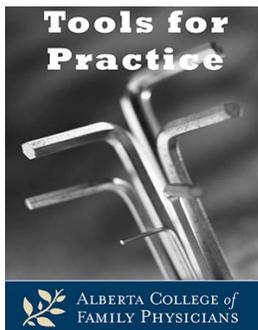


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**Reviewed: April 30, 2015**  
**Evidence Updated: Meta-analysis**  
**Bottom Line: No change**  
**First Published: September 6, 2011**



## **Antidepressants for preventing headaches: Which work and how well?**

**Clinical Question: In the prevention or prophylaxis of headaches (including migraines), which antidepressants work and how effective are they?**

**Bottom-line: Daily tricyclic antidepressants, particularly amitriptyline, effectively reduce headache severity and frequency (for 1 in 8 over placebo). They are effective regardless of headache type and the benefit improves with time.**

### **Evidence:**

- Two systematic reviews and meta-analyses provide the best evidence:
  - Tricyclic antidepressants (TCA):<sup>1</sup> 37 trials (17 tension, 13 migraine, rest mixed); 3,176 patients, mean age 40, 73% female.
    - Versus Placebo, daily TCA resulted in statistically significant:
      - Reduced “burden of headache” (standard mean difference -0.96, -1.39 to -0.53).
      - More patients experienced 50% reduction in headaches: 38.4% versus 24.9%, Number Needed to Treat (NNT)=8.
      - Both migraine and tension type benefited.
      - Benefit improved with time.
      - Higher adverse events with TCA (NNT to harm=5) but no difference in withdrawal.
    - Versus Selective Serotonin Re-uptake Inhibitor (SSRI): TCA’s were superior.
    - Versus other agents: Limited data but direct comparisons suggest no efficacy difference between TCA and topiramate (two trials) or beta-blockers (three trials).
  - No evidence to support the use of SSRI or SNRI antidepressants for migraine prophylaxis:<sup>2</sup> 11 trials, 585 patients.

### **Context:**

- A review of all medications for migraine prophylaxis places amitriptyline (with propranolol and nadolol) as first line agents.<sup>3</sup>

- Dual benefits with amitriptyline can be achieved when patients have co-morbid depression and/or early insomnia.<sup>3</sup>
- Blood pressure medicines for headache prophylaxis are covered in the next Tools for Practice (#52).
- Majority of TCA trials used amitriptyline (30 of 37 trials) at doses of 10-150 mg, mean 80 mg)<sup>1</sup>
  - Slow titration can maximize benefit while limiting adverse events.
- Beta-Blockers, some anticonvulsants and some blood pressure medications (other than just beta-blockers) have also been shown to be effective for migraine prevention.<sup>4-6</sup>
  - For example, NNT is 4-7 for topiramate producing 50% reduction in migraine frequency.<sup>4</sup>

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