OPIOID DOSE CONVERSIONS

JOSEPH CAMMILLERI, PHARM.D., BCACP, CPE
AMBULATORY CARE CLINICAL PHARMACIST
PAIN MANAGEMENT
UF CLINICAL ASSISTANT PROFESSOR
UF HEALTH JACKSONVILLE

OBJECTIVES

• Review opioid rotations
• Discuss incomplete cross tolerance
• Evaluate equianalgesic opioid conversion tables
• Demonstrate ability to perform opioid equianalgesic conversions in given cases

DISCLOSURE

Nothing to disclose

DANGERS ASSOCIATED WITH OPIOID ROTATIONS

• Variations in response to different opioids
  • Pharmacodynamic and Pharmacokinetic properties
  • Patient variables
• Limitations of the Equianalgesic tables
  • Evidence is lacking
  • Numerous tables available and ratios vary considerably
  • Confusing conversion recommendations

2016 ANNUAL MEETING

OPIOID ROTATION

• Definition: Change in opioid drug with the goal of improving outcomes or reduce adverse effects
• Usual reasons to consider an opioid rotation
  • Tolerance
  • Side effects
  • Insurance changes
• Concerns surrounding opioid rotations
  • Opioid rotation protocols with well defined outcomes are lacking
  • Limitation of equianalgesic tables
  • Incomplete cross tolerance

2016 ANNUAL MEETING

Incomplete Cross Tolerance

• Difficult to anticipate or study
• Subtle differences in molecular structure of each opioid
• Individual patient's opioid receptors response to the new molecular structure

2016 ANNUAL MEETING

OPIOID ROTATION

• Difficult to anticipate or study
• Subtle differences in molecular structure of each opioid
• Individual patient's opioid receptors response to the new molecular structure

2016 ANNUAL MEETING

OPIOID ROTATION

• Definition: Change in opioid drug with the goal of improving outcomes or reduce adverse effects
• Usual reasons to consider an opioid rotation
  • Tolerance
  • Side effects
  • Insurance changes
• Concerns surrounding opioid rotations
  • Opioid rotation protocols with well defined outcomes are lacking
  • Limitation of equianalgesic tables
  • Incomplete cross tolerance

2016 ANNUAL MEETING

Incomplete Cross Tolerance

• Difficult to anticipate or study
• Subtle differences in molecular structure of each opioid
• Individual patient's opioid receptors response to the new molecular structure

2016 ANNUAL MEETING

OPIOID ROTATION

• Definition: Change in opioid drug with the goal of improving outcomes or reduce adverse effects
• Usual reasons to consider an opioid rotation
  • Tolerance
  • Side effects
  • Insurance changes
• Concerns surrounding opioid rotations
  • Opioid rotation protocols with well defined outcomes are lacking
  • Limitation of equianalgesic tables
  • Incomplete cross tolerance

2016 ANNUAL MEETING

Incomplete Cross Tolerance

• Difficult to anticipate or study
• Subtle differences in molecular structure of each opioid
• Individual patient's opioid receptors response to the new molecular structure

2016 ANNUAL MEETING

OPIOID ROTATION

• Definition: Change in opioid drug with the goal of improving outcomes or reduce adverse effects
• Usual reasons to consider an opioid rotation
  • Tolerance
  • Side effects
  • Insurance changes
• Concerns surrounding opioid rotations
  • Opioid rotation protocols with well defined outcomes are lacking
  • Limitation of equianalgesic tables
  • Incomplete cross tolerance

2016 ANNUAL MEETING

Incomplete Cross Tolerance

• Difficult to anticipate or study
• Subtle differences in molecular structure of each opioid
• Individual patient's opioid receptors response to the new molecular structure

2016 ANNUAL MEETING

OPIOID ROTATION

• Definition: Change in opioid drug with the goal of improving outcomes or reduce adverse effects
• Usual reasons to consider an opioid rotation
  • Tolerance
  • Side effects
  • Insurance changes
• Concerns surrounding opioid rotations
  • Opioid rotation protocols with well defined outcomes are lacking
  • Limitation of equianalgesic tables
  • Incomplete cross tolerance

2016 ANNUAL MEETING

Incomplete Cross Tolerance

• Difficult to anticipate or study
• Subtle differences in molecular structure of each opioid
• Individual patient's opioid receptors response to the new molecular structure

2016 ANNUAL MEETING

OPIOID ROTATION

• Definition: Change in opioid drug with the goal of improving outcomes or reduce adverse effects
• Usual reasons to consider an opioid rotation
  • Tolerance
  • Side effects
  • Insurance changes
• Concerns surrounding opioid rotations
  • Opioid rotation protocols with well defined outcomes are lacking
  • Limitation of equianalgesic tables
  • Incomplete cross tolerance

2016 ANNUAL MEETING

Incomplete Cross Tolerance

• Difficult to anticipate or study
• Subtle differences in molecular structure of each opioid
• Individual patient's opioid receptors response to the new molecular structure

2016 ANNUAL MEETING
**OPIOID ROTATIONS**

- Assess the situation to find out why the rotation is occurring
- Use this opportunity to hit all the *WHYS* and the *HOWS*
  - Why a rotation might be helpful
  - Why it is necessary to follow the instructions closely
  - Why adjuvants and nonpharmacological options are just as important
  - How to convert from one agent to another
  - How to monitor for any different side effects
  - How to use the short acting agents for breakthrough (if applicable)


---

**EQUIANALGESIC TABLES**

<table>
<thead>
<tr>
<th>Opioid</th>
<th>IV (mg)</th>
<th>PO (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>10</td>
<td>30</td>
</tr>
<tr>
<td>Hydrocodone</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>
<tr>
<td>Hydromorphone</td>
<td>1.5</td>
<td>7.5</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>0.3</td>
<td>0.4(SL)</td>
</tr>
<tr>
<td>Codeine</td>
<td>100</td>
<td>200</td>
</tr>
<tr>
<td>Meperidine</td>
<td>100</td>
<td>300</td>
</tr>
</tbody>
</table>

*What about Methadone??? Never ever use an equianalgesic table to calculate methadone!!!*

**2016 ANNUAL MEETING**

**5 STEP APPROACH TO OPIOID CONVERSION**

1. Globally assess the patient
2. Determine the total daily usage of the current opioid
3. Decide on which opioid analgesic will be used for the new agent and review established conversion tables
4. Individualize the dosage based on assessment and ensure adequate access to breakthrough medication
5. Establish frequent patient follow up and reassessment


---

**METHADONE DOSAGE CONVERSION**

<table>
<thead>
<tr>
<th>Morphine Dose (mg/day)</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;100</td>
<td>3:1</td>
</tr>
<tr>
<td>101-300</td>
<td>5:1</td>
</tr>
<tr>
<td>301-600</td>
<td>10:1</td>
</tr>
<tr>
<td>601-800</td>
<td>12:1</td>
</tr>
<tr>
<td>≥801</td>
<td>20:1</td>
</tr>
</tbody>
</table>

*Modified Morley-Makin UK Model (Friedman)*

- < 1000mg/day morphine < 65yo = 10:1
- < 1000mg/day morphine > 65yo = 20:1


---

**METHADONE DOSAGE CONVERSION**

- Methadone prescribing info:
  - < 100mg MS (20-30% ME)
  - 101-300mg MS (10-20% ME)
  - 301-600mg MS (8-12% ME)
  - 601-800mg MS (5-10% ME)
  - >801mg MS (<5% ME)

  *MS= morphine sulfate ME= methadone equivalents*

  *Individualize dosing for each patient:*
  - Patient’s degree of opioid tolerance
  - Age
  - Medical status of the patient
  - Concurrent non-opioid analgesics and medications with CNS activity
  - Possible drug interactions with other medications
  - Type and severity of the patient’s pain


---

**EQUIANALGESIC CONVERSIONS**

- Step 1: Calculate total amount of opioid in 24 hours
- Step 2: Convert to morphine equivalents by using Equianalgesic Table
  - **Remember: Do Not use Equianalgesic Table for Methadone**
- Step 3: Set up proportion
- Step 4: Adjust dose for incomplete cross tolerance
- Step 5: Determine dosing interval based on new drug dosing recommendations
- Step 6: Consider addition of breakthrough medication (15% of TOTAL DAILY dose) for dosage titration
- Step 7: Follow up with patient and readjust dosing based on IR formulation use

**McPherson, Mary Lynn M. Demystifying Opioid Conversion Calculation: A Guide for Effective Dosing. ASHP 2010**

---
THE EQUIANALGESIC CALCULATION

\[
\text{mg TDD new opioid} \times \frac{\text{equianalgesic factor new opioid}}{\text{mg TDD current opioid} \times \text{equianalgesic factor current opioid}} = X
\]

Example:

10mg TDD oral morphine
120mg TDD oral hydrocodone

(Patient taking hydrocodone ER 40mg q12h and hydrocodone/apap 10/325mg four times a day so total dose is 120mg)

Therefore, X = 120mg oral morphine equivalence (ME)

What strength of fentanyl patch should you recommend?

Hint: The number of mcg per hour of TDF should be about half the number of milligrams of oral morphine per day.

Proper Recommendation: Transdermal Fentanyl Patch 50mcg Apply 1 patch topically q72 hours

PATIENT EDUCATION

- Review all proper counseling points for patch use including patch placement and disposal
  - Placement:
    - Flat dry skin area on upper arm, chest, flank, or back
    - Free of irritation, excess hair, past radiation treatment
  - Disposal:
    - Fold the patch in half so that the adhesive side is inward and immediately flush down the toilet
  - When should the patient take his last Hydrocodone ER?
    - Patient should be told to take the last dose of Hydrocodone ER at the same time the TDF is applied

CHANGING FROM A TDF TO ANOTHER LONG ACTING OPIOID

- Remove the TDF patch
  - 1st 12 hours:
    - Patient to use only the BTP medication
  - 12 hours after patch removal:
    - Begin 50% of calculated schedule opioid regimen and use BTP medication prn
  - 24 hours after patch removal:
    - Increase to 100% of calculated schedule opioid regimen and use BTP medication prn

Fentanyl blood levels

Max concentration achieved in 24-36 hours

Last dose will taper down as fentanyl levels increase

Hydrocodone blood levels

KEEP CALM ONLY ONE LEFT
### Equianalgesic Tables

<table>
<thead>
<tr>
<th>Opioid</th>
<th>IV (mg)</th>
<th>PO (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>10</td>
<td>30</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>---</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>
<tr>
<td>Hydromorphone</td>
<td>1.5</td>
<td>7.5</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>0.1</td>
<td>---</td>
</tr>
<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>Meperidine</td>
<td>100</td>
<td>300</td>
</tr>
</tbody>
</table>

Methadone-naltrexone 100-4mg Q12h and Morphine IR 30mg (5 tablets daily)
Patient is on 350mg morphine daily

### Opioid IV (mg) PO (mg)

- **Morphine**: 10mg IV, 30mg PO
- **Hydrocodone**: --- IV, 30mg PO
- **Oxycodone**: 10mg IV, 20mg PO
- **Oxymorphone**: 1mg IV, 10mg PO
- **Hydromorphone**: 1.5mg IV, 7.5mg PO
- **Fentanyl**: 0.1mg IV, --- PO
- **Buprenorphine**: 0.3mg IV, 0.4mg PO
- **Codeine**: 100mg IV, 200mg PO
- **Meperidine**: 100mg IV, 300mg PO

### EQUIANALGESIC TABLES

<table>
<thead>
<tr>
<th>Opioid</th>
<th>IV (mg)</th>
<th>PO (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>10</td>
<td>30</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>---</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>
<tr>
<td>Hydromorphone</td>
<td>1.5</td>
<td>7.5</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>0.1</td>
<td>---</td>
</tr>
<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>Meperidine</td>
<td>100</td>
<td>300</td>
</tr>
</tbody>
</table>

### Equianalgesic Calculation

- \[ \text{new opioid TDD} = \text{equianalgesic factor} \times \text{current opioid TDD} \]
- \[ \text{new opioid PO} = \text{equianalgesic factor} \times \text{current opioid PO} \]
- \[ \frac{\text{new opioid TDD}}{\text{new opioid PO}} = \frac{\text{equianalgesic factor}}{\text{equianalgesic factor oral}} \]
- \[ \frac{350 \text{mg TDD oral ME}}{30 \text{mg oral morphine}} = \frac{20 \text{mg po oxycodone}}{30 \text{mg oral morphine}} \]

**X** = 233mg TDD oral oxycodone

### ADDITIONAL POINTS

- Start low and go slow
- Be conservative
- Avoid benzodiazepines and opioids
- Recommend dispense naloxone

### Rescue Medication

- Very important to supply during titration period
- 5-10% of **Total Daily Dose**
- **Total daily dose Oxycodone is 160mg**
  - 10% of 160mg: 16mg oxycodone
  - Reasonable rescue: Oxycodone 15mg po q4h BTP
- **Proper Recommendation**
  - Oxycodone ER: 80mg po q12h
  - Oxycodone: 15mg po every 4 hours pm BTP