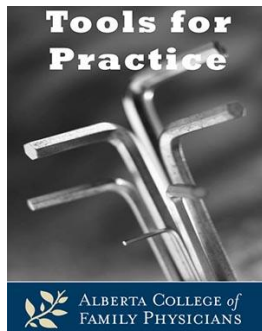


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July 16, 2018



Anxiously Awaiting Evidence: Pregabalin in generalized anxiety disorder

Clinical Question: Is pregabalin effective for generalized anxiety disorder (GAD)?

Bottom Line: Evidence for pregabalin in GAD is inconsistent and at high-risk of bias (industry-written, short-term, poorly described methods, high drop-outs, and run-in periods that overinflate benefit). If real, an additional one in 6-8 people may respond to pregabalin compared to placebo at 4-8 weeks. However, the change in anxiety scales was not clinically meaningfully different than placebo for the average patient.

Evidence:

- All Randomized Controlled Trials (RCTs) written by industry.
- One systematic review, four RCTs:¹
 - Versus placebo (one RCT, n=271):
 - Response: 59% versus 44% placebo, not statistically different.
 - Changes in anxiety scale: ~3-4 points out of 56, not always statistically significant, likely not clinically meaningful.
 - Versus benzodiazepines:
 - Response (one RCT, n=454): 300 mg statistically better than alprazolam (61% versus 43%) but higher doses no difference.^{1,2}
 - Change in anxiety scale (one RCT, n=271): No difference.
 - Overall adverse effects: 67% placebo, 73% pregabalin 50 mg, 89% pregabalin 200 mg, 91% lorazepam.¹
- Four other RCTs (273-374 patients each):
 - Change in anxiety scale: ~3 points out of 56. Statistically different, not clinically meaningful.³⁻⁶
 - Response rates 50-60% versus 27-46% placebo. Statistically different in ¾ studies.^{3,5,6} Number Needed to Treat (NNT)=6-8.
 - Trend to higher response rates with lorazepam (61% versus 46%).⁶
- Other systematic reviews provided standard mean differences (clinically uninterpretable).^{7,8}
- RCT versus sertraline:⁹ No difference anxiety scale or adverse effects.

- As adjunct: RCT of 356 patients.¹⁰
 - If inadequate response to antidepressant, randomized to pregabalin 150-600 mg/day or placebo. At eight weeks:
 - Mean change in anxiety scale: 1.2 (statistically, but not clinically different).
 - Response (anxiety scale): 48% versus 35%, NNT=8.
 - Response (global improvement scale) or remission: No difference.
 - Stopped due to adverse effects: 4% versus 2%, Number Needed to Harm=47.
- Limitations: <80% completed study;³⁻⁶ short-term (4-8 weeks);¹⁻⁶ selective reporting;⁶ quality markers inadequately described;³⁻⁶ run-in which can overinflate benefit.^{2,4-6}

Context:

- Several studies show lower anxiety scores within one week, but usually not a clinically meaningful difference.^{3,4,6}
- Weight gain at one year (all indications): 17% gained >7% of their body weight and mean gain=2.2kg.¹¹
- Canadian guidelines recommend pregabalin or antidepressants first-line or as adjunct.¹²

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Disclosures:

Authors do not have any conflicts of interest to declare.

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