

Compliance a Challenge for Older Epilepsy Patients

BY MITCHEL L. ZOLER
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PHILADELPHIA — Compliance with antiepileptic drugs was worse in the elderly than in younger patients, and noncompliant patients were more likely to have serious sequelae including death, based on results from two separate studies.

Nonadherence among patients aged 65 years or older occurred in 41% of 1,278 patients studied, Dr. Alan B. Ettinger reported at the annual meeting of the American Epilepsy Society. In contrast, in an independent study of 33,658 Medicaid patients in three states the rate of noncompliance among all adults aged 18 years and older was about 26%, reported Annie Guérin, a researcher at Analysis Group Inc. in Boston.

Nonadherence is more likely to be a problem for the elderly because of several factors including their higher likelihood of living alone or having dementia, said Dr. Ettinger, director of the Comprehensive Epilepsy Center at Long Island Jewish Hospital in New Hyde Park, N.Y. The elderly are also more susceptible to complications of noncompliance because of their comorbidities, such as their higher prevalence of osteoporosis, which can boost the risk of bone fracture in a fall during a seizure, Dr. Ettinger said in an interview.

His study included elderly individuals with epilepsy who were patients in any of 30 health plans that covered about 38 million U.S. patients during January 2000–December 2005. Epilepsy patients were identified by at least one diagnosis of epilepsy or nonfebrile convulsions during the study period and by getting at least two prescriptions for antiepileptic drugs. Patients were judged compliant with their medications if they filled prescriptions and had at least one antiepileptic drug on hand for at least 80% of the days when they were prescribed the drug (a medication possession ratio—MPR). Patients

with an MPR of less than 80% were considered nonadherent. The average age of the elderly patients in the study was 73 years.

Of the more than 1,200 elderly epilepsy patients identified in the study series, 41% had an MPR of less than 80%. Within the nonadherent group 25% had poor adherence, with MPR rates of less than 60%, Dr. Ettinger said.

Nonadherent patients were much more vulnerable to having a serious seizure, with a 14% rate of serious seizures in patients with a MPR of less than 60%, and a 12% rate in those with a MPR of less than 80%. In compliant patients (MPR of 80% or higher), the rate of serious seizures was about 8%. Nonadherence was also linked to a significant, \$2,400 increase in the average cost of health care, compared with the compliant, elderly patients.

Physicians who care for elderly patients with epilepsy need to educate them about the importance of compliance with antiepileptic drugs, and they need to use social services and family members to help maintain compliance. Another important step is to assess how well patients feel when taking antiepileptic

drugs. It may be necessary to switch patients to drugs that are better tolerated if adverse effects are an issue. The better tolerated antiepileptic drugs are generally the newer agents, such as gabapentin, pregabalin, lamotrigine, and levetiracetam.

The study was sponsored by GlaxoSmithKline, which markets lamotrigine (Lamictal). Dr. Ettinger is an adviser to and gives lectures for GlaxoSmithKline. Dr. Ettinger is also a professor of clinical neurology at Albert Einstein College of Medicine, New York.

A companion study presented by Dr. Ettinger and his associates reviewed 18,073 adult patients, aged 18-64 years, with epilepsy from more than 40 million people insured by any of 75 health plans in the United States during January 2000–December 2005. During the study period, 2,467 of these patients had a serious seizure.

Adherence to antiepileptic drug prescriptions dropped markedly with time during the first year after prescriptions began, so that by a year after starting a prescription only about 60% of patients were adherent.

The analysis showed a significant link between adherence and the risk of having a serious seizure. Patients who were compliant with their medications and had a MPR of at least 80% were 16% less likely to have a serious seizure than noncompliant patients. Serious seizures were significantly more likely in men, compared with women. And patients who had a change in the type of antiepileptic drug they were prescribed were 2.5-fold more likely to have a serious seizure than those who didn't switch drugs.

Despite this link between drug switching and increased seizure risk, prescribing a simpler dosing regimen using a newer antiepileptic drug may reduce the risk of serious seizures by boosting adherence, Dr. Ettinger and his associates concluded.

A second study of the impact of adherence on outcomes involved 33,658 patients aged 18 years or older with epilepsy who were treated through Medicaid in Florida, Iowa, or New Jersey during 1997-2006. During this time the patients received medication prescriptions for more than 525,000 quarters, and during 26% of these quarters the patients were noncompliant, with a MPR of less than 80%.

After controlling for baseline demographic and clinical differences, nonadherent patients were about threefold more likely to die than adherent patients, reported Ms. Guérin and her associates from the Analysis Group, Inc. in a poster at the meeting. Additional analyses of these data showed that the noncompliant patients were more often age 65 or older, women, nonwhite, and had more comorbidities based on having a higher Charlson comorbidity index. After controlling for baseline demographic and clinical differences, noncompliant patients were more likely to be hospitalized, had more inpatient days, were more likely to require emergency room visits, and had higher health care costs, compared with compliant patients.

The studies by the Analysis Group were also sponsored by GlaxoSmithKline. ■

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Investigational Device Promising for Uncontrolled Seizures

BY DOUG BRUNK
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SAN DIEGO — The RNS System, an investigational device that delivers responsive stimulation to the brain of patients with uncontrolled seizures, shows promise in clinical trials, but the technical learning curve is currently steep, Dr. Ryder Gwinn said at the annual meeting of the Congress of Neurological Surgeons.

"Programming experience is growing but it's still not where we need to be," said Dr. Gwinn, director of surgical epilepsy at the Swedish Neuroscience Institute, Seattle. "It's still very complex. I am very frequently changing parameters in order to reach seizure freedom. However, I believe that the system will become much easier to use as a result of the clinical trials currently underway."

Dr. Ryder disclosed that he is a steering committee member for the devices' manufacturer, NeuroPace Inc., but he has not received consulting fees outside of the study budget. He also has no personal financial interest in the company.

The RNS System is a fully implanted, microprocessor-controlled device that uses up to nine contacts for stimulation. About the size of an iPod, it detects electrographic

patterns from intracranial electrodes and delivers up to five separate programmable therapies. It stores up to 32 minutes of electrocorticogram data that can be downloaded to a laptop at any time.

Benefits of the device include focal treatment that leaves functional neuronal circuits intact, Dr. Gwinn said. In addition, a decision to treat "can be made without significant concern for functional consequences, and it doesn't preclude later alternative treatments."

Concerns about the use of such technology include the fact that localization of focus could be critical to success. "Early seizure detection is important for contingent stimulation, and potentially abnormal tissue or aberrantly organized circuits would be left intact," he noted.

In a recent feasibility study, Dr. Gwinn and his associates at 11 centers used the RNS System in 65 patients aged 18-65 years who had simple or complex partial seizures.

Patients were eligible for the trial if they had failed treatment with a minimum of two antiepileptic drugs; had a minimum of four seizures per month for 3 months; and had an established region of epileptiform activity. The primary end point was safety and preliminary evidence of efficacy. Response rate was defined as



COURTESY DR. RYDER GWINN

The RNS System delivers up to five separate programmable therapies.

a greater than 50% reduction in seizures.

Of the 65 patients implanted with the RNS System, 50 received stimulation, one patient had a device that was never turned on, and 14 patients were in a sham-stimulation group (therapy off).

After a mean 847 days of follow-up, the researchers observed a responder rate of 32% in patients with complex partial seizures, 63% in patients with generalized tonic-clonic seizures, and 26% in those with total, disabling seizures (sim-

ple partial motor seizures, complex partial seizures, and generalized tonic-clonic seizures combined).

As of June 5, 2007, there were 15 serious adverse events, including one case of focal status epilepticus, one case of erosion from the leads, and one case of tissue infection, all of which resolved. Other adverse events included one case each of increase in seizure severity, confusion, sensitivity to visual stimuli, and sudden unexplained death in epilepsy (SUDEP). None of these adverse events were thought to be definitively related to the use of the device.

The researchers concluded that contingent stimulation appears to benefit patients with uncontrolled seizures. "More stimulation seems to be better, but early stimulation is often not enough to have an impact," Dr. Gwinn pointed out. "No parameters so far can reliably eradicate seizures altogether."

He and his associates at 28 centers are currently enrolling patients aged 18-70 years in a similar but larger pivotal study. The recruitment goal is 240 patients.

For now, the therapy appears to be safe. "Stimulation has been applied to all lobes, including the medial temporal lobe," Dr. Gwinn said. ■