OTC Pain Management

University of Hawai‘i Hilo Pre-Nursing Program
NURS 203 – General Pharmacology
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Objectives

- Understand the definition of pain and the components of that definition
- Know the MOA for OTC pain medication
- Know the major ADRs & interactions of OTC pain medications
- Know indication for OTC pain medications
Overview

- NSAIDS
  - Ibuprofen
  - Aspirin
  - Naproxen
- Acetaminophen
- Combinations
  - Excedrin®
- Topical
  - Menthol
  - Capsaicin
Pain

- What is pain?
  - Pain is made up to 2 components
    - Physical – sensation of pain
    - Psychological – emotional reaction to that sensation

OMG! I can’t believe I just did that. Ow! That really hurts….I wonder if I broke my thumb. *%@%# am I gonna have to go to the doctor? I can’t miss anymore work this year…….
Physical component

- **Nociceptors**
  - Nerve cell ending that initiate the sensation of pain
  - Frequency of firing (action potentials) determines the intensity of the pain

- **Prostaglandins**
  - Important local hormones important in the sensation of pain
  - PGE2 – vasomotor tone, capillary permeability, smooth muscle tone, platelet aggregation, endocrine & exocrine functions, and CNS
Inflammatory cytokines

- Cytokines (Histamine)
  - Lipoxygenase
    - LTB4
      - Attracts Neutrophils
  - Phospholipase A2
  - Arachidonic Acid
  - Cyclooxygenase
  - COX 1&2
  - Others
  - PGE2
    - Fever & Pain
    - Others
  - Arterial dilation/Increased venule permeability
  - Bronchoconstriction
  - Attracts Neutrophils
  - Others
Psychological component

- Age
- Gender
- Anxiety/Emotions
- Experiences
- Culture

OMG! I can’t believe I just did that. Ow! That really hurts….I wonder if I broke my thumb. *@%# am I gonna have to go to the doctor? I can’t miss anymore work this year…….
Emotions Involved in Tolerance

- Anxiety
- Depression
- Anger
- Fear
Which is **TRUE** of pain/pain management

- A patient’s perception of chronic pain can be paired with vital sign changes
- Severe chronic pain cannot be effectively controlled
- Opioids are addictive and a treatment of last resort because of unmanageable adverse effects
- The goal of chronic pain management is to keep the dose of medication as low as possible
- Studies show that women are at a greater risk of being undermedicated for pain
Which is **true** of pain/pain management

- A patient's perception of chronic pain can be paired with vital sign changes
- Severe chronic pain cannot be effectively controlled
- Opioids are addictive and a treatment of last resort because of unmanageable adverse effects
- The goal of chronic pain management is to keep the dose of medication as low as possible
- Studies show that women are at a greater risk of being undermedicated for pain
Treatment of Pain

- Ibuprofen
Ibuprofen – Advil/Motrin

- MOA - **Reversibly inhibits cyclooxygenase-1 and 2 (COX-1 and 2) enzymes**, which results in decreased formation of prostaglandin precursors; has antipyretic, analgesic, and anti-inflammatory properties. Other proposed mechanisms not fully elucidated (and possibly contributing to the anti-inflammatory effect to varying degrees), include inhibiting chemotaxis, altering lymphocyte activity, inhibiting neutrophil aggregation/activation, and decreasing proinflammatory cytokine level.
Ibuprofen

- **Kinetics**
  - Onset – 30-60 minutes (oral)
  - Duration 6-8 hours
  - Highly protein bound (>99%)
  - Metabolized – liver
  - Excreted – urine (only 1% unchanged drug)

- **ADRs**
  - Epigastic pain, heartburn, & nausea (take with food)
  - Tinnitus
  - CV – edema & fluid retention

- **Pregnancy**
  - Not recommended

- **Interactions**
  - Anticoagulants, ACEI & ARBs, & others
Aspirin

- MOA - Irreversibly inhibits cyclooxygenase-1 and 2 (COX-1 and 2) enzymes, via acetylation, which results in decreased formation of prostaglandin precursors; irreversibly inhibits formation of prostaglandin derivative, thromboxane A\(_2\), via acetylation of platelet cyclooxygenase, thus inhibiting platelet aggregation; has antipyretic, analgesic, and anti-inflammatory properties.
Aspirin

- **Kinetics**
  - Absorbed – Rapid
  - Duration – 4-6 hours
  - Distributes – into most fluids & tissues readily
  - Metabolized – liver
  - Excreted - Urine

- **ADRs**
  - Bleeding
  - CV – edema, arrhythmia, hypotension
  - GI – ulcer, heartburn, nausea, stomach pain

- **Pregnancy**
  - Not recommended

- **Interactions**
  - Anticoagulants, ACEI & ARBs, other salicylates
Naproxen - Aleve

- MOA - Reversibly inhibits cyclooxygenase-1 and 2 (COX-1 and 2) enzymes, which results in decreased formation of prostaglandin precursors; has antipyretic, analgesic, and anti-inflammatory properties. Other proposed mechanisms not fully elucidated (and possibly contributing to the anti-inflammatory effect to varying degrees), include inhibiting chemotaxis, altering lymphocyte activity, inhibiting neutrophil aggregation/activation, and decreasing proinflammatory cytokine levels.
Naproxen

- **Kinetics**
  - Duration - >12 hours
  - Onset – 30-60 minutes
  - Protein binding - >99%
  - Half life – 12-17 hrs (increased in renal impairment)
  - Metabolized – liver
  - Excreted - Urine

- **ADRs**
  - CV – edema
  - Dizziness, drowsiness, HA
  - Bruising, itching, & rash
  - Tinnitus
  - Shortness of breath

- **Pregnancy**
  - Not recommended

- **Interactions**
  - Anticoagulants, ACEI & ARBs, others
Acetaminophen - Tylenol

- MOA - Although not fully elucidated, believed to inhibit the synthesis of prostaglandins in the central nervous system and work peripherally to block pain impulse generation; produces antipyresis from inhibition of hypothalamic heat-regulating center

- Theories
  - COX inhibitor
  - Endocannabinoid
  - Serotonin
Acetaminophen

- **Kinetics**
  - Onset - < 1hr
  - Duration 4-6 hrs
  - Protein binding only
    10-25% at therapeutic doses (> at toxic)
  - Metabolism – glucuronidation & CYP2E1
  - Half life – changes with age & renal fx
  - Excretion - urine

- **ADRs**
  - Nausea & vomiting
  - Rash & hypersensitivity
  - Generally well tolerated

- **Pregnancy**
  - Recommended

- **Interactions**
  - Minor
  - Avoid in EtOH abuse & liver disease
**Acetaminophen**

- **Kinetics**
  - Onset - < 1 hr
  - Duration 4-6 hr
  - Protein binding - 10-25% at therapeutic doses, > at toxic levels
  - Metabolism - glucuronidation & CYP2E1
  - Half life - changes with age & renal fx
  - Excretion - urine

- **ADRs**
  - Nausea & vomiting
  - Rash & hypersensitivity

- **Pregnancy**
  - Recommended

- **Interactions**
  - Minor

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**This is important!!!**

**ADULT PATIENTS MUST NOT EXCEED MORE THAN 4 GRAMS IN 24 HOURS.**

Accumulation of a dangerous metabolite via the CYP2E1 route. (NAPQI)

Glucuronide metabolism is saturable.

- Liver damage
- Liver failure
- Death

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**WAIT!!!**

Acetaminophen is a pain-relieving medication often used for fever reduction and pain relief. It is commonly found in over-the-counter (OTC) products. The term “Acetaminophen” is also used to refer to the active ingredient in many OTC pain relievers and fever reducers.

**Kinetics**
- **Onset**: Acetaminophen typically begins to take effect within minutes to 1 hour after oral administration.
- **Duration**: The duration of action for Acetaminophen is generally 4 to 6 hours.
- **Protein Binding**: The extent of protein binding for Acetaminophen is variable and depends on the dose and the therapeutic range. At therapeutic doses, 10-25% of the drug is bound to plasma proteins, while at toxic levels, the binding increases significantly.
- **Metabolism**: Acetaminophen is primarily metabolized in the liver through glucuronidation and to a lesser extent by cytochrome P450 enzymes (CYP2E1).
- **Half-life**: The half-life of Acetaminophen varies with age and renal function, with older adults and those with renal impairment having a longer half-life.
- **Excretion**: Acetaminophen is excreted primarily in the urine.

**ADRs**
- Nausea and vomiting
- Rash and hypersensitivity

**Pregnancy**
- Acetaminophen is generally considered safe during pregnancy, but as with all medications, it should be used cautiously and under the guidance of a healthcare provider.

**Interactions**
- Minor interactions may occur, but they are generally not clinically significant.

**Important Note**: **ADULT PATIENTS MUST NOT EXCEED MORE THAN 4 GRAMS IN 24 HOURS.** The risk of liver damage increases with higher doses and prolonged use. Acetaminophen overdose can lead to severe liver damage, liver failure, and death.

**Glucuronidation**: Glucuronidation is a phase II metabolic process that involves the conjugation of a drug with glucuronic acid. It is a major mechanism of detoxification for many drugs, including Acetaminophen. Glucuronidation is also a saturable process, meaning that as the body becomes more saturated with glucuronic acid, the rate of conjugation decreases, potentially leading to accumulation of toxic metabolites.

**CYP2E1**: Cytochrome P450 2E1 (CYP2E1) is an enzyme involved in the metabolism of various drugs and toxins. In the case of Acetaminophen, CYP2E1 is responsible for the metabolism of a dangerous intermediate, N-acetyl-p-benzoquinone imine (NAPQI), which can cause liver damage if not detoxified properly.

**Liver Damage**: The liver plays a crucial role in detoxifying medications. Damage to the liver can result in impaired metabolism of Acetaminophen, leading to increased levels of NAPQI and potentially severe liver injury. This is particularly concerning at toxic levels of Acetaminophen ingestion, where the risk of liver damage is significantly increased.

**Liver Failure**: Chronic liver disease can affect the ability of the liver to metabolize Acetaminophen, increasing the risk of liver injury. Patients with liver disease should use Acetaminophen cautiously, and the dosage should be adjusted accordingly.

**Death**: Acetaminophen overdose is a medical emergency, and prompt treatment is necessary to prevent serious complications, including liver failure and death.
Excedrin – acetaminophen, aspirin, & caffeine

- MOA – Caffeine – adenosine antagonist/sympathomimetic/cerebral vasoconstriction

Amounts of dopamine & norepinephrine
Excedrin

- Indications
  - Minor aches & pains
  - Headache (migraine)

- Administration
  - Take with food to avoid GI upset

- Dosing
  - Available with different strengths of each component

- ADRs
  - GI upset, hepatotoxicity, hypersensitivity, & skin reactions
  - Rebound headache

- Interactions
  - Similar to individual components
    - Anticoagulants, ACEI & ARBs, etc.
Topicals

- Menthol
- Capsaicin
Topicals

- Menthol
  - When applied to the skin, menthol dilates the blood vessels, causing a sensation of coldness followed by an analgesic effect. It relieves itching and is used in creams, lotions, or ointments in pruritus and urticaria. It has also been applied to the forehead, presumably as a counter-irritant, for the relief of headache.

- Capsaicin
  - Causes depolarization of nociceptive nerve fibers, initiation of action potential, and pain signal transmission to the spinal cord; capsaicin exposure results in desensitization of the sensory nerve and inhibition of pain transmission initiation. In arthritis, capsaicin induces release of substance P, the principal chemomediator of pain impulses from the periphery to the CNS, from peripheral sensory neurons; after repeated application, capsaicin depletes the neuron of substance P and prevents reaccumulation. The functional link between substance P and the capsaicin receptor, TRPV1, is not well understood.
Topicals

- Menthol
- ADRs
  - Local
    - Contact dermatitis
  - Systemic
    - Toxic if too much consumed – severe abd pain, N&V
- Interactions
  - No known drug interactions

- Capsaicin
- ADRs
  - Local
    - Redness & pain
  - Systemic
    - Some – well tolerated
- Interaction
  - No known drug interactions
Questions

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