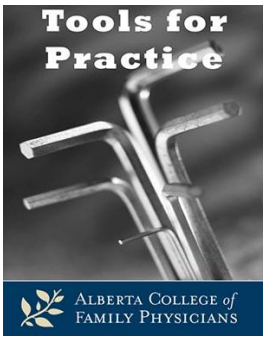
Tools for Practice is proudly sponsored by the Alberta College of Family Physicians (ACFP). ACFP is a provincial, professional voluntary organization, representing more than 4,600 family physicians, family medicine residents, and medical students in Alberta. Established over sixty years ago, the ACFP strives for excellence in family practice through advocacy, continuing medical education and primary care research. www.acfp.ca

December 11, 2017



Any Other "Doobie"ous Effects of Medical Cannabinoids?

Clinical Question: Besides pain, are medical cannabinoids effective for other conditions?

Bottom Line: For most conditions (example anxiety), cannabinoid evidence is sparse (at best), low quality and non-convincing. Dronabinol/nabilone improve control of nausea/vomiting post-chemotherapy for 1 in 3 users over placebo. Nabiximols likely improve multiple sclerosis spasticity ≥30% for ~1 in 10 users over placebo. Patients' preference for cannabinoids exceeds cannabinoids effectiveness.

Evidence:

- Two comprehensive systematic reviews (SR) suggest reasonable evidence for nausea/vomiting (from chemotherapy) and spasticity.[1,2] In other conditions, high-level evidence is too sparse, low quality and/or negative. Examples:
  - Glaucoma: One Randomized Controlled Trial (RCT) (6 patients): No benefit.[1,2]
  - Anxiety: One RCT (24 patients) on simulated public speaking: More improvement on mood scale.[2]
- Nausea/vomiting (mostly dronabinol/nabilone 1-day post-chemotherapy): Seven SRs of 5-30 RCTs (635-1,772 patients).[1,3-8] Statistically significant unless indicated.
  - Meta-analyses for control of nausea/vomiting.[1,5,7]
    - Versus placebo:[3] 47% versus 13%, Number Needed to Treat (NNT)=3.
    - Versus neuroleptic:[3] 31% versus 16%, NNT=7.
    - Others find similar.[1,5,7]
  - Patient preference exceeds effectiveness: NNT=2 versus placebo and NNT=3 versus neuroleptic.[6,8]
    - Suggests something other than effectiveness influences preference.
  - Not chemotherapy-related:
    - Palliative care (cancer/HIV): One SR, symptoms unchanged.[6]
    - Post-Op: One RCT (60 patients), nabilone versus metoclopramide: No difference.[9]
  - No clear difference between nabilone or dronabinol.[5,7]

- Spasticity (mostly nabiximol, ~70 days, multiple sclerosis): Five SRs of 3-17 RCTs (481-2,280 patients), versus placebo.[1,10-13]
  - Meta-analysis of meaningful change in symptoms:[3] 50% versus 35%, NNT=7.
    - Others find similar.[1,10]
  - ≥30% improvement in spasticity:[10] 35% versus 25%, NNT=10.
  - Four meta-analyses of mean change in scale:
    - Two meta-analyses:[1,10] 1.3 versus 0.97 placebo (clinical significance ~1.1).[10]
    - Two meta-analyses: Not statistically significant.[1,13]

Context:

- Issues:
  - Quality often poor.[1]
  - Many studies small/short.[1,8]
  - Blinding not possible: Example, 85-95% of patients and clinicians know who's on cannabinoids.[8,14]
- Approved indication:
  - Nabilone (Cesamet™): Chemotherapy-induced nausea/vomiting.
  - Nabiximol (Sativex™): Adjunctive therapy for spasticity of multiple sclerosis and pain from multiple sclerosis or cancer.
- For pain[15] and adverse events[16] see Tools for Practice #199 and #200.
- Although evidence for seizure is sparse, one RCT suggests potential in children with Dravet epilepsy.[17]

Authors:
G. Michael Allan MD CCFP, Jamil Ramji BSc BSP ACPR, Danielle Perry BScN MSc Candidate

Disclosure:
Authors do not have any conflicts of interest to declare.

References:

1. Whiting PF, Wolff RF, Deshpande S, *et al*. JAMA. 2015; 313(24):2456-73.
2. National Academies of Sciences, Engineering, and Medicine. 2017. The health effects of cannabis and cannabinoids: The current state of evidence and recommendations for research. Washington, DC: The National Academies Press. doi: 10.17226/24625. 2017. Available at: https://www.nap.edu/catalog/24625/the-health-effects-of-cannabis-and-cannabinoids-the-current-state. Last Accessed: September 4, 2017.
3. Allan GM, Finley CR, Ton J, *et al*. Can Fam Physician, 2018, in press.
4. Cotter J. Oncol Nurs Forum. 2009; 36(3):345-52.
5. Machado Rocha FC, Stefano SC, *et al*. Eur J Cancer Care. 2008; 17(5):431-43.
6. Mucke M, Carter C, Cuhls H, *et al*. Der Schmerz. 2016; 30(1):25-36.
7. Smith LA, Azariah F, Lavender VT, *et al*. Cochrane Database Syst Rev. 2015;11:CD009464.
8. Tramer MR, Carroll D, Campbell FA, *et al*. BMJ. 2001; 323(7303):16-21.
9. Canadian Agency for Drugs and Technologies in Health. Nabilone for Non-chemotherapy Associated Nausea and Weight Loss due to Medical Conditions. Ottawa, ON: CADTH, 2014. Available at: https://cadth.ca/sites/default/files/pdf/htis/2017/RC0905%20Nabilone%20for%20Non-Chemotherapy%20Nausea%20and%20Weight%20Loss%20Final.pdf. Last Accessed: September 4, 2017.
10. Wade DT, Collin C, Stott C, *et al*. Mult Scler. 2010; 16(6):707-14.
11. Koppel BS, Brust JC, Fife T, *et al*. Neurology. 2014; 82(17):1556-63.

12. Lakhan SE, Rowland M. BMC Neurol. 2009; 9:59.
13. Meza R, Pena J, Garcia K, *et al*. Medwave. 2017; 17(Suppl1):e6865.
14. Canadian Agency for Drugs and Technologies in Health (CADTH). Cannabinoids for the management of neuropathic pain: Review of clinical effectiveness. Ottawa, ON: Canadian Agency for Drugs and Technologies in Health; 2010. (CADTH 2010b)
15. Allan GM, Finley CR, Hauptman R, et al. Tools for Practice. Available at: https://www.acfp.ca/wp-content/uploads/tools-for-practice/1510681044_tfp199mmandpainfv.pdf. Last accessed: December 8, 2017.
16. Allan GM, Ton J. Tools for Practice. Available at: https://www.acfp.ca/wp-content/uploads/tools-for-practice/1511480622_tfp200harmsmmfv.pdf. Last accessed: December 8, 2017.
17. Devinsky O, Cross JH, Laux L, *et al*. N Engl J Med. 2017 May 25; 376(21):2011-20.

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.