Neurostimulation Works in Early Parkinson's

Brain stimulation may offer benefits earlier in the course of Parkinson's disease than it is currently used, researchers found.

In a randomized, controlled trial, patients with early motor complications had a 26% increase in quality of life scores if they had neurostimulation compared with a 1% worsening for those on standard medical therapy, G. Deuschl, MD, of the University of Kiel in Germany, and colleagues reported online in the New England Journal of Medicine.

Since the treatment appears better than standard medical therapy "before the appearance of severe disabling motor complications," it may be an option for patients "at an earlier stage than current recommendations suggest," they wrote.

Mark Stacy, MD, of Duke University, who was not involved in the study, said some doctors have already been practicing that way.

"Many of us are already using the treatment earlier on, so this data is important because it confirms what we believe," Stacy said in an interview with MedPage Today. "It gives us more confidence to think about this with our patients. It helps us to provide data to people ... [to show comparative outcomes] 2 years in."

Neurostimulation is already an established treatment for advanced Parkinson's disease. But Deuschl and colleagues hypothesized that it would benefit patients in earlier stages of the disease as well.

They conducted the 2-year EARLYSTIM trial, enrolling 251 Parkinson's patients with early motor complications. Patients had a mean age of 52 and had had the condition for a mean of 7.5 years.

They were randomized to either neurostimulation of the subthalamic nucleus, or to standard medical therapy.

The primary endpoint was quality of life at 2 years as measured by the Parkinson's Disease Questionnaire (PDQ-39). Secondary outcomes included Parkinsonian motor disability, activities of daily living, levodopa-induced motor complications, and time with good mobility and no dyskinesia.

Overall, the team found that neurostimulation improved quality of life at 2 years by a mean 7.8 points, compared with a worsening of 0.2 points for those on medical therapy, a significant difference of \( P=0.002 \).

It also proved superior for the secondary endpoints, with significant mean differences in scores between groups for:

- Motor disability (16.4 points, \( P<0.001 \))
- Activities of daily living (6.2 points, \( P<0.001 \))
- Levodopa-induced motor complications (4.1 points, \( P<0.001 \))
- Time with good mobility and no dyskinesia (1.9 hours, \( P=0.01 \))

The differences were typically driven by improvements in the neurostimulation arm and not worsening in the medical therapy arm. For instance, there was no significant change from baseline in motor score and only minimal worsening in activities of daily living for those on medical therapy.

Deuschl and colleagues reported no significant differences in serious adverse events, which occurred in 54.8% of neurostimulation patients and 44.1% of those in the medical therapy group.
Two patients in the neurostimulation group and one in the medical therapy group committed suicide. Suicidal ideation and suicide attempts were of similar frequency in the two groups, but depression was more frequent among neurostimulation patients -- suggesting that stimulation isn't associated with a greater risk of suicide, they wrote.

Also, serious adverse events related to surgical implantation of the device occurred in 17.7% of patients, and that included a brain abscess and a case of unspecific edema -- both of which "resolved completely," they reported.

In an accompanying editorial, Caroline Tanner, MD, PhD, of Stanford University, called it "one of the most rigorously conducted trials of neurostimulation," but warned that the patients in the trial don't represent most patients with Parkinson's disease -- given that all were younger than 60 at the time of surgery, they didn't have dementia, and they all had a good response to levodopa challenge.

Only 11% of Parkinson's cases are diagnosed before age 60, Tanner wrote, and about a third tend to have dementia.

"Whether these results would be obtained in older patients with Parkinson's disease or in less-experienced medical centers is not known," she wrote.

Tanner was also cautious about suicide in the neurostimulation group. Since the risk of suicide appears to persist for years after surgery, she wrote that "careful and sustained monitoring should be a requirement."

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The researchers reported relationships with Medtronic, Lundbeck, Teva, Union Chimique Belge, Bayer, Meda, Onon, GlaxoSmithKline, Boehringer Ingelheim, Desitin, Gianni Public Relations, Eumecom, Cephalon, Abbott Laboratories, GE Healthcare, Bayer Schering, Thieme, Ipsen, Merck, Merz, Aqueuttant, Novartis, Eutherapie, BioProject, and Roche.

Tanner reported relationships with the Michael J. Fox foundation, ADAMAS Pharma, Impax Pharma, Parkinson's Institute, Parkinson's Disease Foundation, and Brin Foundation.

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