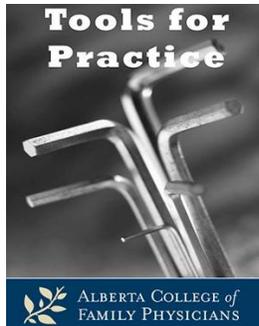


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Pain getting on your nerves? Tricyclic antidepressants for neuropathic pain

Clinical Question: What are the benefits and harms of using tricyclic antidepressants (TCAs) for neuropathic pain?

Bottom Line: Compared to placebo, TCAs may provide a 30% reduction in pain for an additional 1 in 4-6 people with neuropathic pain, with 1 in 5 experiencing an adverse event and 1 in 11 stopping medication because of side effects. Overall, evidence is limited by inconsistent outcome reporting in small studies of short duration.

Evidence:

- Systematic review of 10 Randomized Control Trials (RCTs) of amitriptyline involving 588 patients with predominantly diabetic neuropathy (DN) or post herpetic neuralgia (PHN), followed 3-52 weeks:¹
 - At least moderate (30%) pain relief: 64% versus 32%, Number Needed to Treat (NNT)=4.
 - Desipramine and imipramine similar.
- Systematic Review (four amitriptyline RCTs, 384 patients with DN, PHN, mixed neuropathy, followed 4-9 weeks):²
 - Inconsistently defined pain relief (examples $\geq 50\%$ pain reduction or patient-reported moderate pain relief): 39% versus 20%, NNT=6.
 - At least one adverse effect (six RCTs, 519 patients):
 - 55% versus 36%; Number Needed to Harm (NNH)=5.
 - Common adverse effects include sedation, dry mouth, vertigo.^{3,4}
 - Withdrawal due to adverse effects (three RCTs, 303 patients):
 - 16% versus 7%; NNH=11.
- Other systematic reviews did not provide meta-analyses.⁵⁻⁷ Individual study highlights:
 - 30% pain reduction: 40% nortriptyline versus 37% placebo; patient-reported 'a lot' of pain relief: desipramine 17-31% versus 4-8% placebo; patient-reported 'good' pain relief: imipramine 23% versus 5% placebo.
- Limitations:
 - Inconsistent outcome reporting.
 - Small study sizes and short duration (may overestimate treatment effect).
 - Largest systematic review did not report adverse effects.¹

- No adverse effects analysis at varying doses despite wide dose ranges (10-150 mg).⁵
- Some crossover designs did not use washout period.

Context:

- Guidelines^{8,9} recommend TCAs as a first-line agent for treating neuropathic pain.
- Other treatments for neuropathic pain have similar benefit (NNT of 5-8):
 - Gabapentin, pregabalin, serotonin-noradrenaline reuptake inhibitors, tramadol, and opioids.¹⁰
 - Desipramine and nortriptyline¹¹ may be better tolerated than imipramine and amitriptyline, particularly in geriatrics.¹²
- TCAs cost ~\$25-75 for 90 days (25 mg). Others:¹³⁻¹⁴
 - ~\$60 duloxetine, ~\$65 gabapentin, ~\$110 pregabalin.¹³

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