



Vickie F. Ingledue, MD;
Anne Mounsey, MD
Department of Family
Medicine, University of
North Carolina at Chapel
Hill

PURLs EDITOR

James J. Stevermer, MD,
MSPH

Department of Family
Medicine, University
of Missouri-Columbia

Treating migraine: The case for aspirin

High-dose aspirin is an effective treatment for acute migraine. So why aren't more physicians recommending it?

PRACTICE CHANGER

Recommend aspirin 975 mg (3 adult tablets) as a viable first-line treatment for acute migraine. Consider prescribing metoclopramide 10 mg to be taken with aspirin to markedly decrease associated nausea and help achieve maximum symptom relief.¹

STRENGTH OF RECOMMENDATION

A: Based on a Cochrane meta-analysis of 13 good quality, randomized controlled trials (RCTs).

Kirthi V, Derry S, Moore RA. Aspirin with or without an antiemetic for acute migraine headaches in adults. *Cochrane Database Syst Rev.* 2013;(4):CD008041.

ILLUSTRATIVE CASE

During a routine physical, a 37-year-old patient asks you what she should take for her occasional migraines. She describes a unilateral headache with associated nausea, vomiting, phonophobia, and photophobia. What medication should you recommend?

Migraine headache affects more than 37 million Americans.² Women are 3 times more likely than men to suffer from migraine, with the highest prevalence among those between the ages of 30 and 50 years.^{3,4} More than 50% of patients report that episodes cause severe impairment, resulting in an average loss of 4 to 6 workdays each year due to migraine.^{5,6}

Do you recommend this low-cost option?
Although many patients try over-the-counter

headache remedies for migraine, when they do seek medical care for this condition, most (67%) turn to their primary care providers.⁷ But despite a 2010 Cochrane review showing aspirin's efficacy for acute migraine,⁸ our experience—based on discussions with physicians at numerous residency programs—suggests that family physicians are not likely to recommend it.

Further evidence of the underuse of aspirin for migraine comes from a 2013 review of national surveillance studies,⁵ which found that in 2009, triptans accounted for nearly 80% of antimigraine analgesics prescribed during office visits.⁵ Thus, when the Cochrane reviewers issued this update of the earlier meta-analysis, we welcomed the opportunity to feature a practice changer that might not be getting the “traction” it deserves.

STUDY SUMMARY

Multiple RCTs highlight aspirin's efficacy
The 2013 Cochrane reviewers used the same 13 good quality, double-blind RCTs involving 4222 participants as the earlier review; no new studies that warranted inclusion were found. A total of 5261 episodes of migraine of moderate to severe intensity were treated with either aspirin alone or aspirin plus the antiemetic metoclopramide.¹

Five studies had placebo controls, 4 had active controls (sumatriptan, zolmitriptan, ibuprofen, acetaminophen plus codeine, and ergotamine plus caffeine among them),

INSTANT POLL

How often do you prescribe aspirin to your patients who experience acute migraine pain?

- Often, because research has shown this agent to be effective
- Rarely, because patients are unwilling to accept anything other than a prescription medication
- Rarely, as I've had very good success with triptans
- Never

jfponline.com

and 4 had both active and placebo controls. Primary outcomes were pain-free status at 2 hours and headache relief (defined as a reduction in pain from moderate or severe to none or mild without the use of rescue medication) at 2 hours. Sustained headache relief at 24 hours was a secondary outcome.

Patients self-assessed their headache pain, using either a 4-point categorical scale (none, mild, moderate, or severe) or a 100 mm visual analog scale. On the analog scale, <30 mm was considered mild or no pain; ≥30 mm was considered moderate or severe.

Study participants were 18 to 65 years of age (the mean age range was 37-44), and their symptoms met International Headache Society criteria for migraine with or without aura.⁹ All participants had migraine symptoms for ≥12 months, with between one and 6 attacks of moderate to severe intensity per month prior to the study period.

In 6 studies (n=2027), investigators compared either 900 or 1000 mg aspirin alone with placebo. For both primary outcomes, aspirin alone was superior to placebo, with a number needed to treat (NNT) of 8.1 for 2-hour pain-free status and 4.9 for 2-hour headache relief. In 3 studies (n=1142), aspirin was superior to placebo for 24-hour headache relief, with an NNT of 6.6. Aspirin plus metoclopramide was also better than placebo for primary and secondary outcomes, with an NNT of 8.8 for 2-hour pain-free status, 3.3 for 2-hour headache relief, and 6.2 for 24-hour headache relief. Based on subgroup analysis, aspirin plus metoclopramide was more effective than aspirin alone for 2-hour headache relief ($P=.0131$), but equivalent for 2-hour pain-free status and 24-hour headache relief. The addition of metoclopramide to aspirin significantly reduced nausea ($P<.00006$) and vomiting ($P=.002$).

In 2 studies (n=726), aspirin alone was equivalent to sumatriptan 50 mg for reaching pain-free and headache relief status at 2 hours. Two additional studies (n=523) compared aspirin plus metoclopramide with sumatriptan 100 mg and found them to be equal for 2-hour headache relief, but the aspirin combination was inferior to the triptan for pain-free status at 2 hours (n=528). Data were insufficient to compare the efficacy of aspirin with zolmitriptan, ibuprofen, or acetaminophen plus codeine.

There were no reports of gastrointestinal bleed or other serious adverse events attributable to aspirin therapy. Most adverse effects were mild or moderate disturbances of the digestive and nervous systems, with a number needed to harm of 34 (95% confidence interval, 18-340) for aspirin (with or without metoclopramide) vs placebo.

WHAT'S NEW

A reminder of aspirin's efficacy in treating migraine

The update of this meta-analysis confirms that high-dose aspirin (900-1000 mg) is an effective treatment for migraine headache in adults between the ages of 18 and 65 years. The addition of metoclopramide reduces nausea and vomiting, but offers little if any benefit for headache/pain relief.

CAVEATS

Lack of comparison with other treatments

Data were insufficient to compare the efficacy of aspirin with zolmitriptan, other non-steroidal anti-inflammatory drugs alone, or acetaminophen plus codeine. Aspirin should be used with caution in patients with chronic renal disease and/or a history of peptic ulcer disease.

CHALLENGES TO IMPLEMENTATION

Patients want a prescription

Patients often expect a prescription when they visit a physician with complaints of migraine headache and may feel shortchanged if they're told to take an aspirin. Providing a prescription for the antiemetic metoclopramide, as well as a brief explanation of the evidence indicating that aspirin is effective for migraine, may adequately address such expectations. **JFP**

ACKNOWLEDGEMENT

The PURLs Surveillance System was supported in part by Grant Number UL1RR024999 from the National Center for Research Resources, a Clinical Translational Science Award to the University of Chicago. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Center for Research Resources or the National Institutes of Health.

Copyright © 2014. The Family Physicians Inquiries Network. All rights reserved.



The addition of metoclopramide to aspirin reduces nausea and vomiting, but offers little, if any, benefit for headache/pain relief.

CONTINUED

References

1. Kirthi V, Derry S, Moore RA. Aspirin with or without an antiemetic for acute migraine headaches in adults. *Cochrane Database Syst Rev.* 2013;(4): CD008041.
2. Migraine. National Headache Foundation Web site. Available at: http://www.headaches.org/education/Headache_Topic_Sheets/Migraine. Accessed January 10, 2014.
3. Lipton RB, Stewart WF, Diamond S, et al. Prevalence and burden of migraine in the United States: data from the American Migraine Study II. *Headache.* 2001;41:646-657.
4. Victor TW, Hu X, Campbell JC, et al. Migraine prevalence by age and sex in the United States: a life-span study. *Cephalgia.* 2010;9:1065-1072.
5. Smitherman TA, Burch R, Sheikh H, et al. The prevalence, impact, and treatment of migraine and severe headaches in the United States: a review of statistics from national surveillance studies. *Headache.* 2013;53:427-436.
6. Hu XH, Markson LE, Lipton RB, et al. Burden of migraine in the United States: disability and economic costs. *Arch Intern Med.* 1999;159:813-818.
7. Gibbs TS, Fleischer AB Jr, Feldman SR, et al. Health care utilization in patients with migraine: demographics and patterns of care in the ambulatory setting. *Headache.* 2003;43:330-335.
8. Kirthi V, Derry S, Moore RA, et al. Aspirin with or without an antiemetic for acute migraine headaches in adults. *Cochrane Database Syst Rev.* 2010;(4): CD008041.
9. The international classification of headache disorders. 2nd ed. *Cephalgia.* 2004;24(suppl 1):S9-S160.

New name, same valuable source of pain management information

CURRENT PAIN PERSPECTIVES™

For information on pain management, go to our Web site at www.currentpainperspectives.com and check out these articles:

- Diagnosing fibromyalgia and myofascial pain syndrome: A guide
- Neurogenic thoracic outlet syndrome: Often overlooked, but treatable
- How best to prevent acute pain from becoming chronic?

