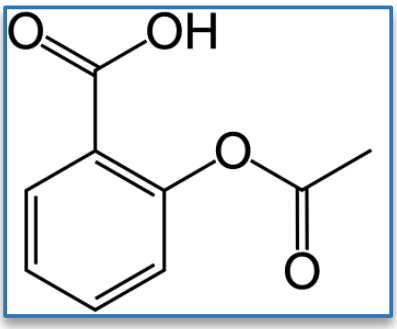
NSAIDs

Celecoxib, Diclofenac, Ketoralac



Mechanism of Action

1. Most NSAIDs are non-selective COX-1 and COX-2 inhibitors
    - COX-1 – "Housekeeping" enzyme, regulates normal cellular processes, expressed in most tissues
    - COX-2 – Expressed in brain, kidney, and bone. Increased during states of inflammation
2. Selective COX-2 inhibitors thought to target inflammation with reduced toxicity
3. Similar analgesia effect, reduced gastroduodenal toxicity, minimal effect on platelets, low-risk for bronchospam in aspirin-induced asthma

Dosing

Celecoxib
- 400 mg initial dose or 200 mg BID
- Patients with indications for cardioprotection require aspirin

Diclofenac
- 50 mg TID, or 100 mg initial dose
- Interacts with CYP2C9 drug metabolism
- Mostly COX-2 selective at recommended doses

Ketorolac (IV)
- 30 mg once, or 15-30 mg q6h, maximum 120 mg/day for five days

Duration

Generally can be divided into "short-acting" and "long-acting"

Short-acting (< 6 hours)	Long-acting (>6 hours)
• Ibuprofen • Diclofenac • Ketorolac • Indomethacin	• Naproxen • Celecoxib • Meloxicam

Opioid Reduction

- Meta-analysis of 52 RCTs demonstrated Ketorolac reduced opioid consumption by **25-45%** thereby reduced opioid side-effects of ileus, nausea, vomiting
- Cochrane review reported that Celecoxib delays and decreases the need for rescue opioid analgesics without significant side effects

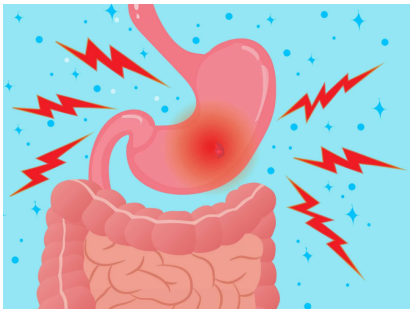
*Ketorolac has ***not*** been associated with an increase in postoperative bleeding
- Meta-analysis of 27 RCTs with 2,314 patients showed postoperative bleeding was not significantly increased with ketorolac (pain control was also found to be superior compared to controls!)

NSAIDs – Adverse Effects

Gastrointestinal
- Mild: Dyspepsia, nausea
- Severe: Strictures, ulcers
- Risk increased by prior hx of GI event, age >60, high dose of NSAID, concurrent use of glucocorticoids or antiplatelet agents

Renal
- Can precipitate both acute and chronic renal failure
- Higher risk in pts with HTN, DM, or HF and those taking diuretics, ACE inhibitor, or aminoglycosides

Cardiovascular
- COX-2 vs COX-1 risk controversial, however most NSAIDs shown to have some cardiac risk
- Risk increased (RR of 1.44) with high frequency (>22 days/month) or dose. More moderate use did not confer substantial risk



References:
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