The Walton Centre
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Excellence in Neuroscience

ESCALATING SEIZURES GUIDELINE

Author and Contact details:	Guleed Adan, James Mitchell, Christine Burness Christine.Burness@thewaltoncentre.nhs.uk	
Responsible Director:	Medical Director	
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Scope:	All trust employees. This guideline has been developed for the management of adult hospital in patients with escalating seizures. The management of convulsive status epilepticus is covered by the Status Epilepticus Guideline.	
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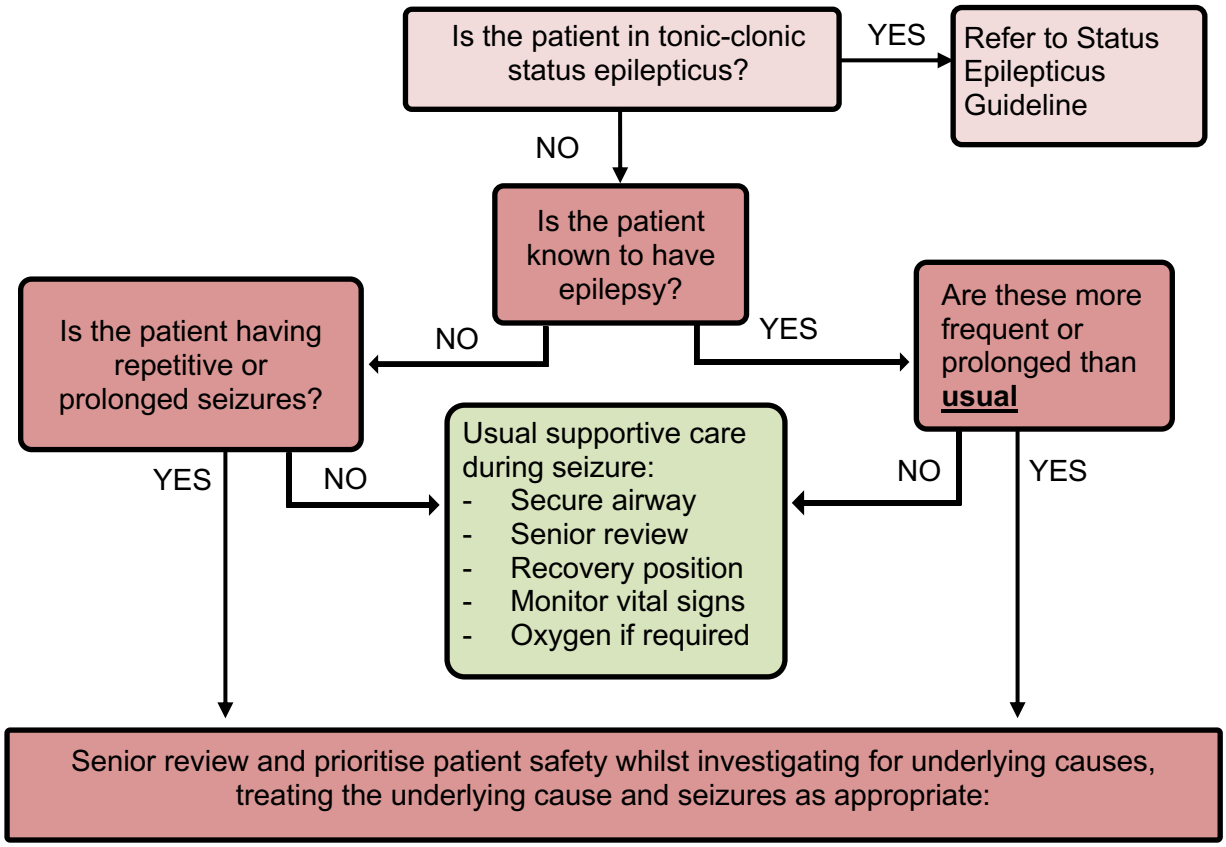
Assessment of patients with recurrent seizures

This algorithm should be used in the management and assessment of patients with repetitive or prolonged convulsive OR non-convulsive seizures.



Identify provoking factors

<u>If known epilepsy:</u>
-poor antiepileptic drug compliance
-reduced antiepileptic drug absorption
-sleep deprivation
-specific provoking factors for individual patient
-systemic infection

<u>All patients:</u>
-Acute brain injury eg stroke
-CNS inflammation
-CNS infection
-CNS space occupying lesion
-hypo/hyperglycaemia
-hyponatraemia
-hypomagnesaemia
-hypocalcaemia
-uraemia
-alcohol withdrawal
-recreational drug use

Investigations to consider

-Serum biochemistry
-Serum inflammatory markers
-Urine dip / MC&S
-CXR
-12 lead ECG (especially if on sodium channel blockers)
- Lumbar puncture
- Toxicology
- Cross sectional brain imaging

Actions to consider

-IV access
-Oral / IV benzodiazepines
-Escalate AED treatment and consider loading dose
-Senior review
-Discuss with neurology and critical care colleagues

Always consider whether events may be dissociative (functional) seizures

<u>For patients in non-convulsive status epilepticus</u>
-Investigate and treat provoking factors
-Appropriate escalation of treatment (IV antiepileptic drug)

<u>CAUTION</u>

Consider the risks of using multiple drugs with same mechanism of action, particularly sodium channel blockers.

Reassess for status epilepticus regularly.
Request senior review.

1 Introduction

Many patients with refractory epilepsy will have frequent seizures. Self - terminating, brief seizures do not require emergency drug treatment. Those who do may have existing epilepsy care plans for rescue medication (usually buccal midazolam) on EP2 which can be followed.

Patients with escalating seizure frequency and duration require investigation to identify the underlying aetiology and provoking factors. Appropriate pharmacological management should be used early to reduce the risk of progression to convulsive (generalised tonic-clonic) status epilepticus, which carries a high mortality and morbidity.

2 Clinical decision making and patient management

When assessing patients with seizures in an inpatient setting, initial management should use an ABCDE approach to maintain patient safety.

2.1 Convulsive (tonic-clonic) status epilepticus

If the patient is in generalised tonic-clonic status epilepticus (a convulsive seizure duration of 5 minutes or more with impaired awareness, or incomplete recovery between multiple convulsive seizures with impaired awareness) then the patient should be assessed and treated in line with the Status Epilepticus Guideline.

2.2 Other status epilepticus

There are many subtypes of status epilepticus other than convulsive (tonic-clonic) status epilepticus.

For a comprehensive review of the classification of status epilepticus please see the 2015 Report of the ILAE Task Force on Classification of Status Epilepticus [1].

When managing patients with status epilepticus, other than convulsive (tonic-clonic) status epilepticus the following principles should be considered:

- The diagnosis of status epilepticus type and aetiology should be determined early.
- Patients with generalised epilepsy syndromes in non-convulsive status

epilepticus tend to have a favourable prognosis and rarely need to be treated aggressively. Treat with higher doses of the patient's usual AntiEpileptic Drugs (AEDs) [2].

- In most patients with non-convulsive status epilepticus, non-sedating AEDs are preferred in order to facilitate repeated patient assessment [3].
- In patients with non-convulsive status epilepticus in the context of coma or critical illness, particularly post brain injury or intracranial haemorrhage, a more aggressive treatment approach should be taken. [3].

Treatment decisions must ultimately be made on a case-by-case basis, given the lack of high quality evidence from clinical research in this area.

2.3 Identify provoking factors in all patients with escalation of seizure severity and/or frequency

For patients with epilepsy, it is important to determine whether current seizures are an escalation of their usual seizure frequency, duration and type.

If the patient does not have an established diagnosis of epilepsy, a thorough screen for underlying causes should be undertaken and the following aetiological factors for acute symptomatic seizures considered:

- Ischaemic Stroke
- Hypoxaemia
- CNS inflammation
- Traumatic brain injury
- Intracerebral haemorrhage
- CNS infection
- Alcohol withdrawal
- Recreational drug use
- Metabolic derangement (including but not limited to hypoglycaemia, hyperglycaemia, hyponatraemia, hypercalcaemia, hypomagnesaemia and uraemia)

If the patient does have epilepsy, clinical assessment for underlying cause should also include:

- Medication compliance
- Recent changes in medication

- Systemic infection or metabolic derangement
- Alcohol withdrawal, acute or progressive CNS pathology

At all stages, it is important to assess whether the events are epileptic in nature or attributable to non-epileptic causes (e.g. dissociative seizures).

3 Investigations

If there is an escalation of seizure frequency, seizure severity or seizure duration then further investigations are likely to be required.

For patients with epilepsy who present with their usual seizures, it may be that no investigation is indicated.

If the patient does not have a diagnosis of epilepsy, and they are having frequent epileptic seizures then a more thorough search for underlying provoking factors is warranted.

Investigations to be considered will depend on the clinical context and individual patient assessment but may include:

- 12 lead ECG
- Blood tests including inflammatory markers, biochemistry and blood glucose measurement
- Chest X-ray
- Cross sectional brain imaging
- Lumbar puncture
- Urine and serum toxicology
- Antiepileptic drug (AED) levels if relevant

4 Management

The treatment approach is similar for acute repetitive seizures and prolonged seizures. Urgent therapy with a rapidly acting AED is required, in order to reduce the risk of convulsive status epilepticus. When managing patients:

1. Gain IV access.
2. Consider Benzodiazepines (IV lorazepam 4mg is the preferred agent, to be repeated after 5 minutes. If no IV access available, buccal midazolam 10 mg is an acceptable alternative). Caution with patients with respiratory failure or low body weight.
3. Consider escalation of usual antiepileptic drug therapy, particularly if

history of poor compliance/ reduced absorption.
4. Consider loading with non-sedating antiepileptic drug.
5. Escalate to neurology registrar or consultant.

There is no robust evidence for drug choice for escalating seizures other than in convulsive status epilepticus. Where an additional parenteral AED is required due to ongoing escalation of seizures despite the treatment of underlying provoking factors and benzodiazepine administration, levetiracetam, phenytoin or valproate should be considered (taking into account seizure type).

The doses below are based on the Established Status Epilepticus Treatment Trial (ESETT) [4], and lower incremental doses may be deemed appropriate in escalating seizures which do not meet the criteria for status epilepticus.

IV Levetiracetam up to 60mg/kg, maximum 4500mg over minimum 10 minutes

OR

IV Phenytoin 20mg/kg (rate 50mg/min, reduce to 25mg/hr in elderly or patients with cardiac disease) – with cardiac monitor, maximum 2g over 40 minutes

OR

IV Valproate up to 40mg/kg, maximum 3000mg over minimum 5 minutes

Phenytoin administration requires cardiac monitoring and should only be given via wide bore intravenous access given the risk of tissue necrosis and extravasation.

CAUTION: consider possibility of adverse events when prescribing multiple medications with the same mechanism of action (please refer to appendix 2. of the Status Epilepticus Guidelines).

5 Escalating dissociative seizures

Prolonged dissociative (functional) seizures can commonly be mistaken for tonic-clonic status epilepticus. These patients are at risk of iatrogenic harm from inappropriate IV therapy and intubation [5].

It is key to make a diagnosis of dissociative (functional) seizures early. They may occur alone or in conjunction with an established diagnosis of epilepsy [6]. The following features raise clinical suspicion of dissociative seizures [7,8,9]:

- History of self terminating prolonged events lasting for over 5 minutes
- Waxing and waning course
- Pelvic thrusting
- Asynchronous movements
- Closed eyes
- Ictal crying
- Recall of the event
- Peri-ictal social interaction
- Side to side head/body movements during an event
- Active resistance to eye opening/ geotropic gaze
- Flutter or blinking on eyelash rub
- Absence of post-ictal confusion after a convulsive seizure

Note that the final clinical diagnosis should encompass all available clinical information, and should not rely on any single sign alone.

In patients with suspected escalation of dissociative seizures it is important to seek neurological opinion early, consider the need for psychological interventions and signpost patients to relevant patient information charities (www.neurosymptoms.org OR www.nonepilepticattacks.info)

6 Patient escalation

Escalating frequency of epileptic seizures leads to an increased risk of status epilepticus. Patients should therefore be discussed with the SMART and critical care team for consideration of more intensive monitoring in a HDU or ITU setting. The need for EEG monitoring should be considered.

7 References

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