Sustained-Release Niacin for Prevention of Migraine Headache

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Considerable advances in the diagnosis and treatment of migraine headache have occurred during the past decade, but treatment options for acute migraine attacks have expanded at a faster rate than those for prophylaxis. We describe a patient whose migraine headaches responded dramatically to sustained-release niacin as preventive treatment. Niacin is not generally considered to be effective for migraine prevention. However, low plasma levels of serotonin have been implicated in migraine pathogenesis, and niacin may act as a negative feedback regulator on the kynurenine pathway to shunt tryptophan into the serotonin pathway, thus increasing plasma serotonin levels. Sustained-release niacin merits further study as a potentially useful preventive therapy for migraine headache.

Migraine headache is a common disorder, affecting approximately 18% of women and 6% of men in the United States. Despite considerable advances during the past decade, the condition remains undiagnosed and undertreated in many cases. The advances have occurred primarily in the treatment of acute migraine, and, unfortunately, advances in specific prophylactic therapy have not been as robust. Therefore, any treatment that shows efficacy for the prevention of migraine and can advance our knowledge and therapeutic options is noteworthy. We describe a patient whose migraine headaches responded dramatically and consistently to sustained-release niacin.

REPORT OF A CASE
A 62-year-old woman with a 40-year history of migraine headaches presented to our medical center for evaluation of increasingly frequent attacks. Her headaches had started when she was in her mid-20s and occurred once or twice per month. They typically began in the occipital region, progressed to encompass the entire head, and lasted 24 to 48 hours. The headaches were accompanied by nausea, vomiting, photophobia, phonophobia, and exacerbation with movement. There were no identifiable triggers, and associated symptoms were less severe. The headaches were unresponsive to oral sumatriptan (25- and 50-mg tablets) and ice packs and responded only partially to zolmitriptan (2.5-mg tablets).

Nine months previously, the patient had experienced 2 major life stressors—the death of a son and a transcontinental move. Subsequently, her headache pattern changed dramatically. The headaches occurred 2 or 3 times per week but were slightly less intense than in the past, and the associated symptoms were less severe. The headaches were unresponsive to oral sumatriptan (25- and 50-mg tablets) and ice packs and responded only partially to zolmitriptan (2.5-mg tablets).

The patient’s medical history was notable for fibromyalgia, depression, chronic fatigue syndrome, and osteoarthritis. Her medications included oral hormone replacement therapy, lorazepam (0.5 mg orally once per week as needed for insomnia), and multivitamins. Results of neurologic and general physical examinations were unremarkable.

Two weeks previously, a friend who had recently started taking niacin as a cholesterol-lowering agent told the patient that since he had been taking the niacin, he had not had any migraine headaches, which had plagued him for many years. The patient decided to try niacin on her own and started taking 750 mg/d of an over-the-counter form of sustained-release niacin, cutting the scored tablet in half and taking 375 mg twice daily. She reported no migraine headaches since she started taking niacin.

We recommended that she continue the niacin therapy at the current dosage (375 mg orally twice daily) and take zolmitriptan (5.0 mg orally) as needed for acute attacks. Several other nonprescription options were discussed including riboflavin, magnesium, and feverfew. She was cautioned that niacin could produce benign skin flushing and, rarely, liver failure with extremely high doses. She was encouraged to use the zolmitriptan early in the course of an acute migraine episode.

At 3-month follow-up, the patient reported that 2 weeks after our consultation she had lowered her dosage of niacin to 375 mg/d because she had been headache-free for 1
month on the regimen of 750 mg/d. After lowering the dosage of niacin, she experienced 2 mild migraine headaches in the subsequent 2 months, both of which immediately resolved with a single 5.0-mg oral dose of zolmitriptan. She has continued to take 375 mg of sustained-release niacin daily and has had no other headaches or any adverse effects.

DISCUSSION
The goals of preventive treatment of migraine headache are to (1) reduce the frequency, severity, and duration of the attacks; (2) improve treatment responsiveness of acute attacks; and (3) improve function and reduce disability. According to the recent US Headache Consortium guidelines, pharmaceutical preventive therapies have been categorized on the basis of clinical efficacy, adverse events, safety profile, and clinical experience. Currently, preventive therapies are divided into 5 groups, ranging from those with proven high efficacy and mild to moderate adverse effects (group 1) to those proven to have limited or no efficacy (group 5).1

Niacin is not generally considered for the prevention of migraines. A thorough review of the literature revealed only anecdotal mention of niacin alone for treatment of migraine2 and 1 report that niacin may be useful as an adjunctive therapy for acute migraine.3

Our patient's experience suggests that niacin may be useful in migraine prevention. Niacin and its derivatives act as negative feedback regulators (Figure 1) on the kynurenine pathway, which is responsible for the conversion of tryptophan (a serotonin precursor) to nicotinic acid (niacin).4 Therefore, higher plasma concentrations of niacin may shunt tryptophan into the serotonin pathway, increasing the plasma serotonin level.3,4

Low systemic and central nervous system levels of serotonin have been strongly implicated in migraine pathogenesis.5 During migraine attacks, there is mobilization of serotonin, as evidenced by low platelet serotonin levels and increased urinary excretion of 5-hydroxyindoleacetic acid, its primary metabolite. In addition, serotonin is a pivotal neurotransmitter involved in central antinociception, and the dorsal raphe, which is the central repository for serotonin, has been implicated as a migraine generator on the basis of elegant positron emission tomographic studies of migraine sufferers during attacks.6,7

Sustained-release forms of niacin have been associated with hepatic toxicity when used as a substitute for immediate-release forms at doses appropriate for the treatment of hypercholesterolemia (1-2 g 2 or 3 times per day).8 No specific reports or recommendations about such toxicity at lower doses of the sustained-release form are available. One other important potential adverse effect is cutaneous flushing, which can be mild to severe and lessens with concomitant use of aspirin or nonsteroidal anti-inflammato-

tory drugs.8 The incidence of headache in patients using slow-release niacin is lower compared with placebo. The over-the-counter formulation comes scored and can be divided.8 Our patient reported no adverse effects.

CONCLUSION
Although conclusions cannot be drawn from a single case, sustained-release niacin merits further study as a potentially useful preventive therapy for migraine headache, especially in patients whose migraine headaches are resistant to other, more conventional, treatments.

REFERENCES