Pain Management in Advanced Illness and Co-morbid Substance Use Disorder
Hospice and Palliative Nurses Association (HPNA) E-Learning

Pain Management in Advanced Illness and Co-morbid Substance Use Disorder
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Disclosures
• Anne F. Walsh has no real or perceived conflicts of interest that relate to this presentation.
• Kathleen Broglio
  - Speakers bureau: Genentech, Teva Consulting: Purdue Pharmaceuticals, Emmi Solutions, Mundi Pharmaceuticals
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Objectives
1. Discuss the current state of substance abuse and governmental response to decrease abuse and diversion
2. Describe a comprehensive pain assessment
3. Discuss pertinent elements of a pain management plan in those with co-morbid substance use disorder
4. Discuss the role of breakthrough medications, opioid rotation, and titration
Overview

• Pain is prevalent in advanced disease and may not be adequately managed
• People with histories of substance abuse face greater risks of being undertreated
• Pain should be treated in this population while providing safeguards to prevent misuse

Substance Use Disorder

• Dependence on and abuse of alcohol and/or drugs including nonmedical use of prescription drugs taken voluntarily for their effect on the central nervous system or to prevent withdrawal
• Prevalence estimated to be more than 23.5 million in U.S.
• Prevalence in those with advanced disease unknown

Substance Use Disorder

• DSM-V combines the DSM-IV categories of substance abuse and substance dependence into a single disorder specific to each substance of abuse (e.g., alcohol use disorder) on a continuum from mild to severe based on 11 symptoms

References:
Substance Abuse Disorder

• Presence of at least 2 of 11 criteria, which are clustered in four groups
  • Impaired control
  • Social impairment
  • Risky use
  • Pharmacologic dependence
    0:1: No diagnosis
    2-3: Mild Substance Use Disorder
    4-5: Moderate Substance Use Disorder
    6+: Severe Substance Use Disorder


Addiction

• Primary, chronic neurobiological disease with genetic, psychosocial, and environmental factors influencing its development and manifestation
• Characterized by behaviors that include one or more of the following:
  • Impaired control over drug use
  • Compulsive use
  • Continued use despite harm
  • Craving


Physical Dependence

• State of adaptation that is manifested by a drug class
• Syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood levels of drug and/or administration of an antagonist

Tolerance

- State of adaptation in which the exposure to a drug induces changes that result in a diminution of one or more of the drug’s effects over time
- Decreases the opioids side effects such as nausea, pruritus, and respiratory depression
- May decrease the analgesic’s ability to reduce pain at the current dose


Growth in Opioid Prescribing

- National Institute on Drug Abuse reports number of opiate prescriptions increased three fold between 1991 and 2009 to over 200 million
- Concurrent increase in illicit use of opioids and associated morbidity and mortality


Past Year Initiates of Specific Illicit Drugs among Persons Aged 12 or Older: 2012

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

Sales, Deaths, Treatment Admissions
Rates of prescription painkiller sales, deaths and substance abuse treatment admissions (1999-2010)

Drug Overdose Deaths
• Leading cause of injury death in 2012
• Among ages 25-64 caused more deaths than motor vehicle accident (MVA) deaths
• 117% increase from 1999 -2012
• Overdose deaths involving opioid analgesics
  • 4,030 deaths in 1999, and 16,007 in 2012
  • 53% of drug overdose deaths (22,114) involved pharmaceutical drugs

* Center for Disease Control and Prevention. Prescription Drug overdose in the United States.
http://www.cdc.gov/homeandrecreationalsafety/overdose/facts.htm
Responding to America’s Prescription Drug Abuse Crisis
• Office National Drug Control Policy collaborative plan released April 2011 key elements
  • Expansion of state-based prescription drug monitoring programs
  • Medication disposal
  • Education for providers and patients
  • Reduction of “pill mills” and doctor shopping through law enforcement


FDA Risk Evaluation Mitigation Strategies (REMS) for opioids
• REMS may be required to ensure benefits of a drug outweigh risks associated with the drug – Food and Drug Administration Amendment Act (FDAAA) 2007
• Final REMS for extended release and long-acting opioids approved July 2012
• Multiple elements include prescriber and patient education


Elements of REMS
• Responsibility of pharmaceutical manufacturers to provide educational activities
  • Start date of CE activities March 2013
• Patient counseling regarding responsibilities and safety
• Updated patient medication guide about safe use and disposal
FDA Guidance to Industry

• 2012 issued guidance to pharmaceutical manufacturers for future opioid development to ensure that the opioids are more difficult to tamper with and have reduced likeability.
• Does not affect opioids already on the market
• Unintended effect
  - Cost burden may be placed on consumer for newer formulations


Abuse-Resistant Formulation

• Resists physical and mechanical manipulation aimed at disrupting the controlled release (CR) feature
• Cannot be chewed or crushed
• Cannot be snorted
• Cannot be injected

Irritants in Abuse Deterrence

• Cleared by the liver
• Does not cause irritation to the GI tract

Irritation if not administered orally
Agonist-Antagonist Formulation

Agonist (example: hydromorphone, morphine, oxycodone)
Antagonist: naloxone, naltrexone

Simultaneous release of agonist and antagonist

Case Study

• JW 68-year-old man with widely metastatic pancreatic cancer status post Whipple procedure; currently receiving chemotherapy seen by palliative care
• Uncontrolled abdominal pain with radicular symptoms to the back
• History of substance abuse recent urine toxicology positive for cocaine/heroin; occasional alcohol (ETOH) use; smokes one pack cigarettes daily
• Lives with daughter who appeared intoxicated during home visit

Case Study

• Pain severity 10/10, stabbing/shooting with no exacerbating factors
• MD unwilling to prescribe opioids
• Takes acetaminophen 500 mg q4h without relief; gets some relief from oxycodone 5mg/acetaminophen (APAP) 325mg which he obtains from visits to the emergency room
• Previously tried adjuvants (gabapentin, duloxetine) without relief, does not want to try again
• Refuses referral to interventional radiology
Pain Assessment

- Location
- Duration
- Onset
- Characteristics
- Severity

- Aggravating factors
- Relieving factors
- Associated symptoms
- Adverse side effects


Location

- Ask about all locations of pain
  - Ask patient to point to area of pain
  - Determine if dermatomal/myotomal
  - Determine if there is radicular spread
Duration and Onset

- When did it start?
- How long has there been a problem?
  - Is it chronic versus acute?
- Patterns of pain if episodic?
  - How long is each episode?
  - Does it occur at specific times of day?
  - Is it related to any activity?

Characteristics

- Ask patient to describe how pain feels
- If patient is unable to describe give examples
  - Throbbing, stabbing, shooting, burning, pins and needles, etc.
- Key point of asking about characteristic is to attempt to establish if pain is neuropathic, nociceptive, inflammatory

Severity

- Ask about pain at worst, best, in the last week, and now
- Explain use of pain scale used when eliciting information
  - Use scale appropriate to age and cognitive level
Aggravating/Relieving Factors

- Aggravating factors
  - What makes it worse?
  - How long do pain flares last?
- Relieving factors
  - What makes it better (medications, rest, activity, heat, ice, complimentary therapies)
  - Past successful treatments

Associated Symptoms

- Appetite changes, weight loss or gain
- Changes in ability to perform ADLs
- Changes in relationships
- Mood changes
- Sexual disturbances
- Sleep disturbances

Adverse Effects

- Adverse side effects of pain or medications
  - Anorexia
  - Constipation
  - Lack of sexual desire
  - Nausea/vomiting
  - Pruritus
  - Sedation
  - Sweating
Assessing Risks

- Ask about current/history of use of illicit drugs, tobacco or alcohol
- Be specific when asking about drug use – ask when last used
  - Ex: have you used marijuana, cocaine, heroin, prescription drugs not used for pain management
- Assess for co-morbid psychiatric conditions
- Assess safety of home environment
- Be observant for signs of aberrant behavior

Indicators of Aberrant Behavior

- Prescription forgery
- Abuse of illicit drugs
- Multiple prescription losses
- Selling prescription drugs
- Multiple dose escalations without provider acknowledgement
- Stealing or borrowing other’s drugs
- Obtaining prescription drugs from non-medical sources

Follow-up Assessments

- Use of the 5 A’s to reassess
  - Analgesia (better, worse, the same)
  - Activities of daily living (psychosocial functioning/may not be applicable in advanced disease)
  - Adverse side effects
  - Signs of aberrant drug-taking behavior
  - Affect (or mood)

Case Study

- JW agreed to discontinue use of illicit substances
- Patient-prescriber agreement completed
- Agreed to use of one prescriber, one pharmacy, and weekly visits
- Agreed to random urine toxicology screens
- Started on fentanyl transdermal 12 mcg/hr patch and a limited supply of morphine sulfate 15 mg PO q2h PRN breakthrough pain
- Home care referral medication management and family support

Designing a Treatment Plan

- Collaboration between providers
- Complete documentation of all prescriptions
- Use of prescription drug monitoring program (PDMP)
- Frequent follow up visits with assessment for appropriate use of analgesics

Treatment Plan

• Consider use of patient-prescriber agreements
• Urine toxicology screens when appropriate
• One prescriber/one pharmacy
• Use of lock boxes in home

• Pasuk S.D, Kirsh E. L. What approaches should be used to minimize opioid diversion and abuse in palliative care. In: Goldstein NE, Morrison RS, eds. Evidence Based Practice of Palliative Medicine. Philadelphia PA: Elsevier, 2013: 87-92

Treatment Plan

• Medication management
  • Use of abuse deterrent extended release or long acting opioids when possible
  • Limited use or avoidance of short acting opioids
  • Use of low street value opioids to prevent diversion
  • Use of nonopioids and nondrug adjuvants
  • Limited supply of medications


Treatment Plan

• Patients in recovery or maintenance programs
• Communication with maintenance program especially if treatment will include opioids
• Use of extended release opioids with limited doses of breakthrough medication
• Possible addition of extra doses of methadone to provide pain management
• Patient/family education

Case Study

- Fentanyl patch was titrated up to 50 mcg/hr as breakthrough doses exceeded five times daily
- Fentanyl patch discontinued and extended release morphine started after three weeks due to severe contact dermatitis
- Morphine immediate release prescribed for breakthrough pain two times daily

Breakthrough Pain
Opioid Titration
Opioid Rotation

Breakthrough Pain

- Transitory increase in pain when baseline pain controlled on an analgesic regimen¹
- Incidence 40-80% for those with cancer²
- Causes multifactorial and include
  - End of dose failure
  - Incident pain (i.e. from activity)
  - Spontaneous/idiopathic pain²

## Treating Breakthrough Pain

- Use 10-15% of total daily dose of opioids as breakthrough dose
- Give oral breakthrough medications every 2 hours as needed, IV medications every 1 hour
- Increase dose of extended-release opioid if amount of breakthrough doses exceeds three times daily

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## Breakthrough Medications

- Consider using same agent as extended release agent except in the case of methadone
- Use single agent products versus those combined with acetaminophen
- May consider use of rapid onset breakthrough medications (transmucosal fentanyl), but consider risk factor in terms of abuse/diversion

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## Opioid Titration

- Titration often necessary in setting of worsening disease states
- Rate of titration
  - Based on total quantity of breakthrough medication consumed in last 24 hours
  - 30% to 50% of current daily dose of extended release medications

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**Opioid Titration**

- Increment may be larger if pain is severe or smaller in those with advanced debility or major organ failure
- Titrate methadone only every 5-7 days
- Titrate breakthrough medications to equal 10-15% of total daily opioid dose

**Opioid Rotation**

- Trials of different opioid drugs to attain most favorable balance between analgesia and adverse effects
- Clinical improvement seen in more than 50% of patients after rotation


**When to Rotate Opioids**

- Inadequate analgesia despite opioid titration
- Inability to escalate opioid due to adverse side effects
- Rapid dose escalation without pain relief
- Different route of administration needed (i.e. transdermal)
**How to Rotate Opioids**

- Calculate current dose of extended release opioids in terms of morphine equivalent
- Calculate morphine equivalent dose of new opioid and reduce the dose of the new opioid by 25-50%
  - Do not reduce dose when rotating to fentanyl transdermal
  - When rotating to methadone the dose may be reduced by up to 90% (expert consultation recommended)


**Case Study**

- JW required multiple escalations of his opioid medications until pain was better controlled
- There were no emergency department (ED) visits for pain management and there were no requests for early refills
- As disease progressed he was transitioned to hospice care and died peacefully at home

**Summary**

- Pain can be effectively controlled in those with histories of substance abuse
- Careful assessment and follow-up is necessary
- Treatment plans should be comprehensive to safeguard against misuse or diversion
- Medications should be titrated to effect and rotated if analgesia not achieved or adverse side effects develop