BASICS OF OPIOID PRESCRIBING
10:30 - 11:45AM

ACPE UAN: 107-000-14-013-L01-P 0.125 CEU/1.25hr
Activity Type: Application-Based

Learning Objectives for Pharmacists: Upon completion of this CPE activity participants should be able to:
1. Identify the top opioid prescribing issues
2. Define REMS and its requirements, use, and application to practice
3. Describe appropriate opioid prescribing and dispensing protocols
4. Describe appropriate monitoring of opioid therapy
5. List strategies for preventing or managing adverse effects of opioid use

Speaker: James Bell, MD, is the full-time medical director for the Palliative Care and Hospice programs at St. Luke’s Hospital in Cedar Rapids. He joined the Hospice team part-time in 1989 while he also served the community as a family physician. Dr. Bell was instrumental in the development and implementation of the inpatient and outpatient Palliative Care programs, established in 2005 and 2009, respectively. In 2008, he became the full-time medical director for Palliative Care and Hospice. He is board certified in Hospice and Palliative Medicine as well as family medicine.

Speaker Disclosure: James Bell reports no actual or potential conflicts of interest in relation to this CPE activity. Off-label use of medications will not be discussed during this presentation.
Basics of Opioid Prescribing

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Faculty Disclosure

- Dr. Bell reports he does not have actual or potential conflicts of interest associated with this presentation
- Dr. Bell has indicated that off-label use of medications will not be discussed during this presentation.
Learning Objectives

Upon completion of this activity participants should be able to:

1. Identify the top opioid prescribing issues
2. Describe appropriate opioid prescribing
3. Describe appropriate monitoring of opioid therapy
4. List strategies for preventing or managing adverse effects of opioid use

Pre-Assessment Questions

- Patients with chronic pain are less likely to present with objective findings (i.e. – tachycardia) compared to those with acute pain
  
  • A True
  • B False
Pre-Assessment Questions

- Which of the following are etiologies for pain?
  - A Physiologic process
  - B Spiritual causes
  - C Anxiety
  - D All of the above

Pre-Assessment Questions

- Which one of the following opioid-induced adverse effects requires proactive management/prevention?
  - A Nausea
  - B Vomiting
  - C Sedation
  - D Constipation
Acute Pain

- Identifiable cause
- Resolves in days/weeks
- Adaptive
- Results in
  - Anxiety
  - Increased BP, pulse, respirations
  - Muscular tension

Chronic pain

- May be multifactorial
- Duration indeterminate
- Maladaptive
- Patient may appear depressed rather than painful
Types Of Pain

**NOCICEPTIVE**
Direct stimulation of intact receptors along normal nerves
- Somatic
  - Receptors in skin, muscles/joints
  - Easy to describe and localize
- Visceral
  - Receptors in hollow structures (i.e. GI, GU)
  - Difficult to describe/localize—often colicky.

Types Of Pain

**NEUROPATHIC**
Disorder of peripheral or central nerves
- Different mechanisms—compression, transection, infiltration, ischemia
- Varied types—peripheral, deafferentation (phantom, post-herpetic), sympathetic

COMPLICATED!
Opioids

- Produce analgesia by interaction with receptors in brain and spinal cord (and to lesser degree, peripheral nerves)
- *Mu* receptor is dominant
- Theoretically no ceiling dose

**Perception/modulation:**
- Tricyclic antidepressants
- SSRIs, SSNRIs
- Alpha blockers (clonidine)

**Transduction:**
- Prostaglandin inhibitors (NSAIDs, steroids)
- Anticonvulsants
- Anesthetics
- Capsaicin, other topicals
- Opioids (when nerves “primed”)

**Transmission:**
- NMDA receptor blockers (ketamine, methadone, dextromethorphan)
- Opioids – primary receptors are in spinal cord
TOTAL PAIN

Pathologic Process

Depression

Anger

Spiritual/Existential Distress

Anxiety

Insomnia

Opioids

- Classified by interaction with receptors
  - **Pure agonist**: morphine, hydromorphone, oxycodone, hydrocodone, codeine, meperidine, fentanyl
  - **Mixed agonist/antagonist**: butorphanol, pentazocine, nalbuphine
  - **Partial agonist**: buprenorphine
  - **Pure antagonist**: naloxone, naltrexone
Opioids

Mixed agonist/antagonist drugs
- Claim to be less addicting, less respiratory depression– not substantiated
- Will potentiate withdrawal in patients being treated with pure agonists–
  - NEVER administer to patient on pure agonist!
- Have analgesic ceiling
- May cause psychosis

Pain Ladder

Step 1: Non-Narcotic Analgesic
- Acetaminophen
- NSAIDs

Step 2: Mild Opioids
- Codeine
- Hydrocodone
- Oxycodone

Step 3: Strong Opioids
- Morphine
- Fentanyl
- Methadone
- Hydromorphone
Tramadol

- Synthetic non-opioid codeine analog
- Roughly equivalent to Tylenol #3
- No anti-inflammatory effects
- May produce dependence

Opioids

<table>
<thead>
<tr>
<th>Parenteral or oral</th>
<th>Oral only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>Oxycodone</td>
</tr>
<tr>
<td>Hydromorphone (Dilaudid)</td>
<td>Hydrocodone</td>
</tr>
<tr>
<td>Meperidine (Demerol)</td>
<td>Codeine</td>
</tr>
</tbody>
</table>
### Opioids

#### Ultra short

**Fentanyl**
- IV (50-100 X potency of morphine)
  - Single dose 100 mcg = 5-10 mg morphine
  - Acts in 5-15 minutes
- Transmucosal (OTFC– Actiq)
  - For breakthrough pain in cancer patients only
  - Must be on opioids for at least 1 week, 60 mg morphine/day or 50 mcg duragesic or equivalent.
  - Special precautions in children
- (Transdermal) (Duragesic)

#### Short acting

- Oral dosing:
  - Onset 20-30 minutes
  - Peak effect 60-90 minutes
  - Duration 2-4 hours
  - Don’t exceed 4 hour dosing interval!
  - May be dose escalated every 2-4 hours for poorly controlled pain.
## Opioids

- **Codeine (Tylenol #3)**
  - Emetogenic
- **Oxycodone (Percocet, Vicodin, Oxyfast)**
  - In chronic dosing, about as potent as morphine
- **Hydrocodone (Lortab)**
  - Slightly less potent than morphine

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## Opioids

**Meperidine (Demerol)**

- Converted to long-acting toxic metabolite
  - Causes tremor, myoclonus and seizures
  - Risk highest with prolonged use, renal insufficiency
  - Only indicated for short term, procedural pain
    - No more than 48 hours
    - No more than 600 mg IV/24 hours
# Opioids

**Combination products**

*Available as combinations with*

- Acetaminophen, aspirin, ibuprofen.

- Typically use for episodic or breakthrough pain
- Don’t use more than one combination drug at a time.

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## Long Acting Opioids

- **Oral**
  - MS Contin
  - OxyContin
  - Methadone

- **Transdermal**
  - Fentanyl patch
Long Acting Opioids

- **MS Contin** (morphine)
  - May dose q8-12 hours
- **OxyContin**
  - Dose q12 hours

Both—
- Must be taken intact (do not crush)
- Provide onset of pain relief in 2 hours
- May be dose escalated every 24 hours
- No difference in toxicity/addiction potential

Long Acting Opioids

**Transdermal fentanyl**

- Onset 13-24 hours
- Duration 48-72 hours
- Dose escalate every 3 days
- Place on hairless, non-irradiated skin
Methadone

**Advantages**
- Mu/delta agonist
- NMDA antagonist
- Least expensive potent opioid
- Clearance not affected by renal/hepatic disease

**Disadvantages**
- Complex pharmacology
- Duration of action changes with prolonged use
- Dose conversions complex
- Drug interactions
- Prolongs QT interval

**Indications**
- May be first line drug for
  - Neuropathic pain
  - Bone pain
  - Chronic renal failure
- Indicated for morphine adverse effects
  - Sedation
  - Delirium
  - Nausea/vomiting
Methadone

**DOSING**

Multiple dosing models
- May schedule q6-q12 hours with q 3 hour prn dosing
- May dose q 3 hour prn with schedules dose calculated on day 6.
- May add low dose methadone to other opioids when doses begin to escalate
- Starting dose typically 2.5-5 mg every 8 hours
- Conversion depends on prior opioid dose and length of use
- Be cautious with dose adjustments more frequently than every 4 days
- Maximum starting dose 30-40 mg q 8 hours no matter what.
- Available tablets, solution, concentrate
- May be given PO, rectal, subcutaneous, IV

<table>
<thead>
<tr>
<th>Drug</th>
<th>IV/PO Dose</th>
<th>PO Dose</th>
<th>Ratio PO/IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>MORPHINE SULFATE</td>
<td>10 mg</td>
<td>30 mg</td>
<td>3:1</td>
</tr>
<tr>
<td>CODEINE</td>
<td>130 mg</td>
<td>200 mg</td>
<td>1.5:1</td>
</tr>
<tr>
<td>OXYCODONE</td>
<td>NA</td>
<td>30 mg</td>
<td></td>
</tr>
<tr>
<td>HYDROCODONE</td>
<td>NA</td>
<td>30-45 mg</td>
<td></td>
</tr>
<tr>
<td>HYRDOMORPHINE</td>
<td>1.5 mg</td>
<td>7.5 mg</td>
<td>5:1</td>
</tr>
<tr>
<td>MEPERIDINE</td>
<td>75 mg</td>
<td>300 mg</td>
<td>4:1</td>
</tr>
<tr>
<td>METHADONE (acute)</td>
<td>10 mg</td>
<td>20 mg</td>
<td>2:1</td>
</tr>
</tbody>
</table>

**EQUIANALGESIC DOSING**

<table>
<thead>
<tr>
<th>MORPHINE DOSE/DAY</th>
<th>METHADONE:MORPHINE</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;90</td>
<td>1:5</td>
</tr>
<tr>
<td>90-300</td>
<td>1:10</td>
</tr>
<tr>
<td>&gt;300</td>
<td>1:12-20</td>
</tr>
</tbody>
</table>
Management

- Begin with short-acting opioids
- Switch to long-acting drugs when 3-4 doses daily are required to control pain
- Calculate 24 hour dose
- Breakthrough: 10-20% total daily dose

Opioids

Dose Escalation
Increase by a percentage of current dose based upon pain rating
- Mild pain (1-3/10): 25% increase
- Moderate pain (4-6/10): 25-50% increase
- Severe pain (7-10/10): 50-100% increase
Opioids

Dose escalation
Frequency of escalation depends on opioid
- Short acting oral: q 2-4 hours
- Long acting oral except methadone: q 24 hours
- Methadone, transdermal fentanyl: q 72 hours.

Opioids

Opioid rotation
Consider changing to a different opioid when reaching high doses of 1 drug (i.e. morphine 300 mg/day po)
Opioids

- Example:
  - 67 y/o female with pancreatic cancer on Oxycontin 10 mg bid and Percocet 5/325 1 q 4 hours prn. Has received 5 doses for breakthrough in last 24 hours and now rates pain at 6/10. Convert to appropriate new drug/dose.

- Total 45 mg oxycodone/day
- 45 mg oxycodone=45 mg morphine
- Increase by 25-50%= 60 mg morphine
- MS Contin 30 mg bid or 20 mg tid
- Breakthrough 10-20%= MSIR 10 mg po q 2 hours prn.
Opioids

- Over the next 2 days, pt requires total of 80 mg po for breakthrough, then becomes unable to swallow and is moaning. Options?

1. Total daily dose = MSContin 60 mg + MSIR 40 mg = 100 mg Morphine/24 hr
2. May switch to Duragesic—
   - 100 mg morphine = 50 mcg Duragesic patch
   - Will still require po/sl for pain, at least 20 mg Roxanol q 4 hours for next 18-24 hours with 20 mg q 1-2 hours for breakthrough
   - OR
3. Convert to IV drip—
   - 100 mg morphine po/day = 33 mg morphine IV/day, increase by 25-50% to 50 mg/day
   - 2 mg/hr with 5-10 mg IV bolus q 2 hours for breakthrough.
Opioids

Over the next 8 hour shift, the pt receives 4 doses of 10 mg IV q 2 hours. She appears comfortable after each dose for about 90 minutes. What would you recommend?

Dose escalation—
10 mg morphine x 4 = 40 mg morphine IV
Plus 2 mg/hour x 8 = 16 mg
40 + 16 = 56 mg IV/8 hours = 7 mg/hour new dose rate. What would you give for breakthrough?
Opioids

7 mg/hour x 24 hours = 168 mg IV morphine
Increase bolus to approx. 20 mg morphine IV q 2 hours for breakthrough.
Now, convert the drip to Dilaudid.

Opioids

10 mg Morphine IV = 1.5 mg Dilaudid IV
So
7 mg Morphine IV/hour = 1 mg Dilaudid IV/hr
Breakthrough dose could be Dilaudid 2-3 mg IV q 2 hours.
Adverse effects

- Respiratory depression
- Nausea/vomiting
  - antiemetics
- Constipation
  - laxatives
- Sedation
  - Methylphenidate, modafinil

Adverse effects

- Neurotoxicity
  - Myoclonus
  - Renal failure leads to metabolite accumulation (ie M3G)
  - Rotate opioids
  - Clonazepam, preservative-free solutions
Opioids

Dependence
- Neuroadaptation
- Characterized by abstinence syndrome upon withdrawal
- If dose reduction required, decrease by 50% every 2-3 days, avoid antagonists

Opioids

Tolerance
- Reduced effectiveness to given dose over time
- Not clinically significant with chronic dosing
- If dose increasing, suspect disease progression
Opioids

**Addiction**
- Psychological dependence, compulsive use, loss of control, loss of interest in activities
- Continued use of drugs despite harm
- Rare outcome of pain management especially if no history of abuse

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Opioids

**Addiction**
- Consider
  - Substance use (true addiction)
  - Pseudoaddiction (undertreatment of pain)
  - Behavioral/family/psychological disorder
  - Drug diversion
Opioids

- Substance abusers may have legitimate pain needs
- Treat compassionately
- Consider contracting, consultation with pain/addiction specialists

Post-Assessment Questions

- Patients with chronic pain are less likely to present with objective findings (i.e. – tachycardia) compared to those with acute pain

- A True
- B False
Post-Assessment Questions

• Which of the following are etiologies for pain?

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Post-Assessment Questions

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