Status epilepticus: a neurological emergency

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Epidemiology

Based on United States data, it is estimated that 6,500 to 15,000 people in Canada each year will have generalized convulsive status epilepticus (GCSE),\(^3\) with a mortality of 20%.\(^3\) The incidence of GCSE is highest in the first decade of life and after age 60.\(^3\)

Definition

Epidemiological literature defines status epilepticus as a fixed and persistent seizure lasting at least 30 minutes,\(^4\) the time interval after which irreversible damage occurs to neurons. However, clinically it is important to initiate treatment before 20 minutes and a more practical definition is: “either continuous seizures lasting at least five minutes or two or more discrete seizures between which there is incomplete recovery of consciousness.”\(^5\)

Clinical features

Initially, patients with status epilepticus will present with obvious seizure symptoms, such as tonic, clonic or tonic-clonic movements. However, as the condition progresses the clinical manifestations become subtle and the only signs of an underlying disorder may be minor twitching or in some cases no motor activity.\(^6\) Electroencephalography (EEG) monitoring will be required to detect cerebral epileptic activity. EEG is also useful in distinguishing status epilepticus from pseudoseizures, also known as nonepileptic status. Pseudoseizures clinically resemble a seizure, but do not show epileptic activity on EEG and may be precipitated by suggestions or commands. It is the other main condition in the differential diagnosis of multiple seizures and is implicated as the cause about half the time.\(^7\)

Physiologic changes that occur in GCSE can be temporally divided into two phases: Phase I (0-30 minutes) in which compensatory mechanisms are still intact, and phase II (>30 minutes) when more serious symptoms develop due to a failure of the compensatory mechanisms. This classification is clinically useful because the development of phase II symptoms should prompt admission to an intensive care unit. (See Table 1).

Pathophysiology

The pathophysiology of status epilepticus remains largely unknown. An insight into the possible mechanism of SE came from reports of patients who consumed mussels contaminated with domoic acid, an analogue of the excitatory neurotransmitter glutamate.\(^8\) This incident suggests that excessive activation of excitatory receptors can cause status epilepticus.

Other evidence demonstrates that status epilepticus can be caused by substances, such as penicillin, which antagonize the neurotransmitter GABA.\(^9\) GABA is the main inhibitory neurotransmitter in the brain and so failure of effective inhibition may lead to prolonged seizures. Ultimately, status epilepticus involves a disorder of the body’s normal mechanism to terminate a seizure, which can be due to excessive excitation or lack of inhibition.

Causes - acute and chronic

The causes of status epilepticus can be divided into acute and chronic. It is important to distinguish between them since the prognosis, management and response to treatment differs.

Acute causes of status epilepticus include metabolic disturbances (e.g. electrolyte imbalances, renal failure, sepsis), CNS infection, stroke, head trauma, drug toxicity and hypoxia. Chronic processes that cause status epilepticus include preexisting epilepsy, discontinuation of antiepileptic medication or sub-therapeutic levels of medication, and seizures due to chronic ethanol abuse. Other processes such as CNS strokes and tumours can present with status epilepticus after a latent period of weeks to years.

Cases of status epilepticus due to chronic processes respond well to anticonvulsant medication. In contrast, seizures due to acute causes are typically difficult to control and have a higher mortality.\(^10\)

Management

The management of status epilepticus includes standard measures that would be implemented in any medical emergency, including evaluation of the airway, breathing and circulation. The next steps in management are to order blood work and administer glucose, thiamine and antiepileptic drugs.

Relevant investigations to order include: CBC, electrolytes, calcium, magnesium, liver function, kidney function, serum levels of antiepileptic drugs, toxicology and clotting parameters. A lumbar puncture should be performed if infection is suspected.

Furthermore, two IV lines are recommended for administering glucose, thiamine, anticonvulsant drugs, normal saline and vasopressors. Thiamine is given to patients who are malnourished or have a history of alcohol abuse since they are at risk for Wernicke’s encephalopathy.

Some special considerations in the management of GCSE are in order:

- A priority in management is maintaining a patent airway and adequate ventilation.
Patients should be protected from injury, however, restraints are not recommended as they may cause fractures.

Arterial-blood gas measurements are useful and often show a metabolic acidosis, which will correct itself once the seizures stop; sodium bicarbonate should be used only in extreme situations.\textsuperscript{11}

Hyperthermia occurs frequently in about 29-79\% of patients and should be treated immediately with passive cooling.

### Principles of drug therapy

The initial treatment of GCSE is combined IV lorazepam and phenytoin; it controls 80\% of seizures in patients with GCSE.\textsuperscript{12}

Benzodiazepines are fast-acting, potent antiepileptic drugs, and include diazepam, lorazepam, midazolam, and clonazepam. Diazepam and lorazepam may both be considered in initial therapy, however lorazepam is preferred because of its duration of action of 12-24 hours versus diazepam's 15-30 minutes duration of action.\textsuperscript{13} Adverse effects of IV benzodiazepines include respiratory depression and hypotension.

Phenytoin is usually administered intravenously after a benzodiazepine (e.g. lorazepam). Adverse effects associated with phenytoin are cardiac rhythm disturbances (incidence of 7\%) and hypotension (incidence of 29\%). IV phenytoin may also rarely cause "purple glove syndrome" a tissue injury caused by venous irritation resulting in extravasation.

Phenobarbital has a depressant effect on respiratory drive, level of consciousness and blood pressure. For these reasons, it is recommended only when benzodiazepine and phenytoin therapy fails, and administration should ideally be carried out in an intensive care unit.

Status epilepticus that does not respond to a benzodiazepine, phenytoin or phenobarbital is considered refractory and will require therapy with propofol and/or midalozam.

### Out-of-hospital Treatment

In situations when IV administration of drugs and monitoring equipment are not available, treatment options include parenteral or rectal diazepam, sublingual lorazepam and intramuscular midazolam.

### References