Opioids and Marijuana: Unknowns in Chronic Pain Management

Kevin L. Kraemer, MD, MSc
Professor of Medicine and Clinical & Translational Science
Chief, Section of Treatment, Research, and Education in Addiction Medicine (STREAM)
Division of General Internal Medicine
University of Pittsburgh
Marijuana Laws in the United States

Outline

• Trends in Opioid Prescribing and Opioid Harms
• Evidence Base for Medical Marijuana for Pain
• Pennsylvania Medical Marijuana Policy and Procedures
In the United States…

- 11% of US adults report chronic pain
- Late 20th and early 21st century
  - Pain as the “Fifth vital sign”
  - 2001 Pain Management Mandate (JCAHO) – required that pain be recognized, assessed, documented, and treated
  - → 4-fold increase in opioid prescriptions
- In 2014, 10 million persons report using prescription opioids non-medically
- Prevalence of opioid use disorder as high as 26% in primary care patients receiving opioids for chronic non-cancer pain
Opioid Prescription Trends

Source: IMS National Prescription Audit (NPA) & Vector One ®: National (VONA).
Drugs Involved in U.S. Overdose Deaths, 2000 to 2016

- Synthetic Opioids other than Methadone, 20,145
- Heroin, 15,446
- Natural and semi-synthetic opioids, 14,427
- Cocaine, 10,619
- Methamphetamine, 7,663
- Methadone, 3,314

Source: CDC Wonder
Age-adjusted drug overdose death rates: United States, 2015

National rate = 16.3 per 100,000

- Dark blue: Statistically higher
- Light blue: Statistically the same
- Light green: Statistically lower

12 recommendations in 3 key areas:

- Determining When to Initiate or Continue Opioids for Chronic Pain (3 recommendations)
- Opioid Selection, Dosage, Duration, Follow-up, and Discontinuation (4 recommendations)
- Assessing Risk and Addressing Harms of Opioid Use (5 recommendations)
UPMC Pain Strategy

- Improve opioid and non-opioid care
  - Best Practices Requirements for All PCPs: 2-hour online Safe and Competent Opioid Prescribing Education (SCOPE)
  - 90/90 Plan for Selected Primary Care and Specialty Providers
- Expand multidisciplinary pain services
- Disseminate Pain Resource Nurse (PRN) Program
- Deploy the HCAHPS Pain Toolkit
- EPIC Pain Management Synopsis (Dashboard)

Source: Executive Summary of Recommendations from the System-Wide Steering Committee for Pain Medicine
What is the Role of Medical Marijuana in Chronic Pain Management...and potentially in Addressing the Opioid Epidemic?
Medical Cannabis Laws and Opioid Analgesic Overdose Mortality in the United States, 1999-2010

Medical Cannabis Laws and Opioid Analgesic Overdose Mortality in the United States, 1999-2010

Could Medical Cannabis Break the Painkiller Epidemic?

A body of research suggests yes, but scientists are having to fight red tape to study whether medical marijuana could substitute for opioid drugs

By Jeremy Hsu on September 1, 2016
Outline

• Trends in Opioid Prescribing and Opioid Harms

• Evidence Base for Medical Marijuana for Pain

• Pennsylvania Medical Marijuana Policy and Procedures
Marijuana for Chronic Pain

• First used as medicinal agent as early as 2700 BC in China

• Sir William Osler: “Cannabis indica is probably the most satisfactory remedy for migraines” (1892)

• In US, most commonly used illicit drug, 12% prevalence (2015)

• As of April 2017, 29 states and the District of Columbia have legalized the medical use of marijuana
Cannabis vs. Cannabinoids

- Cannabinoids are a diverse set of chemicals that act on cannabinoid receptors (CB1 and CB2) in the brain:
  - *Phytocannabinoids* found in cannabis plants (e.g., psychoactive tetrahydrocannabinol (THC), cannabidiol); ~113 different cannabinoids in cannabis
  - *Synthetic cannabinoids* (e.g., nabilone (Cesamet), dronabinol (Marinol))
  - *Endocannabinoids* (produced naturally in the body by animals)
Medical cannabis use is associated with decreased opiate medication use in a retrospective cross-sectional survey of patients with chronic pain. J Pain. 2016 Jun;17(6):739-44.

- **Aim:** Examine if medical marijuana for chronic pain changed patterns of opioid use.
- **Methods:** Cross-sectional retrospective online survey of 244 patients with chronic pain who patronized a medical cannabis dispensary
- **Results:** Medical marijuana use associated with a 64% decrease in any opioid use, decreased number and side effects of medications, and improved quality of life (45%)
- **Conclusion:** Medical marijuana may benefit some chronic pain patients
Aim: Determine long-term effect of medicinal cannabis on pain and quality of life in patients with intractable chronic pain

Methods: In 274 patients with chronic pain, primary outcome was the change in the pain symptom score at the 6-month follow-up

Results:
- At follow-up, the pain symptom score decreased from median 83.3 to 75.0 ($P<0.001$)
- Opioid consumption at follow-up decreased by 44% ($P<0.001$)

Conclusions: Medicinal cannabis in this open-label, prospective cohort resulted in improved pain symptoms and reduction in opioid use
3 Recent Meta-analyses on Marijuana and Pain
## Cannabinoids for Medical Use: A Systematic Review and Meta-analysis


### Improvement in Pain With Cannabinoid vs Placebo by Study

<table>
<thead>
<tr>
<th>Cannabinoids</th>
<th>Cannabinoid Events</th>
<th>Placebo Events</th>
<th>Odds Ratio (95% CI)</th>
<th>Favors</th>
<th>Placebo</th>
<th>Favors</th>
<th>Cannabinoid</th>
<th>Weight, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetrahydrocannabinol (smoked)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abrams et al,77 2007</td>
<td>13 25</td>
<td>6 25</td>
<td>3.43 (1.03-11.48)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6.51</td>
</tr>
<tr>
<td>Nabiximols</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GW Pharmaceuticals,22 2005</td>
<td>54 149</td>
<td>59 148</td>
<td>0.86 (0.54-1.37)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>19.02</td>
</tr>
<tr>
<td>Johnson et al,69 2010</td>
<td>23 53</td>
<td>12 56</td>
<td>2.81 (1.22-6.50)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>10.87</td>
</tr>
<tr>
<td>Langford et al,65 2013</td>
<td>84 167</td>
<td>77 172</td>
<td>1.25 (0.81-1.91)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>20.19</td>
</tr>
<tr>
<td>Nurmiiko et al,76 2007</td>
<td>16 63</td>
<td>9 62</td>
<td>2.00 (0.81-4.96)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>9.84</td>
</tr>
<tr>
<td>Portenoy et al,67 2012</td>
<td>22 90</td>
<td>24 91</td>
<td>0.90 (0.46-1.76)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>14.04</td>
</tr>
<tr>
<td>Selvarajah et al,70 2010</td>
<td>8 15</td>
<td>9 14</td>
<td>0.63 (0.14-2.82)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4.63</td>
</tr>
<tr>
<td>Serpell et al,88 2014</td>
<td>34 123</td>
<td>19 117</td>
<td>1.97 (1.05-3.70)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>14.91</td>
</tr>
<tr>
<td><strong>Subtotal I² = 44.5%, (P = .94)</strong></td>
<td>241 660</td>
<td>209 660</td>
<td>1.32 (0.94-1.86)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>93.49</td>
</tr>
<tr>
<td><strong>Overall I² = 47.6%, (P = .64)</strong></td>
<td>254 685</td>
<td>215 685</td>
<td>1.41 (0.99-2.00)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>100.00</td>
</tr>
</tbody>
</table>

- **Chronic neuropathic pain:**
  - 11 studies: “a higher proportion of intervention patients had clinically significant pain relief up to several months later”
  - Meta-analysis of 9 studies: patients receiving cannabis more likely to report 30% or better neuropathic pain (risk ratio 1.43)

- **Chronic pain** due to multiple sclerosis (9 studies), cancer (3 studies), and other causes (5 studies):
  - insufficient evidence to show a benefit
Safety Issues

• **Potential short-term adverse effects**: dizziness, dry mouth, nausea, fatigue, somnolence, euphoria, vomiting, disorientation, drowsiness, confusion, short-term memory, loss of balance, hallucination, psychosis, pulmonary effects, car crashes

• **Risk of illicit use and addiction**:
  - “Overall, from 1991-1992 to 2012-2013, illicit cannabis use increased significantly more in states that passed MML than in other states (1.4-percentage point more; SE, 0.5; P = .004), as did cannabis use disorders (0.7-percentage point more; SE, 0.3; P = .03).” ([JAMA Psychiatry. 2017 Jun 1;74(6):579-588. doi: 10.1001/jamapsychiatry.2017.0724](https://doi.org/10.1001/jamapsychiatry.2017.0724))
Limitations of Studies

- Most included few or highly selected subjects
- Short duration
- Variable cannabinoid dose and different methods of delivery
- Uncertain effect of cannabinoids when used with other pain treatments (e.g., no studies directly compare cannabinoids with opioids)
Conclusions Regarding Medical Marijuana for Chronic Pain

- Limited evidence to suggest moderate effectiveness for chronic neuropathic pain
- Efficacy of cannabis for other types of chronic pain is uncertain due to lack of controlled clinical trials
- Best formulation and dose is uncertain
- Higher quality studies are needed…but federal barriers to cannabis-related research in US will need to be relaxed
When to Consider Prescribing Medical Marijuana
(Adapted from Hill KP. JAMA 2015;313(24):2474-83)

- Debilitating medical condition that RCTs suggest may respond to medical marijuana
- Multiple failed trials of 1st and 2nd line therapies
- Failed trial of FDA approved cannabinoid (dronabinol (Marinol) or nabilone (Cesamet))
- Absence of substance use disorder or unstable active mental health disorder
- Residence in state with medical marijuana laws
Outline

• Trends in Opioid Prescribing and Opioid Harms
• Evidence Base for Medical Marijuana for Pain
• Pennsylvania Medical Marijuana Policy and Procedures
Pennsylvania Medical Marijuana Program (medicalmarijuana.pa.gov)

• 4/17/16: Signed into law by Governor Tom Wolf
• 1/17/17: Released applications for growers/dispensaries
• 6/20/17: Permits awarded to 12 growers/processors
• 6/29/17: Permits awarded to 27 dispensaries (out of planned 52), each dispensary has 6 months to become operational
• 7/27/17: State launches practitioner registry for medical marijuana
• Early 2018: Anticipated availability to eligible patients
Pennsylvania Medical Marijuana Program: Qualifying Conditions

- ALS (Lou Gehrig's disease)
- Autism
- Cancer
- Crohn's disease
- Epilepsy
- Glaucoma
- HIV/AIDS
- Huntington's disease
- Inflammatory bowel disease
- Intractable seizures
- Intractable spasticity
- Multiple Sclerosis
- Neuropathies
- Parkinson's disease
- Post-traumatic stress disorder
- Sickle cell anemia
- Severe chronic or intractable pain
Pennsylvania Medical Marijuana Program

- **Vehicle:** pill, oil, topical forms (including gel, creams or ointments), a form medically appropriate for administration by vaporization or nebulization (excluding dry leaf or plant form), tincture, and liquid
- **Possession Limit:** 30 days at a time
- **Patient Steps:** Register with the Department of Health → Obtain a physician’s certification → Apply for a medical marijuana ID card and submit the application fee → Obtain medical marijuana from an approved dispensary
Pennsylvania Medical Marijuana Program

- **Physician Steps:**
  - Decide if you wish to provide medical marijuana
  - Join Physician Registry
  - Complete 4-hour in-person, online, or combined training
- Pennsylvania’s law explicitly protects prescribers from arrest, prosecution, or penalty, or denied any right or privilege including civil penalty or disciplinary action
Summary - Take Home Points

• Observational data suggest medical marijuana use may decrease opioid use for chronic pain
• Meta-analyses suggest marijuana may be effective for chronic neuropathic pain but its efficacy for other types of pain is uncertain
• In early 2018, medical marijuana will be available to prescribe in Pennsylvania – what will you do?
References

Questions?