Therapeutic Effectiveness... What Does the Evidence Say?

1. Explain the limitations of available evidence on the safety and effectiveness of cannabis for therapeutic purposes
2. List the disease states/conditions for which cannabis or cannabinoids may provide benefit
3. Recommend reliable evidence sources for health care providers
Is Cannabis Effective for Treating Medical Conditions?

Navigating The Evidence So Far...
• Challenged by bias and lack of high-level research
• Paucity of robust evidence investigating the use of cannabis and/or cannabinoids for therapeutic purposes
• Prescription cannabinoids have received most focus, rather than plant-based cannabis
• Key evidence on efficacy includes:
  – RCTs, systematic reviews and meta-analyses
  – Clinical practice guidelines
  – Curated and peer-reviewed summaries of best available evidence

Even best-available evidence still has limitations.
• Short duration of studies
• Lack of standardized measures (for pain)
• Blinding/placebo control challenges
• Use of cannabinoids as third or fourth line adjunctive, not as a replacement
• Studies have used different cannabis (strains, extracts, different prescription cannabinoids) making study comparisons challenging
"Indications"

Recommendations and guidelines based on best-available evidence do not always align. There are four conditions/symptoms where current best available evidence suggests, overall, the use of cannabis and/or cannabinoid medications may be effective in situations where potential benefits outweigh the risks:

• Improving patient-reported multiple sclerosis spasticity symptoms
• As antiemetics in the treatment of chemotherapy-induced nausea and vomiting
• Treatment of chronic neuropathic pain in adults
• Treatment of Pediatric seizure disorders (Dravet syndrome, Lennox-Gastaut syndrome)

Effect of cannabis/cannabinoids on MS symptoms:

<table>
<thead>
<tr>
<th>Study</th>
<th>Type</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allen et al. Can Fam Physician 2018</td>
<td>Systematic review of systemic reviews</td>
<td>“Reasonable evidence” of improvement; Consider use only after trials of other therapies; nabiximols&gt;nabilone; recommend against medical cannabis</td>
</tr>
<tr>
<td>Whiting et al. JAMA 2015</td>
<td>Systematic review and meta-analysis</td>
<td>“Moderate quality evidence” to support use</td>
</tr>
<tr>
<td>Koppel et al. Neurology 2014</td>
<td>Systematic review</td>
<td>“Probably effective”</td>
</tr>
</tbody>
</table>

### Effect of cannabis/cannabinoids on CINV:

<table>
<thead>
<tr>
<th>Study</th>
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<td>Systematic review of systemic reviews</td>
<td>“Reasonable evidence” of improvement Consider use only after trials of other therapies; use medical cannabinoids as adjuncts; recommend nabilone; recommend against nabiximols and medical cannabis</td>
</tr>
<tr>
<td>Whiting et al. JAMA 2015</td>
<td>Systematic review and meta-analysis</td>
<td>“Low quality evidence” associated with improvement</td>
</tr>
<tr>
<td>Smith et al. Cochrane Database of Systematic Reviews 2015</td>
<td>Systematic review</td>
<td>“May be useful!”</td>
</tr>
</tbody>
</table>

### Effect of cannabis/cannabinoids on pain:

<table>
<thead>
<tr>
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<th>Conclusion</th>
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</thead>
<tbody>
<tr>
<td>Stockings et al..Pain.2018</td>
<td>Systematic review and meta-analysis</td>
<td>“unlikely” that cannabinoids are highly effective in non-cancer pain (with exception of MS pain)</td>
</tr>
<tr>
<td>Allen et al. Can Fam Physician 2018</td>
<td>Systematic review of systematic reviews &amp; Guideline for prescribing medical cannabinoids in primary care</td>
<td>“uncertainty” re effectiveness; neuropathic pain only, small benefit; Use after other trials, more evidence for nabiximols, recommend against medical cannabis</td>
</tr>
<tr>
<td>Mucke et al. Cochrane Database of Systematic Reviews (2018)</td>
<td>Systematic review: Cannabis-based medicines for chronic neuropathic pain in adults</td>
<td>Poor quality evidence (limitations); harms might outweigh benefits</td>
</tr>
<tr>
<td>Meng et al. Anesthesia and Analgesia (2017)</td>
<td>Systematic review and meta analysis</td>
<td>Cannabinoids superior to placebo (6/11 trials); suggestive evidence nabiximols&gt;nabilone</td>
</tr>
<tr>
<td>Whiting et al. JAMA 2015</td>
<td>Systematic review and meta-analysis</td>
<td>“Low quality evidence” associated with improvement</td>
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</table>
Effect of cannabis/cannabinoids on pediatric seizure disorders:

Only one systematic review has been published, although individual studies within the review suggest promising effects on children.

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</tr>
</thead>
<tbody>
<tr>
<td>Stockings et al. Journal of Neurology, Neurosurgery &amp; Psychiatry 2018</td>
<td>Systematic review (epilepsy)</td>
<td>Qualitative evidence that cannabinoids reduced seizure frequency; RCTs in children and adolescents</td>
</tr>
</tbody>
</table>

Possible Clinical Uses for Cannabis

- Appetite stimulant (HIV/AIDS, cancer)
- Irritable Bowel Syndrome (IBS), Inflammatory Bowel Disease (IBD), Crohn’s Disease
- Motor disorders (Parkinson’s Disease, Huntington’s Disease, Tourette’s Syndrome, Dystonia)
- Post-Traumatic Stress Disorder (PTSD), Anxiety, Depression
- Sleep Disturbances
- Glaucoma
- Pain associated with rheumatic conditions: e.g., fibromyalgia, rheumatoid arthritis
- Amyotrophic Lateral Sclerosis
- Cancer, including glioma
- Anorexia Nervosa
- Dementia
- ...and much more
Cannabis and Opioid Sparing Effects?

- Some retrospective observational trials w/ patient self-reported surveys show ↓ in opioid use or substituting cannabis for opioids:
  - 25% reduction in opioid OD death based on ICD codes reported in US states with legalization of medical cannabis
  - VA Canada – veterans with opioid prescriptions ↓ in 2017-2018 vs. 2012-2013 while number of veterans with authorization for cannabis ↑ in 2017-2018 vs. 2012-2013
  - Reduction in opioid prescribing in US states with legalized medical cannabis


Cannabis and Opioid Sparing Effects?

- General association still unclear
- Cannot determine causation or assess impact of other variables
- Most data based on survey, epidemiology or population level data

Other Canadian Evidence Resources for Clinicians

Use With Caution

Clinicians are encouraged to avoid drawing conclusions on the effectiveness of cannabis as a medical treatment from research or other information provided by:

• Licensed cannabis providers or retailers
• News publications
• Cannabis medical clinics
• Cannabis advocacy groups
• Any other organizations with a commercial interest in cannabis use
References


References

References

• Information for Health Care Professionals; Cannabis (marihuana, marijuana) and the cannabinoids, Health Canada October 2018 https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/information-medical-practitioners/information-health-care-professionals-cannabinoids.html


• RxTx [Internet]. Ottawa (ON): Canadian Pharmacists Association; c2018. CPS online: Cannabis; [cited 2019 July 2019]. Available from: www.myrxtx.ca


Please proceed to the next module:
Pharmacokinetics and Routes of Administration:
Considerations for Dosing and Titrating