Medical Marijuana: Health Benefits and Considerations

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Outline Draft:

I. Introduction

A. What is marijuana (MJ)? (SLIDE 2)

1. Cannabis (CB) – *cannabis sativa* plant w/ many chemicals & psychoactive effects

2. Marijuana (MJ) – dried leaves, flower, & stems from CB plant

a. Includes many chemicals or "cannabinoids"

1'. Tetrahydrocannabinol (THC) – responsible for most of usual high

2'. Cannabadiol (CBD) – no high but some medicinal properties

b. Will use term "MJ"; will use THC/CBD if individual components specified in study

B. MJ Background (SLIDE 3)

1. 22.2 million people in US used MJ in past month[1]

2. MJ legalization in US is rapidly changing[2]

a. 1996: CA 1st state to allow medical MJ

b. By 2019, 33 states & DC permit medical use[3]

c. 10 states & DC permit recreational use

3. There are pros and cons of medical MJ: (SLIDE 4)

a. ↓ Pain

b. ↑ Appetite

c. ↓ Nausea

d. ↓ Seizures

e. ↑ Driving after MJ

f. ↑ Poison control calls

g. ↓ Perception of harm

h. ↑ Problems for youth

C. This lecture covers (SLIDE 5)

1. Background & MJ components

2. Disorders/symptoms where MJ has proven benefits

3. Disorders w/ limited data

4. Clinical considerations

5. Policy implications

D. Case example (Edna) (SLIDE 6)

1. Edna: 46 yo ♀, living in Colorado, started experiencing unusual symptoms

2. No history of MJ use

3. Blurred vision, leg tingling, & face numbness

4. Began experiencing trouble walking & muscle spasms

5. Made primary care appt to evaluate symptoms

6. We will follow Edna's case through this lecture

II. MJ Background & components (SLIDE 8)

A. Delta-9-tetrahydrocannibinol (Δ^9-THC)

1. Major psychoactive MJ component

2. THC potency: ↑ in recent years

1'. US: 1995→ 2014: ↑ potency 4% → 12%[4]

2'. High potency concentrates (e.g., dabs) are prevalent

B. Cannabidiol (CBD):

1. Non-intoxicating; absent of craving → no drug misuse liability[5]

2. May ↓ undesirable THC effects (e.g., intoxication, sedation)[6]

3. May have medical benefits (e.g., ↓ seizures)

C. Other potentially therapeutic cannabinoids: (SLIDE 9)

1. >100 cannabinoids identified & all work together[7] including the following
2. Terpenes: substance in many plants (e.g., oranges)
    a. Cannabinoids & terpenes work together →boost MJ effects[7]
    b. May treat pain & inflammation[7]
3. Cannabigerol (CBG): non-intoxicating cannabinoid
    a. ↓ Inflammation in bowel disease & ↑ appetite in animals[8]
    b. ↓ Intraocular pressure in glaucoma eye disease[9]
4. Cannabichromene (CBC): non-intoxicating
    a. CBC+THC ↓ inflammation in animals[10]
    b. Blocks pain & inflammation associated w/ osteoarthritis[11]

C. FDA approved cannabinoid drugs (SLIDE 10)

1. Dronabinol (Marinol): synthetic oral THC
    a. Affects brain area controlling nausea, vomiting, & appetite
    b. Rx nausea & vomiting from chemotherapy
    c. Rx appetite & weight loss in AIDS
2. Nabilone (Cesamet): Synthetic oral THC
    a. ↓ Brain signals controlling nausea & vomiting
    b. Rx severe nausea and vomiting from chemotherapy
3. Nabixmols (Sativex): CBD + THC (SLIDE 11)
    a. Mouth spray
    b. Helps w/ muscle spasms
4. Cannabidiol (Epidiolex): Plant-derived CBD
    a. No high or euphoric effects
    b. Approved by FDA to Rx pediatric epilepsy

D. Defining a randomized controlled trial (RCT) (SLIDE 12)

a. Type of research design
b. Patients get different experimental Rx at random

c. Gold standard for demonstrating drug effects

III. Diseases & symptoms with data-based effectiveness:

A. Chronic pain (SLIDE 14)

1. Most common condition for medical MJ; affects ~30% of adults[12]

2. Opioids commonly prescribed for chronic pain: ~259 million prescriptions[13]

a. ↑ Risk of misuse & overdose[14]

b. US opioid overdose ↑ 4x over past 15 yrs[15,16]

1'. 1999: 1.5/100,000 people/yr

2'. 2009: 6/100,000 people/yr

c. ↑ Drug availability worsens US opioid epidemic[17]

3. 28 RCTs w/ ~2,500 chronic pain participants → MJ ↓ pain compared to placebo[18]

B. Severe nausea (SLIDE 15)

1. MJ ↓ vomiting animal studies[19]

2. Some patients prefer MJ over other antiemetics (anti-nausea drugs)

3. 28 trials show MJ effective Rx for nausea & vomiting[18] (e.g., from chemotherapy)

a. Placebo-controlled study with dronabinol on chemotherapy nausea/vomiting[20]

b. Dronabinol similar to other meds for Rx of nausea/vomiting[19]

C. Severe muscle spasms (SLIDE 16)

1. E.g., spinal injury & multiple sclerosis (a progressive neuron deterioration disease)[21,22]

2. 15+ studies suggest MJ may ↓ spinal and MS symptoms

a. 16% of MS patients use MJ for Rx symptoms[23]

b. MJ improves pain & muscle spasms in several MS studies[24]

1'. Placebo-controlled study on nabiximols w/ ~200 subjects with MS

2'. Pain ↓ in subjects who received nabiximols

D. Check-in w/ Edna (SLIDE 17)

1. Attended primary care appt
2. Dr. suspected MS & began ruling out other conditions
3. Underwent extensive testing including brain scans
4. Started Edna traditional meds. for symptom management

IV. Possible additional med MJ uses (limited data)

A. Seizures: (e.g., lost consciousness/fall to floor & jerking movements) (SLIDE 19)

1. Affects ~2.75 million in US
2. Impairs cognitive development & impacts quality of life
3. Both THC & CBD (key components in MJ) ↓ seizures in animals[25,26]
4. Human studies are lacking
    a. No high-quality RCTs for CBD or THC in Rx of seizure[27]
    b. Insufficient data for MJ for ↓ seizures
    c. Despite this MJ used widely w/o data as anti-seizure Rx
    d. CBD OK for pediatric seizures[28]
    e. Studies with CBD as seizure Rx (SLIDE 20)
        1'. Seizure patients took CBD (Epidiolex) orally in 2 placebo-controlled RCTs[29]
        2'. ~40% ↓ in seizure frequency over 14 wks treatment period
        3'. Non-placebo-controlled study w/ 214 patients → 12 wks oral CBD
        4'. Seizures ↓ 54%

B. Crohn's disease: deterioration of colon with abdominal pain and bleeding (SLIDE 21)

1. MJ effective Rx for other abdominal disorders in animals[30]
2. Case report (no controls): MJ helped patients with digestive disorders[31]
3. Human study of MJ for patients with Crohn's disease[32]
    a. Retrospective observational study of 30 Crohn's patients already using MJ

b. Self-report general medical well-being ↑ after initiating MJ

C. Glaucoma: ↑ eye pressure & can → blindness[33] (SLIDE 22)

1. Optic nerve damage often caused by ↑ intraocular pressure[34]

2. MJ may ↓ eye pressure[35]

3. Single trial: small placebo-controlled study of MJ[18]

a. Short-term (~2 hrs) intraocular pressure ↓

b. Pressure returned after 4 hours[35]

D. Cancer (SLIDE 23)

1. MJ Rx to ↑ appetite, ↓ cancer pain, & ↓ chemotherapy nausea

2. Study in patients w/ advanced cancer → pain responds poorly to opiates

a. Placebo-controlled study w/ 3 doses of nabiximols

b. More pain ↓ w/ nabiximols > placebo in low/med doses[36]

3. Placebo-controlled study in patients w/ cancer pain despite opiate use

a. Patients received THC:CBD, THC alone, or placebo

b. Pain ↓ after THC:CBD compared to placebo; not THC alone[37]

4. No human studies on MJ for Rx of cancer itself

E. Neuropathic pain: pain from nerve damage (e.g., burning pain in feet) (SLIDE 24)

1. Affects ~2% of population

2. Patients use MJ to ↓ pain, ↑ sleep & mood

3. Placebo-controlled study[38]

a. 4 MJ doses in neuropathic pain patients

b. High dose MJ (~9%) ↓ pain, ↑ sleep

c. Lower doses & placebo did not help pain or sleep

F. HIV, AIDS, & cachexia/wasting syndrome (SLIDE 25)

1. Cachexia: severe weight/muscle loss, no appetite, weakness

2. Impacts patients w/ HIV/AIDS

2. Evidence for MJ Rx still unclear[39]

3. One study found MJ didn't ↑ appetite or life quality[40]

4. Contradicts patients who swear by MJ for relief from wasting & ↓ appetite

5. 1 in 3 AIDS patients use MJ on their own for symptom Rx[41]

G. Hepatitis C (SLIDE 26)

1. MJ doesn't Rx Hep C or assoc liver disease/cirrhosis

2. MJ may ↓ nausea assoc w/ Hep C meds

a. MJ may help w/ med adherence → better outcomes

b. May ↓ unpleasant med side effects

3. One study found MJ worsens Hep C by ↑ fibrosis (↑ connective tissue in liver)[42]

4. Alt study concluded MJ did not alter Hep C outcomes[43]

H. Dementia (↓ thinking abilities) diseases (e.g., Alzheimer's) (SLIDE 27)

1. No RCTS w/ MJ for agitation in Alzheimer's or other dementia[44]

2. Small 1-wk dronabinol study w/ dementia[46]: ↓ agitation/aggression, ↑ appetite[45]

3. Small study w/ dronabinol for not eating: Rx→ ↑ weight[46]

4. Dronabinol effective for nighttime agitation in small study[47]

I. Post-traumatic stress disorder (PTSD): severe stress following trauma (SLIDE 28)

1. No good RCTS w/ MJ for PTSD[44], may ↑ sleep quality[48] & ↓ nightmares[49]

2. Retrospective chart review study (90% patients w/ PTSD)[50]

a. Patients received nabilone for insomnia & nightmares; 91% had MJ dependence

b. Nabilone assoc w/ ↑ in sleep, ↓ nightmares

3. Retrospective chart review of PTSD patients w/ nightmares (SLIDE 29)

a. Rx w/ nabilone

b. ~70% reported ↓ or cessation of nightmares and ↑ sleep[51]

4. 2 ongoing studies w/ MJ for PTSD (no results yet)[52]:

a. Study 1: veterans w/ PTSD receive 1 of 3 MJ doses or placebo

b. Study 2: 1-yr observation w/ MJ users vs. nonusers on PTSD symptoms

J. Anxiety (SLIDE 30)

1. No RCTs w/ MJ for anxiety

2. Ongoing study w/ MJ for anxiety[52]

a. Study w/ anxiety patients using high-CBD tincture (liquid dropper under tongue)

b. Outcomes: mood, quality of life, sleep, & general health

H. Check in w/ Edna (SLIDE 31)

1. MS Rx side effects difficult to tolerate

2. Tried many Rx w/ poor results

3. Dr. suggested medical MJ for MS symptoms

4. Edna obtained medical MJ card

V. Clinical Considerations (SLIDE 33)

A. Dose varies widely in active compound

1. Research MJ: low dose: ~3% THC, high dose: ~12% THC

2. Street doses: 10 – 90% THC

B. Unclear which compounds result in desired effect

C. Decreased perception of harm

1. Non-medical users may believe recreational use is harmless

2. E.g., Edna's family members may perceive ↓ harm from MJ

D. Patients seeking MJ for questionable symptoms may be malingering (faking bad)

E. Unclear how to assess for Cannabis Use Disorder (CUD) (SLIDE 34)

1. DSM-5 CUD Criteria[53]: mild, moderate, severe

a. Tolerance: ↑ amount needed for same effect

b. Larger amounts used

c. Much time spent using

d. Attempts to cut down

e. Neglecting major roles

f. Engagement in important activities ↓

g. Interpersonal problems

h. Physical/psychological problems

i. Hazardous use (e.g., driving)

j. Craving

k. Withdrawal

l. Dr. plans to monitor for these symptoms in Edna

2. CUD withdrawal syndrome: (SLIDE 35)

a. Mood effects: irritability, anger, depression

b. Anxiety

c. Sleep difficulty: insomnia

d. ↓ appetite

e. Restlessness

f. Cognitive ↓

g. Phys symptoms: abdominal pain, tremors, sweating, fever, chills, headache

VI. Policy Implications

A. Cons of recommending medical MJ: (SLIDE 37)

1. Driving after MJ use has ↑ in med MJ states[54,55]

2. Poison control center calls ↑ from ~50 in 2006 to ~250 in 2014 in med states[56]

3. Perception of MJ harm ↓ by 10% among teens in med MJ states

4. Risk of ↑ MJ use & probs for young adult MJ cardholders[57]

5. Doctors can't "prescribe" & can't indicate dosage/amount[58] (SLIDE 38)

   a. ~90% of residents/fellows feel unprepared to recommend MJ[59]

   b. ~65% feel unable to answer MJ questions[59]

6. Only some states require MJ education for Drs. to rec MJ

7. Medical training usu. not req. for dispensary staff to make recs[60]

   a. Dispensary – designated locale for MJ sale/purchase

      1'. Both medical & recreational dispensaries

      2'. Sell wide variety of MJ in many forms

      3'. Must have Dr. recommended med card for medical dispensaries

      4'. "Budtenders" help patients w/ MJ selection for conditions

   b. Staff make recs based on personal opinion[61]

   c. Majority of dispensaries in CO rec MJ for morning sickness[61]

   d. Desire for sales vs. science may drive recommendations

8. Risk of drug interactions due to ↓ research

B. Pros of recommending MJ for symptom Rx: (SLIDE 39)

1. Very effective for some illnesses

2. States permitting medical MJ → ↓d opioid overdose[62]

3. States permitting medical MJ → ↓d opioid prescriptions for those w/ Medicare[63]

4. Medical MJ associated w/ 64% ↓ in opioid use[64]

5. MJ patients report better quality of life & ↓ med. side effects[64]

C. Edna's positive outcome (SLIDE 40)

1. Began using MJ for MS symptom Rx

2. Found low-dose edible that improved symptoms

3. Began ↓ poorly tolerated medications w/ doctor supervision

4. Successfully controlled MS symptoms w/ medical MJ

5. Edna advocates for MJ benefits

VII. Conclusion (take away points) (SLIDE 41)

A. MJ very promising for some conditions (e.g., chronic pain) Stat

B. MJ is not a panacea for all illnesses

C. Drs. Must attend to clinical considerations when rec. MJ

D. Several policy implications of rec. MJ

E. More MJ research is essential

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