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often it is precipitated by an acute illness. In one study of hospitalised patients with a median age of 65 years, de novo status epilepticus was most commonly caused by stroke and metabolic derangements [45-49]. De Lorenzo's review of common causes of SE in older patients emphasises the importance of cerebrovascular disease as a factor in SE (Table 1 and 2). Alcohol intoxication or withdrawal is less commonly a cause in older patients but should still be considered. In some cases, no obvious cause may be found. There is also an association with advanced Alzheimer's disease, which has been identified as a risk factor for new onset generalized tonic-clonic seizures in older adults.

Table 1: Causes of epilepsy in older patients

- Cerebrovascular disease 40%
- Toxic/metabolic 15%
- Brain tumours 10%
- Head trauma 5%
- Dementias <5%
- CNS infections 1%

(Adapted with permission from Kramer 2001)49

Table 2: Causes of SE in older patients

- Cerebrovascular accident (CVA) 21%
- Remote symptomatic (mainly previous CVA) 21%
- Low anticonvulsant drug concentrations 21%
- Hypoxia 17%
- Metabolic 14%
- Alcohol 11%
- Tumour 10%
- Infection 6%
- Anoxia 6%
- Haemorrhage 5%
- CNS infection 5%
- Trauma 1%
- Idiopathic 1%
- Other 1%

(Adapted with permission from DeLorenzo 1996.35

### Investigation

Blood investigations should include full blood count and CRP to check for infection, biochemistry for electrolyte abnormalities, calcium and glucose level [50]. CK rises with seizure activity. Prolactin is not useful in status epilepticus as it returns to normal with persistent seizures. An arterial blood gas will reveal hypoxia or evidence of metabolic disarray. Antiepileptic drug levels should be assayed if the patient has been prescribed them, and liver function checked. A toxicology screen may be useful [51].

Brain imaging is mandatory, with either CT or MRI. ECG helps to rule out cardiac arrhythmias such as long QT syndrome which may present as seizures and a lumbar puncture is indicated if central

nervous system infection is possible. In the event of doubt about the diagnosis an EEG may help to clarify the matter. It is also useful for diagnosis of non-convulsive SE, which may develop from convulsive SE but be easily missed by the clinician. One EEG study found that focal variant patterns considered as epileptiform abnormalities, or non-specific abnormalities are more frequently recorded in older age groups [52-54]. However a later study comparing changes on EEGs in young patients (20 to 59 years) and older patients (over 60 years of age) who had epilepsy found decreased background rhythm, rhythmicity, and amplitude in the older group.

### Initial treatment

Early treatment is important as longer seizure duration leads to less response to treatment and more neuronal damage. The priorities are to stop the seizure and apply basic life support immediately. Airway, breathing and circulation should be assessed and intervention made if necessary. The patient should be kept in a safe area away from objects that may cause injury if struck [55]. Nothing should be put in the mouth. IV access should be established. A fingerprick test for blood glucose level should be performed, and IV dextrose given if necessary. Iamline should be administered where malnutrition is suspected.

### Pharmacologic therapy

Immediate treatment is initially with a benzodiazepine. Lorazepam is the preferred first line agent due to its favourable pharmacokinetics. It rapidly achieves high concentration in the brain and appears to have a lower risk of seizure recurrence than diazepam [56-58]. A Cochrane review found that lorazepam is better than diazepam or phenytoin alone for cessation of seizures and carries a lower risk of continuation of status epilepticus requiring a different drug or general anaesthesia. The incidence of respiratory depression is higher in older people. One small prospective observational study suggested that in critically ill older patients with NCSE, giving intravenous benzodiazepines was associated with increased risk of death.

### Second line therapy

Most guidelines recommend intravenous phenytoin as second line if benzodiazepines have failed. It has established efficacy and its side effects are known. It may produce hypotension and cardiac arrhythmias and cardiac monitoring is recommended. These problems are seen more often in patients over 50 years [59-63]. The infusion site reaction called "purple glove syndrome" is thought to be due to local thrombosis. It is less common if using the prodrug fosphenytoin, but this is more expensive. Fosphenytoin can be given intramuscularly if intravenous access is difficult to establish. Sodium valproate has been suggested as an alternative second line agent, but is approved for this in some countries only. Two small randomised comparative studies of phenytoin and valproate favoured valproate. Valproate also appears to have a low incidence of cardiovascular side effects [64].

In older people, there appears to be no uncontroversial drug of first choice. Age-related changes such as progressive decline in AED protein binding by albumin, increased volume of distribution, and slow elimination can affect pharmacokinetics and pharmacodynamics. Older people are often on other medications, which makes drug interaction more likely. They appear to be more responsive to antiepileptic drug therapy than younger groups, but are also more likely to experience side effects at lower serum antiepileptic drug concentrations. A 1994 trial found a mean side effect rate of 20% with valproate or phenytoin [65-67]. Just over 20% of patients were not satisfactorily controlled. First choice of an AED is also made difficult by the paucity of evidence-

based data on their use in elderly patients, especially in the very old and those with comorbidities. Recent small case series have suggested that intravenous levetiracetam may be useful in older patients. No trials were found comparing treatment options for SE in younger and older patients. Trials comparing different treatments tended to have a younger cohort than would be generally seen in clinical practice [68].

As is standard practice in Geriatric Medicine, the treatment should be tailored to the patient. For example, antacids and enteral feeding decrease the absorption and efficacy of phenytoin. Valproate levels may be decreased and phenytoin levels may be increased in patients taking both medications. Carbamazepine is metabolized in the liver, and as hepatic function can be reduced in older people, levels should be monitored closely. It also has a greater association with hyponatraemia in old age. The VA Cooperative Study on epilepsy in the elderly demonstrated that lamotrigine and gabapentin were better tolerated than carbamazepine [69-71]. Newer drugs include topiramate and lacosamide but experience is limited. Topiramate has been reported to have adverse effects on cognition, even in younger patients, which leads to a high discontinuation rate.

#### Refractory SE

In some cases SE does not resolve despite the application of first and second line treatments. It is then termed refractory SE. Anaesthetic agents (such as pentobarbital, propofol, or midazolam) and mechanical ventilation may be necessary. It is estimated that SE becomes refractory in 9% to 40% of cases. Mortality for RSE is as high as 48% and only about a third of patients return to their premorbid functional baseline [72].

#### ICU management

Ala-Kokko looked at incidence of infections in patients with status epilepticus requiring intensive care and effect on resource utilization. He concluded that the infection rate of status epilepticus patients was high and nosocomial infections were associated with more severe illness, treatment escalation, prolonged hospital stay and enhanced resource utilization. In one study of critically ill older patients with NCSE, those who were managed outside of ICU had significantly shorter hospital stays (22.3 vs. 39.2 days) [73-76].

#### Surgical management

A small range of case reports and series has reported the use of surgery such as temporal lobectomy in the management of epilepsy, however this is infrequent in status epilepticus and the oldest patient reported was 45 years [77-79]. NCSE is not a surgical condition. The oldest patient reported was 45 years [77-79].

Aspiration pneumonia

Pulmonary oedema

Sepsis

Chronic encephalopathy

#### Prognosis

The prognosis is related to the aetiology and duration of the seizures. For example, when SE complicates acute ischaemic stroke, mortality is 3 times higher than in stroke alone [17]. Primary predictors

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