Pain Management in Individuals with Serious Illness and Co-morbid Substance Use Disorders

Kathleen Broglio, DNP-APN-BC, ANP-BC, ACHPN, CPE, FPCN
Nurse Practitioner Section of Palliative Care
Assistant Professor of Medicine
Dartmouth Hitchcock Medical Center
Lebanon, NH
Kathleen.broglio@hitchcock.org

Disclosures

- Royalty: UpToDate
- Legal Consulting- TASA

Objectives

- Describe scope of substance use disorders in the United States
- Discuss key components of a comprehensive pain and opioid risk assessment
- Describe universal precautions approach to opioid management in serious illness with co-morbid substance use disorder
What is the current challenge you face in the care of these patients?

The Goal: Effective and Safe Pain Management

Where we are now

Doing *some* of the right things *some* of the time for *some* of our patients with serious illness, pain, and pain with opioid use disorder

Where we want to be

Doing *all* the right things *all* of the time for *all* of our patients with pain

Clarifying Terminology

- **Substance use disorder (SUD)** - use of alcohol or another substances for non-medical reasons - result in impairment in daily life or noticeable distress
- **Addiction** - neurobiological disease - compulsive craving and use despite the risk for harm
- **Physical dependence** - altered physiologic state caused by repeated administration of a drug that necessitates the continued administration of the drug to prevent the appearance of withdrawal or abstinence syndromes characteristic for that drug; DOES NOT necessarily constitute addiction
- **Tolerance** - state in which, after repeated administration of a drug, a given dose produces a decreased effect or a decreased side effect or in which increasingly larger doses are needed to obtain the same effect as that of the original dose

Substance Use Disorders

- In 2014, 21.5 million people aged 12 or older had a substance use disorder (SUD) in past year
  - 17.0 million people alcohol use disorder
  - 7.1 million with an illicit drug use disorder
  - 2.6 million alcohol use and illicit drug use disorder

Source: Centers for Behavioral Health Statistics and Quality, 2015. [http://www.samhsa.gov/]

Opioid Use Disorder

Substance Use Disorder

- In 2015, more than 2 million individuals sought treatment for a substance use disorder (including opioids)
- In 2011, about 300,000 people received methadone in opioid treatment programs (OTPs) and more than 32,000 individuals were treated with buprenorphine
- The numbers of people on Medication Assisted Treatment (MAT) for opioid use disorder is expected to increase with the ability of nurse practitioners and physician assistants to prescribe buprenorphine for opioid use disorder


Substance Use Disorders 2015

http://www.samhsa.gov/
**Medication Assisted Treatment**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Action</th>
<th>Dose</th>
<th>Where is it obtained?</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methadone</td>
<td>Full mu-opioid agonist – can reduce craving for 24 hours</td>
<td>Usual: 60-120 mg PO once daily – patient goes to opioid treatment program clinic daily for observed dosing</td>
<td>Must be administered through a federal Opioid Treatment Program</td>
<td>Provides analgesia for 6-12 hrs.; more than once daily dosing necessary for pain management; many drug-drug interactions; may trigger nausea in opioid-naive patients</td>
</tr>
<tr>
<td>Buprenorphine/naloxone</td>
<td>Partial mu-agonist - occupies mu receptors</td>
<td>Sublingual/transmucosal: 8-24 mg once daily; implant: every 6 months</td>
<td>Can be prescribed by physicians, nurse practitioners and physician assistants who have waiver with special DEA number</td>
<td>May provide analgesia for 6-12 hours; may need buprenorphine and naloxone implants every 6 months; can be removed prior to six months; less drug-drug interactions than methadone</td>
</tr>
<tr>
<td>Naltrexone</td>
<td>Full mu-receptor antagonist</td>
<td>50 mg orally daily; 380 mg monthly intramuscular depot injection</td>
<td>Injection administered by any clinician who is prescriber</td>
<td>Also used for Alcohol Use Disorder. Will block the effects of opioids</td>
</tr>
</tbody>
</table>

Where Pain Relievers Were Obtained for Most Recent Nonmedical Use among Past Year Users Aged 12 or Older: 2011-2012

![Diagram showing where pain relievers were obtained for nonmedical use]

SCOPE OF PROBLEM IN PALLIATIVE CARE AND HOSPICE
What about Opioid Misuse Risks in those with Cancer?

- Emerging literature – those with cancer screened for substance abuse risk had same level of risk as seen in chronic non-cancer pain


What we know or don’t know...

- Data scope of problem hospice and palliative care is limited
- Risks for opioid misuse and diversion when patients are receiving home hospice services
  - May be limited oversight a where large quantities of opioids may be in home to manage uncontrolled symptoms
- Risks may be higher in home population than previously reported - more than seventy percent of diverted prescription drugs are obtained by family and friends


What we know or don’t know...

- Training policies lacking for substance abuse and diversion issues within hospices (Virginia)
- Majority of palliative care programs surveyed
  - Did not have policies in place for addressing substance abuse or diversion issues
  - Were not consistently screening patients for the risk of substance use disorder
- Recent survey - less than 50% palliative medicine fellows had received adequate training in addiction and managing opioid misuse
  - Majority did not feel prepared to treat pain in this population

MANAGING PAIN IN SERIOUS ILLNESS

Think about these patients...

- 50 y.o. woman with metastatic pancreatic cancer, cancer related pain, has active cocaine abuse
- 68 y.o. woman with lung cancer, pain from tumor invasion, runs out of pills each week prior to visit. Family member reports son is taking medications
- 55 y.o. woman with lymphoma in remission. Residual pain, requests for increasing opioids, frequent ED visits. Urine screen negative for opioid you have prescribed
- 74 y.o. woman metastatic pancreatic cancer, severe pain, has received multiple prescriptions for opioids in the last few days, but reports she has none left
- 26 y.o. with metastatic sarcoma found injecting crushed opioids in his hospital room
- 58 y.o. woman with metastatic NSCLC with pathologic fracture in the left femur with uncontrolled pain on 700 mg MEDD – did not report had been on buprenorphine 24 mg daily

Pharmacologic Approaches

- Mainstay of treatment in serious illness
- WHO ladder approach to pain management
  - Oral
  - Around the clock
  - Individualized
- Use of multimodal analgesia
  - Non-opioids, adjuvant therapies provide analgesia and may be opioid sparing

Multimodal analgesia is optimal but opioids often become mainstay for severe pain. However the focus for the rest of this presentation will be on safe opioid management.

Universal Precautions Approach to Pain Management

Universal Precautions

- All patients treated as if they are at risk for addiction
- Originally developed for use in chronic pain management
- Effective strategy as clinicians may not always identify “at-risk” individual
- Reduces the stigma associated with labeling an individual as “at-risk”

Components of Universal Precautions

• Elements in opioid prescribing include:
  – Comprehensive pain assessment
  – Opioid risk assessment
  – Differential diagnosis for the pain report
  – Informed consent
  – Clear documentation of the treatment plan, decision making, and goals for opioid therapy
  – Ongoing reassessment of analgesia effect
  – Use of urine drug screening as needed


Pain Assessment

• Assessment should include
  – other past successful treatments both pharmacologic and non-pharmacologic
  – associated symptoms such as depression, anxiety or insomnia
  – risk of opioid misuse if opioids are a consideration for treatment
  – Assessment of possible opioid withdrawal


Signs and Symptoms of Opioid Withdrawal

• Tachycardia
• Sweating
• Restlessness
• Pupil dilation
• Bone/Joint aches
• Runny Nose
• Gastrointestinal upset
• Tremor
• Yawning
• Anxiety
• Gooseflesh skin

Consider use of Clinical Opioid Withdrawal Scale
Wesson & Ling, J Psychoactive Drugs, 2003; 35: 253-259
Opioid Risk Evaluation

- Detailed history essential to assess for risk for abuse
- Many tools available but have not been validated in population with serious illness
- Evaluation tools such as the Opioid Risk Tool (ORT), Revised Screener and Opioid Assessment for Patients with Pain (SOAPP-R) and the Diagnosis, Intractability, Risk, Efficacy (DIRE) have been recommended.

Risk Stratification

- Establish level of risk based on clinical interview, history and results of opioid risk tools
- Level of risk determines frequency of follow-up, use of pill counts, frequency of random urine drug screens
- NO established guideline but multiple suggested strategies

Sample Risk Stratification

- Low:
  - Clinical assessment that the patient is likely to have "therapeutic" opioid behavior, AND
  - SOAPP-R score less than 9, AND
  - Morphine Equivalent Daily Dose (MEDD) <100 mg
- Moderate risk:
  - Clinical assessment that the patient is at increased risk for misuse of opioids OR
  - SOAPP-R score 10-21 OR
  - Morphine Equivalent Daily Dose (MEDD) >100 mg
- High risk:
  - Clinical assessment that the patient is at high risk for misuse of opioids, OR
  - SOAPP-R score 22 or higher

Dartmouth Hitchcock Palliative Care Opioid Prescribing Guidelines. 2016 (unpublished)
Example of Management

- All patients will have initial urine drug screen and sign patient provider agreement
- Moderate to high risk patients will have increased frequency of visits (may be weekly), prescription drug monitoring program checked on each visit, pill counts, more frequent urine drug screens (frequency to be determined by prescriber)
- Moderate to high risk patients will complete Current Opioid Misuse Measure at every visit

Dartmouth Hitchcock Palliative Care Opioid Prescribing Guidelines. 2016 (unpublished)

Opioid Management Guidelines

<table>
<thead>
<tr>
<th>Stratification</th>
<th>Low (“Standard”)</th>
<th>Medium</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Criteria</td>
<td>Clinically-assessed low risk AND SOAPP-R &lt; 9 AND MEDD &lt; 100mg</td>
<td>Clinically-assessed medium risk OR SOAPP-R = 10-21 OR MEDD &gt; 100mg</td>
<td>Clinically-assessed high risk OR SOAPP-R &gt; 22</td>
</tr>
<tr>
<td>Action (f/u visits)</td>
<td>Random UDS at least yearly</td>
<td>Additional monitoring at clinician’s discretion</td>
<td>Additional monitoring at clinician’s discretion</td>
</tr>
</tbody>
</table>

Unpublished Data Dartmouth Hitchcock Medical Center

Informed Consent Patient/Prescriber Agreements

- Informed consent outlines the risk, benefits, and expectations
- Experts recommend the use of treatment agreements – Relatively weak evidence regarding the efficacy of agreement to reduce misuse and abuse
- Can be helpful when evidence of aberrant behavior

Components of PPA

- Frequency prescriptions will be filled
- Compliance monitoring
- Safeguarding opioids
- Why and how to discontinue opioids
- Places for signature and dating of PPA

Should be written at literacy level of patient population

Urine Drug Testing (UDT)

- Objective measure to see if the patient is taking what is being prescribed and to evaluate for the presence of illicit drugs or medications that have not been prescribed
- Although robust evidence for the use of UDT to prevent misuse is lacking, experts recommend prior to initiation and periodically when patient is on chronic opioid therapy


Types of UDT

- Screening – Rapid turnaround
  - Immunoassay analysis
  - Low/no sensitivity synthetic or semisynthetic
  - Variable specificity
- Confirmatory – Slower turnaround
  - Analyzed GC-MS
  - High sensitivity
  - Can detect individual drugs
  - Recommended for use in pain medicine

Prescription Drug Monitoring Programs (PDMP)

- All 50 states and one US territory had operational PDMP programs. Programs state-specific - differ in accessibility and functionality.
- Early data from PDMPs indicate programs may decrease abuse or misuse.
- Difficult to check the status in neighboring states unless have reciprocal programs.
- In certain states, PDMP mandatory prior to prescribing opioids; early data showed changes in prescribing patterns in these states.

PDMP and Electronic Prescribing

- Use of PDMPs may be useful in Palliative care and hospice setting to track prescriptions.
- Hospice prescribers may be exempt from checking PDMPs.
- AT present Opioid Treatment Programs (methadone maintenance) exempt reporting.
- Electronic prescribing of opioids:
  - may improve opioid tracking.
  - may decrease the risk of prescription forgery.
  - mandated in certain states.
  - use likely to increase over time.

Opioid Selection

- Mu-agonist opioids trigger the 'reward' system:
  - producing euphoria through binding to GABAergic interneurons.
  - inhibit dopamine production.
- Activation of reward system can trigger craving and possible misuse of opioids.
- Immediate-release opioids (i.e. oxycodone, hydromorphone):
  - faster onset/increase of blood levels.
  - can trigger the 'reward' system.
- Use of an extended release opioid (i.e. morphine ER, transdermal fentanyl) or a long acting formulation (i.e.; methadone):
  - decreases 'reward' or 'likeability' component of medication's effect.

Opioid Selection

- Consider use of abuse deterrent extended release opioids – but be aware may have problems with cost/authorizations
- Minimize use of immediate release breakthrough medications
- Be aware of certain formulations that are higher risk for diversion: e.g. Oxycodone IR 30 mg
- If concerned utilize opioids with ‘less likeability’
  - Morphine less likeability than oxycodone
- Low street value and/or more difficult to abuse
  - Fentanyl patch
  - Morphine IR

Patients in Medication Assisted Treatment

- Close collaboration with facility is essential
- Maintenance dose may not be sufficient to manage the pain
- Treatment program may continue the maintenance dose but another opioid or additional methadone added in divided doses may be necessary
  - Ex: methadone maintenance 80 mg daily, methadone 40 mg in afternoon and night prescribed for pain (methadone duration of pain relief 6-12 hours, reduces craving 24 hours)
  - As disease advances may consider prescribing all opioids for ‘pain management’ when patient can no longer go to methadone maintenance

Buprenorphine

- Partial mu agonist, partially activates the receptor; analgesia at lower doses
- Ceiling effect at higher doses (32mg/d); blocks full mu effect and prevents effect from other mu agonists
- Poor GI bioavailability, fair sublingual
- Some drug/drug interactions due to CYP450 3A4

References:

2. Walsh & Broglio. NCNA. 2016: (in press)

Savage. The ASAM principles of Addiction Medicine. 2014:1500-29

Buprenorphine
Medication Assisted Treatment

- Sublingual tablet, film usually combined with naloxone (except in pregnancy) for addiction treatment (8 mg-24 mg daily)
- Naloxone minimizes overdose risk if used for injection
- Six month implant delivering about 8 mg daily buprenorphine
- **DO NOT CONFUSE WITH**
  - Weekly low dose patch for analgesia
  - LA buccal film for analgesia

With buprenorphine use

- Mu opioid receptors occupied but not activated
- If patient requires opioids for pain – **WILL REQUIRE** much higher doses to overcome occupied mu opioid receptors
- If buprenorphine discontinued takes about 72 hours to disassociate from mu opioid receptors

Buprenorphine use in serious illness

- Sparse data
- Consider use when opioid requirements less than about 240 mg daily
- Consider utilizing with split dosing along with multimodal analgesia

NB: if using for opioid use disorder MUST have waiver to prescribe
Designing Safe Treatment Plan

- Complete documentation of the plan of care easily accessed by all team members
- Specific instructions on the time of medication administration (i.e., 800 a.m., 400 p.m.) versus every 8-hour dosing may minimize confusion
- For those with breakthrough pain who require the use of immediate release opioids
  - May be necessary to make medication time contingent or related to a painful activity versus relying on the pain severity as an indicator

Savage. The ASAM Principles of Addiction Medicine, 2014:1500-29.

Follow up...

- Frequent follow-up visits to assess for appropriate use of prescribed medications, including urine drug screens when indicated
- Frequent home care visit for patients seen by palliative care or hospice at home
- In cases of cross-coverage, detailed plan should be documented to ensure consistency
- Limited supply of opioids should be prescribed and dispensed especially for high-risk patients

Follow up…

• For those individuals at very high risk for opioid misuse, consideration for daily visits, using fentanyl patches in the home or clinical setting, without dispensing a supply of oral pain medications
• Family and/or friends (when appropriate) help ensure compliance
• Keep medications safely secured in lockboxes to prevent diversion or theft

Substance Abuse and Mental Health Services Administration. (SMA) 13-4742; 2013

Reassessment Tools

• Current Opioid Misuse Measure (COMM)\(^1\)
  – Useful to detect challenges with opioid use once patient started on opioids
• Pain Assessment Documentation Tool (PADT)\(^2\)
  – The 4 ‘A’s’ – analgesia, activity, adverse side effects, aberrant behavior
• These tools may reflect changes in risk status of patient and need for more frequent visits and monitoring


Opioid Reversal

• Educate individuals and families on measures in the event of adverse events such as oversedation (if death is not intended outcome)
• All states have legislation to improve naloxone access for laypersons
• Naloxone intramuscular and intranasal forms for laypersons available in many states
• Educate caregivers to administer naloxone in event of overdose

Medication Disposal

- Safe disposal of medications or the use of Drug Enforcement Agency (DEA) take back programs
- In hospice setting, policies for proper medication disposal after a patient dies or when there is a rotation to another opioid before the previous opioid supply is finished

Acute care or inpatient hospice setting

- Patient controlled analgesia (PCA) may provide pain benefit through small incremental dosing which is preferable to intermittent clinician bolus dosing which may trigger the reward system
  - PCA also allows the individual some control over the bolus dosing
  - May reduce the perception that there is ‘drug-seeking’
  - Lockboxes or methods of securing the medication minimize the risk of tampering
- For those actively abusing drugs, extra precautions necessary when has intravenous access to prevent use of illicit substances
- In certain cases, visitor restriction or searching of patient’s belongings may be necessary to prevent substance abuse in the inpatient setting

Conclusion

- Pain is prevalent in individuals with serious illness and comorbid substance use disorder and requires a comprehensive assessment and treatment plan
- A comprehensive pain assessment includes risk assessment for misuse of opioid medications
- ‘Universal precautions’ should be utilized when designing an opioid pain management treatment protocol for all individuals
- Pain management in individuals with serious illness and comorbid substance use disorder requires a unified interdisciplinary team approach