Anti-inflammatory agents

NSAIDS – Classification

1. Asprin
2. Non-acytylated salicylates – anti-inflammatory actions, less COX inhibition and analgesia than asprin
3. COX 2 selective inhibitors – celecoxib, meloxicam
    1. Half the GI side effects, same analgesia and anti inflammatory
    2. Don't effect platlet function at normal doses
    3. Can increase incidence of edema and HTN and associated with increased incidence of thrombotic vascular events
    4. Renal toxic
4. Non selective COX
    1. Diclofenac – used as post surgical eye drops for inflammation
    2. Ibuprofen – closes PDA in preterm babies, causes less fluid retention and decreased urine output when compared to indomethacin
    3. Indomethacin – reduce neutrophil migration, lower T and B cell proliferation, inhibits phospholipase A and C. Probenecid prolongs indomethacin half life

Paracetamol

- Analgesic and anti-pyretic with no significant anti inflammatory properties
- Weak COX 1 and 2 inhibitor
- Pharmacokinetics
  - A: PO administration, absorption related to rate of gastric emptying – peak blood concentration 30 – 60 minutes
  - D: Slightly bound to plasma proteins
  - M: Hepatic metabolism to inative metabolites → sulphate and glucuronides, T1/2 is 2 – 3 hours (can double in toxicity)
  - E: Less than 5% is excreted unchanged

Paracetamol

- Toxicity
  - 10g/24 hours of 200mg/kg
  - Can cause severe hepato toxicity and associated renal tubular necrosis
  - N/V/D and abdominal pain are usual symptoms
  - Normal hepatic conjugation pathways become saturated – toxic metabolite NAPQ accumulates and cause oxidative liver damage
  - 4^{th} hour paracetamol levels and commencement of NAC which replaces glutathione

Paracetamol metabolism pathway

Paracetamol normogram

Colchicine

- Pharmacokinetics:
  - A: Good bio-availability, peak plasma levels in 2 hours
  - D: Low Vd
  - M: Hepatic
  - E: GIT and urine
- Pharmacodynamics:
  - No change in urate levels
  - Binds to intracellular protein tubulin → prevents polymerisation into microtubules → and inhibits leukocyte migration and phagocytosis
  - Also inhibits leukotriene B4 synthesis
  - Relieves pain and inflammation from gout within 12 – 48 hours
- Side effects: Diarrhoea, nausea, vomiting, abdominal pain
- Overdose: Burning throat pain, fast ascending CNS depression

Allopurinol

- Used for gout prophylaxis
- Reduced total uric acid body burden by inhibiting Xanthine oxidase (allopurinol metabolised by XO but the metabolite alloxanthine inhibits XO)
- Can precipitate gout – so need cover with cholchicine or NSAID when commencing
- Pharmacokinetics:
  - A: 80% after oral administration
- S/E: GI upset, nausea, vomiting, diarrhoea, 3% get allergic maculopapular rash, necrotising vasculitis, aplastic anaemia – all areas
- Need to dose reduce chemotherapeutics when given concurrently – target uric acid level below 6mg/dL