NSAID & ANTIPYRETIC- ANALGESICS

It is a class of drug ~ analgesic, antipyretic & anti-inflamatory action in diff. measures. In contrast to morphine they do not depress CNS, do not produce physical dependence, no abuse liability & r particulary effective in inflamatory pain.

They act mainly on peripheral pain mechanism, but also in CNS to raise pain threshold.

NSAID/ANTIPYRETIC-ANALGESIC

- NON SELECTIVE COX INHIBITORS
  - SALICYLATES
    - ASPIRIN
  - PROPIONIC-ACID DERIVATIVE
    - IBUPROFEN
    - NAPROXEN
    - KETOPROFEN
  - FENAMATE
    - MEPHENAMIC ACID
  - ENOLIC ACID DERIVATIVE
    - PIROXICAM
    - TENOXICAM
  - ACETIC ACID DERIVATIVE
    - KETOROLAC
    - INDOMETHACIN
  - PYRAZOLONE DERIVATIVE
    - PHENYL-BUTAZONE
- PREFERENTIAL COX-2 INHIBITOR
  - NIMUSELIDE
  - DICLOFENAC
  - ACECLOFENAC
  - MELOXICAM
- SELECTIVE COX-2 INHIBITOR
  - CELECOXIB
  - ETORICOXIB
  - PARECOXIB
- ANALGESIC-ANTIPYRETIC & POOR ANTI INFLAMMATORY ACTION
  - PARA-AMINO PHENOL DERIVATIVE
    - [PARACETAMOL (Acetaminophen)]
  - BENZOXAZOCINE DERIVATIVE
    - [NEFOPAM]

M/A → ① NSAID blocks PG (prostaglandin) synthesis.

② Cytokines & other signal molecules at the site of inflammatn induce COX-2 enzyme (inducible isoform) COX-1 & (housekeeping function)

③ These enzymes act on arachidonic acid to produce enzyme prostacyclin (PGI_2) & thromboxane A_2 (TXA_2).

④ This leads to generation of PGs locally which mediate many inflamatory changes

CYTOKINE → COX-1/COX-2 ⟶ ARACHIDONIC ACID ⟶ PG

Most NSAID inhibit COX-1 & COX-2 nonselectively bt now some selective COX-2 inhibitors have been produced.

ASPIRIN inhibits COX irreversibly, return of cox activity depends on synthesis of fresh enzyme.

Other NSAIDs r competitive & reversible inhibitors of COX, return of activity depends on their dissociat^n from enzyme (depending on pharmacokinetic characteristic of comp.)

USES of NSAID –

1) **Analgesia** – Blocks the pain sensiting mechanism by inhibiting COX-2 primarily. It constitute peripheral component of analgesic action. ∴ more effective against inflamat^n associated pain.

2) **Antipyretic** – It lowers body temp. in fever, but do not cause hypothermia in normothermic individual

Fever during infect^n & tissue injury is produced thru the generat^n of pyrogens including ILs, TNFα, interferons etc vich induce PGE_2 product^n in hypothalamus & raise its temp set point.

NSAID block the action of pyrogen bt not dat of PGE_2 injected in hypothalamus

3) **Antinflammatory** → The most imp. mechanism of antinflamatory action of NSAID is inhibition of COX-2 mediated enhanced PG synthesis at site of injury. Inhibition of cox-1 also contributes to supression of inflamat^n, espacially in initial stages. *(Nimusulide is potent antinflamatory bt weak COX inhibitor)

[* Inflamat^n is result of participat^n of large no. of vasoactive, chemotactic & proliferative factors at diff. stages & there r many target for antinflamatory action. Activated endothelial cells express adhesion mol. [ELAM-1, ICAM-1] on their surface & play a key role in directing circulating leucocytes to the site of inflam (chemotaxis).