Review: Some drugs are effective for preventing migraine headache; limited evidence exists on the relative effectiveness of drugs

Pringsheim T, Davenport WJ, Becker WJ. ***Prophylaxis of migraine headache****. CMAJ. 2010;182:E269-76.*

Clinical impact ratings: GM ★★★★★★☆ N ★★★★★☆☆

Question
Which drugs are effective for preventing migraine headaches?

Review scope
Included studies evaluated drugs that are commonly used in North America and Europe for preventing migraine headaches in adults who met International Headache Society or ad hoc criteria for migraine. Studies of chronic headache (daily, tension-type, or migraine) were excluded. The most consistently reported outcome was responder rate (≥ 50% reduction in migraine frequency).

Review methods
MEDLINE and EMBASE/Excerpta Medica were searched (to Apr 2008) for double-blind, randomized controlled trials (RCTs), and the Cochrane Library was searched for systematic reviews. 1 Cochrane review evaluating propranolol (26 placebo-controlled trials, *n* = 668; limited data reported for drug–drug comparisons) and 59 RCTs evaluating 17 drugs met the selection criteria. Drugs evaluated were flunarizine, botulinum toxin type A, topiramate, divalproex sodium, pizotifen, amitriptyline, feverfew, gabapentin, nadolol, venlafaxine, verapamil, riboflavin, magnesium, butterbur, lisinopril, candesartan, and coenzyme Q10. Most trials were placebo-controlled. Data were not reported for all eligible trials.

Main results
The main results are in the Table. Divalproex sodium, topiramate, and propranolol reduced migraine frequency (Table); botulinum toxin had no effect.

Drug treatment for preventing migraine headaches*

Comparisons	Number of trials (*n*)	Selected findings	
		Reduction in migraine frequency†	Adverse effects‡
Divalproex sodium vs placebo	3 (510)	OR 2.74, 95% CI 1.48 to 5.08	Greater at higher doses
Topiramate vs placebo	4 (828)	OR 2.44, CI 1.81 to 3.28	Greater at higher doses
Amitriptyline (comparisons NR)	4 (NR)	Amitriptyline beneficial for migraine prophylaxis in all RCTs (data NR).	Occasional
Propranolol vs placebo§	26 (668)	RR 1.94, CI 1.61 to 2.35	Infrequent
Butterbur vs placebo	2 (NR)	50 mg twice daily: OR 2.24, CI 0.64 to 7.81 (2 RCTs) 75 mg twice daily: OR 2.16, CI 1.06 to 4.38 (1 RCT)	Infrequent
Botulinum toxin type A (comparisons NR)	8 (NR)	No effect (6 RCTs); subgroup treatment benefit (1 RCT); data not interpretable (1 RCT)	Infrequent
Pizotifen vs placebo	5 (NR)	Pizotifen beneficial in all RCTs (data NR).	Occasional
Flunarizine vs placebo	6 (NR)	Flunarizine reduced migraine frequency in all RCTs (data NR).	Occasional

**NR = not reported; OR = odds ratio; RCT = randomized controlled trial; RR = risk ratio; other abbreviations defined in Glossary. Only drugs with > 1 RCT reporting data are included in the table.*

†ORs and RRs > 1 favor treatment for ≥ 50% reduction in migraine frequency.

‡Led to treatment discontinuation in < 10% of patients (infrequent) or 10% to 25% of patients (occasional).

§Data from a Cochrane review.

Conclusion
Some drugs prevent migraine headache in adults; limited evidence exists on the relative effectiveness of different drugs.

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For correspondence: Dr. T. Pringsheim, University of Calgary, Calgary, AB, Canada. E-mail tmprings@ucalgary.ca.

Commentary
Migraine headache is a common problem encountered by primary care physicians—an estimated 18.2% of women and 6.5% of men suffer from this disorder (1). When severe, migraine headaches are highly associated with depression, decreased quality of life, and disability.

Overall, this comprehensive review of pharmacologic therapies for prevention of migraine headache has no important methodological flaws. It confirms conclusions of previous guidelines about the efficacy and safety of β-blockers (propranolol, nadolol, metoprolol), certain anticonvulsants (divalproex sodium, topiramate, gabapentin), and antidepressants (amitriptyline, venlafaxine) (2, 3). Additional medications that were not included in previous guidelines were also reviewed. Other antihypertensive drugs (lisinopril, candesartan), vitamin preparations (riboflavin, coenzyme Q10), and miscellaneous medications (magnesium, butterbur) were reviewed and considered as potential secondary choices for treatment.

The authors suggest which medications may be used for first-, second-, or third-line treatment based on strength of evidence for efficacy, their impression of clinical effectiveness, and frequency of adverse effects. They accurately state that there is little evidence for increased efficacy of one medication over another in head-to-head RCTs and instead suggest that the choice of medication could be based on such clinical circumstances as comorbid conditions or sensitivity to medication side effects.

Migraine prophylaxis remains a clinical challenge. Patients with severe headaches resulting in disability, with frequent headaches that put them at risk for medication-overuse headache, and with variant migraines syndromes (i.e., hemiplegic migraine) that are associated with important morbidity should all be considered candidates for prophylactic medications. This review gives the practitioner evidence-based options from which to choose.

Renato Roxas Jr, MD
Wayne State University School of Medicine
Detroit, Michigan, USA

References

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