Emergency management of the paediatric patient with generalized convulsive status epilepticus

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The present guideline paper addresses the emergency management of generalized convulsive status epilepticus (CSE) in children and infants older than one month of age. It replaces the previous statement from 1996, and includes a new treatment algorithm and table of recommended medications, reflecting new evidence and the evolution of clinical practice over the past 15 years. The document focuses on the acute pharmacological management of CSE, but some issues regarding supportive care, diagnostic approach and treatment of refractory CSE are discussed.

Key Words: *Convulsions; Emergency management; Paediatrics; Seizures; Status epilepticus*

La prise en charge d'urgence du patient pédiatrique en état de mal épileptique convulsif généralisé

Les présentes lignes directrices portent sur la prise en charge d'urgence de l'état de mal épileptique convulsif (ÉMÉC) généralisé chez les enfants et les nourrissons de plus d'un mois. Il remplace le document de 1996 et inclut un nouvel algorithme de traitement et un nouveau tableau des médicaments recommandés qui reflètent les nouvelles données probantes et l'évolution de la pratique clinique depuis 15 ans. Le document s'attarde sur la prise en charge pharmacologique aiguë de l'ÉMÉC, mais certaines questions relatives aux soins de soutien, à la démarche diagnostique et au traitement de l'ÉMÉC réfractaire sont abordées.

BACKGROUND AND EPIDEMIOLOGY

The conventional definition of convulsive status epilepticus (CSE) is continuous generalized tonic-clonic seizure activity with loss of consciousness for longer than 30 min, or two or more discrete seizures without a return to baseline mental status (1). More recently, the terms 'early' or 'impending' status epilepticus have been based on a definition of continuous or intermittent seizures lasting longer than 5 min without full recovery of consciousness between seizures. It has been shown that early treatment is more effective in stopping the seizure, and treatment delay results in increased morbidity and mortality (2).

The annual incidence of CSE in children is reported as 10 to 73 episodes/100,000 children and is highest (135/100,000 to 156/100,000 children) in children younger than two years of age (3). Common etiologies are listed in Table 1 (3). Mortality has been reported to be between 2.7% and 8%, with an overall morbidity (mainly newly diagnosed neurological disorders) of between 10% and 20% (2).

The present guideline paper addresses CSE in children and infants older than one month of age. It replaces the statement published in 1996 (4).

PROTOCOLS AND GUIDELINES

There is limited evidence in paediatrics on which to base a 'gold standard' protocol for the management of CSE. There are many different variations of guidelines, protocols and algorithms endorsed by organizations and institutions around the world, based on a combination of evidence, consensus opinion, local

TABLE 1
Common etiologies of convulsive status epilepticus in children and incidences from population-based studies

Acute
Acute symptomatic (17% to 52%)
Acute CNS infection (bacterial meningitis, viral meningitis or encephalitis)
Metabolic derangement (hypoglycemia, hyperglycemia, hyponatremia, hypocalcemia or anoxic injury)
Antiepileptic drug noncompliance or withdrawal
Antiepileptic drug overdose
Non-antiepileptic drug overdose
Prolonged febrile convulsion (23% to 30%)
Remote (16% to 39%)
Cerebral migrational disorders (lissencephaly or schizencephaly)
Cerebral dysgenesis
Perinatal hypoxic-ischemic encephalopathy
Progressive neurodegenerative disorders
Idiopathic/cryptogenic (5% to 19%)

CNS Central nervous system. Adapted from reference 3

experience and drug availability (2-10). Despite the minor variations in detail, in many ways they are quite similar.

In the highly stressed setting of this type of medical emergency, a familiar standardized protocol of recommended management saves time, prevents errors and facilitates care. Although the outcome is mainly determined by its cause, the duration of CSE is very important. A timely approach may be more important than

the exact individual pharmacological interventions. Particular local expertise or resource limitations may provide legitimate reasons to adapt or adjust the recommended protocol. For individual children, who are known to respond well to specific medications, a more tailored approach may be more appropriate.

The objectives for the acute management of CSE are as follows:

1. Maintenance of adequate airway, breathing and circulation (ABCs).

2. Termination of the seizure and prevention of recurrence.

3. Diagnosis and initial therapy of life-threatening causes of CSE (eg, hypoglycemia, meningitis and cerebral space-occupying lesions).

4. Arrangement of appropriate referral for ongoing care or transport to a secondary or tertiary care centre.

5. Management of refractory status epilepticus (RSE).

1. MAINTENANCE OF ADEQUATE ABCs

Inability to maintain the airway is the most important immediate risk to the patient with CSE. Factors responsible for the airway and ventilation being at risk include a clenched jaw, poorly coordinated respirations, and production of secretions and vomitus. Hypoxia is frequently present. Management of the airway includes positioning the child on his/her side and suctioning the easily accessible secretions. The teeth should not be pried apart. After suctioning, the patient should be repositioned on his/her back and a chin lift or jaw thrust should be applied, if necessary, to help open the airway. Oxygen (100%) should be given by face mask, and cardiorespiratory and oxygen saturation monitors should be used. Breathing should be carefully monitored. Assisted ventilation should be considered if the child shows signs of respiratory depression or if oxygen saturations remain low despite receiving 100% oxygen by face mask.

Increased heart rate and blood pressure (BP) are usually observed in the convulsing patient. They should return to normal when the seizure stops. Bradycardia, hypotension and poor perfusion are ominous signs. They imply severe hypoxia and an immediate need to establish the airway and ventilate the patient, either by bag-valve mask ventilation or intubation. Intravenous (IV) access should be obtained immediately (two large-bore IV lines if possible) and the bedside blood glucose level should be checked. Further testing should be considered once the ABCs have been stabilized.

2. TERMINATION OF THE SEIZURE AND PREVENTION OF RECURRENCE

Principles of treatment and monitoring
The major goal of treatment is to stop the seizure and, in doing so, prevent brain injury. In animal models, ischemic and excitotoxic neuronal cell loss starts to occur after 30 min of seizure activity. Seizures that last longer than 5 min to 10 min are at high risk of continuing for at least 30 min, so early treatment is associated with the best outcome. This is the rationale behind assuming that any child who arrives in the emergency department with acute tonic-clonic generalized convulsions is in early CSE, which should immediately trigger the first-line treatment with benzodiazepines as per the management protocol (Figure 1).

Anticonvulsant drug therapies for CSE are listed in Table 2 and Figure 1. If IV access is unavailable, then other routes (eg, buccal, intranasal and rectal) should be used while efforts to establish access continue. Consideration should be given to starting an intraosseous (IO) line if IV access is not possible and the seizure is prolonged or the patient is decompensating.

Because of the time required to administer many of the second-line treatments (eg, phenytoin and phenobarbital), preparations to give these should start at the same time as administering the first dose of benzodiazepine. Regardless of the particular institutional protocol being followed, some of the frequent problems encountered include the following (5):

- Inadequate doses of benzodiazepines.

- Treating with more than two doses of benzodiazepines and a delay in initiating second-line treatment (usually fosphenytoin/phenytoin or phenobarbital).

- Delay in initiating the RSE treatments (usually rapid sequence induction/intubation and initiation of midazolam infusion).

It is important to obtain a brief history including any history of seizure disorder, other symptoms (eg, fever), medication usage and allergies to medications. This can be completed by a designated person not immediately involved in the acute resuscitation. This history will allow a simultaneous search for cause (Table 1) and focused physical examination to be completed while termination of the seizure is undertaken.

A bedside glucose determination will establish the need for a bolus of dextrose. If the blood glucose level is 2.6 mmol/L or lower, then the recommended management is 2 mL/kg to 4 mL/kg of 25% dextrose water or 5 mL/kg of 10% dextrose water (0.5 g/kg) by IV. If the patient is hypoglycemic, the bedside glucose level should be rechecked 3 min to 5 min postbolus, and a repeat bolus should be given as necessary. Increased intracranial pressure (ICP) or sepsis should be suspected and treated as needed.

During the administration of medications, pulse rate, respiratory rate, BP, cardiac monitoring and oxygen saturation via pulse oximeter should be followed on a regular basis. Anticonvulsant medications may cause loss of airway reflexes, respiratory depression, hypotension and cardiac arrhythmias. Monitor the child's temperature and aim for normothermia using acetaminophen and ibuprofen as appropriate.

First-line treatment
First-line treatment usually begins outside the hospital. It has been shown that prehospital treatment of children reduces seizure length but often is not utilized (11). Benzodiazepines are the first-line drugs of choice in the treatment of CSE. If used within the first 20 min of seizure onset, termination rates of seizures can be as high as 70% to 85% (5). Because IV administration results in more rapid onset of action and improved bioavailability and efficacy, IV access should be obtained as soon as possible.

Prehospital: Treatment varies depending on local practices and availability, but options include the following: buccal or rectal lorazepam; buccal or intranasal midazolam; and rectal diazepam (for dosing details see Table 2). Buccal midazolam has been shown to control seizures in 56% of children compared with rectal diazepam (27%) (12). Two further studies (13,14) showed a 70% to 75% response to buccal midazolam compared with a 57% to 59% response to rectal diazepam. In one trial (15), intranasal midazolam (88%) was shown to be as effective as IV lorazepam (92%) in the treatment of prolonged febrile convulsions of at least 10 min. If available, some would consider buccal (16) or intranasal midazolam (2) to be the first-line management in children without IV access.

In hospital: IV lorazepam is usually the first-line treatment. It has a longer-lasting anticonvulsant activity and causes less respiratory depression than diazepam (17). It has been shown to be more effective than diazepam or phenytoin in stopping seizures (18). Note that repeat doses are much less likely to be effective (17% versus 85% for the first dose [12]). If children have received

benzodiazepines in the prehospital setting, one repeat IV dose may be adequate (5) before moving to second-line treatments if necessary. Because timing is critically important, if no IV access is available, a second dose of benzodiazepine (lorazepam, midazolam or diazepam) should be given through the buccal, intranasal, rectal or intramuscular (IM) route while IV access is being obtained. Treatment with more than two doses of benzodiazepines is associated with respiratory depression (11).

Second-line treatment

Fosphenytoin/phenytoin is generally preferred over phenobarbital because it is less likely to cause respiratory depression and alter the level of consciousness of the child (3), which can complicate the assessment. If no IV access is available, then IM fosphenytoin, IO phenytoin or rectal paraldehyde are alternative options. Note that evidence for the safety and efficacy of IO phenytoin or phenobarbital is scant.

Phenytoin and fosphenytoin: Phenytoin has been shown to control 60% to 80% of seizures with a 20 mg/kg dose (19). It must be administered in normal saline (NS) because it precipitates in glucose-containing solutions. It is infused over approximately 20 min. Because of its high pH, extravasation of phenytoin can result in severe subcutaneous irritation ('purple glove syndrome') characterized by edema, discolouration and pain distal to the site of administration. This side effect does not occur with fosphenytoin (20 mg/kg/dose), which is a water-soluble prodrug of phenytoin. In addition to more rapid IV infusion, fosphenytoin may be given by IM injection, but it is more expensive and is not universally available (5). Side effects of both phenytoin and fosphenytoin include cardiac arrhythmias, bradycardia and hypotension, so continuous BP and electrocardiogram monitoring is recommended during infusion.

Phenobarbital: Early trials suggest that phenobarbital has similar anticonvulsant activity to phenytoin, but a greater incidence of respiratory depression, especially when used in conjunction with benzodiazepines. The mechanism of action is similar to benzodiazepines, so it may be less effective in treating seizures refractory to these drugs (5). It is still routinely used for the treatment of neonatal seizures, as well as for children who are already on phenytoin maintenance. The loading dose is 20 mg/kg in NS or 5% dextrose water over 20 min. Side effects include sedation, respiratory depression and hypotension, especially if a benzodiazepine has already been given.

Paraldehyde: The mechanism of action is unknown. In the only published randomized controlled trial (20) to date, IM paraldehyde was found to be inferior to intranasal lorazepam as a first-line treatment in sub-Saharan Africa. In a prospective observational study (11), children who received IV phenytoin were nine times more likely to stop seizing than those who received rectal paraldehyde. There are, however, case series showing benefit in a minority of cases for which other anticonvulsant drugs have failed. Because of side effects reported with IV and IM use (eg, cyanosis, cough, hypotension and pulmonary edema), only the rectal route with dilution in oil is recommended. A dose of 0.4 mL/kg is mixed in an equal amount of oil to a maximum total volume of 20 mL (5). Paraldehyde is available through Health Canada's Special Access Programme but, currently, is only used in certain regions of Canada. Many authorities no longer recommend paraldehyde use, while others incorporate it only in cases for which there is no IV access.

Sodium valproate: There is increasing interest in the use of IV sodium valproate as a second- or third-line treatment. Initial

open-label randomized trials look promising, with similar efficacy to phenytoin, fewer adverse effects and, specifically, no respiratory or cardiovascular compromise (3). The IV loading dose is 30 mg/kg over 5 min, followed by a 10 mg/kg bolus if needed. The maintenance dose is 10 mg/kg by IV every 8 h (9). Its role as a second-line treatment requires further investigation in well-controlled paediatric trials.

Pyridoxine: For children younger than 18 months of age in whom seizures may be caused by an undiagnosed metabolic disorder such as pyridoxine-dependent epilepsy, a trial of pyridoxine (vitamin B_6) 100 mg by IV initially and then 50 mg IV or by mouth twice a day, should be considered (9).

3. DIAGNOSIS AND INITIAL THERAPY OF LIFE-THREATENING CAUSES OF CSE

Investigations should be individualized according to the clinical scenario (Table 1). The most common cause of CSE is a prolonged febrile seizure. Children experiencing this type of seizure may not require an extensive workup. The same may apply to children with a known seizure disorder who are already on anticonvulsant therapy. However, a full clinical assessment should involve a search for precipitating causes, focusing on signs of infection, meningeal irritation, trauma, focal neurological deficits and intoxication. It is important not to mistake decorticate or decerebrate posturing for seizures.

When the etiology of the seizure is unclear, the following investigations should be considered (1): blood for electrolytes, glucose (to verify earlier bedside determination), complete blood count and differential, cultures (if sepsis is suspected), and capillary or arterial gas (perfusion must be adequate for capillary gas). Anticonvulsant levels should be measured for patients on long-term anticonvulsant therapy. Urine and blood can be sent for toxicology screening. Serum calcium, blood urea nitrogen, magnesium, liver enzymes, lactate and ammonia may be required in selected cases. A decision regarding the need for lumbar puncture (LP) should be deferred until the patient's vital signs are stable, there is no suspicion of increased ICP and the convulsion has stopped. If sepsis is believed to be likely, IV antibiotics may be given immediately after blood cultures without waiting to perform the LP. Prolonged attempts at obtaining cultures should not delay treatment.

A history of trauma, evidence of increased ICP, focal neurological signs, unexplained loss of consciousness or suspicion of cerebral herniation are some of the indications for a computed tomography (CT) scan of the head. Head CT may be performed after the ABCs have been stabilized and the convulsion has terminated (1).

If there are clinical indications of raised intracranial pressure or herniation, these must be treated immediately before further investigation. A normal CT scan does not exclude significantly increased ICP. LP must be deferred if clinical or radiological signs of increased ICP are present.

Intoxication should always be considered as a possibility. If intoxication is proven or strongly suspected, and the convulsive activity has stopped, the use of activated charcoal may be considered once the airway is protected, either through intubation or after the child has woken up sufficiently to protect his own airway.

Non-CSE

If the child's level of consciousness does not recover as expected after the convulsion has stopped, or if neuromuscular paralysis is

Pre-Hospital Management of Status Epilepticus

Lorazepam buccal/PR 0.1 mg/kg (max 4 mg)
OR
Midazolam buccal 0.5 mg/kg (max 10 mg)
or intranasal 0.2 mg/kg (max 5 mg/nostril)
OR
Diazepam PR 0.5 mg/kg (max 20 mg/dose)

Hospital Management of Status Epilepticus

A = support airway
B = 100% oxygen, assess breathing, O$_2$ saturation monitor
C = cardiorespiratory monitor, check pulse/blood pressure
Establish IV access
Rapid glucose test, consider critical labs*****
Monitor for respiratory depression, hypotension, arrhythmias

Rapid IV access? — Yes →

Lorazepam IV 0.1 mg/kg (max 4 mg) give over ½-1 minute
OR
Midazolam IV 0.1 mg/kg (max 10 mg)
OR
Diazepam IV 0.3 mg/kg
[max 5 mg (<5 yrs) 10 mg (≥5 yrs)] give over 2 minutes

No ↓

Lorazepam buccal/PR 0.1 mg/kg (max 4 mg)
OR
Midazolam buccal 0.5 mg/kg (max 10 mg)
OR intranasal 0.2 mg/kg (max 5 mg/nostril)
OR intramuscular 0.2 mg/kg
OR
Diazepam PR 0.5 mg/kg (max 20 mg/dose)

Still seizing? — Yes → Repeat above × 1 within 5 minutes

Still seizing? — Yes → Repeat above × 1 within 5 minutes
OR
if IV access then switch
to IV route

No ↓
Monitor, investigate**†**

No ↓
Monitor, investigate**†**

Still seizing? — Yes → **Is IV access present?** — Yes →

Fosphenytoin IV**‡**
20 mg PE/kg in NS or D5W
(max 1000 mg): give over 5-10 minutes
OR
Phenytoin IV
20 mg/kg in NS over 20 minutes
(max 1000 mg)
OR
Phenobarbital IV
20 mg/kg in NS or D5W over 20 minutes
(max 1000 mg)

No ↓
Monitor, investigate**†**

No ↓
Consider insertion of IO

Fosphenytoin intramuscular
20 mg PE/kg
(max 1000 mg PE)**§**
OR
Paraldehyde PR**¶**
400 mg/kg (0.4 mL/kg/dose)
Max 10 g (10 mL)
Dilute 1:1 in oil
OR
Phenytoin IO******
20 mg/kg in NS (max 1000 mg)

Still seizing after 5 minutes? — Yes →
Use **Phenobarbital** as above
if fosphenytoin/phenytoin used
OR
use **Fosphenytoin** or **Phenytoin**
if phenobarbital already used

No ↓
Monitor, investigate**†**

Still seizing after 5 minutes? — Yes →
Use **Paraldehyde** as above
if fosphenytoin/phenytoin used
OR
Use **Fosphenytoin** or **Phenytoin**
as above if paraldehyde used

No ↓
Monitor, investigate**†**

Seizure stops within 10 minutes? — Yes → Monitor, investigate**†**

No**††** ↓

Refractory Status Epilepticus

Continued on the next page

1st line – 1st 10 minutes
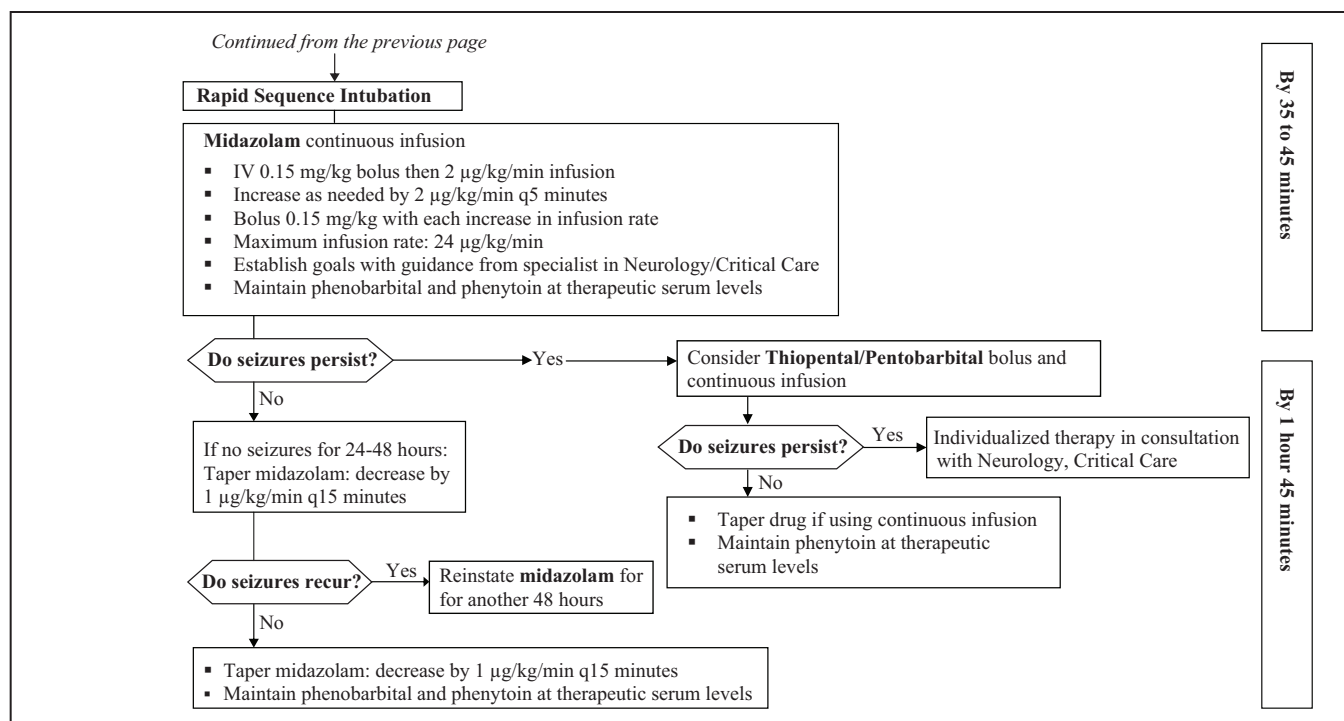
2nd line - 2nd 20 minutes

Figure 1) *Guidelines for emergency department management of convulsive status epilepticus (CSE) in infants (older than one month of age) and children. *Consider critical laboratory tests (labs): includes electrolytes, glucose, blood gas and calcium. Consider complete blood count/differential, anticonvulsant levels, liver function tests, toxicology screen, metabolic screen and blood culture when appropriate. For further detail, see the section entitled, "Diagnosis and initial therapy of life-threatening causes of CSE"; †Investigate, monitor: see section entitled, "Diagnosis and initial therapy of life-threatening causes of CSE"; ‡Fosphenytoin (if available) is preferred as the initial loading dose. Otherwise, use phenytoin unless the patient is already on phenytoin maintenance or a neonatal patient, in which case phenobarbital should be considered first; §Maximum (max) dose per intramuscular (IM) site is 3 mL (if child is heavier than 30 kg, IM dosing may not be practical because multiple IM sites are required); ¶Paraldehyde is available through Health Canada's Special Access Programme but, currently, is only used in a few parts of the country; **Intraosseous (IO) phenytoin 20 mg/kg in normal saline (NS) (max 1000 mg) is an option, but evidence for safety and efficacy is scant; ††In children younger than 18 months of age, consider a trial of intravenous (IV) pyridoxine (vitamin B_6) 100 mg initially, then 50 mg IV or by mouth twice a day. D5W 5% dextrose water; PE Phenytoin equivalent; PR Per rectum; q Every; yrs Years. Adapted from The Hospital for Sick Children (Toronto, Ontario) and BC Children's Hospital (Vancouver, British Columbia)*

being used, then an electroencephalogram (EEG) should be performed to exclude non-CSE. If an EEG cannot be obtained, then empirical treatment for non-CSE may be indicated (10).

4. ARRANGEMENT OF APPROPRIATE REFERRAL FOR ONGOING CARE OR TRANSPORT TO A SECONDARY OR TERTIARY CARE CENTRE

Children without a previous history of epilepsy or febrile seizures who present with CSE should be referred to either a secondary or tertiary care hospital for further treatment and investigation. Unstable vital signs or continuing CSE require transport to a paediatric intensive care unit. Stabilization of the child before transport must be discussed with a physician skilled in paediatric emergency medicine or critical care.

5. MANAGEMENT OF RSE

CSE that is unresponsive to two different antiepileptic medications (eg, a benzodiazepine and phenytoin) is considered to be refractory, although some authorities have added a duration criterion such as longer than 30 min or longer than 60 min (3,21). Studies in children have indicated that CSE lasts longer than 1 h in 26% to 45% of patients (21). These children are unlikely to respond to other

second-line anticonvulsants. Therefore, escalation to anesthetic support with subspecialist and intensive care consultation and initiation of a midazolam infusion should be considered within 20 min to 30 min of starting the CSE algorithm (Figure 1).

It is recognized that paralysis may aid ventilation and prevent the motor manifestations of seizures, but it does not terminate the seizure activity in the brain. At this point, the patient's care is beyond the scope of the usual emergency department setting, and transfer to a paediatric intensive care unit with neurological consultation for further management will be necessary. Management will depend on the previous experience in the individual centre involved, and may include intermittent or constant EEG monitoring.

Pharmacotherapy in RSE (Figure 1)

There are currently no published controlled trials examining different treatment options for RSE in children. A number of Canadian hospital guidelines have incorporated a continuous infusion of midazolam as the first step. If this fails, then anesthetizing doses of barbiturates should be considered. Most recently, the use of topiramate and levetiracetam has been suggested, but the role of these drugs remains unclear at the present time.

TABLE 2
Anticonvulsant drug therapies for convulsive status epilepticus

Drug and route	Dose	Maximum	Rate	Repeat	Risks	Comments
First-line treatments						
Lorazepam (IV, IO, buccal, PR)	0.1 mg/kg	4 mg	<2 mg/min (IV over 0.5–1 min)	Every 5 min ×2	Hypotension, respiratory depression, sedation	Use sublingual tablets for buccal route. For PR route, dilute injection to 2 mg/mL in D5W or NS
Midazolam						
Buccal	0.5 mg/kg	10 mg		Every 5 min ×2	Hypotension, respiratory depression, sedation	
Intranasal	0.2 mg/kg	5 mg/nostril				
IM	0.2 mg/kg					
IV	0.1 mg/kg					
Diazepam						
IV	0.3 mg/kg	5 mg (<5 yrs) 10 mg (≥5 yrs)	<2 mg/min (IV over 2 min)	Every 5 min ×2	Hypotension, respiratory depression, sedation	
PR	0.5 mg/kg	20 mg				
Second-line treatments						
Fosphenytoin (IV, IM)	20 mg/kg phenytoin equivalents	1000 mg	IV over 5–10 min (in NS or D5W)		Decreased risks compared with phenytoin	Expensive
Phenytoin* (IV)	20 mg/kg	1000 mg	1 mg/kg/min (over 20 min in NS)		Hypotension, bradycardia, arrhythmia	Must be given in nonglucose-containing solution
Phenobarbital[†] (IV, IO)	20 mg/kg	1000 mg	1 mg/kg/min (over 20 min in NS or D5W)		Respiratory depression (especially if benzodiazepine has been used), hypotension, sedation	First choice in neonates, or if on phenytoin maintenance
Paraldehyde[‡] (PR)	400 mg (0.4 mL/kg/dose)	10 g (10 mL/ dose)			Mucosal irritation	Dilute 1/1 in oil in glass syringe

*If a patient is already receiving phenytoin, a partial loading dose of 5 mg/kg may be given. Subsequent doses may be given based on anticonvulsant levels; [†]If a patient is already on phenobarbital, a dose of 5 mg/kg may be given. Subsequent doses may be given based on anticonvulsant levels; [‡]Paraldehyde is available through Health Canada's Special Access Programme but, currently, is only used in certain regions of Canada. D5W 5% dextrose water; IM Intramuscular; IO Intraosseous; IV Intravenous; NS Normal saline; PR Per rectum; yrs Years

Midazolam: Midazolam is a fast-acting benzodiazepine with a short half-life. It is believed to be effective in the management of RSE and is administered by IV access with a bolus dose followed by continuous infusion. A loading dose of 0.15 mg/kg (maximum 8 mg) is followed by an infusion rate of 2 µg/kg/min. This can be titrated up by increasing by 2 µg/kg/min every 5 min until seizure control is achieved or a maximum of 24 µg/kg/min is reached (9,10). Side effects include hypotension (21). Therefore, BP should be monitored judiciously, and low BP should be treated by giving 20 mL/kg IV boluses of NS.

Barbiturates (thiopental and pentobarbital): Thiopental is dosed at 2 mg/kg to 4 mg/kg bolus followed by 2 mg/kg/h to 4 mg/kg/h. Increases of 1 mg/kg/h can be used every 30 min as needed, with a 2 mg/kg bolus with each increase in the infusion rate to a maximum of 6 mg/kg/h. If midazolam and phenobarbital are currently being used, they should be discontinued, whereas phenytoin should be maintained at therapeutic serum levels. Once seizures are controlled for 48 h, the infusion rate of thiopental is decreased by 25% every 3 h; phenobarbital is restarted while tapering (9).

If pentobarbital is used, it can be administered as a 10 mg/kg bolus, followed by a continuous infusion at 0.5 mg/kg/h to 1 mg/kg/h (10). Studies in children reported an efficacy for pentobarbital of 74% to 100% and a high incidence of hypotension (21).

Other pharmacotherapy: Other options include propofol (10), topiramate (9) and levetiracetam (3,21). These drugs may be useful in the management of RSE, but should be used by specialists with experience in their use.

CONCLUSION

There have been a number of changes in the emergency management of CSE over the past 15 years based on the emergence of new evidence and medications. It is important for all those involved in the acute medical management of children to have an up-to-date, evidence-based approach to the emergency management of children with CSE.

REFERENCES

1. Riviello JJ, Ashwal S, Hirtz D, et al. Practice parameter: Diagnostic assessment of the child with status epilepticus (an evidence-based review): Report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. Neurology 2006;67:1542-50.
2. Sofou K, Kristjánsdóttir R, Papachatzakis NE, Ahmadzadeh A, Uvebrant P. Management of prolonged seizures and status epilepticus in childhood: A systematic review. J Child Neurol 2009;24:918-26.
3. Singh RK, Gaillard WD. Status epilepticus in children. Curr Neurol Neurosci Rep 2009;9:137-44.
4. Canadian Paediatric Society, Emergency Paediatrics Section. Management of the paediatric patient with generalized convulsive status epilepticus in the emergency department. Paediatr Child Health 1996;1:151-5.
5. Yoong M, Chin RF, Scott RC. Management of convulsive status epilepticus in children. Arch Dis Child Educ Pract Ed 2009;94:1-9.
6. Appleton R, Choonara I, Martland T, Phillips B, Scott R, Whitehouse W. The treatment of convulsive status epilepticus in children. The Status Epilepticus Working Party, Members of the

Status Epilepticus Working Party. Arch Dis Child 2000;83:415-9.

7. Kälviäinen R. Status epilepticus treatment guidelines. Epilepsia 2007;48:99-102.

8. Great Ormond Street Hospital for Children, UCL Institute of Child Health. North Central London Epilepsy Network. Clinical Guideline: Convulsive Status Epilepticus (CSE). <http://www.ich.ucl.ac.uk/clinical_information/clinical_guidelines/cmg_guideline_00038> (Accessed on December 6, 2010).

9. Guidelines for prolonged seizures and status epilepticus in infants (age > 1 month), children and adolescents. In: Lau E, ed. 2009/10 Drug Handbook and Formulary. Toronto: The Hospital for Sick Children, 2009:322-4.

10. Child Health BC. The BC Children's Emergency Clinical Practice Guidelines. Management of Convulsive Status Epilepticus in Infants and Children. <http://www.childhealthbc.ca/guidelines/category/4-convulsive-status-epilepticus> (Accessed on December 6, 2010).

11. Chin RF, Neville BG, Peckham, C, Wade A, Bedford H, Scott RC. Treatment of community-onset, childhood convulsive status epilepticus: A prospective, population-based study. Lancet Neurol 2008;7:696-703.

12. McIntyre J, Robertson S, Norris E, et al. Safety and efficacy of buccal midazolam versus rectal diazepam for emergency treatment of seizures in children: A randomised controlled trial. Lancet 2005;366:205-10.

13. Scott BC, Besag FM, Neville BG. Buccal midazolam and rectal diazepam for treatment of prolonged seizures in childhood and adolescence: A randomised trial. Lancet 1999;353:623-6.

14. Mpimbaza A, Ndeezi G, Staedke S, Rosenthal PJ, Byarugaba J. Comparison of buccal midazolam with rectal diazepam in the treatment of prolonged seizures in Ugandan children: A randomized clinical trial. Pediatrics 2008;121:e58-64.

15. Lahat E, Goldman M, Barr J, Bistritzer T, Berkovitch M. Comparison of intranasal midazolam with intravenous diazepam for treating febrile seizures in children: Prospective randomised study. BMJ 2000;321:83-6.

16. Appleton R, Macleod S, Martland T. Drug management for acute tonic-clonic convulsions including convulsive status epilepticus in children. Cochrane Database Syst Rev 2008;(3):CD001905.

17. Appleton R, Sweeney A, Choonara I, Robson J, Molyneux E. Lorazepam versus diazepam in the acute treatment of epileptic seizures and status epilepticus. Dev Med Child Neurol 1995;37:682-8.

18. Prasad K, Al-Roomi K, Krishnan PR, Sequeira R. Anticonvulsant therapy for status epilepticus. Cochrane Database Syst Rev 2005;(4):CD003723.

19. Wilder BJ. Efficacy of phenytoin in treatment of status epilepticus. Adv Neurol 1983;34:441-6.

20. Ahmad S, Ellis JC, Kamwendo H, Moyneux E. Efficacy and safety of intranasal lorazepam versus intramuscular paraldehyde for protracted convulsions in children: An open randomised trial. Lancet 2006;367:1591-7.

21. Abend NS, Dlugos DJ. Treatment of refractory status epilepticus: Literature review and a proposed protocol. Pediatr Neurol 2008;38:377-90.

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