Anti-inflammatory drugs

NSAIDS (non-steroidal Anti-inflammatory drugs)

① Non-selective COX inhibitors inhibits both COX-1 COX-2

- Salicylic acid derivative : Aspirin
- Acetic acid derivatives : Indomethacin, sulindac, etodolac
- propionic acid derivates : ibuprofen, ketoprofen, naproxen fenoprofen
- Fenamates : Mefenamic
- Oxicams : piroxicam, meloxicam
- Miscellanous : Heteroaryl acetic acids diclofenac, tolmetin ketorlac

② Selective COX-2 inhibitors

Celecoxib

③ Central effect (CNS)

Acetaminophen - panadol

Aspirin (Acetyl salicilyc Acid)

• kinetics (Absorption)
Acid → well absorbed in the stomach

Dual Route of elimination
two routes of elimination according to concentration
① First order elimination – therapeutic dose
② zero order elimination - overdose

Increase in elimination by Alkalization of urine. ← Elimination by kidneys

MOA: COX inibitor – COX-1 Side effects ✗
COX-2 inflammation ✓

↓ [PG] prephiral & centrall
↓ V.D ↓chemotaxis ↓ immune cell activation
Effects: ① Anti-inflammatory endgenous pyrogen
② Anti-pyretic ↓PG-E2 ↓IL-1 cut. VD
③ limits the spread of infections

change

pH → HCO_3 --- metabolic

pH → CO_2 --- Respiratory

① Respiratory ~~Acidosis~~ Effects

Aspirin increases the excretion of HCO_3 Metabolic acidosis which induces Respiratory center to release CO_2 ⟶ Hyperventilation, Respiratory alkalosis

High toxic dose → patients die due to respiratory + metabolic Acidosis

∴ depending on the dose Aspirin can cause Metabolic Acidosis, Respiratory alkalosis Respiratory acidosis

But never Metabolic Alkalosis

② cardio - no effects

③ G.I.

→ Acute gastric ulcer, stomach burn Empty stomach (Ion trap)

→ chronic peptic ulcer prolonged use

caused by natural stomach HCl; Attack thin mucosa due to prolonged inhibition of PG_1-E_1, E_2

→ Reye's syndrome - necrosis in brain & liver in children that take aspirin

④ Hematologic effects

→ prevents platelets aggregation ↓ TXA_2

- low dose aspirin (75 mg) is given as anti-thrombotic to patients who are susceptible to thrombosis ↓ platelets adherens inhibition ↓ inhibits ADP release by platelets
- it inhibits TXA_2 produced by platelets while maintaining PGI_2 of endothelium ← more sensitive

irreversible effect of Aspirin on COX causes damage that stays till the end of ½ of platele life

this is the reason why Aspirin is stopped a week prior to surgery

⑤ kidneys - Analegesic nephropathy (NSAIDS)

PE_2, PE_1 ⇒ Regulate Renal blood flow

↓ PGIs ↓ Renal blood flow ↑ Renin-Angiotensin as a compensatory reflex

Salt & water retention

contraindication

diuretics, beta-blockers

Contraindications for using Aspirin

⇒ Gout; Hyperurecimia ↑ uric acid
Acute Attack of gout

75-150 mg - anti thrombotic dose
doesn't affect the uric acid
cardiovascular disease + Gout on low dose
no problem :)

(b) Metabolic effect of aspirin
→ uncoupling of oxidative phosphorylation
at toxic doses
O_2 ⇏ ATP
O_2 → Hyperthermia

Uses of Aspirin

1. Analegesic
2. Anti-pyretic
3. Anti-rheumatic
4. Anti-thrombotic 75-150 mg
   - Hypertension + end organ damage
   - cardiovascular disease
     - ↳ transient ischemic attack
       ischemic heart disease
   - Hypertension, 50 years, DM
   - 10 years - C.V. Risk score above than 20%
5. Keratolytic
   for warts
   ↗ salicilyc acid
   additive
6. couter - irritant

Adverse effects

1. G.I ulcers
2. liver → mild Hepatic injury
   ~~→ Reye syndrome~~
3. uterus
   prolonged labor
   due to ↓PG1
   no contractions
4. Blood - thinning
5. Hyper-sensitivity Rxn
   aspirin-induced asthma
   Acute Attack, broncho constriction
   ↓leukotrien B4

Contraindications

1. Gastric ulcers
2. Hemophilia, hemoragic blood disease
3. surgery / recent operation
4. severe hypertension - fatal bleeding
5. children
6. 3rd trimester / near full term pregnant women

Drug - Drug interactions

1. Beta - blockers, loop diuretics
2. prednisone - Gout
3. Anti - acids chemical complex w/ drugs
4. plasma protein bound drugs e.g warfren

Acute Aspirin toxicity

Symptomps: hyperpyrexia
Metabolic acidosis - Hyperventilation
tachypnoea
Earliest sign

Treatment:
- Gastric lavage غسيل معدة
- IV fluids + Bicarbonates for dehydration
- vitamin k IM, slow IV to regenerate the clotting factor + stop bleeding
- Hemodialysis 100 mg/dl of aspirin

Diclofenac → voltaren
More nephrotoxic, less gastic irritant than aspirin

*propionic Acid derivates:
ibuprofen, naproxen, fenoprofen, ketoprofen
↓ nephrotic syndrome

Indomethecin
pore potent than aspirin not give
Most toxic; neurotoxicity ⇝ Epilepsy, CNS
Ductus arteriosus Indomethecin closes this open Artery

Dysmenorrhea: painful menstural symptomps
Indomethecin is the wort preferred drug to treat dysmenorrhea
Best options: diclofenac, ibuprofen, ketoprofen

Oxicam

piroxicam – long half-life 36h
same side effects as aspirin

selective COX-2 inhibitors

celecoxib — less G.I irritant
Renal injury
C.V. increases TXA_2
and platelet aggregation
→ thrombosis, clots