Management of Addiction Issues in Complex Pain

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Disclosures

• Relevant financial relationship(s) and nonfinancial relationship(s):
  – Dr. Fellers, co-editor and author of *Treating Comorbid Opioid Use Disorder in Chronic Pain*, is employed by MaineHealth and Maine Medical Center

• Disclosure:
  – Financial: Author for Springer Publishing, receive royalty payments
  – Nonfinancial: I have no relevant nonfinancial relationship(s) to disclose
Objectives

• Provide background of current theories of pain and addiction
• Describe differences in pain perception by patients with addiction
• Understand how to manage addiction patients with complex pain
Background

• How many people with chronic pain may have addiction?
  
  32%

• How many people with opioid use disorder report chronic pain?
  
  29-60%

Pain Theories

• What is the purpose of pain?
  – Identifies injury and disease
  – Motivates to protect from further damage
  – Provides lesson about the environment
Pain Theories

• Specificity Theory
  – Pain is an independent sense, with its own unique receptors, pathways, and “brain center”

• Pattern Theory
  – Perception of pain depends upon the temporal and spatial pattern of stimulation

Pain Theories

• Gate Control Theory
  – "Gate" in the spinal cord controls the flow of pain signals from the periphery to the central nervous system
  – i.e. TENS unit

Pain Theories

- Biopsychosocial Model
  - Pain is more than a biological phenomenon
  - Involves psychological and social factors
  - Informs multimodal approach to complex pain

Addiction Theories

• Positive reinforcement
  – Mesocorticolimbic dopamine system involved in reward
  – Drugs of abuse enhance dopamine release within the nucleus accumbens, including opioids

Addiction Theories

• Negative reinforcement
  – Locus coeruleus noradrenergic system important for arousal and psychological stress
  – Opioid withdrawal leads to hyperactivity of system

Addiction Theories

- Genetic factors account for between 40 and 60 percent of a person’s vulnerability to addiction
  - Altered response to the drug
  - Changes in drug metabolism

- Environmental factors
  - Each adverse childhood experience increased the likelihood of early initiation into illicit drug use by 2- to 4-fold
  - Peer influences
  - Drug availability
Pain and Addiction

• Progression to opioid use disorder is not assured
  – Tolerance and withdrawal will develop

• Opioid use during acute pain is protective against addiction
  – Pain provides a natural counterbalance to opioid-induced reward and tolerance

Pain and Addiction

• Does chronic exposure to opioids alter pain perception?
• Waccholtz et al looked at four groups ($n=30$) with chronic pain:
  – Methadone maintenance
  – Buprenorphine maintenance
  – History of opioid maintenance but prolonged abstinence
  – Opioid naïve controls

Pain and Addiction

• What did they find?

• Differences in the groups:
  – Sensitivity to pain and ability to tolerate pain significantly lower among those with an opioid use disorder history compared to opioid naïve
  – Prolonged abstinence did not alter it
  – Prolonged abstinence does improve sense of control over opioid cravings

Treatment

• What makes treating pain in patients with addiction so challenging?

• Three main challenges:
  – Rewarding aspect of opioids
  – Opioid tolerance
  – Opioid-induced hyperalgesia (OIH)
Opioid Tolerance

• Without use or tolerance, we are at “normal”
Opioid Tolerance

• Repeated use leads to tolerance
• No use with tolerance leads to withdrawal

Drug effects:
- Euphoria
- Decreased pain perception
- Sedation
- Respiratory depression
- Constipation
- Miosis

Tolerance effects:
- Dysphoria
- Increased pain perception
- Restlessness
- Tachypnea
- Diarrhea
- Mydriasis

Normal

[Diagram showing balance between drug effects and tolerance effects]
## Opioid Withdrawal Symptoms

<table>
<thead>
<tr>
<th>Early to Moderate</th>
<th>Moderate to Advanced</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety, dysphoria, irritability</td>
<td>Broken sleep</td>
</tr>
<tr>
<td>Fatigue, headache, restlessness, craving</td>
<td>Muscle and bone pain</td>
</tr>
<tr>
<td>Yawning, lacrimation, rhinorrhea,</td>
<td>Myoclonus</td>
</tr>
<tr>
<td>Perspiration, piloerection</td>
<td>Vasomotor symptoms</td>
</tr>
<tr>
<td>Tachypnea</td>
<td>Hypertension, tachycardia, hyperthermia</td>
</tr>
<tr>
<td>Anorexia</td>
<td>Abdominal cramps, nausea, vomiting</td>
</tr>
<tr>
<td>Mild mydriasis</td>
<td>Severe mydriasis</td>
</tr>
</tbody>
</table>
# Opioid Withdrawal Time Course

<table>
<thead>
<tr>
<th>Drug</th>
<th>Effect wear off</th>
<th>Start</th>
<th>Peak</th>
<th>End</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl</td>
<td>1 hour</td>
<td>3-5 hours</td>
<td>8-12 hours</td>
<td>4-5 days</td>
</tr>
<tr>
<td>Meperidine</td>
<td>2-3 hours</td>
<td>4-6 hours</td>
<td>8-12 hours</td>
<td>4-5 days</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>3-6 hours</td>
<td>8-12 hours</td>
<td>36-72 hours</td>
<td>7-10 days</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>4-5 hours</td>
<td>4-5 hours</td>
<td>36-72 hours</td>
<td>7-10 days</td>
</tr>
<tr>
<td>Heroin</td>
<td>4 hours</td>
<td>8-12 hours</td>
<td>36-72 hours</td>
<td>7-10 days</td>
</tr>
<tr>
<td>Morphine</td>
<td>4-6 hours</td>
<td>8-12 hours</td>
<td>36-72 hours</td>
<td>7-10 days</td>
</tr>
<tr>
<td>Codeine</td>
<td>4 hours</td>
<td>8-12 hours</td>
<td>36-72 hours</td>
<td>7-10 days</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>4-8 hours</td>
<td>8-12 hours</td>
<td>36-72 hours</td>
<td>7-10 days</td>
</tr>
<tr>
<td>Methadone</td>
<td>8-12 hours</td>
<td>36-72 hours</td>
<td>8-12 days</td>
<td>14-21 days</td>
</tr>
</tbody>
</table>
Assessing Opioid Withdrawal

• Clinical Opiate Withdrawal Scale (COWS)
• Standardized instrument based on objective and subjective symptoms

5-12 = Mild
13-24 = Moderate
25-36 = Moderately Severe
>36 = Severe
Opioid-Induced Hyperalgesia

• Paradoxical increase in pain sensitivity due to opioid therapy
• Mechanism though to be glutamate (NMDA) dysfunction
• Increase in opioid dose will not improve pain

Treatment

• Differs based on type of pain
  – Chronic
  – Acute

• Also depends on patient
  – In recovery
  – On methadone maintenance
  – On buprenorphine maintenance
  – Actively using
Treatment

• General principles:
  – Complete a thorough assessment
  – Prioritize non-opioid analgesics
    • Acetaminophen
    • NSAIDs
    • Antidepressants, anticonvulsants
    • Regional anesthesia
  – Use nonpharmacological treatment
    • Therapeutic exercise
    • Physical therapy
    • Complementary medicine
  – Treat comorbidities
## Treatment

<table>
<thead>
<tr>
<th>Analgesic</th>
<th>Addictive</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>No</td>
<td>Potentiates analgesia without potentiating respiratory and sedative side effects.</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>No</td>
<td>Are used to relieve numerous types of pain, especially bone, dental, and inflammatory, and enhance opioid analgesia</td>
</tr>
<tr>
<td>SNRIs</td>
<td>No</td>
<td>Are used to relieve several nonstructural types of pain (e.g., migraine, fibromyalgia, low back pain) and probably others</td>
</tr>
<tr>
<td>TCAs</td>
<td>No</td>
<td>Have demonstrated efficacy in migraine prophylaxis, fibromyalgia, many neuropathic pains, vulvodynia, and functional bowel disorders</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>No*</td>
<td>Some have demonstrated efficacy in relieving fibromyalgia, migraine prophylaxis, neuropathic pains</td>
</tr>
</tbody>
</table>

Treatment

• When opioids are needed consider:
  – Avoid opioid patient had trouble with
  – Avoid IV boluses
  – Patient-controlled analgesia
  – Using longer acting opioids
Methadone

• Full agonist at μ opioid receptors, 24 hour half-life
• Pain control lasts about 6-8 hours
• Potent opioid with excellent oral bioavailability
• Has some NMDA antagonism therefore offers some protection against OIH
• Side-effects include weight gain, QTc prolongation, sex hormone suppression, sedation, constipation
Methadone

• Continue maintenance dose
• Consider splitting for 3-4 administrations
• Additional opioids may be required for acute pain
• Will require larger and more frequent administration
Buprenorphine

- Partial agonist at μ opioid receptors (about 60%), 36 hour half-life
- MUST BE IN WITHDRAWAL to start it
- Poor bioavailability, requires sublingual administration
- Combination product includes naloxone, potent μ opioid receptor antagonist that is not absorbed sublingually
Buprenorphine

• Does have analgesic effects lasting 6-8 hours
• Because it is a partial agonist, its dose–response curve plateaus limiting efficacy in severe pain
• May need to be discontinued so that full agonist opioids for pain can be used
• Substitute about methadone 30mg for buprenorphine 12-16mg
Switch to Buprenorphine

• Patients \((n=35)\) on high-dose opioids (MME=550) with unsatisfactory pain control

• After two months:
  – Reduction in pain \((7.2 \rightarrow 3.5, \ p<0.001)\)
  – Quality of life improvement \((6.1 \rightarrow 7.1, \ p=0.005)\)

Active Substance Use

• Refer for addiction treatment
• May begin methadone in hospital to manage tolerance
• Use of adjuvant ketamine peri-operatively
Resources

Managing Chronic Pain in Adults With or in Recovery From Substance Use Disorders

TIP 54

Substance Abuse and Mental Health Services Administration