Classification of NSAIDs

- Based on their anti-inflammatory action:

A. Weak or No clinically useful anti – inflammatory action eg. Paracetamol

B. Mild to moderate anti-inflammatory action eg. Aspririn

C. Marked Anti-inflammatory action eg. Diclofenac

A. Weak or No clinically useful anti – inflammatory action

1. **Paracetamol or Acetaminophen (Panadol):**

- Paracetamol has an analgesic and antipyretic properties with a devoid of anti-inflammatory effect.
- It inhibits PGs in brain and therefore acts as analgesic and antipyretic but it has less effect on peripheral PGs responsible for inflammation.

It probably act on another enzyme, (COX_3), in CNS, which may be a splice variant product of COX_1 gene, to produce analgesic or antipyretic effects.

- It is a weak inhibitor of COX1 or COX2

In periphery , it has no significant anti-inflammatory action . In tissues , p-aminophenols trap free radicals which are important for formation of hydro-peroxidase that is essential for the activity of COX .

In inflamed tissues, large amounts of peroxide radicals are produced which swamp this action of

p-aminophenols ; thus hydroperoxidase continue to be formed, and COX_2 remain active in inflammatory cells at inflamed sites

Safest for peptic ulcer: paracetamol

- It neither affects platelet function nor GI irritation
- The oral dose for adults as analgesic or antipyretic is 0.5 -1 g X 3/d.
- Maximum daily dose is 4 g

➢ Therapeutic uses: First choice antipyretic

1. It is effective in mild to moderate pain e.g. headache, dysmenorrhoea (menstrual pain)
2. It is a substitute for analgesic & antipyretic effects of aspirin particularly in

   A. children with viral infection

   B. patients with peptic ulcer since it causes no gastric irritation

➢ Adverse effects include:

1. Skin rash occurs infrequently
2. Hepatic and renal necrosis with large and prolonged doses (quinone metabolite). Antidote is N- acetyl cysteine binds and inactivates the toxic quinone metabolite

B. Mild to moderate anti-inflammatory action

1. **Aspirin (Acetylsalicylic acid)**

Irreversibly inhibits Cox

why?

- It is a weak organic acid and is unique among NSAIDs.
- Mechanism of action:

Aspirin Irreversibly inhibits Cox by acylating active site of enzyme, so preventing formation of thromboxane, prostacyline & other PGs.

- Other NSAIDs are reversible inhibitors of Cox

- Therapeutic uses:

1. **Anti-inflammatory use :**

- RA, OA and other inflammatory joint disease.
- Dose is 4-6 g / d in 3-4 divided doses

2. **Analgesic and anti-pyretic use:**

- Fever, headache, toothache, and muscular and joint pain
- Dose is 325-650 mg X 3 / d

3. **Anti-platelet use :**

- Low dose of aspirin 80-100 mg daily are used to prophylactically decrease incidence of transient ischemic attacks (TIAs) & strokes

- Adverse effects:

1. GIT:

- Epigastric distress, nausea, vomiting and bleeding

2. Bleeding tendency

3. Hypersensitivity:

- About 15% of patients develop allergy

4. Specific adverse effects :

A. Reye's syndrome:

- Use of Aspirin in children with viral infections (e.g. measles, influenza, or chickenpox) may rarely cause Reye's syndrome (extensive fatty infiltration of liver with liver damage and failure)

B. Salicylism :

- It is mild salicylic acid intoxication. Symptoms include: confusion, tinnitus, deafness, sweating, vomiting and others
- Contraindications:
- Aspirin should be avoided in patients with peptic ulcers, asthma and febrile children due to viral infections.
- Drug interactions:
- Aspirin should be avoided or used with caution in patients taking warfarin, phenytoin or valporic acid. Aspirin displaces these drugs from binding of plasma protein resulting in high drug concentrations and therefore toxicity

2. Propioinc acid derivatives

- This class includes Ibuprofen , ketoprofen and Naproxen : Very effective in Dental pain
- All are reversible non-selective inhibitors of Cox that inhibit synthesis of PGs
- All possess anti-inflammatory, analgesic & antipyretic activities
- They cause less GI side effects than aspirin and therefore are preferred for chronic use in inflammatory joint diseases and in musculo-skeletal disorders
- Most common adverse effects ranges from GI dyspepsia to bleeding

3.Fenamates : Additional to naproxen, fenamates good for dental pain

- Main example is Mefenamic acid (ponstan)
- No clear advantages over other NSAIDs and may cause GI side effects. It has little anti-inflammatory action (milde).
- Indications:
- Short-term treatment of pain in soft-tissue injuries, dysmenorrhea, and in RA and OA
- Adverse effects:
- Severe diarrhea associated with inflammation in bowel and hemolytic anemia

C. Marked Anti-inflammatory action

1. Arylacetic acid derivatives :

1-Diclofenac potassium ;preferred for hypertensive patients
2-Diclofenac sodium

- Main example is Diclofenac (Voltaren)
- It is a potent Cox inhibitor with anti-inflammatory, analgesic & antipyretic activities (accumulates in synovial fluid)

So,Very good for chronic conditions

- It is potent than indomethacin or naproxen
- Indications:
- long-term treatment of RA and OA
- short-term treatment of acute musculoskeletal pain, postoperative pain, and dysmenorrhea
- Side effects:

a. GI irritation to bleeding
b. Fluid retention, edema, and rarely impairment of renal function

2. Acetic acid derivatives:

- Indomethacin (Indocin) and sulindac
- All possess anti-inflammatory, analgesic and antipyretic properties
- They are not generally used to lower fever

A. Indomethacin :

- It is more potent than aspirin, but toxicity limits its use to short-term dosing
- Indications:
- It is useful in treatment of RA,OA, ankylosing spondylitis (AS), and acute gout

2. Closure of patent ductus arteriosus in neonate : given by IV infusion within 72 h of birth

- Side effects :
- CNS : (35-50%)headache, dizziness and others
- GI disturbances: Diarrhea, ulcers, bleeding

B. Sulindac :

- This is a pro-drug ; it is converted to active sulfide metabolite in liver
- It is less potent than indomethacin
- It causes less adverse effects than indomethacin & other NSAIDs
- It is useful in treatment of RA,OA, AS and acute gout

3. Oxicam derivatives :

- Piroxicam (Feldene) and meloxicam (Mobic)
- Able to inhibit Cox-1 and Cox-2 but meloxicam shows preferential COX-2 selectivity (preferential Cox-2 inhibitor)
- Are used to treat RA, OA, AS Most patients of these diseases treated by oxicam derivatives
- They have long half-life, once daily
- Piroxicam has more GI side-effects than most other NSAIDs
- Meloxicam has significantly less GI side-effects compared to piroxicam and other NSAIDs

4. Selective Cox-2 inhibtors (coxibs)

- Celecoxib, rofecoxib, valdecoxib and etoricoxib
- Analgesic and anti-inflammatory properties by selectively inhibiting the Cox-2 biosynthesis
- **Hypothesis**: Cox-2 isoform is up regulated in the site of inflammation mediating inflammation by catalyzing the biosynthesis of PGE2 and PGI2 , and these PGs are also formed by Cox-1 in gastric epithelium where they act as cytoprotective mediators.

- proinflammatory PGs are inhibited and simultaneously sparing the PGs catalyzed by Cox-1 necessary for physiologic functions
- They exert anti-inflammatory properties with less or none of typical adverse effects associated with NSAIDs treatment on GIT and kidney.
- **Indications:**
- Patients who require chronic use of NSAIDs & are at high risk for NSAIDs-induced ulcer

- Inflammatory and painful conditions such as RA, OA, headache, menstrual, dental and postoperative pain
- Long acting, once daily
- **Side effects:**
- Most common abdominal pain, diarrhea, dyspepsia
- Hypersensitivity:sulphonamide hypersensitive patients (urticaria, angioedema, sweet, rash... Etc)

- **Contraindications:**
- COX-2 inhibitors should be avoided in patients with chronic renal insufficiency, severe heart disease & hepatic failure.

- Rofecoxib and valdecoxib was withdrawn from market because its use was associated with increased risk of stroke, heart attack, and sudden cardiac death.

Questions from the archives

patient comes to hospital with thrompocytopenic purpura history. He complains from almost everyday headache with dull feeling, and this headache begins afternoon and persists till sleeping. A drug to control headache is perscribed to the patient, what is it?
A Paracetamol
B Meloxicam
C Ibuprofen
D naproxen
E aspirin

Answer: A

A 55 year old man with history of coronary artery disease present to the emergency department with chest pain. He has a known history of hypertension and diabetes mellitus.
An ECG shows ST-segment elevation and a diagnosis of MI is made.
Which of the following medications should be administered immediately to help reduce mortality by preventing thrombus formation :
A Ibuprofen.
B Naproxen.
C Acetaminophen.
D Aspirin.
E Diclofenac.
Answer: D

Which of the following is selective COX-2 inhibitor :
A Meloxicam.
B Diclofenac.
C Naproxen.
D Sulindac.
E Etoricoxib.
Answer : E

medicine that relieves the pain of osteoporosis and at the same time the patient has heart disease?
What medicine should not be taken?

celecoxib

Boy has been diagnosed with viral infection in the stomach, the doctor prescribed anti-inflammatory and anti-pyretic drug
The boy developed serious symptoms like brain hydrocephalus and liver disease and heart disease plus kidney disease, the boy died 5 days later.
Which drug was given to the boy:

Aspirin

)65yrs old alcoholic woman was administered to the ER by her husband with hearing loss and bradycardia and hyperglycemia and hypertension with creatinine elevation and hypercalicemia, her husband said she took a drug for an attempting to a suicide.
Which drug has been taken :

Aspirin

Which of the following medications would represent arthritis therapy that is least likely to cause gastric ulceration?
Select one:
A Aspirin
B Acetaminophen
C meloxicam
D Rofecoxib
E Piroxicam
Answer:C

A patient was given celeocoxib, what were the possible findings to prescribe this drug for him:

A Peptic ulcer.
B Diabetes mellitus.
C He suffered from skin allergy due to taking sulfonamide.
Answer: A