Febrile convulsions in children

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ABSTRACT

The term febrile convulsion is not a diagnostic entity. It simply describes any seizure that occurs in response to a febrile stimulus. It usually occurs between the age of 3 months and 5 years and occurs in 2-4% of young children. The typical febrile convulsion is a generalized tonic clonic seizure lasting between a few seconds and 15 minutes, followed by a period of drowsiness. Febrile seizures tend to occur in families, although the exact mode of inheritance is not known. Viruses are the most common cause of illness in children admitted to the hospital with a first febrile seizure. Routine laboratory studies are not indicated for patients who have febrile seizures and should be performed only as part of the evaluation for a source of fever. Prognosis is generally good. Only a small minority of children develop epilepsy or recurrent non-febrile seizures. Children with febrile seizures are at no greater risk of intellectual impairments than their peers. Treatment to prevent recurrence has not been shown to prevent later development of epilepsy.

Keywords: Febrile convulsions, epilepsy, viral infections, prognosis.

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Febrile convulsions are the most common type of seizure in children.[1] They are generally of excellent prognosis. However, as they may signify a serious underlying acute infectious disease, such as sepsis or bacterial meningitis, each child must be carefully examined and appropriately investigated to see whether there is an associated cause for the fever.[2] Febrile seizures are to be distinguished from epilepsy which is characterized by recurrent non-febrile seizure.[3]

A febrile seizure is an event in infancy or childhood usually occurring between 3 months and 5 years of age, associated with fever but without evidence of intracranial infection or defined cause. Seizures with fever in children who have suffered a previous non-febrile seizure are excluded. This definition excludes seizure that accompany neurologic illnesses such as meningitis, encephalitis, or toxic encephalopathy. Seizures in these instances may carry a more ominous prognosis than that of febrile seizure owing to the effects of associated illness. The mean age is 17-23 months.[1] In practice they are rarely seen before the age of 9 months and after 5 years old.[2]

Clinical features. Febrile seizure, usually occurs early in the course of febrile illness and is often the first sign.[4] These convulsions are associated with a rapidly rising temperature and usually develop when the core temperature reaches 39°C or higher. The seizure may be of any type but is typically generalized, tonic-clonic, of a duration of a few seconds to 15 minutes, followed by a brief post-ictal period of drowsiness, less commonly, they may be focal motor or tonic. Occasionally, there may be more than one seizure in 24 hours or the seizure may last more than 15 minutes. Febrile convulsions have been divided into 2 subgroups: Simple febrile seizure, which lasts less than 15 minutes and are generalized tonic-clonic and not repeated in the same episode; and complex febrile seizures, which are prolonged to last longer than 15 minutes, multiple and occur within 24 hours or are focal[4] or have post-focal paresis.

Two large studies have demonstrated that in about one fifth of children, the first febrile seizure either was focal, multiple (more than one seizure in 24 hours or prolonged over 15 minutes.[5,6] Hot water epilepsy is a type of hyperthermic seizure similar to

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febrile convulsion but differs from it with respect to stimulus and rate of rise in temperature in a susceptible individual.[7]

Epidemiology. Febrile convulsions occur in 2-4% of young children in the United States, South America, and western Europe. They are reported to occur more frequently in Asian countries. They are slightly more common in males.[4] Several large prospective studies have determined that in approximately 20% of cases the first febrile seizure was complex. The most common age of onset is in the 2nd year of life.

Genetics. Febrile seizures tend to occur in families, although the exact mode of inheritance is not known, children who have febrile seizure more often tend to have a history of febrile convulsions in close relatives. It has long been recognized that there is a significant genetic component for susceptibility to this type of seizure. Wallace, Berkovic and co-workers recently reported linkage of a putative autosomal dominant febrile convulsion to chromosome 8Q13-21. There is also a report for another autosomal dominant febrile convulsion gene locus on chromosome 19P.[8] Parents may be told that the risk of another child having febrile convulsions after one is affected is one in five, if both parents and a previous child have had febrile convulsion, the risk for another sibling is one in three.[9] The seizure incidence in offspring of individuals with a history of febrile convulsions was 10% (only febrile convulsions in 64% of the affected offspring). Offspring of females with affected parents were not at increased risk, pathological children EEG findings of the probands were not related to an increased risk in offspring.[10]

Etiology. The exact role of fever in the etiology of febrile convulsion is not clear but there is a positive family history in 7-31% of cases.[1] The definitive degree of fever is uncertain. In one series it was shown that at the time of convulsions, 75% of patients had a temperature over 39°C. Viruses are the most common cause of illnesses in children admitted to the Hospital with a first febrile seizure.[11] Seizures that occur after immunizations are likely to be febrile, occurring in response to temperature elevation, particularly those occurring within 48 hours of DPT and 7 to 10 day after measles immunization.[12] Children of preschool age are subject to frequent infections and accompanying high fever, which in combination with a relatively low seizure threshold, allows for the common occurrence of febrile seizure. The infections commonly associated with febrile convulsion are shown in Table 1.

Hypozincemia in febrile convulsion has been reported. Serum and CSF Zn levels are decreased in children with febrile seizures. Zinc deprivation may play a role in the pathogenesis of febrile seizures.[13]
Risk factors for a first febrile seizures are:[4] Family history of febrile seizure; Neonatal discharge > 28 days; Delayed development; Child care attendance; Low serum sodium; Very high fever.

Natural history and prognosis. It is exceedingly unlikely that death or permanent motor disability will occur as a result of a febrile seizure although 0.4 percent experienced a transient focal weakness or Todd's paralysis following the seizure.[5]

Recurrences. The likelihood of recurrence of febrile seizures varies with age. The younger the child at the first febrile seizure, the more likely is a recurrence. Fifty percent of those children whose first seizure occurs under the age of one year will have at least one recurrence, whereas only 20 percent of those who have their first febrile seizure after the age of 3 years will have a recurrence.[14] About 75 percent of recurrences take place within 1 year, and about 90 percent within 2 years. There is no increased likelihood of recurrence if the seizure is complex (i.e focal, lasting over 15 minutes followed by transient or persistent neurologic deficit or multiple in one day).[5,6]

Family history of febrile seizures is another reported risk factor for recurrence.[4,5] Predictors of recurrence of febrile convulsion are shown in (Table 2).[4,5,27]

Epilepsy. Although it has been reported that febrile seizure preceded 15% of cases of childhood onset epilepsy, because febrile seizures are a much

Table 1 - Infections commonly associated with febrile convulsions.

Upper Respiratory tract infection
Otitis Media
Pneumonia
Influenza
Gastroenteritis
Urinary tract infection
Human herpes virus 6 (exanthem subitum)

Table 2 - Factors that predict recurrence of febrile convulsion.

Young age at onset
History of febrile seizures in first degree relatives
Short duration of fever before the initial seizure
Relatively lower fever at the time of the initial seizure
Possible family history of afebrile seizure

Table 3 - Risk factors for the development of epilepsy following febrile seizures.

Suspect or abnormal development before the 1st seizure
Family history of afebrile seizure
Complex first febrile seizure

more common occurrence than childhood epilepsy, fewer than 5% of children who have febrile seizures actually develop epilepsy.[4] All types of epilepsy including absence, generalized tonic-clonic and complex partial can be seen in patients who have a history of febrile convulsion.[4] Risk factors for the development of epilepsy following febrile seizure are shown in Table 3. In one study analysis of a large family and critical review of the literature led to the concept of a genetic epilepsy syndrome termed generalized epilepsy with febrile seizures plus (GEFS+), GEFS has a spectrum of phenotypes including febrile seizures, febrile seizures plus (this comprised childhood onset (median, 1 year) of multiple febrile seizures, but unlike the typical febrile convulsion syndrome, attacks with fever continued beyond 6 years of age, or afebrile seizures occurred) and the less common myoclonic-astatic epilepsy. Molecular genetic study of such large families should allow identification of genes relevant to febrile seizures and generalized epilepsies.[15] The association between febrile convulsions and temporal lobe epilepsy with mesial temporal sclerosis is recognized. A prolonged febrile convulsion was the most important determinant of this association.[16] The long term prognosis in term of subsequent epilepsy, neurological, motor, intellectual, cognitive, and scholastic ability was not influenced by the type of treatment applied in early childhood.[17] There is a preferential association of febrile convulsion with temporal lobe foci and a weaker association between febrile convulsion and generalized epilepsy . Febrile convulsion doesn't appear to be a clear risk factor for extra temporal epilepsy.[18] The relationship between febrile seizures and later epilepsy is frequently genetic, recent clinical and molecular genetic studies suggest that there are a number of syndrome specific genes for febrile seizures.[19]

Intellectual and motor function. There is no evidence that febrile seizure causes a decrease in intellectual function. In a more recent British study, there were no significant behavioral differences between children with a history of febrile convulsions and the rest of the population.[6] In the British National Child Development study, children with febrile seizures did not show any deficits in school performance at 7 and 11 years.[20] In children with prolonged febrile convulsion, non-verbal intelligence was found to be significantly lower as compared with children with simple febrile seizures and controls. Children with multiple recurrence of febrile convulsion performed poorer in all tests when compared with children with only one febrile seizure or with control.[21]

Management. Routine laboratory studies are not indicated for patients who have febrile seizure and should be performed only as part of the evaluation for a source of fever. Management of the normal infant who has simple febrile convulsion includes:- A careful search for the cause of fever; Active measure to control the fever including the use of antipyretics; Reassurance of the parents, short-term anticonvulsant prophylaxis is not indicated; Prolonged anticonvulsant prophylaxis for prevention of recurrent febrile convulsion is controversial and no longer recommended; Antiepileptics such as phenytoin and carbamezapine have no effect on febrile seizures. Phenobarbitone has fallen into disfavor because of the high incidence (30-50%) of behavioral side effects.[1] Sodium valproate has become the most widely used drug for continuous prophylaxis.[1] Treatment to prevent recurrence should be recommended in only a small minority of children who have febrile convulsion.[4] Investigation for a child with febrile convulsions:- 1. Investigate the cause of fever; 2. Exclude meningitis; a. Child under 6 months, convulsion with fever mean central nervous system infection until proven otherwise.[1] b. Child between 6 months and 18 months signs of meningitis are few, so lumber puncture at the time of the first febrile convulsion is advisable.[1] c. Child over 18 months.

If the child appears well, fully conscious with no sign's of meningitis, and has an obvious source of infection, lumbar puncture can be avoided. Review the child regularly over the next 24 hours. If the child dose not recover consciousness on arrival at the hospital, or because valium has been given, a detailed examination must be performed to rule out signs of increased intracranial pressure or focal neurological abnormality. PCR including quantitative assays, may identify primary, HHV-6 and HHV-7 infections in febrile children when an appropriate combination of clinical specimens is used.[22] The levels of Tumor necrosis factor-alpha (TNF-alpha), interleukin-1 alpha and IL6 as proinflammatory cytokines in CSF to facilitate differentiation between acute encephalitis/encephalopathy and prolonged febrile seizure. Elevated concentration of the CSF proinflammatory cytokines, TNF-alpha, IL-1 beta, and IL-6, indicate acute encephalitis/encephalopathy rather than febrile seizures.[23] The continuation of routine immunizations may arise as a question in the child who has had febrile seizures. A history of seizure within 3 days following DPT immunization is considered reason for not repeating the DPT, even though most of these seizures are probably febrile seizures. The American Academy of Pediatrics (AAP) also recommends deferral of immunization with pertussis vaccine in a child with a history of any type of seizure who is not "stable".[24] This does not preclude immunization of the child with a history of what clearly are febrile convulsions, however in each individual case risks and benefits of the vaccine should be discussed with parents and re-evaluated at each medical visit. If immunizations are given, close observance and prompt treatment of fever with antipyretics should be emphasized, particularly

within 48 hours of DPT and 7 to 10 days after measles immunization.

Brain CT scan in children with febrile convulsion. Brain CT is not indicated in the management of simple or complex febrile convulsion. Brain CT may be justifiable, but may not be clinically useful in the management of febrile convulsion patients with prior neuro-develpomental deficits.[25]

Electroencephalography. An EEG performed within one week of the febrile convulsion will show an abnormal result in one third of cases. Posterior slow activity, which may be bilateral or unilateral, is not predictive of subsequent epilepsy. An EEG is indicated for atypical febrile seizure or for the child at risk for developing epilepsy. An atypical febrile convulsion includes a seizure persisting for more than 15 minutes repeated convulsions for several hours or days, and focal seizure.[2] An abnormal EEG will not identify those children who will subsequently develop epilepsy and should not be used as a basis for deciding which children need anticonvulsant medications.

Prophylaxis. Intermittent prophylaxis. Regular use of diazepam suppositories or solution given at the start of febrile illness will prevent the recurrence of convulsion. It will reduce the convulsion rate from 27% to 12% of cases.[1] At the onset of each febrile illness, diazepam 0.3mg/kg/8 hours by mouth is administered for the duration of the illness (2-3 days), side effects are usually minimal, but symptoms of lethargy, irritability and ataxia may be reduced by adjusting the dose.[2] If treatment is prescribed, oral diazepam (valium) is preferable.[4] A study evaluated the efficacy of diazepam and chloralhydrate given rectally for the prophylaxis of recurrence of febrile seizure showed that diazepam is more effective than chloralhydrate in the prevention of recurrence of febrile seizures.[26]

Indications for continuous prophylaxis. Children under one year old and those who have prolonged convulsion; Repeated seizure during the same febrile episode; First degree-relative with history of afebrile seizure; Abnormal development before the febrile convulsion occurred. These are not absolute indications for continuous prophylaxis, provided rectal diazepam is available to the parents.

Long term management. The approach should focus on decreasing parental anxiety; Prophylaxis by means of medications is controversial; Antipyretics alone have not been shown to be effective in preventing recurrences of febrile seizures; There is no evidence that treatment to prevent recurrences can prevent the subsequent development of epilepsy.

Should certain drugs be contraindicated in children who have had febrile seizure or who present a risk of convulsion? Camphor known to be toxic and its use must be avoided in young children, other terpens given to children with colds may be convulsant if they are used for prolonged treatment or associated with other convulsant drugs (sympathomimetics, piperazine derivatives, antihistamines). We propose that the above mentioned drugs and that potential convulsant drugs and their association be used with caution.[27]

Prognosis. Febrile convulsion generally have an excellent prognosis.[2] In the majority of patients there is no tendency for the seizure to recur in adult life.[28] Recurrence of febrile convulsion is age-related, under one year there is a 50% chance of recurrence and 90% of recurrences take place within 2.5 year[3] after the first febrile seizure approximately 33% of children will have experienced one or more recurrence and about 9% of children who have febrile seizure will have three or more.

In conclusion, febrile convulsions are the most common type of seizure in childhood.[1] It is the most common cause of status epilepticus in childhood.[2] Only a small minority of children will develop epilepsy or recurrent non-febrile seizure later there is no evidence of risk of brain damage.[4] Treatment to prevent recurrences has not been shown to prevent later development of epilepsy.[3]

Prolonged anticonvulsant prophylaxis for prevention of febrile convulsion is controversial,[2] and requires further study and elucidation.

Potential risk of anticonvulsant should be weighed against benefits.[4] The majority of children who have febrile seizure require no treatment other than parental reassurance and will have a good outcome.[4] No currently available treatment has been shown to be both completely safe and effective.[4]

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