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The management of febrile seizures

Parents and caregivers should be reassured that after a febrile seizure the child's risk of having an afebrile seizure or developing epilepsy is very low.

ABSTRACT: Seizures during a febrile illness ("febrile seizures") are common in children between 3 months and 6 years of age. In most cases, a clinical history and physical examination can be used to determine the prognosis of a child presenting with a febrile seizure, which is usually excellent. Electroencephalography and neuroimaging are of limited value, and treatment with antiepileptic medications is rarely indicated.

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Seizures with fever occur in 3% to 5% of children in North America and Europe[1,2] and in up to 14% of children of Asian origin.[3] In most children, these seizures are the manifestation of an underlying genetic abnormality that is expressed over a relatively small number of years and is associated with an excellent prognosis. Very occasionally seizures that are due to an underlying brain lesion or infection, or to a more serious genetic abnormality, may also occur initially at a time of fever.

A febrile seizure (FS) is a disorder that presents between 3 months and 6 years of age with convulsions and fever but without evidence of intracranial infection or defined cause.[4] Population studies have found the vast majority of children have an excellent prognosis after FS.[5,6] These studies demonstrate that the risk of developing epilepsy after FS is not much greater than in the general population; there is no evidence that the seizures influence cognitive functioning; and very few children require treatment with prophylactic antiepileptic medication. These studies also demonstrate that clinical factors alone can be used to establish the prognosis and that laboratory investigations are of little value in this regard.[5,6]

Simple versus complex febrile seizure

Two major population studies, the National Collaborative Perinatal Project (NCCP)[5] and the Child Health and Education (CHES),[6] have used certain clinical features to categorize febrile seizures as simple or complex. A febrile seizure is considered complex if the seizure is focal or prolonged (longer than 15 minutes), or if there is more than one seizure in 24 hours. These studies demonstrate that approximately 80% of febrile seizures are simple. Focal seizures occurred in 4% of all FS, and the seizure lasted more than 15 minutes in 8% of cases and more than 30 minutes in 4% to 5% of cases.[5,7] Recurrent seizures within 24 hours occurred in 16% of cases. Characterization of FS as complex is of limited value in predicting the risk of later epilepsy. Whereas a child with a simple FS has a 98% probability of

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not developing epilepsy, a child with a complex FS has an 85% to 95% probability of *not* developing epilepsy.[5,8]

When do investigations help?

Although febrile seizures are common and the prognosis is excellent in nearly all children, it is important to recognize that fever and seizures are symptoms of a variety of different diseases. Thus, the occurrence of a seizure during a febrile illness may be symptomatic of an acute infection that requires treatment, such as bacterial meningitis or viral encephalitis.

Lumbar puncture

A diagnosis of bacterial meningitis or viral encephalitis should be considered in those children presenting with clinical features of these diseases and in those who have received antibiotics that may have masked these clinical features.[9] A practice parameter recommends that a lumbar puncture (LP) be performed following a febrile seizure if meningeal signs are present.[10] The same parameter recommends that LP be strongly considered if the child is younger than 12 months of age or has received antibiotics prior to the seizure, and LP be considered if the child is younger than 18 months. Bacterial meningitis has been found in 1.8% to 5.4% of children presenting with a febrile seizure.[9] However, these studies were performed prior to the use of vaccines against the bacteria commonly associated with meningitis in children under 2 years of age, meaning that today the incidence of bacterial meningitis is much lower in areas where immunization is available. However, the decreased incidence also means that many physicians have limited experience in the diagnosis of bacterial meningitis and it would seem prudent to err on the side of caution. The clinical condition of the child, the length of time since the seizure occurred, and the experience of the physician are factors that will determine whether to perform a lumbar puncture. Treatment with meningitic doses of an appropriate antibiotic and acyclovir should be instituted when there is concern that the seizure may be due to meningitis or encephalitis.

Blood glucose

Blood glucose should be measured if the seizure is longer than 15 minutes in duration or ongoing when the patient is assessed, and if the patient has a depressed level of consciousness for a prolonged period following the seizure. Blood glucose should also be checked at the bedside and 5 mL/kg of 10% dextrose should be administered if the level is less than 3 mmol/L.

Other laboratory tests

If the seizure is prolonged or ongoing when the patient is assessed, a blood culture and urine culture should also be performed and treatment with antibiotics for meningitis and with acyclovir should be strongly considered until an LP can be performed and the diagnosis clarified.

Laboratory investigations after a simple febrile seizure depend on the clinical condition of the child and should be guided by an appropriate clinical recommendations for children of that age presenting to the emergency department with fever.[11]

Neuroimaging

Imaging of the brain is not indicated after a simple febrile seizure.[11] A computed tomography head scan should be performed if there is a postictal neurological deficit persisting for more than a few hours. Elective neuroimaging should be considered when there are clinical features of a neurological disorder such as micro- or macrocephaly, neurocutaneous abnormalities, pre-existing neurological deficit, or when there is recurrent complex FS, particularly where there is doubt whether the seizures are occurring at times of fever.[12] Magnetic resonance imaging has a higher sensitivity than CT for brain lesions that present with seizures.

Electroencephalography

Electroencephalography (EEG) is not helpful in children with simple FS. Epileptiform abnormalities are relatively common in children with benign FS. Generalized spike-wave discharges occur in 49% and photosensitivity in 42% of children with benign FS followed until 11 to 13 years of age.[13] Although these abnormalities occur most often between 5 and 6 years of age, a proportion will appear at an earlier age. Thus, epileptiform abnormalities are common in children with FS and are a poor predictor of later epilepsy. In addition, first febrile seizures occur before 3 years of age in 89% of children with FS[6] and EEG has a low sensitivity in that age group.[14]

The role of EEG following a complex febrile seizure has received limited attention. In one study, EEG performed during the wake and sleep states within 1 week of a complex febrile seizure was normal in all 33 children.[15] EEG may be helpful in children who remain encephalopathic for longer than normal following a febrile seizure or who experience a focal seizure lasting longer than 30 minutes.

Risk of further febrile seizures

Approximately 30% to 40% of children who have a febrile seizure will have a recurrence,[16] usually within 12 months.[5,17] A higher risk of recurrence exists if the first seizure occurs when the patient is younger than 15 months,[16] there is a history of FS in a first-degree

Table. Factors that influence recurrence of seizures.

	Recurrent febrile seizure	Later afebrile seizure
Febrile seizure in first-degree relative	Yes	Undetermined
Afebrile seizure in first-degree relative	No	Undetermined
Developmental delay	No	Yes
Neurological abnormality	No	Yes
Age < 15 months at febrile seizure	Yes	Undetermined
Shorter duration of fever prior to seizure	Yes	Undetermined
Height of temperature	Inversely	Undetermined
Focal or prolonged febrile seizure	No	Yes
Multiple seizures in 24 hours	Possibly	No

relative,[16] there is a shorter duration of fever prior to the seizure,[17] and when the febrile seizure occurs at a lower temperature.[17] In contrast, the presence of a complex first febrile seizure, a history of developmental delay, and a family history of epilepsy have no influence on the recurrence rate of febrile seizures.[17] In addition, patients who have a febrile seizure lasting longer than 30 minutes had only a 2% risk of a second lengthy febrile seizure[5] (see **Table**).

Risk of afebrile seizures

The risk of having an afebrile seizure or developing epilepsy following a febrile seizure is very low. The risk of an afebrile seizure is 3% at 7 years of age,[5] 2.5% at 10 years of age,[2] and 5% at 20 years of age.[18] However, the risk of developing epilepsy in patients who have their first afebrile seizure following a febrile seizure is between 70% and 85%.[2,18]

The most important factor influencing the risk of developing epilepsy following a febrile seizure is the neurological function of the child prior to the febrile seizure. Forty percent of children with cerebral palsy, mental retardation, or both prior to the febrile seizure developed epilepsy compared with 2.9% of those without neurological deficit.[18] In contrast, only 0.9% of children with normal neurological development and no history of epilepsy in the immediate family had an afebrile seizure by 7 years of age, a figure only slightly higher than in the general population.[5] The occurrence of a complex febrile seizure has only a limited effect on the risk of developing epilepsy by 7 years of age. Whereas 2% of children developed epilepsy following a simple febrile seizure, 4% to 12% developed epilepsy following a complex febrile seizure in the NCCP study.[5,8]

Neurological outcome

Children with febrile seizures whose neurological development is normal at the time of the first seizure perform as well as other children in terms of their academic progress, intellectual function, and behavior at 10 years of age. This is true for children with both simple and complex FS and for those with recurrent FS.[19] Similarly, when children with febrile seizures are compared with their siblings at the age of 7 years, there are no differences in the mean full-scale IQ scores, and poor academic achievement is as common in siblings as in children who have had febrile seizures.[20] Furthermore, the mean IQ of those with recurrent seizures and those with seizures lasting 30 minutes or longer is not different from that of their siblings. Thus, the prognosis for neurological development is excellent.

Treatment

Most febrile seizures are brief and the seizure has usually ended prior to the child being assessed. If the seizure has not stopped, treatment with intravenous lorazepam (0.1 mg/kg over 1 min; maximum dose 4 mg), intravenous diazepam (0.3 mg/kg over 2 min; maximum dose 5 mg in infants and 10 mg in older children) or buccal midazolam (0.5 mg/kg; maximum dose 10 mg) is indicated.[21] Rectal diazepam (0.5 mg/kg; maximum dose 10 mg) may also be administered, but is less effective than buccal midazolam.[21]

A benign form of seizure that occurs in association with viral gastroenteritis, and in the absence of dehydration or electrolyte disturbance, has a prognosis similar to that of FS.[22] These seizures occur in children in the same age group affected by FS and may or may not be associated with fever. Such seizures appear to be unrelated to FS in that only 7% of patients have a family history of FS and only 5% have a history of FS. The seizures are brief and generalized and last less than 3 minutes in 87% of children. They occur in clusters over a period that can be as long as 24 hours in 75% of children and recurrent episodes are rare.[23] Treatment with antiepileptic drugs does not abort the cluster in most children.[23] A retrospective study reported that a single dose of chloral hydrate (50 mg/kg/d) was effective in stopping a cluster in 19 of 22 patients (86%), whereas diazepam was effective in only 2 of 16 patients (13%).[24] Care must be taken in monitoring young children receiving chloral hydrate, which may cause excessive sedation, vomiting, hyper-

activity, and respiratory complications.[25]

The second step in management is to exclude a serious underlying cause such as meningitis. This can usually be achieved by clinical assessment, with the proviso that the characteristic features of meningitis may not be present in children under 18 months of age and may be masked in those who have received antibiotics. Treatment with meningitic doses of an appropriate antibiotic and acyclovir should be instituted when there is concern that the seizure may be due to meningitis or encephalitis.

An integral part of the management of a first febrile seizure is reassurance of the family. A first seizure can be a terrifying experience for many parents, who may think initially that their child is dying. The challenge is to help the family deal with the emotional trauma and to appreciate the excellence of the prognosis. It is important for the family to understand that there is no increased risk of intellectual delay or school difficulties and that febrile seizures less than 30 minutes in duration do not result in brain damage. Similarly, the family should appreciate the low risk of developing epilepsy and the lack of benefit in using antiepileptic drug treatment to lower that risk. Finally, the family should understand that EEG and neuroimaging are of little value.

This information should be discussed with the family when the child is seen at the time of the febrile seizure. The ability of the family to fully understand all of the information at that time is likely to be limited by their emotional state, and it can be helpful for arrangements to be made for the family to receive further education at a later visit. It is important to provide the family with information on the risk of a further febrile seizure and how to deal with such an event. The information can be given in pamphlet form along with the addresses of reliable websites (e.g., www.epilepsy.com/epilepsy-febrile.html; www.patient.co.uk/showdoc/23068735/).

Prevention and treatment of recurrent febrile seizures

Cooling the child and using antipyretics does not reduce the frequency of recurrent FS.[26] Antipyretics can make the febrile child more comfortable but the parents should be dissuaded from the aggressive use of these drugs.

Several medications have been found to reduce the risk of a recurrent febrile seizure. Most physicians consider that the benefit of reducing seizure frequency is usually outweighed by the potential side effects of treatment. However, there may be situations where drug treatment has a role. Thus, in the very small number of children who have very frequent febrile seizures, reduction in the frequency of these episodes may reduce the stress on the family. Similarly, prophylactic treatment should be considered in children who live remote from medical help and who have a history of a prolonged febrile seizure.

Daily oral phenobarbital reduces the frequency of recurrences, but has a high incidence of behavioral and cognitive side effects.[27] Furthermore, in a placebo-controlled study of children with FS, the mean IQ of those who had received daily phenobarbital was 7 points lower than controls after 2 years and 5 points lower after the medication had been discontinued.[28] Daily oral valproic acid is also effective in reducing the frequency of recurrent FS,[29] but the high incidence of fatal liver failure in infants and young children[30] suggests that the risks of this drug outweigh the benefits in this situation. Daily carbamazepine and phenytoin are not effective in preventing recurrences.[31]

The academic progress and behavior of children with febrile seizures is similar to that of other children.

Benzodiazepines may reduce the frequency of recurrent febrile seizures. Intermittent rectal diazepam administered at a dose of 5 mg every 8 hours when the temperature is above 38.4 °C is effective in reducing the frequency of recurrences.[32] Intermittent oral diazepam at a dose of 0.3 mg/kg every 8 hours when the child is febrile is also effective in prevention of recurrent FS, but drowsiness, ataxia, or both occur in 30% of the children and limit the usefulness of oral diazepam. Intermittent clobazam (given as soon as the fever occurs for

Key points for management of febrile seizures

- Febrile seizures occur in 3% to 5% of children between 3 months and 5 years of age.
- When a child presents with a seizure and fever, it is important to rule out bacterial meningitis.
- Children with febrile seizures do as well at school as their siblings who do not have febrile seizures.
- The risk of developing epilepsy is approximately 1% in children with simple febrile seizures.
- Use of prophylactic antiepileptic medication is not recommended.
- Electroencephalography and neuroimaging are not indicated in children with simple febrile seizures.
- Counseling and reassurance of caregivers are very important aspects of management.

48 hours at a dose of 0.3 to 1.0 mg/kg up to a maximum dose of 10 mg b.i.d.) has been shown in a placebo-controlled study to be effective in reducing febrile seizure recurrence.[33] Intermittent clobazam has also been shown to be associated with fewer side effects than intermittent oral diazepam in children with febrile seizures.[33,34]

Parents of children who have had a prolonged febrile seizure and families living at a significant distance from medical help can be taught how to administer rectal diazepam (0.3 mg/kg) or buccal midazolam (0.5 mg/kg; maximum dose 10 mg) at home if the seizure lasts longer than 5 minutes.

All parents should be informed that there is no evidence that treatment with antiepileptic drugs influences the risk of developing epilepsy.

Summary

Febrile seizures are a common disorder in children between 3 months and 6 years of age, and are associated with an excellent prognosis. The risk of developing epilepsy is very small and neurological development and school progress are unaffected by the seizures. EEG and neuroimaging are not helpful and treatment with an antiepileptic drug is rarely indicated.

Competing interests

None declared.

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