

Lamotrigine Effective Add-On for Seizures

Adjunctive treatment reduces frequency of primary generalized tonic-clonic seizures.

BY DIANA MAHONEY
New England Bureau

LOS ANGELES — Adjunctive therapy with lamotrigine significantly reduced the number of primary generalized tonic-clonic seizures in children and adolescents in whom such seizures are inadequately controlled with other antiepileptic drugs alone, judging from findings reported by Dr. Edwin Trevathan.

The investigators, who had funding from GlaxoSmithKline, conducted a subanalysis of a larger double-blind, placebo-controlled study that had looked at the safety and efficacy of lamotrigine (Lamictal) as an adjunctive therapy in both adults and children experiencing primary generalized tonic-clonic (PGTC) seizures, Dr. Trevathan said at the annual meeting of the Child Neurology Society.

The approved pediatric indications of lamotrigine are management of simple or complex partial seizures or Lennox-Gastaut syndrome, a devastating childhood epileptic encephalopathy. The drug is not approved for use in children under 2 years of age.

During his presentation, Dr. Trevathan said that “remarkably few randomized control trials have focused on PGTC seizures exclusively—even though it is one of the more serious forms of epilepsy—and fewer still have focused on children with these seizures,” he said.

In the larger study, 117 children, adolescents, and adults with EEG-confirmed PGTC seizures who were taking one or two concurrent antiepileptic drugs who also experienced three or more PGTC seizures during an 8-week baseline phase were randomized to adjunctive treatment with lamotrigine (58) or placebo (59).

In the majority of patients, epilepsy ideology was classified as idiopathic. Patients with evidence of partial seizures were excluded from the study, he said.

Data were collected at baseline, during the 7-12-week dose-escalation phase, and during the 12-week maintenance phase, when the dosage of the study drug and concurrent antiepileptics was held constant.

The results showed that lamotrigine reduced PGTC seizures significantly relative to baseline during both the dose-escalation and maintenance phases individually and during the entire combined treatment period, said Dr.

Trevathan, director of pediatric and developmental neurology at Washington University, St. Louis.

In the post hoc subgroup analysis looking at only the results for adolescents and children—21 of whom were randomized to lamotrigine and 24 who got placebo—lamotrigine reduced the number of PGTC seizures from baseline by 77% during the entire treatment period compared with 40% for placebo. “Although the analysis was not powered to evaluate this subset of patients, the reduction is statistically significant,” Dr. Trevathan noted.

In the dose-escalation and maintenance phases, lamotrigine therapy was associated with a seizure frequency reduction from baseline in children of 72% and 83% respectively, compared with 30% and 42% in the placebo group.

There were no reports of drug-induced serious rashes—rare cases of toxic epidermal necrolysis or Stevens-Johnson syndrome have been reported with lamotrigine treatment—in either treatment group.

The most common adverse events reported during treatment were headache (10% with lamotrigine vs. 25% with placebo), nasopharyngitis (14% for lamotrigine vs. 4% for placebo), and convulsion (10% for lamotrigine vs. 13% for placebo). One patient from each treatment group dropped out of the study because of an adverse event.

“The magnitude of the effect that lamotrigine had on seizures in the subgroup analysis was approximately the same as was seen in the overall trial—basically a median percent reduction that was about twofold higher than placebo,” Dr. Trevathan said.

“Despite the fact that the subgroup analysis was underpowered because of the small sample size, it’s quite clear from this data that lamotrigine appears efficacious in these patients,” he pointed out.

Because PGTC seizures are associated with a range of potentially injurious physiologic and behavioral changes before, during, and after they occur, and because they can have life-threatening complications, “effective control of these seizures is especially critical in the vulnerable child and adolescent populations,” said Dr. Trevathan. “We hope the results of this analysis will encourage more clinical trials of children and adolescents who suffer from these seizures.” ■

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Pediatric Epilepsy Surgery Fails To Aid Later Cognitive Function

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

WASHINGTON — Childhood epilepsy surgery isn’t associated with a long-term improvement in cognitive functioning, Janet Olds, Ph.D., and her colleagues reported in a poster at the joint annual meeting of the American Epilepsy Society and the American Clinical Neurophysiology Society.

While findings from previous studies have shown that the surgery has no short-term effect on childhood cognition, little was known until now about its long-term effect on adult cognition, noted Dr. Olds, a psychologist at the Children’s Hospital of Eastern Ontario.

She assessed cognitive function in 50 adults (mean age 22 years) with a history of childhood epilepsy; 34 had undergone epilepsy surgery at least 2 years prior to assessment.

Of these, 21 were seizure-free and 13 continued to have seizures. The other 16 subjects, who served as controls, had never had surgery for their epilepsy as children and continued to have seizures as adults.

Seizure-free surgical subjects were taking a mean of one antiepileptic drug. Both the surgical group with continued seizures and the nonsurgical group were taking a mean of two antiepileptic drugs.

All of the subjects completed a neuropsychological assessment consisting of measures of intelligence, memory, and executive functioning (Wechsler Adult Intelligence Scale, vocabulary and block design; Wechsler Memory Scale, logical memory and memory for faces; Wisconsin Card Sort Test). Scores were compared with the subjects’ pre- and postsurgical scores on the same tests.

There were no group differences in problem solving as reflected in the Wisconsin Card Sort Test. Surgery subjects who continued to have seizures scored lower on vocabulary and verbal memory tests, com-

pared with both the seizure-free surgery group and the no-surgery group.

When the scores in two surgical groups were compared, the seizure-free group did better on vocabulary and block design, compared with the group still having seizures. However, there were no differences in scores across the three test periods, indicating no significant change in functioning over time.

It’s important to include a discussion of cognitive function when counseling par-

ents about the potential impact of epilepsy surgery, said Mary Lou Smith, Ph.D., the study’s principal investigator. The majority of research suggests that cognitive skills won’t change—a fact that can be construed in a positive, as well as potentially negative, light.

“In essence, this is good news, although not necessarily the good news those parents would like to hear,” Dr. Smith, of the

University of Toronto, said in an interview. “[Parents] may wish, and often do, that their child will show improved cognitive function after surgery.”

She added that it is important to remember that the study’s conclusions are based on group numbers and that within each group, some children do better or worse than the study’s findings indicate.

Unfortunately, Dr. Smith said, there’s no consensus on what factors predict who will improve and who will deteriorate.

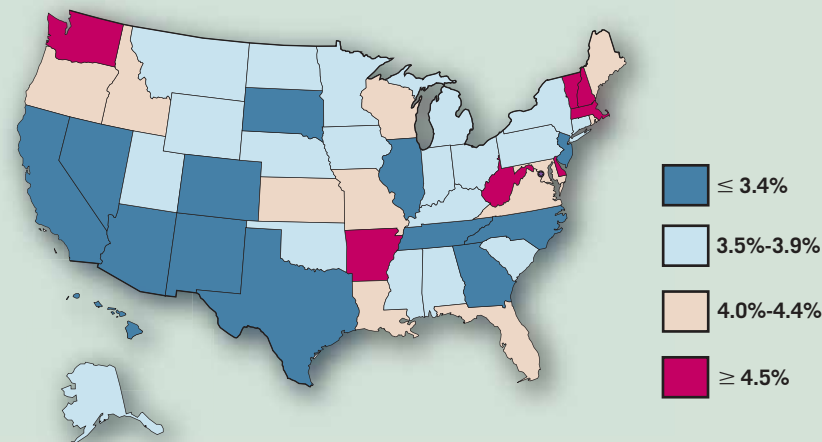
“The few studies that have included a comparison group of children with intractable epilepsy who don’t have surgery show that the proportion who shows increases or decreases is the same in both surgical and nonsurgical groups,” she commented.

The general conclusion is that as long as the eloquent cortex remains intact, there is no particular cognitive risk or benefit associated with the surgery, said Dr. Smith. ■

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DATA WATCH

Prevalence of Chronic Emotional, Behavioral, Or Developmental Problems in Children



Note: Includes children with problems that required treatment or counseling.
Source: 2001 data, Centers for Disease Control and Prevention