Cochrane for Clinicians

Putting Evidence into Practice

These are summaries of reviews from the Cochrane Library.

The series coordinator for *AFP* is Corey D. Fogleman, MD, Lancaster General Hospital Family Medicine Residency, Lancaster, Pa.

A collection of Cochrane for Clinicians published in *AFP* is available at http://www.aafp.org/afp/cochrane.

CME This clinical content conforms to AAFP criteria for continuing medical education (CME). See CME Quiz Questions on page 708.

Author disclosure: No relevant financial affiliations.

Gabapentin for the Prophylaxis of Episodic Migraine in Adults

COREY D. FOGLEMAN, MD
Lancaster General Hospital Family Medicine Residency, Lancaster, Pennsylvania

Clinical Question

Does gabapentin (Neurontin) help prevent episodic migraines?

Evidence-Based Answer

Gabapentin does not decrease the frequency of migraine headaches and is not recommended for prophylactic therapy. (Strength of Recommendation: B, based on inconsistent or limited-quality patient-oriented evidence.)

Practice Pointers

Worldwide, migraine has a lifetime prevalence of 18% in women and 10% in men.[1] Therapeutic options are usually divided into prophylactic and abortive. Avoidance of triggers may be beneficial. Effective prophylaxis can range from acupuncture to medications such as propranolol, topiramate (Topamax), and valproic acid (Depakene), all of which have shown consistent positive benefit in systematic reviews.[2-5]

Previously published systematic reviews by these same authors gave cautious support for the use of gabapentin for migraine prophylaxis based on poor-quality evidence. However, new data from not-yet-published industry-sponsored trials of gabapentin for migraine have come to light during litigation against the drug manufacturer. These data have led the authors to change their conclusion based on the results of five studies involving 1,009 patients.

Four trials with a total of 351 patients compared gabapentin in a dosage of 900 to 2,400 mg per day with placebo. The meta-analysis found no significant reduction in the frequency of migraine headache (mean difference in the number of headaches = –0.44; 95% confidence interval, –1.43 to 0.56). Pooled results of two studies with 235 patients comparing the proportion of responders (at least 50% improvement in frequency of headaches) between those treated with up to 2,400 mg of gabapentin vs. placebo failed to show a difference (odds ratio = 1.59; 95% confidence interval, 0.57 to 4.46). One study analyzed prophylactic use of the prodrug gabapentin enacarbil (Horizant) titrated up to 3,000 mg daily and failed to find any benefit.

Patients taking gabapentin often reported adverse effects, most commonly dizziness (number needed to harm [NNH] = 7), drowsiness (NNH = 9), and abnormal thinking (NNH = 20).

According to the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society, prophylaxis should be offered to anyone whose daily activities are severely impaired, or when acute drug treatment is inadequate. The antiepileptic drugs topiramate and valproic acid are considered first-line prophylactic agents. However, the guidelines state that the evidence is inadequate to recommend the use of gabapentin for migraine prevention.[6] Because gabapentin is not effective and commonly causes adverse effects, family physicians should consider alternatives when offering prophylaxis for migraine headache.

SOURCE: Linde M, Mulleners WM, Chronicle EP, McCrory DC. Gabapentin or pregabalin for the prophylaxis of episodic migraine in adults. *Cochrane Database Syst Rev.* 2013;(6):CD010609.

The practice recommendations in this activity are available at http://summaries.cochrane.org/CD010609.

REFERENCES

1. Vos T, Flaxman AD, Naghavi M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010 [published correction appears in *Lancet.* 2013;381(9867):628]. *Lancet.* 2012;380(9859):2163-2196.
2. Linde K, Allais G, Brinkhaus B, Manheimer E, Vickers A, White AR. Acupuncture for migraine prophylaxis. *Cochrane Database Syst Rev.* 2009;(1):CD001218.
3. Linde K, Rossnagel K. Propranolol for migraine prophylaxis. *Cochrane Database Syst Rev.* 2004;(2):CD003225.

4. Linde M, Mulleners WM, Chronicle EP, McCrory DC. Topiramate for the prophylaxis of episodic migraine in adults. *Cochrane Database Syst Rev.* 2013;(6):CD010610.
5. Linde M, Mulleners WM, Chronicle EP, McCrory DC. Valproate (valproic acid or sodium valproate or a combination of the two) for the prophylaxis of episodic migraine in adults. *Cochrane Database Syst Rev.* 2013;(6):CD010611.
6. Silberstein SD, Holland S, Freitag F, Dodick DW, Argoff C, Ashman E. Evidence-based guideline update: pharmacologic treatment for episodic migraine prevention in adults: report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society [published correction appears in *Neurology.* 2013;80(9):871]. *Neurology.* 2012;78(17):1337-1345.

Progestin-Only Contraceptives: Effects on Weight

JOSEPH R. YANCEY, MAJ, MC, USA, and MEGHAN RALEIGH, MAJ, MC, USA
Fort Belvoir Community Hospital, Fort Belvoir, Virginia

Clinical Question

Do progestin-only contraceptives cause weight gain?

Evidence-Based Answer

There is little evidence that progestin-only contraceptives cause weight gain; in this review, mean weight gain was less than 2 kg (4.4 lb) for most studies up to 12 months. (Strength of Recommendation: B, based on inconsistent or limited-quality patient-oriented evidence.)

Practice Pointers

More than 99% of all U.S. women 15 to 44 years of age who are or have been sexually active have used some form of contraception. Of those who use contraception, nearly one-fourth have tried depot medroxyprogesterone acetate (DMPA; Depo-Provera). The most common reason given for discontinuation of DMPA was weight gain.[1] This Cochrane review examined 16 studies on various forms of progestin-only contraceptives and their association with weight gain. The data from these studies were too varied to be combined for meta-analysis. Most of the studies examined DMPA, but others looked at progestin-only implants, oral contraceptives, and intrauterine devices (IUDs). Only one study examined weight change in women taking different types of oral progestin-only contraceptives. The mean weight change in each group was small.

Ten studies examined weight gain in women using DMPA. Three of the studies compared the weight gain in DMPA users with the gain in women using combined estrogen-progestin contraceptives. None of the studies found a significant difference between the two groups, although one study noted that DMPA users had a significant increase in body fat (mean difference = 11%; 95% confidence interval [CI], 2.64 to 19.36) and a greater decrease in lean body mass (mean difference = –4%; 95% CI, –6.93 to –1.07) when compared with those using no hormonal method.

Five studies examined weight gain in women using different formulations or doses of injectable progesterone. None of the studies showed a significant difference in weight gain among various doses or formulations. The mean weight change in these patients was small.

Two studies examined weight gain in those using DMPA vs. those using nonhormonal IUDs. One study showed no significant difference. The other showed a statistically significant weight gain in the DMPA group at one year (mean difference = 2.28 kg [5.07 lb]), two years (mean difference = 2.71 kg [6.02 lb]), and three years (mean difference = 3.17 kg [7.04 lb]). Of note, this weight gain was significant only for patients categorized as normal weight or overweight; women who were obese showed no significant weight gain on DMPA.

One study involving the levonorgestrel-releasing intrauterine system (Mirena) found that women who used this method had an increase in body fat (2.5% vs. –1.3%; $P = .029$) and a decrease in lean body mass (–1.4% vs. 1.0%; $P = .027$) compared with a similar group who used a nonhormonal IUD. Despite the small difference in body composition, no significant change in body weight was noted between the two groups.

Several studies compared women using the six-capsule levonorgestrel implant (no longer available in the United States) with those using other hormonal and nonhormonal contraceptives. The implant group experienced more weight gain at one year

than a group using a nonhormonal IUD (mean difference = 1.10 kg [2.44 lb]; 95% CI, 0.36 to 1.84), but there was no difference at three years. In another study, the implant group gained more weight than a group using a barrier method or no contraceptives (mean difference = 0.74 kg [1.64 lb]; 95% CI, 0.52 to 0.96). A study of women 15 to 30 years of age using the levonorgestrel implant or DMPA showed no significant weight change between the two groups at one year. None of the studies in the review evaluated the newer etonogestrel implants (Implanon, Nexplanon).

Overall, there is little evidence that progestin-only contraceptives cause weight gain. The mean weight gain was less than 2 kg for most studies up to 12 months. Multiyear studies showed more weight gain, but the gain was similar when comparing women who used progestin-only contraceptives and those who did not. This suggests that weight gain over time may occur regardless of contraceptive use. The two studies looking at body mass showed that progestin-only contraceptive users had greater increases in body fat and decreases in lean mass than users of nonhormonal methods. This could be caused by a hormone-mediated increase in fat deposition. Having frank discussions with patients about the average weight gain that occurs with progestin-only contraceptive use may decrease discontinuation rates of this method.

SOURCE: Lopez LM, Edelman A, Chen M, Otterness C, Trussell J, Helmerhorst FM. Progestin-only contraceptives: effects on weight. *Cochrane Database Syst Rev.* 2013;(7):CD008815.

The practice recommendations in this activity are available at http://summaries.cochrane.org/CD008815.

The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the U.S. Army, the U.S. Army Medical Department, the Department of Defense, or the U.S. government.

REFERENCE

1. Daniels K, Mosher WD, Jones J. Contraceptive methods women have ever used: United States, 1982–2010. National Health Statistics Reports, no. 62. Hyattsville, Md.: National Center for Health Statistics; 2013. ■