REVIEW ARTICLE / PREGLEDNI ČLANAK

FEBRILE SEIZURES IN THE EMERGENCY DEPARTMENT: ASSESSMENT AND MANAGEMENT

FEBRILNE KONVULZIJE U HITNOM BOLNIČKOM PRIJEMU: PROCJENA I ZBRINJAVANJE

***Martina Matolić[1], Višnja Nesek Adam[1,2,3]**

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Abstract

Febrile seizures (FS) are the most common neurological disorder in children aged 6 months to 5 years. These seizures are typically benign and occur during a febrile event (at least 38°C), without the presence of central nervous system infections, metabolic disorders, or a history of epilepsy.

The cause of FS seems to be multifactorial. Genetic predisposition has been recognized, although the mode of inheritance is not well known. Fever as a trigger of FS is requisite and up to 82 % of FS occur during viral infections, while bacterial infections are less often as a trigger. Febrile seizures are categorized as: simple or complex. Division is based on the presence of focal signs, duration and recurrence within a single infectious episode.

Prehospital and emergency management should address primarily on stabilizing the child ABC's (airway, breathing and circulation). Most febrile seizures will resolve before children arrive at the Emergency Department. For those that have not resolved and are lasting more than five minutes, benzodiazepine is recommended to terminate the seizure. Rectal diazepam and buccal midazolam are the first choice as rescue therapy, especially if IV access is not available. Prognosis is favorable and there is a low risk of developing epilepsy.

Sažetak

Febrilne konvulzije (FK) su najčešći neurološki poremećaj kod djece u dobi od 6 mjeseci do 5 godina. Najčešće su benigne i javljaju se tijekom febrilnog stanja (najmanje 38°C), bez prisutnosti infekcija središnjeg živčanog sustava, metaboličkih poremećaja ili povijesti epilepsije. Uzroci febrilnih konvulzija su višestruki, a genetska predispozicija je jedan od uzroka, iako način nasljeđivanja nije poznat. Povišena tjelesna temperatura je glavni okidač napadaja, a 82 % febrilnih konvulzija dešava se tijekom virusnih infekcija, dok su bakterijske infekcije rjeđe. Febrilne konvulzije dijele se na jednostavne i složene, a podjela se temelji na postojanju žarišnih ispada, trajanju i ponovnoj pojavi unutar 24 sata.

Većina febrilnih konvulzija prestaj i prije dolaska djeteta u hitni bolnički prijem. Djecu čiji napad traje treba stabilizirati (ABC pristup) te zaustaviti napad. Prva linija terapije u zaustavljanju napada su benzodiazepini. Rektalni diazepam i bukalni midazolam su lijekovi izbora ako se ne može uspostaviti intravenski put. Prognoza febrilnih konvulzija je dobra, većina prolazi spontano i ne zahtijeva liječenje te ima nizak rizik od razvoja epilepsije.

1 Clinical hospital "Sveti Duh", Zagreb, Croatia

2 Josip Juraj Strossmayer University of Osijek, Faculty of Dental Medicine, Osijek, Croatia

3 University North, Varaždin, Croatia

4 Libertas – International University, Zagreb, Croatia

*** Corresponding author:**

Martina Matolić
Clinical Hospital Sveti Duh,
Sveti Duh 64, Zagreb, Croatia
email: martina.matolic@gmail.com

Martina Matolić
ID: 0009-0004-3293-6089

Višnja Nesek Adam
ID: 0000-0002-6521-4136

Introduction

Febrile seizures (FS) represent the most common neurological disorder in children aged 6 months to 5 years. FS in childhood are mostly of benign character. They are defined as seizure during a febrile event (at least 38°C) without central nervous system infection, metabolic disorders or history of epilepsy (1).

The prevalence among children ranges between 2% and 5% in Europe and the United States, and up to 12% in some parts of Asia. The peak incidence of first febrile seizure occurs during the second year of children's lives (2). There is a slight male predominance.

Etiology

The cause of FS seems to be multifactorial. Genetic predisposition has been recognized, although the mode of inheritance is not well known. Polygenic inheritance has been suggested (3,4). If a child has febrile seizures there is 10 % to 45 % risk that their siblings will also have one. Susceptibility to FS is linked to several genetic loci such as 2q,5q,8q,19p and 19q. The most robust linkage is on chromosome 2q and specifically to genes responsible for sodium channel receptors and genes responsible for the immune-inflammatory response (5).

The cause of febrile seizures seems to be multifactorial, with genetic predisposition playing a significant role.

Fever as a trigger of FS is requisite and up to 82 % of FS occur during viral infections, while bacterial infections are less often as a trigger (6). The most common viruses associated with FS are: human herpesvirus 6, influenza, parainfluenza, adenovirus, respiratory syncytial virus and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (7). SARS-CoV-2 causes a febrile illness in children but it is not a trigger for FS. One study reviewed data of 8854 children aged from 0 to 5 years, diagnosed with COVID-19. Only 0,5 % of them were diagnosed febrile seizures (8).

It is still an issue for debate whether the maximum temperature or the rate of temperature rise determines the risk for febrile seizures (3). Temperature above 38°C remains a trigger for onset a febrile seizure.

Clinical signs and symptoms

Febrile seizures are categorized as: simple or complex. Division is based on the presence of focal signs, duration and recurrence within a single infectious episode. 20 % to 35 % of FS are classified as complex and their prevalence increases up to 45 % in children under 12 months of age (9).

Febrile seizures are classified as simple or complex, with complex seizures being more common in younger children and those with previous neurological issues.

A prolonged FS may result in a febrile status epilepticus (FSE). The definition means a continuous seizure (more than 5 minutes) without neurological recovery.

Simple febrile seizures

Simple febrile seizures are generalized tonic-clonic spells, and also tonic-atonic spells can be seen. The facial and respiratory muscles are also involved. They last less than 15 minutes and most of simple FS are shorter, with median duration of 3-4 minutes (10). A deep breath and closed eyes are signs of the end of seizures. Simple FS do not recur in 24-hour period.

After a simple FS children return to baseline condition very quickly and without any neurologic disorders. The postictal period can be associated with confusion or agitation and drowsiness.

Complex febrile seizures

Complex FS can be focal or generalized prolonged seizures, lasting more than 15 minutes. They are recurring in 24 hours during the same illness. Complex FS are associated with postictal neurologic abnormalities: prolonged drowsiness, transient hemiparesis (Todd paresis). Open and deviated eyes are a clinical feature of ongoing seizure.

Children with complex FS are often younger and have more likely abnormal development and previous neurologic impairment.

Diagnostic assessment

Febrile seizure is a clinical diagnosis and is defined by the following features:

1. A child aged between 6 months and 5 years
2. A seizure associated with high fever (≥38°C)
3. Absence of central nervous system infection
4. Absence of acute metabolic disorders that can cause seizures
5. No history of previous febrile seizures and no pre-existing neurologic abnormalities

Main points to examine after the first febrile seizure:

1. Medical history and physical examination to identify fever causes
2. Characteristics and duration of the seizures and post seizure status
3. Family history of FS and epilepsy

4. Pre-existing neurologic abnormalities
5. Recent illness and the use of antibiotics
6. Recent vaccination and immunization status against Haemophilus influenzae type b and Streptococcus pneumoniae

For children with simple FS who are well-appearing, diagnostic testing is unnecessary in most cases. The focus is on the assessment of the underlying febrile illness and parent education about recurrent febrile seizures and low risk of future epilepsy.

Febrile seizures in children 6 months to 5 years are usually benign, but complex cases need careful evaluation and may require lumbar puncture and brain imaging.

Signs for recurrence of FS

1. Age younger than 18 months
2. Fever duration of less than one hour and on lower level of temperature before seizure onset
3. Family history of FS
4. Preexisting neurologic abnormalities

Signs of future risk of epilepsy:

1. Age older than 3 years of the first FS
2. Family history of epilepsy
3. Multiple episodes of FS and complex FS
4. Pre-existing neurologic abnormalities

Children presenting with complex FS, specially if it is the first one, require more individualized approach. Physical and neurologic examination includes attention to:

1. Vital signs
2. Level of consciousness
3. Presence of meningismus
4. Tense or bulging fontanelle
5. Focal differences in muscle tone

Abnormalities in any of these signs should direct us to expanded diagnostics: routine laboratory testing, lumbar puncture, brain multislice computed tomography (MSCT), elective electroencephalography (EEG) and elective magnetic resonance imaging (MRI) of brain.

Indications for lumbar puncture:

1. Signs of meningitis/encephalitis
2. Age under 12 months
3. Unknown/uncomplete immunization status
4. Recent antibiotic treatment (can mask signs of meningitis)

Urgent brain MSCT should be done in children with abnormally large head, abnormal neurologic examination with focal features, or when there are symptoms of increased intracranial pressure (11).

Management

Prehospital and emergency management should address primarily on stabilizing the child ABC's (airway, breathing and circulation). Most febrile seizures will resolve before children arrive at the Emergency Department (ED).

For those that have not resolved and are lasting more than five minutes, benzodiazepine is recommended to terminate the seizure (12). Rectal diazepam and buccal midazolam are the first choice as rescue therapy, especially if IV access is not available (13). Both of them have rapid onset and limited adverse events (in terms of respiratory depression). Table 1 shows the first-line medication for febrile seizures.

Febrile status epilepticus rarely stops spontaneously and after initial benzodiazepine administration and repeated dose after 5 minutes, there is a need for additional antiseizure medications such as levetiracetam, valproate or phenobarbital (Table 2) (14).

Febrile status epilepticus rarely stops spontaneously and requires prompt intervention with benzodiazepines, followed by additional antiseizure medications if seizures persist."

Table 1. First line medication for febrile seizure

diazepam	0,3-0,5 mg/kg rectally – max dose 20 mg 0,2 mg/kg IV – max dose 10 mg 0,2 mg/kg intranasally – max dose 20 mg
midazolam	0,3-0,5 mg/kg buccally – max dose 10 mg 0,2 mg/kg intranasally -max dose 10 mg 0,1-0,2 mg/kg IM -max dose 10 mg
lorazepam	0,1 mg/kg IV – max dose 4 mg

Table 2. Second line medication for febrile seizure

LEVETIRACETAM	60 mg/kg IV
VALPROATE	20-40 mg/kg IV
PHENOBARBITAL	20 mg/kg IV

Most children with febrile seizures do not require hospital admission and can be safely discharged after a period of observation, provided they return to their neurological baseline. Before discharge, it is essential to reassure and educate parents on appropriate fever management and symptom monitoring.

Hospital admission should be considered in the presence of any of the following factors: a Glasgow Coma Score (GCS) below 15 more than one hour after the seizure, complex febrile seizures, signs of meningeal irritation, age under 18 months, prior antibiotic use before seizure onset, or incomplete or unknown immunization status.

Conclusion

Febrile seizures are the most common type of seizures in young children with relatively high recurrence rate. Prognosis is favorable and there is a low risk of developing epilepsy. Classification of febrile seizures on simple and complex type is helping ED staff in diagnostic and therapeutic management.

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