A Provider's Guide to Medical Cannabis: THC and CBD Putting the Evidence to Work for Improved Patient Care

What is Medical Cannabis?

- Cannabis is a genus of flowering plants. It produces a resin containing several different cannabinoids
- Delta-9-tetrahydrocannabinol (or THC) is the main active cannabinoid in Cannabis
- Cannabidiol (CBD) is the main active cannabinoid in Hemp. Hemp is Cannabis with <0.3% THC concentration
- THC is responsible for the mood altering effects of cannabis
- THC is used by patients with pain, anxiety, insomnia, chemotherapy induced nausea, muscle spasticity, and reduced appetite
- CBD is used by patients with seizures, pain, inflammation, anxiety, insomnia, nausea, and IBD

Clinical Evidence: Why would you recommend medical cannabis for your patients?

In 2017, an ad hoc committee of the National Academies of Science, Engineering, and Medicine published the report *The Health* Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research. In the report, the committee presented nearly 100 conclusions related to the health effects of medical cannabis. Some of their conclusions include:

There is conclusive or substantial evidence that cannabis or cannabinoids are effective:

- For the treatment for chronic pain in adults (cannabis)
- Antiemetics in the treatment of chemotherapy-induced nausea and vomiting (oral cannabinoids)
- For improving patient-reported multiple sclerosis spasticity symptoms (oral cannabinoids)

There is moderate evidence that cannabis or cannabinoids are effective for:

• Improving short-term sleep outcomes in individuals with sleep disturbance associated with obstructive sleep apnea syndrome, fibromyalgia, chronic pain, and multiple sclerosis (cannabinoids, primarily nabiximols)

There is limited evidence that cannabis or cannabinoids are effective for:

- Increasing appetite and decreasing weight loss associated with HIV/AIDS (cannabis and oral cannabinoids)
- Improving clinician-measured multiple sclerosis spasticity symptoms (oral cannabinoids)
- Improving symptoms of Tourette syndrome (THC capsules)
- Improving anxiety symptoms, as assessed by a public speaking test, in individuals with social anxiety disorders (cannabidiol)
- Improving symptoms of posttraumatic stress disorder (nabilone; one single, small fair-quality trial)

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Chronic Pain

- Evidence shows there is synergistic anal gesia with greater-than-additive effects
 between cannabinoids and opioids¹
- There is no enhancement of cardiorespiratory suppression with combination treatment^{1,2}
- The treatment of chronic pain in this open-label, prospective cohort resulted in improved pain and functional outcomes, and a significant reduction in opioid use⁹
- Use of marijuana for chronic pain, neuropathic pain, and spasticity due to multiple sclerosis is supported by highquality evidence³

Anxiety Existing preclinical evidence strongly

supports CBD as a potential treatment

for generalized anxiety disorder, panic

sessive-compulsive disorder, and post-

traumatic stress disorder when admin-

When co-administered with THC, CBD

was able to attenuate the anxiogenic

effect of high doses of THC. CBD was

able to reduce post-stress anxiety in

healthy subjects submitted to simulat-

Cannabis consumption affects anxiety-

related behaviors in a dose-dependent

disorder, social anxiety disorder, ob-

Sleep Disturbance

- In patients with unremitted PTSD, treatment with orally absorbable
 THC had beneficial effects on global symptom severity, sleep quality, frequency of nightmares, and PTSD hyperarousal symptoms⁷
- CBD may hold promise for
 REM sleep behavior disorder and
 excessive daytime sleepiness, while
 nabilone may reduce nightmares
 associated with PTSD and may improve sleep among patients with
 chronic pain⁸

THC

THC is a CYP450 inhibitor -2C9 and 3A4.

- FDA approved synthetic THC*
- Dronabinol— oral chemotherapy induced nausea/ vomiting and weight loss in patients with HIV
- Nabilone— oral chemotherapy induced nausea/ vomiting

Adverse Effects

THC: orthostatic hypotension, • tachycardia, decreased intraocular pressure, nystagmus, conjunctival injection, lethargy, decreased concentration, psychomotor impairment, euphoria, acute panic or paranoid reaction, altered motivation, increased appetite, tolerance

Vermont Medical Cannabis Dispensaries

Champlain Valley Dispensary— Burlington, South Burlington Southern Vermont Wellness– Brattleboro, Middlebury Grassroots Vermont—Brandon PhytoCare Vermont— Bennington

Start with 2mg of THC. Increase by 0.5mg every 2 days until symptom relief is achieved. -Paul Jerard, PA-C. Vermont Cannabinoid Clinic

Dosing Recommendations: THC

Chronic Pain: 2mg—10mg Sleep Disturbance: 2mg—5mg Anxiety: 2mg—25mg MS Spasticity: 2mg—5mg Anti-emetic: 2mg—25mg

Cannabinoids

Pharmacology

- Cannabinoids binds to CB1 receptors in the CNS and CB2 receptors, mostly expressed in cells of the immune system, with varying affinity.
- THC is a stronger agonist than CBD.
- Clinically significant drug-drug interactions due to CYP450 inhibition by medical cannabis have not been reported.
- *Synthetic cannabinoids are associated with more morbidity and mortality than phytocannabinoids (naturally occurring cannabinoids)

Relative Contraindications to Medical Cannabis

- Pregnant or breast feeding mothers—possible link between smoking cannabis during pregnancy and low birth weight
 - Adolescents heavy users show disadvantages attention, learning, and processing speed. Resolves within 3 months of abstinence
- Children—possibility for severe disorientation, confusion, and anxiety. Long term studies have not been done
- Cannabis Hyperemesis Syndrome

Routes of Administration

- Smoking—fastest onset < 5 mins, duration 2-3 hours
- Vaping—onset < 5 mins, duration 2-3 hours</p>
- **Concentrates**—wax, shatter, distillate. Most potent products with the highest levels of cannabinoids. Used in smoking or vaping or creation of infused products
- Edibles/Capsules—longest onset 60-90 minutes, duration 6-8 hours
- Tinctures—most accurate dosing method, onset 15-30 minutes sublingually or 60-90 minutes when ingested, duration 4-6 hours
- Transdermal Patches/Gel Pens—quick onset, long duration of effect
- Creams/Ointments—regional pain relief, onset 30
 minutes, duration 2-4 hours

Dosing Recommendations: THC/CBD combo*

For the cannabinoid naïve patients, <u>START LOW</u> and suggest 1:1 products of THC:CBD Chronic Pain: 2mg/10mg—10mg/25mg Sleep Disturbance: 2mg/10mg—5mg/40mg Anxiety: 2mg/10mg—10mg/25mg MS Spasticity: 2mg/20mg—5mg/50mg *The combination of THC and CBD increases clinical efficacy while reducing adverse events⁴

CBD

CBD is a CYP450 inhibitor—2C19 and 3A4

CBD is a weak partial agonist and can antagonize the effect of THC at CB receptors

FDA approved synthetic CBD*

Epidiolex—oral. Seizures

 associated with Lennox Gastaut Syndrome or
 Dravet Syndrome in pa tients 2years of age or older

Adverse Effects

CBD: fatigue, diarrhea, weight change¹⁰

Ensuring Your CBD is Good Quality

- Choose CBD products made with American grown hemp (VT, CO, OR, WA, KY, TN)
- Choose "full spectrum" CBDrich hemp extracts
- Look for labels that indicate the amount of THC/CBD per serving, not whole bottle
- Beware of companies that make explicit health claims this is illegal
- Seek out CBD-rich products derived from high-resin cannabis grown sustainably
- Avoid vape cartridge products with thinning agents propylene glycol and ethylene glycol
- Beware companies claiming to source CBD from seed or stalk

Dosing Recommendations: CBD

Chronic Pain: 10mg—25mg Sleep Disturbance: 10mg—40mg Anxiety: 10—25mg MS Spasticity: 20mg—50mg IBD: 200-300mg BID

Resources for Providers:

-Vermont Cannabinoid Clinic: Medical Guidance for Medicinal Cannabis

Paul Jerard, PA—C pbj@vtcclinic.com

-Ada Puches, Community Outreach Coordinator

Champlain Valley Dispensary and Southern Vermont Wellness

ada@cvdvt.org

-Vermont Marijuana Registry – http://medicalmarijuana.vermont.gov

-Project CBD— projectCBD.org

California-based nonprofit dedicated to promoting and publicizing research into the medical uses of cannabidiol (CBD)

-The University of Vermont's Free Cannabis Speakers Series—

learn.uvm.edu/com/program/cannabis-speaker-series-from-botany-to-medicine/

-The Society of Cannabis Clinicians—cannabisclinicians.org

-United Patient's Group—unitedpatientsgroup.com

-Healer.com

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