**Introduction**

Febrile seizures and status epilepticus are common neurological emergencies seen in pediatric patients that require prompt recognition and management by pharmacists. Febrile seizures affect 2-5% of children between 6 months to 5 years of age and are defined as seizures accompanied by fever without central nervous system infection. Status epilepticus refers to continuous seizure activity lasting more than 5 minutes or recurrent seizures without full recovery in between. If not treated quickly, status epilepticus can lead to permanent neurological damage and even death.

Pharmacists play a vital role in optimizing anticonvulsant therapy, educating families, and preventing medication errors in pediatric patients with these conditions. Key aspects in febrile seizures include risk stratification for recurrence, appropriate use of testing, and judicious use of anticonvulsants to minimize adverse effects. For status epilepticus, rapid benzodiazepine administration, escalation to second-line agents, and aggressive management of refractory cases are critical. This section will cover the clinical features, diagnosis, pathophysiology, and management of both febrile seizures and status epilepticus with a focus on pharmacotherapy. Key guidelines and evidence for treatment will be presented along with clinical insights and scenarios.

**Clinical Presentation**

**Febrile Seizures**

Febrile seizures affect 2-5% of children between 6 months to 5 years of age and are defined as seizures accompanied by fever without central nervous system infection. They are usually generalized in nature, lasting less than 15 minutes. Common precipitating illnesses include otitis media, upper respiratory infections, roseola, gastroenteritis.

* Risk factors:
* Age < 18 months
* Family history of febrile seizures
* Rapid rate of temperature rise
* Low degree of fever at time of seizure
* Short duration between onset of fever and seizure

* Symptoms:
* Behavioral changes, irritability
* Eye deviation or twitching
* Jerking of limbs or facial muscles
* Loss of muscle tone
* Temporary apnea

**Status Epilepticus**

Status epilepticus refers to prolonged continuous seizure activity lasting more than 5 minutes or recurrent seizures without full recovery in between. Subtypes include convulsive status epilepticus which is a prolonged convulsive seizure and nonconvulsive status epilepticus which is a prolonged change in mental status without convulsions.

Etiologies include acute causes such as CNS infections, metabolic abnormalities, drug noncompliance, drug overdose; remote causes like cerebral migrational disorders, perinatal brain injury, neurodegenerative disorders; and cryptogenic causes with unknown etiology.

* Symptoms:
* Convulsions with loss of consciousness
* Confusion or delirium
* Autonomic instability: Hypertension, tachycardia, hyperthermia
* Focal neurological deficits post-seizure

**Pathophysiology**

The exact mechanism of febrile seizures is unknown but fever lowers the seizure threshold in the developing brain. Febrile seizures likely result from the immature brain's inability to compensate for the physiological changes of fever. There is no clear evidence that febrile seizures cause permanent neuronal damage or structural abnormalities in the brain. The slightly increased risk of future epilepsy is likely from genetic predisposition rather than brain injury from the seizures themselves.

Status epilepticus results from failure of the body's endogenous mechanisms to terminate seizure activity. An imbalance occurs between excitatory neurotransmitters like glutamate and inhibitory ones like GABA. With prolonged seizure activity, GABA receptors undergo structural changes causing benzodiazepine resistance. Unopposed glutamate excitation leads to neuronal injury and death via mitochondrial dysfunction. Metabolic changes include increased glucose utilization, lactic acidosis, hyperthermia, and autonomic instability.

**Diagnostic Approach**

Febrile Seizures

* Neurological exam: Assess for meningeal signs, focal neurological deficits
* Lumbar puncture: If meningeal signs present or suspicion for CNS infection
* EEG: Not routinely needed
* Neuroimaging: Only if focal findings or persistent neurological abnormalities

Status Epilepticus

* Bedside glucose test: Rule out hypoglycemia
* Laboratory studies: Serum glucose, electrolytes, blood gas, renal function tests, drug levels
* Toxicology screen if overdose suspected
* EEG: Confirms seizure activity and monitors response to treatment
* Neuroimaging: If focal findings or history of trauma
* ECG: Assess for arrhythmias

**Management - Overview**

For febrile seizures, priority is identifying and treating the source of the fever. Anticonvulsant therapy is not routinely required. Intermittent oral diazepam can be considered for recurrent febrile seizures to reduce risk of recurrence. Patient education on febrile seizure first aid and follow-up monitoring is also important.

In status epilepticus, the main priorities are maintaining the ABCs (airway, breathing, circulation), rapidly administering benzodiazepines to stop the seizure, and escalating to second-line agents if needed. It is also critical to identify and correct the underlying etiology, prevent systemic complications, provide neuroprotection, and utilize aggressive support measures for super-refractory cases.

**Pharmacotherapy**

Febrile Seizures

Emergency Management

* **Lorazepam**0.1 mg/kg IV/IO (max 4 mg) or diazepam 0.2-0.5 mg/kg IV/IO/PR (max 10 mg)
  + Can repeat every 5-10 minutes until seizure controlled
* **Midazolam**0.2 mg/kg IN/buccal (max 10 mg)
  + Easy to administer, absorbs quickly
* **Supportive care:**
  + Antipyretics: acetaminophen, ibuprofen
  + Cooling measures
  + Oxygenation, airway management
  + Identify source of fever and treat infection

Prophylaxis

* *Not routinely recommended*
* Increased risk of recurrence if:
* Age < 12 months
* Seizure with low-grade fever
* Brief time between fever onset and seizure
* Strong family history
* **Oral diazepam:**
* 0.33 mg/kg/dose every 8 hours during febrile illness
* Reduces recurrence risk by ~40%
* Risk of respiratory depression
* Side effects: sedation, ataxia
* Chronic anticonvulsants generally not recommended
* Phenobarbital, valproic acid, primidone lower recurrence risk
* Toxicities outweigh benefits for most patients

Status Epilepticus

Emergency management

* First-line:**IV lorazepam** 0.1 mg/kg (max 4 mg) OR IV diazepam 0.3-0.5 mg/kg (max 10 mg)
* Repeat every 5 minutes until seizure controlled
* Faster absorption with lorazepam, longer duration with diazepam
* Second-line:**IV fosphenytoin** 20 mg PE/kg; IV valproic acid 20-40 mg/kg; IV levetiracetam 20-60 mg/kg
* Load fosphenytoin at maximum rate of 150 mg/min
* Monitor valproic acid levels, avoid in liver impairment
* Levetiracetam generally well tolerated

Refractory status epilepticus

**IV anesthetics:**

* Propofol starting at 2-5 mcg/kg/min, titrate up to 5-10 mcg/kg/min
* Midazolam 0.2-2 mg/kg bolus, then 0.05-2 mg/kg/hr infusion
* Pentobarbital typical starting dose 5-15 mg/kg, then 0.5-5 mg/kg/hr

**Adjuvant therapy:**

* Ketamine loading dose 1.5 mg/kg IV, then infusion 2.5 mg/kg/hr
* Hypothermia goal temp 32-34°C
* IV magnesium sulfate 40 mg/kg loading dose
* Key is EEG monitoring to titrate anesthetic infusion

Key Points

* Give oxygen, secure airway early
* Shock resistant peripheral IV access
* Bedside glucose, anticonvulsant levels
* Treat underlying cause: thiamine if suspected alcohol withdrawal
* Avoid phenytoin in neonates (purple glove syndrome)
* Monitor for hypotension, arrhythmias

**Key Guidelines and Evidence**

Febrile Seizures

* Guideline for the Neurodiagnostic Evaluation of the Child with a Simple Febrile Seizure (AAN, 2010)
* Neuroimaging not needed in neurologically normal child 1B
* EEG not recommended 1B
* LP should be strongly considered if meningeal signs or <12 months without Hib vaccine 1B
* Clinical practice guideline for the long-term management of the child with simple febrile seizures (AAP, 2008)
* Anticonvulsants not routinely recommended due to side effects 1B
* Intermittent oral diazepam can be considered to reduce recurrence 1B

Status Epilepticus

* Treatment of Convulsive Status Epilepticus in Children and Adults (Epilepsy Foundation Guideline, 2016)
* Administer benzodiazepine as soon as possible 1A
* Fosphenytoin is preferred 2nd line agent in children 1B
* Levetiracetam, valproic acid alternatives for 2nd line 1B
* Urgent control of systemic and respiratory complications 1C

**Clinical Scenarios**

Clinical Scenario 1:

A 10-month old girl presents with a witnessed tonic-clonic seizure at home associated with a fever of 38.9°C (102°F). Her parents report this is her third febrile seizure in the past 6 months. On examination, she is sleepy but consolable and has no meningeal signs or focal neurological deficits.

Clinical Scenario 2:

A 5 year-old boy with a history of epilepsy presents with 2 witnessed focal seizures that have continued for over 10 minutes. He receives lorazepam which stops the seizure temporarily but a third seizure begins 5 minutes later.

Answer Key for Scenario 1:

This presentation is consistent with a simple febrile seizure. LP and neuroimaging are not necessary given normal post-ictal exam. Testing should focus on identifying the source of fever, likely a viral infection. Intermittent oral diazepam could be considered for febrile illness in this patient given her young age and seizure recurrence. The benefits of reducing recurrence risk must be weighed against the potential for medication side effects and adverse events. Parents should receive education on febrile seizure first aid and precautions.

Answer Key for Scenario 2:

This patient is now in status epilepticus. Urgent escalation to a second-line anticonvulsant is indicated given failure of lorazepam to terminate the seizures. Fosphenytoin would be a reasonable choice given the patient’s history of epilepsy. The patient should be transferred to the ICU for further management. EEG monitoring and evaluation for an underlying etiology are critical steps.

**Tips for Board Exam Questions**

* Know criteria for simple vs complex febrile seizures and implications for workup
* Identify scenarios requiring LP based on history and exam
* Recall anticonvulsant options for febrile seizure prophylaxis and emergency treatment
* Stages of status epilepticus: early, established, refractory
* Initial benzodiazepines, second-line agents, and options for refractory cases
* Differentiate convulsive vs nonconvulsive status epilepticus

**Summary**

Febrile seizures and status epilepticus are medical emergencies requiring prompt recognition and management. However, febrile seizures are ultimately benign in most children and rarely require chronic anticonvulsants due to side effects.

Pharmacists should be prepared to assist in risk stratification, administration of emergency anticonvulsants, and prevention of medication errors. For status epilepticus, priority is terminating seizures quickly with benzodiazepines while identifying the underlying etiology. Multimodal management and aggressive support are crucial in refractory cases to avoid permanent neurological injury.

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