Management of status epilepticus

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Abstract

Convulsive status epilepticus (CSE) is a neurological emergency. It can be the brain’s response to a variety of acute cerebral insults, or a complication of chronic neurological conditions. Management focuses on maintaining vital functions, stopping the seizure and identifying and treating the underlying cause. Morbidity and mortality have improved over recent years, probably because of more aggressive use of anti-convulsant medication in the acute phase and improved paediatric emergency and intensive care. Neurological sequelae are cause- and age-dependent. The highest morbidity and mortality is seen in the group of children with symptomatic CSE. More accurate epidemiological data is now being gathered on CSE in children, which has refined our understanding of the problem. Much work has gone into the development of evidence-based national guidelines on the optimal management in children, and new evidence from both epidemiological studies and the Cochrane review are informing improvements to the guidelines.

Keywords  acute management; children; generalised tonic-clonic seizure; review; status epilepticus

Introduction

Convulsive status epilepticus (CSE) is a potentially life-threatening neurological emergency, with a risk of serious neurological sequelae. Both the underlying condition, and CSE and its treatment carry a significant morbidity. There has been better understanding of CSE over recent years, with paediatric epidemiological studies showing that morbidity and mortality in children with CSE are lower than in adults, although children are more commonly affected by CSE.

This article focuses on CSE as this is the most common presentation of status epilepticus (SE) in children, and the most dangerous. The convulsive element may be tonic-clonic, tonic or clonic, and may start as a focal seizure with secondary generalisation. We will be discussing CSE in children over 28 days of age because neonatal SE has a different aetiology, treatment recommendations and outcomes.

CSE should be seen as a symptom of a cerebral insult, either acute, acute on chronic (often referred to as remote symptomatic) or part of a chronic neurological condition. It occurs when the body’s innate mechanisms to terminate a seizure fail. It is not a single disorder, but is seen as a complication of many disorders. The seizure has local effects on the brain, which continue to be investigated and debated, and also causes systemic compromise, which worsens the longer the seizure continues. Although the main concern is to stop the seizure, while maintaining vital functions, rigorous effort must be made to identify and treat the underlying cause, as in some instances (e.g. hypoglycaemia) the seizure will continue until this is managed.

Definition of CSE

The International League Against Epilepsy (ILAE) defined SE in 2001 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’. The definition of CSE used in many articles is of a generalised seizure lasting 30 minutes or longer, or repeated tonic-clonic convulsions occurring over a 30-minute period without recovery of consciousness between each convolution.

Most generalised tonic-clonic seizures (GTCS) self-terminate after 2 or 3 minutes. GTCS that last longer than 5 minutes may not stop on their own and become increasingly resistant to treatment. If a seizure lasts for 30 minutes, the child is at high risk of metabolic decompensation. For these reasons, in practical terms, treatment for CSE should be started once a GTCS has lasted for 5 minutes.

The 2001 ILAE-proposed classification of epilepsy recognises that there are as many types of SE as there are types of seizures. The most clinically useful distinction is between convulsive or generalised tonic-clonic status epilepticus (CSE) and other focal, absence or non-convulsive types of SE (NCSE). Although this is not addressed by the ILAE classification system, in general, types of SE other than CSE are less likely to lead to rapid systemic compromise. Although needing prompt intervention, the management of these is less urgent and requires an individual response depending on the patient and seizure type.

Epidemiology

In the UK, the best available evidence about the incidence of CSE is the North London convulsive Status Epilepticus in childhood Surveillance Study (NLSTEPSS). This prospective population-based study, based in an urban resource-rich setting, took place over a 2-year period (2002–2004). It included 226 children and has been reported by Chin and colleagues. The incidence of CSE was 18–20 per 100,000 children per year. Extrapolated to the paediatric population of England and Wales, about 3200–4300 episodes of CSE will occur every year in England and Wales. This will be the first episode of CSE for 1650–2240 children. The incidence of CSE was highest in children under 1 year of age (51 per 100,000 per year), then those aged 1–4 years (29 per 100,000 per year), then 5–9 years (9 per 100,000 per year), then 10–15 years (2 per 100,000 per year). Studies in adult populations have estimated an incidence of 4–6 per 100,000 per year (although the
The higher incidence in infants and toddlers is due to more acute symptomatic causes in this age group, such as febrile seizures.

Aetiology

CSE in children is most often not a symptom of an underlying seizure disorder or an epilepsy but represents a response to an acute cerebral insult. The ILAE has produced a recommended classification system according to aetiologies, which can be useful to think of when forming a differential diagnosis.

- **Acute symptomatic CSE** is SE in a previously neurologically normal child, within a week of an underlying aetiology.
- **Prolonged febrile convulsion (PFC)** is a subtype of acute symptomatic SE. PFC occurs in 5% of children experiencing febrile seizures and has a much better outcome than other acute symptomatic causes such as meningitis.
- **Remote symptomatic CSE is SE** in the absence of an acute insult but with a history of a pre-existing central nervous system (CNS) abnormality.
- **Remote symptomatic with an acute precipitant** is seen in children with a static encephalopathy who have an acute provocation for their CSE (e.g. meningitis in a child with cerebral palsy and epilepsy) or a blocked ventriculo-peritoneal shunt in a child with treated hydrocephalus.

Children with a progressive CNS disorder are included in the remote symptomatic group. Table 1 gives examples of potential causes.

CSE can also be seen as the first seizure presentation in 12% of children with epilepsy. Around 10–25% of children with epilepsy will have at least one episode of CSE. When it occurs in a child with epilepsy it could be due to an intercurrent illness, non-concordance with or changing of antiepileptic drugs (AEDs), or due to an acute symptomatic cause. The classification of the CSE is the same as their type of epilepsy.

The cause of CSE in the NLSTEPSS cohort is shown in Table 2. These results are in keeping with previous studies that have shown that less than one-third of cases of CSE in children are caused by an underlying epilepsy. Aetiology is also age-dependent. A febrile aetiology is more common in the under 2s and a cryptogenic or remote cause is more common in older children.

The NLSTEPSS cohort also provided a very important reminder that not everyone in CSE with a fever is having a prolonged febrile convolution. In the children in CSE who were febrile, 12% had acute bacterial meningitis (11 children) and 8% (seven children) had a viral CNS infection. Some of these were initially diagnosed as a prolonged febrile convolution. This emphasises the point that care must be taken in finding the underlying cause in all children with CSE.

Pathology and pathogenesis

CSE occurs when the mechanisms required for seizure termination fail. A seizure is a disturbance of cortical function due to a sudden, abnormal, excessive and disorganised discharge of neurons. This leads to an alteration of consciousness and abnormal motor activity. The abnormal activity of the neurons greatly increases the cerebral metabolic rate, causing increased consumption of oxygen, glucose, adenosine triphosphate and other cell substrates. There is a compensatory increase in cerebral blood flow, stimulated by a sympathetic response, which leads to tachycardia and raised blood pressure. The catecholamine release also stimulates hyperglycaemia initially. As the seizure continues, there may be systemic compensation, especially if respiration is ineffective, leading to hypoxia and respiratory acidosis. The excessive muscle activity can exhaust glycojen stores, and hypoglycaemia and anaerobic metabolism ensue. In turn this can lead to metabolic acidosis, organ failure, and cardiac and respiratory arrest.
Benzodiazepines and phenobarbital act via GABAA receptors, leading to loss of GABA-mediated inhibition of seizures. Because enon of epileptogenesis (seizures beget seizures) could potentially potential for future seizures is not clear in children. This phenom-

apses, alterations in receptors and ion channels) can enhance the activation of phospholipase A and a secondary influx of calcium to the cell membrane, inhibition of mitochondrial function and toxicity. Activation of the NMDA receptor can lead to destruction at high concentrations, a phenomenon known as excitatory neuro-
toxicity. As the CSE progresses, a dynamic process involving changes at cellular level in the brain is seen. There is time-dependent loss of synaptic gamma aminobutyric acid (GABA) receptors, leading to loss of GABA-mediated inhibition of seizures. Because benzodiazepines and phenobarbital act via GABA receptors, this explains why benzodiazepines are less effective as the seizure progresses. It is interesting though that midazolam, which works in a similar manner, may be effective by infusion in resistant CSE when other benzodiazepines have failed.

In the acute phase, CSE is dangerous because it impairs vital functions. In the longer term, there is debate about whether the actual seizure itself causes long-term cerebral damage. Glutamate, the main excitatory neurotransmitter via the N methyl D aspartate (NMDA) receptor, is thought to have a directly toxic effect on cells

Table 2

<table>
<thead>
<tr>
<th>Underlying cause of CSE in NLSTEPSS</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolonged febrile seizure</td>
<td>32%</td>
</tr>
<tr>
<td>Acute symptomatic</td>
<td>17%</td>
</tr>
<tr>
<td>Remote symptomatic</td>
<td>16%</td>
</tr>
<tr>
<td>Remote with acute cause</td>
<td>16%</td>
</tr>
<tr>
<td>Idiopathic epilepsy-related</td>
<td>10%</td>
</tr>
<tr>
<td>Cryptogenic epilepsy-related</td>
<td>2%</td>
</tr>
<tr>
<td>Unclassified</td>
<td>7%</td>
</tr>
</tbody>
</table>

CSE, convulsive status epilepticus; NLSTEPSS, North London convulsive Status Epilepticus in childhood Surveillance Study.

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poral lobe epilepsy is still debated. Whether the changes caused by CSE (such as inflammation, loss of and changes in nerve syn-

apses, alterations in receptors and ion channels) can enhance the potential for future seizures is not clear in children. This phenom-

emon of epileptogenesis (seizures beget seizures) could potentially be influenced by therapeutic interventions.

**Management**

The goals in the management of CSE are to maintain vital func-
tions whilst stopping the seizure and to identify and treat the underlying cause. This should be achieved through a structured approach (such as that taught on Advanced Paediatric Life Sup-
port (APLS) courses), by a team, and advice from the most ex-
perienced clinician available. A large number of interventions, both therapeutic and diagnostic, need to be carried out in a short period of time. In the acute treatment phase, parents and carers may be very frightened about the health of their child, and it is important that they are provided with a clear, contemporaneous explanation of what is happening.

**CSE management guidelines**

In the UK in 2000, the Status Epilepticus Working Group pub-
lished recommendations for a treatment protocol for CSE in children. These were based on a comprehensive literature review and subsequent expert consensus. These guidelines have been included in National Institute for Clinical Excellence (NICE) and Scottish Intercollegiate Guidelines Network (SIGN) guidance and the APLS manual. Systematic reviews from the Cochrane Col-
laboration (2002, 2005, 2008) and further prospective population-based studies and randomised controlled trials are being reviewed to update the practice parameter.

**Out-of-hospital treatment**

One issue not addressed by the current guideline is out-of-hos-
pital emergency medication (from parents and carers or para-
medics). Receiving more than two doses of benzodiazepines is associated with an increased risk of need for paediatric intensive care unit (PICU) admission because of respiratory depression, rather than because of ongoing seizure. The use of pre-hospital treatment is now more widespread and this could lead to multiple ineffective doses of benzodiazepines. The APLS algorithm also emphasises that, in the presence of serious systemic compromise, it may be appropriate to proceed more rapidly to tho-

dentone and intubation.

Diazepam as rectal gel has been the most popular out-of-
hospital drug in the UK for many years. However, the rectal route can be difficult in a convulsing child and is embarrassing in public places. Carers in some school or residential settings are not permitted by their employers to administer medication by this route. Midazolam can be given safely via the buccal route and is replacing rectal diazepam as the preferred rescue medication for out-of-hospital situations. Midazolam has been recommended as the first-choice benzodiazepine in the management of CSE in a paper from the Netherlands.

There are guidelines available to ambulance services, including the Pre-Hospital Paediatric Life Support algorithm (the pre-
hospital version of APLS). However, these are constrained by the unlicensed status of midazolam and the skills and training level of the paramedics. Most are still based on rectal diazepam but all reinforce the need for urgent hospital transfer.

**On arrival in hospital**

Despite the many different causes of CSE, the initial treatment of a child presenting to hospital in CSE is the same. NICE and SIGN guidelines recommend that local protocols for the management of CSE be in place. Constant re-assessment of the child should be made throughout the process, to gather information pointing to the underlying cause, which will direct further interventions and treatment. Close and skilled nursing observation of temperature, blood pressure, heart rate, respiratory rate and oxygen saturations are needed. A ward-test glucose should be done. The APLS guidelines are probably the most widely taught and followed in the UK. These provide advice on how to manage such children in the first hour of their presentation and are recommended. Teams should know who to talk to if the CSE continues.

History taking should concentrate on antecedents to this epi-
sode, any previous episodes and treatment and an accurate semio-
logy and chronology of this seizure. Information from paramedics is often useful. The child needs a careful examination on arrival and this may need repeating. In the acute phase, a primary survey/secondary survey approach is best including level of consciousness, signs of an acute insult and general neurological examination.
**Differential diagnosis**

The guidelines emphasise that there are other neurological conditions that present with alteration of consciousness, real or apparent, and/or abnormal movements, tone and posture and which need to be differentiated from CSE. Table 3 shows the main differential diagnoses to be considered. A careful history and clinical examination will distinguish between these conditions in most patients.

**Investigation**

A ward-test glucose should be done immediately. CSE usually causes hyperglycaemia initially, therefore, if hypoglycaemia is found, further investigations should be carried out as well as treatment. Further investigations are guided by the clinical situation, and not all may be needed.

The American Academy of Paediatrics published a practice parameter (evidence-based review) on the diagnostic assessment of the child with SE in 2006, which offers a review of the usefulness of each investigation. The Royal College of Paediatrics and Child Health Guideline Appraisal and Summary 31 (decreased conscious level) provides advice on investigation, some of which is relevant to CSE. Table 4 shows some tests that may be of use.

Investigations should be mainly aimed at explaining the aetiology. For a first episode, urea, electrolytes and calcium should be done but not as a routine for all CSE. Full blood count, liver function tests, C-reactive protein, coagulation studies and blood and urine culture are commonly requested in seriously ill children, particularly when sepsis is suspected. Initially, the child may be too unstable to have a lumbar puncture. When there is concern about a CNS infection, treatment with antibiotics and acyclovir should be given until a lumbar puncture can be done and infection confidently excluded. Guidelines for safe lumbar puncture in the acute phase are included in APLS.

In most cases, AED levels are not useful. They might show non-concordance with treatment (by being unrecordable) but AED levels are often not representative of level of seizure control. Low AED levels were seen in only one out of 226 children in the NLSTEPSS cohort. Neuroimaging should only be done after the child in CSE is stabilised and the seizure controlled. It is not recommended in all cases of CSE. At least 8% of children in CSE will have an imaging abnormality, but this may not be relevant to the CSE. Imaging is indicated in a first event when there is no obvious cause in a previously well child or where the history suggests a focal onset. If the child’s level of consciousness remains low or there are new neurological signs, senior advice should be sought as well as imaging. Computed tomography is often sufficient in the acute situation and presents fewer practical difficulties compared with magnetic resonance imaging. Inborn errors of metabolism may account for some cases of CSE. Although they are individually rare, they may be treatable.

**Drug treatment**

Drugs used in CSE should ideally be efficacious, safe, and rapid in onset. Benzodiazepines (midazolam, lorazepam and diazepam) are currently regarded as the best first-line drugs. Phenytin, phenobarbital and paraldehyde are often used as second line. In the resuscitation situation, intravenous access in young children can be very difficult and other routes, such as buccal or rectal, are often used. The intra-osseous route may be used. Treatment can potentially cause respiratory arrest, hypotension and cardiac arrhythmias. The timing of each drug class in the treatment protocol is based on understanding of the time-dependent receptor changes that occur during the evolution of CSE, and the time taken for the drugs to reach therapeutic levels following administration.

**Table 3**

**Differential diagnosis of CSE**

- Extensor tonic posturing due to RiCP
- Dystonia, including status dystonicus
- NEAD, also known as pseudo-seizures
- Acute movement disorders, including chorea and tics
- Acute encephalopathy

CSE, convulsive status epilepticus; RiCP, raised intra-cranial pressure; NEAD, non-epileptic attack disorder.

**Table 4**

**Potentially useful investigations in CSE**

**In all cases**

- Ward-test glucose (with appropriate further tests before treatment if low)

**In some cases**

- Urea, electrolytes, calcium
- True blood glucose
- Full blood count
- C-reactive protein
- Liver function tests
- Capillary blood gas
- Coagulation studies
- Blood culture
- Urine culture
- Lumbar puncture (glucose, lactate, microbiology and viral studies with paired true blood samples)
- Bacterial and viral PCR tests

**Sometimes useful (once child stable)**

- Neuroimaging (CT easier than MRI acutely)

**Sometimes useful (dependent on history and initial investigation)**

- ECG
- Ammonia
- Urine amino and organic acids
- Specific enzyme assays (speak to a consultant with an interest in IEM)
- Urine toxicology screening

**Rarely useful (acutely)**

- AED levels
- EEG

CSE, convulsive status epilepticus; PCR, polymerase chain reaction; CT, computed tomography; MRI, magnetic resonance imaging; ECG, electrocardiogram; IEM, inborn errors of metabolism; AED, antiepileptic drug; EEG, electroencephalogram.
NLSTEPSS was conceived as an observational study, but further examination of the data, published in 2008, looks at the outcomes from treatment. The effectiveness of early (pre-hospital) treatment was confirmed to reduce the incidence of prolonged CSE. Within hospital, intravenous lorazepam was 3.7 times more likely to stop CSE than intravenous diazepam. Children who received phenytoin as second line were nine times more likely to respond than children who were treated with rectal paraldehyde. Chin and colleagues comment that rectal paraldehyde is inferior to phenytoin in this situation and, particularly with the misinterpretation of the published guidelines apparent from their study, should not be part of CSE management. Paraldehyde may still have a role for some children on an individual basis.

**Benzodiazepines**

Benzodiazepines act as GABA agonists, suppressing brain activity. Respiratory depression is more often seen when the intravenous route is used, particularly with multiple doses. Benzodiazepines are rapidly redistributed from the brain to adipose tissue, which can lead to recurrence of seizures. Lorazepam binds more tightly to benzodiazepine receptors than others and this may explain why clinically it has a longer duration of action. Lorazepam is usually given intravenously. There are reports of its use rectally and nasally, but its efficacy by these routes is not established.

The recent studies evaluated in the 2008 Cochrane Review confirmed the superiority of lorazepam compared with diazepam in the acute treatment of acute tonic-clonic convulsions. Children who receive lorazepam are less likely to require additional drugs to terminate the seizure, fewer develop respiratory depression, and fewer require PICU admission.

Buccal midazolam is better than rectal diazepam where intravenous access is unavailable and intranasal midazolam is as effective as intravenous diazepam in the treatment of prolonged febrile convulsions. It is this evidence that has led to a change in out-of-hospital and first-line treatment to buccal midazolam. In addition to its greater efficacy and safety, the buccal route is far preferred by patients and carers.

**Second-line treatments**

Phenytoin acts by stabilising neuronal membranes. It must be infused slowly at 1 mg/kg/min and under cardiac monitoring, as it may cause cardiac arrhythmias. The efficacy of phenytoin as second line was demonstrated in the NLSTEPSS study and it causes less sedation and respiratory depression than barbiturates. Paraldehyde is a polymer of acetaldehyde. It is well absorbed rectally and distributes quickly to the brain. Clinical effects are noticed before maximal blood levels are reached. The risks of respiratory and cardiac depression after paraldehyde administration are low. There is considerable clinical experience of its effectiveness in CSE but few controlled studies. In the current APLS guidelines paraldehyde is recommended to be given at the same time as the phenytin infusion starts, if not already given, as it will be effective before the phenytoin infusion reaches therapeutic levels. A response to phenytoin is seen during the infusion in 85% of responders. If CSE continues after this, it should be classed as refractory and rapid sequence induction of anaesthesia with thiopentone is recommended. Figure 1 shows an example of a local guideline from Manchester Children’s Hospitals (based on the 2000 Status Epilepticus Working Party Guidelines), for the acute management of CSE.

**Refractory CSE**

Refractory CSE is the persistence of seizure activity despite appropriate medical and AED therapy. In children, it is associated with a poorer neurological outcome in survivors and has a higher mortality. An American study from 2001 put this as high as 30%, although a Finnish study (with a low prevalence of acute symptomatic causes) from 2004 showed no mortality.
The treatment of children in refractory CSE must take place in the PICU and be discussed with a consultant paediatric neurologist. It is important to ensure that all appropriate investigations for an underlying cause have been carried out. Therapeutic trials of pyridoxine (or pyridoxyl phosphate), biotin and folinic acid may be indicated. Thiopentone and midazolam (by high dose infusion up to 24 mcg/kg/min) are the drugs most often used in refractory CSE. There is debate as to whether additional measures to prevent brain injury (neuroprotection) are beneficial in PICU, over and above the achievement of seizure cessation.

Children who have needed airway protection because of respiratory depression will also be managed on PICU. In the NLSTEPSS cohort (Chin and colleagues), children who required PICU admission for respiratory depression were more likely to have received more than two doses of benzodiazepines. Only one in six of the children admitted to PICU had been appropriately treated before arrival in Accident and Emergency (A&E). In the 2007 review by Appleton and colleagues, of the 137 children admitted to Royal Liverpool Children’s Hospital PICU in CSE, 13% required ventilatory support in A&E because of respiratory insufficiency rather than ongoing seizure activity. The best way to avoid PICU admission is by effective early treatment of CSE.

**Outcome**

Recent outcome data show that morbidity and mortality rates overall are low, in the absence of an acute or progressive insult. Outcome is affected mainly by the cause and seizure duration. The improvement in reported outcomes may be related to better initial treatment, especially pre-hospital, more structured acute management of the seriously ill child, and developments in PICU care. Historical data often reported mixed adult (who have a worse outcome, in general) and paediatric populations. More information is now available from prospectively gathered data from more representative populations.

**Mortality**

CSE is more common in children than adults, but has a lower mortality. Acute mortality in children is 2.7–5.2%, but for those who require PICU admission, it is 5–8%. In the NLSTEPSS cohort, 5% of children admitted to PICU died. A recent review of PICU admissions for CSE by Appleton and colleagues reported zero mortality. Duration of seizure does have an effect on mortality, but the main factor is the underlying cause.

**Risk of recurrence of CSE**

The likelihood of a further episode of CSE is mainly determined by the underlying cause. In children with febrile CSE and idiopathic CSE it is low, at less than 4%. The likelihood rises in the acute, remote and progressive symptomatic groups. Children with pre-existing neurological abnormalities are at higher risk, as are children younger than 5 years. The treating clinician should always consider training the parents in the use of buccal midazolam at home to try to reduce the length of any future seizure. All families should be given first aid advice.

**Risk of development of epilepsy**

CSE may be the first seizure presentation of an epilepsy, although this may be difficult to determine until further seizures have occurred. It has been suggested that an episode of CSE may cause subsequent epilepsy, but this is generally not thought to be the case. Again, the risk of development of epilepsy comes down to the cause of CSE. More than 50% of children with an acute symptomatic cause or previous neurological impairment will develop epilepsy after a prolonged first seizure. The risk of later epilepsy after PFC is not higher than that after a brief febrile convulsion in otherwise healthy children.

**Risk of subsequent neurological impairment**

Neurological complications can range from subtle impairment of higher function (poor attention, concentration or behavioural difficulties) and focal neurological deficits through to a persistent vegetative state. Again, the cause of CSE is the main determinant of poor outcome, being highest in the acute (20% have new deficits) and remote symptomatic groups. In children without an acute or progressive neurological disorder, outcome is much better, with few children with febrile CSE developing new neurological dysfunction.

**Follow-up**

After a first episode of CSE, training in the giving of rescue medication is needed. It is no longer felt necessary for children to be admitted to hospital for test doses of buccal midazolam, but carers must be shown how to draw it up and give it appropriately. In some children with epilepsy, who have recurrent CSE, an individualised management plan is needed. Certain children respond better to certain drugs, or are sensitive to adverse effects from benzodiazepines. An individual plan to optimise care should be drawn up with parents and carers, and disseminated to all appropriate parties including school, the general practitioner, community paediatrician, ambulance service, A&E and PICU. The epilepsy nurse specialist is invaluable in ensuring all this is done. Duration of follow-up to monitor for complications of CSE should be decided on a case-by-case basis.

**Prevention**

Strategies for the primary prevention of CSE include public health measures to reduce infectious diseases, especially meningitis, and head injuries (accidental and non-accidental). Parents and carers can be educated about the management of the feverish child and the first aid care of a seizure. Once medical care is sought, then all levels of staff involved, from paramedics onwards should be appropriately skilled in the current management of CSE. Within hospital, the most experienced clinician available should oversee treatment.

**Further research**

Comparative studies of the effectiveness of drugs used for CSE are needed at all stages from out of hospital treatment up to drugs for resistant CSE on PICU. New areas of interest include the role of intravenous levetiracetam and sodium valproate as second-line treatments. Interventional studies requiring informed consent are difficult to design for acute situations. Prospective observational studies are possible, but yield less robust information. Because outcome in CSE is mainly determined by cause and there are so many potential causes, any treatment study has to include large numbers to detect a difference in outcome. Fortunately, research
in the UK is now on a more national collaborative footing with organisations such as the Medicines for Children Research Network and Comprehensive Research Networks.

Summary

CSE is more common in children than adults, but has a better outcome. However, it is still a neurological emergency, with the potential to cause severe neurological impairment and death. A structured approach to the child in CSE is needed, focusing on the maintenance of vital functions, the cessation of the seizure, and the treatment of the underlying cause. The underlying cause should be carefully looked for as this is the main determinant of outcome, and may need specific treatment. The evidence base for management is expanding and the national guidelines are being updated to include this new information.

FURTHER READING

GUIDELINES


JOURNAL ARTICLES


BOOKS


Shorvon S. Status epilepticus: its clinical features and treatment in adults and children. Cambridge: Cambridge University Press, 1994 [A comprehensive review of SE; should be read in conjunction with the 2007 Epilepsia supplement (48 Suppl. 8) detailing the consensus from the first London Colloquium on SE, which provides an update.]

WEBSITES


Practice points

- CSE in children is an emergency, potentially associated with high morbidity and mortality
- Recognise CSE, treat it early and appropriately – the longer it continues, the harder it is to stop
- Pre-hospital care is safe and effective
- Attention must be paid to basic life support measures and a structured approach to the seriously ill child adopted
- It is necessary to identify and treat the underlying cause. The outcome is largely dependent on the underlying cause
- Maintain a high index of suspicion for bacterial meningitis in children with a first-ever episode of CSE associated with fever
- Do not forget to look for an acute precipitant in a child who may have a history of epilepsy or neurological impairment
- National Guidelines for the management of CSE exist, and local guidelines should be in place – be familiar with these, and understand the rationale behind them
- Seek advice from a paediatric neurologist
- Audit should be used to check on guideline adherence
- Clear communication at all stages with parents, carers, team members and community professionals is vital