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
Somative vs visceral

WHO 3-Step Ladder

Step 1 - Mild

Aspirin

Acetaminophen

NSAIDs

Step 2 - Moderate

Codeine/…

Hydrocodone/…

Oxycodone/…

…/acetaminophen or NSAID

Tramadol

Step 3 - Severe

Morphine

Hydromorphone

Methadone

Oxycodone

Fentanyl

Always consider adding an adjuvant Rx

“Adjuvant Analgesic”

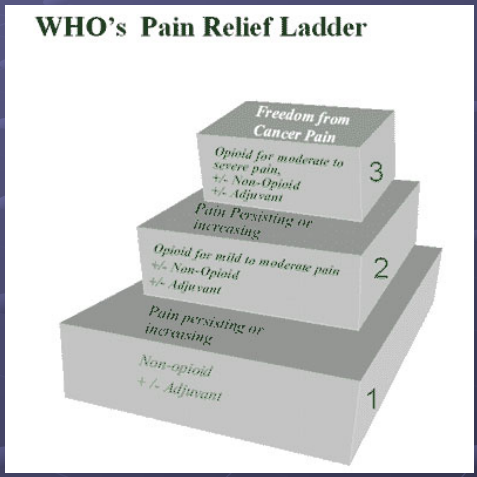
- Drug which has a primary indication other than pain management
- Acts as analgesic in some painful conditions
  - Antidepressants
  - Corticosteroids
  - Anticonvulsants
  - Local anesthetics
  - Osteoclast inhibitors
  - Radiopharmaceuticals
  - Muscle relaxants
  - Benzodiazepenes

Our Case

- Continuous pain
- Moderate intensity
- Chronic, non-neuropathic
- Worsens with certain activites

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
  - μ–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-evaluarte 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 4hours 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
    - 120mg oxycodone/24 hours
- Oxycodone ER 60mg q 12 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 C_{max} reached
    - po ≈ 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

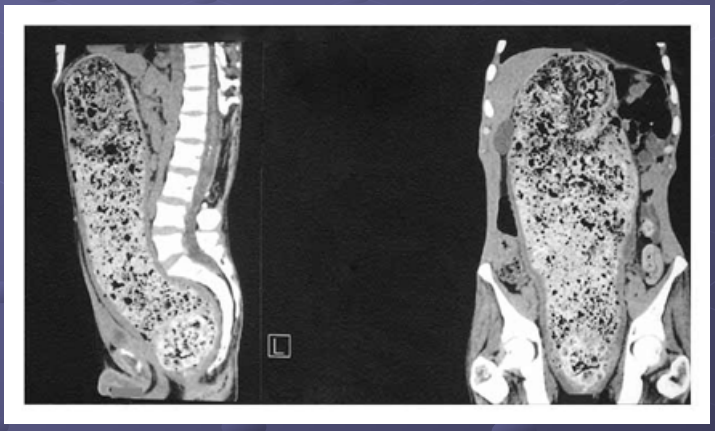
po / pr (mg)	Analgesic	SC / IV / IM (mg)
100	Codeine	60
15	Hydrocodone	-
4	Hydromorphone	1.5
15	Morphine	5
10	Oxycodone	-

Conversion

- Oxycodone 120mg x $\frac{\text{Morphine 15mg}}{\text{Oxycodone 10mg}}$
  =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…..

http://www.stritch.luc.edu/lumen/MedEd/softchalkhdht/kristopaitisendoflife/index.html