandins synthesis inhibiton



# Physiological Functions of Prostaglandins

- Pain: PGI<sub>2</sub> and PGE<sub>2</sub> sensitize nerve endings to bradykinin, histamine
- Inflammation: PGI<sub>2</sub>, PGD<sub>2</sub> and PGE<sub>2</sub> are vasodilators (edema, erythema)
- Protection of the gastric mucosa: PGI<sub>2</sub>
- Maintenance of renal blood flow: PGE<sub>2</sub>
- Fever: PGE<sub>2</sub>
- Platelets: PGl<sub>2</sub> and PGD<sub>2</sub> inhibit platelet aggregation.

TXA<sub>2</sub> stimulates platelet aggregation

- Uterus: PGD<sub>2</sub> contracts uterus
- Other:PGE<sub>2</sub> keeps ductus arteriosus open following birth

## Role of PGs in inflammation

#### By 2 roles:

- Promote development
- Modulate and regulate inflammatory cell function { Gordon et al 1976 }
- PG can induce pain , edema , redness and vasodilation when they are induced by other mediators .
- PG inhibits lysosomal enzyme release during phagocytosis, enhances chemotaxix , chemokinesis

{ Estensen et al 1973 }

- Inhibit clonal proliferation of macrophages stem cells migration of macrophages
- On lymphocytes it supress cell transformation { Mihas 1975

# Role in Bone Resorption

- In number of ways and may induce bone resorption by facilitating the release of osteoclasts activating factor from lymphocytes { Yoneda & Mundy 1979 }
- Inhibit bone collagen formation which result in inhibition of the repair of resorbed bone { Raisz & Koolemans – Beynen 1974 }

# Role in periodontal destruction

#### Production of arachidonic acid metabolites:

Recently the role of host's immuno inflammatory system is understood. After activation of inflammatory cells in the periodontium by bacteria, phospholipids in the plasma membrane of cells become available for actions by phospholipase. This leads to free arachidonic acid in the area [AAP 1992]

# INDICATIONS OF NSAIDS IN DENTISTRY

- Irreversible pulpitis
- Apical periodontitis
- Acute alveolar abscess
- Infected cyst
- Sinusitis
- TMJ Arthritis
- MPDS
- After tooth extraction
- Dry socket
- Recurrent apthous ulcers
- Lichen planus
- Agranulocytosis
- Cyclic neutropenia

# GENERAL CONTRAINDICATIONS

- Ulcer
- Asthma
- Patient with nasal polyp
- Diabetes
- Gout
- Influenza (Reye's syndrome)
- Hypo coagulation state
- Chronic allergic disorders
- Chronic liver disease
- Renal failure
- Salicylate allergy
- Breast feeding mothers
- Pregnancy

# NSAIDs as Host Modulation Therapy

Treatment concept that aims to reduce tissue destruction and stabilize or even regenerate the periodontium by modifying or downregulating destructive aspects of host response and upregulating protective or regenerative responses.

### (CARRANZA)

HMTs are systemically or locally delivered pharmaceuticals that are prescribed as part of periodontal therapy and are used as adjuncts to conventional periodontal treatments.

- HMTs offer the opportunity for modulating or reducing this destruction by treating aspects of the chronic inflammatory response.
- HMTs do not "switch off" normal defense mechanism or inflammation; instead, they ameliorate excessive of pathologically elevated inflammatory processes to enhance opportunities for wound healing.

- NSAIDS block PGE2 production, thereby reducing inflammation & inhibiting osteoclast activity in periodontal tissue
- Studies have shown that systemic NSAIDS such as indomethacin, flurbiprofen & naproxen administered daily for upto 3 yrs significantly slowed the rate of alveolar bone loss compared with placebo
- However daily administration for extended period is necessary for periodontal benefits

# **ASPIRIN**

- Acetylsalicylic acid
- Pharmacological actions
- Analgesic, antipyretic, antiinflammatory actions
- Metabolic effects: Blood sugar may decrease, plasma free fatty acid & cholesterol levels reduced
- Respiration: Hyperventilation in salicylate poisoning
- Acid base & electrolyte balance: Compensated respiratory alkalosis
- CVS: Vasodilation, increase in cardiac output
- GIT: Epigastric distress, nausea & vomiting
- Blood: Prolongs bleeding time

### ADVERSE EFFECTS:

- Nausea, vomiting, epigastric distress, increased blood loss in stools
- Rashes, fixed drug eruptions, urticaria, rhinorrhea, angioedema, asthma, anaphylactoid reaction
- Salicylism dizziness, tinnitus, vertigo, impairment of hearing & vision, excitement & mental confusion, hyperventilation & electrolyte imbalance
- Acute salicylate poisoning: Fatal dose in adults 15-30g, lower in children

- USES:
- Analgesic
- Antipyretic
- Acute rheumatic fever
- Rheumatoid arthritis
- Osteoarthritis
- Postmyocardial infarction
- Patent Ductus Arteriosus
- Familial colonic polyposis
- Prevention of colon cancer
- Treatment of Bartter's syndrome

- Precautions & Contraindications:
- Peptic ulcer
- Bleeding tendencies
- Children with chicken pox or influenza
- Chronic liver disease
- Diabetics
- Pregnancy
- Breast feeding mothers

#### Dose

- 0.3-0.6 g 4-6 hrly orally

### INDOMETHACIN

- Indole derivative
- Potent inhibitor of PG synthesis & suppresses neutrophil motility
- Well absorbed orally & t ½ is 2-5 hrs
- Adverse effects: Gastric irritation, nausea, anorexia, gastric bleeding & diarrhoea, frontal headache, dizziness, ataxia, mental confusion, depression, psychosis, leukopenia, rashes, increased risk of bleeding
- Contraindicated in machinery operators, drivers, psychiatric patients, epileptics, kidney disease, pregnant women & children
- Dose: 25-50mg BD-QID
- Commercially available as-Idicin, Indocap, Indoflam : 25mg, 75mg tab

## **IBUPROFEN**

- Propionic acid derivative
- Adverse effects:
- Gastric discomfort, nausea & vomiting
- Headache, dizziness, blurring of vision, tinnitus & depression
- Avoided in pregnancy, peptic ulcer patient & asthmatic patients

- USES:
- Analgesic & Antipyretic
- Rheumatoid arthritis, osteoarthritis, musculoskeletal disorders
- Soft tissue injuries, fractures, vasectomy, tooth extraction
- Postpartum & postoperatively : suppress swelling & inflammation
- Dose: 400-800 mg TDS
- Comercially available as-Brufen, Emflam, Ibusynth: 200, 400, 600mg tab. Ibugesic: 100mg, 400 mg tab.

### DICLOFENAC SODIUM

- Aryl-acetic acid derivative
- Well absorbed orally
- Plasma t ½ 2 hrs
- Adverse effects: Epigastric pain, nausea, headache, dizziness, rashes
- Uses: Rheumatoid arthritis, ankylosing spondylitis, dysmenorrhea, post traumatic & post inflammatory conditions
- Dose: 50mg TDS, then BD oral, 75mg deep i.m.
- Commercially available as:
  - Voveran, Diclonac, Movonac: 50 mg tab.
  - Diclomax: 25, 50 mg tab.

# KETOROLAC

- Pyrrolo-pyrrole derivative
- Potent analgesic & modest anti inflammatory
- Rapidly absorbed after oral & i.m administration
- Plasma t ½ is 5-7 hrs
- Adverse effects: Nausea, abdominal pain, dyspepsia, ulceration, loose stools, drowsiness, headache, dizziness, nervousness, pruritis, pain & fluid retention
- Not be given to patients on anticoagulants

#### USES:

- Postoperative & acute musculoskeletal pain: 15-30 mg
   i.m or i.v every 4-6 hrs
- Used for renal colic, migraine, pain due to bony metastasis
- Orally in a dose of 10-20 mg 6 hrly.
- Commercially available as –
  Ketorol, Zorovon, Ketanov, Torolac : 10mg tab.