

# Febrile Seizure Guidelines Reflect New Findings

BY DIANA MAHONEY

FROM PEDIATRICS

Identifying the cause of fever should be the top priority when evaluating infants or young children after a simple febrile seizure, and the differential diagnosis should always include meningitis, according to a new clinical practice guideline published by the American Academy of Pediatrics.

In most situations, however, “a simple febrile seizure does not usually require further evaluation, specifically electroencephalography, blood studies, or neuroimaging,” the AAP Subcommittee on Febrile Seizures wrote.

The new guideline replaces the 1996 AAP practice parameter for the neurodiagnostic evaluation of healthy infants and children 6-60 months of age who have had a simple febrile seizure and who present for evaluation within 12 hours of the event (*Pediatrics* 1996;97:769-72).

The new document is based on a comprehensive review of the evidence-based literature published from 1996 to February 2009, with an emphasis on research that differentiated simple febrile seizures from other seizure types. The final recommendations, presented as action statements relating to the use of lumbar puncture, electroencephalography, laboratory testing, and neuroimaging, were developed based on the quality of supporting evidence and the balance of benefit and harm if the given policy is carried out, said lead author Dr. Patricia K. Duffner, professor of neurology and pediatrics at the State University of New York at Buffalo, and her associates (*Pediatrics* 2011;127:389-94).

Dr. Duffner noted in an interview that the biggest change is in the recommendation regarding lumbar punctures. In the prior guideline, lumbar punctures were strongly considered for children aged 6-12 months and considered for those aged 12-18 months. With the advent of routine immunizations for *Haemophilus influenzae* and *Streptococcus pneumoniae*, the risk of simple febrile seizures being caused by bacterial meningitis is much reduced, she said. The caveat is the child

who has not been immunized and the child who is on antibiotics which may mask the infection. In those cases, the physician will need to be more cautious in his/her evaluation of the child.

According to the document:

► **Lumbar puncture.** It is strongly recommended for children who present with febrile seizure and have meningeal signs and symptoms, including neck stiffness, Kernig signs, or Brudzinski signs, or those whose history or exam suggests possible meningitis or intracranial infection. The procedure is optional for infants between 6 and 12 months who have not received scheduled *Haemophilus influenzae* type b (Hib) or *S. pneumoniae* immunizations or when immunization status is unknown, and for children with febrile seizure who have been pretreated with antibiotics, which could potentially mask the signs and symptoms of meningitis.

Since the previous practice parameter was published, there has been widespread immunization in the United States for two of the most common causes of bacterial meningitis in this age range: Hib and *S. pneumoniae*. Compliance with all recommended immunizations does not completely eliminate the possibility of bacterial meningitis from the differential diagnosis, but “current data no longer support routine lumbar puncture in well-appearing, fully immunized children who present with a simple febrile seizure. Moreover, although approximately 25% of young children with meningitis have seizures as the presenting sign of the disease, some are either obtunded or comatose when evaluated by a physician for the seizure, and the remainder most often have obvious clinical signs of meningitis (focal seizures, recurrent seizures, petechial rash, or nuchal rigidity),” the guideline says.

► **Electroencephalography (EEG).** It should not be used routinely in the evaluation of simple febrile seizures in otherwise neurologically healthy children. “There is no evidence that EEG readings performed either at the time of presentation after a simple febrile seizure or within the following month are predictive of either recurrence of febrile

seizures or the development of afebrile seizures/epilepsy within the next 2 years,” the authors wrote.

► **Measurement of serum electrolytes, calcium, phosphorus, magnesium, blood glucose, or complete blood cell count.** Such measurements should not be performed routinely for the sole purpose of identifying the cause of a simple febrile seizure. “When fever is present, the decision regarding the need for laboratory testing should be directed toward identifying the source of the fever rather than as part of the routine evaluation of the seizure itself,” Dr. Duffner and her associates concluded.

► **Neuroimaging.** It is not recommended for the routine evaluation of children who present with simple febrile seizures.

“The literature does not support the use of skull films in evaluation of the child with a febrile seizure,” they explained, nor have data been published that support or negate the need for CT or MRI in this population.

Data do show that “CT scanning is associated with radiation exposure that may escalate future cancer risk. MRI is associated with risks from required sedation and high cost,” the authors said.

All of the authors filed conflict of interest statements with the AAP, and any conflicts have been resolved through a process approved by the Board of Directors. The AAP reported having neither solicited nor accepted any commercial involvement in the development of the revised guideline. ■

## Lumbar Puncture Advice Helpful

The guidelines on when to do a lumbar puncture “in the context of lack of immunization and pretreatment with antibiotics will be most useful with regard to decision making in this carefully defined patient population,” Dr. Jeffrey Buchhalter said in an interview. The authors “were very specific regarding age of inclusion and consideration of only simple febrile seizures in their recommendation.”

“My general impression is that many individuals who evaluate children with simple febrile seizures recognize the very low utility of neuroimaging but obtain head CT anyway due to concern regarding litigation if anything is missed. The strong recommendation not to obtain skull films is appropriate, but in my experience has not been used with any frequency during the last decade,” he said.

“The guidelines make sense as so much credence is given to observational studies – what we commonly

see in clinical practice. Furthermore, the recommendations take into account a benefit/harm consideration that each clinician confronts. Thus, implementation should occur with a caveat regarding perceived medical-legal liability regarding neuroimaging and other testing.

“However, a potential reason not to implement these guidelines is precisely because of the lack of high-quality evidence proving or disproving each recommendation. This is an interesting conundrum that we face in creating guidelines that are truly evidence based yet clinically relevant,” Dr. Buchhalter concluded.



DR. BUCHHALTER is chief of neurology at Phoenix Children's Hospital. Dr. Buchhalter has received personal compensation for activities with the National Institute of Neurological Disorders and Stroke, and he has received research support from Ovation Pharmaceuticals, Inc. and Pfizer Inc.

## IV Levetiracetam Aided Newborns With Acute Seizures

BY DIANA MAHONEY

FROM THE ANNUAL MEETING OF THE AMERICAN EPILEPSY SOCIETY

SAN ANTONIO – Intravenous levetiracetam safely and effectively halted acute neonatal seizures within 72 hours in a retrospective study of 22 newborns treated with the drug at a Texas hospital.

The findings, if validated through larger studies, could represent a major shift in the management of neonatal seizures, said Dr. Owais Ahmed Khan of Scott & White Healthcare in Temple. “The antiepileptic medications that are currently approved for neonatal seizures – including phenobarbital, phenytoin, and lorazepam – are effective in less than 50% of newborns and can have serious long-term effects.”

Neonatal seizures affect 1-4 of 1,000 live births in

North America and are a major predictor of adverse neurologic outcomes, “yet very few antiepileptic medications carry [a Food and Drug Administration–approved] indication for their treatment,” Dr. Khan said at the meeting.

Intravenous levetiracetam (Keppra) is approved as adjunctive treatment for various seizure types in children aged 16 years and older, but “it is being increasingly used off label in pediatric patients because of literature documenting efficacy and safety in adults, along with favorable anecdotal reports in younger patients,” he said.

To evaluate the efficacy and tolerability of IV levetiracetam therapy for acute seizure management in neonates, Dr. Khan and colleagues reviewed the charts of all term and near-term neonates who received the drug at their institution between January 2007 and December 2009. The 12 female and 10 male newborns typically received a bolus dose of 50 mg/kg of levetiracetam fol-

lowed by a maintenance dose of 25 mg/kg every 12 hours, infused over 15 minutes to 1 hour.

“Nineteen of the newborns [86%] experienced immediate seizure control within 1 hour of the loading dose,” Dr. Khan reported.

After the loading dose, no further seizures were recorded while on IV levetiracetam in seven (32%) of the newborns. Seizures stopped altogether within 24 hours of the loading dose in 14 patients (64%) and within 48 hours in 19 patients (86%). All 22 were seizure free within 72 hours, he said.

All of the newborns were switched to oral levetiracetam while in the hospital, and 81% were discharged home on levetiracetam monotherapy, Dr. Khan reported. No major or immediate adverse effects were reported during follow-up of 2-6 months.

Dr. Khan and his colleagues had no disclosures. ■