Generalized tonic-clonic status epilepticus in the elderly in China

Andrew C.F. Hui¹, Anita K. Lam², Adrian Wong¹, Kai-Ming Chow¹, Eric L.Y Chan², Simon L. Choi², Ka-Shing Wong¹

¹ Department of Medicine and Therapeutics, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong SAR
² Department of Medicine and Geriatrics, Caritas Medical Centre, Shamshuipo, Hong Kong SAR, China

ABSTRACT – The proportion of elderly people in China is projected to increase rapidly but there is limited information on status epilepticus (SE) in this population. We evaluated retrospectively the etiology, response to treatment, outcome and predictors of mortality in a group of elderly patients with generalized tonic-clonic SE in Hong Kong, China. Factors for increased mortality were analyzed using a logistic regression model. Of the 80 acute admissions for SE from two large urban hospitals over a seven-year period, 1996-2002, the two leading causes were attributed to cerebral infarct (n=28, 35%) and cerebral haemorrhage (n=14, 17.5%). The mean age was 74.2 years (range 60-93 years). At six months from the onset of seizures, 26 patients (32.5%) had made a good recovery but another 28 (35%) had died. Results showed that mortality was associated with increasing age (OR 1.08, 95% CI 1.01-1.16) and SE due to an acute symptomatic disturbance (OR 4.90, 95% CI 1.17-13.67). SE is associated with significant morbidity and mortality in this age group.

Key words: epilepsy, status epilepticus, predictor, Chinese, mortality, elderly

The incidence of status epilepticus (SE) shows a bimodal distribution with a second peak in the elderly, as there is an increased prevalence of neurologic and systemic conditions that predispose this group to seizures (DeLorenzo et al. 1996, DeLorenzo 1997, Hesdorffer et al. 1998, Wu et al. 2002, Logroscino et al. 2001). Estimates of status epilepticus among people aged 60 and above in the US vary from 22.3 to 96.1/100000, which is two to four times that of the general population (DeLorenzo et al. 1996, DeLorenzo 1997, Hesdorffer et al. 1998, Wu et al. 2002, Logroscino et al. 2001). Mortality in the elderly is also considerably higher at 38%, rising to 50% in those over 80 years of age, compared with adults (26%) or paediatric patients (3%) (DeLorenzo et al. 1996, Waterhouse and DeLorenzo 2001). Convulsive SE in older people is associated with different aetiologies and outcomes but few series have focused on this group as most reports are based on SE in children or adults in general (Sung and Chu 1989, Celesia et al. 1972). The objective of this study is to study the causes and outcome of generalized tonic-clonic SE, and predictors of excessive mortality in elderly patients in Hong Kong, China.
Methods

The series consisted of consecutive patients, 60 years of age or over who were admitted to two regional government hospitals in neighbouring health care districts, (the Prince of Wales Hospital and the Caritas Medical Centre from Hong Kong, China), with a diagnosis of generalized tonic-clonic SE. We collected information retrospectively from consecutive, unselected patients who were admitted between January 1996 and December 2002. To ensure that we obtain as complete a dataset as possible, we used multiple, overlapping databases. Patient identification was based on the records of the electro-diagnostic unit, the computerized admission and discharge records of the medical department, and the emergency department of both hospitals (International Classification of Disease codes 345.2, 345.3, 345.7, 780.39). The following exclusion criteria applied: i) patients under the age of 60; ii) patients in which other forms of status were predominant: complex partial, simple partial or myoclonic SE.

Definitions

Status epilepticus was defined as: i) continuous seizure activity lasting 30 minutes or more; ii) recurrent seizure activity lasting 30 minutes or more without full return of consciousness. Generalized tonic-clonic seizure was defined using recommendations of the International Classification of Epileptic Seizures, according to the description from witnesses, nursing and medical staff (Commission on Classification and Terminology of the International League Against Epilepsy 1981). Information from the medical records of cases that fulfilled the diagnosis criteria for SE was reviewed by two independent reviewers. A standardized data sheet was used in order to achieve consensus and accuracy. Relevant details were noted: patients’ name, age and sex; pre-morbid state and co-morbidities, history of epilepsy and antiepileptic drug use, seizure type, etiology, results of laboratory and brain imaging, duration of hospital stay and outcome. The patients were also categorized into groups with newly diagnosed seizures or with prior epilepsy. We used the Glasgow Outcome Score (GOS) at six months after the onset of SE as a measure of functional status; this was recorded as part of standard aftercare in survivors (Jennett and Bond 1975). This score ranges from 1 (death) to 5 (good recovery). Poor outcome was defined as death, or deterioration to grades 2 or 3 on the GOS among survivors. Conforming to institutional guidelines, baseline electrolytes such as glucose, renal and liver function tests and cranial computed tomography were performed in all patients admitted with SE. Firstline anticonvulsive therapy, based on published recommendations (Dodson et al. 1993), consisted of intravenous diazepam or lorazepam, followed by phenytoin loading of 15-20 mg/kg, however second-line agents such as midazolam, propofol, phenobarbitone or thiopentone infusions were not standardized.

Etiology was defined as the presence of a remote or acute symptomatic injury that was assumed to have caused the episode, following the modified classification of Hauser and Kurland (Hauser and Kurland 1975). The criteria for designating etiology were as follows: – antiepileptic drug non-compliance. This required laboratory and historical support of non-compliance; – alcohol/drug. Status due to alcohol-related or drug-induced seizures required history of relevant drug ingestion and laboratory support; – cerebrovascular disease (infarct or haemorrhage). The diagnosis was based on a definite clinical history of focal neurological deficit of sudden onset of over 24 hours duration and/or consistent abnormality on imaging; – central nervous system infection. This required clinical features of CNS infection with compatible CSF findings; – hypoxic. This diagnosis was made if there was a history of respiratory or cardiac arrest without other cause for developing SE; – metabolic. Metabolic disorders such as hyponatraemia or non-ketotic hyperosmolar syndrome required the presence of abnormalities sufficiently severe to cause seizures; – tumour. Compatible lesions on cranial CT or MR scanning were necessary to attribute tumour as a cause; – head injury. This diagnosis was made if there was a history of trauma sufficient to produce coma of 24 hours duration, neurological deficit or CT evidence of post-traumatic changes; – cryptogenic. The episode was labeled cryptogenic if there was insufficient clinical, laboratory or radiological evidence to support a specific cause. Delay in treatment was defined here as initiation of antiepileptic drugs (AED) 30 minutes after the onset of SE as reported by witnesses or medical personnel. Patients with recurrent or continuous seizures lasting more than 60 minutes were regarded as being in refractory SE.

Statistical analysis

Data were analyzed using SPSS 9.0 for Windows, Chicago, IL, USA. Continuous variables were compared using the two-tailed t-test or the Mann-Whitney test for non-normally distributed data, while categorical variables were compared using chi-squared or Fisher’s exact test as appropriate. To identify independent risk factors for excess mortality following SE, clinical variables associated with death in a univariate analysis were entered into a logistic regression model. Age was analyzed as a continuous variable and the presence of an acute/remote symptomatic injury; gender; etiology and delay in treatment were analyzed as categorical variables. The predictive factors for excess mortality were determined in the multivariate logistic regression model after adjustment for age, sex, acute symptomatic, delay in treatment and etiology. Statistical significance was taken as 0.05.
Results

The records of 80 patients with onset of SE at age 60 or over were identified and retrieved for review. This group comprised 41 men and 39 women, mean age 74.2 years (range 60 to 93 years). Fifteen (18.5%) had a prior history of epilepsy and 45 (56.2%) had been admitted with an acute symptomatic injury. The most common etiology was cerebral infarct of which 19 were remote symptomatic and 15 acute, followed by cerebral haemorrhage of which seven were remote symptomatic and seven acute (table 1). Among these 34 cases with cerebral infarct, six had coexisting dementia. No cause was found in five (6.25%) cases. The mean duration of hospitalization was 15.1 days (SD 13.8 days). Twenty-six patients (32.5%) made a good recovery, another 26 (32.5%) had a poor GOS score compared with pre-morbid at six months after the onset of SE: 28 (35%) had died; in total 54 (67.5%) cases of SE resulted in poor outcome. Mortality and poor outcome according to each age category is shown in figure 1. There was a delay in instituting treatment in 18 cases (23%), while refractory SE developed in 17 (21%). After correction for the above factors, multivariate analysis revealed that increasing age (OR 1.08, 95% CI 1.01-1.16) and SE due to an acute symptomatic disturbance (OR 4.90, 95% CI 1.17-13.67) were associated with increased mortality.

Discussion

Age is an important factor in the etiology and outcome of epilepsy (Towne et al. 1994, Shorvon 1999, Claassen et al. 2002). While idiopathic epilepsy syndromes are more common in children and have a more favorable prognosis, epilepsy in older patients is usually due to the effects of...
acute and remote symptomatic neurologic insults. In contrast to reports on SE from the US and Europe in a general adult population, we found that cerebrovascular disease was the most frequent underlying cause, while alcohol-related and antiepileptic drug withdrawal were uncommon causes (Aminoff et al. 1980, Lowenstein and All-}


Although this study was conducted in government hospi-
tals, 95% of patients with acute, convulsion-related disor-
ders are admitted to such public institutions (Department
of Health of Hong Kong, 2002). Because of the limited size
of the sample population, this may not represent the total
number of SE; other predictors for death may be identified,
with larger numbers. Another source of bias is the retro-
spective nature of the study, which may have led to
underestimations.

It is difficult to separate the effects of seizures per se from
the consequences of the underlying pathology; in gener-
alized tonic-clonic SE, recent studies have highlighted the
heterogeneous nature of this condition and the impor-
tance of the underlying cause in determining outcome
(Logrosino et al. 2002). In a report of 31 patients with a
mean age of 66 years who developed SE after a stroke
(constituting 19% of all cases who develop first-time sei-
zuers after a stroke), Rumbach found that the immediate
prognosis was poor, but SE did not necessarily lead to
subsequent epilepsy (Rumbach et al. 2000). Mortality after
stroke is higher in those who develop status compared with stroke alone (Waterhouse et al. 1998).

This report has focused on generalized tonic-clonic SE,
however other forms of status are being increasingly rec-
ognized, namely non-convulsive SE, which is regarded as
a complex partial or absence status. Both forms are less
common but they can occur in elderly patients with or
without a history of epilepsy. In one series of late-onset
absence SE, patients’ age ranged from 48 to 81 years with
a mean of 58.6 years (Thomas et al. 1992). Drug with-
drawal and metabolic derangement have been the most
frequently reported triggers for these episodes.

Seizures in general are especially debilitating in the eld-
erly. Loss of confidence, loss of independence and pro-
gression to nursing homes are common (Luehdorf et al.
1986, Dodrill and Wilensky 1990, Ettinger and Shinnar
1993, Stephen and Brodie 2000). Currently, 10% of the
population of China are classified as elderly. By 2020 this
figure is expected to rise to 17%, which would have an
immense impact on medical services and society (United
Nations Secretariat 2004). As stroke is the most common
cause of SE, the prevention of cerebrovascular disease
would, in theory, reduce the burden of status epilepticus in
this age group.

### Table 2. Results of univariate analysis.

<table>
<thead>
<tr>
<th>Univariate</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lower</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;0.05</td>
<td>1.02</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
</tr>
<tr>
<td>NS</td>
<td>0.34</td>
</tr>
<tr>
<td><strong>History of epilepsy</strong></td>
<td></td>
</tr>
<tr>
<td>NS</td>
<td>0.18</td>
</tr>
<tr>
<td><strong>Class</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;0.01</td>
<td>1.61</td>
</tr>
<tr>
<td>&lt;0.05</td>
<td>0.10</td>
</tr>
<tr>
<td>NS</td>
<td>0.00</td>
</tr>
<tr>
<td><strong>Aetiology</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;0.01</td>
<td>1.61</td>
</tr>
<tr>
<td>&lt;0.05</td>
<td>0.10</td>
</tr>
<tr>
<td>NS</td>
<td>0.00</td>
</tr>
<tr>
<td><strong>Refractory</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;0.001</td>
<td>3.32</td>
</tr>
<tr>
<td><strong>Delay in treatment</strong></td>
<td></td>
</tr>
<tr>
<td>NS</td>
<td>0.70</td>
</tr>
<tr>
<td><strong>Days hospitalized</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;0.05</td>
<td>0.88</td>
</tr>
</tbody>
</table>

* Risk factors of p<0.05 in univariate regression were submitted to stepwise multivariate model.
Acknowledgements. We thank Dr C.Y. Man for assistance in the preparation of the manuscript.

References


