The Yin and Yang of clinical decision making before prescribing medical marijuana

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Conflict of interest statements:
\begin{itemize}
\item Sharon Cirone
\item Ruth Dubin: none
\item Mel Kahan: none
\item Lori Montgomery: none
\end{itemize}

Learning objectives:
At the end of this workshop the participants will be able to
\begin{itemize}
\item Understand the potential impact of the new marijuana prescribing legislation.
\item Conduct an assessment of the potential risks and harms of medical marijuana.
\item Come to a patient-centered, evidence-based decision about safe marijuana prescribing.
\end{itemize}

Audience feedback: Show of hands
\begin{itemize}
\item How many of you have patients who have asked for or use cannabis?
\item How many of you have concerns and worries about patients requesting medical cannabis?
\item How many of you are comfortable prescribing medical cannabis?
\end{itemize}
A sampler of recommendations:  
# 2 (of 13)

• If considering authorizing dried cannabis for treatment of neuropathic pain, the physician should first consider a) adequate trials of other pharmacologic and non-pharmacologic therapies and b) an adequate trial of pharmaceutical cannabinoids (Level I).

Recommendation 4

Dried cannabis is not appropriate for patients who:
• a) Are under the age of 25 (Level II)
• b) Have a personal history or strong family history of psychosis (Level III)
• c) Have a current or past cannabis use disorder (Level III)
• d) Have an active substance use disorder (Level III)
• e) Have cardiovascular disease (angina, peripheral vascular disease, cerebrovascular disease, arrhythmias) (Level III)
• f) Have respiratory disease (Level III) or
• g) Are pregnant, planning to become pregnant, or breastfeeding (Level III)

Recommendation 5

Dried cannabis should be authorized with caution in those patients who:
• a) Have a concurrent active mood or anxiety disorder (Level II)
• b) Smoke tobacco (Level II)
• c) Have risk factors for cardiovascular disease (Level III) or
• d) Are heavy users of alcohol or taking high doses of opioids or benzodiazepines or other sedating medications prescribed or available over the counter (Level III)
Recommendation 7

Physicians should assess and monitor all patients on cannabis therapy for potential misuse or abuse (Level III).

- If the patient does not use substances problematically and begins cannabis treatment, the physician should ask the patient at each office visit about cognitive and mood-altering effects, as well as compliance with the dosing recommendations and use of any other substances. Periodic urine drug screens are advised.

Recommendation 9

The physician should regularly monitor the patient’s response to treatment with dried cannabis, considering the patient’s function and quality of life in addition to pain relief (Level III). The physician should discontinue authorization if the therapy is not clearly effective or is causing the patient harm (Level III).

Recommendation 10

- Patients taking dried cannabis should be advised not to drive for at least:
  - a) Four hours after inhalation (Level II)
  - b) Six hours after oral ingestion (Level II)
  - c) Eight hours after inhalation or oral ingestion if the patient experiences euphoria (Level II)

What’s an FP to do? Case #1: Mr J.

- 45 year old man, prior history of left L5/S1 discectomy due to persistent pain/foot drop. Good results X 3 years then pain returned after minor injury at work
- Despite physiotherapy, referrals to orthopedics, injections—epidural steroids, IV lidocaine, pain worsened
- Mood: depressed—early childhood adversity, shunned by family (religious differences), benefits cut off by workmen’s compensation,
- Given venlafaxine by psychiatrist: severe suicidal ideation, ended up admitted overnight
- Not willing to try any more drugs!
Mr J’s pain drawing

- Pain descriptors:
  - Numbness
  - Burning
  - Pins and needles
  - Aching
  - Stabbing
  - Like electric shocks

Mr J’s SENSORY EXAM

- Cotton balls
- Safety pin
- Brush
- Tuning fork
- Warm and cold water

Symptoms and physical exam:

- patient has allodynia, hyperalgsia around scar, in dermatome and generally over entire back
- Reduced range of motion, stiff gait, has to stand all the time as too painful to sit down

Began using marijuana on his own: significant pain relief, sleep better, mood up and down

- FP advised re safer use (Do not mix with tobacco, use vapourizer)
- Opioid Risk tool score: 4 (personal history of alcohol abuse, depression)
- Trial of nabilone: not covered, could not afford
- Trial of pregabalin: afraid to try
- Continued to use marijuana: used orally in butter/brownies
- Previously was on the MMAR (specialist supported use of mj)
Audience Feedback

• How many of you would agree with this patient’s treatment
• What might you have done instead?
• What worries you about this patient?

Six years Later:

• Still having good pain relief
• Sleep better
• **Function better**
• Eventually accepted for LTD, insurance claim accepted
• Enjoyed fishing, plans to open a bait shop
• Has now got a partner in his life
• No adverse effects (urine drug screens as normal)
• No escalation of dose, no aberrant behaviours etc
• Still drinking some beer, less than before

What was the most important factor in this patient’s symptomatic improvement?

• Use of medical marijuana?
• Acceptance for long-term disability and financial stability?
• Longterm relationship?
• Supportive relationship with an understanding primary care provider?
• Who cares? He now has some quality of life.

THE DARK SIDE OF MEDICAL CANNABIS:

• Tweet sent by [http://medpotnow.com/cannabis-menu/](http://medpotnow.com/cannabis-menu/)
  “Potent indica dominant hybrid that may take you to a galaxy far, far away”
  (indica 70%, sativa 30%, 25% THC; $10 per gram)
ASK THE ADDICTION SPECIALIST
(SHARON CIRONE)
• DO YOU HAVE ANY CONCERNS WITH THE ABOVE PATIENT’S MANAGEMENT?
• WHAT IF HE WAS 18 YEARS OLD? (note 20% of people under 18 have chronic pain, and 5 to 8% are seriously disabled – Jen Stinson, RN PhD – Sick Kids)
• WHAT ABOUT HIS HISTORY OF ALCOHOL MISUSE?
• WHAT IF HE BREAKS UP WITH HIS GIRLFRIEND AND STARTS DRINKING MORE ALCOHOL?
• WHAT ABOUT THE MEDICAL DISPENSARY’S ADVERTISEMENTS?

Youth with Chronic Pain :
• Acute pain is common
• Chronic pain not a common presentation
• Adequate trials of non-pharmacotherapy interventions
• Trials of pharmacotherapy
• Pharmaceutical cannabinoids
• Avoid smoked cannabis: risk vs benefit

Teenage Brain Development and Vulnerability to Drug Use

Neurocognitive Effects of Cannabis Use
• Decreased IQ
• Neurocognitive damage
• Risk of addiction
The Link between Cannabis Use and Psychosis

- Increasing presentations of cannabis induced psychosis
- Exploring the link
- Increased access with new legislation?

Message for youth and parents

“Regular cannabis use is not safe”

“Delay the onset of cannabis use past the sensitive period of significant neuromaturation”

Youth, Alcohol and Substance Use

- Student surveys of last year use: >50% alcohol, up to 25% marijuana, <10% daily use
- Polysubstance Use
- Deaths are associated with oversedation and poor decision making

Youth, Alcohol and Substance Use

- Marijuana is associated with legal consequences
- Requests for prescribing for harm reduction
Youth, Emotional Distress and Chemical Coping

- Distress tolerance
- Undifferentiated mental health and psychiatric illnesses
- "Self medicating"
- "hand, pill and mouth disease"
- Healthy coping behaviors
- Resilience

Licensed Producers

LSD, Girl Guide Cookies

Nyce N’ Ez, Happy Face

Case # 2: Pain description: Mel Kahan

- 37 year old man requests medical marijuana
- Has four year history of severe back pain
- Localized to lower back, sometimes down legs
- Triggered by lifting a heavy object
- Pain is constant, 5-7/10

Pain description (2)

- Renders him unable to work, interferes with his sleep, makes him depressed
- Exam shows discomfort on lateral bending, nil else
- X-ray shows mild degenerative changes
Medications
- Hydromorph Contir 18 mg BID
  - Helps a little bit
- Clonazepam 0.5 mg tid
- Citalopram 20 mg OD
- Discontinued meds
  - NSAIDs - ineffective
  - Nabilone (cesamet) - ineffective

Psychosocial
- Is unable to work because of back pain and depression - on provincial disability plan
- Lives alone, not active
- Smokes 1 pack of cigarettes per day
- Drinks small amounts on occasion
- No other substance use
- Is depressed because of pain
  - No history of anxiety, psychosis, suicide ideation or attempts

His cannabis use history:
- Smokes 4-5 joints/day on average, 1 joint every 4-6 hours, two at night for sleep
- Not sure of size or potency of joint
- Assuming 500 mg/joint, then he’s smoking 2 – 2.5 grams/day, within the 1-3 grams/day promoted by the cannabis companies
- Doesn’t know potency
- Does admit to feeling anxious in the AM “Doc that’s why I need my clonazepam”

HE INSISTS THAT HE HAS TO USE CANNABIS
Questions

• Would you prescribe for him? Why or why not?
• What further information do you want?

Cannabis use disorder

• Signs of cannabis use disorder:
  • Smoking large amounts eg 2+ grams/day
  • Spending large amounts of time smoking
  • Poor social, work, school function
  • High value placed on cannabis (salience)
  • No clear medical indication

Cannabis Use Disorder

DSM-V Criteria (see Turner et al CFP 60:803 – Sept 2014)

A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by 2 or more of the following in a 12-month period:

1. Cannabis is often taken in larger amounts or over a longer period than was intended
2. A persistent desire or unsuccessful efforts to cut down or control use
3. A great deal of time is spent on activities necessary to obtain, use, or recover from the substance
4. Craving, or a strong desire or urge to use cannabis
5. Recurrent cannabis use resulting in a failure to fulfill major role obligations at work, home, or school

### Definition of Addiction

American Academy of Pain Medicine, American Pain Society, American Society of Addiction Medicine

Addiction is a primary, chronic, neurobiologic disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving.

*From: Definitions Related to the Use of Opioids for the Treatment of Pain, 2001.*

### Management

- Don’t prescribe dried cannabis to this patient!
- Provide advice on tapering
- Consider use of pharmaceutical cannabinoids to relieve withdrawal symptoms
- Counsel on harms of cannabis
  - Patients with CUD will likely experience improved pain, mood and function with abstinence
- Refer for addiction treatment

### Medical marijuana and other drugs

- Patients who report using medical marijuana, when compared to other patients with similar pain conditions:
  - Are more likely to use opioids problematically
  - Are more likely to use cocaine
  - Have worse psychosocial function

### Management

- Patients who request medical marijuana and are currently using other drugs problematically:
  - Don’t prescribe for pain unless evidence available:
    - I.e. Neuropathic pain not responding to other Rx
  - Patient should agree to treatment for concurrent problem
  - Taper prescribed opioids and benzodiazepines
Assessment

• In all patients requesting medical marijuana:
  • Take a detailed history of current use of marijuana, alcohol, tobacco, opioids, cocaine and other drugs
  • Ask about past use
  • Ask if have received ever received treatment for problematic substance use
  • Consider screening tools eg CAGE-AID

Ask the pain specialist? (Lori)

• What can you offer this patient in lieu of medical cannabis?
• How can a provider say “no” and still remain patient-centered

The “bottom line”

• Physicians are expected to know and comply with the regulations and policies of their College.
• Physicians are not obliged to complete a medical document for medical marijuana if they are unfamiliar with its treatment use or feel it is medically inappropriate.

http://www.cmpa-acpm.ca/cmpapd04/docs/resource_files/web_sheets/2013/com_w13_005_e.cfm

The “bottom line”

• If a physician chooses to complete a medical document, it is important that a meaningful consent discussion be held, and that the consent discussion be captured in the medical record.
• Members should not hesitate to contact the CMPA for advice on this issue.

http://www.cmpa-acpm.ca/cmpapd04/docs/resource_files/web_sheets/2013/com_w13_005_e.cfm
Neuropathic pain
Fibromyalgia
Back pain
HIV neuropathy
MS pain
Muscle spasm
Myofascial pain
Pelvic pain
Migraine
Tension headache

Clearly proven
risks and benefits for pain patients

References:


3. Cannabinoids

HIV neuropathy:
Abrams et al

- 2007 RCT HIV medication-related neuropathy
- N=50
- Smoking 0.9g cigarettes, 3.56% THC or placebo
- 5-day inpatient intervention phase
- Previous cannabis use required ("so that they would know how to inhale and what neuropsychologic effects to expect")

References:
HIV neuropathy: Abrams et al

- 52% of cannabis patients had >30% reduction in VAS, compared to 24% of placebo group
- Median reduction in pain levels was 34%
- No discontinuations due to side effects
- No changes in mood reported

Mixed neuropathic pain: Wilsey et al

- 2008 crossover RCT mixed neuropathic pain conditions
- N=38
- Smoking high dose (7%), low dose (3.5%) or placebo, total 9 puffs per session
- Previous cannabis use required (“to minimize psychoactive adverse effects”)
- Tested VAS and experimental pain

Mixed neuropathic pain: Wilsey et al

- 0.0035 points per minute decrease in VAS
- VAS ~5.5 - 3 vs 5.5 - 4
- No difference in experimental pain
- No difference in analgesia between low (3.5%) and high (7%) dose, described as a “ceiling effect”
- Impairments greater with high dose
- Analgesia began to diminish within 1-2 hours after dose

Neuropathic pain: Ware et al

- 2010, Crossover design, unblinded by the end
- N= 21, former marijuana smokers
- THC Concentrations of 0%, 2.5%, 6%, 9.4%
- 25mg tid for five days each dose
- Reduction in pain of 0.7 points on 10 point scale
- Statistically significant improvement in sleep
- No difference in mood or QOL
Neuropathic pain: Ware et al

- Well-designed study; rigorous methods
- Outcomes carefully considered
- Abuse monitored
- All previous MJ smokers
- Low dose (25mg tid), concentration THC 9.4%
- 2.35 mg total available Δ9-THC
- Very small magnitude of effect
- Effectively a five-day trial

Wilsey: mixed neuropathic pain

- 2013 double-blind, placebo-controlled, crossover study
- N=39 (13 central, 26 peripheral NeP)
- Previous cannabis use required “to reduce the risk of adverse psychoactive effects in naïve individuals”
- Vapourized medium-dose (3.53%), low-dose (1.29%), or placebo cannabis
- Flexible dose – 4 puffs, then 4-8 puffs 2h later, to overcome “robust placebo response”


- Significant difference from placebo not evident until 120 minutes after initial dose, drops off 1-2 hours later
- 57% of cannabis patients saw >30% reduction in VAS, compared to 26% of placebo
- No difference in analgesia between low and medium doses
- Unblinded for 63% placebo, 61% low dose, 89% medium dose
- Analgesia not associated with feeling “high”; “high” and “stoned” more likely with medium dose


Eisenberg: mixed neuropathic pain

- N=8
- Open-label, single dose study
- Stable medical regimen for 60 days that included cannabis
- Battery-operated, palm-sized, hand-held thermal-metered-dose inhaler, designed to vaporize multiple doses of processed cannabis
- Each dose heated to 190-C
- 19.2% THC, 0.1% cannabidiol, and 0.2% cannabinol
- 15.1mg (+/- 0.1mg) cannabis; 3.08 ± 0.02 mg Δ9-THC

Eisenberg: mixed neuropathic pain

- Blood samples at 1, 2, 3, 4, 5, 10, 15, 30, 60, 90, and 120 minutes after inhalation for monitoring THC and active metabolite
- Pain on VAS at baseline, 20min and 90min
- Adverse events recorded at 5, 15, 30, 60, and 120 minutes
- Satisfaction with MDI compared with the current method of use (smoking) on VAS: “not at all” at 0, “very much” at 10, at 120 minutes
- PRIMARY OUTCOME: inter-individual variability of Δ9-THC


Evidence to date (all neuropathic pain)


Eisenberg: mixed neuropathic pain

- 15.1mg (+/- 0.1mg) cannabis
- Blood samples at 1, 2, 3, 4, 5, 10, 15, 30, 60, 90, and 120 minutes after inhalation for monitoring THC and active metabolite
- Pain on VAS at baseline, 20min and 90min
- Adverse events recorded at 5, 15, 30, 60, and 120 minutes
- Satisfaction with MDI compared with the current method of use (smoking) on VAS: “not at all” at 0, “very much” at 10, at 120 minutes


Eisenberg: mixed neuropathic pain

- Higher and more predictable bioavailability
- Cmax interindividual variability of the Syqe Inhaler is 25.3%
- 47–85% for vaporizer
- 32–116% for smoking
- 42–115% for oral administration
- 59–67% for oromucosal delivery

Evidence to date

• Average N=30
• Duration of studies ≤5 days
• All previous smokers of marijuana
• Amounts ranging 25mg-900mg
• Smoking or vapourizing
• THC ≤9.4%
  • One study 20% not an efficacy study, n=8
• Reduction in pain ranging from 0.7 to 3 points on the NRS

A logical approach in this patient

• Evidence is in its early stages, and this isn’t a therapy for everyone
• The evidence we have suggests that if cannabis is going to be helpful, it is in very low doses compared to what this patient is using
• Benefits may be in reducing pain related distress
• There are many other ways of reducing this distress
• Evidence is evolving on a virtually daily basis, and it’s logical to return to this discussion regularly

Audience Questions and feedback