



Meds for Essential Tremor: Steady solution or shaky science?

CLINICAL QUESTION

How effective are beta-blockers and other first line agents for essential tremor?

BOTTOM LINE

Older, small randomized controlled trials (RCTs) show that propranolol improves tremor severity (~2-points more than placebo on 10–15-point scales) and leads to feeling “definitely better” in 64-100% versus 14-20% (placebo) at 2-6 weeks. Benefit is seen from 90 mg/day, with 120–240 mg/day most studied. Primidone and topiramate may improve function based on limited RCTs.

EVIDENCE

- Results statistically significant unless stated.
- Systematic reviews of patient-oriented outcomes not found. Patient-reported outcomes from double-blind, placebo-controlled RCTs, mainly in upper limb tremor, described here.
- Propranolol:
 - Tremor (patient-rated): 9 of 9 RCTs report benefit over placebo. Examples:¹⁻⁹
 - Proportion of patients “definitely better” at 2-6 weeks:
 - RCT (10 patients): 100% versus 20% placebo, number needed to treat (NNT)=2 (PEER calculation).¹

- RCT (7 patients): 64% versus 14% placebo,² NNT=2.
- Severity on 10-15 point scales (baseline scores not provided). At 2-3 weeks:
 - Three RCTs (9-23 patients): Placebo score 5-12 points. Propranolol ~1.6-2.0 points better than placebo, likely clinically meaningful. Two RCTs statistically different; one not.³⁻⁵
- Function: No difference.⁶
- Sotalol: Two RCTs (9-17 patients).
 - Tremor (scale: 0-100, baseline: 34): At 14 days, placebo score: 31. Sotalol: 9 points better than placebo, likely clinically meaningful.¹⁰ Other RCT similar.³
- Metoprolol, atenolol:
 - Symptoms: No difference from placebo.^{3,5,9,10}
 - Metoprolol: Inferior to propranolol.^{5,11} Example: At 14 days, metoprolol tremor score 4.8 on 10-point scale. Propranolol 1.5 points better.
- Primidone: Two RCTs (22 patients each).^{12,13}
 - Functional rating (lower=better function, baseline=8). After four weeks, placebo score=7.8 on 15-point scale. Primidone 2.6 points lower (statistics not reported), likely clinically meaningful.
- Topiramate: Largest RCT (223 patients).¹⁴
 - "Good/very good outcome:" 69% versus 15% placebo, NNT=3.
- Limitations:
 - Many RCTs/systematic reviews report tremor amplitude/frequency but clinical significance unclear.¹⁵
 - Patient and clinician-rated symptom improvement differ.
 - Numerous symptom scales (many unvalidated), frequent incomplete reporting.

CONTEXT

- Guidelines: Propranolol, topiramate and primidone first-line.^{16,17}
 - Options: Alprazolam,¹⁸ gabapentinoids (inconsistent benefit),^{6,19-23} botulinum toxin.²⁴
- Propranolol dosing:
 - Lower doses (possibly as low as 90mg/day) similarly effective to higher (320mg)^{2,4,5}
 - "As needed": No RCTs.

REFERENCES

1. Tolosa ES, Loewenson RB. Neurology 1975; Nov;25(11):1041-4.
2. Morgan M, Langton Hewer R, Cooper R. J Neurol Neurosurg Psychiatry. 1973 Aug;36(4):618-24
3. Jefferson D, Jenner P, Marsden CD. J Neurol Neurosurg Psychiatry. 1979; Oct;42(10):904-9.
4. Cleeves L, Findley LJ. J Neurol Neurosurg Psychiatry. 1988 Mar;51(3):379-84

AUTHORS

Allison Paige, MD CCFP,
Samantha S. Moe, PharmD
 ACRP

*Authors do not have any
 conflicts of interest to declare.*

5. Calzetti S, Findley LJ, Perucca E, *et al.* J Neurol Neurosurg Psychiatry. 1982 Oct;45(10):893-7.
6. Gironell A, Kulisevsky J, Barbanj M *et al.* Arch Neurol. 1999 Apr;56(4): 475-80.
7. Teravainen H, Huttunen J, Larsen TA. Acta Neurol Scand. 1986 Jul;74(1):34-7.
8. Winkler GF, Young RR. N Engl J Med. 1974 May 2;290: 984-88.
9. Larsen TA, Teravainen H, Calne DB. Acta Neurol Scandinav. 1982 Nov;66:547-554.
10. Leigh PN, Jefferson D, Twomey A, *et al.* J Neurol Neurosurg Psychiatry. 1983 Aug;46(8): 710-5.
11. Larsen TA, Teravainen H. Adv Neurol. 1983;37:247-251.
12. Gunal DI, Afsar N, Bekiroglu N, *et al.* Neurol Sci. 2000 Oct;21(5): 315-7.
13. Findley LJ, Cleeves L, Calzetti S. J Neurol Neurosurg Psychiatry. 1985 Sep;48(9):911-915.
14. Ondo WG, Jankovic J, Connor GS, *et al.* Neurology 2006 Mar 14;66(5):672-7.
15. Zhang, JJ, Yan R, Cui Y, *et al.* eClinicalMedicine. 2024 Oct 18;77:102889.
16. Ferreira JJ, Mestre TA, Lyons KE, *et al.* Mov Disord. 2019 Jul;34(7): 950-8.
17. Zappia M, Albanese A, Bruno E, *et al.* J Neurol. 2013 Mar;260(3):714-40.
18. Bruno E, Nicoletti A, Quattrocchi G *et al.* Cochrane Database Syst Rev. 2015 Dec 6;2015(205(12):CD009681.
19. Pahwa R, Lyons K, Hubble JP, *et al.* Mov Disord. 1988 May;13(3): 465-7.
20. Ondo W, Hunter C, Vuong KD, *et al.* Mov Disord. 2000 Jul;15(4): 678-82.
21. Ferrara JM, Kenney C, Davidson AL, *et al.* J Neurol Sci. 2009 Oct 15;285(1-2): 195-7.
22. Zesiewicz TA, Sullivan KL, Hinson V, *et al.* Mov Disord. 2013 Feb;28(2):249-50.
23. Zesiewicz TA, Ward CL, Hauser RA, *et al.* Mov Disord. 2007 Aug 15;22(11):1660-3.
24. Brin MF, Kyons KE, Doucette J, *et al.* Neurology. 2001 Jun 12;56(11):1523-8.

IN PARTNERSHIP WITH



Tools for Practice are peer reviewed and summarize practice-changing medical evidence for primary care. Coordinated by **Dr. Adrienne Lindblad**, the articles are developed by the Patients, Experience, Evidence, Research (PEER) team, and supported by the College of Family Physicians of Canada, and the Alberta, Ontario, and Saskatchewan Colleges of Family Physicians. Feedback is welcome and can be sent to toolsforpractice@cfpc.ca. Archived articles can be found at www.toolsforpractice.ca

This communication reflects the opinion of the authors and does not necessarily mirror the perspective and policy of the College of Family Physicians of Canada.