Menstrual Migraines: Are They Double the Trouble?

BY BETSY BATES
Los Angeles Bureau

LOS ANGELES — Migraine headaches were twice as likely during the menstrual cycle, and menstrual migraines lasted longer, were somewhat more painful, and proved significantly more resistant to treatment than migraines suffered during other times of the month, according to a study released at the annual meeting of the American Headache Society.

Dr. Brenda F. Pinkerman of the James A. Haley Veterans' Hospital in Tampa, Fla., reported a sharp spike in migraines on day 1 of the menstrual cycle in a prospective study of 107 women with a history of menstrual-related migraine.

The women were subjects in a larger study cosponsored by Ohio University in Athens and the National Institutes of Health. To be eligible, patients had to have a history of disabling migraines 3-20 days a month. Those enrolled in the menstrual migraine portion of the study had a mean age of 35 and suffered from migraines a mean 9 days per month.

The odds ratio of a migraine was 1.91—almost a doubling of risk—in a 4-day window beginning 2 days prior to and ending 2 days after day 1 of the menstrual cycle, compared with any other time of the month.

Perimenstrual migraines were significantly different from those occurring at other times of the month in a few ways, including the following:

- ► Duration: 23 hours, compared with 16 hours.
- ► Disability: occurs in conjunction with 86% of menstrual headaches vs. 76% of other headaches.
- ► Doses of triptans: two vs. 1.6; and rescue medications: 2.3 vs. 1.7.
- ► Pain-free response to medication at 2 hours: 7% vs. 13%.
- ► Recurrence after 4 pain-free hours: 36%, compared with 20%.

Other poster presentations at the meeting detailed the efficacy of rizatriptan administered early in the course of menstrual migraines and the safety and tolerability of frovatriptan taken prophylactically each month in women with regular menstrual cycles.

The TAME (Treat a Migraine Early) trials randomized 94 patients to take a single 10-mg dose of rizatriptan or placebo within 1 hour of the onset of any migraine occurring during the 2 days before to 3 days following day 1 of their menstrual cycles.

Freedom from pain at 2 hours was reported by 40 of 63 subjects (63.5%) taking rizatriptan, compared with 9 of 31 (29%) assigned to placebo, a highly significant difference. Nausea was significantly less common in subjects taking rizatriptan, although photophobia and phonophobia responses did not reach significance in the Merck-sponsored, multicenter study presented by Dr. Vincent Martin of the University of Cincinnati.

A final poster featured results from a yearlong, open-label extension study of frovatriptan used to prevent migraines in 308 patients with regular menstrual cycles and a history of menstrual migraine. Women were instructed to take two 5-mg doses of frovatriptan 2 days before the expected onset of menstruation, followed by 2.5 mg of frovatriptan twice daily for the next 5 days.

Dizziness, the most common side effect, occurred in about 7% of patients. The drug was well tolerated, with just 25 patients discontinuing long-term treatment for reasons other than migraine, reported Dr. Anne MacGregor of the City of London Migraine Clinic.

Perimenstrual migraines occurred in 44% of women taking prophylactic frovatriptan for a year—on par with the 41% who experienced perimenstrual migraines during a 3-month randomized, double-blind, placebo-controlled trial of 433 patients. In that pivotal study, 67% patients assigned to placebo experienced migraines.

The consistency of incidence data in the two trials suggests "durability of effect with continued use," Dr. MacGregor and associates noted in their poster's conclusion. "In addition, there was no evidence of rebound migraine."

The study was sponsored by Endo Pharmaceuticals of Chadds Ford, Pa., manufacturer of frovatriptan. ■

Frovatriptan Appears to Curb Menstrual Migraine

BY HEIDI SPLETE
Senior Writer

WASHINGTON — Women who took 2.5 mg of frovatriptan either once or twice daily for 6 days at the time of menstruation had significantly fewer—and less severe—menstrual migraines, compared with women who took a placebo, reported Dr. Marie Pinizzotto and her colleagues at Endo Pharmaceuticals.

The women on either regimen of frovatriptan also reported significantly fewer headaches in general and less functional impairment compared with the placebo group.

Data from the randomized, double-blind, three-way crossover study were presented in a poster at the annual meeting of the American College of Obstetricians and Gynecologists. The study was sponsored by Vernalis Development Ltd., and Endo Pharmaceuticals Inc.

Frovatriptan has been approved by the Food and Drug Administration for the acute treatment of migraines, both with and without aura, in adults, but it has not been approved for the prophylactic prevention of migraines.

The manufacturers are seeking an additional indication for the prophylactic treatment of menstrual migraines.

The patients in the study were randomized to receive each of the two treatment regimens or a placebo over the course of three different 6-day periods from 2 days before to 4 days after the onset of menstruation.

The incidence of pure menstrual migraines, defined as migraines that occurred during the time period from 2 days before to 3 days after the onset of menstruation, was significantly lower in both frovatriptan groups, compared with placebo.

These distinctive headaches occurred in 38% of the twice-daily frovatriptan group, compared with 51% of the once-daily group and 67% of the placebo group.

The intent-to-treat analysis included 179 women aged 18 years and older with at least a 1-year history of menstrually-related migraines. The mean age was 37 years, and 82% were white. On average, the study participants had a history of migraines greater than 10 years, and the average number of migraine attacks was one per month during the year prior to the study.

Moderate to severe headaches were reported by 25%, 32%, and 46% of women in the twice-daily frovatriptan, once-daily frovatriptan, and placebo groups, respectively. The incidence of functional impairment was 14%, 24%, and 35%, respectively.

Adverse events seen in the study included headache, nausea, dizziness, and nasopharyngitis. The incidence of these events was similar between the two groups, with the exception of upper respiratory tract infections, which were significantly more common in the patients treated with twice-daily frovatriptan.

Migraine With Aura Raises Risk of Coronary Heart Disease

BY DOUG BRUNK
San Diego Bureau

SAN DIEGO — Healthy women aged 45 years and older who have migraine with aura have a significantly increased risk of coronary heart disease, myocardial infarction, coronary revascularization, and angina, results from the largest study of its kind demonstrated.

On the other hand, migraine without aura was not associated with any such outcome, Dr. Tobias Kurth reported at the annual meeting of the American Academy of Neurology. "Since migraine without aura is far more common than migraine with aura, for most migraine patients our data indicate no increased risk of coronary heart disease," said Dr. Kurth of the preventive medicine division at Brigham and Women's Hospital, Boston.

Dr. Richard B. Lipton, who was invited to discuss the work, said the findings warrant being vigilant for coronary heart disease (CHD) risk factors in patients who have migraine with aura. This would include working with patients to modify CHD risk factors, noted Dr. Lipton, vice chair of neurology at Albert Einstein College of Medicine, New York. "It may be possible to devise risk factor modification strategies that might include aspirin or folate," he said.

The findings warrant being vigilant for CHD risk factors in all patients who have migraine with aura.

DR. LIPTON

In a study funded by the National Institutes of Health, Dr. Kurth and his associates followed 27,840 women aged 45 years and older who were enrolled in the Women's Health Study. All study participants were free of cardiovascular disease at baseline. The researchers used a Cox proportional hazards model to evaluate the association between migraine and risk of subsequent CHD and angina, while adjusting for cardiovascular risk factors including age, blood pressure, smoking status, body mass index, alcohol consumption, and exercise habits. The average follow-up was 10 years. "All women were age 45 or older, health professionals, and mostly white," Dr. Kurth added.

In the baseline questionnaire study, participants were asked if they ever had a migraine, and if they had a migraine in the previous year. "If the woman answered yes to the latter question, we asked further details about her migraine, including a question about aura," Dr. Kurth said. Women who did not report migraine served as the referent group.

At baseline, 5,125 (18%) reported a history of migraine and 3,610 (13%) reported current migraine. Of those who reported current migraine, 1,434 (40%) reported aura.

During 10 years of follow-up, 625 coronary heart disease events and 408 angina events occurred.

Compared with women who reported no history of migraine, women who reported migraine with aura had a 1.7-fold increased risk for CHD; a 2-fold increased risk for myocardial infarction; a 1.7-fold increased risk for coronary revascularization; and a 1.7-fold increased risk for angina. On average, the risk for all of these factors reached statistical significance in the sixth year of follow-up, said Dr. Kurth, also of Harvard Medical School, Boston.

Migraineurs without aura had no increased risk for any of the outcome events. ■

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