Cannabis in the Elderly: The Blunt Truth

Janna Hardland, MD
Geriatric Fellow
Division of Geriatric Medicine
University of Colorado SOM
Geriatric Medicine Grand Rounds
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Outline

- Brief history of Cannabis
- Current marijuana laws
- Demographics
- Endocannabinoid system
- Pharmacology of Cannabis
- Review of evidence for medical use
- Pharmacokinetics
- Practical tips and tricks
Objectives

- Describe the endocannabinoid system and its role in the pharmacology of Cannabis
- Discuss the current evidence for use of Cannabis in conditions common among older adults
- Apply knowledge of pharmacology and evidence in order to develop practical advice for patients

History of Cannabis

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
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<tbody>
<tr>
<td>???</td>
<td>Origin of Cannabis</td>
</tr>
<tr>
<td>4000 BC</td>
<td>Beginning of use by humans</td>
</tr>
<tr>
<td>2737 BC</td>
<td>First documentation of medicinal use</td>
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<tr>
<td>1839 AD</td>
<td>William O'Shaughnessy discovers therapeutic properties</td>
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<tr>
<td>1854 AD</td>
<td>Cannabis listed in US Dispensatory</td>
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<tr>
<td>1933 AD</td>
<td>Prohibition ends</td>
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History of Cannabis

- 1937: Marihuana Tax Act
- 1942: Removed from US Pharmacopoeia
- 1970: Controlled Substances Act
- 1971: UN Convention on Psychotropic Substances
- 1978: Robert Randall lawsuit
- 1985: dronabinol and nabilone approved by FDA

Current US Cannabis Laws

- Cannabis remains a schedule I drug
- Conflict between federal and state laws
- Federal Law: Illegal to possess, cultivate, sell, or prescribe cannabis
- State Laws:
  - Variable legalization
  - Variable decriminalization
Legalization

Legalized for recreational & medical use
Medical use only

Legalized for recreational & medical use:
Washington
Washington D.C.
Oregon
Alaska
Colorado
California
Massachusetts
Nevada
Maine

Legalization & Decriminalization
Demographic Trends in Cannabis Use

- National Survey on Drug Use and Health, 2006-13:
  - 47,140 respondents aged ≥50 years old
  - ~40% ≥65 years old
  - Past-year cannabis use: ’06/’07 vs ‘12/’13
    - All adults ≥50 years old
      - 2.8% → 4.8% (p <0.001)
      - 71.4% relative increase
    - Adults ≥65 years old
      - 0.4% → 1.4% (p = 0.002)
      - 250% relative increase

Demographic Trends: Medical Marijuana

- Colorado has the largest medical marijuana population
  - 114,713 registered users
  - 29 per 1000 adults
- Nationwide:
  - 441,279 registered users
  - 7.6 per 1000 adults
Demographic Trends: Colorado

- Colorado registry dates back to 2001
- Decline in male dominance of participation
  - 68% → 65%
- 20% of participants ≥61 years old
  - 15.9% 61-70 years old
  - 4.1% ≥71 years old
- Nearly 5,000 users over 70!
Anatomy of Cannabis

Chemical Composition

- Over 460 known chemicals in Cannabis
- More than 100 cannabinoids
  - Δ-9-tetrahydrocannabinol (THC)
  - Cannabidiol (CBD)
  - Many others: 11-OH-Δ-9-THC, Δ-8-THC, CBN, CBL, CBC, CBG
Endocannabinoid System

- Maintains homeostasis
- Modulates neurotransmitter release
  - ACh
  - NE
  - DA
  - 5HT
  - GABA
  - Glutamate
- Prevents excessive neuronal activity
Endocannabinoid System

CB₁ >> CB₂
In central and peripheral nervous system

Endocannabinoid System
Pharmacology of Cannabis

- Partial agonist at CB₁
- Partial agonist at CB₂
- Affinity: CB₁ >> CB₂
- Lower affinity than synthetics
- Low affinity: CB₁, CB₂
- Indirectly modulates CB₁ activity
- 5HT-1A agonist
- TRPV-1 agonist

Acute Effects of THC

- Altered thinking, judgement
- Intensification of sensation
- Increased appetite
- Euphoria
- Altered pain sensitivity
- Impaired coordination
- Slowed reaction time
- Anxiety, paranoia
- Impaired memory
Acute Effects of THC

- Tachycardia
- Postural hypotension
- Possible anticholinergic effects
- Severe psychological effects with overdose
- Psychomotor effects are additive with alcohol, benzodiazepines, opiates
- Withdrawal effects can be seen

Chronic Effects

- Bone Health:
  - May increase bone turnover
  - May reduce bone mineral density
- Reproductive:
  - Reduces testosterone
Chronic Effects

- Respiratory:
  - Symptoms of chronic bronchitis
  - May increase risk of respiratory cancer
  - May impair alveolar macrophages

- Cognitive:
  - Impaired memory
  - Impaired attention
  - Impaired executive function

Qualifying Diagnoses

- Cancer
- Glaucoma
- HIV/AIDS
- Cachexia
- Persistent muscle spasms
- Seizures
- Severe nausea
- Severe pain
- Parkinson’s Disease
- Dementia
Review of Current Evidence

- Antiemetic effects
- Appetite stimulation
- Analgesic effects
- Parkinson’s Disease
- Glaucoma
- Dementia

Bjore Emoji Rating Scale
(patent pending)

Review of Current Evidence

- Antiemetic Effects:
  - >30 studies: synthetic THC, few inhaled marijuana
  - Max age: 82
  - Mixed results:
    - Superior to placebo
    - Superior to phenothiazine antipsychotics
    - Equivalent to metoclopramide
    - Equivalent to haloperidol
    - No evidence of superiority to 5-HT₃ or NK₁ antagonists
Review of Current Evidence

- Anorexia and Cachexia:
  - Few randomized trials
  - Max age: 73
  - Results in advanced cancer & HIV/AIDS
    - May stimulate appetite
    - May stabilize weight
    - Less appetite stimulation than megestrol
    - Less weight gain than megestrol

Review of Current Evidence

- Analgesic Effects:
  - ~30 randomized trials
  - Max age: 70
  - Mixed results:
    - May reduce chronic pain
    - May reduce neuropathic pain
    - No effect on post operative pain
    - One CBD trial with no effect
Review of Current Evidence

• Glaucoma Effects:
  • Max age: 71
  • Reduces Intraocular Pressure
  • Effects on intraocular pressure are short lived
  • Tolerance develops quickly

Review of Current Evidence

• Parkinson’s Disease Effects:
  • Few studies
  • Max age: 78
  • Minimal Effect:
    • No change in Parkinsonian symptoms
    • No change in efficacy of levodopa
    • Minimal effect on levodopa induced dyskinesia
Review of Current Evidence

- Dementia:
  - Qualifying diagnosis in 40% of states with legal medical marijuana
  - 3 randomized trials + case reports
  - Short duration: 3-6 weeks
  - Low doses: 4.5-5 mg daily
  - Mixed results:
    - Possible weight increase
    - Possible improvement in behaviors

Other Considerations

- Of 105 trials including adults ≥65, only FIVE report data separately for older adults
- More adverse effects overall, primarily sedation
Pharmacokinetics

<table>
<thead>
<tr>
<th></th>
<th>Bioavailability</th>
<th>Time to Onset</th>
<th>Time to Max Effect</th>
<th>Duration of Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhaled THC</td>
<td>18-50%</td>
<td>3-5 mins</td>
<td>10-60 mins</td>
<td>2-4+ hrs</td>
</tr>
<tr>
<td>Oral THC</td>
<td>5-20%</td>
<td>30-120 mins</td>
<td>60 mins – 8+ hrs</td>
<td>5 hours - ???</td>
</tr>
<tr>
<td>Buccal THC/CBD</td>
<td>***</td>
<td>15-30 mins</td>
<td>1-3 hours</td>
<td>***</td>
</tr>
<tr>
<td>Oral CBD</td>
<td>13-19%</td>
<td>***</td>
<td>***</td>
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</tr>
</tbody>
</table>

Pharmacokinetic Considerations

- Extensive 1st pass metabolism
- Potential for drug interactions
  - CYP2C9
  - CYP3A4
- Highly lipophilic
- Possible accumulation with repeated dosage
Practical Tips

- **C. indica vs C. sativa?**
  - Depends:
    - Indica = sedating, “body high”
    - Sativa = “invigorating”
    - Look for high CBD strains of either
- **THC content?**
  - Lower is better
- **THC vs CBD?**
  - Try CBD first

Practical Tips

- **Route of administration:**
  - Oral:
    - Be patient!
  - Inhaled:
    - Worse than cigarettes
    - Easier to titrate
  - Vaporized:
    - Less toxins than smoking
  - Sublingual:
    - May be a good pharmacokinetic compromise
  - Topical:
    - We really don’t know
Practical Tips

• Concerning adverse effects:
  • Tachycardia
  • Postural hypotension
  • Anticholinergic effects
  • Psychoactive effects
  • Potential for drug interactions

• No one is counseling our patients if we don’t do it

Future Directions

• Additional studies in older adults, particularly for pain and dementia
• Data on pharmacokinetics in older adults, particularly topical, sublingual, and other novel methods
• Studies on use of CBD for pain, dementia with behaviors, psychosis with Parkinson’s disease
• Coming soon to a grand rounds near you!
  Data on marijuana use in Seniors Clinic presented by Dr. Ian Reynolds
References


References

- Medicines.org.uk/emc
References

- www.colorado.gov
- Sativex Product Monograph

References
