Seizure-Free Children Can Be Weaned Off AEDs

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SEATTLE — Most children with epilepsy who become seizure free with antiepileptic drug therapy are able to stop taking the drugs without developing intractable seizures, according to findings from a population-based cohort study.

Dr. Katherine C. Nickels said that about a third of children with epilepsy experience a recurrence after becoming seizure free on antiepileptic drugs (AEDs) and stopping therapy. More than half of those who resume AEDs are rapidly able to regain seizure control.

To put the findings in perspective, she noted the 20% rate of intractable seizures is similar to that seen among children with a new diagnosis of epilepsy.

"Children who achieve seizure freedom on antiseizure medications can be considered for antiseizure medication withdrawal without high risk of intractable epilepsy," Dr. Nickels reported at the annual meeting of the American Epilepsy Society. Dr. Nickels said she had no disclosures to report in association with the study.

"Antiepileptic medications may have serious side effects, including cognitive slowing, weight change, fatigue, and hepatotoxicity," she said.

Children who become seizure free while taking AEDs are often weaned off of them, but there is a concern that seizures will recur and—most worrisome—that they will be intractable when they do.

"The current data regarding the risk of recurrence of seizures as well as the risk of intractable seizures following medication withdrawal varies widely from one study to the next," said Dr. Nickels, a pediatric neurologist at the Mayo Clinic, Rochester, Minn. Moreover, "many of them are not population based."

Using data from the Rochester Epidemiology Project, she and her coinvestigators reviewed the medical charts of all children aged 1 month to 16 years who received a new diagnosis of epilepsy while living in Olmsted County during 1990-2000 and had follow-up of at least 5 years after their first seizure. To be included in the study, children were required to have had two or more unprovoked seizures in the absence of any progressive neurologic disorder and to be receiving AEDs daily.

The investigators focused on the group who became seizure free and discontinued their AEDs. They reviewed the medical charts of these children through their last follow-up to assess seizure recurrence (defined as occurrence of at least one seizure) and the development of intractable seizures (defined as occurrence of at least one seizure every 3 months during the last year of follow-up and failure of at least two AEDs to control the seizures at maximum tolerated doses).

A total of 152 children fit the study criteria. Some 56 (37%) became seizure free and were weaned off of the drugs. Their mean duration of seizure freedom while on treatment had been 2.3 years.

After a mean follow-up of 8 years, 20 (36%) of this group had a recurrence of seizures. Among these children, 15 restarted AEDs, 4 remained off AEDs with rare or no additional seizures, and 1 died of sudden unexpected death in epilepsy.

After a mean follow-up of 5.7 years in the 15 children who restarted AEDs, 10 again became seizure free within 2 years, whereas 5 never did. Of those five children, three—5% of the total stopping AEDs or 20% of the total restarting them—had intractable seizures.

An analysis of the time until seizures recurred among the children with this outcome showed that 55% had their recurrence within 1 year of stopping AEDs, said Dr. Nickels. But 20% had their recurrence more than 5 years after stopping.

Finally, an analysis of the time until regaining freedom from seizures among the 15 children who had a recurrence and restarted AEDs showed that 8 became seizure free within 1 year and another 2 achieved this status within 2 years. The remaining five children never regained freedom from seizures. ■

MRI Seldom Affects Therapy For Child's Afebrile Seizures

SEATTLE — Magnetic resonance imaging seldom changes the acute management of children with new-onset afebrile seizures who have a normal computed tomography scan, according to a study of more than 1,000 children.

In the retrospective study reported at the annual meeting of the American Epilepsy Society, Dr. Dewi Depositario-Cabacar, a neurologist with the Children's National Medical Center in Washington, and her colleagues assessed imaging findings and management among children seen at the center for new-onset afebrile seizure-like events that occurred during an 86-month period from October 2000 through December 2007.

MRI altered acute management in only 5% of the children with a normal CT scan but abnormal MRI.

DR. DEPOSITARIO-CABACAR

All of the children were evaluated according to a standardized protocol that included a head CT scan. Some also underwent MRI on a 1.5-Tesla scanner at their treating physician's discretion.

Results showed that 1,278 children with new-onset afebrile seizures had a noncontrast head CT, and 710 of them also had an MRI.

Of the 489 children with a normal CT scan who underwent MRI, 165 (34%) had abnormal MRI findings.

The most common finding was an incidental abnormality (seen in 23% of this subgroup). The most common nonincidental findings were dysplasia (13%), focal signal hypodensities or hyperdensities (13%), vascular abnormalities (7%), atrophy/encephalomalacia (6%), and mesial temporal sclerosis (6%).

The MRI findings altered acute management in only eight (5%) of the children who had a normal CT scan but an abnormal MRI scan. These children had final diagnoses of meningoencephalitis, new arterial strokes, toxoplasmosis, low-grade gliomas, and sinus thrombosis.

"However, all of the children had focal abnormalities by history or by examination," Dr. Depositario-Cabacar noted. In addition, two children had known contributing medical factors: acute myeloid leukemia in one child and cardiac surgery in another.

In an additional analysis of the 30 children with nonspecific CT findings who underwent MRI, 10 (33%) had new findings on MRI. These findings were vascular abnormalities, infection, dysplasia, and delayed myelination.

"This study confirms that MRI is superior to CT in identifying and delineating abnormalities," Dr. Depositario-Cabacar said of the findings.

However, she concluded, among children having a first afebrile seizure and a normal CT scan, there is a low probability that MRI findings will alter management acutely.

Dr. Depositario-Cabacar reported that she had no conflicts of interest to report in association with the study. ■

Poor Seizure Control Associated With Neuropsychological Decline in Children

SEATTLE — Poor early control of seizures adversely affects neuropsychological development among school-aged children who are otherwise healthy, new data from a prospective, longitudinal study show.

"It's critical to delineate the timing and the course of neuropsychological deficits [in the childhood onset of epilepsy] and to identify the risk factors associated with them," said Philip S. Fastenau, Ph.D., lead author of the study.

Dr. Fastenau and his coinvestigators enrolled children 6-14 years old who had a first recognized seizure, an IQ of at least 70, and no other chronic conditions affecting their activities of daily living. The children were matched with biological sibling controls who were of similar age, sex, and IQ, and had been raised in the same home.

Over the next 3 years, the investigators assessed seizure control every 9 months and performed neuropsychological testing at baseline (a mean of 2.4 months after seizure onset), at 18 months, and at 36 months.

The results were based on 209 children with new-onset seizures and 143 matched siblings. At baseline, half of those in the seizure group were receiving antiepileptic drugs, according to Dr. Fastenau, a neuropsychologist at the Case Medical Center, Cleveland. He reported having no relevant conflicts of interest with the study.

During the 3-year follow-up, 27% of the children with new-onset seizures did not have any recurrence, 61% had recurrent seizures (at least one more seizure, but not at every follow-up), and 12% had persistent seizures (seizures at every follow-up). In analyses that controlled for potential confounders, processing speed was similar across all three seizure groups and the sibling control group at baseline, Dr. Fastenau reported at the annual meeting of the American Epilepsy Society.

However, the 3-year change differed significantly. Processing speed increased for the siblings and the children who did not have a recurrence. In contrast, it decreased among children with recurrent seizures, and even more so among those with persistent seizures. Similarly, verbal memory and learning did not differ across groups at baseline, but the change during follow-up did.

Verbal memory and learning improved with time in the siblings and children with no recurrence of seizures, but worsened among the children with persistent seizures, a difference that was significant. It remained constant in the children with recurrent seizures.

At baseline, children with persistent seizures had significantly poorer attention, executive processing, and construction skills, compared with the siblings. During the 3-year follow-up, these skills increased in all four groups. However, the gain was significantly smaller in the persistent seizure group, compared with the sibling group.

"Seizure recurrence and persistent seizures, in particular, are associated with neuropsychological decline within the first 3 years after onset," Dr. Fastenau said.

"In children with school-age onset [of seizures], complete seizure control is critical for optimizing cognitive development, but this goal might need to be balanced against the iatrogenic effects of some antiepileptic drugs," he said. ■