Can Cannabis Treat My IBD?

JAMI KINNUCAN, MD
Discuss complimentary and alternative medicine (CAM)

Why do patients use CAM?

Review of cannabis

Review of studies of cannabis in IBD

Questions
What do we mean by “complementary and alternative medicine” (CAM)?

A group of diverse medical and health care practices and products not presently part of conventional medicine

- **Complementary** - when used in conjunction with conventional medicine
- **Alternative** - when used as alternative to conventional medical therapy

### Natural Products
- Dietary supplements
- Herbs
- Vitamins
- Minerals
- Probiotics
- Cannabis

### Mind/Body Practices
- Large and diverse group of procedures/techniques
- Yoga
- Chiropractic/osteopathic manipulation
- Meditation
- Massage therapy
- Acupuncture
- Relaxation techniques
- Tai chi
- Qi Qong
- Healing touch
- Hypnotherapy
- Movement therapies

The National Center for Complementary and Integrative Health (NCCIH)
IBD patients are using CAM based therapies to treat symptoms but not telling providers

In 2007, National Health Interview Survey reported that 38% of US adults were using CAM based therapies.

National Center for Complementary and Integrative Health Reports estimates that Americans spend more than $30 billion out-of-pocket for treatments.

However many do not disclose use to health care provider:
- Fear of disapproval, assumption of lack of knowledge, do not recognize as “medical treatment”

CAM based approach in IBD patients

- 30-50% of IBD patients report CAM use
- Of the users, <50% report use to medical provider

Top reasons why IBD patients use CAM based therapies

<table>
<thead>
<tr>
<th>Direct disease benefits</th>
<th>Indirect disease benefits</th>
<th>Reasons they don’t</th>
</tr>
</thead>
<tbody>
<tr>
<td>Search for optimum therapy</td>
<td>Take control over treatment</td>
<td>Lack of knowledge/understanding</td>
</tr>
<tr>
<td>Want better control of symptoms and disease</td>
<td>Better quality of life due to control of treatment options</td>
<td>Lack discussion with medical provider</td>
</tr>
<tr>
<td>Avoidance of steroid-based therapies</td>
<td>Considered “safer” than conventional therapy</td>
<td></td>
</tr>
<tr>
<td>Unable to deal with the side effects of conventional therapies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ineffective conventional medical therapies</td>
<td></td>
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CAM approaches have challenges

• The data is not robust and often not performed in randomized controlled trials (similar to FDA approved drugs)
• Published data often doesn’t come up in MEDLINE search
• No regulation or testing of efficacy prior to marketing
• Small number of participants in studies and the mix of patients included → hard to generalize to you!
• Often not recognized or covered by insurance companies

Koretz, RL and Rotblatt M. CGH 2004
Cannabis
The low down: *Cannabis* plant

- **Cannabis sativa**
  - Marijuana: THC high (>0.3-40%)
  - Hemp: THC low (<0.3%)

- **Cannabis indica**
  - Marijuana

*Image of Cannabis plant*
The low down: *Cannabis sativa*

Composed >70 active compounds or phytocannabinoids

- **Δ-9-tetrahydrocannabinol (THC)**
  - Psychoactive effects

- **Cannabidiol (CBD)**
  - Anti-inflammatory
  - Immune modulation
## Synthetic cannabinoids

<table>
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<tr>
<th>Drug</th>
<th>Mechanism</th>
<th>Approved indications</th>
</tr>
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<tbody>
<tr>
<td>Nabilone (Ceseamet)</td>
<td>THC analog</td>
<td>Nausea/vomiting (chemo induced)</td>
</tr>
<tr>
<td>Dronabinol (Marinol)</td>
<td>THC analog</td>
<td>Nausea/vomiting (chemo induced) AIDS associated anorexia</td>
</tr>
<tr>
<td>Nabiximols (Sativex)</td>
<td>THC analog</td>
<td>*Not FDA approved in US Cancer related pain Neuropathic pain MS spasticity</td>
</tr>
<tr>
<td>Epidiolex</td>
<td>CBD analog</td>
<td>Epilepsy (2 forms) *Just approved 2018</td>
</tr>
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</table>
The endocannabinoid system: a simplified version

- Endocannabinoid system (ECS) is found throughout the body
- Main receptors CB1 + CB2
- CB1 mainly found in the brain and CNS and lesser in peripheral tissues
- CB2 is mainly found in peripheral organs with immune potential

THC=Tetrahydrocannabinol
CBD=Cannabidoil
CBN=Cannabinol
Cannabis Administration

- Product labelling is not standardized
- Different formulations of CBD:THC
  - THC 0.3-40% (average 20-40%)
- Routes of administration
  - Inhalation- tobacco paper (cigarettes, cigars, pipes, blunt)
  - Inhalation- vaporizer, vaping, water pipes, pen (oil)
  - Oral- leaf, hashish, oil (foods, teas, pills, lozenges)
  - Sublingual (oil)
  - Rectal- suppository/enema
- Studies have looked at various routes and formulations → limitations

Cannabis timeline

- 2700 BC
- Mid 1800s
- 1850
- 1971
- 1992
- 1996
- 2008
- 2018
Where is cannabis legal NOW?

As of June 2019

DISCLAIMER: It is still considered Schedule I drug under the Federal Controlled Substance Act

Image adapted from www.disa.com Aug 1, 2019
Michigan Cannabis Laws

As of November 2018 we have to consider both medical cannabis and recreational cannabis laws.

<table>
<thead>
<tr>
<th>Medical Cannabis</th>
<th>Recreational Cannabis</th>
</tr>
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<tbody>
<tr>
<td>Qualifying conditions*</td>
<td>Law impacts adults (≥21y)</td>
</tr>
<tr>
<td>16 ounces (solid)</td>
<td>Possession</td>
</tr>
<tr>
<td>7g (gaseous)</td>
<td>≤ 2.5 ounces (out of home)</td>
</tr>
<tr>
<td>36 fl ounces (fluid)</td>
<td>≤ 10 ounces (in home)</td>
</tr>
<tr>
<td>Growth of ≤ 12 plants (locked)</td>
<td>Growth of ≤ 12 plants (&lt;15g)</td>
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<tr>
<td>Caregiver growth of ≤ 12 plants</td>
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## Michigan Cannabis Laws

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<th>Recreational Out of Home (&lt;2.5)</th>
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<td><img src="#" alt="Images" /></td>
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Michigan: Obtaining Medical Marijuana

Eligible Patient

Physician*

*Provide written documentation as treating physician and the patients’ diagnosis


Qualifying conditions

Amyotrophic lateral sclerosis (ALS)
Alzheimer’s disease
Cachexia/Wasting Syndrome
Cancer
Crohn’s disease
Glaucoma
Hepatitis C
HIV/AIDS
Nail Patella
Seizures
Severe & chronic pain
Severe & persistent muscle spasms
Severe nausea
What are legal implications for you?

- Despite laws at STATE level, cannabis (but not hemp) is still considered a scheduled I substance through CSA
  - However people acting in compliance with state laws unlikely to have federal implications

- Patients should consider…
  - Potential (though VERY unlikely) for federal prosecution
  - Implications for employment, school, camp and travel
  - Driving implications
  - Drug interactions?
  - Special considerations: aging population, pregnancy and children
Common provider questions as it pertains to legality around medical cannabis

What if I only met the patient once, can I certify their use?

Will I be prosecuted for recommending/suggesting cannabis to a patient?

Does malpractice insurance cover medical cannabis?

Are there known drug interactions?

Does my hospital have a policy regarding certification?

What is the optimal dose, route of administration, common complications?
Cannabis- What is the “right” dose?
What are the gastrointestinal effects of cannabis?

↓ esophageal sphincter relaxation

? ↑ fibrosis (HCV)

Association acute pancreatitis (rare)

↓ gastric motility

↓ gastric acid secretion

↓ bowel motility, secretion, colonic tone

↓ visceral pain

Imaged adapted from Goyal et al. Eur Jour Gastroenterol & Hepatol 2017
Why even talk about Cannabis in IBD?
IBD patients are using cannabis

- In Canadian study (pre 2018) up to 50% IBD patients using to relieve abdominal pain, diarrhea, appetite

- Older data in the US, up to 12% report current use with 40% report prior use
  - 2012 → 2017 one study 2x rates of cannabis use, however appeared to be for recreational use > medicinal use

- Pediatric study showed up to 70% report current/past use
  - Up to 70% did not disclose to health care provider

Phatak UP et al. *J Pediatrc Gastroenterol Nutr* 2017
Merker et al. *Inflamm Bowel Dis* 2018.
Overall clinical effects in IBD patients

- Abdominal pain (75-95%)
- Diarrhea (29-85%)
- Nausea (46-86%)
- Joint pain (48%)
- Steroid requirement (small study)
- Appetite (70-100%)

# What is known about cannabis in Crohn’s disease?

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<td>Naftali (2018)(^3)</td>
<td>50</td>
<td>CBD:THC oil</td>
<td>No Δ clinical or endo scores ↑ QOL, sleep, mood, bloat, abd pain*</td>
<td>None reported</td>
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\(^{1}\)Naftali T et al. CGH 2013  \(^{2}\)Naftali T et al. DDS 2017  \(^{3}\)Naftali T et al. UEG. Abstract  

*p<0.04
Synthetic cannabinoid in IBD

Open-label phase 2a study looking at CB2 agonist to treat abdominal pain in CD (n=14)

- Showing safety and tolerability of Olorinab (CB2 agonist)
- Outcome: reduction in abdominal pain scores (but not inflammation)

More pain free days, improved patient reported outcomes

75% each group with adverse effects (not severe)

- Early exploratory data

What is known about cannabis in ulcerative colitis?

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<td>THC cigs x8w</td>
<td>No Δ clinical symptoms</td>
<td>↑ memory changes</td>
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<td>↓ clinical symptoms* ↓ endo disease activity* No Δ CRP, fecal calprotectin</td>
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What are the risks to consider?

- Long-term effects have not been well studied
- Large study published looking at risks in all cannabis users
  - Risk for addiction to other substances, diminished life achievement, increased motor vehicle accidents, chronic bronchitis, psychiatric disturbances, cannabis withdrawal
- Several adverse clinical effects to consider
- Drug interactions to consider, do we even know them all?
- There have been no deaths associated with cannabis use alone (typically with co-substance use)
- Concerns about use in IBD
  - More likely to stop treatments, increased risk for surgery

Volkow ND et al. NEJM. 2014.
Negative clinical effects

- Sedation, ataxia, dizziness
- ↑ psychosis, anxiety
- ↔ change lung function
  *tobacco dependent
- ↑ HR → ?increased risk of arrhythmia
- Acute bronchitis (self-limited)
- ↓ sperm count
- Delayed ovulation

Cannabis hyperemesis syndrome (CHS)
A few words on cannabis hyperemesis syndrome (CHS)

- Chronic cannabis users with cyclical episodes of nausea and vomiting
- Now international diagnostic criteria
- Mechanism is not entirely clear
  - Low dose CBD → anti-nausea effects
  - High dose CBD → pro-nausea effects

Rome IV Criteria
1. Stereotypical episodic vomiting resembling CVS (≥ 3/year)
   - Mimics CVS related to onset, duration, frequency
2. Presentation after prolonged, excessive cannabis use
   (>1y use, >4x/week)
3. Relief of vomiting episodes by sustained cessation of cannabis use
   (6 months or span 3 cycles)

Supportive: May be associated with prolonged hot baths/showers

Treatment
STOP CANNABIS

Goyal et al. Eur Jour Gastroenterol & Hepatol 2018
Venkatesan T et al. Neurogastroenterology & Motility 2019
Cannabis use and sleep

- Cannabis use is often cited by patients/general public to improve sleep disturbances

- Early studies showed low dose can improve sleep parameters
  - ↓ sleep onset latency
  - ↓ wake after sleep onset
  - ↑ slow wave sleep

Some concerns should be considered
- ↑ cannabis requirement required to achieve same level of sleep improvement
- Chronic use (5x/week) → ↑ sleep disturbances
- Cannabis withdrawal → sleep disturbances up to 45d

Babson et al. *Curr Psychiatry Rep.* 2017
Summary: Cannabis in IBD

• Animal studies show possible benefit of activation of the CB2 receptors
• Large percentage of IBD patients have used or are currently using cannabis to manage IBD-related symptoms
• Majority of current users do not share with their providers
• There are a few small studies have shown that cannabis use + traditional medical therapy can IMPROVE patients symptoms but NOT disease activity
Take Home Messages

1. There are some patients that might benefit from using cannabis in ADDITION to traditional medical therapy.

2. There is NO study that has shown that cannabis can replace medical therapy.

3. No clear benefit in patients who are otherwise feeling well (disease already in remission).

4. Nothing is risk free… Have to weigh the risks/benefits of use.

5. If you are using or want to use, discuss with your medical provider.
“There cannot be two kinds of medicine—conventional and alternative. There is only medicine that has been adequately tested and medicine that has not, medicine that works and medicine that may or may not work. Once a treatment has been tested rigorously it no longer matters whether it was considered alternative at the outset”

Angell M, Kassirer JP. NEJM 1998