The Perils of Pain

Underwriting Chronic Pain, Medical Marijuana and Opiate Use

Steven L Cooper, MD, DBIM
2nd VP and Senior Medical Director

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Case Study #1

A 45 year old man is applying for $500K PERM. He has a history of low back pain following a work injury in 2013. He was out of work briefly on STD but is back to work full-time. He sees a primary care doctor and a pain specialist. He is on Vicodin and Neurontin, prescribed by the pain specialist who he sees regularly. There are PRN visits to the PCP, for URI’s and other acute illnesses.

An Rx search reveals results consistent with the APS. There are no other medications or prescribing physicians noted.

What is the risk?
Case Study #2

A 44 year old woman is applying for $500,000 of TERM. APS review reveals that she is on Oxycontin for chronic pain. The pain is not well described; numerous times she presents to her doctor saying ‘I hurt all over’. A phone call from 2011 is recorded where she states that she needs a new prescription for her pain pills because she accidently flushed her old one down the toilet.

In March of 2012 her doctor refers her to a pain specialist and notes that he thinks she is ‘dependent’ on Oxycontin. She does not appear to have seen the specialist. She hasn’t seen her PCP since June 2012, but states on the app that she is still on Oxycontin.

What is the risk?
How significant is Chronic Pain?

- The total annual incremental cost of health care due to pain ranges from $560 billion to $635 billion (in 2010 dollars) in the United States, which combines the medical costs of pain care and the economic costs related to disability days and lost wages and productivity. Institute of Medicine Report from the Committee on Advancing Pain Research, Care, and Education: *Relieving Pain in America, A Blueprint for Transforming Prevention, Care, Education and Research*. The National Academies Press, 2011

- More than half of all hospitalized patients experienced pain in the last days of their lives and although therapies are present to alleviate most pain for those dying of cancer, research shows that 50-75% of patients die in moderate to severe pain. A Controlled Trial to Improve Care for Seriously Ill Hospitalized Patients. [http://jama.ama-assn.org/cgi/content/abstract/274/20/1591](http://jama.ama-assn.org/cgi/content/abstract/274/20/1591)

- An estimated 20% of American adults (42 million people) report that pain or physical discomfort disrupts their sleep a few nights a week or more. National Sleep Foundation ([http://www.sleepfoundation.org](http://www.sleepfoundation.org)). Sleep in America poll. 2000
<table>
<thead>
<tr>
<th>Condition</th>
<th>Number of Sufferers</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic Pain</td>
<td>100 million Americans</td>
<td>Institute of Medicine of The National Academies</td>
</tr>
<tr>
<td>Diabetes</td>
<td>25.8 million Americans (diagnosed and estimated undiagnosed)</td>
<td>American Diabetes Association</td>
</tr>
<tr>
<td>Coronary Heart Disease (heart attack and chest pain)</td>
<td>16.3 million Americans</td>
<td>American Heart Association</td>
</tr>
<tr>
<td>Stroke</td>
<td>7.0 million Americans</td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td>11.9 million Americans</td>
<td>American Cancer Society</td>
</tr>
</tbody>
</table>
Definition of ‘Chronic’ Pain

- Some studies use duration of 6 months or more

- Others use duration of 3 months and longer

- Some suggest that any pain lasting longer than reasonably expected for the tissues involved to heal should be considered chronic
Causes of chronic pain

- Low back pain
- Arthritis, especially osteoarthritis
- Headache
- Multiple sclerosis
- Fibromyalgia
- Shingles
- Nerve damage (neuropathy)
Mortality of Chronic pain

• The problem with most studies regarding chronic pain and mortality is that they are not adjusted for co-morbid conditions such as smoking, physical activity, psychiatric and other medical conditions.

• However the general conclusion of most studies is that chronic pain in and of itself does not lead to an increase in all-cause or cause specific mortality.

• The factor that is important in the mortality risk is the use of opiate medication to treat the pain.
Changes in Management of Chronic Pain

- Prior to 1997 physicians did not commonly treat non-cancer pain with opiate medication.
- The guidelines encouraged expanded use of opiate pain medication for any type of chronic pain.
WHO Analgesic Ladder

- **Mild pain**
  - Non-opioid
    - (Acetaminophen [paracetamol], aspirin, NSAID)
    - ± adjuvant

- **Mild to moderate pain**
  - Opioid
    - (Codeine, Tramadol, etc.)
    - ± non-opioid,
    - ± adjuvant

- **Moderate to severe pain**
  - Opioid
    - (Morphine, Fentanyl, etc.)
    - ± non-opioid,
    - ± adjuvant

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Relationship Between Chronic Pain and Suicide

- Chronic pain is associated with increased risk of suicidal ideation (lifetime prevalence around 20% compared to 13-15% of general population)
- Chronic pain is associated with an increased risk of suicide attempts (lifetime risk 5-14% compared to 4-6% for general population) – Drug overdose accounts for the majority of these attempts
- Risk of completed suicide is at least doubled – Drug overdose accounts for the majority (75%) of completed suicides

Death Related to Pain Medication

• Even though suicide risk is high, most deaths occur due to accidental overdose of pain medication
• Most of these are due to opiates
• TOLERANCE is a major factor in this – tolerance is when an increasing dose of medication is needed, over time, to achieve the same effect due to diminished physiologic effect
Unintentional Overdose

• The rate of unintentional overdose death in the US more than doubled between 1999 and 2007 Bohnert AS, Valenstein M, Bair MJ, Ganoczy D, McCarthy JF, Ilgen MA, Blow FC JAMA. 2011;305(13):1315

• A study of 100,000 patients with chronic pain found a linear correlation between the annual overdose rate and the daily opiate dose Dunn KM, Saunders KW, Rutter CM, Banta-Green CJ, Merrill JO, Sullivan MD, Weisner CM, Silverberg MJ, Campbell CI, Psaty BM, Von Korff M Ann Intern Med. 2010;152(2):85

• In the above study risk was highest on initiation of opiate treatment and after dose escalation, indicating importance of close monitoring
Opiates Differ in Potency and Duration

• It is important to have an understanding of the strength of various opiate medications
• There are numerous charts and calculators on the internet that can provide this information
• Most commonly used guideline is to refer to opiates by their ‘morphine equivalence’ – how much of a dose of morphine is required to provide the same analgesic affect
<table>
<thead>
<tr>
<th>Analgesic/opioid</th>
<th>Strength (morphine)</th>
<th>Equivalent dose (10 mg morphine)</th>
<th>Bioavailability</th>
<th>Half-life of active metabolites (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>1/360</td>
<td>1000 mg</td>
<td>60-90%</td>
<td>3-12</td>
</tr>
<tr>
<td>Diflunisal (NSAID, non-opioid)</td>
<td>1/160</td>
<td>1600 mg</td>
<td>80-90%</td>
<td>3-9</td>
</tr>
<tr>
<td>Dextropropoxyphene</td>
<td>1/10 to 1/20</td>
<td>130-200 mg</td>
<td></td>
<td>4-12</td>
</tr>
<tr>
<td>Codeine</td>
<td>1/20</td>
<td>200 mg</td>
<td>&lt;90%</td>
<td>2.5-3 (CYP 2C9, 1.94)</td>
</tr>
<tr>
<td>Tramadol</td>
<td>1/10</td>
<td>100 mg</td>
<td>68-72%</td>
<td>5.5-7 (rebound)</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>1/10</td>
<td>40 mg</td>
<td></td>
<td>2-3</td>
</tr>
<tr>
<td>Methadone</td>
<td>0.36</td>
<td>28 mg</td>
<td>60-60%</td>
<td>3-6</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>0.6</td>
<td>17 mg</td>
<td>28-30%</td>
<td>3-8</td>
</tr>
<tr>
<td>Morphine (oral)</td>
<td></td>
<td></td>
<td></td>
<td>2-3</td>
</tr>
<tr>
<td>Oxycodone</td>
<td></td>
<td></td>
<td>&gt;87%</td>
<td>3-4.5</td>
</tr>
<tr>
<td>Methadone - Acute</td>
<td>3.4</td>
<td>2.5-3.33 mg</td>
<td>40-90%</td>
<td>16-50</td>
</tr>
<tr>
<td>Morphine (IV)</td>
<td>4</td>
<td>2.5 mg</td>
<td>100%</td>
<td>2-3</td>
</tr>
<tr>
<td>Dihydrocodeine (heroin, IV)</td>
<td>1.9-1.3</td>
<td>2.3-6.2 mg</td>
<td>100%</td>
<td>2-3</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>5</td>
<td>2 mg</td>
<td>40-35%</td>
<td>2-3</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>7</td>
<td>1.4 mg</td>
<td>10%</td>
<td>7.25-9.43</td>
</tr>
<tr>
<td>Methadone - Chronic</td>
<td>7.5</td>
<td>1.35 mg</td>
<td>40-90%</td>
<td>15-60</td>
</tr>
<tr>
<td>Levoethanol</td>
<td>8</td>
<td>1.3 mg</td>
<td>70%</td>
<td>11-16</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>40</td>
<td>0.25 mg</td>
<td>30-40% (transdermal)</td>
<td>20-70, mean 37</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>50-100</td>
<td>0.1-0.2 mg</td>
<td>33% (oral), 92% (transdermal)</td>
<td>0.04 (IV), 7 (transdermal)</td>
</tr>
<tr>
<td>Sufentanil</td>
<td>500-1000</td>
<td>10-20 mg</td>
<td></td>
<td>4.4</td>
</tr>
<tr>
<td>Etorphine</td>
<td>1,000-3,000</td>
<td>3.3-10 μg</td>
<td></td>
<td>7.7</td>
</tr>
<tr>
<td>Carfentanil</td>
<td>10,000-100,000</td>
<td>0.1-1.0 μg</td>
<td></td>
<td>7.7</td>
</tr>
</tbody>
</table>
Of particular concern...

Methadone
- Used in treating opiate addiction
- 2nd line drug for pain control
- Very long half-life
- Tolerance leads to increasing dosages
- Respiratory depression = death

Suboxone
- Used to wean patients off of opiates
- It reduces withdrawal symptoms and cravings
- Continued use suggest possibility of addiction to Suboxone
- There is no set length of appropriate maintenance treatment with Suboxone but a high level of scrutiny should be employed and each case is IC
## Factors for rating Chronic Pain

<table>
<thead>
<tr>
<th>Favorable features</th>
<th>Unfavorable features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Localized, well-defined source of pain</td>
<td>Diffuse or poorly localized, and ill-defined sources of pain</td>
</tr>
<tr>
<td>Pain present &lt; 2 years</td>
<td>Pain present &gt; 2 years, the longer the worse</td>
</tr>
<tr>
<td>Minimal physical and functional impairment</td>
<td>Limited physical mobility or other functions</td>
</tr>
<tr>
<td>Socially engaged, reasonably active, with leisure or work interests</td>
<td>Socially isolated, limited activities and interests, unemployed, receiving disability benefits</td>
</tr>
<tr>
<td>No associated depression or other psychiatric or medical diagnoses</td>
<td>Associated depression or other psychiatric or medical diagnosis</td>
</tr>
<tr>
<td>Managed primarily by one physician</td>
<td>Managed by multiple physicians or referral to pain treatment center</td>
</tr>
<tr>
<td>Prescriptions written by one physician</td>
<td>Visits to emergency room or multiple physicians for pain symptoms or prescriptions</td>
</tr>
<tr>
<td>Intermittent or continuous use of one or two medications at low dosages</td>
<td>Continuous use of multiple medications at high</td>
</tr>
<tr>
<td>No benzodiazepine prescription</td>
<td>Benzodiazepine prescription, especially alprazolam (Xanax)</td>
</tr>
<tr>
<td>No physician expressed concern about medications or combinations, or about alcohol misuse</td>
<td>Physician expressed concern about medications or combinations, or about alcohol misuse</td>
</tr>
</tbody>
</table>
Medical Cannabis

• Cannabis has been cultivated as an elixir for pain control since as far back as 2000 years BCE

• Increasing reports of addiction, psychosis and other adverse effects of smoked cannabis led to the Marihuana Tax Act in the 1930’s

• This and other legislative actions posed nearly insurmountable obstacles for physicians to prescribe medical cannabis

• Mounting scientific evidence for the pain-relieving properties of cannabis over the past 2 decades has led to relaxing and eliminating laws in many states
Medicinal Marijuana

2011 State Marijuana Laws

- States with legal medical marijuana
- States with decriminalized marijuana possession laws
- States with both medical marijuana and decriminalization laws

Compliance Number
California Eligibility for Cannabis Card

1. Acquired immune deficiency syndrome (AIDS)
2. Anorexia
3. Arthritis
4. Cachexia
5. Cancer
6. Chronic pain
7. Glaucoma
8. Migraine
9. Persistent muscle spasms, including, but not limited to spasms associated with multiple sclerosis
10. Seizures, including, but not limited to seizures associated with epilepsy
11. Severe nausea
12. Any other chronic or persistent medical symptom that either:
   a. Substantially limits the ability of the person to conduct one or more major life activities as defined in the Americans and Disabilities Act of 1990 (Public Law 101-336).
   b. If not alleviated, may cause serious harm to the patient’s safety or physical or mental health.
Medicinal Marijuana

• Marijuana (cannabis) has several pharmacologically active components, including delta-9-tetrahydrocannabinol and cannabidiol.

• 2 medications containing synthetic THC are FDA approved for the treatment of chemotherapy-associated nausea and vomiting: Marinol and Cesamet.
Venice Beach, California
One of the 1st scientifically validated papers looking at the use of cannabis for pain control was published in 1997.

It was the result of a randomized, placebo-controlled study looking at the effect of smoked cannabis on neuropathic pain in HIV patients with associated sensory neuropathy.

Pain relief was found to be comparable to pain relieve from oral drugs (gabapentin or opioids).

Abrams et Neurology 2007:68;515-521
Sativex (not approved yet in US)
Cannabis and Mortality

• No mortality related to cannabis itself
• Cannabis consumption is related to multi-factorial deaths including marijuana related accidents and deaths attributable to alcohol and illicit drugs
• Cannabis dependence is associated with morbidity, including impaired occupational and social functioning, and various psychiatric disorders such as perceptual disturbances and disordered thought process
• Controversial: link between cannabis and psychosis
There is insufficient evidence, particularly because of the low number of studies, to assess whether the all-cause mortality rate is elevated among cannabis users in the general population. Case-control studies suggest that some adverse health outcomes may be elevated among heavy cannabis users, namely, fatal motor vehicle accidents, and possibly respiratory and brain cancers. The evidence is as yet unclear as to whether regular cannabis use increases the risk of suicide.

There is a need for long-term cohort studies that follow cannabis using individuals into old age, when the likelihood of any detrimental effects of cannabis use are more likely to emerge among those who persist in using cannabis into middle age and older. Case-control studies of cannabis use and various causes of mortality are also needed.

Practical Considerations

- Legitimate users of medical marijuana are likely ratable based on their underlying condition with no added mortality
- The problem lies in determining whether or not recreational use is occurring as well and to what extent
- Also must consider the combined use of medical marijuana and opiate medication – in theory appropriate medical marijuana use should reduce or eliminate need for opiates, but each case needs to be evaluated carefully
An article published in the August 25th, 2014 issue of JAMA Internal Medicine states:

Medical cannabis laws are associated with significantly lower state-level opioid overdose mortality rates. Further investigation is required to determine how medical cannabis laws may interact with policies aimed at preventing opioid analgesic overdose.
Thank You!

Any Questions?