Medical Cannabis in Utah

For The

Ogden Surgical-Medical Society

Presented
by

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This presentation has no commercial content and is not supported by a commercial vendor, and I have no financial links to any medical cannabis company.

FIRST: A BOTANY LESSON

Cannabis

- Flowering plant native to central and eastern Asia
- Three species
  - sativa
  - indica
  - ruderalis
    - (+ multiple cultivars)

FIRST: A BOTANY LESSON

- Used by humans for millennia
- 4000 BCE: first documented cultivation
- 1000 BCE: recovered from tombs in Asia
- Uses include: fiber, food (seeds are highly nutritious), religion
- Medicinal
- Recreational

(anthropological theory-burning the trash?)

LEARNING OBJECTIVES

1. Review the endocannabinoid system

- physiology
- pathology
- pharmacology

LEARNING OBJECTIVES

2. Discuss the principles of medical cannabis recommending

- indications
- dosing
- toxicity
- monitoring

THE ENDOCANNABINOID SYSTEM

(WHO KNEW?)

- Discovered in 1990 by an Israeli researcher: Dr.Mechoulam
- Evolutionary-ancient intercellular signaling system
- Phytocannabinoids mimic the actions of endocannabinoids
- Endogenous ligands (fatty acid derivatives) are manufactured by many cell types

THE ENDOCANNABINOID SYSTEM

The endocannabinoid system (ECS) is an internal homeostatic system present in all vertebrates that plays a critical role in the nervous system and regulates multiple physiological processes, including appetite, digestion, mood, coordination, and other processes. The ECS also influences immunomodulation, cardiovascular functions, sensory integration, tumor surveillance, fertility, bone physiology, the hypothalamic-pituitary-adrenal axis, neural development, and intraocular pressure. *

* This information is based upon numerous studies done and published between 2008 and 2013.

THE ENDOCANNABINOID SYSTEM

- Endogenous cannabinoids include: Anandamide (THC mimics this), and 2-AG (2-Arachidonoylglycerol) (CBD mimics this)
- CB 1 Receptors (are G protein receptors): present in all chordates
  - (**brain**, lungs, vascular system, muscles, reproductive organs, immune system, liver, bone marrow, pancreas)

THE ENDOCANNABINOID SYSTEM

- CB 2 Receptors (also G protein receptors: found in: spleen, bones, skin, immune system, liver, bone marrow, pancreas

ENDOCANNABINOID NEUROPATHOLOGY

(HISTORICAL, CLINICAL OBSERVATIONS)

- Patients with mutated enzyme for endocannabinoid clearance: had twice normal levels of anandamide and an absence of pain and anxiety
- Patients with MS, ALS and experimental neuropathy have increased CB2 expression
- Marijuana is known to heighten sensory perception, including touch, smell, sight, taste and hearing. For some patients, this can be an undesirable effect.

PHARMACOLOGY (FOR CBD)

- Weak CB1 and CB2 antagonist
- Does not involve direct binding
- Increases availability of endocannabinoids
- FDA statement for Epidiolex: obtain serum transaminases (ALT and AST) and total bilirubin levels in all patients prior to treatment

PHARMACOLOGY (FOR CBD)

- Is lipophilic: consuming fatty foods with CBD can increase absorption and blood levels up to 4-5 times; and, poorly penetrates skin unless put in a hydrophilic vehicle.
- Lacks psychoactive effects
- In rats: decreases inflammatory response, improves fracture healing
- In humans: decreases inflammation in vitro

PHARMACOLOGY (FOR THC)

- THC is a CB1 and CB2 agonist
- Causes psychoactive effects
- Can decrease nausea/vomiting associated with chemotherapy
- Improves appetite (studied in HIV patients)
- Reduces pain, especially neuropathic (usually in combination with some amount of CBD)
- Reduces muscle spasticity (usually with CBD)

(**Note**: CBD can counter psychoactive effects of THC)

PHARMACOLOGY (FOR THC)

Cytochrome (CYP) P450 enzymes metabolize both THC and CBD.

- THC is metabolized by CYP3A4, CYP2C19 and CYP2C9.
- CBD is metabolized by CYP3A4, CYP2C19 and potentially by CYP2C9 and CYP1A1/1A2.
- Studies suggest that both THC and CBD **inhibit** CYP3A4, CYP2C19, CYP2C9 and CYP1A1/1A2,

PHARMACOLOGY (FOR THC)

- THC and CBD inhibit CYP3A4, so can increase the availability of drugs metabolized by this system, e.g. sertraline (Zoloft)
- THC and CBD inhibit CYP2C9 also, and both these pathways metabolize fluoxetine (Prozac), thus increasing the availability of fluoxetine.
- THC and CBD inhibit CYP2C9 which is responsible for metabolizing warfarin, so **cannabis can greatly increase bleeding times** in those patients.
- THC and CBD **also increases the bleeding times for patients on Direct Oral Anticoagulants (DOACs**), but the mechanism is not known. (these drugs are not metabolized by the p450 enzyme systems, rather, they are excreted in the urine.

MEDICAL CANNABIS RECOMMENDING

Indications: *

Conclusive or substantial evidence:

- Chronic pain
- Chemotherapy induced nausea/vomiting
- Spasticity with multiple sclerosis
- Lennox-Gastaut and Dravet seizure syndromes

(recently added seizures secondary to Tuberous Sclerosis)

* Study by the National Academy of Sciences

MEDICAL CANNABIS RECOMMENDING

Indications:

Moderate evidence:

- Sleep disturbance

Limited evidence:

- Appetite and weight gain
- PTSD (symptom control)
- Social anxiety

MEDICAL CANNABIS RECOMMENDING

Indications:

No or insufficient evidence:

- Cancer
- Epilepsy (exception being the Lennox-Gastaut and Dravet syndromes)
- ALS, Huntington’s, Parkinson's
- Irritable bowel syndrome
- Opiate addiction

MEDICAL CANNABIS CONTRAINDICATIONS

Contraindications:

- Pregnancy and lactation (adverse neurodevelopmental effects on fetus/infant)
- Heart disease (angina due to tachycardia and hypotension due to THC)
- Relative contraindication for those <21 years old
- Smoking or vaping in patients with COPD and asthma

MEDICAL CANNABIS RECOMMENDING

- Like other controlled drugs
- Review prior medical records
- Comprehensive history and physical
- Check the Controlled Substances Database (notation about checking the EVS)
- Plan for follow-up care
- Proper documentation
- Communication with other care-givers

MEDICAL CANNABIS RECOMMENDING

- "Qualified" recommender
- ***Start Low, Go Slow***
- Discuss options for medication delivery
  - (oral, inhaled, sub-lingual)
- Plan for follow-up care
- CBD: 2.5 – 10 mg/kg p.o. in 2 divided doses
- THC: 2 – 10 mg p.o. q8h (note: greater than 30 mg/day associated with increased adverse effects)

TIMING OF VARIOUS DOSAGE FORMS

- Inhalation: **onset** seconds to minutes, peak blood level in 30 minutes, **duration** 2- 4 hours.
- Sublingual/oromucosal: **onset** 15 – 45 minutes, **duration** 90 minutes to several hours.
- Oral/edible: **onset** 1 – 3 hours, **duration** 6 – 8 hours

  (Note: risk with oral administration is that patient will not wait enough time to feel effect of dosage and may repeat doses resulting in excessive medication.)
- Topical: variable onset and variable duration.
- Suppositories: **onset** 15 – 45 minutes, **duration** 2-4 hours.

MEDICAL CANNABIS PATIENT FOLLOW-UP

Monitor:

- Treatment response
  - Helping/not helping
  - Side effects
  - Adverse psychological effects
- Drug-drug interactions (warfarin, clobazam)
- LFTs
- Hyperemesis?
- Vaping “unregulated” products?

MEDICAL CANNABIS PATIENT FOLLOW-UP

Monitor:

- Common side effects of CBD: diarrhea, somnolence, decreased appetite, change in weight, increased liver enzymes
- Common side effects of THC: somnolence, increased appetite with weight gain, undesired psychological effects, undesired enhancement of sensory inputs

MEDICAL CANNABIS TOXICOLOGY

Driving/Safety Sensitive Operations:

- Avoid for 4 hrs after inhalation
- Avoid for 6 hrs after oral ingestion
- Avoid for 8 hrs if euphoria was experienced
- Specific jobs (aviation) – no use within 28 days

MEDICAL CANNABIS TOXICOLOGY

Buyer Beware with OTC CBD products:

A 2017 analysis of online retail purchases of 84 CBD products from 31 companies found that 43% contained more CBD than was indicated on the label and that 26% contained less CBD than was indicated on the label; additionally, THC was found in 18 out of the 84 samples even though none of the labels indicated that the products contained THC.

MEDICAL CANNABIS TOXICOLOGY

Urine testing:

- Presence of cannabinoids can persist for days to weeks

Oral fluid cannabinoids:

- Present for 1-2 hours after use
- Brushing teeth removes cannabinoids from oral fluid

MEDICAL CANNABIS

Not a “cure all” treatment, but can provide important options for treatment of difficult conditions that do not respond to conventional therapy. **Note:** controlling **symptoms** is **not** the same as controlling the disease.

Side Note: 36 states now have legalized medical marijuana.

Must be treated like any other medication:

- Clear indications for recommending
- Based on a thorough patient evaluation
- Side effects, drug interactions explained
- Dosing: ***“start low, go slow“***

MEDICAL CANNABIS

Cannabinoid Product Board

(name will change as of July 1 to:

The Cannabis Research Review Board)

https://medicalcannabis.utah.gov/resources/cannabinoid-product-board/

This Board is currently composed of 4 physicians (family medicine, internal medicine, pain medicine and psychiatry), and 2 professors from the College of Pharmacy at the U of U. They have researched and published guidance documents (on the website) on several conditions for which medical cannabis may be used.

Note: they also hold monthly meetings that are open to the public. Currently via Zoom meetings.