Deep Brain Stimulator Approved for OCD

BY ALICIA AULT

The Food and Drug Administration has approved humanitarian use of Medtronic's experimental deep brain stimulation device to treat severe obsessive-compulsive disorder.

It is the first approval for deep brain stimulation for a psychiatric condition. The technique is being studied for a variety of neurologic and psychiatric disorders, including treatment-refractory depression and Tourette syndrome.

Under the special Humanitarian Device Exemption (HDE) approval, Medtronic can market its device, Reclaim DBS Therapy, for obsessive-compulsive disorder (OCD). But the company will likely not pursue any marketing since it has not proved effectiveness, Mark Rise, Ph.D., a distinguished scientist in Medtronic's neuromodulation division, said in an interview. Also, under FDA rules, Medtronic can recover only the cost of research, development, fabrication, and distribution for Reclaim.

Medtronic will not pursue further development of Reclaim for OCD and is not sponsoring any studies in that condition. Instead, it will pursue the indication of treatment-resistant depression for the device, Dr. Rise said.

To gain HDE approval, a device must be intended to treat or diagnose a condition affecting fewer than 4,000 people per year in the United States. (Reclaim for OCD is currently intended to treat severe OCD patients for whom medication and psychotherapy is not working.) Also, a manufacturer has only to "demonstrate the safety and probable benefit" for a device to receive approval.

"Deep brain stimulation using the Reclaim system may provide some relief to certain patients with severe obsessive-compulsive disorder who have not responded to conventional therapy," said Dr. Daniel Schultz, director of FDA's Center for Devices and Radiological Health. It is not a cure, however. "Individual results will vary and patients implanted with the device are likely to continue to have some mild to moderate impairment in functioning.

The agency approved Reclaim after reviewing data on 26 patients with treatment-resistant OCD. The most recent update of data on those patients was presented at the American Association of Neurological Surgeons annual meeting in April 2008.

According to the FDA, on average, patients had a 40% reduction in symptoms after 12 months of therapy. ■

Alcohol Abuse May Lead Depression's Development

BY MARY ANN MOON

Alcohol abuse and dependence appear to lead to major depression, rather than vice versa, according to a collection of statistical analyses reported in the Archives of General Psychiatry.

Researchers used data from the Christchurch Health and Development Study, a cohort of 635 boys and 630 girls born in urban New Zealand in 1977 and followed through age 25, to examine the well-known relationship between alcohol abuse or dependence and depression. They used several advanced statistical modeling methods to explore possible causal pathways between the two disorders, said David M. Fergusson, Ph.D., and his associates at the University of Otago, Christchurch.

At age 24-25 years, approximately 14% of the sample met DSM-IV criteria for alcohol dependence (6%) or abuse (8%), and 14% met criteria for major depression.

At all ages, there were clear and significant trends for alcohol abuse to be associated with depression, such that subjects who abused alcohol were nearly twice as likely to fulfill criteria for major depression as were those who did not abuse alcohol. In contrast, major depression did not appear to predispose subjects to alcohol abuse.

In addition, the relationship between alcohol abuse and depression was not found to arise from some common factor underlying both disorders, Dr. Fergusson and his colleagues said (Arch. Gen. Psych. 2009;66:260-6).

The researchers noted that these results contradict those of previous studies, some of which have suggested that the causal relationship moves in the opposite direction because some people with depressive symptoms self-medicate with alcohol. ■

CLINICAL GUIDELINES FOR FAMILY PHYSICIANS

Second-Generation Antidepressants

BY NEIL S. SKOLNIK, M.D., AND NATALIE E. LINGENFELTER, D.O.

The American College of Physicians developed evidence-based recommendations for the treatment of depressive disorders using second-generation antidepressants. Evidence was examined for acute, continuation, and maintenance phases of major depressive disorder and dysthymia for response to treatment as well as full remission of symptoms (Ann. Intern. Med. 2008;149:725-33).

Guidelines are most useful when they are available at the point of care. A free and concise handheld computer version of this guideline is available for download at www.redi-reference.com.

No significant difference was found among second-generation antidepressants with regard to efficacy, effectiveness, or quality of life. Success in maintaining response or remission was similar among the various agents including selective serotonin reuptake inhibitors (SSRIs: citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline), serotonin norepinephrine reuptake inhibitors (SNRIs: mirtazapine, venlafaxine), selective serotonin norepinephrine reuptake inhibitors (SSNRIs: duloxetine), and other second-generation drugs (bupropion, nefazodone, trazodone).

In 6-12 weeks of acute phase treatment, 38% of patients failed to respond and 54% failed to achieve remission. In one study, switching to sustained-release bupropion, sertraline, or extended-release venlafaxine helped an additional one in four patients achieve remission. Patients who fail to respond to first- and second-line therapies may require the use of multiple agents.

Examination of the treatment of depressed patients with accompanying symptom clusters, including anxiety, insomnia, melancholia, pain, and psychomotor changes, revealed no significant difference in the efficacy of second-generation antidepressants at relieving depression in patients with these symptom clusters. Treatment of symptom clusters in patients with accompanying depression was examined and, again, no significant difference in efficacy was seen for the relief of accompanying anxiety, insomnia, pain, or somatization. Efficacy of second-generation antidepressants was evaluated in select subgroups and special populations, with no differences found on the basis of age, sex, race, ethnicity, or comorbidities.

The most common adverse events associated with second-generation antidepressants were nausea, vomiting, diarrhea, constipation, dizziness, headache, insomnia, and sexual dysfunction. Side effects were similar among the drugs, with a few subtle differences. Venlafaxine had higher rates of nausea and vomiting than other SSRIs. Sertraline had a higher incidence of diarrhea. Greater weight gain was reported with use of mirtazapine and paroxetine. Trazadone was associated with more somnolence. Bupropion had a significantly lower risk of sexual dysfunction, and paroxetine was associated with increased risk. Weak evidence exists that bupropion may be associated with an increased risk for seizures, and venlafaxine may be associated with an increased risk for cardiovascular events. There was no difference among second-generation antidepressants with regard to increased risk of completed suicide, though the SSRIs showed an increased risk of nonfatal suicide attempts (odds ratios of 1.57 and 2.25 in two different meta-analyses).

Current evidence does not definitively support the use of one second-generation antidepressant over another. The following recommendations are based on the compilation of available data.

▶ **Agent selection:** Select second-generation antidepressants for the treatment of acute major depression based on side effect profiles, cost, and patient preference.

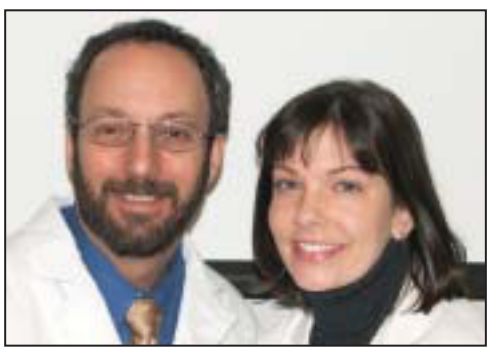
▶ **Patient assessment:** 1-2 weeks after initiation of antidepressant therapy, begin assessing patient status, response, and adverse effects regularly. The Food and Drug Administration recommends close monitoring for increases in suicidal thoughts or behaviors after starting antidepressants. Monitoring for increased agitation and negative changes in behaviors and thoughts should begin 1-2 weeks after starting therapy because increases in agitation may indicate a heightened risk for suicide.

▶ **Treatment modification:** If, after 6-8 weeks of therapy, the patient does not experience an adequate response to treatment, modify therapy. Monitor the patient for response to treatment to decide whether to switch antidepressants or add additional medications.

▶ **Response times:** For treatment of first episodes of major depression, therapy should be continued for 4-9 months after adequate response. Longer durations of therapy are appropriate for patients with two or more episodes.

The Bottom Line

Selection of second-generation antidepressant should be made on the basis of side effects, cost, and patient preference. Patients should be monitored closely for response and side effects, including suicidal ideations. Therapy should be changed if it is ineffective after several weeks of therapeutic dosing. Therapy should be continued for a minimum of 4 months after symptom resolution to prevent recurrence.



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