A PALLIATIVE CARE PROVIDER’S PERSPECTIVE ON MEDICAL CANNABIS

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Share something you learned about medical cannabis...
AND
What would you like to learn about medical cannabis today?

SESSION OBJECTIVES:
• Build your knowledge base about potential benefits and risks of medical cannabis
• Describe the certification process
• Develop tools to advise patients about medical cannabis

TODAY WE WILL REVIEW:
• One provider’s perspective entering the Wild West
• A brief overview of:
  • History of cannabis medicine
  • Endocannabinoid system
  • Clinical research
• The certification process
• What I take into account when advising patients
What are our patients seeing online?

LESS IS MORE BETTER LIVING THROUGH CHEMISTRY

WE ALL NEED TO BALANCE:

- Enormous public demand
- Limited current evidence — does not mean no benefit
- Potential benefit and safety
CANNABIS AND CANCER: “SIBERIAN ICE MAIDEN”

A BRIEF HISTORY OF CANNABIS MEDICINE:

- Humans may have cultivated Cannabis for at least 12,000 years
- 1838 – introduced to Western medicine
- 1890 – “In almost all painful maladies I have found Indian hemp by far the most useful of drugs”
- 1942 – Cannabis is removed from the USP
- 1964 – THC is discovered by Dr. Raphael Mechoulam

Have you ever heard of the endocannabinoid system?
WHAT ARE CANNABINOIDS?

- Endocannabinoids:
  - Anandamide
  - 2AG
- Phytocannabinoids:
  - THC
  - CBD
- Synthetic Cannabinoids:
  - Dranabinol (Marinol)
  - Nabilone (Cesamet)
  - Nabiximols (Sativex) – whole plant extract, 1:1 THC/CBD oral mucosal spray.

ISSUES IN CANNABINOID RESEARCH:

- Small studies
- Short duration
- Most include patients with prior history of cannabis use
- Interventions studied are different than what most patients are accessing
- Unblinding was very common
Cannabis for pain

**ANALGESIC EFFECTS OF CANNABINOIDS:**

- Affects descending and ascending pain transmissions
- May target affective qualities of pain
- May attenuate low grade inflammation
- May potentiate the effects of opioids


**≥30% IMPROVEMENT IN PAIN:**

<table>
<thead>
<tr>
<th>Original investigation</th>
<th>Cannabinoids for Medical Use A Systematic Review and Meta-analysis</th>
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<tr>
<td>Methods</td>
<td>Cannabinoids for Medical Use A Systematic Review and Meta-analysis</td>
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OR = 1.41
Cannabis is an old drug that interacts with our body in many ways. We do not fully understand it. Current evidence is limited, though the potential may be significant.
SHORT TERM SIDE EFFECTS ARE USUALLY MILD:
- Tachycardia, vasodilation, hypertension, postural hypotension
- Coughing, wheezing from vaping
- Dry mouth, reddening of the eyes, blurred vision
- Dizziness, headache
- Increased appetite
- Euphoria, anxiety, sedation
- Impaired motor function
- Hyperemesis syndrome – can be treated with a hot shower

SERIOUS AND LONG TERM SIDE EFFECTS:
- High dose: Tachycardia, paranoia, delusions, anxiety, insomnia, hallucinations
- Decreases in cognition, mood, motivation
- Dependence/cannabis use disorder
- Brain maturation in youth
- Short term memory and cognition
- Lung damage in heavy users from contaminants

CAUTIONS AND CONTRAINDICATIONS:
- Pregnancy and lactation
- History of psychosis, schizophrenia
- Medication interactions
- Act 16 states patients under the influence may not work in: electricity, public utilities, permit chemicals, mining, public health/safety risk

Obtaining Medical Cannabis in Pennsylvania
PENNSYLVANIA ACT 16 DEFINES:

- Qualifying conditions
- Patients
- Certifying physicians
- Dispensaries
- Product
- Research

THERE ARE CURRENTLY 21 QUALIFYING CONDITIONS:

- Amyotrophic Lateral Sclerosis
- Autism
- Cancer, including remission therapy
- Crohn’s Disease
- Damage to the nervous tissue of the central nervous system (brain-spinal cord) with objective neurological indication of intractable spasticity, and other associated neuropathies
- Dyskinetic and spastic movement disorders
- Epilepsy
- Glaucoma
- HIV/AIDS
- Huntington’s Disease
- Inflammatory Bowel Disease
- Intractable Seizures
- Multiple Sclerosis
- Neuropathies
- Opioid use disorder for which conventional therapeutic interventions are contraindicated or ineffective, or for which adjunctive therapy is indicated in combination with primary therapeutic interventions
- Parkinson’s Disease
- Post-traumatic Stress Disorder
- Severe chronic or intractable pain of neuropathic origin or severe chronic or intractable pain
- Sickle Cell Anemia
- Terminal Illness

QUALIFYING CONDITIONS, CONTINUED

HOW PATIENTS CAN GET MEDICAL MARIJUANA IN PENNSYLVANIA

1. REGISTER for the Medical Marijuana Program at https://www.health.pa.gov.
2. OBTAIN a physician’s certification that you suffer from one or more of the sixteen medical conditions.
3. COMPLETE an application to acquire a medical marijuana identification card.
4. VISIT a dispensary to purchase medical marijuana.

https://www.health.pa.gov/topics/programs/MedicalMarijuana/Pages/Patients.aspx
CERTIFICATION REQUIRES AN ASSESSMENT:

- Physician determines that the patient:
  - Has a serious medical condition documented in the EHR
  - Is likely to receive therapeutic or palliative benefit based on:
    - Professional opinion
    - PMH as documented
    - Controlled substance history, review of PDMP

MY GOALS IN THE ENCOUNTER

- Assess:
  - Patient's goals and the symptoms they are looking to treat
  - Prior experience and SEs
  - Medical conditions with special attention to:
    - Frailty
    - Medication interactions
    - Route of delivery
- Describe the process for obtaining certification
- Discuss dosing and product choice
- Manage expectations
- Follow-up & learn from my patients

RATIO OF THC:CBD MAY BE PATIENT AND CONDITION SPECIFIC:

- Naïve patients: include at least some CBD
- Neuropathic pain: possible synergy with THC/CBD → may need to trial agents empirically
- Nausea/anorexia: THC most studied

ACTIVITY OF THE AVAILABLE FORMS:

- Vaporization or nebulization
- Tincture/Oil
- Pill/capsule
- Topical
- Plant material for vaporization
GENERAL GUIDELINES:
• Store safely, away from children, in a cool, sealed, dark location.
• Begin with a low dose
• Take a few small doses/day
• Do not redose orally too quickly (may need to wait 30min-2hr to feel effect), effect may last hours
• Increase gradually, looking for balance of function vs SEs/euphoria
• Use only as directed by dispensary professional
• Be alert for adverse effects

BOTTOM LINE
• The evidence for medical cannabis is limited
• Patient expectations and demand is high
• With time we will learn more about which patients and conditions are best candidates for use
• Educate yourself!

What will you take away from this talk about medical cannabis?

Questions?
There is a tension as we have researched this:

On the one hand evidence for MMJ efficacy is quite limited, on the other hand it may be comparatively safe and worth a try.
PRECLINICAL STUDIES OF MMJ IN CANCER:

- 1975 NCI study: THC and CBD inhibited the growth of Lewis lung adenocarcinoma cells in vitro in mice and rats.
- Combined with gemcitabine, cannabinoids reduce the viability of pancreatic cancer cells.
- Adding THC to temozolomide reinstated glioma suppression in tumors that had become resistant to chemotherapy.

“But again, mice and rats are not people, and what is observed in vitro does not necessarily translate into clinical medicine. The preclinical evidence that cannabinoids might have direct anticancer activity is provocative as well, but more research is warranted.”

PRECLINICAL DATA SUPPORTS USE IN CIPN:

- Activation of the CB1 and CB2 receptors suppresses the development of vincristine-induced peripheral neuropathy in rats.
  - Br J Pharmacol 2007; 152:765-77
- Administration of Anandamide attenuated CIPN in mice receiving daily cisplatin.
  - J Neurosci 2012; 32:7091-101
- Cannabidiol pretreatment stops paclitaxel induced neuropathy in mice.
  - Br J Pharmacol 2014; 171:636-45

Brief Report
A Double-Blind, Placebo-Controlled, Crossover Pilot Trial With Extension Using an Oral Mucoadhesive Cannabinoid Extract for Treatment of Chemotherapy-Induced Neuropathic Pain
Mary C. Lynch, MD, Bisson, Philip C. V. Brant, MD, MPH, and Barbara J. DeBose, MD
# NABIXIMOLS VS PLACEBO IN CIPN:

<table>
<thead>
<tr>
<th>Method</th>
<th>Group 1</th>
<th>Group 2</th>
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<tbody>
<tr>
<td>Disease</td>
<td>Numb</td>
<td>Normal</td>
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<tr>
<td>Study design</td>
<td>Double-blind study</td>
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<td>Number</td>
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## Participants

- **Inclusion criteria:** Numbet of participants in the 1-month placebo group, including patients with inflammatory pain.
- **Exclusion criteria:** Patients with active cancer, severe liver disease, or renal failure.

## Maintaining Homeostasis:

- **Pain, Stress**
- **Control energy balance**
- **Immune regulation**

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**“Modern-day scientists have increasingly been turning their attention to cannabis due to its potential to inhibit or destroy cancer cells, and at the very least, manage the pain and symptoms that come with the illness. But then, ancient people seem to have known that already.”**

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CANNABIS USE DISORDER

Some criteria as with other drugs of abuse:
1 in 10 who try cannabis for an addiction (lower than with other drugs of abuse)

Connection between marijuana use and psychiatric conditions is unknown. Cannabis use is highly associated with psychiatric disorders but unclear if causal or makes it worse. Be wary of use with schizophrenia/psychotic disorders as connection is stronger. MJ may also worsen PTSD.
- Cannabis withdrawal syndrome
- Cannabis intoxication disorder

ADDICTION

Dependence (regular use despite mental and physical impairment and withdrawal symptoms upon stopping) is 21.7-38%

Withdrawal symptoms can include anger, aggression, anxiety, anorexia, insomnia, stomach pain, tremors and headache

Higher concentrations of THC (preparations such as oils) cause rapid spikes in dopamine which the beginning of addiction

USES

THC – nausea/vomiting, appetite, some pain. Important for spasticity (MS).
CBD – anti-seizure, anti-spasmodic, anti-inflammatory, antipsychotic. Less clear how it works. Doesn’t bind to CB1 receptors, so doesn’t cause as much anxiety, euphoria. Pain control.

Indications:
- Autoimmune disease
- Migraine – NSAIDs boost endocannabinoid levels

ROUTE-DEPENDENT EFFECTS

Smoked: Fast (seconds-minutes), max dose 30min, subsides over 1-3hrs
Vaping: Seems to avoid lung damage due to contaminants
Eating: Slower onset (30min-2hrs), longer duration (5->8hrs). THC converted in the liver to a longer-acting metabolite. Harder to titrate due to delayed and variable onset.
SL Tincture: Avoids 1st pass metabolism.
Topical: Variable absorption
Rectal: Rapid absorption. Avoids 1st pass metabolism. 2nd highest bioavailability after vaping.
THERE ARE IMPORTANT MEDICATION INTERACTIONS

Avoid CYP3A4, CYP2D6 inhibitors — cannabis is metabolized by these enzymes so medications can be anticipated to inhibit elimination or increase concentration:

- Amiodarone, cimetidine, fluoxetine, ketoconazole, metronidazole, voriconazole, clarithromycin, erythromycin, cyclosporine, verapamil

Rifampin, a CYP3A4 inducer decreases levels.

Anticipate interaction with anticholinergic, CNS depressant, and sympathomimetic medications.

Cannabis may decrease levels of epileptic medications.

Be aware of additive SEs with multiple medications.

SAFETY

Ecological data that shows in states with MMJ laws there are decreased opioid-related adverse events (ie MVAs, o/ds) on a statewide level, but this data is inconsistent.

Unknown risks in pregnancy, advised against use although rates of use are increasing.

HISTORY-TAKING

Add questions about cannabis to your medical history — find out what they’re using, what they’re hoping from it, route, how much.

Consider treatment and its SEs, e.g. radiation in the mouth or chest may affect SL absorption, or vaping may be a bad idea.

CERTIFICATION LETTER INCLUDES

Certification Letter:
- Pt’s info
- Practitioner’s info
- Date
- Specific medical condition
- A statement by the practitioner that the patient has a medical condition, and the pt is under the practitioner’s continuing care for the condition
- Length of time symptoms existed, cannot exceed 1 year
- Recommendations, restrictions, or limitations as to dosage or form or CCB recommendation that pt consult with onsite practitioner or dispensary
- How to proceed
- Any other relevant information
- A statement that if the pt is homebound
- A statement that you have explained potential risks and benefits of use and documented in EHR, including that informed consent has been obtained
- A statement that a false statement is punishable by law.
AFTER CERTIFYING

Submit original certification (w/ signature) to DOH, can be done electronically
Give pt a copy of certification
Scan copy into chart
Notify dispensary if pt has a reaction to marijuana
You can modify the certification, but not w/in the first 30 days (except by reaching out to DOH).
Need to notify DOH immediately if: pt no longer has serious medical condition, pt died, use of MMJ would no longer be therapeutic or palliative
You may w/draw certification at any time by notifying DOH and pt at any time in writing.

META-ANALYSIS OF PATIENTS >30% REDUCTION IN PAIN WITH CANNABINOIDS VS PLACEBO:

We need to walk a fine line between dismissing very real potential and promoting quackery
THE CANNABIS PLANT:

- Phytocannabinoids:
  - THC - tetrahydrocannabinol
  - CBD - cannabidiol
  - CBN - cannabinol
  - CBG - cannabigerol
  - THCV - tetrahydrocannabivarin

THC VS. CBD

THC
- Responsible for the psychoactive effects and pain-relieving properties

CBD
- Counteracts the negative effects of THC on memory, mood, cognition
- Potential analgesic, antiepileptic, anti-nausea, anti-emetic, anti-inflammatory, anxiolytic properties