Developing an Effective Oral Analgesic Regimen

Theresa Kristopaitis, MD
Department of Internal Medicine, Division of General Medicine
Associate Medical Director, Loyola Hospice
General Principles

- Assess pain thoroughly
- Know your patient
- Know the medications
- Dose to reduce pain by at least 50%
- Reassess frequently
Pain

Pain is a personal, complex experience with 3 components

- Sensory
- Emotional
- Cognitive
Review

Neuroscience lectures on pain physiology!
P&T lectures on NSAIDs and opiates!
Pain pathophysiology

Acute pain
- identified event, resolves days–weeks
- usually nociceptive

Chronic pain
- cause often not easily identified, multifactorial
- indeterminate duration
- nociceptive and/or neuropathic

Nociceptive pain – results from actual or potential tissue damage. Result of ongoing activation of nociceptors on primary afferent nerves by noxious stimuli

Somatic vs visceral
WHO 3-Step Ladder

**Step 1 - Mild**
- Aspirin
- Acetaminophen
- NSAIDs

**Step 2 - Moderate**
- Codeine/…
- Hydrocodone/…
- Oxycodone/…
- …/acetaminophen or NSAID
- Tramadol

*Always consider adding an adjuvant Rx*

**Step 3 - Severe**
- Morphine
- Hydromorphone
- Methadone
- Oxycodone
- Fentanyl
“Adjuvant Analgesic”

- Drug which has a primary indication other than pain management
- Acts as analgesic in some painful conditions
  - Antidepressants
  - Corticosteroids
  - Anticonvulsants
  - Local anesthetics
  - Osteoclast inhibitors
  - Radiopharmaceuticals
  - Muscle relaxants
  - Benzodiazepenes
Our Case

- Continuous pain
- Moderate intensity
- Chronic, non-neuropathic
- Worsens with certain activities
Where to begin?

- Begin low dose immediate release oral opioid
  - Examples
    - Hydrocodone 5mg
    - Morphine 5mg
    - Oxycodone 3mg
    - Hydromorphone 1mg

Hospice and Palliative Care Training for Physicians: UNIPAC 3
Assessment and Treatment of Physical Pain Associated with Life-Limiting Illness, CP Storey et al, ed

EPERC, Fast Facts
Immediate Release Oral Opioid

Administered as
- single agents
- combination products

Peak analgesic effect occurs in 60-90 minutes

Expected total duration of analgesia of 2-4 hours.

Standard reference sources generally cite q 4 hour dosing interval for the single-agent opioids
Combination opiate/nonopiate

-50 different opioid combination products
  - Contain either acetaminophen, aspirin or ibuprofen, with an opioid
  - range of tablet strengths and liquids
  - typically used for moderate pain that is episodic
    - For persistent pain administered on around-the-clock basis
Step 2 Opioid Combos

- **Potency**
  - Oxycodone > hydrocodone > codeine
  - Propoxyphene = aspirin or acetaminophen

- The dose limiting property of all the combination products is?
  - aspirin, acetaminophen or NSAID
WHO Step 2
Tramadol

Centrally acting synthetic analgesic
- $\mu$–opioid receptor binding
- Weak inhibition of serotonin uptake
- Weak inhibition of norepinephrine uptake
Our patient

On Percocet

- Combination opioid/nonopioid
  - Oxycodone/acetaminophen
  - Strengths
    - 2.5/325
    - 5/325
    - 7.5/325
    - 7.5/500
    - 10/325
    - 10/650
Initial Plan

- Oxycodone/acetaminophen
  - 2.5/325 q 6 hours
- Not helping - still 5-6/10 pain
- Titration
  - Increase 25-50% for mild-moderate pain
  - Increase 50-100% for moderate – severe pain
- Side effect evaluation
  - Sedation
EPIC In-Box

- Oxycodone/acetaminophen
  - 5/325 tab
  - 1-2 tabs every 6 hours as needed
Case Options?

- Increase dose of oxycodone/acetaminophen?
  - 10/325 tabs – take 1 ½, not relieved, take 2
- Change dosing interval?
  - Q 4 hours
- Scheduled vs PRN dosing?
  - Scheduled
- Change to another opiate combo?
  - Oxycodone most potent
- Change to non-combo opiate?
  - Soon - reaching acetaminophen max
- Add breakthrough dose of opiate?
  - Yes, but will need an agent without acetaminophen
- Add an adjuvant?
  - Re-evaluate characteristics of pain
- Begin long acting opiate?
  - When stable daily dosage requirements determined
Plan

Oxycodone 10/325
- 1 1/2 tabs q 4 hours scheduled
- 2 days later, a little better, not sleepy
- 2 tabs q 4 hours scheduled

- Titrated oxycodone from 40mg /24 hours to 120mg/24 hours
  (acetaminophen 3900mg/24 hours)

Relief!!
Q 4 hour ATC meds?
Extended-release opiate preparations

- Improve compliance, adherence
Extended Release Opiates

NEVER!!!!!

In opiate naïve patients!!!!!
Extended Release Preparations

- Extended Release Oral Morphine
- Extended Release Oral Oxycodone
- Transdermal Fentanyl
Extended-release opiate preparations

- **Morphine**
  - Morphine ER, MS Contin, Kadian, Avinza

- **Oxycodone**
  - Oxycodone ER, Oxycontin

- **Fentanyl**
  - Transderm patch (Duragesic)
Extended-release opioid preparations

Dose q 8, 12, or 24 h (product specific)
- Don’t crush or chew capsules
- No capsules down feeding tubes

Adjust dose q 2–4 days (once steady state reached)

Fentanyl transderm q 72 hours
- Adjust dose at 6 days (once steady state achieved)
Extended-release opioid preparations

- Should not be used for rapid titration in patients with severe pain
Case - How?

- Oxycodone 10/325
  - 2 tabs q 4 hours
- Oxycodone ER 60mg q 12 hours

120mg oxycodone/24 hours
Breakthrough Pain

- Incident
  - Activity related, identifiable precipitant
    - Anticipate and premedicate with short acting agents

- Idiopathic, spontaneous
  - Unpredictable
  - PRN opiate, consider adjuvant

- End-of-dose failure
  - Increase dose or shorten time between doses of long-acting agent
Breakthrough Pain

- Use immediate-release opioids
  - 10%–15% of 24-hr dose
  - offer after Cmax reached
    - po \approx q 1hr
  - or 50% regular 4 hour dose

- Do NOT use extended-release opioids
Our Case

- Oxycodone 120mg/24 hours
  - 10-15%
- Oxycodone 15mg PO q 1 hour PRN
  breakthrough pain
Follow-up

- Oxycodone ER 60mg q 12 hours
- Oxycodone 15mg breakthrough
  - 3 weeks later EPIC in-box
  - Has taken 4 breakthrough doses daily x 4 days
    - Re-evaluate pain
- 60mg additional oxycodone
- Increase oxycodone ER to
  - 90mg q 12 hours
- New breakthrough dose?
  - Oxycodone 20mg q 1 hours PRN
Could we use extended release morphine?

Could we use transdermal fentanyl?
Fentanyl

- Lipid soluble
  - Crosses skin and oral mucosa
- Transdermal fentanyl
  - 25 μg patch ≈ 45–135 (likely 50–60) mg PO morphine / 24 h
Fentanyl Transdermal Patch

- onset after application ≈ 24 hours
- effect 72 hours (some patients 48 hours)
- ensure adherence to skin
- increased absorption with increased body temp
- may not be as effective in cachexia (minimal adipose tissue)
Our patient

- Convert to Fentanyl
  - Oxycodone 120mg/24 hours
## Equianalgesic doses of opioid analgesics

<table>
<thead>
<tr>
<th>po / pr (mg)</th>
<th>Analgesic</th>
<th>SC / IV / IM (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>Codeine</td>
<td>60</td>
</tr>
<tr>
<td>15</td>
<td>Hydrocodone</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>Hydromorphone</td>
<td>1.5</td>
</tr>
<tr>
<td>15</td>
<td>Morphine</td>
<td>5</td>
</tr>
<tr>
<td>10</td>
<td>Oxycodone</td>
<td>-</td>
</tr>
</tbody>
</table>
Conversion

- **Oxycodone** 120mg x **Morphine** 15mg
  - Oxycodone 10mg
  - = 180mg morphine equivalent

  - 25 µg patch ≈ 50 mg PO morphine / 24 h

Fentanyl 75mcg/hr patch q 72 hrs
  + breakthrough
Bowel regimen

NEJM March 2005
Final Comments

- Physical pain is the most common source of “suffering”
Total Pain

Dame Cicely Saunders
- Physical
- Emotional
- Social
- Spiritual
Questions?

Practice.....