Pain Module

Section 2 Treatment
Pharmacologic
Non Steroidal Anti-inflammatory Drugs (NSAIDs)
NSAIDs
Examples

• aspirin
• ibuprofen (Advil, Motrin, Caldolor--IV form)
• naproxen (Aleve, Naprosyn)
• indomethacin (Indocin)
• ketoprofen (Orudis)
• ketorolac (Toradol)
• meloxicam (Mobic)
• diflunisal (Dolobid)
• piroxicam (Feldene)
• sulindac (Clinoril)
• tolmetin (Tolectin)
• nabumetone (Relafen)
• choline magnesium trisalicylate (Trilisate)
• celecoxib (Celebrex)
How do NSAIDs reduce pain?

- NSAIDs work at the site of injury by inhibiting the cyclo-oxygenase 2 (COX-2) enzyme which produces the pain/inflammation/fever-promoting prostaglandins.

- Unfortunately, nonselective NSAIDs also inhibit the COX-1 enzyme which produces prostaglandins that protect the stomach and intestinal lining, help the blood to clot, and support renal function. The more a NSAID blocks COX-1, the greater is its tendency to cause ulcers and promote bleeding.
COX-2 Inhibitor NSAID--celecoxib

• A selective NSAID, celecoxib (Celebrex), blocks COX-2 but not COX-1 thus reportedly causing fewer side-effects e.g., less platelet effects and fewer ulcers (although GI effects increase with longer duration of therapy).

• Celecoxib is the only COX-2 inhibitor available in the U.S. Rofecoxib (Vioxx) and valdecoxb (Bextra) were withdrawn because they reportedly caused increased risk of heart attacks and strokes with long term use.

• Celecoxib, while it has fewer side-effects than the nonselective NSAIDs, is no more effective as an analgesic and is more expensive.
NSAIDs: Indications and Advantages

- More effective than are opioids for pain caused by inflammation e.g., fractures, soft tissue trauma, incisions, post-op pain, toothaches, menstrual cramps, arthritis, renal & biliary colic, some headaches, cold and flu symptoms.
- Synergistic with opioids e.g., less opioid is needed.
- Most forms inexpensive.
- Many forms available without prescription.
- Variety of routes—PO, IV, IM, rectal, topical preparations.
- Low drug abuse potential although some people eat NSAIDs like candy.
General Information about NSAIDs

• Ceiling effect (cannot keep increasing NSAID dose without life-threatening side-effects).
• It is impossible to predict which NSAID will be best tolerated by a particular patient.
• No one NSAID has demonstrated superiority over others for pain relief.
• Marked individual variation in response. In other words, a particular NSAID may be very effective for one person, yet be ineffective for another.
• Marked variation in side-effects from one person to another.
• Drug-to-drug variation in toxicities partly determined by COX-1 selectivity e.g., some NSAIDs are known to cause more gastric distress and bleeding than others e.g., ketorolac.
• Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals.
• Be aware of possible drug interactions e.g., anticoagulants, antihypertensives.
NSAIDs: Potential Side-Effects and Toxicities

- Diarrhea
- Dyspepsia
- Abdominal pain
- Hypertension
- Fluid retention & edema
- Bronchospasm
- Gastric & duodenal ulcers
- Perforation and hemorrhage of the esophagus, stomach, and the small or large intestine.
- Renal papillary necrosis & insufficiency
- Liver damage

- Severe or fatal allergic reactions
- Serious skin reactions e.g., exfoliative dermatitis, Stevens-Johnson Syndrome, & toxic epidermal necrolysis.
- Cardiovascular thrombotic events, myocardial infarction, and stroke. Research has shown that COX-2 NSAIDs are associated with increased cardiovascular risk. There is a huge, multi-state, clinical trial (PRECISION) underway to help clarify this issue.
Risk Factors for NSAID-Related Side-Effects

- Prior history of GI ulcer
- High doses and chronic use of NSAIDs
- Concurrent use of two or more NSAIDs
- History of an allergic reaction to NSAIDs
- Asthmatic
- Smoker
- Older age
- Combination with steroids, blood thinners, or alcohol
- Impaired renal function, heart failure, liver dysfunction.
- Hypertension (NSAIDs increase blood pressure)

Because many NSAIDs are available without a prescription, people may believe the drugs are harmless.

Potentially life-threatening side effects can occur at any time during therapy, most often without any warning signs.
Contraindications

NSAIDs are contraindicated in the following situations:

- Known allergies to sulfa drugs, aspirin or any NSAIDs.
- Hx of peptic ulcers.
- Treating pain right before or after coronary artery bypass graft surgery (possible pro-thrombotic action of certain NSAIDs).
- Organ disease—cardiac, renal, liver.
- Pregnancy, especially late in the term because they may cause premature closure of the fetal ductus arteriosus. Additionally, NSAIDs may cause renal problems in the fetus and are linked with premature birth and miscarriage.
Ketorolac (Toradol)

- No more potent than other NSAIDs, but is available in a parenteral form for patients who are NPO.
- PO Toradol not recommended-- is more expensive and no more effective than PO ibuprofen.
- IM injection considered painful.
- Maximum IV dose 30 mg. Can burn the vein. Dilute and administer slowly.
- The duration of ketorolac (Toradol) is not to exceed 5 days (regardless of route of administration) because doing so will likely increase the frequency and severity of toxicities.
Bleeding and NSAIDs

• Aspirin is the only NSAID that inhibits the clotting of blood for the life of the platelet (4 to 7 days).
• Other NSAIDs inhibit platelet aggregation only during the time the drug is in the systemic circulation. Note that Cox-2 inhibitors (Celecoxib) do not affect platelets.
• Patients with stents and/or cardiac disease, who are receiving aspirin or other anticoagulant therapy to prevent blood clot formation, may be subject to emboli formation if the aspirin or anticoagulant is stopped abruptly. Patients having surgery must discuss with their doctor if they are to stop their aspirin or anticoagulant and if so, for how many days prior to surgery.
GI Ulcer Prevention

• Enteric-coated NSAIDs, food, or antacids do not protect the patient from the risk of systemic side effects, although taking NSAIDs with food, an antacid, and sitting upright for 30 minutes will help decrease the local gastric effects of the NSAID.

• A cytoprotective agent is recommended for individuals who will benefit from an NSAID, but who also have a high GI risk factor profile. Misoprostol (Cytotec), sucralfate, proton pump inhibitors, and H2-receptor antagonists are effective at reducing the risk of NSAID-induced ulcers. Note that misoprostol should not be taken by women who are pregnant because the drug could cause a miscarriage, premature birth or birth defects. **Patients who are prescribed misoprostol** must be warned not to give the drug to others.
Patient/Family Education

NSAIDs should only be taken:
• exactly as prescribed
• at the lowest dose possible
• for the shortest time needed
• with food

Avoid taking multiple medications that contain the same active ingredient. Read the label! Many products contain a NSAID.

Do not take an NSAID if hx of asthma attack, hives, or other allergic reaction with aspirin or any other NSAID medicine.

NSAIDs should not be taken with alcohol, as the combination can increase the risk of GI bleeding.

These medicines should never be used right before or right after coronary artery bypass graft surgery.
Patient/Family Education

• Get emergency help right away for the following symptoms: shortness of breath or trouble breathing, slurred speech, chest pain, swelling of the face or throat, weakness in one part or side of the body, or any other emergent type symptoms.

• Call doctor for nausea, vomiting of blood, more tired or weaker than usual, bloody or tarry stools, jaundice, unusual weight gain, stomach pain, skin rash or blisters with fever, flu-like symptoms, swelling of the arms and legs, hands and feet.

These are not all the possible side effects of NSAIDs.