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Surgical Deactivation of Trigger Sites for Migraine—Effective Treatment or Expensive Placebo?

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BOSTON—Can surgery to decompress nerves at migraine trigger sites alleviate, or even eliminate, the disorder? Physicians sought to answer this question during a debate at the 2013 International Headache Congress.

Bahman Guyuron, MD, Chair of the Department of Plastic and Reconstructive Surgery at University Hospitals Case Medical Center in Cleveland, presented evidence that an outpatient surgical technique can reduce the number of migraine headaches by at least 50% for approximately 80% of patients. Dr. Guyuron began his research on migraine 13 years ago and left his career in cosmetic surgery eight years ago for an academic position.

Hans-Christoph Diener, MD, PhD, Chair of the Department of Neurology at the University of Duisburg–Essen, Germany, cited multiple methodologic shortcomings in a placebo-controlled trial presented as evidence for the surgery's effectiveness. Rather than supporting the surgical treatment of migraine, the current data indicate that it "is an invasive and expensive placebo treatment," he said.

Patients Had Reduced Migraine Frequency After Surgery

Dr. Guyuron first became interested in treating migraine when several patients who had undergone forehead rejuvenation, which involves the removal of forehead muscles that cause frown lines and the detachment of a small nerve in the temple, later told him that they no longer had headaches. When he and his colleagues performed a retrospective study of 314 patients who had undergone forehead rejuvenation, they found that 39 patients had either complete elimination of or significant improvement in their migraine headaches. The study's average follow-up time was 47 months.

After developing a surgical method for treating migraine, Dr. Guyuron and a neurologist operated on 22 patients with migraine who previously had filled out questionnaires and responded favorably to Botox injections. Of these patients, 10 had complete elimination of headaches, 11 had significant improvement, and one had no response to surgery.

Dr. Guyuron later developed an operation to decompress the occipital nerve in an effort to treat migraine in patients who complained of pain starting at this site. He and his neurology colleagues conducted a prospective, randomized study in which 100 subjects were assigned to surgery and 25 were assigned to a control group. A total of 89 surgical patients completed a one-year follow-up, and 82 of them had at least 50% reduction in

migraine frequency, intensity, and duration. Migraine was eliminated in 31 patients, and 57% had improvement. In the control group, 19 patients completed a one-year follow-up, and three patients had 50% improvement.

At the recommendation of a neurologist, Dr. Guyuron designed a sham surgery to study the real surgery in a placebo-controlled trial. He and his colleagues randomly assigned 49 migraineurs to a treatment group and 26 to a placebo group. At one year, 41 patients in the treatment group had a reduction in migraine headaches of at least 50%. Fifteen patients in the sham surgery group had a similar response. In addition, 28 patients in the real surgery group had complete elimination of migraine during the study, compared with one subject in the sham surgery group.

Adverse effects of the surgery were minor, said Dr. Guyuron. Transient numbness along the sensory distribution of the target nerve was common, and one patient had permanent numbness. Several patients had hollowing of the temple but were unaware of this outcome.

Response to Surgery May Be Equivalent to Placebo Effect

Based on the current evidence, surgical treatment of migraine "should be strongly discouraged," said Dr. Diener. He pointed out various methodologic flaws that he said detracted from the placebo-controlled trial. For example, the investigators screened 317 patients and administered onabotulinumtoxin A at the trigger points of 130 patients. The 76 patients who responded to onabotulinumtoxin A were chosen for the trial. "Botulinum toxin is not superior to placebo in episodic migraine," said Dr. Diener, "so you are using an ineffective therapy with a responder rate similar to placebo to pick out the patients who will undergo surgery."

Surgery was performed on either the frontal, temporal, or occipital region of each patient. In light of the numbers of patients randomized to receive real versus sham surgery (19 vs 10 for the frontal approach, 19 vs eight for the temporal approach, and 11 vs seven for the occipital approach), "this study is clearly underpowered," said Dr. Diener. "We know that a 2:1 randomization increases the expectation and therefore increases the placebo response."

Another problem, according to Dr. Diener, is that the study's primary end point was an index of headache frequency, intensity, and duration. The International Headache Society strongly discourages the use of indices as end points because they are highly nonlinear and nearly impossible to analyze statistically, he said. The statistical methods used in the study were not appropriate for an index and did not enable analysis of variance, he added.

Migraine was eliminated in 57% of patients in Dr. Guyuron's study, but the cure rate in previous randomized, placebo-controlled drug trials is approximately 5%, said Dr. Diener. Comparing Dr. Guyuron's study with open trials of patent foramen ovale closure for migraine might explain this discrepancy. "All the open trials have a cure rate of about 50%, but the only properly conducted randomized trial had a cure rate of 4%," said Dr. Diener. Patients who had migraine elimination in Dr. Guyuron's study "were responders to placebo, and this is the only way to show a success rate of 50%," said Dr. Diener. "There was no cure of migraine."

Another problematic aspect of Dr. Guyuron's study is that patients were examined by neurologists before undergoing surgery, but not after surgery. In addition, the study's premise that migraine results from trigger sites is implausible, said Dr. Diener. "Migraine is a complex disease of the brain. How could surgery affect the epigenetics of 22 different genes," he asked.

"The study, unfortunately, has basically all the methodologic mistakes that can be made in a randomized trial," added Dr. Diener. "If you actually want to use a placebo, use acupuncture. It will not hurt anyone."

—Erik Greb
Senior Associate Editor

Suggested Reading

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