Botox May Reduce Frequency of Migraines

ARTICLES BY
MICHELE G. SULLIVAN

PHILADELPHIA — OnabotulinumtoxinA appears to be a safe, effective, and well-tolerated headache prophylactic for patients with chronic migraine.

Two large randomized controlled trials showed that the toxin significantly reduced migraine frequency and improved headache-related disability over a 24-week period, Dr. David W. Dodick reported at the International Headache Congress.

The studies—PREEMPT 1 and 2—were conducted at 22 centers in North America and Europe, and included 1,384 patients (average age 41 years). Each trial consisted of a 4-week baseline period, during which patients kept a daily headache diary, followed by 24 weeks of treatment during which patients received two injection cycles of either placebo or onabotulinum toxin A (Botox), which has not been approved by the Food and Drug Administration for migraine prophylaxis. From 24 to 56 weeks, there was an open-label trial consisting of three injection cycles of the study drug, said Dr. Dodick of the Mayo Clinic Arizona, Phoenix.

At baseline, patients reported a mean of 20 headache days per month, 19 of which were considered migraine days, with a mean of 290 cumulative headache hours. The mean score on the Headache Impact Test–6 (HIT-6) survey was 65, indicating severe impact. Most of the patients (93%) also reported severe headache-related disability, and 65% were overusing acute pain medications.

The Botox group had a significantly greater reduction in headache days and migraine days than did those taking placebo.

DR. DODICK

During the double-blind phase, patients randomized to the treatment group received two injection cycles (one every 12 weeks) of onabotulinumtoxinA 155 U.

The medication was injected at 31 sites across seven muscle areas in the head and neck. At the physicians' discretion, an additional 40 U could be injected among three additional muscle groups; the maximum dose was 195 U.

The study's main end point was frequency of headache days; secondary end points were frequency of migraine days, moderate/severe headache days, monthly headache hours, and proportion of patients with a severe HIT-6 score.

At 24 weeks, patients in the active group had a significantly greater reduction in headache days and migraine days than did those taking placebo (–8 vs. –6). The HIT-6 score also declined significantly more among the active group (–5 points vs. –2 points). Patients receiving the study drug had a greater decrease in cumulative headache hours per month (–120 vs. –80), and a lower proportion had a severe score on the HIT-6 survey (68% vs. 78%).

"The only outcome that was not statistically significantly better among the active group than the placebo group was the percentage overusing acute pain medications. However, the use of triptans did decrease significantly in the active group compared to the placebo group," Dr. Dodick said at the congress, which was sponsored by the International Headache Society and the American Headache Society.

Adverse events occurred in 62% of those taking the study drug and 52% of those taking placebo—a significant difference, he said.

There were also significantly more treatment-related adverse events in the onabotulinumtoxinA group (29% vs. 13%). One serious treatment-related adverse event did occur in the active group—a severe postinjection migraine that required hospitalization.

Adverse events occurring in more than 5% of the entire study group were neck pain (9%) and upper respiratory infection (5%).

Four patients in the active group and one in the placebo group discontinued active injections because of an adverse event.

The study was sponsored by Allergan Inc., manufacturer of the study drug. Dr. Dodick reported having received honoraria from the company. ■

Stroke, Heart Attack Found Higher in Migraine Patients

PHILADELPHIA — Migraine with or without aura is associated with a significant increase in the risk of cardiovascular disease, including stroke and heart attack.

Numerous studies have hinted at the association between migraine with aura and cardiovascular events, Dr. Marcelo E. Bigal reported at the International Headache Congress. But the population-based study he performed with his colleague, Dr. Richard Lipton, was the first to examine the association in a large national sample in which migraine, with and without aura, had been officially diagnosed according to accepted standards.

Dr. Bigal of Merck Research Laboratories, Whitehouse Station, N.J., and his coauthor, Dr. Lipton of Albert Einstein College of Medicine, New York, extracted their data from the American Migraine Prevalence and Progression Study. It was the largest study of migraine sufferers ever conducted, analyzing symptoms and treatment patterns in a representative sample of 162,576 Americans aged 12 years and older.

The cardiovascular substudy included data on 6,102 adults with migraine and 5,243 controls. Overall, migraineurs were significantly more likely than controls to have diabetes (13% vs. 9%), hypertension (33% vs. 26%), and hypercholesterolemia (33% vs. 26%).

Framingham risk scores also were significantly higher for overall migraine and for those with migraine with and without aura (mean 11) than they were for controls (mean 9). Myocardial infarction had occurred in 2% of controls and 4% of migraineurs, which yielded an unadjusted odds ratio of 2.2. Stroke occurred in 1.2% of the controls and 2% of the migraineurs—a significant 60% increased odds. Rates of stroke were higher in those who had migraine with aura (4%) than without aura (1%).

The significantly increased risks remained after adjusting for sex, age, disability, triptan use, diabetes, smoking, hypertension, and high cholesterol. Overall, migraineurs were twice as likely as controls to have had a heart attack and 50% more likely to have had a stroke. Migraineurs with aura were three times more likely than controls to have had either of those outcomes. Migraineurs without aura were twice as likely as controls to have had a heart attack, but had no increased risk of stroke.

"Both migraine with and without aura are associated with cardiovascular disease, and providers should be aware of these associations to properly identify individuals at particularly high risk, as well as to plan treatment that targets not only migraine, but the complications potentially associated with it," Dr. Bigal said at the congress, which was sponsored by the International Headache Society and the American Headache Society.

Dr. Bigal is a full-time employee of Merck Research Laboratories. Dr. Lipton has received research grants and honoraria from Merck and is a member of its advisory board. ■

Migraine With Aura Increases Risk of Cardiovascular Death

PHILADELPHIA — Men and women with a history of migraine with aura were significantly more likely to die from cardiovascular disease than were those without headache.

Women with nonmigraine headache were also significantly more likely to die from cardiovascular disease than were women without headache, but the hazard ratio was smaller, Dr. Larus S. Gudmundsson wrote in a poster presented at the International Headache Congress. The International Headache Society and the American Headache Society sponsored the congress.

Dr. Gudmundsson of the University of Iceland, Reykjavik, and his colleagues used data extracted from the Reykjavik Study, a population-based cohort of adults followed from middle age, representing 474,360 person-years of observation. The cohort comprised 18,882 subjects who were a mean of 53 years old at baseline. Baseline interviews took place between 1967 and 1991.

The investigators divided the cohort into four categories: those without a headache once or more per month; those with nonmigraine headache; those with migraine without aura; and those with migraine and aura. Auras were defined as visual, sensory, or both. Patients with nonaura headache symptoms, including nausea, unilateral location, and photophobia, were placed in the "with migraine without aura" category.

After entering the study, subjects were followed for up to 40 years (mean follow-up 26 years). Statistics on those who died during that time were obtained from the Icelandic government and hospital records.

Cox regression analysis was used to control for age, body mass index, smoking, blood pressure, hypertension medication, oral contraceptive use, diabetes, and lipid levels.

During assessment of all-cause mortality, both men and women with migraine and aura were at a significantly increased risk of death, compared with subjects without headache (20%). For cardiovascular death, the hazard ratio was 1.38 among men with migraine and aura and 1.18 among women with migraine and aura.

Adults who had migraine without aura did not have an increased risk of cardiovascular death, compared with those without headache.

However, women with nonmigrainous headaches were at a slightly—though still statistically significant—elevated risk of cardiovascular mortality, compared with women without headache (HR 1.14). The risk did not change significantly for men with nonmigrainous headache.

The authors pointed out that the increased risk of death, while significant, was not as great as the risks conferred by other common factors. "The risk is relatively low when compared with conventional risk factors such as hypertension, high cholesterol, and smoking," they said.

Conflict of interest disclosures were not available for Dr. Gudmundsson. ■

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