New Migraine Guidelines Rank Rx, OTC Efficacy

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NEW ORLEANS -- Seven different drugs are proven to be effective for preventing episodic migraine attacks and another half-dozen are probably helpful, according to new guidelines released here by the American Academy of Neurology (AAN).

An evidence review by the AAN and the American Headache Society also identified several over-the-counter (OTC) products, including herbal supplements, with either proven or probable efficacy.

The announcement accompanied publication of two practice guidelines on prevention of episodic migraine -- one for prescription products and another for nonsteroid anti-inflammatory drugs and "complementary" therapies -- in the April 24 issue of *Neurology*.

Prescription drugs listed as having proven effectiveness against migraine, defined as a significant benefit in at least two high-quality randomized trials, included one triptan agent, three beta-blockers, and three anti-epileptic drugs.

Action Points

Preventive treatments in patients with migraine can reduce episodic migraine attacks but are frequently not used by those who might benefit.

Note that these new guidelines from the American Academy of Neurology review available evidence for the efficacy of certain prescription drugs, as well for over-the-counter and complementary treatments.

Only one OTC product has established efficacy, according to the guideline: the herbal supplement known as Petasites or butterbur.

The guidelines did not address the use of Botox or other botulinum toxin-based drugs for migraine because these were covered in a separate AAN review published in 2008.

That review indicated that botulinum toxin was "probably ineffective" for preventing episodic migraine. However, Botox is now approved for preventing chronic migraine and the AAN indicated that a new guideline is now in development.

Specific prescription drugs with a Level A recommendation, indicating proven efficacy in at least two high-quality trials, included:

- Divalproex sodium (Depakote)
- Sodium valproate (Depacon)
- Toprimate (Topamax)
- Metoprolol (Lopressor, Toprol-XL)
- Propranolol (Inderal)
- Timolol (Blocadren, but no longer sold under that name in the U.S.)
- Frovatriptan (Frova)

Another half-dozen prescription drugs, including antidepressants, beta-blockers, and triptans, were rated as "probably effective" on the basis of one high-quality or two moderate-quality trials, the

review found.

No nonsteroidal anti-inflammatory drugs (NSAIDs) received the highest rating for proof of efficacy, but several -- including naproxen (Naprosyn, Aleve), ibuprofen (Advil), ketoprofen (no branded version in the U.S.), and fenoprofen (Nalfon) -- are probably effective.

Other OTC products with probable efficacy included magnesium, riboflavin, histamine SC, and the herbal supplement feverfew (MIG-99).

Listed as "probably" or "possibly" ineffective were a range of agents:

Lamotrigine (Lamictal)

Clomipramine (Anafranil)

Acebutolol (Sectral)

Clonazepam (Klonopin)

Nabumetone (Relafen)

Oxcarbazepine (Trileptal)

Telmisartan (Micardis)

Montelukast (Singulair)

In between, rated as "possibly effective" or with inadequate or conflicting evidence on efficacy, were more than 30 treatments in 15 classes.

The AAN first published recommendations for episodic migraine prophylaxis in 2000.

At a press briefing announcing the new guideline, lead author Stephen Silberstein, MD, of Thomas Jefferson University in Philadelphia, said that it contained three major changes from the 2000 edition.

Topiramate had been elevated to Level A on the strength of five randomized trials conducted since the initial guideline was published, he said.

And two drugs receiving a high rating in the initial edition -- verapamil (Calan) and gabapentin (Neurontin) -- had been downgraded because the current evidence failed to clearly support their efficacy.

He emphasized that the review did not address the magnitude of any given drug's efficacy -- only the strength of evidence backing their superiority relative to placebo.

Silberstein noted that prophylactic treatments would benefit an estimated 38% of all migraine sufferers. In terms of who would be a candidate, "there are no absolutes," he said, but such factors as having very frequent attacks, use of acute medications beyond recommended limits, or failure of acute medications to provide relief are common identifiers.

Still, only about one-third of patients who could be such candidates are receiving any kind of preventive treatment, he said.

A migraine patient at the press briefing, Gina Gjorvad, described her own treatment history, starting at age 11 when she was advised to take OTC medications.

After reaching adulthood, her physician recommended nortriptyline as a daily prophylactic medication. "I found that that did not provide much relief" in terms of attack frequency or severity, Gjorvad said.

She was switched to topiramate, which Gjorvad said was somewhat helpful, reducing the attack frequency by half.

But that still left with 8-10 attacks per month. She then changed neurologists consequent to a relocation, and her new doctor upped the dose, which has now reduced the frequency to about 3 per

month, she said.

Silberstein commented that several aspects of her experience were unfortunately common among migraineurs.

Too often, he said, prophylactic medications are not recommended to patients who would benefit from them, and are then told to take drugs that either don't work or are given doses too low to be effective.

The guideline development had no commercial funding.

Silberstein reported consulting or other fees from AGA, Allergan, Amgen, Capnia, Coherex, Colucid, Cydex, GlaxoSmithKline, Lilly, MAP, Medtronic, Merck, Minster, Neuralieve, NINDS, NuPathe, Pfizer, St. Jude Medical, and Valeant, Endo, and Novartis. Other guideline authors reported relationships with numerous commercial entities, including medical publishers, pharmaceutical companies, and device manufacturers.

Primary source: Neurology
Source reference:
Silberstein S, et al "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" *Neurology* 2012; 78: 1337-45.

Additional source: Neurology
Source reference:
Holland S, et al "Evidence-based guideline update -- NSAIDs and other complementary treatments for episodic migraine prevention in adults: Report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society" *Neurology* 2012; 78:1346-53.