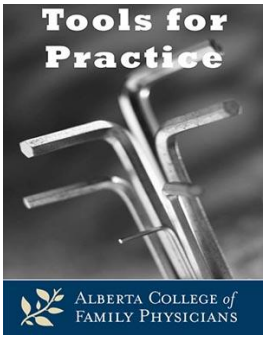
Tools for Practice is proudly sponsored by the Alberta College of Family Physicians (ACFP). ACFP is a provincial, professional voluntary organization, representing more than 4,800 family physicians, family medicine residents, and medical students in Alberta. Established over sixty years ago, the ACFP strives for excellence in family practice through advocacy, continuing medical education and primary care research. www.acfp.ca

June 18, 2018



Nerve-ous About Opioids? Treatment of neuropathic pain with opioids

Clinical Question: What are the risks and benefits of opioids for neuropathic pain?

Bottom Line: Compared to placebo, high-dose opioids moderately (at least 30%) reduce pain for an additional 1 in every 5-8 people over 4-12 weeks. Opioid-related adverse events lead to discontinuation for 1 in every 11-12 people over placebo. Other medications (like tricyclic antidepressants, gabapentin/pregabalin, and duloxetine) are similarly effective with less adverse events. Opioids should only be considered in patients with refractory pain after multiple therapeutic trials.

Evidence:

- Four systematic reviews of 5-31 Randomized Control Trials (RCTs) with 236-1,769 patients followed for 4-12 weeks. Mean age ~60, all versus placebo, in diabetic neuropathy, phantom limb pain, or post-herpetic neuralgia. Morphine equivalent dosing ranged from 7.5 mg/day to 180-240 mg/day.[1-5]
  - Pain control:
    - Moderate pain relief (at least 30% improvement) or much/very much improved on a Patient Global Impression of Change scale:[1,2]
      - Morphine: 63% versus 36%, Number Needed to Treat (NNT)=4.
      - Oxycodone as monotherapy and/or add-on: 44% versus 27%, NNT=6.
        - Monotherapy NNT=5 or add-on NNT=8.
    - At least 33% improvement (morphine and oxycodone):[3,4]
      - 57% versus 34%, NNT=5.
      - Meta-analysis by Tools for Practice authors (five RCTs, 429 patients): Reduce pain 1.2 points more than placebo on 10-point scale.
  - Function:
    - General activity, normal work activities, social relations, sleep, and life enjoyment: Unclear clinical benefit.[3]
      - Example: Outcomes improved between ~0.7 to ~1.7 points out of 10 with morphine or oxycodone versus placebo.
    - Mood and walking measures: No benefit.

- Adverse Events:
  - Morphine, oxycodone, and methadone versus placebo:
    - Withdrawal due to adverse events: [3,4] Number Needed to Harm (NNH)=11-12.
    - Constipation (NNH=4-5),[2,3] dizziness (NNH=8),[2,3] drowsiness/somnolence (NNH=6-7),[2,3] nausea (NNH=6),[2,3] vomiting (NNH=12).[3]
- Limitations: Concomitant pain treatment unclear, RCTs had small sample sizes and short duration of studies.

Context:

- Guidelines suggest serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants, or gabapentin/pregabalin as first-line agents for neuropathic pain.[6,7]
  - Generally, work as well (similar NNT) as high-dose opioids.[8]
  - Opioids inconsistently recommended: From not starting in primary care without specialist advice[6] to second-line therapy.[7]
- Between 2006-2008, 58% of drug-related deaths in Ontario were opioid-related.[9]

Authors:
Joey Ton BScPharm PharmD, Danielle Perry BScN MSc Candidate, G. Michael Allan MD CCFP

Disclosure:
Authors do not have any conflicts of interest to declare. (Authors JT and DP are supported by the Physician Learning Program.)

References:

1. Cooper TE, Chen J, Wiffen PJ, *et al*. Cochrane Database Syst Rev. 2017; 5:CD011669.
2. Gaskell H, Derry S, Stannard C, *et al*. Cochrane Database Syst Rev. 2016; 7:CD010692.
3. McNicol ED, Midari A, Eisenberg E. Cochrane Database Syst Rev. 2013; 8:CD006146.
4. Sommer C, Welsch P, Klose P, *et al*. Schmerz. 2015; 1:35-46.
5. Busse JW, Craigie S, Juurlink DN, *et al*. CMAJ. 2017; 189(18):E659-E666.
6. National Institute for Health and Care Excellence. NICE Guideline (CG96). Available from: https://www.nice.org.uk/guidance/cg173/evidence/neuropathic-pain-pharmacological-management-full-guideline-191621341. Last Accessed: March 6, 2018.
7. Moulin D, Boulanger A, Clark AJ, *et al*. Pain Res Manag. 2014; 6:328-35.
8. C-TOP Tool. Available at: www.pain-calculator.com. Last Accessed: March 28, 2018.
9. Madadi P, Hildebrandt D, Lauwers A, *et al*. PLoS One. 2013; 8(4):e60600.

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.