Cannabis and Cancer

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Disclosures

- No Financial disclosures
- Clinical experience is in DC
  - Geriatrics
  - Palliative care
  - Chronic Pain, Neurodegenerative conditions (Parkinson’s, Alzheimer’s)
  - Cancer Support Care
- Paid consultant for DC RX (DC government sponsored education initiative) – some slides designed by DC RX
- Founder and Medical Director of MKCI – DC Based organization providing comprehensive integrative treatment for patients with Alzheimer’s disease
Cannabis as Medicine

- Interest waned in early 1900’s with advent of opiates, barbiturates, chloral hydrate, aspirin and syringes
- First federal restrictions in 1937 with Marihuana Tax Act ($1/oz for medical use, $100/oz for recreational users)
- AMA virtually alone in opposing act
  - Believed objective data re: harmful effects were lacking
  - Act would impede future clinical investigations
    - Removed from US Pharmacopoeia in 1942

Courtesy of Dr. Donald Abrams (personal friend and mentor)
“Marijuana” or “Marihuana”

- Originates from Mexican Spanish; the exact meaning is not known.
- The term was popularized by Harry Anslinger in the 1930s. Anslinger was the first commissioner of the Federal Bureau of Narcotics (which later became the DEA).
“Cannabis”

- Genus name originates from κάνναβις, written by Herodotus in 440 BCE.
- Main segregates include Cannabis *sativa* and Cannabis *indica*, best separated at the botanical rank of variety, rather than species.
TERMINOLOGY

“Hemp”

- Cannabis plant with a THC content less than 0.3%, grown for its seed and fiber
- Has been used commercially in thousands of products for more than 12,000 years
- Can describe any industrial or nutritional product from cannabis that is not used as a drug
There are three commonly recognized “strains” of cannabis – *C. sativa*, *C. indica*, and *C. ruderalis*. “Strain” names should not be confused with the formal botanical taxa *C. sativa* and *C. indica* because they do not correlate.

Cannabis vendors often characterize “Sativa” as a high-THC* plant, “Indica” as a mixed THC-CBD** plant, and “Ruderalis” as a high-CBD plant. However, these concepts are simplistic and often inaccurate (McPartland 2014).

* THC = tetrahydrocannabinol  
** CBD = cannabidiol
Cannabinoids
THC

THC discovered in 1964

- Psychoactive
- Anti-inflammatory
- Neuro-protective
- Anti-nausea
- Analgesic (neuropathic, chronic, and cancer pain)
- 11-OH-THC, the metabolite formed when THC undergoes first-pass metabolism, is estimated to be 4 times more potent than THC.
Cannabinoids
CBD

CBD
discovered in 1940

- Non-psychoactive, with no significant affinity for CB1 and CB2 receptors
- Blocks formation of 11-OH-THC (the most psychoactive metabolite of THC)
- Potent CYP450 3A1 inhibitor
- Modulates effects of THC; reduces THC-associated anxiety, dysphoria, panic reactions, and paranoia
- Paradoxically, CBD mitigates the side effects of THC while improving THC’s therapeutic activity (Izzo et al 2009; Russo 2011).
Cannabinoids
Manifold targets of CBD and minor cannabinoids

- CBD targets other receptors (GPR55, TRPV1, TRPV2, TRPA1, PPARγ, 5-HT1A, α3 glycine, etc).
- CBD inhibits adenosine uptake (caffeine, in contrast, increases adenosine), inhibits FAAH (increasing AEA), inhibits release of proinflammatory cytokines (TNF-α, IL-6, IL-1β), and acts as an antioxidant and free radical scavenger that is more potent than Vitamin C or Vitamin E.

(McPartland et al 2015)
Endogenous Cannabinoid System

- Synthesis
- Endocannabinoids
- Cellular uptake
- Metabolism
- CB2 Receptor
- CB1 Receptor
- CBx Receptor
- VR1 Receptor

Signal Transduction

- Immune function
- Cell proliferation
- Inflammation
- Pain

Appetite
- Immune function
- Muscle control
- Pain
- IOP

Cognition
- Emesis
- Neuroexcitability
- Reward
- Thermoregulation

Pain
- Vaso-dilation
- Inflammation
Tommy Chong on His Prostate Cancer: 'Cannabis Is a Cure'

2:06 PM PDT 6/13/2012 by Erik Pedersen
CELEBRITY NEWS

Tommy Chong: “I Got Diagnosed With Rectal Cancer,” in Treatment Now

By Madeline Boardman  June 17, 2015

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Related videos
Case – 59 year old man with chemotherapy induced neuropathy

- Severe chronic neuropathy
- Response to medications poor or side effects
- Other Symptoms: weight loss, poor appetite - “food does not taste good”
- BMI on 1st visit 18.5
- Goals – control pain and gain some weight.
- 8 weeks after recommendation – gained 5 lbs, no side effects, reports use twice daily with vaporizer, pain is mostly controlled, occasionally needs to use extra few doses/day.
- Tolerating euphoria well and the only problem - COST but “it is worth it”
Anti-cancer activity

- Potent autophagy-mediated apoptotic signaling in vitro and in vivo in many cancer cell lines and models
- Both THC and CBD induce apoptosis
- No large animal studies or human studies
- No studies comparing different THC:CBD ratios
- Not possible to guide patients beyond very general statements
- Large amount of outlandish claims
- In my opinion cannabinoids alone are NOT ENOUGH!

Visˇnja Bogdanovic´, 2017
Cannabis in Palliative Medicine -

“Moving forward to the present moment, I prefer that this type of care be termed “cannabinoid integrative medicine” (cim),” - S.K. Aggarwal, MD PhD*

Euphoria is often described as a “side-effect” in trials

Is it really an “adverse experience” or improved quality of life?

In palliative care improved quality of life is the main goal

No other single treatment can help to increases appetite, decreases nausea and vomiting, and improve pain and sleep. And can be combined with opioids without added toxicity/side effects

S.K. Aggarwal, 2016 Curr Oncol
Large Cancer Center Study

- 2010-11 -12 months study period at Sheba Medical Center, Tel Aviv University Affiliated Cancer center
- 17,000 total cancer patients
- 279 patients obtained permit from the center’s authorized oncologist
- Median age of users was 60 years old
- 57% were women
- 84% had metastatic disease
- Symptoms were co-managed with palliative care team – standard of care

Barliz Waissengrin 2015
Results

- About half were recommended by oncologist and others found information from friends and other sources and requested it.
- Most indications: pain 76%, anorexia 56%, generalized weakness 52%, nausea 41%.
- 46% died within 6 months.
- Of remaining about half renewed cannabis order in 6 months – about half did not find it helpful or had some other reasons not to renew it.
- 90% smoked it – (likely since this study was done 6 years ago.)
Fig. 1. Efficacy of cannabis use in patients, as perceived by patients who completed a detailed questionnaire (n = 69).
CONCLUSIONS FOR: THERAPEUTIC EFFECTS

There is **conclusive or substantial evidence** that cannabis or cannabinoids are effective:
- For the treatment for chronic pain in adults (cannabis) (4-1)
- Antiemetics in the treatment of chemotherapy-induced nausea and vomiting (oral cannabinoids) (4-3)
- For improving patient-reported multiple sclerosis spasticity symptoms (oral cannabinoids) (4-7a)

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) (4-19)

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) (4-4a)
- Improving clinician-measured multiple sclerosis spasticity symptoms (oral cannabinoids) (4-7a)
- Improving symptoms of Tourette syndrome (THC capsules) (4-8)
- Improving anxiety symptoms, as assessed by a public speaking test, in individuals with social anxiety disorders (cannabidiol) (4-17)
- Improving symptoms of posttraumatic stress disorder (nabilone; one single, small fair-quality trial) (4-20)

There is **limited evidence** of a statistical association between cannabinoids and:
- Better outcomes (i.e., mortality, disability) after a traumatic brain injury or intracranial hemorrhage (4-15)

There is **limited evidence** that cannabis or cannabinoids are **ineffective** for:
- Improving symptoms associated with dementia (cannabinoids) (4-13)
- Improving intraocular pressure associated with glaucoma (cannabinoids) (4-14)
- Reducing depressive symptoms in individuals with chronic pain or multiple sclerosis (nabiximols, dronabinol, and nabilone) (4-18)
Common Modes of Administration and Formulations

- **Inhalation by smoking or vaporization**
  - (herbal cannabis, resin, concentrates)

- **Oral**
  - (prescription cannabinoids, edibles, tinctures)

- **Oro-mucosal or sublingual**
  - (lollipops, lozenges, nabiximols)

- **Topical or Rectal**
  - (herbal cannabis, resin, concentrates)
Cannabis Toxicity/Addiction

Active/Lethal Dose Ratio and Dependence Potential of Psychoactive Drugs

Legend:
- Narcotics
- Depressants
- Stimulants
- Anesthetics
- Hallucinogens
- Cannabis

R. S. Gable, et al 2006
Conclusions

- Cannabis is the single best Palliative Medicine treatment we have.

- Cannabis is proven effective treatment for number of conditions:
  - Chronic Pain
  - Cancer/Chemotherapy induced Nausea and Vomiting

- Anti-proliferative effects are clinically lacking any evidence but in vitro and in small animal models appear to be very promising and SHOULD be researched

- Cannabis alone can have some efficacy for variety of conditions but alone it is just one tool! Best of integrative medicine is finding synergism between different approaches.
Rita M., a 67-year-old retired schoolteacher, presented in the fall of 2010 with mild bloating and digestive symptoms, including pain that was relieved with bowel movements. She was evaluated and treated with a BRAT diet for 1 month with worsening of symptoms. Within a month of her first presentation a vaginal ultrasound showed bilateral pelvic masses; her CA125 level was >4,000. Total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed and the patient received treatment with intravenous and intraperitoneal chemotherapy, including Taxol, cisplatin, and carboplatin, for stage IIIC ovarian neoplasia. In addition to conventional care Rita consulted integrative oncology providers. With a broad integrative team including medical and surgical oncologists, her primary care physician, acupuncture, naturopathic physicians, nutritionists, and mental health providers she navigated multiple fistula formation and resolution. She also experienced significant fatigue, nausea and vomiting, and moderate neuropathy.
Thank you - Questions