Migraines Spike, Last Longer During Menstruation

BY BETSY BATES
Los Angeles Bureau

LOS ANGELES — Migraine headaches were twice as likely during the menstrual cycle, and they 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—nearly 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 number of ways, including the following:

- Duration: 23 hours, compared with 16 hours
- Disability: occurring in conjunction with 86% of menstrual headaches vs. 76% of other headaches
- Doses of triptans: 2 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 prior to the expected onset of menstruation, followed by 2.5 mg of frovatriptan twice daily for the next 5 days.

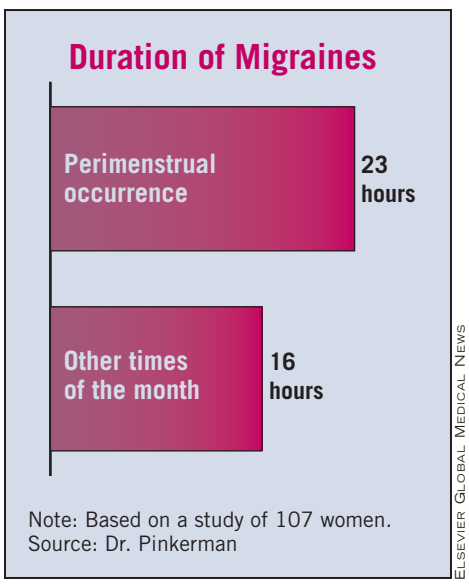
Dizziness, the most common side effect, occurred in about 7% of patients.

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, the investigators found that 67% patients assigned to placebo experienced migraines.

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



Siblings of Fibromyalgia Patients Have Heightened Pain Sensitivity

BY ROXANNE NELSON
Contributing Writer

SAN ANTONIO — Women with fibromyalgia and their siblings experience a generalized sensitivity to pain and lower levels of serum serotonin, according to new research.

These are the preliminary results of an ongoing study, said Dr. Laurence A. Bradley, who presented the study at the annual meeting of the American Pain Society.

Several recent studies have shown that first-degree relatives of women with fibromyalgia have higher lifetime rates of major depressive and anxiety disorders, compared with first-degree relatives of those with rheumatoid arthritis. Other research has found that fibromyalgia and reduced pressure pain thresholds aggregate in families.

"Some studies show that female relatives of the fibromyalgia probands display higher rates of psychiatric disorders than do male relatives," said Dr. Bradley, who is a professor of medicine in the division of clinical immunology and rheumatology at the University of Alabama, Birmingham.

The goal of the current study was to measure pain sensitivity and blood serum levels of serotonin in female patients with fibromyalgia, sex-matched healthy controls, and the siblings of both the fibromyalgia probands and the controls.

It is unknown if the first-degree relatives of women with fibromyalgia exhibit the same pain sensitivity, Dr. Bradley explained, and if there are differences in the expression of serotonin in these relatives as well as in the patients. It is also unclear to what degree serotonin levels may mediate differences in pain sensitivity, not only in patients vs. controls but also in relatives of patients vs. relatives of controls.

Thus far, the study has enrolled 49 families, and includes 16 probands with fibromyalgia; 5 male and 11 female proband siblings; 23 female, pain-free, control individuals; and 8 male and 15 female control siblings. All of the participants had blood drawn for measurement of serum serotonin, and underwent testing for pain thresholds. Pain sensitivity was measured after stimulation of pressure points and control points. Thermal heat and ischemic pain threshold tolerance was also evaluated in all study participants.

The pain threshold and serum serotonin levels were measured between probands vs. controls and proband siblings vs. control siblings. Dr. Bradley and his colleagues also evaluated the group differences in pain thresholds after controlling for the influence of serotonin.

"We found that not only were pain thresholds lower in probands as compared with healthy controls, but we also saw the same pattern in proband relatives as compared with the relatives of the control group," Dr. Bradley said. Lower levels of serum serotonin also were seen in both the patients and their siblings, compared with controls.

However, analysis revealed that serum serotonin levels partially mediated these group differences in pain threshold only for ischemic stimulation. Thus, serotonin appears to have a limited influence on pressure and thermal pain thresholds.

"The fact that we found only a modest relationship between ischemic pain thresholds and serotonin in patient probands and controls helps explain why early studies using tricyclic antidepressants and pressure point stimulation found no changes in pain response," Dr. Bradley said. In future studies, "we need to look at multiple factors such as differences in family environments and gene variances," he said. ■

TMS Studied for Ability to Short-Circuit Migraines

BY BETSY BATES
Los Angeles Bureau

LOS ANGELES — A handheld transcranial magnetic stimulation device delivered mixed results in a small study of patients with migraine headaches, Dr. Yousef Mohammad reported at the annual meeting of the American Headache Society.

Numerically, the device extinguished more migraines within 2 hours than did a sham device that made an audible buzz but delivered no magnetic pulses to the head, said Dr. Mohammad.

Among 23 patients who received two brief magnetic pulses, 30 seconds apart, 17 (74%) were headache-free or reported only minimal pain at 2 hours, compared with 9 of 20 patients (45%) randomized to sham device treatment. But perhaps because of the small sample size, the difference was not statistically significant, said Dr. Mohammad, a member of the neurology faculty at Ohio State University, Columbus.

The transcranial magnetic stimulation (TMS) treatment significantly reduced photophobia and phonophobia at 2 hours, compared with placebo, and more patients receiving TMS treatments rated the effectiveness as "excellent" or "very good."

Statistical trends were seen in the ability of TMS to reduce nausea and restore patients to normal functioning at 2 hours post treatment, although these end points also failed to reach statistical significance, he reported. The only adverse event found was left-sided numbness reported by one patient, but this symptom developed before administration of TMS.

Dr. Mohammad pointed out that the study design called for patients to receive their TMS or sham treatments at a hospital, leading to delays that potentially outlasted the device's potential to abort a migraine.

Patients with a history of migraine with aura were instructed to report to preselected hospitals immediately upon experiencing an aura. The TMS device or the sham device was placed either over the occipital region, if only aura was present, or over the area of maximum pain, if the headache had begun.

Efforts are underway to develop a user-friendly portable device that patients could use at home at the first sign of an impending migraine. This version of the device will be put to the test in a large, multicenter trial that will also use sham devices as placebo, said Dr. Mohammad, who disclosed that he is an investigator for Neuralieve Inc., the commercial sponsor of the study. ■