Review Article

Febrile Seizure – An Overview

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ABSTRACT

Febrile seizures are the most common seizures of childhood, occurring in 2 to 5 percent of children between six months to five years of age. As defined by the American Academy of Paediatrics (AAP), febrile seizures occur in the absence of intracranial infection, metabolic disturbance, or history of febrile seizures, and are classified as simple or complex. Simple febrile seizures represent 65 to 90 percent of febrile seizures and require all of the following features: duration of less than 15 minutes, generalized in nature, a single occurrence in a 24-hour period, and no previous neurologic problems .Initial evaluation should determine whether the features of a complex seizure are present and identify the source of fever. Routine blood tests, neuroimaging, and electroencephalography are not recommended. In the unusual case of febrile status epilepticus, intravenous lorazepam and buccal midazolam are first-line agents. After an initial febrile seizure, physicians should reassure parents about the low risk of long-term effects, including neurologic squeal, epilepsy, and death. However, there is a 15 to 70 percent risk of recurrence in the first two years after an initial febrile seizure. This risk is increased in patients younger than 18 months and those with a lower fever, short duration of fever before seizure onset, or a family history of febrile seizures. This literature review gives an overall view of etiology, risk factors, clinical parameters and the demographical profile of children with febrile seizure.

Keywords: Febrile seizure, classification, anticonvulsants, epilepsy.

INTRODUCTION

Febrile seizures are one of the most common types of seizures in childhood from which 2-5 percent of children suffer, usually occurs between 3 months and 5 years old and generally have excellent prognosis[1].It has been reported that 1 in every 25 children will experience febrile seizure at least once in their childhood[2].The International League Against Epilepsy (ILAE)has defined febrile seizure as seizure events in infancy or childhood featured with a temperature over 38℃ without any evidence of acute electrolyte imbalances or central nervous system infections[3]. There are three types of febrile seizures; simple FS, complex and febrile status epilepticus. Recurrence may be seen and the average risk of recurrence is 30-40%[4].The major risk factors for recurrence are the first FC under the age of 15 months, positive family history, and a complex type first seizure[5].

Febrile seizure arises from a wide array of genetic and environmental factors though the main case for this disorder still needs to be recognised. Various risk factors are said to play a role in aetiology of FS are gender, developmental delay, breast-feeding duration, sudden high body temperature, maternal history of alcohol consumption/smoking, family history,[6] bacterial and viral infections,[7]certain vaccinations,[8] and iron and zinc deficiencies[9]. Severe electrolyte imbalance, i.e., hypocalcaemia or hyponatremia, and hypoglycaemia are reported to be the etiology of seizure in less than 1% of children [10]. Although mild traumatic brain injury in children is associated with a low risk for posttraumatic seizures, the rate of post traumatic seizure may be as high as 19% in severe cases[11].

The standardized mortality rate (SMR) in patients with a newly diagnosed unprovoked seizure ranges from 2.5 to 4, varying with the study population and design. The SMR is highest in the youngest patients and in those with symptomatic seizures[12]. In most children with newly diagnosed epilepsy, the long-term prognosis of epilepsy is favourable, and patients with idiopathic etiology will eventually reach remission[13].Despite of advancement in the diagnosis and treatment of epilepsy many children with epilepsy function poorly with an excessive incidence of psychosocial difficulties and behavioural problems as compared to healthy children or children with other chronic illnesses [14, 15].

Objectives

To evaluate the clinical,etiological and demographical profile of febrile seizure in children.

Definition

The international league against epilepsy defines febrile seizure as a seizure occurring in childhood after one month of age associated with febrile illness that is not caused by an infection of the central nervous system[16].Febrile seizure diagnosed children cannot have a history of neonatal seizures,a previous unprovocated seizure or meet criteria for other acute symptomatic seizures.

According to the National Institute of Health, febrile seizure usually occurs between the age of 3 months and 5 years without evidence of intracranial infection or defined cause[17]. The children with neurodevelopment abnormalities may also have febrile seizure, therefore the joint working group of British physicians and paediatricians have therefore limited their definition to include neurologically normal children.

Risk Factors

- Genetics
- Prolonged neonatal hospitalization
- Maternal smoking
- Infections such as frequent throat infections, pneumonia within 6 months of age

Bethune et al stated that any of the above risk factor has a 28% risk of febrile seizures and parents of these children receive counselling concerning the possibility of febrile seizures[18]. Nelson in an American study noticed that the maternal smoking is the only preventable risk factor in case of febrile seizures. A Meta analysis study done up to 1986 has shown that younger age is one of the main risk factor for febrile seizure. The younger the age, the greater is the risk case control studies suggest that the iron and zinc deficiencies may also be risk factors for febrile seizures[19].

Epidemiology

Febrile seizures are one of the neurologic disorders in the paediatric age group, mostly affected between the age group of 6 months and 5 years of age. The febrile seizure is usually seen all ethnic group, but it has been more frequently observed in the Asian population but i.e., almost 5 – 10% of Indian children and 6-9% of Japanese[20] and the incidence is high in 14% Guamese[21]. The investigators of the United States, Finland, and Japan observed seasonal and diurnal variations in the occurrence of seizures. Febrile seizures usually occur in winter season and in the afternoon[22]. A study performed in Italy, on 188 febrile seizure children found that there is a significant increase in febrile seizure during 6 pm to 11.59 pm and a seasonal peak in January [23].

Pathophysiology

Febrile seizure is an age dependant response of immature brain to fever[24]. At the time of maturation there is an enhanced neuronal excitability that causes the child to develop seizures, this usually seen in age below 3 years of age when of seizure threshold is low[24].

First the elevated brain temperature alters many of neuronal functions, including certain temperature sensitive ion channels[25]. This cause neuronal firing and increases the chances of generating massive neuronal activity i.e.; seizures, an inflammatory process which includes secretion of cytokine in the periphery and the brain is known to be part of this mechanism.

Second it was discovered that both fever and hyperthermia are provoking seizures. The fever promoting pyrogen interleukin 1β contributes to fever[26].

Third hypothermia induced hyperventilation and alkalosis have been a pivotal element in the generation of FS. Out of which alkalosis provokes neuronal exitability[27].

Clinical Evaluation

A detailed history of patient should be taken in order to find out the etiology of fever onset of fever[28].The patient's family history should be verified to know the chances of hereditarily inherited.

Vitals should be monitored. Physical examination should be done to find out underlying cause of fever like erythromatous bulging eardrum beefy red pharynx, erythromatous tonsils etc[28]. The examination shared also search for the signs of meningitis such as irritability, depressed sensorium, nuchal rigidity etc. Above all neurological examination and fundus examination should be done

Diagnostic Evaluation

Blood tests are usually unnecessary in this case but in certain serious cases if the child is ill. A complete blood test is done to find out the chances of bacteraemia[29]. Lumbar puncture is not necessary for children who have rapidly reached normal baseline[30]. The AAP strongly recommends lumbar puncture for children <12 months of age with febrile seizure[31].

EEG should be considered in children who have prolonged or complex seizure, have a recurrence not associated with fever or children with recurrent febrile seizure associated with neurological defects[32]. MRI and CT should be considered in patients with high intracranial pressure.

Complications

Febrile seizures can be extremely frightening and emotionally traumatic for patients. The condition can cause anxiety to patients who may be under the feeling that their child might die during seizure or brain damage[33-35].

It is the seizure type that defines risk of future epilepsy. Children with simple febrile seizures have a slightly higher risk of subsequent epilepsy of around 1% compared with the incidence in the general population of approximately 0.5%[36]. The risk of future epilepsy in children with complex febrile seizures is around 4.6%,depending on the number of the complex features[37].

Encephalopathy is a rare complication with febrile seizures[38]. Recent evidence shows that missense mutations in sodium channels SCN1A and SCN2A genes may predispose children to severe febrile seizures[39]. Prolonged seizures may cause disruption in white matter

maturation along with neuroplasticity and microsterilural recognition.

Bertelsen et al followed a population based study of children born in Denmark from 1990 through 2007 of total 906,379 followed 21,079 developed attention deficit hyperactivity disorder[40]. It shows that when the studies are carried out in large scale it provides more information about development of attention deficit hyperactivity disorder.

Febrile seizures may also increase the risk of subsequent Tourette syndrome[41]. Using the Taiwan national health insurance research database; Tu et al conducted a retrospective study on 1586 patients with febrile seizure[41]. They foundthe incidence of Tourette disease is higher in case with febrile seizure.

Management

Intervention to stop the seizure is unnecessary as it may get resolve by the time the physician evaluates the child. If the seizure continuous for a long time the child is treated with intravenous lorazepam (0.05-0.1 mg/kg) or diazepam (0.1-0.2mg/kg) which is very effective in treatment of seizure[42, 43]. A 2018 Cochranesystemic review showed that intravenous lorazepam was more effective than diazepam to stop tonic clonic convulsions in children and both of them had similar rate of respiratory depression[44]. When the intravenous route is unavailable diazepam administered rectally (0.5mg/kg), buccal (0.5mg/kg) or intranasally (0.2mg/kg) and midazolam administered buccally (0.2mg/kg) or intranasally(0.2mg/kg) are safe and more effective[45, 43].

Vital signs such as temperature, heart rate, respiratory rate and blood pressure should be monitored during seizure[36]. Hypoxic children should be given with the supplemental oxygen using nasal cannular, head box, face mask or high flow delivery derive to maintain SaO_2>92%.Removal of excessive clothing and blankets and giving of antipyretics may reduce the fever[42,45].Febrile seizures can be anxiety-provoking for parents because of poor parental knowledge. It has been found that parental anxiety should be minimized with an educational intervention[46]. Parents should be aware of the first aid treatment in order to avoid a panic situation. Most of the cases, febrile seizures do not require hospitalisation.

Prevention

Children with febrile seizures have chances of developing epilepsy and recurrent febrile seizure[47].A 2017 cochrane systemic review showed that administration of valproic acid (10-15mg/kg/day) or Phenobarbital (5-8 mg/kg/day) in daily divided doses for children below 2 years is effective in prevention of febrile seizure. But there is about 20-40% chances of adverse effects on chronic anti epileptic therapy[48]. ADR of valproic acid include flu like symptoms,headache, nervousness, insomnia, alopecia, renal toxicity, pancreatitis, GI disturbances and hepatotoxicity. ADR of phenobarbitol include dizziness, loss of appetite, nausea, vomiting, transient sleep disturbances, loss of balance and hyper activity[49]. Anti epileptic drugs like phenytoin and carbamazepine are said to be ineffective in prevention of seizure[49].

Diazepam when given orally or rectally at appropriate doses (0.3-0.5 mg/kg) is found to be very effective in case of recurrence of febrile seizures[49]. But there are some cases where the seizure occurs before the fever is noticed. Under such conditions the intermittent diazepam therapy is impractical[49].Adverse effects of diazepam include nausea, constipation, drymouth, slurred speech, ataxia[48]. Other antiepileptic medications that have been used for intermittent prophylaxis include oral clobazam and levetiracetam[50].

Both acetaminophen (15mg/kg/dose) every 6 hours and ibuprofen (5mg/kg/dose) every 8 hours are effective to relieve the discomfort of the child[51].

CONCLUSION

Febrile seizures are one of the most common types of seizure that affects the paediatric age group. Children between 6 months and 5 years of age are mostly affected. Simple febrile seizures are common whereas only 15-20% is complex febrile seizures. Children with complex febrile seizures are at risk of developing epilepsy. Almost one third of children have chances of recurrence, but they outgrowth the condition by 6 years of age.

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