Disclosures

Bonnie Morgan has no real or perceived conflicts of interest that relate to this presentation.

Objectives

1. Recognize principles of effective pharmacological pain management.
2. Recognize principles of effective nonpharmacological pain management.
Categories of Analgesics

**Opioids**
- Morphine
- Oxycodone
- Fentanyl
- Hydromorphone
- Methadone
- Hydrocodone
- Tramadol

**Adjuvants/Co-Analgesics**
- Corticosteroids
- Anticonvulsants
- Antidepressants
- Topical agents

**Non-Opioids**
- Acetaminophen
- NSAIDs/Aspirin

**Opioids to Avoid**
- Mixed agonist–antagonists
- Meperidine
- Codeine

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**Acetaminophen**
- Analgesic, antipyretic actions, no anti-inflammatory effect
- Routes: oral, rectal, IV
- Maximum daily dose: 4000 mg (U.S. FDA, 2011)
- Reduced doses or avoidance in the following:
  - Hepatic insufficiency
  - History of significant alcohol use
  - Elderly
- May be present in other medications

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**Nonsteroidal Anti-inflammatory Drugs (NSAIDs)**
- Actions – analgesic, antipyretic, anti-inflammatory
- Non-selective and selective Cox-2 inhibitors
- Adverse effects
  - Gastrointestinal (GI), renal, inhibits platelet aggregation
  - Cardiovascular effects, hypersensitivity reactions
  - Central nervous system (CNS) effects
  - Dose escalation is limited by analgesic ceiling
**Opioid Types**

- Types
  - Pure agonists
  - Antagonists
  - Partial agonists
  - Mixed agonist-antagonists
- Action – bind to receptors in the brain, spinal cord and peripheral nervous system

**Common Opioids**

- Morphine
- Codiene
- Hydrocodone
- Oxycodone
- Fentanyl
- Methadone
- Tramadol

**Constipation**

- Most common side effect of opioids; principle reason they are stopped
- Prevention is the goal
- Opioids delay gastric emptying
- Bowel regimen: NECESSARY!!!
- Assess frequently
- Use combination of laxative (stimulant) and a stool softener
- Methylnaltrexone (Relistor)
  - Opioid receptor agonist

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Nausea & Vomiting/Pruritis

- Nausea and Vomiting
  - Stimulation of chemoreceptor trigger zone (CTZ), ↓ GI motility, vestibular imbalance
  - Treatment – may need antiemetic initially
  - Tolerance usually develops in a few days

- Pruritus
  - Due to associated histamine release; common with morphine
  - May be generalized, usually localized to face, neck, chest
  - Usually not accompanied by rash
  - Treatment – antihistamine
  - Tolerance usually develops in a few days

Sedation

- Greatest risk when opioids are started or dose increased
- Tolerance will occur over period of days to weeks
- Caution in patients with sleep apnea or renal failure and the elderly

Respiratory Depression

- Rare occurrence
- Sedation precedes respiratory depression
- Tolerance develops rapidly with steady dose
- Risk factors
  - Sleep apnea with obesity
  - Concomitant use of benzodiazepines or sedatives
  - Chronic lung disease
  - Elderly
- Reducing risk
  - Titrate appropriately
  - Monitor for sedation
  - Avoid administration of two or more sedating drugs
  - Educate patient and caregivers
Opioid Active Metabolites

- Meperidine
  - Should not be used due to active metabolite that can cause seizures
- Morphine and hydromorphone
  - Active metabolites excreted by the kidney
  - Accumulate in the elderly and those with renal dysfunction

Opioid-Induced Neurotoxicity

- Myoclonic jerking more common with high-doses and prolonged use
- Associated with metabolite accumulation in presence of renal dysfunction
- Frequently missed in assessments
  - Unusual/unpredictable painful sensations
  - Pain out of proportion to disease condition
  - Pain continues despite increasingly higher opioid doses
  - Sudden decreased level of consciousness (LOC), or confusion/hallucinations
- Treatment
  - Benzodiazepines, switching opioids, hydration

<table>
<thead>
<tr>
<th>Routes of Administration</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td>Least invasive, safest, use when patient can swallow</td>
</tr>
<tr>
<td>Rectal/Intrastomal</td>
<td>Bioavailability varies based on individual absorption; do not use with anal lesions, diarrhea, thrombocytopenia, or neutropenia</td>
</tr>
<tr>
<td>Parenteral</td>
<td>IV/subcutaneous; severe pain requiring rapid titration</td>
</tr>
<tr>
<td>Transmucosal</td>
<td>Buccal or sublingual delivery; lipophilic drugs more easily absorbed; usually liquid; hydrophilic opioids mostly swallowed and absorbed in GI tract</td>
</tr>
<tr>
<td>Transdermal</td>
<td>Fentanyl is most common; delayed onset of action (12-24 hours); do not use in opioid-naive patient</td>
</tr>
<tr>
<td>Epidural/intrathecal</td>
<td>Severe uncontrolled chronic pain especially in lower extremities; cost, care issues, and potential adverse effects must be weighed</td>
</tr>
<tr>
<td>Intramuscular (IM)</td>
<td>Not Recommended</td>
</tr>
</tbody>
</table>
Adjuvants for Analgesia

- Drugs with other indications that may be analgesic in specific circumstances
- Often used for chronic neuropathic pain
- May be a coanalgesic to opioids
- Less often may be primary therapy
- Multimodal therapy for mixed pain syndromes

<table>
<thead>
<tr>
<th>Antiepileptic Drugs</th>
<th>Major Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gabapentin</td>
<td>Sedation, ataxia, dizziness, dependent edema</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>Similar to above; may use lower doses</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Bone marrow depression, vertigo; requires serum monitoring, costly</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Ataxia, rash, hepatotoxicity; requires serum monitoring</td>
</tr>
<tr>
<td>Valproic acid</td>
<td>Nausea and vomiting (N/V), sedation, ataxia, thrombocytopenia, neutropenia; requires serum monitoring</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>Sedation, physical dependence; useful for anxiety associated with pain</td>
</tr>
</tbody>
</table>

Antidepressants

- Tricyclic antidepressants
  - Amitriptyline – not recommended – anticholinergic side effects
  - Desipramine and nortriptyline – most recommended
    - Start with low dose at bedtime – may cause sedation and enhance sleep
    - Increase by 10-25 mg every few days based on patient response
    - May take 3-7 days to see effect; maximum dose of both drugs – 75-100 mg/day
    - Monitor adverse side effects – sedation, orthostatic hypotension, anticholinergic side effects – including urinary retention
  - Selective serotonin re-uptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs)
Other Adjuvants

- Local anesthetics
  - Lidocaine patch 5%
  - Lidocaine infusions
- Corticosteroids
  - Used in metastatic bone pain
  - Pain associated with liver metastasis

Opioid Equianalgesic Conversion

- Considerations for opioid rotation
  - Unacceptable side effects with current opioid
  - A change in route of administration is needed
  - The patient is on an opioid/non-opioid formulation and dose escalation is needed
- Use opioid equianalgesic dosing chart as a guide for converting from one opioid to another
- Incomplete cross tolerance
  - When converting from one drug to another AND pain is well controlled, consider reducing the dose by 25%
- Frequent reassessment and availability of breakthrough doses is essential

Equianalgesic Dosing Guide

<table>
<thead>
<tr>
<th>Drug</th>
<th>Parenteral Route</th>
<th>Enteral Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>10 mg</td>
<td>30 mg</td>
</tr>
<tr>
<td>Codeine</td>
<td>130 mg</td>
<td>200 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(not recommended)</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>50-100 mcg</td>
<td>TIRF</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>Not available</td>
<td>30 mg</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>1.5 mg</td>
<td>7.5 mg</td>
</tr>
<tr>
<td>Levorphanol</td>
<td>2 mg acute</td>
<td>4 mg acute</td>
</tr>
<tr>
<td></td>
<td>1 mg chronic</td>
<td>1 mg chronic</td>
</tr>
<tr>
<td>Methadone</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>Not available</td>
<td>20 mg</td>
</tr>
</tbody>
</table>
Equianalgesic Conversion Process

The equianalgesic conversion process is discussed in more detail in the Basic Opioid Conversion Calculations module, which is part of the CHPN Review Course.

Calculating Breakthrough Doses

- Always order a “rescue” dose with long-acting opioids
- Breakthrough short-acting doses should increase as long-acting opioids are increased
- Recommend 10-20% of total 24-hour opioid dose given q 1-2 hours
- Parenteral administration – give 50-100% of the hourly rate every 15 minutes for bolus dose
- Increase baseline dose if more than 3 rescue doses (oral) are used in 24 hours

Nonpharmacological Interventions

- Use concurrently with medications
- Physical modalities
  - Physical and occupational therapy
  - Heat, cold, exercise – passive or active range of motion
  - Transcutaneous nerve stimulation
  - Therapeutic touch, Reiki
Nonpharmacological Interventions

- Cognitive behavioral interventions
  - Relaxation, guided imagery, mindfulness, distraction
  - Pet therapy, creative arts, reframing
  - Hypnosis, counseling, prayer
  - Spiritual reflection, meditation
  - Patient and family education

Anticancer therapy

- Palliative radiation
  - Used to manage pain and other distressing symptoms
  - Bleeding, compression of vital organs, brain mets, ulcerating skin lesions
  - Treatment of choice for spinal cord compression, bone pain, superior vena cava (SVC) syndrome
  - External beam radiation most common; IV Strontium-89 may be used
- Palliative chemotherapy
  - Tumor shrinkage, reduction in organ obstruction
- Bisphosphonates to control pain in multiple myeloma or bony mets

Pain During the Final Days of Life

Nonverbal assessment

- Furrowed brow
- Guarding and vocalization
- Assume pain is present
  - Consider a trial of an opioid if opioid naive
  - If opioid tolerant, continue dose with adjustments as necessary
  - Change route
  - Renal dysfunction – decrease in renal clearance
    - Sedation may increase
Palliative Sedation

• Intractable suffering
• Medications
  - Benzodiazepines
  - Opioids
  - Barbiturates
  - Ketamine
  - Propofol

Pain Management Principles in Palliative Care

• Conduct a thorough assessment
• Document completely
• Provide continuity of care
• Reassess with every intervention

Pain Principles

• Oral route when possible
• Consider buccal, transdermal, sublingual, rectal prior to parenteral routes
• Avoid IM routes
• IV or subcutaneous routes for severe, escalating pain
• Subcutaneous route in home setting
Pain Principles

• Constant pain – use around the clock (ATC) dosing
  • Long acting opioid with short acting medication for breakthrough pain (BTP)
• Titrate based on patient’s self-report
• Use equianalgesic conversions when switching opioids and/or routes

Breakthrough Pain Principles

• Generally, increase if more than 3 rescue doses are needed in 24 hours
• BTP dose = 10 to 20% of the total 24 oral morphine equivalent dose
• Educate patients/families to take pain med when pain first starts, not when it has become unbearable
• Use nonpharmacologic approaches
• Manage constipation