New study identifies best treatment for childhood epilepsy

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One of the oldest available anti-seizure medications, ethosuximide, is the most effective treatment for childhood absence epilepsy, according to initial outcomes published in this week's *New England Journal of Medicine*.

OHSU Doernbecher Children's Hospital is one of 32 comprehensive pediatric epilepsy centers nationwide selected to participate in this landmark clinical trial as part of the NIH Childhood Absence Epilepsy Study Group.

The study group compared three medications typically used to treat the most common childhood epilepsy syndrome, childhood absence epilepsy, which is characterized by frequent non-convulsive seizures that cause the child to stop what he or she is doing and stare for up to 30 seconds at time.

Prior to this study, there was no definitive evidence on which drug worked best.

"Much of our scientific understanding of childhood epilepsy care today comes from historical experience or studies involving adult patients with related, but not identical, conditions," explained Colin Roberts, M.D., OHSU Doernbecher's principal investigator for the study, assistant professor of pediatrics and neurology, and director of OHSU Doernbecher's Pediatric Epilepsy Program,

"This study is an important milestone in our understanding of childhood absence epilepsy. Never before have we been able to document in such a comprehensive, scientific fashion the best options to treat children with this condition."

The study group enrolled 453 children newly diagnosed with childhood absence epilepsy from July 2004 to October 2007. Study participants were randomly assigned to ethosuximide, valproic acid or lamotrigine. Drug doses were incrementally increased until the child was seizure-free. After 16 weeks of therapy, the researchers found ethosuximide and valproic acid were significantly more effective than lamotrigine in controlling seizures, with no intolerable side effects. They also determined ethosuximide was associated with significantly fewer negative effects on attention.

Nick and Michelle Skimas, of Vancouver, Wash., enrolled their daughter Julia in the study in April 2007. Julia stopped having seizures after starting medication.

Before diagnosis and treatment, Julia, now 8, would stop abruptly while reading aloud, pause for 10 to 15 seconds, then resume where she left off, not aware that anything had occurred. Michelle assumed Julia was just taking breaks to look at the pictures.

This went on for two to three weeks, and Michelle didn't think anything of it. Then, while on a family vacation, Julia suddenly stopped in the midst of pitching a baseball and began slowly turning in a circle. Julia was unaware of what was happening and had no recollection of what had occurred.

"That did it," said Michelle. "We took Julia to be evaluated as soon as we got back." After an EEG, and an MRI to rule out a brain tumor, Julia was diagnosed with childhood absence epilepsy. Her primary care

physician recommended she enroll in a new drug trial at OHSU Doernbecher. Nick and Michelle were leery of giving their daughter medication, but Roberts and his team explained that without treatment Julia's seizures would have a serious impact on her learning and development.

"They said to think of Julia's brain as a classroom in which one child is continuously disruptive. The rest of the class can't function. It was a hard decision, but we are glad we participated. We feel blessed that she has been seizure-free for more than 2 ½ years."

The national study group recommended long-term follow up for the study participants and recently received a five-year extension from the NIH.

Julia, who stopped taking the medication several months after she became seizure-free because it increased her BMI, or body mass index, continues to participate in the newly extended trial, representing one of three study groups: participants who took medication, became seizure-free and stopped taking the medication. The other groups comprise children who are taking the medication but still having seizures, and children taking the medication who are not experiencing seizures, respectively.

"We told Julia all along that what she was doing could very well help other kids in her position, and now she knows it did. That will make a big difference in her life," said Michelle.

"The initial outcomes from this study describe one of many aspects of childhood absence epilepsy evaluated by the study group. Collaborative studies like this lay the groundwork for many critically important studies to follow that will define the proper care of children with seizures," said Roberts.

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