

Abuse, Cardiovascular Risk Linked in Adult Migraineurs

BY SHERRY BOSCHERT

FROM THE ANNUAL MEETING OF THE AMERICAN HEADACHE SOCIETY

LOS ANGELES — Adults with migraines who also had cardiovascular risk factors were 39%-83% more likely to report having been abused or neglected as children compared with migraineurs without cardiovascular problems in a study of 1,348 patients.

In addition, a linear relationship was found between the risk of stroke/transient ischemic attack (TIA), myocardial infarction, or both and the total number of types of abuse reported by patients, Dr. Gretchen E. Tietjen reported at the meeting.

"This certainly suggests that childhood maltreatment may adversely influence cardiovascular status—both disease and risk factors—in adulthood," she said.

Previous studies have identified associations between childhood maltreatment and adult morbidities, including cardiovascular disease. But this is the first study to look at those associations in migraineurs.

Headache specialists determined the migraine diagnosis and attack frequency for the patients at 11 U.S. and Canadian headache centers. Patients reported whether they had been told by a physician that they have cardiovascular disease, specific cardiovascular risk factors, or other comorbidities while completing a self-administered electronic questionnaire, which included the Childhood Trauma Questionnaire to identify childhood maltreatment.

One or more cardiovascular risk factors was reported by 71% of patients, including hypertension, hyperlipidemia, obesity, obstructive sleep apnea, or ever having smoked. A small percentage of patients reported a history of stroke or TIA (5%) or prior MI (4%).

The questionnaire asked about physical, sexual, or emotional abuse and about physical or emotional neglect. Migraineurs with cardiovascular disease were more likely to report childhood abuse rather than less-severe neglect, compared with migraineurs without cardiovascular disease, reported Dr. Tietjen and her associates in the American Headache Society's Women's Issues Research Consortium.

Patients with one or more cardiovascular risk factors said they had experienced more types of abuse as children compared with migraineurs without cardiovascular risk factors, said Dr. Tietjen, professor and chair of neurology at the University of Toledo, Ohio. (See chart.)

Because the analysis was controlled for age, race, gender, income, education, and each of the other in-



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Major Finding: Adults with migraines who had cardiovascular risk factors were 39%-83% more likely to report abuse or neglect during childhood, compared with migraineurs without cardiovascular problems.

Data Source: Cross-sectional study of 1,348 adult migraine patients at 11 U.S. and Canadian headache centers.

Disclosures: Dr. Tietjen has received research grants from GlaxoSmithKline, and consulting fees and honoraria from MAP Pharmaceuticals.

dividual risk factors, "those are pretty significant differences," she said. "I certainly think that abuse is related to migraine in some way, but how well it fits in" remains to be determined in future studies of better databases.

"I'd really like to look at young people—people that are in the 18-to-24 range, where maybe migraine is all they have, but if they have a history of abuse it may mean that they are predisposed to develop some of these other conditions," Dr. Tietjen said in an interview at the meeting. Cognitive-behavioral therapy might help these young people change their response to stressful stimuli.

A separate analysis of the study's data identified three constellations of comorbidities in migraineurs with distinct demographic, headache, and psychosocial profiles, Dr. Tietjen reported in a separate presentation at the meeting.

One group of 231 patients reported a relative absence of comorbid conditions. Another 669 patients fit into a group of "pain conditions," including irritable bowel syndrome, chronic fatigue syndrome, fibromyalgia, interstitial cystitis, uterine fibroids, and arthritis. The remaining 448 patients were grouped in "metabolic and psychiatric conditions," including hypertension, diabetes, hyperlipidemia, depression, and anxiety.

Compared with the group without comorbidities, the pain and metabolic/psychiatric groups were older, more likely to be white, had more headaches per month, were more likely to have chronic migraine, and had higher disability scores on the six-item Headache Impact Test. The two comorbidity groups were associated with a doubling or tripling in risk for childhood maltreatment, especially emotional abuse, in an adjusted logistic regression analysis, Dr. Tietjen said.

Patients in the pain or metabolic/psychiatric comorbidity groups were three times as likely as the no-comorbidity group to report childhood emotional abuse or emotional neglect and twice as likely to report physical or sexual abuse. Reports of physical neglect were twice as likely in the pain group and three times as likely in the metabolic/psychiatric group, compared with the control group.

Future studies of general populations with headache should carefully classify them by headache criteria, Dr. Tietjen and her associates suggested. A better understanding of the link between adverse childhood experiences and migraine might improve understanding of the pathophysiology and lead to better therapies, she said.

'This certainly suggests that childhood maltreatment may adversely influence cardiovascular status.'

DR. TIETJEN

Odds Ratios for Type of Childhood Abuse Associated With CV Risk Factors

Type of maltreatment	One or more cardiovascular risk factors present	P value
Emotional abuse	1.83	<0.001
Physical abuse	1.70	0.002
Emotional neglect	1.51	0.002
Physical neglect	1.40	0.045
Sexual abuse	1.39	0.032

Note: Based on self-reports by 1,348 adult patients with migraine at 11 U.S. and Canadian headache centers.

Source: Dr. Tietjen

Migraine Drug Has Similar Effects in Patient Subgroups

BY SHERRY BOSCHERT

FROM THE ANNUAL MEETING OF THE AMERICAN HEADACHE SOCIETY

LOS ANGELES — The experimental drug telcagepant for acute migraine therapy appears to be tolerated by patients with stable coronary artery disease and to be consistently effective in various subgroups of patients, according to several analyses of randomized, double-blind, placebo- or active-controlled studies.

Previous studies have shown that telcagepant, an oral calcitonin gene-related peptide (CGRP) receptor antagonist, is effective in acute treatment of migraine (Neurology 2009;73:970-7; Lancet 2008;372:2115-23; Neurology 2008;70:1304-12).

The new analyses were led by employees of Merck, which is developing telcagepant and which funded the studies. Merck also had been developing the drug for migraine prophylaxis, but stopped those trials when some patients taking twice-daily doses for 3 months developed elevated liver enzyme levels, a company spokeswoman said in an e-mail interview after the meeting. Following discussions with the Food and Drug Administration at the end of 2009, Merck is conducting an additional safety study this year before regulators consider the drug further—a 6-month study of 4,500 females with menstrually associated migraine who will take 140 mg of telcagepant or placebo once daily for 7 consecutive days on a monthly basis.

No Cardiovascular Problems Noted

A double-blind, crossover study randomized patients with migraines and stable coronary artery disease to one of two treatment groups. Patients in the first group treated up to 12 moderate to severe migraines with telcagepant in a 280-mg tablet plus a 300-mg capsule during a 6-week period, then treated 12 more migraines in the next 6-week period with acetaminophen 1,000 mg. Patients in the second group got placebo for the first moderate to severe migraine attack, then acetaminophen for up to 11 more migraines in the first 6-week period; in the second 6 weeks, up to 12 migraines were treated with the telcagepant regimen.

Final data were available to analyze safety in 184 patients and efficacy in 105 patients.

Adverse events were reported within 48 hours of treatment by 17 of 98 patients on telcagepant (17%) and 9 of 86 patients on acetaminophen (10%), reported Dr. Tony Ho, senior director of clinical research at Merck Research Laboratories, North Wales, Penn., and his associates. Drug-related adverse events were reported by eight patients (8%) on telcagepant and four (5%) on acetaminophen. No patients stopped treatment because of adverse events.

Three serious vascular events—two reports of chest pain after telcagepant and one report of renal artery stenosis after acetaminophen—were sent for adjudication by a blinded independent expert committee. The committee declared all to be non-thromboembolic events, and each occurred longer than 48 hours after migraine treatment. No patients had transaminase elevations three times the upper limit of normal or higher.

The study did not find significant differences in efficacy, perhaps because of the small number of patients, the investigators suggested. No pain was reported in 13 (25%) of 52 patients 2 hours after taking telcagepant, compared with 10 (19%) of 53 patients on placebo.

The apparent lack of a significant risk of using telcagepant in patients with coronary artery disease is a huge plus. The drug could be an alternative for patients who can't take triptans, Dr. Leslie Kelman, medical director of the private practice Headache Center of Atlanta, said in an interview. He was not involved in the telcagepant studies.

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