Pain Management in the Hospital

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“Pain is a more terrible lord of mankind than even death itself.”

Albert Schweitzer
Overall message

- Pain management is an essential component of comprehensive care and should begin at the onset of pain and not wait for the diagnosis of cause but rather occur concurrently with other workup.

- Our patient satisfaction scores demand that we realize that Pain is an Emergency!
Secondary Message

Palliative Care Teams exist to serve and educate with the hope that in the future the provision of symptom management will rival that of our magnificent technologically driven diagnostics and therapeutics.
Objectives:
Participant should be able to:

1) Understand the new FDA REMS
2) Discuss appropriate pain management by understanding the pharmacology
3) Define tolerance, addiction and physical dependence and understand the relationships
4) Review short term and long term side effects of opioids and their treatment
5) Convert opioids through equianalgesic dosing
An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage

IASP – International Association for the Study of Pain
Professional Barriers to Pain Management

- Lack of knowledge of pain mechanism
- Fear of producing addiction
- Concern about tolerance
- Concern about side effects
- Tolerance, addiction, dependence
- Fear of regulatory scrutiny

FDA “REMS”

Part of a multiagency federal effort to address prescription drug abuse and misuse and further educate all clinicians

REMS
(Risk Evaluation and Mitigation Strategy)

- Reason: currently a prescription drug abuse epidemic in the USA
- Pharmaceutical companies required to offer CME (~3 hours) to address appropriate prescribing of LA and ER opioids
- First programs available March 2013
Based on the 2010 National Survey on Drug Use and Health, public health experts estimate

- more than 35 million Americans age 12 and older used an opioid analgesic for non-medical use some time in their life—an increase from about 30 million in 2002.3

- In 2009, there were nearly 343,000 emergency department visits involving nonmedical use of opioid analgesics.4

- In 2008, nearly 36,500 Americans died from drug poisonings, and of these, nearly 14,800 deaths involved opioid analgesics.5

- Improper use of any opioid can result in serious side effects including overdose and death, and this risk can be greater with ER/LA opioid analgesics.
Expected results of the prescriber education in this REMS are that the prescribers will:

a. Understand how to assess patients for treatment with ER/LA opioid analgesics.

b. Be familiar with how to initiate therapy, modify dose, and discontinue use of ER/LA opioid analgesics.

c. Be knowledgeable about how to manage ongoing therapy with ER/LA opioid analgesics.

d. Know how to counsel patients and caregivers about the safe use of ER/LA opioid analgesics, including proper storage and disposal.

e. Be familiar with general and product-specific drug information concerning ER/LA opioid analgesics.
## Drugs included

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Fentanyl Patch</td>
<td>Morphine ER</td>
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<tr>
<td>Oxycontin</td>
<td>Kadian (24*)</td>
</tr>
<tr>
<td>Opana (oxymorphone ER)</td>
<td>Panadone (HMER)</td>
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<tr>
<td>Dolophine (methadone)</td>
<td>Exalgo (HMER)</td>
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<tr>
<td>Tapentadol ER</td>
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The DOs and DON’Ts of Extended-Release / Long-Acting Opioid Analgesics

DO:
- Read the Medication Guide
- Take your medicine exactly as prescribed
- Store your medicine away from children and in a safe place
- Flush unused medicine down the toilet
- Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Call 911 or your local emergency service right away if:
- You take too much medicine
- You have trouble breathing, or shortness of breath
- A child has taken this medicine
WHO 3-step Ladder

1 mild
ASA
Acetaminophen
NSAID’s
± Adjuvants

2 moderate
A/Codeine
A/Hydrocodone
A/Oxycodone
Tramadol
± Adjuvants

3 severe
Morphine
Hydromorphone
Methadone
Fentanyl
Oxycodone
± Adjuvants

Pain management

- Don’t delay for investigations or disease treatment
- Unmanaged pain $\Rightarrow$ nervous system changes
- Treat underlying cause of pain
Mixing Opioids

Double, double toil and trouble;
Fire burn, and caldron bubble.
(Shakespeare: Macbeth)
Opioid pharmacology . . .

- Conjugated in liver (little liver function required)
- Excreted via kidney (90-95%)
- First-order linear kinetics
- Simplified Cmax after
  - PO ≈ 1 hr
  - SC, IM ≈ 30 min
  - IV ≈ 10 min
- Half-life at steady-state
  - PO/PR/SC/IM/IV ≈ 4 hrs
  - Steady state after 4-5 half-lives (20 hours)

PRESCRIBING FOR PAIN - The Right Frequency

A. Pain free interval
B. Pain recurs - patient waits until “needs” to take again
C. Patient waits, after asking, until meds received
D. Patient waits for meds to be absorbed
E. Total time patient is in pain.
Routine oral dosing
Immediate-release preparations

- (Codeine, hydrocodone), morphine, hydromorphone, oxycodone

  Dose q 4 h when stable (but initially may need q 1 hr)

  Adjust oral dose daily

  - Mild/moderate pain \(\uparrow 25-50\%
  
  - Severe/uncontrolled pain \(\uparrow 50-100\%

*Adjust more quickly for severe, uncontrolled pain (or with IV/SQ!)*
Routine oral dosing
Extended-release preparations

- Improve compliance (less bolus effect)
- Dose q 8, 12, or 24 h (product specific)
  - Don’t crush or chew tablets
  - May flush time-release granules down feeding tubes (Kadian is a Q 24 hour drug)
- Adjust dose q 2-4 days (once steady state is reached)
Breakthrough dosing

- Use immediate-release opioids
  - 10-15% of 24 hr dose
  - offer after Cmax reached
    - PO/PR $\approx q\ 1\ h$
    - SC, IM $\approx q\ 30\ min$
    - IV $\approx q\ 10–15\ min$

- Do NOT use extended-release opioids for breakthrough dosing
When would you expect a patient to report the maximal analgesic effect after taking a dose of acetaminophen/oxycodone?

1. 30-45 minutes
2. 60-90 minutes
3. 120-150 minutes
4. 180-210 minutes

Bar graph showing:
- 40% for 60-90 minutes
- 20% for 30-45 minutes
- 20% for 120-150 minutes
- 20% for 180-210 minutes
A 28 year old woman is hospitalized for an exacerbation of rheumatoid arthritis. She has chronic low back pain from steroid-induced compression fractures. You prescribe both a long acting and short-acting oral morphine.

How often can she take the short-acting oral morphine for pain?

1. Every 1 hour
2. Every 4 hours
3. Every 6 hours
4. Every 8 hours
What medication should also be prescribed for this patient?

1. Docusate (Colace)
2. Bisacodyl (Ducolax)
3. Lactulose (Chronulac)
4. Senna concentrate (Senokot)
Addiction . . .

- Psychological dependence
- Compulsive use
- Loss of control over drugs
- Loss of interest in pleasurable activities due to preoccupation with drug
- Continued use of drugs in spite of harm
- Rare outcome of pain management (<1%)
- Physical dependence and tolerance are not necessary
- CANNOT cure in the hospital
A 72 y/o man with lung cancer and bone mets has increasingly severe pain over the left hip. The pain began 6-8 weeks ago and was initially controlled with acetaminophen/oxycodone tables using 4-6 tablets/day. The pain has increased and he is using 12 tabs/day with only partial pain relief. The pain is constant, aching and well localized; there is no referred pain.

Increasing pain in this patient most likely represents:

1. new-onset depression
2. opioid addiction
3. opioid tolerance
4. worsening metastatic cancer
Tolerance

- Reduced effectiveness to a given dose over time due to neuro adaptation
- If dose is increasing, rule out disease progression prior to assuming tolerance
Physical dependence

- A process of neuro adaptation

- Abrupt withdrawal may → abstinence syndrome

- If dose reduction required, reduce by 50% q 1-2 days

(not synonymous with addiction)
Pain that is poorly responsive to opioids

If dose escalation ➔ adverse effects

Add therapy to counteract adverse effect

Try Alternative

Route of administration

Opioid ("opioid rotation")

Coanalgesic
Ongoing assessment

- Increase analgesics until pain relieved or adverse effects
  (no ceiling dose of opioids)

- Driving is safe if:
  Pain controlled, dose stable, no adverse effects
Opioid Induced Hyperalgesia

- Can occur in long term opioid usage (high dose drug induced pronociceptive process)
- Treatment is opioid rotation to a lower equianalgesic dose or opioid tapering and addition of adjunctive medication
<table>
<thead>
<tr>
<th>PO/PR (mg)</th>
<th>Analgesic</th>
<th>SC/IV/IM (mg)</th>
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<tbody>
<tr>
<td>100</td>
<td>Codeine</td>
<td>-</td>
</tr>
<tr>
<td>15</td>
<td>Hydrocodone</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>Hydromorphone</td>
<td>1</td>
</tr>
<tr>
<td>15</td>
<td>Morphine</td>
<td>5</td>
</tr>
<tr>
<td>10</td>
<td>Oxycodone</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Fentanyl</td>
<td>0.050</td>
</tr>
<tr>
<td>150</td>
<td>Tramadol</td>
<td>-</td>
</tr>
</tbody>
</table>

Morphine 50 mg/24 hours = fentanyl 25 mcg patch q 48-72 hours
Changing Opioids

- Incomplete Cross-tolerance

  Start with 50-75% of published equianalgesic dose
  More if pain, less if adverse effects

You are caring for a patient with diabetic neuropathy treated with 180 mg Morphine ER q 12 hours and taking 6 breakthrough doses of 30 mg Morphine IR daily. She is now severely nauseated and you wish to convert to an IV morphine drip. What would be the appropriate IV dose of Morphine for equianalgesic effect?

1. 22.5 mg/hr IV morphine
2. 10 mg/hr IV morphine
3. 7.5 mg/hr IV morphine
4. 15 mg/hr IV morphine
Convert the dose of Morphine from the prior question to IV dilaudid. Do not adjust for incomplete cross tolerance.

1. 7.5 mg/hr
2. 5 mg/hr
3. 2 mg/hr
4. 1.5 mg/hr
After three days of oral morphine a decision is made to discontinue long acting morphine and begin using a fentanyl patch due to difficulty swallowing. Therapeutic analgesic levels should not be expected after the first application of a fentanyl patch until:

1. 2-6 hours
2. 7-12 hours
3. 13-24 hours
4. 25-36 hours

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Opioid allergy

- Anaphylactic reactions are the only true allergies and are very unusual
  Present with Bronchospasm
- Urticaria and wheezing can be true allergies; need careful assessment
- Nausea/vomiting, constipation, drowsiness, confusion
  (Adverse effects, not allergic reactions)
# Acute Opioid Adverse Effects

## Common
- Constipation
- Dry mouth
- Nausea/vomiting
- Sedation
- Sweats

## Uncommon
- Bad dreams/hallucinations
- Dysphoria/delirium
- Myoclonus/seizures
- Pruritus/urticaria
- Respiratory depression
- Urinary retention

Develop Tolerance for all common except constipation
Constipation

- Opioid effects on CNS, spinal cord, myenteric plexus of gut
- Easier to PREVENT than treat!
- Bulk-forming agents not recommended
- Stimulant laxatives (Senna, bisacodyl)
- Combine with a stool softener
- Add an osmotic agent

TITRATE to RELIEF
Respiratory depression . . .

- Opioid effects differ for patients treated for pain
  
  Pain is a potent stimulus to breathe

  Drowsiness precedes respiratory depression

  Pharmacologic tolerance to respiratory depression occurs very rapidly
Respiratory Depression

- Management
  - Identify, treat contributing causes
  - Reduce opioid dose
  - Observe
  - If unstable vital signs
    - Naloxone 0.04 mg IV q 1 min
  - Careful observation for the next hour
You have given a young woman an initial dose of Percocet and she develops nausea. Which one of the following statements concerning nausea while taking opioids is true:

1. Nausea to opioids is due to bowel distention and stimulation of the vagus nerve
2. Nausea to opioids is usually accompanied by itching
3. Nausea to opioids represents a drug allergy
4. Nausea to opioids resolves in most patients within 4-7 days
Nausea/vomiting . . .

- Onset with start of opioids
  Tolerance develops within days
- Prevent or treat with dopamine-blocking antiemetics
  - Prochlorperazine 10 mg q 6 h
  - Haloperidol 1 mg q 12 h
  - Metoclopramide 10 mg q 6 h

Alternate opioid if refractory nausea!
Opioid Neurotoxicity

- Cognitive Dysfunction
- Myoclonus
- Hyperalgesia
- Allodynia
- Seizures
Long term SE of Opioids

- Hormonal Changes
- Immunologic Effects
- Sleep Disorders
Opioids in Renal Failure and Dialysis

- Fentanyl
- Methadone
Adjuvant analgesics

Medications that supplement primary analgesics

May themselves be primary analgesics

Use at any step of WHO ladder

Include anticonvulsants, tricyclics, anticholinergics and corticosteroids
Pain Crisis

- Opioid Naïve (2mg IV)
- Chronic Pain (basal + 15% bolus)
Titration of Narcotic in Crisis

- Pain 1-3: no dose needed; recheck in 30”
- Pain 4-6: give same additional dose; check in 10”
- Pain 7-10: double prior dose and check in 10”
Summary

- Define the type of pain and its likely cause.
- Avoid mixing opioids.
- Increase scheduled and breakthrough doses as needed, but not simultaneously.
- Monitor rapidly increasing doses of opioids for opioid neurotoxicity with sudden allodynia.
- Be alert for opioid neurotoxicities and intervene early.
- Convert between opioids as needed. Remember to always prescribe for breakthrough pain.
“If we know that pain and suffering can be alleviated and we do nothing about it, we, ourselves, are tormentors.”

Primo Levi
If we can relieve torment and do not, then we ourselves become the tormenters.

“We must become the change we want to see”

Mahatma Gandhi