Pain Management

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Objectives

- Common opioids
- Opioid conversions and Equianalgesia
- Inpatient management examples
- Adjuvants
- Common issues
- Aberrant behavior
Total Pain Experience: 4 components

- Physical
- Psychological
- Emotional
- Social/interpersonal
Responsibility in Opioid Prescribing

- It’s our job to judiciously prescribe these drugs
- Use adjuvants if reasonable
- WHO Ladder requires us to use non-opioids before advancing to opioids
- Also employ interventional pain management techniques where possible to try to limit systemic opioids
- Goal is to use the minimum necessary to help the patient function
Interventional Strategies

*Opioid Therapy is the first-line approach for moderate-severe cancer pain.
A-delta and C-PMN fibers
↓
Spinothalamic Tract
→
Myelinated fibers (fast)

Unmyelinated fibers (slow)

Spinothalamic Tract→
Opioids: Mechanism of Action

- Exploitation of the μ (mu), κ, and δ receptors
- These receptors modulate pain in both the PNS and CNS
- Decrease transduction and transmission at periphery
- Decrease pain perception at the cortex
Opioids: Specifics

- Morphine
- Hydrocodone
- Oxycodone
- Transdermal Fentanyl
- Hydromorphone
- Oxymorphone
- Methadone
Morphine

- The prototype
- Standard for comparison
- Metabolized in the liver and renally excreted
- Morphine-3-gluconoride metabolite (M3G) may cause side effects
- Cost effective
- Caution in renal insufficiency
- Both IR/SA and ER/LA options
- Just one of many options for patients
- Long acting versions: MS Contin, Avinza, Kadian
Hydrocodone

- This is the opioid in **Norco/Lortab**
- Comparable potency to morphine
- Now a schedule II, cannot call this in to a pharmacy
- Dosed in combination with acetaminophen which limits use
- ER/LA formulation (**Zohydro ER, Hysingla**)
  - $650 and up for 100 pills
  - Versus $70 for 120 of MS Contin
Oxycodone

- This is the opioid in **Percocet**
- Slightly stronger than morphine 2:3
- Binds to both mu and kappa receptors
- Similar caution with renal failure
- ER/LA version is **OxyContin** (caution with history of addiction)
Hydromorphone

- This is Dilaudid
- Less likely to cause issues in renal failure
- Highly soluble in water, good for subcutaneous infusions
- Long acting version is Exalgo (8, 12, and 16mg) dosed daily
- Stronger than morphine
  - Orally it is 4 times more potent (2mg hydromorphone = 8mg morphine)
  - IV it is 7 times more potent (1mg hydromorphone = 7mg morphine)
Oxymorphone

- Low propensity to release histamine, less pruritis
- Trade name is Opana
- Comes in IR/SA and ER/LA formulations
- 3 times stronger than morphine orally
- 2 times stronger than oxycodone orally
- 10 times stronger than morphine IV
- High abuse potential in the ER/LA form, FDA is recommending removing from the market
Transdermal Fentanyl

- Less histamine release, so less pruritis
- Better for renal failure, less metabolite production
- Dosed in mcg/hr
- Rule of thumb: divide mg of MSE/24 hours by 2 for dose.

**Duragesic** patch is convenient with the following caveats:
- Fever may cause increased absorption
- Requires SubQ fat, not for cachectic patients
- Needs a non-hairy, non-greasy surface
- Adhesion can be a problem
- Have metal in them so risk for local skin burn in MRI
Methadone

- Metabolized by the liver, excreted by the bowel
- Inexpensive
- NMDA antagonist and mu receptor agonist
- Long and variable half-life
- Adjust over longer intervals, no sooner than 4 days
- Can reverse opioid tolerance
- Can prolong QTc (get EKG if over 100mg/24hours)
Methadone dosing

24 Hour Morphine Equivalent | Morphine : Methadone Ratio
---|---
< 30mg | 2:1
31-99mg | 4:1
100-200mg | 8:1
300-499mg | 12:1
500-999mg | 15:1
1,000-1200mg | 20:1
General Prescribing Guidelines

- Start with a short acting, immediate release drug
- By mouth
- Around the clock
- If consistent use, begin a long acting drug
- Do NOT begin ER/LA opioid on a naïve patient
- Dose for breakthrough pain (10-15% of 24-hour requirement)
- Monitor for toxicity
- Must be on a bowel regimen
<table>
<thead>
<tr>
<th>Opioid</th>
<th>IV (mg)</th>
<th>PO (mg)</th>
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<th>Onset (min)</th>
<th>Peak (min)</th>
<th>Comments</th>
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<td>30</td>
<td>3–4</td>
<td>IM 15–30</td>
<td>30–60</td>
<td>Injection: 2, 4, 8, 10, 15 mg/mL syringes</td>
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<td></td>
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<td>IV &lt; 5</td>
<td>10–20</td>
<td>Oral IR: 10, 15, 30 mg tablets</td>
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<td>PO 15–60</td>
<td>60</td>
<td>Oral soln: 10mg/5mL, 20mg/mL</td>
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<td>PR 10–20</td>
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<td>Suppositories: 5, 10, 20, 30 mg</td>
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<td>SC 5–10</td>
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<td><strong>Morphine SR</strong> (MS Contin®, Kadian®, Avinza®)</td>
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<td>Kadian (q12h): 20, 30, 50, 60, 80, 100 mg caps,</td>
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<td>Avinza (q24h): 30, 60, 90, 120 mg caps</td>
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<td><strong>Hydromorphone (Dilaudid)</strong></td>
<td>1.5</td>
<td>7.5</td>
<td>3–4</td>
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<td>30–90</td>
<td>Injection: 1, 2, 3, 4, 10 mg/mL; Tablets: 1, 2, 3, 4, 8 mg; Oral Soln: 1mg/mL</td>
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<td><strong>Fentanyl inj. (Sublimaze)</strong></td>
<td>0.1–0.2</td>
<td>0.2–0.4</td>
<td>3–4</td>
<td>IV: 0.5–1</td>
<td>3–5</td>
<td>Injection: 50 mcg/mL</td>
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<td>PO: 1–2</td>
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<td><strong>Fentanyl tab/loz. (Actiq, Fentora, Onsolis, Abstral)</strong></td>
<td>0.1–0.2</td>
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<td>Buccal: 1–2</td>
<td>Buccal 5–15</td>
<td>25mcg patch = 60mg oral morphine/day</td>
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<td>patches: 12, 25, 50, 75, 100 mcg/hr</td>
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<td>Lortab, Norco: 5, 7.5, 10mg (500, 325mg)</td>
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Opioid Survival Skills

- IV morphine is 3 times as potent as oral (10mg IV = 30mg oral)
- Hydrocodone is about as potent as oral morphine
- Oxycodone is a little stronger than morphine
- Oral dilaudid is 4 times more potent than oral morphine (2mg dilaudid = 8mg morphine or hydrocodone)
- IV dilaudid is 7 times more potent than IV morphine (1mg dilaudid = 7mg morphine)
- IV dilaudid is 5 times more potent than oral dilaudid (1mg IV = 5mg oral)
- Transdermal fentanyl dose is 24-hour oral MS dose divided by 2. (100mg or MS = 50mcg/hr duragesic patch)
Converting opioids

1. Add up the total requirements per 24° (including breakthrough pain)
2. Convert to the new drug and route using an equivalency table
3. Reduce the total amount by about 25-50% (if pain controlled)
4. Divide the dose based on duration of action
5. Calculate a dose for breakthrough (usu. 10-15% of the total given Q 3-4°)
Examples

- Total Dilaudid dose is 12mg IV/SubQ/IM for the day and you want to convert to morphine.
- First, convert IV to PO Dilaudid (Factor of 5), so total Dilaudid is 60mg po.
- Conversion factor to morphine is 4 (30:7.5)
- Total morphine is about 240mg.
- Reduced by 25% is about 180mg total for the day
- MS Contin 90mg BID or MS Contin 60mg TID
- Breakthrough dose MSIR 15mg every 4 hour pm
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|                                     |         |         |                        |             |            | Avinza (q24h): 30, 60, 90, 120 mg caps                                    |
| Hydromorphine (Dilaudid)            |         |         | 3–4                    | 10–20       | 30–90      | Injection: 1, 2, 3, 4, 10 mg/mL; Tablets: 1, 2, 3, 4, 8 mg; Oral Soln: 1mg/mL |
| Fentanyl inj. (Sublimaze)           | 0.1–0.2 | 0.2–0.4 | IV: 0.5–1 PO: 1–2      | 3–5         | 10–30      | Injection: 50 mcg/mL                                                      |
| Fentanyl tab/loz. (Actiq, Fentora, Onsolis, Abstral) |         |         | 3–4                    | 10–20       | 30–90      | Bioavailability different for each product                               |
|                                     |         |         |                        |             |            | Dosing individual for each product                                       |
| Fentanyl patch (Duragesic)          | 72      | 8 – 12 hr | 24 – 36 hr             | 25mcg patch = 60mg oral morphine/day             |
|                                     |         |         |                        |             |            | Patches: 12, 25, 50, 75, 100 mcg/hr                                      |
| Methadone                           |         |         | 6–12                   | 10–20       | 30–60      | PO morphine:methadone ratio (mg/day): < 90 mg (4:1); 90–300mg (8:1); > 300 (12:1) |
| Oxycodone (Oxycontin (CR), OxyIR)   | 20      |         | IR 3–4 PO 30–60        | 30–60       |            | morphine:oxycodone ratio: 3:2                                           |
|                                     |         |         | CR 12                  |             |            | 25% will require q8hr dosing with Oxycodone CR                           |
| Hydrocodone                         | 30      | 3–4     | PO 10–20               | 30–60       |            | Lortab, Norco: 5, 7, 5, 10mg (500, 325mg)                                |
45 yo man with a painful skull base tumor. Admitted to hospital for pain crisis. He is on 60mg MS contin bid at home and taking 6 X10mg oxycodone IR for breakthrough pain. Pain is not controlled. You anticipate surgery and he will need to be NPO for a few days. What is the best strategy? (120mg + 60mg = 180mg oral MSE)

What is this equivalent to in IV MS?
- 60mg IV MS/24hr (180 / 3)

What is the equivalent in Dilaudid?
- 8.5mg IV Dilaudid/24hr (60 / 7)
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<td>Fentanyl patch (Duragesic)</td>
<td>72</td>
<td></td>
<td></td>
<td>8 – 12 hr</td>
<td>24 – 36 hr</td>
<td>25mcg patch = 60mg oral morphine/day Patches: 12, 25, 50, 75, 100 mcg/hr</td>
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Converting to PCA

- 60mg IV/24 hours = 2.5mg IV MS basal rate
- This will give him what he was taking
- Add bolus dosing for breakthrough pain
- 2-3mg with lockout as you feel appropriate
- Maximum hourly dosage is just a matter of math
- Check history on the PCA to tell you usage
From PCA to home regimen

- After 3 days in the hospital his pain is finally controlled. You check the history and he has used 150mg IV MS in 24 hour period consistently. It’s time to go home, what next?
- 150mg IV MS = 450mg oral MS
- MS contin 200mg bid with 60mg IR MS for breakthrough
- 200mcg Duragesic patch with 60mg IR MS for breakthrough
- Methadone?
58 yo lady who has been on opioids for years is on Ms Contin 60mg BID and Norco for a total of 60mg daily for breakthrough pain. She is admitted with a new laryngeal tumor which is painful and is placed NPO. You prescribe 4mg IV morphine q 4 hours for pain. You begin getting calls a few hours after admission. The nurse has been paged all night and she expresses concerns to you that the patient is expressing “drug seeking behaviors.” What should you do?

What is happening here?
Pseudoadiction

- The result of poorly managed pain
- Add up her usual MSE (120mg + 60mg = 180mg daily)
- Her MSE totaled to 180mg/24hours
- =60mg IV morphine/24hours
- You gave her a maximum of 24mg IV/24hours
- For NPO patients on long acting opioids, best idea is to put them on a PCA with appropriate basal rate to cover their baseline requirements.
Opioid Side Effects

- Constipation
- Dry mouth
- Nausea
- Itching
- Urinary retention
- Delirium
- Somnolence
- Sweats
- Respiratory depression
- Painful myoclonus
- Opioid use disorder
Side effects: Management

- Everybody must be on a bowel regimen
  - Miralax 17mg daily or bid
  - Senna
  - MOM
- Increased oral intake, Biotene rinses for dry mouth
- Non-sedating antihistamines for itching
- Opioid rotation for myoclonus or delirium
- Somnolence precedes respiratory suppression
  - Dilute 0.4mg naloxone in 10ml of saline, give 1ml q 5min for partial reversal
Adjuvants

- Glucocorticoids (multipurpose)
  - Bone pain
  - ICP
  - Bowel obstruction
  - Neuropathic pain
- BNZs (clonazepam)
  - Spastic pain
- Cannabis/Cannabinoids
  - Neuropathic pain?
- Topicals for neuropathic pain
  - Lidocaine, Capsaicin, Diclofenac, Doxepin, Ketamine, Gabapentin

- Analgesic antidepressants
  - Neuropathic pain with depression
    - Duloxetine
    - Venlafaxine
- Analgesic anticonvulsants
  - Neuropathic pain without depression
    - Gabapentin
    - Pregabalin
- Bisphosphonates
  - Malignant Bone pain
Adjuvants

- Acetaminophen
- Ibuprofen
- NSAIDS: Naproxen, Celebrex
- Antidepressants: Duloxetine
- Anticonvulsants: Gabapentin
- Interventional pain management

- Physical therapy
- Acupuncture
- Cognitive behavioral therapy
- Integrative medicine/allopathic
  - massage
  - yoga
  - meditation
  - mindfulness
  - art therapy
Common Head and Neck Issues

- Odynophagia
- Skin burns
- Co-morbid mood disorders
- Alcohol/tobacco abuse
- Pain syndromes: very often mixed with somatic and neuropathic qualities
- Osteoradionecrosis of the jaw
Aberrant Behavior

- Opioid overdoses have increased over the past decade
- New guidelines for management of chronic, non-malignant pain introduced this year, 2017
- Palliative care and cancer pain are exempt from these guidelines
- Yet, insurers and pharmacies still can present barriers for opioid dispensing
- We need to understand how to manage the risk of prescribing opioids
**DEFINITIONS**

**Tolerance:**
Drug induced loss of effect over time

**Dependence:**
Development of withdrawal with abrupt cessation or dose decrease

**Abuse:**
Using medications in a way not prescribed

**Addiction:**
Aberrant drug behavior with craving, loss of control, compulsive use despite harm to self

**Diversion:**
Distribution of a drug into the illicit marketplace
Risk Mitigation Strategies

- Screen all patients for potential misuse (We use the Opioid Risk Tool)
- Pain contracts for all moderate to high risk patients
- Stop prescribing if unable to adhere to patient responsibilities
- Urine drug screening initially and routinely
- Mental Health Referrals for high risk
- Weaning prescription versus medical detox if stopping therapy due to misuse
Risk Mitigation Strategies

- Opioid risk tool
- Controlled substance agreement/ pain contract
- Louisiana physician monitoring program
- Urinary drug screen
- Reassessment and documentation, DOCUMENTATION
TIPS

- No refills
- Prescribe enough till next visit
- No prescribing over the phone
- Set expectations
- Use functional pain scale
- No nonsense/zero tolerance policy
- Reassessment and document every visit
Resources

- Portenoy, et al. “Cancer pain management with opioids: Optimizing analgesia” UpToDate online
- Portenoy, et al “Cancer pain management: Adjuvant analgesics (coanalgesics)” UpToDate online
- Portenoy, et al. “Cancer pain management: General principals and risk management for patients receiving opioids” UpToDate online