FDA Neuro Device Trial Slowly Gets Underway

BY MARK HOLLMER

FROM A FOOD AND DRUG ADMINISTRATION WORKSHOP

SILVER SPRING, MD. – The ASK Children study, a Food and Drug Administration–led clinical trial designed to gather data about the use of neurologic devices in children, has enrolled 18 patients since launching in March 2009.

Through 2011, the FDA wants to enroll 100 pediatric and adolescent patients aged 7-15 years who have been implanted with a neurologic-related medical device for up to 1 year.

Despite the slow progress, the agency signaled at the workshop that the trial remains an important priority. The gathering was called to collect information on how to improve regulators' approach to evaluating pediatric neuroprostheses.

The ASK Children (Assess Specific Kinds of Children, askchildrenstudy.org) initiative is an important part of that strategy, said Carlos Peña, Ph.D., senior science policy adviser for the FDA's Office of the Commissioner, and one of the study's two principal investigators. "We have taken the study very seriously," he said.

Through interviews with the children and adolescents, the agency will gather data about scientific and medical device–related issues. Regulators hope the data will lead to more efficient approaches in evaluating the devices and the patients' experiences with them, as well as the development of similar, new technologies.

Requirements Are an Ongoing Issue

Including pediatric needs in the device evaluation process is an ongoing issue for the FDA, and one that has gotten more attention as the agency strives to implement pediatric-focused provisions of the FDA Amendments Act of 2007.

This is an "emerging science area as we continue to learn about the nervous system," said Dr. Peña, who is leading the trial with Kristen Bowsher, Ph.D., an engineer in the FDA's Office of Device Evaluation.

Study organizers hope to enroll 20 children and adolescents each who have been implanted within the last year with five kinds of neurologic devices: deep brain stimulator, spinal cord simulator, cerebral spinal fluid shunt, vagus nerve stimulator, and cochlear implant.

The children will be required to participate in two 1-hour in-person or telephone interviews about 6 months apart. Three sites have been chosen for the study: the FDA Parklawn Building in Rockville, Md.; the Arkansas Children's Hospital in Little Rock; and the Cleveland Clinic. Patients also will be required to answer questionnaires about general quality of life.

Regulators hope to obtain information on human factors, safety, usability, adverse events, and possible postmarket issues immediately following implementation of high-risk devices. The initial study will be expanded in the future into other pediatric-related device areas.

Unique Considerations Are Needed

Dr. Warren Marks, medical director of the movement disorder and neurorehabilitation program at Cook Children's Medical Center in Fort Worth, Tex., said the FDA should consider quality of life factors in evaluating neurologic device use, as well as safety and efficacy, because "there is no really good quality of life measure out there right now."

He argued the trial would gain more relevant data on quality of life if it were to include patients who have had device implants beyond 12 months, rather than limiting the time frame to within 12 months.

Dr. Philip Pearl, chief of the division of child neurology at Children's National Medical Center in Washington, said the upper-age cut-off for classifying child neurology device implant patients as "adolescent" should be extended from 18 to 21 years because the unique emotional needs in dealing with the implants and their related health conditions are still prevalent at that older age.

Workshop attendees pushed for children's devices that are smarter, smaller, and, ideally, self-contained, without exposed wires that children could play with and damage. Lauri Rush, who spoke about her daughter's experience with the device, emphasized the need to factor in a child's active lifestyle with devices such as cochlear implants. "How do you keep on a device while [a child] is in gymnastics?" she asked.

The workshop participants agreed that it is difficult to encourage companies to develop devices for the pediatric population because they do not always see profit potential. The 2007 Amendments Act included a provision allowing device firms to profit from pediatric-targeted indications of humanitarian use devices, though industry says it needs more incentives.

Dr. Marks and Dr. Pearl said they had no conflicts of interest. ■

"The Gray Sheet" and this newspaper are published by Elsevier.

Continued from previous page

asymptomatic at rest and when active. Evidence suggests that cognitive exertion – including doing homework, watching TV, and playing video games – can exacerbate symptoms post concussion.

In the last few years, several states have passed laws requiring educational materials about sports-related concussion for school-aged athletes, coaches, and parents. The AAP began working on the report before the first law was passed, said Dr. Halstead, director of the sports concussion program at Washington University in St. Louis. "We felt there was a need to address specifically the [pediatric] athlete and address all the recent research that has been published on this topic," he said in an interview.

"The recommendations presented aren't significantly different from other recent documents published, but these were primarily published in sports medicine journals, which many pediatricians do not review. We wanted to bring these recommendations to the forefront to the pediatric community, and expand upon the details provided in previous documents published. We have highlighted some of the new research on neuroimaging, balance assessments, long-term complications, education, and neuropsychological testing," Dr. Halstead said.

Dr. Walter added, "I think it is also important to recognize that because we have learned more about concussion diagnosis, treatment, and complications, the treatment that coaches and parents received when they had a concussion themselves at a young age is likely different [from treatment] today." Many parents and coaches don't think concussion is a big deal because they had one when they were younger and they "toughed it out" and "are fine now," said Dr. Walter, program director of pediatric and adolescent sports medicine at Children's Hospital of Wisconsin in Milwaukee.

The authors acknowledged the lack of published baseline neuropsychological data on children younger than 12 years, and noted that assessment by a neuropsychologist might be helpful for children who have had more than one concussion, or whose postconcussive symptoms persist for several months.

Dr. Halstead emphasized the following take-home tips for clinicians:

► Never should young athletes return to play on the day of their concussion, nor should they return to play until they are symptom free both at rest and at exertion.

► A concussion is an injury to the brain, and rest is paramount. "If an athlete injures an ankle or knee and cannot run on it, we wouldn't think twice about resting that injury until it healed. Why should we treat the brain any differently?"

► Doctors are interested in getting an athlete back to play and activity as soon as possible. "But we need to be smart about it and make sure it is safe for that young athlete first."

► Continue to educate everyone involved – coaches, parents, teachers, and athletes – in preventing and managing sports-related concussions.

None of the researchers mentioned in this story had any financial conflicts to disclose. ■

VIEW ON THE NEWS

Awareness Drives Rise in Reports

I'm not surprised by the increase in reports of concussions in young athletes. And because not every kid with a concussion goes to the ED, there are even more injuries occurring that are not being reported.

I think greater awareness and better diagnosis are the main reasons why the number of sports-related concussions is rising. Until 10 years ago, the medical literature focused only on concussions that involved loss of consciousness. But what we have learned in the past decade is that the subtleties of this injury are absolutely critical for diagnosis. (My 2003 paper shows that amnesia or memory loss around the time of the concussion is 10 times more predictive than a loss of consciousness.) Changes in the way we define the injury are driving the rise in reported concussions in young athletes.

As we continue to peel the onion on concussion, we realize that it is an extremely complex injury. We now have animal models that help show what happens in the brain after a concussion. This knowledge base has accumulated at warp speed over the last 10 years, and with that has come better recognition, better management, and better understanding of the injury, as well as more concern.

Most importantly, neurocognitive testing is becoming more widely used as a way to assess sports-related concussion, and it is the key to why there is so much attention now being paid to the injury: We now have a way to measure it by collecting baseline data. The sensitivity and specificity of such tests are impressive.

One of the keys to improving the management of pediatric concussion is to get knowledge related to this injury, as well as its many assessment tools, into pediatric offices. Clinics are available around the United States to help pediatricians who want to incorporate neurocognitive testing into their practices. The American Academy of Pediatrics' report by Dr. Halstead and Dr. Walter lists several assessment tools, and it includes other valuable, relevant information about managing sports-related concussions in young athletes.

MICHAEL COLLINS, PH.D., *is the assistant director of the sports medicine concussion program at the University of Pittsburgh Medical Center. He coauthored the Centers for Disease Control and Prevention's "Heads Up: Brain Injury in Your Practice" tool kit for physicians. He disclosed that he is a cofounder of ImPACT, a computerized neurocognitive testing tool.*