Burning Issues and Aching Questions: Tramadol for osteoarthritic and neuropathic pain

Clinical question: Is tramadol effective for neuropathic or osteoarthritic pain?

Bottom Line: Compared to placebo, tramadol reduces neuropathic and osteoarthritic pain by ≥50% for one in five people with one in 8-12 stopping for adverse effects. Although comparisons are limited, pain control with tramadol appears to be similar to gabapentin (neuropathic pain) and maybe similar or better than opioids or diclofenac (osteoarthritis).

Evidence:

- For neuropathic pain:
  - Tramadol alone: Two systematic reviews [6-7 Randomized Controlled Trials (RCTs)]:1,2
    - ≥50% pain reduction: 46% tramadol, 27% placebo, Number Needed to Treat (NNT)=5 over 4-9 weeks.1
      - Other found NNT=4 at ~6 weeks.2
    - Adverse effects causing withdrawal:1,2 Number Needed to Harm (NNH)=8-12.
  - Tramadol with acetaminophen:
    - RCT (313 diabetic neuropathy patients) versus placebo:3
      - Achieved 30% pain reduction: NNT=6.
    - Open-label RCT (163 diabetic neuropathy patients): No difference in pain intensity versus gabapentin.4
      - Tramadol increased nausea/vomiting, NNH=12.
  - Issues: Possible publication bias,1 high loss to follow-up,2,4 some studies too flawed for meaningful interpretation,2 underpowered.4

- For osteoarthritis:
  - Systematic review (11 RCTs),5,6 targeting ≥50% pain reduction at ~35 days:
    - Versus placebo (four RCTs):
      - 71% versus 51%, NNT=5.
      - More stopping due to adverse effects, NNH=8.
    - Versus other opioids or diclofenac (three RCTs):
      - 63% versus 47%, NNT=7.
• Adverse effects causing withdrawal higher with tramadol in two of three comparisons (including diclofenac).
  ▪ Limitations: Systematic review author employed by manufacturer, most studies manufacturer sponsored, randomization process often not described.
    o Two small RCTs tramadol versus diclofenac: No efficacy difference.\textsuperscript{7,8} Adverse effects higher with tramadol.

**Context:**
- Systematic review of neuropathic pain found NNT and NNH similar for most drugs versus placebo.\textsuperscript{1}
- Osteoarthritis response with opioids: NNT=10, with NNH to stop drug due to adverse effects=21.\textsuperscript{9}
- Underpowered and potentially biased study found tramadol had similar rates of “abuse” with NSAIDs, and lower rates than hydrocodone.\textsuperscript{10}
  o Reports of abuse and deaths from tramadol are increasing.\textsuperscript{11,12}
- Cohort data suggests seizures are rare (<1%), but more likely in those predisposed.\textsuperscript{13-15}
- Tramadol delayed release costs \(~\$75\)/month (200mg daily). Tramacet (two tabs QID) costs \(~\$185\)/month.\textsuperscript{16}
  o Not covered in many jurisdictions due to insufficient evidence of superiority over less expensive agents.\textsuperscript{17}

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**References:**

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