Treating status epilepticus in the community

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Early treatment of status epilepticus is vital so it is important to identify those patients at risk. Carers can then be trained to use buccal midazolam where possible for early intervention.

Status epilepticus is defined as seizure activity lasting for 30 minutes or more, either as a single prolonged seizure or as repeated seizures without recovery in between. Estimates of incidence vary from 4–27 cases per 100,000 adults per year, with a case fatality rate of 7–33 per cent in the first 30 days.¹

Tonic-clonic status epilepticus can lead to respiratory compromise, hypoxia and cardiorespiratory arrest, but ongoing seizure activity beyond about 60 minutes also causes permanent cerebral damage.² It is for this reason that the early treatment of status is vital.

Types of status epilepticus
Most of our discussion will be in reference to tonic-clonic status epilepticus; however, it is important to note that there are other types. Primary or secondary generalised seizures can lead to tonic-clonic status; other types of seizures can also be persistent and prolonged. These other types are not medical emergencies in the same way as tonic-clonic status epilepticus as they usually do not threaten the airway.

Non-convulsive status epilepticus is under-recognised. It usually presents as altered behaviour and confusion, and underdiagnosis is a concern, particularly in the elderly. In a patient with known epilepsy who presents with altered behaviour, it should certainly be considered; however, it can also be a first presenting symptom of epilepsy. An EEG will be diagnostic, and treatment will usually need the advice of a specialist.

Epilepsia partialis continua is another special case of status, where there may be clonic muscle activity in full consciousness. This can be particularly difficult to treat, and it is recommended that a specialist opinion is obtained.

A particularly challenging situation is dissociative, or non-epileptic, status epilepticus (“pseudostatus”) that can

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**Premonitory stage**
- In patients with epilepsy, a prodromal period during which there is a gradual increase in seizure frequency over several hours.
- Rescue treatment, review adherence and regular AEDs.
- Consider buccal midazolam 10mg, or rectal diazepam 10mg (repeated once if necessary).

**Early status**
- The first 30 minutes of seizure activity.
- Buccal or im midazolam 10mg, rectal diazepam 10mg; OR iv lorazepam 4mg; repeat once after 10 mins if seizures continue

**Established status**
- 30–60 minutes of seizure activity.
- Iv phenytoin 15–20mg/kg, 50mg/min; OR iv fosphenytoin; OR iv phenobarbitone 10mg/kg, 100mg/min

**Refractory status**
- More than 60 minutes of seizure activity, despite first- and second-line treatments.
- This is when cerebral damage (from hypoxia, hypoglycaemia and excitotoxicity) will ensue.
- General anaesthesia (thiopentone, propofol or midazolam iv)

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Figure 1. The treatment of tonic-clonic status epilepticus in hospital.
resemble tonic-clonic status. The diagnosis of dissociative seizures is beyond the scope of this article, but where there is doubt about the diagnosis, unless the patient has a videotelemetry confirmed diagnosis of non-epileptic attack disorder, in an emergency it is safer to treat as tonic-clonic status epilepticus.

**Causes and triggers of status epilepticus**

Status epilepticus most commonly arises in patients who do not have a history of epilepsy. It may be associated with any cause of acute cerebral dysfunction, including encephalitis, stroke, traumatic brain injury, alcohol withdrawal, cerebral tumours, and toxic or metabolic insults.

In patients with epilepsy, the GP can play an important role in identifying those at risk and preventing status epilepticus. Triggers and risk factors for status are:

- non-adherence to antiepileptic drug (AED) therapy
- drug changes, including down-titrating AEDs
- initiation of new drug that interacts with AEDs and lowers drug levels
- intercurrent illness eg, chest infection, urinary tract infection
- hypoglycaemia
- alcohol or alcohol withdrawal
- drug overdose.

These patients may also show warning signs of impending status epilepticus. Typically, they may develop an increase in fit frequency or a change in seizure pattern. These are red flags and should prompt a check for triggers and stepping up of treatment by increasing regular AEDs, and considering a short course of rescue treatment. Clobazam 10mg daily for five days can be a useful treatment when patients have more seizures than normal associated with an intercurrent infection or other short-lived trigger, helping to reduce the seizure frequency or severity during a high-risk period.

**Stages of status epilepticus**

Although status epilepticus is defined strictly as an epileptic seizure that continues for more than 30 minutes, in practice most tonic-clonic seizures lasting for more than about five minutes need to be treated as status. This reflects the fact that most tonic-clonic seizures do not last longer than two minutes; however, it is important to bear in mind that this is dependent on patient population. Patients with temporal lobe epilepsy may have prolonged seizures (for more than five minutes) that always self-terminate; furthermore, patients with learning disabilities may have longer-than-normal seizures as their habitual seizure type. A seizure that is twice as long as a normal seizure for that patient should be treated as status.

The first 30 minutes of seizure activity are early status; from 30–60 minutes is established status. Beyond 60 minutes, if seizures continue, status epilepticus is termed refractory. Additionally, in patients with epilepsy there is often a premontory phase, during which the fit frequency increases over several hours, resulting in a cluster of seizures. This is a particularly important stage for the primary care physician to consider, as it provides an opportunity to prevent status from developing. Benzodiazepines such as buccal midazolam (Buccolam; unlicensed in adults) are used during this stage.

**Treatment algorithm for convulsive status epilepticus**

We will concentrate in this article on the premontory and early stages of status, as these are the stages that can be treated in the community. However, Figure 1 outlines a recommended treatment protocol for status. Standard emergency measures,
such as supporting airway, breathing and circulation, are paramount. All of these will be adversely affected by ongoing seizure activity, therefore terminating the seizures needs to be the top priority. Do not forget to check the blood glucose level and to treat hypoglycaemia if necessary.

There is good evidence that treating status in the community reduces the duration of seizures. Benzodiazepines are the drugs of choice. These are the most effective agents available for treating status epilepticus, and the majority of cases will resolve with first-line treatment with benzodiazepines if given early enough.

**Benzodiazepines**

The key here is early administration. Benzodiazepines are agonists at the GABA-A receptor. As a seizure persists, GABA receptors are progressively internalised and become unavailable for modification by benzodiazepines. In one study, buccal midazolam was effective in 100 per cent of children treated within 30 minutes of seizure onset, but in only 50 per cent of children treated after that. Early resolution of status epilepticus will result in reduced need for hospital stays, ITU admissions, and the morbidity associated with both of these factors.

In a hospital setting, the intravenous route of administration is preferred because of speed of onset, and lorazepam (Ativan) is superior to diazepam because of a lower volume of distribution and longer duration of action. However, iv treatment is not practical in the community. The options are rectal diazepam, buccal, intranasal (unlicensed indication) and im midazolam (unlicensed indication). Rectal diazepam has been available for many years, and is very effective. Although the time to onset of action is longer than that of iv diazepam, this is balanced by the length of time taken to obtain iv access. However, rectal administration of medication can be challenging, undignified, and impacted stool can impair absorption of the drug.

Buccal midazolam is as, or more, effective than rectal diazepam and its use has been a game-changer, although it remains unlicensed for use in status epilepticus in adults. It can be supplied to carers and families for use if a seizure lasts longer than five minutes, or during a premonitory phase for a cluster of seizures. NICE suggests supplying buccal midazolam to patients who have had status epilepticus or serial seizures in the past.

There is a theoretical risk of respiratory depression, from repeated doses, and so proper training is essential, and a written care plan should be supplied to care-givers and agreed by relevant medical professionals. A dose of 10mg midazolam is administered between the gum and the inside of the cheek; if this has not taken effect within five minutes, an ambulance should be called. In special circumstances a second dose of benzodiazepine can be given after at least 10 minutes.

Paramedics may use iv lorazepam, rectal diazepam, buccal midazolam or im midazolam after arrival at the scene. The double-blind, randomised Rapid Anticonvulsant Medication Prior to Arrival Trial (RAMPART) clinical trial showed that midazolam injected by im auto-injector was non-inferior to iv lorazepam in terms of efficacy, and could be given more quickly.

**Adverse effects**

Adverse effects of benzodiazepines include respiratory depression and lowering of conscious level; these drugs can also precipitate acute angle closure glaucoma and this should be considered before supplying midazolam for use at home. If carers administer benzodiazepines, they should call an ambulance if there is a concern about respiratory function or airway. Having said this, the risk of respiratory depression from uncontrolled seizures is much higher than from benzodiazepine treatment.

**Epilepsy nurses**

Treatment of epilepsy is increasingly specialised, and the treatment options can be baffling for the non-specialist. The stakes can appear particularly high when you are worried about impending status epilepticus. Epilepsy nurses are increasingly used across the country to provide rapid access to information and support for patients, relatives and non-specialists. While on the whole they do not provide emergency services, the premonitory phase of status epilepticus can last for up to 48 hours in some patients, so find out who your local epilepsy nurse is and use them if you are worried.

**Conclusion**

Steps should be taken in primary care to identify patients at risk of status epilepticus, and to prevent it by improving seizure control or stepping up treatment if fit frequency increases. Early use of benzodiazepines is paramount once status epilepticus occurs, and this means that if patients have had a previous episode of status epilepticus or serial seizures, carers and family should be given (and trained to use) buccal midazolam where possible.

**References**


**Declaration of interests**

Dr Shah has none to declare. Dr Kelso has received honoraria from Eisai and UCB Pharma for speaking at educational symposia.

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