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
    - Morphone: 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 advice⁶ to second-line therapy.⁷
  - Between 2006-2008, 58% of drug-related deaths in Ontario were opioid-related.⁹

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References: