Learning Objectives

Pharmacists:
- Identify issues of opioid misuse and abuse in the US.
- Explain the role of prescription drug monitoring programs to combat opioid misuse and abuse.
- Discuss implications for medication-use policy in hospitals and health systems.
- Describe the role of opioids for various pain syndromes.
- Differentiate the pharmacology of commonly used opioids, including long-acting and short-acting agents.
- Evaluate medication calculations for appropriateness of opioid conversions and titrations.

Conflict of Interest

No conflicts of interest to disclose

Need For Balance

NWH: Context
Treatment of Chronic Pain has Created Silent Epidemic

AAPP COC
Common $30 million to Combat Prescription Drug Overuse

Oregon Board of Medical Examiners: Parenting Decisions - Prescribing either too little or too much pain medication can spoil professional doctor

FDA Commissioner: "We have an important balancing act of trying to ensure that analgesic effective drugs are made available to patients with low real pain and need medical care"

Pharmacist Clinician, Mesilla Valley Hospice

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Public Health Issue

- Chronic pain affects ~100 million Americans
- Costs up to $635 billion/year in medical tx and lost productivity
- During the 1990s, undertreatment of pain was identified as deficiency in medical practice and education
- Increased focus on routine assessment and effective treatment
- Aggressive marketing by drug companies
Public Health Issue

- 46 Americans die each day from prescription opioid overdoses; ~2 deaths/hour; 17,000 annually
- Drug overdose was the leading cause of injury death in 2013, greater than car accidents and suicide
- In 2012, 2.59 million opioid pain medication prescriptions were written, enough for every adult in America to have a bottle of pills

Scope of Problem in New Mexico - 2008

Sources of Medication

Scope of the Problem in NM – Education Requirements

- In 2012, Senate Bill 215 was adopted – revised Pain Relief Act of 1999
- Required all health care professional licensing boards to mandate CME training in treatment of chronic pain
- Development of Governor’s Prescription Drug Abuse and Overdose Prevention and Pain Management Advisory Council
- August 2012 – Rule 16.10.14
  - Physicians and PAs to complete 5 hrs of CME in pain and addiction between November 1, 2012 and June 30, 2014
  - Must sign up with BOP PMP and check PMP each time a new prescription for chronic opioids is written and every 6 months thereafter
Statewide CME

- Development of 5 hr course
  - Basic awareness of epidemic of chronic pain, opioid abuse, addiction, and diversion
  - Management of pain with nonopioid medications
  - Safer opioid prescribing
  - Identification and management of pts at risk for addiction
  - Current state and federal rules and regulations regarding use of PMPs
  - Pre-post surveys to >1000 clinicians that participated in CME course (67% physicians, 30% midlevel providers)
  - Significant improvement in course objectives relating to knowledge, self-efficacy and attitudes regarding pain management

CDC Prescription Drug Overdose: Prevention for States

- NM is one of 16 states to receive funding to advance prevention strategies
- Maximize Prescription Drug Monitoring Programs (PDMPS)
  - Move toward universal registration and use
  - Easier access and use
  - Make data more timely
  - Expand and improve proactive reporting
  - Use data to better understand behavior of overdose epidemic

NM PMP

- Dispensing pharmacy requirements
  - In accordance with 16.19.29.8, shall submit the information in accordance with transmission methods and frequency established by the board; shall report within 1 business day of prescription being filled
  - Data elements to upload through PMP site
    - Dispenser details: DEA #
    - Patient details: name, DOB, gender, address
    - Prescriber details: DEA #
    - Prescription details: Rx #, date written, refills, date filled, product ID, qualification, medication, NDC, quantity, days supply, dosage unit, Rx origin code, partial fill, payment method
  - Also applies to dispensing practitioners

http://www.rld.state.nm.us/boards/Pharmacy_Prescription_Monitoring_Program.aspx
PMP - Perfect Monitoring Program?
- Limitations
  - State-to-state variation
  - Agency that houses PMP
  - Which controlled substances are monitored
  - Proactive vs. reactive
  - Dependent on utilization
  - Not all states share PMP data
- Effectiveness
  - RADARS (Research on Abuse, Diversion, and Addiction-Related Surveillance) data
  - Decrease in number of poison center interventions and decrease in admissions for opioid overdose
  - Florida POMP
    - Associated with 1.4% decrease in opioid prescriptions; 2.3% decrease in opioid volume, and 3.6% decrease in POMP per transaction

Expanded Access to Naloxone
- Amendment to Pharmacist Prescriptive Authority Act to allow prescriptive authority
- Must complete a training course and submit a protocol to the BOP
- Informed consent must be documented
- Pharmacist must notify provider within 15 days of naloxone dispensing

Screening Criteria
- High doses of opioids long-term
- Recently completed opioid detox or inpatient treatment program
- Recently released from incarceration with a past history of opioid abuse
- Recently experienced an overdose
- Households with people at risk of overdose
- Prescribed long-acting opioid
- History of or current polyopioid use
- ≥ 65 years old receiving an opioid
- Concurrent prescription or OTC that could potentiate respiratory depression
- Patients who have difficulty accessing emergency medical services
- Patients as determined by the pharmacist using professional judgment

Just a Retail Pharmacy Problem?
- Even though this isn't the maternity ward, some times it can sure pass

Hospital Pharmacists
- Health-system pharmacists are subject to the same level of DEA scrutiny as retail pharmacists
- Determine controlled substances are ordered for a legitimate medical purpose
- Proper record-keeping and labeling procedures
- Issues of diversion
- Use of opioids for maintenance or detoxification in patients who are addicted

Treating Pain in Hospitalized Patients

- Quality of acute inpatient pain management remains suboptimal and poorly understood
- Many patients have frequent prolonged and unrelieved severe pain episodes
- Patients who abuse pain likely to be minority, but complex cases

Inpatient Pain Management

<table>
<thead>
<tr>
<th>Case</th>
<th>Opioid Treatment</th>
<th>Opioid Spinal</th>
<th>Inpatient Spinal</th>
<th>Risk Score Summary</th>
</tr>
</thead>
</table>
| Case 1 | Morphine-Saline | Morphine-Saline | Morphine | Increased use of inpatient opioids in low risk patients; increased opioid use in high risk patients
| Case 2 | Opiate | Opiate | Opiate | Increased use of inpatient opioids in low risk patients; increased opioid use in high risk patients
| Case 3 | Ketamine | Ketamine | Ketamine | Increased use of inpatient opioids in low risk patients; increased opioid use in high risk patients

Opioid Use for Chronic Pain – Myth or Fact

- Dose escalation is the best response when patients experience decreased pain control.
- Addiction is rare in patients receiving medically prescribed chronic opioid therapy.
- Extended-release opioids have NOT been proven to be safer or more effective than short-acting opioids for managing chronic pain.

Opioid Use for Chronic Pain

- Weak evidence of long-term (i.e., ≥ 6 months) effectiveness of morphine and transdermal fentanyl in reducing pain and improving function
- No evidence of effectiveness of other opioids
- Long-term opioid use may be associated with tolerance, opioid-induced hyperalgesia, physical and psychological dependence, persistent adverse effects, a lower QOL, increased rates of depression, and increased healthcare utilization

Pathogenesis of Pain

- Nociceptive Pain
  - Somatic
  - Visceral
- Non-epithelial, well-localized
- MAnnually joint, rib, chest
- Mass to bone, fractures
- Diffuse, deep-aching, burning
- Poorly localized, extensive, intercostal, unresponsive, persistent, chronic
Pathogenesis of Pain

**Neuropathic Pain**
- Peripheral or Central
- Burning, shooting, pricking, parasthesias.
- Phantom limb pain, SCI pain, stroke, diabetic neuropathy, postherpetic neuralgia.

**Opioid Therapy Strategies**
- For moderate to severe pain, increase opioid total daily dose (TDD) by 50-100%, regardless of starting dose.
- For mild to moderate pain, increase opioid TDD by 25-50%, regardless of starting dose.
- Short-acting, immediate-release opioids can be safely dose escalated every 2 hours.
- Long-acting, sustained-release opioids can be increased every 24 hours (does NOT include transdermal fentanyl or methadone).

**Adjuvant Analgesics**
- **Neuropathic pain**
  - Antidepressants (TCAs, SNRIs, SSRIs)
  - Anticonvulsants
  - Local anesthetics
  - Topicals
- **Bone pain**
  - NSAIDs
  - Corticosteroids
  - Musculoskeletal spasms
  - Muscle relaxants
  - Benzodiazepines
  - Medical cannabis

**Short-Acting Opioids**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Onset</th>
<th>Peak Effect</th>
<th>Duration</th>
<th>Common starting doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>PO: 20-30 min IV: 1-2 min</td>
<td>PO: 60-90 min IV: 10-15 min</td>
<td>PO: 1-4 hrs IV: 2-4 hrs</td>
<td>5 mg PO q4h PRN</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td></td>
<td></td>
<td></td>
<td>1 mg PO q3-4h PRN</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>PO: 20-30 min</td>
<td>PO: 60-90 min</td>
<td>PO: 3-4 hrs</td>
<td>5 mg PO q6h PRN</td>
</tr>
</tbody>
</table>

**Long-Acting Opioids**
- **Morphine ER (MS Contin), oxycodone ER (Oxycontin), hydromorphone ER (Exalgo)**
  - Onset of action within 2 hrs
  - Plateau effect 3-8 hrs, duration 8-12 hrs

**Fentanyl Patches**
- **Good for chronic, stable pain**
  - Should not be prescribed to an opioid naïve patient
  - Are NOT good for rapidly escalating pain due to difficult titration
  - > 12 hr onset of action and 3 days to steady state
- **Dosing/conversion**
  - Fentanyl patch dose (mcg) × 2 = oral morphine equivalent in 24 hrs
  - Example: 25 mcg/hr fentanyl patch = 50 mg oral morphine in 24 hrs
Methadone
- Used to treat opioid dependent patients
- Many characteristics that make it ideal for chronic pain
- Long duration of action, efficacy, low cost
- Mu agonist, NMDA receptor antagonist
- PK properties
  - Basic, lipophilic drug - onset 15-45 minutes after oral
  - Oral bioavailability: 70-80%
  - Widely distributed, retained in tissues
  - Extensively metabolized (3A4, 2B6, 2C8, 2C9, 2C19, 2D6, many drug interactions)
  - Elimination half-life: 5-130 hours (avg 20-35 hours)
  - Takes 4-10 days to achieve steady-state
  - When initiating therapy and with dosage changes

Appropriate Methadone Candidates
- True morphine allergy or hypersensitivity (or other mu agonist)
- Significant renal impairment
- Neuropathic pain
- Opioid-induced adverse effects
- Pain refractory to other opioids or uncontrolled pain
- Cost is an issue
- Long-acting opioid preferred (especially oral solution)

Equianalgesic Opioid Dosing

<table>
<thead>
<tr>
<th>DRUG</th>
<th>EQUIANALGESIC DOSES (MG)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PARENTERAL</td>
</tr>
<tr>
<td>Morphine</td>
<td>10</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>0.3</td>
</tr>
<tr>
<td>Codeine</td>
<td>100</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>0.1</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>N/A</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>1.5</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>100</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>10</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>1</td>
</tr>
<tr>
<td>Temodal</td>
<td>100</td>
</tr>
</tbody>
</table>

Reasons for Changing Opioids
- Lack of therapeutic response
- Development of adverse effects
- Change in patient status
- Other consideration
  - Opioid/formulation availability
  - Formulary issues
  - Patient/family health care beliefs

Incomplete Cross-Tolerance
- With chronic use (> 5-7 days), tolerance to stimulation develops to specific subset of μ receptors
- There may be a more profound response due to stimulation of the new (non-tolerant) receptors
- Equianalgesic dose of the new opioid is often decreased by 25-50% for initial dosing

Opioid Adverse Effects and Treatments

<table>
<thead>
<tr>
<th>Adverse Effect</th>
<th>Duration (days)</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constipation</td>
<td>Chronic – will NOT develop tolerance to opioid</td>
<td>Stimulant (e.g., dexamethasone)</td>
</tr>
<tr>
<td>Nausea/Vomiting</td>
<td>3-7</td>
<td>Dopamine antagonists (propranolol, promethazine, metoclopramide, ondansetron)</td>
</tr>
<tr>
<td>Sedation</td>
<td>2-3</td>
<td>Decrease opioid dose, consider other causes</td>
</tr>
<tr>
<td>Confusion/Hallucinations</td>
<td>&lt; 2 days</td>
<td>Opioid rotation, lower dose, antipsychotic</td>
</tr>
</tbody>
</table>
**Approach to Opioid Conversion**

1. Appropriate, thorough assessment for uncontrolled pain or new pain
2. Determine the total daily (24 hrs) dosage of the current opioid(s) calculating each medication separately (i.e. fentanyl patch, PRN oxycodone use)
3. Convert each opioid to ORAL morphine equivalents using established conversion table
4. Individualize the proper dose of the new opioid taking into account incomplete cross tolerance and current pain control
5. Divide the 24 hour dose as appropriate for the dosing interval of the new opioid based on pharmacokinetics.

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**Let’s Practice…**

- MB is a 72 year old man with multiple myeloma and diffuse bony metastases being admitted to the hospital by his oncologist for escalating pain and sudden onset confusion
- His current pain regimen is extended-release oral morphine 30 mg PO every 12 hours and oral morphine solution 10 mg PO every 4 hours PRN breakthrough (takes 6 times per day)
- Plan is to convert to IV hydromorphone

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**Case**

- **Assessment**
  - Pain unstable and uncontrolled; possible adverse effects of current regimen?
  - **TDD oral morphine**
    - Morphine extended release 30 mg PO q12h = 60 mg
    - Oral morphine solution 10 mg x 6 = 60 mg
    - TDD = 120 mg oral morphine
  - Consult equianalgesic dosing chart for equivalency

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**Setting Up the Conversion Calculation**

1. Calculate the total daily dose of current opioids.
2. Set up conversion ratio between old opioid (and route of administration) and new opioid (and route of administration) as follows:

   \[ \text{mg of current opioid} / \text{mg of new opioid} = \text{equivalent mg new opioid/route} \]

   \[ \text{mg of current opioid} / \text{mg of new opioid} = \text{equivalent mg current opioid/route} \]

   \[ x \text{ mg oral morphine} = 20 \text{ mg oral oxycodone} \]

   180 mg oral morphine = 30 mg oral morphine
   30x = (20)(180)
   \[ x = 120 \text{ mg oral oxycodone per day} \]

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