Fighting the Good Fight: How to Convert Opioids Just Right!

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Disclosures

• Nothing to disclose
Learning Objectives

At the completion of this activity, the pharmacist will be able to:

1. Assess whether a patient is an appropriate candidate for switching among opioids.

2. Describe how to calculate opioid dosages when switching patients among opioids.

3. List factors for consideration when switching patients among opioids.

4. Given a case, accurately perform an opioid calculation between routes and between different opioid analgesics.
Self-Assessment Question

You have a patient taking morphine PO for post-operative pain (post-op day #2) and pain is well-controlled. Select the most appropriate reason to consider rotating to a different agent:

a. She begins to ask for more than prescribed
b. She develops acute kidney injury
c. Her blood pressure runs low
d. She reports nausea with morphine
A patient presents to the pharmacy with a prescription for oxycodone ER 30 mg PO q12h. It is not on formulary for her insurance. Morphine is preferred and you want to call her physician with a recommendation. You call and recommend:

A. Morphine ER 30 mg PO q12h
B. Morphine ER 15 mg PO q12h
C. Morphine ER 45 mg PO q12h
D. Morphine IR 5 mg PO q6h
Mr. Smith is a 68 yo male with metastatic prostate cancer, with diffuse bony metastases. He is admitted to the hospital with pain. On admission, he has AKI with a SCr increase from 1.3 to 2.8. At home he was using MSContin 30mg q8 hours and MS IR 15mg q4 hours PRN for pain. You want to ensure that he has adequate pain control during his hospitalization.
Why Rotate?

• Lack of efficacy
• Availability/Cost
• Tolerability
• Hyperalgesia
• Safety
• Change in patient status
## Dosage Conversion Table

<table>
<thead>
<tr>
<th>Opioid</th>
<th>Parenteral (mg)</th>
<th>Oral (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
<td>0.3</td>
<td>0.4 (SL)</td>
</tr>
<tr>
<td>Codeine</td>
<td>100</td>
<td>200</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>NA</td>
<td>30</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>1.5</td>
<td>7.5</td>
</tr>
<tr>
<td>Morphine</td>
<td>10</td>
<td>30</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>1</td>
<td>10</td>
</tr>
</tbody>
</table>

The mcg/hr dose of transdermal fentanyl (TDF) is ≈ one half the mg/day dose of PO morphine (e.g., 200 mg/24 hours PO morphine =100 mcg/hr TDF

Methadone conversion to morphine is not linear. Consult clinical specialist.
Opioid Selection Considerations

- Age
- Liver and renal function
- Cost/Availability
- Patient preference/experience
- Duration of action
- Body build
- Drug interactions
- Disease-state interactions
Relevant Patient Attributes

- Ability to swallow/PO status
- History of responsiveness
- Opioid allergies
- Body Build?
- Medical conditions
- Other medications
Relevant Patient Attributes

- Patient beliefs, fears, misconceptions
- Patient’s cognitive status
  - Reliability of self-assessment and pain scores
  - Ability to self-monitor
  - Ability to determine/relate need for breakthrough analgesia
Making the Switch

1. Globally assess the patient
2. Determine total daily dose of current opioid
   a. Determine actual use
3. Decide which opioid to switch to
   a. Consult opioid conversion chart
4. Individualize dose
5. Patient follow-up and continued re-assessment
Setting up the Calculation

• Simple ratio
  – Oral morphine to oral morphine is a 1:1 conversion (or 30mg:30mg)
  – Oral morphine to parenteral morphine is a 3:1 conversion (or 30mg:10mg)
  – Oral hydromorphone to oral morphine is a 1:4 conversion (or 7.5mg:30mg)
Setting up the Calculation

• Algebra!
  – Calculate total daily dose of current opioids
  – Set up conversion ratio between current opioid and new opioid (remember route of administration)
  – Cross multiply, solve for “X”

\[
\frac{x}{y} \text{ mg new opioid} = \frac{\text{mg equivalent of new opioid}}{\text{mg of current opioid} \times \text{mg equivalent of current opioid}}
\]
Online Opioid Calculators

- Practical Pain Management
  - [https://opioidcalculator.practicalpainmanagement.com](https://opioidcalculator.practicalpainmanagement.com)
- Global RPh
  - [http://globalrph.com/narcoticonv.htm](http://globalrph.com/narcoticonv.htm)
- Washington State
  - [http://agencymeddirectors.wa.gov/Calculator/DoseCalculator.htm](http://agencymeddirectors.wa.gov/Calculator/DoseCalculator.htm)
  - Disclaimer: “CAUTION: This calculator should NOT be used to determine doses when converting a patient from one opioid to another.”
- Centers for Disease Control and Prevention (CDC)
  - Disclaimer: “Do not use the calculated dose in MMEs to determine dosage for converting one opioid to another”
- CMS
Remember…

- Incomplete cross tolerance
  - Differential binding to major opioid receptors
  - Individual pharmacogenetics involving opioid metabolism and intracellular regulation of downstream responses
  - Opioid ligand-specific G protein interactions due to unique receptor conformational changes
  - Reduce calculated dose by 30-50%
Different Ways to Convert

• Single Step Rotation
  – Stop current opioid
  – Start new opioid
  – Most commonly used

• Step-wise rotation
  – May be preferable with high-dose opioids or methadone
  – Reduce current opioid by 10-30% and start 10-30% of new opioid per week
  – Patient must be able to manage and comprehend complex-dosing schedule
More Evidence Dare (I) Demand?

• Conversion calculation ≠ MEDD calculation
• MEDD = “lumping” all opioids and patients together
• MEDD seen as a way to avoid opioid-induced respiratory depression or possible opioid overdose
• Lack of agreement in terms of MEDD calculations in published guidelines
• Cut-off MEDD =100?
• MEDD cutoff offered but no real alternative solutions offered for replacing opioids
CASE - Revisited

Mr. Smith is a 68 yo male with metastatic prostate cancer, with diffuse bony metastases. He is admitted to the hospital with pain. On admission, he has AKI with SCr increase from 1.3 to 2.8. At home he was using MSContin 30mg q8 hours and MS IR 15mg q4 hours PRN for pain. You want to ensure that he has adequate pain control during his hospitalization.
CASE

• What are you worried about?

• What are your options for pain management?
Case 1: Total Daily Opioid Utilization

Give it a try!
Recommendation

• Step 1: Calculate TDD
  – TDD = 90 mg PO morphine/day

• Step 2: Convert to oral
  \[
  \frac{X \text{ PO Oxycodone}}{90 \text{ mg PO morphine}} = \frac{20 \text{ mg PO oxycodone}}{30 \text{ mg PO morphine}}
  \]
  – \( X = 60 \text{ mg PO oxycodone} \)
  – 60 mg PO oxycodone \( \times 0.5 = \text{ Oxycodone PO 30 mg} \)
  – Oxycodone ER 10 mg PO q8h
Recommendation – Breakthrough Pain

• Step 3: Calculate short-acting breakthrough dose
  – ~10-20% of TDD
    • Offered q 4-6 hours prn
  – Oxycodone IR 5 mg po q4h prn
Other options?

- Fentanyl?

- Hydromorphone?
## Conversion to Fentanyl

### Table 5-1

**Conversion from Oral Morphine to Duragesic**

<table>
<thead>
<tr>
<th>Oral 24-hour morphine (mg/day)</th>
<th>Duragesic® dose (mcg/h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>60–134</td>
<td>25</td>
</tr>
<tr>
<td>135–224</td>
<td>50</td>
</tr>
<tr>
<td>225–314</td>
<td>75</td>
</tr>
<tr>
<td>315–404</td>
<td>100</td>
</tr>
<tr>
<td>405–494</td>
<td>125</td>
</tr>
<tr>
<td>495–584</td>
<td>150</td>
</tr>
<tr>
<td>585–674</td>
<td>175</td>
</tr>
<tr>
<td>675–764</td>
<td>200</td>
</tr>
<tr>
<td>765–854</td>
<td>225</td>
</tr>
<tr>
<td>855–944</td>
<td>250</td>
</tr>
<tr>
<td>945–1034</td>
<td>275</td>
</tr>
<tr>
<td>1035–1124</td>
<td>300</td>
</tr>
</tbody>
</table>

And More Methods...

• Alternative: Fentanyl TDD (mcg/h) = MEDD. ÷ 2

• Transdermal: IV fentanyl ratio is 1:1!
  100 mcg/hour patch = 100 mcg/hr infusion!
Fentanyl Conversion Considerations

• Retrospective review of 2471 consecutive oncology patient visits for opioid rotation from TDF to strong opioids
• Advanced cancer patients (77%)
• Median TDF mcg/hour to net MEDD was 2.4 (0<0.0001) (range 0.3-5.2)
  – Implies 100 mcg/hour TDF = 240 mg MEDD
  – Not equianalgesic ratio, but opioid rotation ratio (ORR)
  – Wide range, use with caution
  – Lower ratio with higher TDF doses (Hyperalgesia?)

Conversion Off Fentanyl

• Conversion Chart Ratio
  → Morphine IV 10 mg = 100 mcg IV Fentanyl

• Other methods
  → Morphine IV 1 mg/hr = Fentanyl IV 25 mcg/hr

• Infusions of > 48 hour duration

• Conversion to alternative long-acting opioid
  – Initiate alternative long-acting ~12 hours after patch removal
Other options?

- **Fentanyl dose?**
  - 90 mg PO morphine/2 = 45 mcg/hour fentanyl
    - Fentanyl 37.5 mcg/hour

- **Hydromorphone dose?**
  - Manufacturer Chart – 90 mg*0.2 = 18*0.5 = 9 mg
    \[ \frac{X \text{ PO Hydromorphone}}{90 \text{ mg PO morphine}} = \frac{7.5 \text{ mg PO hydromorphone}}{30 \text{ mg PO morphine}} \]
    \[ X = 22.5 \text{ mg PO hydromorphone} \]
  - 22.5 mg PO hydromorphone*0.5 = Hydromorphone PO 11.25 mg
  - Hydromorphone ER 12 mg PO daily
Other options?

• Methadone?

• Buprenorphine?
Opioid Conversions to Methadone

• Important to note: conversion to methadone is not linear
  – The higher the opioid dose $\rightarrow$ the more potent methadone becomes
  – Possibly due to less cross-tolerance and additional mechanisms of action
  – Methadone is not associated with metabolites that may contribute to hyperalgesia

• Conversion from methadone to oral morphine: 1:3

• Conversion PO:IV $\rightarrow$ 2:1
Multiple Conversion Methods

<table>
<thead>
<tr>
<th>Morphine Equivalent (ME) Daily Dose (mg/day)</th>
<th>Initial Equianalgesic Dose ratio (PO morphine: PO methadone)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 30</td>
<td>2:1</td>
</tr>
<tr>
<td>30-99</td>
<td>4:1</td>
</tr>
<tr>
<td>100-299</td>
<td>8:1</td>
</tr>
<tr>
<td>300-499</td>
<td>12:1</td>
</tr>
<tr>
<td>500-999</td>
<td>15:1</td>
</tr>
<tr>
<td>≥1000</td>
<td>20:1 or greater</td>
</tr>
</tbody>
</table>

*Decrease calculated dose by 50%

**Quadratic Equation:**
Methadone Daily Dose (mg/day) = 5.3956 + (0.09401[ME] - 0.0000435[ME]^2)

** Avoid using with when converting from ≥1000 mg ME/day
## Buprenorphine Conversions

<table>
<thead>
<tr>
<th>Morphine</th>
<th>&lt; 30 mg</th>
<th>30-80 mg</th>
<th>&gt; 80 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocodone</td>
<td>&lt; 15 mg</td>
<td>15-40 mg</td>
<td>&gt; 40 mg</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>&lt; 15 mg</td>
<td>15-40 mg</td>
<td>&gt; 40 mg</td>
</tr>
<tr>
<td>Tramadol</td>
<td>&lt; 300 mg</td>
<td>300-400 mg</td>
<td>NA</td>
</tr>
<tr>
<td>Codeine</td>
<td>&lt; 90 mg</td>
<td>90-250 mg</td>
<td>&gt; 250 mg</td>
</tr>
</tbody>
</table>

- 5 mcg/hr patch
- Taper to < 30 mg morphine equivalent → 10 mcg/hr patch
- Buprenorphine patch may not be appropriate

Adapted from: Initiating Butrans® in appropriate opioid-experienced patients.
Other options?

• Methadone
  – 90 mg PO morphine/4 = 11.25 mg methadone per day
  – Methadone 3 mg PO q8h or 5 mg PO q12h

• Buprenorphine
  – Not best choice in metastatic cancer patient or acute exacerbation
  – Would need to taper morphine equivalent dose down to 30 mg or less and start 10 mcg/h patch
Special Population: Opioid-Tolerant Patients

• Definition:
  – Patients receiving ≥1 week at least 60mg PO morphine/day, fentanyl patch 25mcg/hr, 30mg PO oxycodone/day, 8mg PO hydromorphone/day, 25mg PO oxymorphone/day, or an equianalgesic dose of another opioid.
Patient Considerations – Opioid-Tolerant Patients

• Identify the at-risk population
• Prevention of withdrawal symptoms
• Effective analgesic treatment in the acute pain phase.
• Multidisciplinary teams for support
• Management of aberrant drug-taking behaviors

Sinatra RS and Jahr JS. General Surgery News, 2011
Opioid-Tolerant Patients

• Replace 75-100% of home opioid requirements
  – Give home regimen or basal infusion
• Will require greater doses for the acute pain
• Utilize multi-modal analgesia
  – Acetaminophen, NSAIDs (if appropriate), anti-convulsants, anti-depressants
  – May require opioid rotation
Adjuvant Considerations

• Multimodal analgesia is more effective and opioid-sparing

• Scheduled acetaminophen – be mindful of maximum doses

• Scheduled NSAIDs – when not contraindicated

• Gabapentin – start 300-900 mg/day; titrate as tolerated; renal dosing
  – Alternative: pregabalin
Adjuvant Considerations

• Selective Serotonin-Norepinephrine Reuptake Inhibitors
  – Venlafaxine, duloxetine
  – Alternative: Tricyclic antidepressants

• Non-pharmacologic interventions

• Invasive techniques (nerve blocks, injections, etc)
Self-Assessment Question

You have a patient taking morphine PO for post-operative pain (post-op day 2) and pain is well-controlled. Select the appropriate reason to consider rotating to a different agent:

a. She begins to take more than prescribed
b. She develops acute kidney injury
c. Her blood pressure runs low
d. She reports nausea with morphine
A patient presents to the pharmacy with a prescription for oxycodone ER 30 mg PO q12h. It is not on formulary for her insurance. Morphine is preferred and you want to call her physician with a recommendation. You call and recommend:

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B. Morphine ER 15 mg PO q12h
C. Morphine ER 45 mg PO q12h
D. Morphine IR 5 mg PO q6h
Things To Keep In Mind

• Safety First!
• Multi-modal analgesia
• Conversion charts and 5-step process serve as a guide
• Allow for individual results based on patient need
• Use conventional equianalgesic ratios as ballpark estimates
• Unlikely any single formula will substitute for a tailored titration
• Always include a scheduled bowel regimen
References

- McPherson ML. Demystifying opioid conversion calculations. Bethesda, MD; American society of health-system pharmacists; 2010.


- CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. Recommendations and Reports. 2016;65(1);149.


References

• Exalgo ER Tablets Package Insert. Conshohocken, PA: Neuromed Pharmaceuticals INC; March 2010


• Buprenorphine buccal film [package insert]. Available at: https://www.belbuca.com/hcp/.