

Adverse Events Occur in 35% of VNS Patients

BY MICHELE G. SULLIVAN
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PITTSBURGH — Treatment-limiting adverse events occurred in more than 30% of patients who received a vagus nerve stimulator for the treatment of seizure disorders, Dr. Phillip Pearl reported at the annual meeting of the Child Neurology Society.

The number of adverse events may increase even more as vagus nerve stimulator (VNS) devices become more common among new populations of patients with seizure disorders, said Dr. Pearl. "I think this is probably the tip of the iceberg and that we will be seeing more cases as more people receive this device and as the longevity of VNS therapy increases beyond what was studied for the initial approval."

Dr. Pearl reported adverse events among 62 patients who had VNS devices implanted in 1998-2005 at the Children's National Medical Center, Washington, where he is a pediatric neurologist. The patients ranged in age from 3 to 29 years (median 12 years). The median duration of therapy was 40 months (range 1-96 months).

Of the 62 patients, 35% (22 patients) had at least one clinically significant adverse event. The most common were persistent drooling (six), coughing (five), throat discomfort or spasms (four), and dysphagia (three). Two patients had difficulty breathing, with one requiring device removal. Two experienced vomiting while the VNS current was delivered, and two more experienced vocal cord weakness. All of these adverse events required some limiting of the current output of the device. Two more patients experienced axillary wound infections that required oral antibiotic treatment.

Of the patients with adverse events, eight needed nonroutine surgical intervention. The device was removed from five patients (8%),

including a 13-year-old girl who developed serious complications from a wound infection requiring intravenous antibiotics. She also needed a percutaneous endoscopic gastrostomy tube because of vocal cord paralysis and persistent dysphagia. The other four explanations were necessary because of persistent problems with breathing, coughing, or throat discomfort.

There were also two lead failures, Dr. Pearl said. One was discovered during a routine device interrogation more than 7 years after the initial implant. The other one was discovered after seizure control worsened.

In addition to these adverse events, there were two patients who experienced unique unanticipated problems.

One was a 13-year-old boy who had received the implant for intractable generalized seizures and was seen at an emergency department for convulsive status.

Peripheral vein access was limited; an emergency physician searching for an access site misidentified the VNS wire in the boy's neck as the jugular vein.

"The wire was stabbed several times until it became apparent that it was not a vein," Dr. Pearl said. Interrogation of the device a few days later showed no evidence of malfunction. One year later, the device did malfunction; the patient experienced increased seizures and needed a replacement.

Finally, Dr. Pearl said, a 25-year-old man with a VNS for intractable absence seizures began to experience tingling in the left side of his neck about 3 months after implantation. There was no indication that the device was malfunctioning, but the tingling did not occur when it was turned off. Subsequent x-rays showed that there was no strain-relief loop in the VNS wire located over the sternocleidomastoid muscle. Rather than have a revision, the patient continues to tolerate the intermittent sensations, Dr. Pearl said. ■

Of 62 patients studied, 35% had at least one significant adverse event. Persistent drooling and throat discomfort were the most common.

High TNF- α in Spinal Fluid Could Be an Early Sign of Neuroinflammation, Autism

CHICAGO — A high level of tumor necrosis factor- α in cerebrospinal fluid, but not serum, may be an early indicator for neuroinflammation and possibly autism, according to a study of eight autistic children with regression.

Although recent reports have found elevated levels of proinflammatory cytokines in brain tissue and cerebrospinal fluid (CSF) of autistic patients, no studies to date have specifically examined the level of tumor necrosis factor- α (TNF- α) in patients with autistic regression, Dr. Michael G. Chez reported during a poster session at the annual meeting of the American Neurological Association.

The mean concentration of TNF- α in the CSF of eight male patients who had autistic regression at an age of 15-24 months was significantly higher than it was in sera collected

at the same time from the patients at ages ranging from 2.1 years to 9.5 years (62.6 pg/mL vs. 3.5 pg/mL), according to Dr. Chez of the department of neurology at Chicago Medical School, North Chicago.

The CSF-to-serum ratio of TNF- α in autistic patients (24.4:1.0) was higher than what has been reported for other inflammation-related disorders, such as meningitis, multiple sclerosis, systemic lupus erythematosus, HIV, traumatic brain injury, dementia, and stroke, all of which had ratios near 1.0:1.0.

The CSF-to-serum ratio of TNF- α in four of the patients who were previously treated with prednisone, thalidomide, or turmeric for "presumed autoimmune issues" was significantly lower than the other four patients who had no prior treatments (6.1:1.0 vs. 33.2:1.0).

—Jeff Evans

Younger, Older Autistic Males Have Smaller Corpora Callosa

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

PITTSBURGH — The corpora callosa of individuals with autism are smaller than those of healthy controls both during early childhood and after age 30 years, according to data presented during a poster session at the annual meeting of the Child Neurology Society.

The differences are especially obvious in the genu, rostrum, and splenium—areas with a high density of thin fibers, which are important in higher-order cortical processing.

"Our findings provide new evidence that, in autism, differences in the pattern of neurological development may continue into the aging process," said Diane L. Williams, Ph.D., who presented the findings.

Dr. Williams of Duquesne University, Pittsburgh, and her colleagues used magnetic resonance imaging to examine the corpora callosa of 80 high-functioning males with autism (aged 9-53 years) and 80 healthy age-matched male controls. Because corpus callosum anatomy has been reported to be affected by handedness and gender, the investigators used only males, and the groups were matched for handedness.

The researchers divided each group into five age categories (10-15.4 years, 15.5-20.4 years, 20.5-25.4 years, 25.5-30.4 years, and 35 years and older). On imaging, the corpus callosum was divided into seven subregions (rostrum, genu, rostral body, anterior midbody,

posterior midbody, isthmus, and splenium), and was measured at the midsagittal slice.

After controlling for IQ, age, and total brain volume, the group with autism had reliably smaller corpora callosa than did controls.

The overall difference was driven by significant differences in the youngest and oldest groups compared with their corresponding control groups. Both autism groups had significantly smaller measurements for the total corpus callosum and the rostrum and genu; the oldest group also had reduced measurements in the splenium.

During adolescence and young adulthood, the size differences normalized. "This should not be interpreted, however, to mean that the integrity and composition of the neural structures are the same at that time," the researchers noted.

Rather, the structure size differences in childhood and later adulthood may reflect a different developmental trajectory, with later maturing and earlier decline than normal controls experienced.

"The suggestion of group differences for the rostrum and genu at early and late ages is consistent with what is known about normal development of these subregions. In normal adults, the anterior white matter, including the genu of the corpus callosum, is the first to decline. In autism, this same developmental pattern may occur, only with a timing difference," the investigators said. ■

β -Blockers May Have Short-Term Benefit for Aphasia

CHICAGO — The β -blocker propranolol may help some aphasic patients communicate more easily, at least in the short term, Dr. Yutaka Tanaka reported in a poster session at the annual meeting of the American Neurological Association.

β -blockers have been shown to lessen performance anxiety in nervous musicians and students.

This gave Dr. Tanaka and his colleagues the idea that the drugs might have the same effect for aphasic patients with performance anxiety.

Aphasic patients have been reported to score better on tests of functional communication than on more formal tests of specific linguistic ability, he said.

The investigators tested patients and controls on naming (Boston Naming Test) and verbal fluency (FAS; listing animals, vegetables, or numbers for 1 minute) for the first time 90 minutes after 10-mg propranolol was administered and at a second visit without any medication,

said Dr. Tanaka, who is a neurologist in private practice in Ikoma-Gun, Japan.

Of 6 patients with Broca's aphasia and 4 with Wernicke's aphasia (mean age of 70 years), all 10 showed significant improvement on all of the tests after receiving propranolol. In all of the patients, the testing occurred more than 6 months after the onset of aphasia.

Propranolol did not significantly alter the performance of nine young or nine elderly control subjects on any of the tests.

Nine middle-aged control individuals significantly improved on two tests of fluency but not on the naming test when pretreated with propranolol, he said.

"We postulate that the patients with aphasia were more anxious than the other groups with regard to language tasks, and thus benefited from treatment with the β -blockers," Dr. Tanaka said.

—Jeff Evans