Harms of Medical Cannabinoids: Up in Smoke!

Clinical Question: What are the harms associated with medical cannabinoid therapy?

Bottom Line: Compared to placebo, medical cannabinoids cause multiple different adverse events in patients, from visual disturbance or hypotension (1 in 3-10) to hallucination or paranoia (1 in 20). Stopping due to adverse effects occurs in 1 in every 8-20 patients. Regardless of the type of medical cannabinoid used, adverse events are common and likely underestimated. Given the extensive harms, potential benefits must be impressive to warrant a trial of therapy.

Evidence:
Eleven systematic reviews with meta-analyses of harm (in general or in treatment of pain/spasticity/nausea and vomiting). Statistically significant unless otherwise noted.

- Total adverse events: Four meta-analyses with 3-29 Randomized Controlled Trials (RCTs), 666-3,714 patients.\(^1\)-\(^5\)
  - Range\(^1\)-\(^3\) from relative risk 1.18 to odds ratio (OR) 3.03.
  - Percent of patients:\(^4,5\) 79-92% cannabinoid versus 56-78% placebo.
    - Number Needed to Harm (NNH)=5-8.
- Serious adverse events: Three meta-analyses with 11-34 RCTs, 1,568-3,248 patients.\(^1,2,6\)
  - Two non-statistically significant.\(^1,2\)
  - Other OR 1.41 (1.04-1.92), absolute numbers not provided.\(^6\)
- Stopped due to adverse events: Seven meta-analyses (2-24 RCTs), 276-2,755 patients.\(^2,5-10\)
  - Range from\(^2,7,8\) OR 2.94 to Risk Ratio 6.85.
  - Actual events:\(^5-9\) 7-14% cannabinoid versus 1-5% placebo, NNH=8-22.
  - One of the seven meta-analyses was not statistically significant.\(^10\)
- Specific adverse events versus placebo:
  - Predictable effects: Sedation\(^8\) NNH=5, feeling high\(^7,8\) NNH=2-4, euphoria\(^7,8\) NNH=9.
Common: Visual blurring/hallucination \( ^{11} \) NNH=3, dizziness \( ^{2,5,8,11} \) NNH=5, speech disorders \( ^{11} \) NNH=5, ataxia/muscle twitching \( ^{11} \) NNH=6, disconnected thought \( ^{11} \) NNH=7, dysphoria \( ^{8} \) NNH=8, hypotension \( ^{8} \) NNH=8, impaired memory \( ^{11} \) NNH=12, disorientation \( ^{11} \) NNH=15.

- Nausea (OR 2.1) and vomiting (OR 1.7) increased, NNH unavailable.\(^2\)

Other: Hallucination \( ^{8} \) NNH=17, paranoia \( ^{8} \) NNH=20.

Versus other agents like prochlorperazine, cannabinoids also increased adverse events: Examples sedation (NNH=7) and dizziness (NNH=3).

Adverse events rates varied little between different cannabinoid products (example nabiximol, nabilone, dronabinol, inhaled marijuana, etc.):\(^2\) NNH=4-7.

Context:

- See Tools for Practice #199 and #201 for potential benefits.
- Many studies enrolled patients with a history of medical or recreational cannabinoid use.\(^{11,12}\) Regular users will:
  - Be more tolerant of cannabinoids and less likely to report adverse events.
  - Recognize if randomized to cannabinoids or placebo (up to 89% of the time).\(^{12}\)

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References:


Tools for Practice is a biweekly article summarizing medical evidence with a focus on topical issues and practice modifying information. It is coordinated by G. Michael Allan, MD, CCFP and the content is written by practising family physicians who are joined occasionally by a health professional from another medical specialty or health discipline. Each article is peer-reviewed, ensuring it maintains a high standard of quality, accuracy, and academic integrity. If you are not a member of the ACFP and would like to receive the TFP emails, please sign up for the distribution list at http://bit.ly/signupfortfps. Archived articles are available on the ACFP website.

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