Management of Status Epilepticus

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Introduction

Status epilepticus (SE) is an acute, life-threatening, neurologic emergency. It is associated with significant morbidity and mortality and prompt initiation of appropriate treatment of both the seizure and the underlying cause is crucial.

The International League Against Epilepsy (ILAE) defines SE as "a condition resulting either from a failure of the mechanisms responsible for seizure termination or from the initiation of mechanisms which lead to abnormally prolonged seizures (after time point t1). It is a condition that can have long-term consequences (after time point t2), including neuronal death, neuronal injury, and alteration of neuronal networks, depending on the type and duration of seizures" (Trinka et al., 2015).

Definition of t1 and t2

Table 1. Operational dimensions with t_1 indicating the time that emergency treatment of SE should be started and t_2 indicating the time at which long-term consequences may be expected

Type of SE	Operational dimension 1 Time (t_1), when a seizure is likely to be prolonged leading to continuous seizure activity	Operational dimension 2 Time (t_2), when a seizure may cause long term consequences (including neuronal injury, neuronal death, alteration of neuronal networks and functional deficits)
Tonic–clonic SE	5 min	30 min
Focal SE with impaired consciousness	10 min	>60 min
Absence status epilepticus	10–15 min[a]	Unknown

[a]Evidence for the time frame is currently limited and future data may lead to modifications.

From Trinka et al *Epilepsia* 2015

t1 indicated in the table above is based on a study by Shinnar et al in 2001 (*Annals of Neurology)* discovering that a seizure that lasts longer than 7 min is unlikely to stop spontaneously in the next few minutes without intervention, and that focal seizures tend to last longer than generalised seizures. These findings led the ILAE to reach a consensus opinion that treatment of convulsive seizures should be initiated at around 5 min and that of focal SE with impaired awareness should be initiated at around 10 minutes.

t2 is derived from experimental evidence looking at the duration of prolonged seizures that result in brain damage. Results of these studies vary widely but for a safe guideline, the ILAE task force suggests a time of t2 at 30 min in convulsive SE. Note that there is limited information to define t1 and t2 for focal SE, and no information for absence SE. It is important to realise that the time limits given for t2 above are meant primarily for operational purposes and are general approximations only. The timing of onset of cerebral damage will vary considerably in different clinical circumstances.

In practice, prompt treatment should be initiated for **any convulsive seizure lasting > 5 minutes** or **any focal seizure with impaired awareness lasting > 10 minutes.**

Refractory status epilepticus (RSE) is when there is failure of the seizure to respond to 2 sequentially administered anti-seizure medications (Vasquez et al., 2019). RSE has a mortality of > 30 % (c.f. 7% for paediatric status epilepticus).

Super-refractory status epilepticus is when SE persists for 24 hours or more after the administration of general anaesthesia or that recurs after general anaesthesia withdrawal (Vasquez et al., 2019).

Features

The first important step in the management of SE is the recognition of SE in a child:

- Generalised convulsive SE (GCSE)
    - Overt GCSE - Combination of tonic (stiffening), clonic (rhythmic), or tonic-clonic movements with loss of consciousness
    - Subtle GCSE – Fine twitching of eyelids, fingers
- Non-convulsive SE- Electroencephalogram documents continued electrographic seizure without overt clinical signs
- Focal impaired awareness SE - Stupor, dreamy affect
- Absence SE – hypo-motor, staring
- Focal motor SE – Twitching of one limb/ body part with preserved consciousness

Physiological changes during Status Epilepticus

Seizures cause physiological changes which include:

- Epinephrine/norepinephrine release
- Respiratory depression
- Neurogenic pulmonary oedema
- Acidosis
- Hyperthermia
- Elevated total white cell counts

If prolonged seizures occur, this can also lead to:

- Hypotension
- Hypoglycaemia
- Rhabdomyolysis with renal failure
- Cerebral edema with risk of death

Investigations

New-Onset Status Epilepticus
Always recommended:

- Serum electrolytes
- Plasma glucose
- CT brain

If clinical suspicion:

- Genetic / metabolic investigations:
  - dysmorphism
  - consanguinity
  - persistent metabolic acidosis, hypoglycaemia
  - neurodevelopment delay or regression

- Urine/ blood toxicology
  - suggestive history
  - high osmolar gap
  - persistent metabolic acidosis

- Lumbar puncture
  - history or physical examination suggestive of meningitis/ encephalitis

- Electroencephalogram (EEG)
  - if refractory or persistent encephalopathy, refer neurologist (consider video EEG)

SE in Known Epileptics
Always recommended:

- Antiepileptic Drug (AED) levels (trough level > 6 hours post last dose of AED preferred)
- Serum electrolytes
- Plasma glucose

Consider:

- CT/ MRI brain
- Lumbar puncture if symptoms or signs of meningitis/ encephalitis
- EEG if persistent encephalopathy

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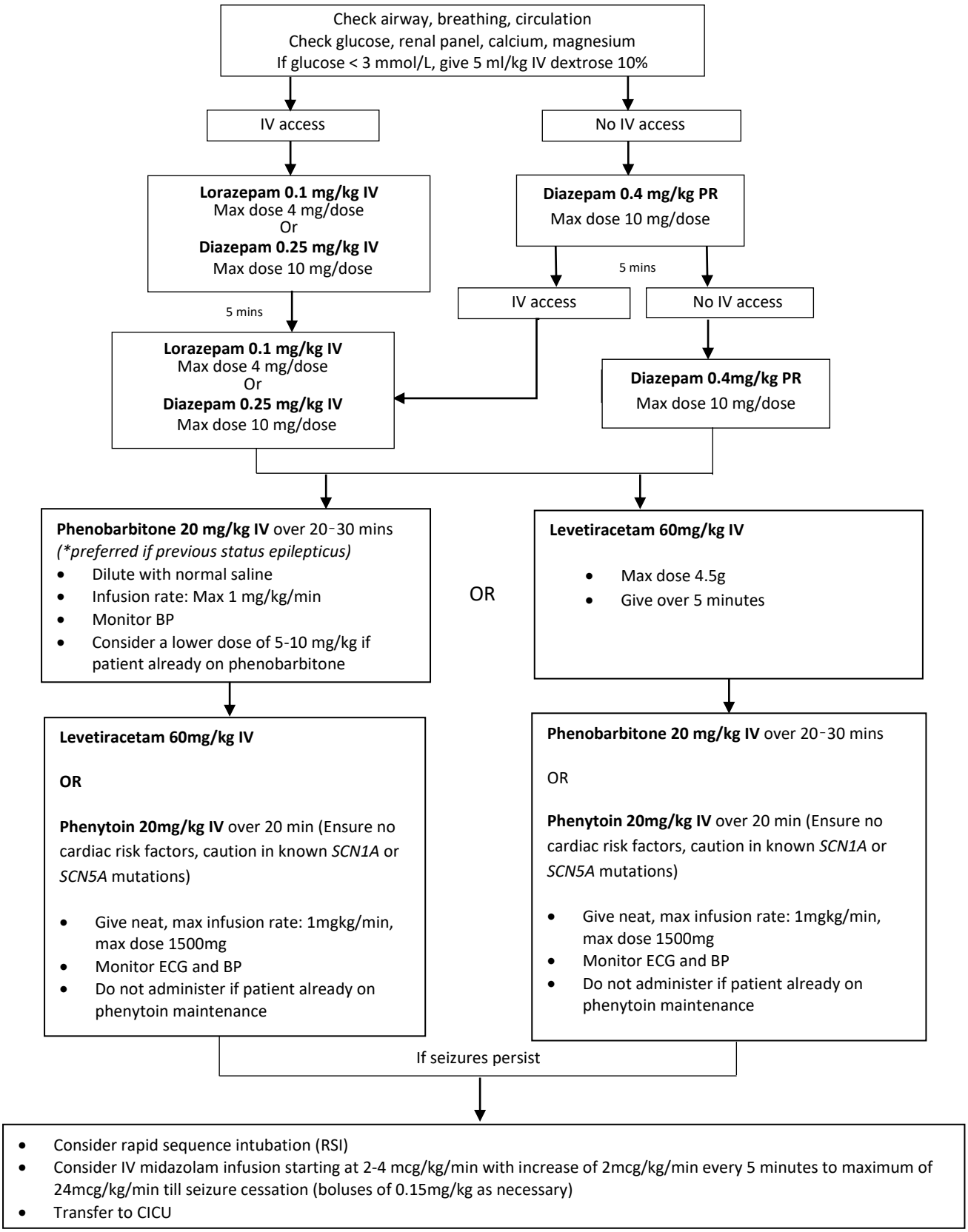

Initiation of other intravenous anti-convulsants

(Consider discussion with Neurology)

Valproate: Load 20 mg/kg/dose over 6-10 minutes. Maintain at 6 mg/kg/dose Q6H.
Avoid if there is suspicion of metabolic/mitochondrial disorder (raised lactate, abnormal LFTs, dysmorphism, consanguinity, unexplained developmental delay)

Levetiracetam: Load 60 mg/kg/dose. Maintain at 30 mg/kg/dose Q12H. For prolonged therapy, convert to enteral formulation: cheaper, good bioavailability.

Phenobarbitone: Load 20mg/kg/day. Maintain at 2.5 mg/kg/dose Q12H.

Thiopentone: Loading 2-5 mg/kg slowly (max dose = 250mg/dose) (beware hypotension) then infusion 1 to 5 mg/kg/hr until therapeutic endpoint achieved.
Inotrope support may be required as thiopentone is increased

Propofol is not recommended for prolonged (> 48 hr) use in refractory paediatric status epilepticus

Oral anti-convulsants

Topiramate: 1-3 mg/kg/day in two divided doses. Increase every 3-5 days. Screen urine calcium/creatinine ratio and renal ultrasound. Monitor pH and avoid if existing renal calculi, nephrocalcinosis.

Use of continuous EEG monitoring

Continuous EEG monitoring is targeted to a therapeutic endpoint. This may include:

- Clinical and electrographic seizure control
- Suppression-burst pattern on EEG

Clarify endpoint when taking over patient. Continuous EEG monitoring is not automated.

If suspected seizure, then:

- **Look** at the patient – observe for clinical evidence of seizure, subtle or otherwise
- **Mark** the event – on the EEG by pressing the event button (Figure 1)
- **Describe** the event – document on the supplied seizure chart
- **Treat** the seizure if high suspicion

Figure 1

References

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