Pain: Objectives

• Describe safe opioid dosing and titration
• Discuss management of patient controlled analgesia (PCAs)
• Apply equianalgesic opioid dosing principles

Pain: Methadone – Does not follow regular opioid principles!

• Recommend consulting Palliative Care or Pain Service for patients in acute pain crisis who are on Methadone

Pain: Why is it important?

- Pandemic
  - Most common:
    - reason patients seek health care
    - symptom in hospitalized adults

Pain: Why is it important?

- Causes distress
- Consequences
  - Increased morbidity
  - High risk for developing chronic pain
- Poorly controlled
  - Only 1 in 4 report control of their pain

Pain: Opioid Therapy

- Routine dosing
- Breakthrough dosing
- Titration
- Choice of opioid
Pain: Opioid Routine Dosing

• Preferred route
  – By the mouth
• Preferred schedule
  – Around the clock


Pain: Opioid Routine Dosing

• Immediate Release (IR)
  – e.g., Morphine IR, Oxycodone IR
  – Schedule
    • Effective analgesic t½ = 2-4 hours
    • q 4 hrs
  – Starting dose
    • Morphine IR 5 mg po q4 hr (2.5 mg in elderly)


Pain: Opioid Routine Dosing

• Sustained Release (SR)
  – e.g., Morphine SR, Oxycodone SR
  – Transition from IR once on stable opioid requirement for at least 48 hours
  – Schedule
    • q 12 hrs (q 8 hrs if rapid metabolizers)
  – Starting dose
    • Take IR total daily dose and convert to SR q12 hr
      • eg. Morphine IR 5 mg po q4 hr
      • = 30 mg/day
      • = Morphine SR 15 mg po BID

EPEC Module 4 1999.
Pain: Opioid Breakthrough Dosing

• Dose
  – IR form
  – Stay with same opioid as scheduled
    • Avoid mixing opioids
  – 10-15% of 24 hour total opioid requirement per breakthrough dose


Pain: Case Study

• 52 y/o M with chronic pain from metastatic colon cancer
• Morphine ER 120 mg po BID
• Breakthrough med?
  1. Morphine IR 10 mg po
  2. Morphine IR 30 mg po
  3. Oxycodone/APAP 5/325 mg 2 tabs po

Pain: Opioid Breakthrough Dosing

• Interval
  – Time to peak effect

EPEC Module 4 1999.
Pain: Opioid Time to Peak Effect

<table>
<thead>
<tr>
<th>Route of Administration</th>
<th>Time to Peak Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td>60 minutes</td>
</tr>
<tr>
<td>IV</td>
<td>10 minutes</td>
</tr>
</tbody>
</table>


Pain: Case Study

- Morphine IR 30 mg po Q1 hour as needed
  - q4 hour for the non-seriously ill patient
Pain: Opioid Titration – How often?

- Immediate release oral
  - every ≥ 1-2 hours
- Sustained release oral
  - every ≥ 48-72 hours
- IV opioids
  - every ≥ 8-15 minutes
- Transdermal Fentanyl
  - every ≥ 72 hours


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Pain: Opioid Titration

<table>
<thead>
<tr>
<th>Pain Severity</th>
<th>Increase Dose By</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>25%</td>
</tr>
<tr>
<td>Moderate</td>
<td>50%</td>
</tr>
<tr>
<td>Severe</td>
<td>100%</td>
</tr>
</tbody>
</table>

EPEC Module 4 1999; NCCN Palliative Care V.1.2010.

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* Pain Pearl *

- Avoid increasing the dose of opioid by more than 100% at any one time!
Pain: Opioid Therapy Recap

- **Routine dosing**
  - Schedule IR q 4 hrs
  - Effective analgesic t½
  - Consider SR
    - once pain/opioid requirements stabilize for 48-72 hrs

- **Breakthrough dosing**
  - Dose: 10-15% of 24 hour total opioid requirement
  - Interval: time to peak effect
    - po = 1 hr
    - iv = 10 min

- **Titration**
  - Mild: ↑ 25%
  - Moderate: ↑ 50%
  - Severe: ↑ 100%

Pain: Choice of Opioid

- What is considered the gold standard opioid?


Pain: Opioid Metabolism

- 90-95% renally cleared
- Avoid Morphine with renal failure
  - Potent active renal metabolites
- Fentanyl, Hydromorphone, and Oxycodone better choices with renal failure

Dean: JPS/M 2004; Macintryre: Br J Anaesth 2001;
Pain: Transdermal Fentanyl

- Chronic, stable pain
- NOT good option for acute pain or cachectic patients
- Slow to titrate
- Poor subcutaneous lipid stores
  – Lower plasma conc in cachectic cancer pts
- Increased absorption with fevers


Pain: Transdermal Fentanyl

- Fentanyl TD ≈ 2x po Morphine equivalent
- Fentanyl 25 mcg/hr patch TD q72 hrs
  ≈ Morphine 50 (50-60) mg oral per day
  ≈ Morphine SR 30 mg po BID

Pain: Pharmacologic Management

- Opioid Therapy
- PCAs
- Equianalgesic Dosing
Pain: PCAs

• Parameters
  – Basal rate
  – Demand dose
  – Lockout time
  – Nurse initiated bolus

Pain: PCA Basal Rate

• Opioid naïve or not???

Pain: PCA Basal Rate

• Opioid naïve; routine post-operative
  – No basal rate
    • Increased rates of respiratory depression
    • No improvement in pain scores

Pain: PCA Basal Rate

- Opioid tolerant
  - Convert 24 hour total opioid requirement to hourly rate (by equianalgesic dosing)

Pain: PCAs

- Parameters
  - Basal rate
  - Demand dose
  - Lockout time
  - Nurse initiated bolus

Pain: PCA Demand Dose

- Opioid naïve or not???
Pain: PCA Demand Dose

- Opioid tolerant
  - 50% of the basal rate (50-100%)
- Opioid naïve, no basal...
  - begin with 1 mg Morphine equivalent
    (0.5 mg in elderly)


Pain: PCAs

- Parameters
  - Basal rate
  - Demand dose
  - Lockout time
  - Nurse initiated bolus

Pain: PCA Lockout Time

- Based on time to peak effect
- 10 minutes is a standard interval
  - No difference in pain level with different intervals

Pain: PCAs

- Parameters
  - Basal rate
  - Demand dose
  - Lockout time
  - Nurse initiated bolus

Pain: PCA Nurse Initiated Bolus

- Variable
- Twice the demand dose


Pain: PCA Titration

- Acute pain control / IR
  - Demand dose
- Chronic pain control / SR
  - Basal rate
Pain: PCA Titration Acute Pain

- Demand dose
  - Can change every 10-15 minutes if needed
  - Practically: change and reevaluate in an hour

- Opioid titration
  - Mild pain: ↑ 25%
  - Moderate pain: ↑ 50%
  - Severe pain: ↑ 100%


Pain: PCA Titration Chronic Pain

- Basal rate
  - Takes 8-24 hours to achieve steady state
  - Do not change more frequently than ≥ 8 hours
    - Every 24 hours reasonable
  - Avoid ↑ by more than 100% at a time


* Pain Pearl *

- Titrate PCA demand dose for rapid pain control
PCA Titration Summary

- Basal rate
  - Change ~ daily based on 24 hour opioid usage in opioid-tolerant

- Demand dose
  - Titrate for acute pain control
    - ↑ 25-50% mild-moderate pain
    - ↑ 50-100% moderate-severe pain

- Lockout time
  - Keep at 10 min

Pain: Pharmacologic Management

- Opioid Therapy
- PCAs
- Equianalgesic Dosing

Pain: Opioid Conversions - Equianalgesic Dosing

1. Calculate total 24 hour total opioid dose
2. Convert to 24 hour new opioid equivalent
3. Adjust by 50-75% for incomplete cross tolerance
4. Triple check calculations
5. Constipation prophylaxis!

EPEC Module 4 1999.
### Pain: Incomplete Cross Tolerance

- When switching from one opioid to another
- Tolerance developed to one opioid may not completely transfer to the new opioid
- Start the new opioid at 50-75% of the equianalgesic dose
  - 60% good generalization


### * Pain Pearl *

- Adjust for incomplete cross tolerance with equianalgesic dose conversions

### Pain: Opioid Conversions- Equianalgesic Dosing

<table>
<thead>
<tr>
<th>Current Opioid</th>
<th>New Opioid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current Opioid</td>
<td>Total 24 hour Current Opioid</td>
</tr>
<tr>
<td>New Opioid</td>
<td>Total 24 hour New Opioid (X)</td>
</tr>
</tbody>
</table>
Pain: Case Study

• 52 y/o M with chronic pain from metastatic colon cancer
• Admitted to the hospital for PNA
• ARF (peak creatinine 2.9)
• Acute pain crisis
• Morphine ER 120 mg po BID and Morphine IR 30 mg po q1 hour prn BTP

Pain: Case Study

• PCA to achieve rapid analgesia
• Switch Morphine to Hydromorphone with ARF


Pain: Case Study: Calculate 24 hour total opioid dose

• Morphine ER 120 mg po BID = 240 mg/day
• Morphine IR 30 mg x 5/day = 150 mg/day

Total Morphine po dose/day
= 240 mg + 150 mg = 390 mg/day
Pain: Case Study - Convert to 24 hour new opioid equivalent

<table>
<thead>
<tr>
<th>Current Opioid</th>
<th>Total 24 hour Current</th>
<th>New Opioid</th>
<th>Total 24 hour New</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine 30 mg PO</td>
<td>Morphine 390 mg/day</td>
<td>Hydromorph 1.5 mg IV</td>
<td>Hydromorph X</td>
</tr>
</tbody>
</table>

\[ X = \text{Hydromorphone 19.5 mg/day IV} \]

Pain: Case Study - Adjust 60% for incomplete cross tolerance

Hydromorphone 19.5 mg/day \( \times 0.6 \)  
= Hydromorphone 11.7 mg/day IV

Pain: Case Study - PCA Parameters

Hydromorphone 11.7 mg/day IV  
\( \div 24 \text{ hours/day} \approx 0.5 \text{ mg/hour} \)

- Opioid: Hydromorphone IV  
- Basal Rate: 0.5 mg/hour  
- Demand Dose: 0.3 mg  
- Lockout Time: 10 minutes  
- Nurse Initiated Bolus: 0.6 mg
Pain: Case Study - Triple check calculations

- Call a colleague or pharmacist who is experienced in opioid calculations

Pain: Case Study - Constipation Prophylaxis

- Senna 2 tablets PO QHS

* Pain Pearls *

- Avoid increasing opioid dose by more than 100% at any one time
- Titrate demand dose on PCA for rapid pain control
- Adjust for incomplete cross tolerance with equianalgesic dose conversions

"Yes! That was very loud Sir, but I said I wanted to hear your HEART!"