CURRENT LITERATURE

CHILDHOOD STATUS EPILEPTICUS

Short-Term Outcomes of Children with Febrile Status Epilepticus

Shinnar S, Pellock JM, Berg AT, O'Dell C, Driscoll SM, Maytal J, Moshe SL, DeLorenzo RJ

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Febrile status epilepticus (SE) represents the extreme end of the complex febrile seizure spectrum. If there are significant sequelae to febrile seizures, they should be more common in this group. We have prospectively identified 180 children aged 1 month to 10 years who presented with febrile SE over a 10-year period in Bronx, New York, and Richmond, Virginia. They were compared with 244 children who presented with their first febrile seizure (not SE) in a prospective study done in the Bronx. The mean age of the children with febrile SE was 1.92 years, and of the comparison group, 1.85 years. Duration of SE was 30-59 min in 103 (58%), 60-119 min in 43 (24%), and $>$ or $=$120 min in 34 (18%). Focal features were present in 64 (35%) of cases. There were no deaths and no cases of new cognitive or motor handicap. Children with febrile SE were more likely to be neurologically abnormal (20% vs. 5%; $p < 0.001$), to have a history of neonatal seizures (3% vs. 0; $p = 0.006$) and a family history of epilepsy (11% vs. 5%; $p = 0.05$) and less likely to have a family history of febrile seizures (15% vs. 27%; $p = 0.01$) than were children in the comparison group. The short-term morbidity and mortality of febrile SE are low. There are differences in the types of children who have febrile SE compared with those who experience briefer febrile seizures. Long-term follow-up of this cohort may provide insight into the relationship of prolonged febrile seizures and subsequent mesial temporal sclerosis.

A Major Role of Viruses in Convulsive Status Epilepticus in Children: A Prospective Study of 22 Children

Juntunen A, Herrgard E, Mannonen L, Korppi M, Linnavuori K, Vaheri A, Koskiniemi M

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A group of 22 previously healthy children with their first convulsive status epilepticus (SE), treated at Kuopio University Hospital, Finland, were prospectively studied. Eleven children had febrile and 11 afebrile SE. Polymerase chain reaction was used to detect specific DNA from CSF, enzyme immunoassays and immunofluorescence assays to detect specific antibodies in serum and CSF, viral cultures were obtained from CSF, throat and stool and antigen detection from throat specimens. Viral infection was identified in 10 of 11 children with febrile SE (91%) and in 7 of 11 with afebrile SE (64%). Human herpes virus 6 infection was identified in 12 children (55%), and in at least six of them the infection was primary. Single cases of human herpes virus 7, parainfluenza 3, adenovirus 1, echovirus 22, rota, influenza A and Mycoplasma pneumoniae infection were diagnosed. CONCLUSION: Viruses, human herpes virus 6 in particular, seem to be major associated factors in convulsive status epilepticus, both febrile and afebrile. Human herpes virus 7 and Mycoplasma pneumoniae are novel agents associated with status epilepticus.

COMMENTARY

Whether prolonged febrile seizures are associated with the development of mesial temporal sclerosis remains an unresolved issue. Drs. Shinnar, Pellock, and colleagues prospectively studied short-term outcomes in a population of 180 children who presented with febrile status epilepticus (FSE). They compared these patients with a group of prospectively followed children presenting with a first febrile seizure. These patients were evaluated at discharge as well as at follow-up of at least one month. Similar identification and evaluation

methods were used in both sites, and all cases were reviewed by two of the investigators (Shinnar and O'Dell). As expected, there were no deaths within 30 days of the episode of FSE or in patients with simple febrile seizures. There were, however, several important differences between the two populations. Patients with FSE had a higher proportion of focal seizures, a higher rate of pre-existing neurologic abnormalities, and a higher likelihood of a family history of epilepsy. Previous retrospective studies have reported that intractable mesial temporal lobe epilepsy commonly has a history of prolonged febrile seizures in childhood (1). Population-based studies and animal studies, however, have suggested that this does not represent a causal relationship; however, pre-existing temporal lobe abnormalities may render patients more vulnerable to damage from prolonged febrile seizures (2,3). Data from the study would certainly seem to support this latter possibility. The study is uniquely important by identifying a large prospective population with plans for ongoing data collection to track the later development of epilepsy as well as the results of detailed follow-up neuroimaging. Future results from this study may therefore be instrumental in resolving the controversy of early childhood factors contributing to the development of mesial temporal sclerosis.

Status epilepticus (SE) in children has been associated with morbidity including long term cognitive deficits, subsequent epilepsy and behavioral disorders. As the incidence of SE in children is highest under two years and is commonly associated with fever, identification of the source of the fever becomes a key element in establishing appropriate and effective treatment for SE. The authors identified 22 consecutive patients with first convulsive SE (11 febrile SE and 11 afebrile SE). Careful evaluation of all patients was conducted by serum, CSF, throat, and stool samples with detailed biological studies, nucleic acid detection, and antigen detection for specific viruses. Ten febrile SE (FSE) patients had evidence of a viral diagnosis, and eight of the afebrile SE (ASE) patients had viral diagnosis or findings. HHV-6 infection was the most commonly reported viral diagnosis in both groups, and it accounted for a larger proportion of the ASE patients. HHV-6 has previously been described to play an important role in non prolonged febrile convulsions as well (4,5). The authors conclude that HHV-6 may account for about 50% of both FSE and ASE and that viral etiologies can be found in the majority of all childhood SE. Although this is a small study, it is interesting that many patients with viral infection as a potential cause for SE did not present with a systemic manifestation of fever. Therefore, a high suspicion for viral infection in all childhood cases of SE should prompt the clinician to perform early viral testing in order to dictate specific therapy. Future studies could be developed to determine if morbidity is diminished with appropriate and promptly administered antivirals in addition to anticonvulsants.

Both of these studies direct the reader's attention to the putative relationship between mesial temporal sclerosis (MTS) and complex febrile convulsions. Because SE itself is associated with a higher incidence of later epilepsy, this controversy centers around whether there are characteristics unique to complex febrile convulsions or whether merely duration of seizure initiates or facilitates the appearance of MTS. Complex febrile convulsions that are focal rather than prolonged may occur in patients with subtle pre-existing temporal pathology that is not diagnosed on the initial magnetic resonance imaging, but later appears as MTS. Febrile convulsions that are complex due to prolonged duration, however, may be associated with development of MTS simply because these seizures are SE. Only large, long-term, prospective, controlled studies of children with FSE without pre-existing neurologic abnormalities can potentially clarify this question. Ultimately, the epileptologist and pediatric neurologist must consider whether knowing the answer to this question can improve patient outcome. Will this knowledge allow earlier epilepsy surgery, prevent the need for epilepsy surgery by diminishing the likelihood of MTS, or simply provide us with better prognostic information for our patients?

by Jane G. Boggs, M.D. and Elizabeth J. Waterhouse, M.D.

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