CANNABINOID THERAPEUTICS

Eloise Theisen, RN, MSN, AGPCNP-BC
Green Health Consultants

Overview

- Demographics
- Special considerations in geriatrics
- Clinical implications
- Case studies
- Misconceptions
- Barriers

Green Health Demographics

- Started in October 2014
- Average age of patient is 76 years old
- Eighty percent are females
- Eighty five percent have never used cannabis before
- Fifty nine percent of patients are coming to cannabis for pain, 35% are coming to cannabis for sleep
- Average number of medications per patient is 7!
- Most common request- ”I don’t want to get high!”

Geriatric Considerations

- By 2040 the number of elderly over the age of 85 is expected to increase to 14.1 million
- Polypharmacy is a huge issue in the elderly
  - *Defined as 5 or more medications for a single patient (does not include supplements/vitamins).*
  - *Polypharmacy increases with age. Patient is assisted living communities and/or skilled nursing facilities can be on 20 different medications daily.*
  - *Risks of drug interactions, compliance adherence and adverse effects increase with each additional medication*

Geriatric Considerations

- BEERS List
  - *A list of potentially inappropriate medications for adults age 65 or older originally developed in 1991 by Dr. Mark Beers.*
    - Excludes end of life or palliative care patients
  - *Reviews the risk versus benefit of pharmaceutical's (prescribed and over the counter) and assesses for adverse pharmacodynamics, pharmacokinetics and drug-drug interactions*
  - *Updated in 2015. Identifies more drug-drug interactions and dose adjustments in liver and kidney disease*

Geriatric Considerations

- Age Related Changes
  - *As the body ages absorption, first pass metabolism, bioavailability, protein binding and renal/hepatic clearance are compromised*
    - Absorption can be decreased
    - Gastric emptying can be delayed
    - pH can be altered
    - Decreased motility of GI tract
  - *First Pass Metabolism*
    - P450 cytochrome primarily expressed in liver. Responsible for metabolizing medications
      - *Less efficient in older adults- upwards of 30%*
      - *Puts patients at risk for increased side effects*
      - *Can be even less effiecent in patients with hepatic disease*

Geriatric Considerations

- Adverse Drug Reactions (ADR)
  - *Defined as a symptom, consequence and/or injury that occurs as a result of medication adminstration*
  - *Polypharmacy puts a patient at an increased risk of ADR*
  - *Incidence in geriatrics is double and accounts for 1/3 hospitalizations related to ADR*
  - *Risk of ADR is 10% with one medication and increases with each additoinal medication. The risk of ADR is 100% when 10 or more medications are prescribed*
  - *ADR categories are side effects, hypersensitivity, idiosyncratic response, toxic reactions, and adverse drug interactions*

Phytocannabinoids

- Found in the cannabis plant and some other plants (Echinacea)

Most common phytocannabinoids

- THCA (raw/non-activated)
  - Anti-inflammatory, anti-spasmotic, anti-cancer
- THC (Delta-9)
  - Analgesic, anti-bacterial, anti-cancer, anti-inflammatory, anti-spasmotic, appetite stimulant, bronchodilator, neuroprotectant
- CBDA (raw/non-activated)
  - Anti-cancer, anti-inflammatory

Phytocannabinoids

- CBD
  - Analgesic, anti-anxiety, anti-bacterial, anti-cancer, anti-convulsive, anti-depressant, anti-emetic, anti-inflammatory, anti-insomnia, anti-spasmotic, anti-psychotic, bone stimulant, neuroprotective
- CBN
  - Analgesic, anti-bacterial, anti-convulsive, anti-insomnia, anti-inflammatory
- Currently identified approx. 114 different cannabinoids

Cannabis Pharmacokinetics and pharmacodynamics

- Drug-drug interactions- essential organs lose efficiency
  - *No safety established with CBD and other medications*
    - CBD can either be an inducer or inhibitor of the P450 pathway
  - *CBD is metabolized by the CYP3A4, CYP2C9 and CYP2C19*
    - CBD can either decrease or increase the serum levels of other medications metabolized through these enzymes
      - *CBD can increase warfarin levels*
  - *THC is metabolized by CYP3A4 and CYP2C9*
    - THC levels can be affected by other medications metabolized through these enzymes
      - *THC can increase warfarin levels*
  - *THC is relatively safe*
    - 80-90% is excreted out within 5 days
      - *Sixty-five percent of cannabis is excreted in feces and approx 20% is excreted in urine*

Adverse Drug Reactions with Cannabis

- THC
  - *Increase heart rate*
  - *Increase appetite*
  - *Sleepiness*
  - *Headaches*
  - *Dizziness*
  - *Decreased blood pressure*
  - *Dry mouth, dry eyes*
  - *Constipation*
  - *Decreased urination*
  - *Hallucination*
  - *Paranoia*
  - *Forgetfulness*
  - *Anxiety*

Adverse Drug Reactions with Cannabis

- CBD
  - *Dizziness*
  - *Lightheaded*
  - *Anxiety*
  - *Increased heart rate*
  - *Decreased appetite*
  - *Jitteriness*
  - *Drowsiness*
  - *Diarrhea*
  - *Palpitations*

Dosing and Administration

- Biggest challenge in cannabis administration.
- No set dosing guidelines
- Patients response varies- best to individualize for each patient.
- Start low and go slow
  - *Average dose is between 2.5-10mg*
- Delivery methods
  - *Smoking/Vaporizing*
    - Onset is immediate- within 5-15 minutes; duration 1-3 hours
    - Good for BTP, anxiety, agitation
    - Bioavailability is around 2-56%
      - *Depth of inhalation determines the amount asorbed*

Dosing and Administration

- Delivery methods cont
  - *edibles, teas*
    - Difficult to dose
    - Onset can take 1-3 hours depending on metabolism
    - Duration can last 5 hours or more, especially in an experienced user
    - THC goes through liver (P450) and become 11-Hydroxy THC
      - *Increase in psychoactivity and unwanted side effects*
    - CBD when ingested can either be an inducer or inhibitor of other medications that use the P450 pathway
    - Bioavailability is between 4-20%
  - *tincture, concentrates, sprays*
    - Generally given sublingual
    - Easier to regulate dosage

Dosing and Administration

- Delivery methods cont
  - *Topical*
    - Varies in consistency. Mostly made with THC. Can be applied to painful, itchy areas.
    - CBD absorbs 10x more into the skin than THC
    - Doesn't have systemic side effects
  - *Transdermal*
    - Avoids first pass metabolism
    - Less side effects
    - Quick onset- starts to work within 20 minutes, last up to 12 hours
  - *Rectal*
    - Avoids first pass metabolism- less psychoactivity
    - Suppositories made with coconut oil and cannabis extract
    - Tush push easier to administer
    - Not always well absorbed

Clinical Implications

- Many people are coming to cannabis as a last resort
- Pharmaceutical medications are less effective and/or have undesirable side effects
  - *Many patients want to wean off their pharmaceuticals*
- Less is more
- A thorough intake is important to establish safe dosing practices and assess for potential drug-drug interactions
- Collaboration among HCP's is essential to preventing medication errors and increasing compliance
- Cannabis is not a silver bullet and requires titration as well as self experimenting to be successful and minimize side effects

Clinical Implications

- Insomnia
  - *Cannabis more effective and safer than pharmaceutical sleep aids*
    - Many sleep aids can cause side effects that are harmful to seniors
      - *Diphenhydramine and Zolpidem are not recommended for patients over the age of 65*
    - Small amounts of THC/CBN at night before bed can assist in falling asleep
      - *Average dose to start is 2.5-10mg*
      - *Myrcene is a great terpene for sleep- it increase sleep latency*
    - Edibles or tinctures will last longer than smoking
      - *Some edible products are appropriate for sleep- consistency of dosing is crucial*
      - *2.5-5 mg is often plenty to induce an adequate nights sleep without leading a hangover in the morning.*

Clinical Implication

- Chronic Pain
  - *Cannabis less toxic than opiates and other non-narcotic pain medications*
    - Doesn't cause constipation, although it can exacerbated it
    - No physical dependence
    - Fewer side effects- no one has ever overdosed on cannabis
  - *Cannabis works synergistically with opiates*
    - Patients use less opiates when medicating with cannabis
  - *Treatment depends on type of pain*
    - Nerve pain, especially chemo induced neuropathy- THCa dominant, CBD in high does
    - Muscle pain- THC dominant
    - Bone pain- CBD/THC
    - Inflammatory- THCa/THC

Clinical Implications

- Anxiety and Depression
  - *Often the result of other problems- pain, insomnia, other health issues, fear of aging/dying, PTSD*
  - *Pharmaceuticals only work in 40% of patients*
    - Many come with terrible side effects
    - Can be addicting and nearly impossible to wean off of completely (benzodiazepines)
  - *On average- 90% of the patients I see are also using cannabis for anxiety and/or depression*
    - Females need 30% less THC then males
    - Too much THC and CBD can cause anxiety
      - *Terpenes play a role as well*

Clinical Implications

- Decreased Appetite/Weight Loss
  - *Could be the result of cancer, aging (taste bud changes), pain, or other medications*
  - *Very few pharmaceutical options available*
    - Dranbinol is approved for appetite loss
      - *Synthetic THC- often not as effective as whole plant cannabis*
    - Megestrol is also approved for appetite stimulation
      - *Hormone that can cause females to bleed again*
      - *Also on the BEERS list*
  - *THC most effective for appetite stimulation*
    - Some females find CBD to increase appetite
    - Strains high in THCV can decrease appetite
    - Men tend to get the “munchies” more then women
  - *CBD can suppress appetite*

Clinical Implications

- Dementia/Alzheimer's and other neurological disorders
  - *Alzheimer's/Dementia patients can exhibit aggressive behaviors, wandering and lack of appetite*
  - *Medications to control behavioral issues come with Black Box Warning*
    - Increased risk of death associated with long term use of medication
      - *Seroquel causes weight gain and somolence*
  - *Parkinson's tremors and rigidity often affect ones quality of life.*
    - Carbidopa and Levodopa often becomes less effective over time
    - Stiffness/rigidity responds well to CBD
    - Tremors respond well to THC/THCa

Case Studies

- L.H. 90 year old female with history of MS, advanced dementia and chronic pain
  - *Resides in assisted living community.*
  - *Was close to being moved to memory care unit*
  - *Had been on opioids for 40 years*
  - *Multiple falls, memory loss and aphasia*
  - *Cannabis naive*
  - *Started her on 2.5 mg CBD and 2.5 mg THC twice a day for pain*
  - *Added 5 mg CBD and 5 mg THC at night for sleep*
  - *Weaned off all opioids. Only using cannabis to manage pain and sleep*

Case Studies

- T.B. 73 year old retired Pediatrician with Parkinson's and dementia
  - *Resides in assisted living community*
  - *Aggressive behavior- walked into other residents rooms*
  - *Wife was called every night around 11 pm to help calm T. B. down*
  - *Cannabis naive*
  - *Started on 2.5 mg THC and 2.5 mg CBD capsules 3 times a day*
  - *Wife stopped getting called after 3 days*
  - *Weaned off seroquel*

Case Studies

- M.M. 75 year old female with Parkinson's disease
  - *Main concerns were fatigue and stiffness*
  - *Stopped Carbidopa and Levodopa- no longer effective*
  - *No other medications*
  - *Cannabis naive*
  - *Started her on 10 mg CBD twice a day via tincture*
  - *Energy increased and stiffness improved*
  - *Able to maintain 10 mg twice a day for 10 months*

Case Studies

- R.M. 71 year old male diagnosed with Parkinson's 18 months ago
  - *Flat affect, constant left arm tremor (worse with stress)*
  - *Tried multiple medications without success*
  - *Told next steps was deep brain stimulation surgery*
  - *Cannabis naïve*
  - *Started on 5mg THCa transdermal patch*
    - Tremors decreased by 50%. Increased dose to 10 mg THCa transdermal

Case studies

- 86 yo female with advance COPD
  - *Lives alone*
  - *C/O Shortness of breath, decreased energy/stamina, poor quality of life*
  - *Cannabis naïve*
  - *Started her on 5 mg THC three times a day*
    - After 1 week added 5 mg CBD in conjunction with THC three times a day
  - *Will begin vaporizer next week- CBD dominant as tolerated*

Case Studies

- P.D. 96 year old female with history of insomnia
  - *On Temazepam 15 mg every night for 7 years.*
  - *Wanted to get off pharmaceuticals and try cannabis for sleep*
    - Felt “hung over in the morning” and was experiencing memory recall difficulties
  - *Started her on CBN 5 mg every night. Increase to 10 then 15 mg with inconsistent results. Difficulty falling asleep. Woke up feeling disoriented*
    - Cannabis naïve and lives alone
  - *Ultimately decided to use cannabis first and if did not help her fall asleep, take temazepam.*
  - *Side effects much less with cannabis*

Misconceptions

- CBD and THCa are non psychoactive
- Psychoactivity cannot be controlled
- Vaporizing is harder to control and high dose and will lead to lung cancer
- The stigma is over
  - *Many of my patients are afraid to tell their adult children!!*
- Cannabis is highly addictive and can lead to harsher drugs
- Dosing is not important
- Cannabis is safe (true) and does not pose a risk of interactions with other medications
- Cannabis does not come with side effects

Barriers

- Consistent strains/supply
- Costs- high CBD oil more expensive
  - *Not covered by insurance*
- HCP cannot legally advise patients where to obtain safe medicine.
- Lack of standards
  - *Not all medicine is created equal*
    - Dosages not always clearly defined on labels
    - Many products are made with butane, hexane, isopropol alcohol
    - Lab testing is expensive and not always done. Many places do not test for terpene content, molds, pesticides or bacteria.
- Lack of qualified health care practitioners available to met the demands
  - *Patients are often afraid to tell their other HCP thereby limiting collaboration*
- Traveling outside of the state with medicine is challenging and often prohibited

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