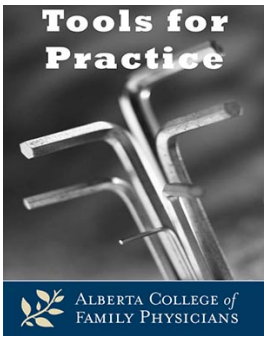
Tools for Practice is proudly sponsored by the Alberta College of Family Physicians (ACFP). ACFP is a provincial, professional voluntary organization, representing more than 4,000 family physicians, family medicine residents and medical students in Alberta. Established over fifty years ago, the ACFP strives for excellence in family practice through advocacy, continuing medical education and primary care research. www.acfp.ca

Reviewed: May 11, 2015
Evidence Updated: Systematic review and 2 RCTs added
Bottom Line: Unchanged
First Published: September 19, 2011



Are antihypertensive medications effective for migraine prophylaxis?

Clinical Question: In patients with frequent and/or severe migraines, are antihypertensive medications effective in reducing frequency or severity of migraines?

Bottom-line: A number of antihypertensive medications are effective in migraine prophylaxis. The best data are for propranolol, which will benefit one in four patients (over placebo).

Evidence:

- Systematic review of propranolol for migraine prophylaxis, 58 trials (5,072 patients).[1]
  - Versus Placebo: Propranolol statistically significantly:
    - Improved migraine control: For example, more patients on propranolol attained a 50% reduction in headaches (57.1% versus 29.7%), Number Needed to Treat (NNT)=4.
    - Increased drop-out due to adverse events (4.1% versus 1.6%), Number Needed to Harm 40.
  - Versus other medications (primarily other beta-blockers & calcium channel blockers): No consistent differences.
    - Low quality studies and heterogeneity make definitive statements difficult.
    - Recent industry-sponsored cross-over trial of 54 patients found candesartan was not inferior to propranolol.[2]
- Randomized Controlled Trial (RCT) with 55 patients on lisinopril 20 mg/day or placebo:[3]
  - Statistically significant reduction in headache frequency: 7.9 days/month on placebo versus 6.6 days/month on lisinopril.
  - Rescue medications and headache severity also reduced.
- RCT with 57 patients on candesartan 16 mg/day or placebo for migraine prophylaxis:[4]
  - Statistically significant reduction in headache frequency: 6.2 days/month on placebo versus 4.5 days/month on candesartan.

    - Rescue medications and sick leave days also reduced.
- Reviews of verapamil, although low quality, suggest it too improves headache.[5,6]
- Recent systematic review found other beta-blockers (timolol, metoprolol, atenolol, nadolol, acebutalol), calcium channel blockers (nimodipine, nicardipine), captopril, candesartan, and clonidine all improve some measures of migraine frequency/severity, although evidence is limited and not all effects consistent.[7,8]
    - Recent small study from Iran suggests enalapril may also be effective.[9]

Context:

- Meta-analysis of 95 hypertension RCTs (24,244 participants) reporting headache among the adverse events:[10]
    - Patients taking any of the four classes of antihypertensives (thiazides, beta-blockers, ACE inhibitors, or ARBs) reported headache less often than those taking placebo.
- Two reviews of migraine prophylaxis[11,12] suggest the following antihypertensives (with starting doses[12]): Propranolol (20 mg BID) is consistently highly recommended,[11,12] followed by nadolol (80 mg OD),[12] metoprolol,[11] lisinopril (20 mg),[11,12] candesartan (16 mg),[11,12] or verapamil (40mg TID).[11,12] Similar recommendations are found in Canadian and US guidelines.[13,14]
- Anticonvulsants and Tricyclic anti-depressants are also effective.[15]

Original Authors:
Michael J Kapusta BSc (medical student), G Michael Allan MD CCFP

Updated:
Adrienne J Lindblad BSP ACPR PharmD

Reviewed:
G Michael Allan MD CCFP

References:

1. Linde K, Rossnagel K. Cochrane Database Syst Rev. 2004; 2:CD003225.
2. Stovner LJ, Linde M, Gravdahl GB, *et al*. Cephalalgia. 2014; 34(7):523-32.
3. Schrader H, Stovner LJ, Helde G, *et al*. BMJ. 2001; 322:10-22.
4. Tronvik E, Stovner LJ, Helde G, *et al*. JAMA. 2003; 289(1):65-9.
5. Markley HG. Am J Med. 1991; 90(5):S48-S53.
6. Solomon GD. Headache. 1989 Jul; 29(7):425-7.
7. Shamliyan TA, Kane RL, Taylor FR. Rockville (MD): Agency for Healthcare Research and Quality (US); 2013 Apr. Report No.: 13-EHC068-EF.
8. Shamliyan TA, Choi JY, Ramakrishnan R, *et al*. J Gen Intern Med. 2013 Sep; 28(9):1225-37.
9. Sonbolestan SA, Heshmat K, Javanmard SH, *et al*. Int J Prev Med. 2013; 4:72-7.
10. Law M, Morris JK, Jordan R, *et al*. Circulation. 2005; 112:2301-6.
11. Fenstermacher N, Levin M, Ward T. BMJ. 2011; 342:d583.
12. Pringsheim T, Davenport WJ, Becker WJ. CMAJ. 2010; 182(7):E269-E276.
13. Pringsheim T, Davenport W, Mackie G, *et al*. Can J Neurol Sci. 2012; 39(2 suppl 2):S1-59.
14. Silberstein SD, Holland S, Freitag F, *et al*. Neurology. 2012; 78:1337-45.
15. Allan GM, Levy M. Tools for Practice #51. Available at http://www.acfp.ca/wp-content/uploads/tools-for-practice/1397836024_20111028_100921.pdf. Accessed May 11, 2015.

Tools for Practice is a biweekly article summarizing medical evidence with a focus on topical issues and practice modifying information. It is coordinated by G. Michael Allan, MD, CCFP and the content is written by practicing

family physicians who are joined occasionally by a health professional from another medical specialty or health discipline. Each article is peer-reviewed, ensuring it maintains a high standard of quality, accuracy, and academic integrity.

The ACFP has supported the publishing and distribution of the Tools for Practice library since 2009. If you are not a member of the ACFP and would like to receive the TFP emails, please sign up for the distribution list at http://bit.ly/signupfortfp. Archived articles are available at no extra cost on the ACFP website.

You can now earn credits on Tools for Practice! In August 2014, the ACFP launched GoMainpro, an online accreditation tool to help facilitate MAINPRO® accreditation for the ACFP's Tools for Practice library which has been accredited for Mainpro-M1 credits by the College of Family Physicians of Canada (CFPC). The combination of the CFPC's Direct Entry Program and GoMainpro's tracking and reporting features provide an easy and convenient way to earn Mainpro-M1 credits.

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