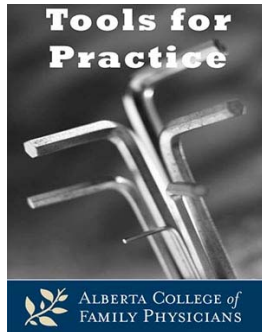


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April 27, 2010



Gabapentin & Chronic Pain: Missing Evidence and Real Effect?

Clinical Question:

What is the evidence to support gabapentin (or pregabalin) in chronic peripheral neuropathic pain?

Evidence:

A review showing gabapentin published research was incomplete or modified and new analysis of gabapentin in chronic pain including unpublished data.

- Review of 20 Randomized Controlled Trials (RCTs) of Gabapentin for off-label use (primarily 17/20 for pain)¹
 - 8 were never published (40%)
 - Reporting of outcomes in 12 published studies
 - Only 4 used the planned primary outcome
 - Of 180 predefined secondary, 122 (68%) not reported
- Meta-Analysis of all trials (including unpublished)²
 - Moderate-marked improvement in pain occurs in 13-17.5% more patients than placebo
 - Number Needed to Treat (NNT) = 6-8 (2 weeks)
 - Efficacy greatest in post-herpetic neuralgia
 - No benefit for acute pain or in dose escalation beyond 900mg (but more adverse events)
 - Adverse events: NNH 8 (dizziness, somnolence, confusion, etc.)

Context:

- Cochrane review³ (published studies only) reported gabapentin gave effective pain relief in chronic pain, NNT 3-4
 - Another review⁴ found similar numbers that worsened with adding unpublished trials.²
- Pregabalin best case: Effective peripheral chronic pain relief is NNT 4-5 but this only includes published data.⁵
 - Common Drug Review⁶ (including unpublished trials) reported pregabalin was intermittently better than placebo but not consistently efficacious.
 - No direct clinical trial evidence for superiority over gabapentin.

- One trial had an active comparator: Pregabalin not superior to placebo but tricyclic antidepressants were.
- Other reviews suggest tricyclic antidepressants are similar⁷ or perhaps superior^{7,8} to gabapentin or pregabalin. This evidence may be biased by time and trial quality⁷
- While publication bias and selective reporting likely occur more in industry funded research, non-profit funded RCTs also selectively report outcomes.⁹

Bottom-line: The apparent benefit of gabapentin in chronic pain was exaggerated by publication and reporting biases. In carefully selected patients with peripheral neuropathic pain, gabapentin may offer moderate or more pain relief for 1 in every 6-8 patients but causes adverse events in a similar number. There is no trial evidence pregabalin is superior to gabapentin.

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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. Archived articles are available on the Toward Optimized Practice and ACFP websites.

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