# Management of convulsive status epilepticus in children

Dipak Ram

Timothy Martland

## Abstract

Convulsive status epilepticus (CSE) is the commonest neurological emergency in children, and is potentially life-threatening. The main principles of management encompass good basic life support, terminating the seizure with suitable drugs, and identifying and treating the underlying cause. The outcome is dependent on the aetiology of CSE and the duration of seizure. National resuscitation guidelines in the United Kingdom now focus on the importance of rapid recognition and treatment of CSE, with appropriate escalation of care involving intensive care at an earlier stage. In recent years, use of other drugs are being explored in various centres as part of the acute management of CSE including sodium valproate, levetiracetam and lacosamide. This ongoing research will provide further fundamental evidence-based information in shaping future guidelines for the optimal management of CSE in children.

**Keywords** acute management; children; emergency; paediatric; review; seizures; status epilepticus

## Introduction

Seizures are paroxysmal disturbances to consciousness, behaviour, sensation or autonomic function caused by disruption to brain function. Most seizures are transient and self-limiting events, enabling the child to return to their baseline state. When they are prolonged, seizures may become difficult to terminate, necessitating emergency treatment.

Convulsive status epilepticus (CSE) is a neurological emergency and if not treated appropriately, causes significant morbidity and mortality. With recent advances in paediatrics, new approaches are being applied to further optimise the management of CSE.

Our article will focus on CSE as this is the commonest presentation of status epilepticus in children (more than 85% of cases). Non-convulsive status epilepticus (NCSE) presents very differently with only minor motor accompaniments and although prompt management is warranted, it does not constitute an emergency. Neonatal status epilepticus will also not be covered in this review as aetiology, management and outcomes differ from presentations in infants and children. Focal motor status epilepticus and *Epilepsia partialis continua* are not included in the standard definition of CSE, and details of this are therefore not discussed in our review.

***Dipak Ram*** *MBBS MRCPCH is a Specialist Registrar in Paediatric Neurology in the Department of Paediatric Neurology, at Royal Manchester Children's Hospital, UK. Conflicts of interest: none declared.*

***Timothy Martland*** *MBChB MRCP MRCPCH is Consultant Paediatric Neurologist in the Department of Paediatric Neurology, at Royal Manchester Children's Hospital, UK. Conflicts of interest: none declared.*

## Definition

Convulsive status epilepticus (CSE) has historically been defined as continuous motor seizure activity or repetitive clustering of seizures with incomplete recovery for more than 30 minutes. This initial definition was based on animal studies which showed that after 30 minutes, damaging physiological effects due to the ongoing seizure activity began to be seen.

From the perspective of managing CSE in children, this is relevant but not directly applicable to the convulsing child. Current opinions suggest a more practical definition, which can be applied to clinical practice in paediatrics. The International League Against Epilepsy (ILAE) defines status epilepticus (SE) as "a seizure that shows no clinical signs of arresting after a duration encompassing the great majority of seizures of that type in most patients or recurrent seizures without interictal resumption of baseline central nervous system function".

In reality, the majority of convulsions terminate spontaneously without intervention in less than 2 minutes. Evidence has shown that generalised tonic-clonic seizures (GTCS) lasting longer than 5 minutes may not stop spontaneously and become increasingly resistant to treatment if not dealt with appropriately. Therefore, it is generally agreed that treatment for CSE should be started 5 minutes after the onset of a GTCS.

## Epidemiology

Population based studies have shown that the annual incidence of CSE in children is about 20 per 100,000 children. This translates to an estimated 10,000 new cases each year in the United Kingdom. In children with a pre-existing diagnosis of epilepsy, about 10–25% will have at least one episode of CSE. They account for just under 5% of admissions to paediatric intensive care units.

## Pathogenesis

Seizures usually terminate due to GABA mediated inhibition of the central nervous system. This pathway is activated when a seizure starts and failure of this mechanism may be one of the reasons for CSE developing.

A seizure involves abnormal discharge of neurons, which increases the cerebral metabolic rate. This in turn leads to increased utilisation of oxygen, glucose and other substrates. The supply of these substrates to the brain is further enhanced by an increase in cerebral blood flow, which is stimulated by a sympathetic response. Initially, this maintains cerebral metabolism but as the seizure continues, hypoxia may impair this and lactate accumulates. Continuing motor activity also causes depletion of glycogen stores in the muscle, leading to anaerobic metabolism and myocardial impairment. This can trigger a cascade of further cellular hypoxia and hypoperfusion, leading to multiorgan failure and death.

## Aetiology

### Febrile CSE

5% of febrile convulsions are prolonged beyond 30 minutes. The concern in any child with febrile CSE is an underlying central nervous system infection. Up to 20% of children who present with febrile CSE are found to have underlying bacterial or viral

meningitis. However, it is important to highlight that in children who present with simple febrile convulsions, less than 1% are due to meningitis. Although febrile CSE may be a first presentation of meningitis, it is not usually the only sign. An irritable child or one who is not recovering as expected post-ictally warrants further investigation. Careful history taking and examination is required to ensure that diagnosis and treatment are not delayed in these circumstances.

There are also genetic epilepsies which may present with recurrent prolonged febrile convulsions in children. Dravet syndrome, previously known as severe myoclonic epilepsy of infancy (SMEI), tends to present with recurrent focal febrile CSE episodes in up to 60% of cases. It is typically caused by a mutation in the *SCN1A* gene, which encodes for voltage-gated sodium channels. These patients are differentiated from other children with febrile CSE with time, as their seizures become more prominent and difficult to manage. It is also associated with a poor neurodevelopmental outcome.

Generalised epilepsy with febrile seizures plus (GEFS+) is another genetic epilepsy which may initially manifest as recurrent febrile CSE episodes. Unlike typical febrile convulsions, these episodes may persist beyond the age of 6 years. There is usually a family history and although most children stop having seizures by mid-adolescence, some continue into adulthood Box 1.

### Afebrile CSE

The first step is to identify the background neurological and developmental status of the child. Children with no background history are more likely to have had acute cerebral insults, such as meningitis, head injuries or electrolyte disturbances leading to CSE. This is not always applicable, as sometimes the first CSE in a previously well child may be the start of a neurological disorder or epilepsy syndrome.

Children with pre-existing neurological and developmental abnormalities may have a predisposition to CSE. For example, children with focal cortical dysplasia or a mitochondrial disorder may present with recurrent CSE episodes due to their underlying diagnosis. It is still crucial to look for acute triggers in these children, as you do not want to miss something reversible such as hypoglycaemia or electrolyte abnormalities Box 2.

### Questions to consider in febrile CSE

1. Could this be meningitis?

- Perform a lumbar puncture in a child who is irritable or is taking longer than expected to recover post-ictally

2. Am I dealing with a genetic epilepsy?

- Think of GEFS+ in a child with recurrent febrile CSE episodes and a family history of this
- Consider Dravet syndrome in a child with recurrent focal febrile CSE episodes even if it has not evolved to different seizure types yet

**Box 1**

### Differential diagnosis

One of the most important points is getting the diagnosis correct before commencing treatment. Non-epileptic attack disorders

### Example of aetiological classification for CSE

1. Child with normal neurological background

- Meningitis/encephalitis
  - Viral or bacterial
  - Autoimmune (e.g. NMDAR/VGKC encephalitis)
- Head injury
  - Traumatic
  - Non-accidental
- Metabolic
  - Hypoglycaemia
  - Electrolyte disturbance
- Haemodynamic instability
  - Hypoxia
  - Hypertensive encephalopathy
- Cerebrovascular disorders
  - Ischaemic stroke
  - Intracranial haemorrhage
  - Venous sinus thrombosis
  - Vasculitis
- Toxicity
  - Drug-induced
- Idiopathic*

2. Child with history of pre-existing neurological/developmental abnormality

- Structural
  - Focal cortical dysplasia
  - Brain tumour
  - Previous brain insult/injury
  - Neurocutaneous disorders (e.g. tuberous sclerosis, neurofibromatosis, Sturge–Weber)
- Metabolic
  - Mitochondrial disorders (e.g. POLG1 mutation)
  - CSF neurotransmitter disorders
- Genetic
  - Known genetic condition associated with epilepsy (e.g. Angelman syndrome)
- Iatrogenic (in children with known epilepsy)
  - Reduction/withdrawal of anti-epileptic drugs
  - Poor absorption of drugs (e.g. gut dysfunction)
- Idiopathic*

*No precipitant found in 8–10% of cases

**Box 2**