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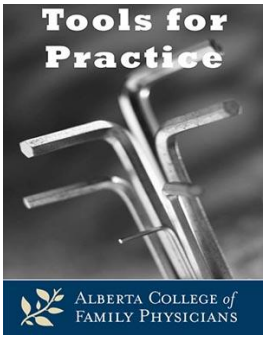

Harms of Medical Cannabinoids: Up in Smoke!

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:[7] Example 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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