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Late onset epilepsy is increasing in incidence. These patients often have significant underlying morbidity. This retrospective study in a tertiary referral centre identified 68 patients aged 65 years or older, with new onset seizures over a four-year period. 81% of patients (n = 55) were followed up at an average of 2.7 years post diagnosis. 38% of patients had evidence of cerebrovascular disease (CT visualised focal infarction, haemorrhage or small vessel ischaemia in 32%, clinical diagnosis with normal CT brain in 6%). No patient was found to have a space-occupying lesion. Of the 55 patients followed up, 45% of these had died at a mean age of 82 years old and 1.9 years post diagnosis (range 12 hours to 5 years). Three patients died as a direct result of seizures (trauma and sepsis). 14 patients died of clearly unrelated causes. Eight patients died from underlying vascular disease or Alzheimerâ s dementia. Patients who died during follow-up were on average 3.4 years older at the time of diagnosis than survivors (p< 0.05). Patients with atrial fibrillation at the time of diagnosis, had increased mortality (relative risk 2.53; 95% C.I. 1.19 â 5.36), but they were older than those without atrial fibrillation. At the time of follow up, 92% of those taking anti-convulsants were maintained seizure free on anticonvulsant monotherapy.

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Author : Timmons Suzanne , Hyland JM, O'Mahony D, Sweeney B, Twomey CB

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Introduction

In adults, the incidence of seizures increases steeply with advanced age[1,2]. Presently, 24% of new diagnoses of seizures are made in persons over the age of 60 years old[3]. As the population ages, elderly patients will make up an increasingly large subgroup of epileptic patients. They are a challenging group to treat because of frequent concomitant illnesses, impaired drug clearance and multiple other medications. However, seizures in the elderly generally respond very well to anticonvulsant therapy[4].

The aim of this study was: 1) to determine the underlying aetiology for seizures in elderly patients in our district and to review the resources used in investigating new onset seizures, 2) to establish current in-hospital prescribing practice for elderly patients with seizures and 3) to follow up these patients with respect to seizure control, medication requirement and mortality.

Methods

Cases were identified from the Hospital Inpatient Enquiry (HIPE) system, which details diagnoses at the time of hospital discharge or death. The initial search yielded 98 cases aged 65 years or older with a diagnosis of epilepsy, seizure or other similar codes, over a four-year period from Jan 1 1995 to Dec 31 1998.

Sixty-eight cases were included in the study (22 patients had a previous diagnosis of seizure; 4 cases were miscoded for age or diagnosis; 4 charts were unavailable).
These patients were then followed up by a telephone call to their General Practitioner or, if they were resident in a Nursing Home, the matron of the Nursing Home. Hospital notes were also reviewed for any subsequent admissions and outpatient visits. Particular emphasis was placed on any alterations to anticonvulsant therapy, the reasons for any such change and current seizure control. If the patient was deceased, details were obtained as to the cause of death.

Statistical analysis was performed using Students t test for the difference between two means, using a two-tailed analysis and taking a p value of <0.05 as significant. Relative risk was calculated in the standard way.

Results

60% of cases were male, of average age 77 years, (range 66-88 years) and 40% were female, of average age 79 years, (range 69-90 years). 45% had been under the care of the geriatric service, 28% general physicians and 26% neurologists.

Seizure type and frequency (Table 1): 51% of seizures were clinically primary generalised tonic-clonic seizures, with 11% of these in status at first presentation. (One patient however had EEG evidence of a focal discharge, indicating probable secondary generalisation). 41% were clinically partial seizures (one-third of these were simple partial seizures, while two-thirds had secondary generalisation). 8% were clinically primary generalised absence seizures - these patients had no obvious limb jerking or focal features but lost contact with their surroundings and were confused post-ictally. 46% of patients presented after a single seizure (mainly tonic-clonic) and 29% after a second seizure, while 13% of cases presented after four or more seizures. Those without obvious ictal features had an average of five seizures before the diagnosis was made.

Table 1 Type of seizure and EEG findings

	Seizure Type		
	Primary Tonic clonic	**Partial seizure (complex or simple)**	**Absence***
Number of patients (% of total)	35 (51%)	28 (41%)	5 (8%)
Number in Status Epilepticus at presentation	4	1	0
Average number of seizures at diagnosis	1.6	2.4	5
Number with EEG performed	14 (40%)	13 (46%)	2 (40%)

Focal discharge on EEG (%)	1 (7%)	5 (38%)	0
* Primary generalised absence seizure			

Table 2 Aetiological factors in late onset seizures:	
Aetiology Number of patients	**(%)**
Cerebrovascular lesion (clinical or CT finding)	26 (38%)
Idiopathic	23 (34%)
Medication related	15 (22%)
Alcohol excess	6 (9%) *
Hyponatraemia	5 (7%)
Alzheimers disease	5 (7%)
Febrile illness	2 (3%)
Hypoglycaemia	1 (1.5%)
(Total)	(120%)
* Inadequately documented	

Table 3 Medication details

	Initial % of patients	Final %	Initial daily dose	Final daily dose
Phenytoin	48%	33%	200 - 300mg	200 - 300mg
Valproate	35%	47%	200 - 600mg	200 - 2400mg
Carbamazepine	17%	20%	200 - 400mg	200 - 800mg
Lamotrigine	0%	2%	25 mg	100mg

EEG findings: Electroencephalogram (EEG) was performed in 43% of cases. Of these, 21% had focal discharges and 7% had generalised slowing (Table 1).
Aetiology: CT brain was performed in 94% of cases and Magnetic Resonance Imaging (MRI) in 2% of cases. 20% had focal cerebrovascular disease: infarct (n = 10) or haemorrhage (n = 3). A further four patients (6%) had clinical evidence of cerebral infarction with normal CT brain. In 12% of cases, the seizure occurred in the first month post cerebral event. A further 12% of patients had evidence of small vessel ischaemia. No tumours or other space occupying lesions were found.
Precipitants: 20% of cases were taking drugs that are known to lower seizure threshold (antipsychotics, antidepressants, levodopa) while 2% had benzodiazepines withdrawn in the days prior to the seizure. 13% had a metabolic disturbance (see Table 2 for details). At least 9% had recent excessive alcohol intake (inadequately documented in many patients), including a clear history of alcohol withdrawal in just one case.

Co-morbidity: 41% of patients had hypertension, 40% had ischaemic heart disease and 19% had both. 15% of cases were in atrial fibrillation and 3% had documented valvular heart disease. 9% of cases had vascular dementia and 7% had Alzheimers dementia.

Treatment: 90% of patients were treated with anticonvulsants (the remainder had either a single seizure or a reversible cause for seizures). 48% received phenytoin, 35% received sodium valproate and 17% received carbamazepine (Table 3). 80% of patients with a single seizure were treated - 44% of these had a structural brain lesion, a focal discharge on EEG, or both; 12% were in status epilepticus; 8% had significant dementia.

Mortality: 55 patients (81% of the total group) were followed up, at an average of 2.7 years since diagnosis. 45% of these patients died, at a mean age of 82 years old and 1.9 years post diagnosis (range 12 hours to 5 years). Three patients (5.5% of the follow-up group) died as a direct result of seizures: one in status epilepticus, one due to a post-ictal subdural haematoma and one due to post-ictal septicaemia. 14 patients died of unrelated causes (e.g. malignancy, biliary sepsis, COPD). Six cases died of vascular disease (stroke, cerebral haemorrhage, severe vascular dementia and peripheral vascular disease) while two cases died of pneumonia due to profound Alzheimers dementia. Patients who died during follow-up were on average 3.4 years older at the time of diagnosis than survivors ($p < 0.05$).

We examined whether any particular features (such as vascular disease, dementia or CT findings) at the time of presentation were predictive of higher mortality (Graph 1). Of these, atrial fibrillation was the only factor associated with an increased risk of death (relative risk 2.53; 95% C.I. 1.19 5.36). Patients in atrial fibrillation were four years older at time of diagnosis than those in sinus rhythm so increased mortality due solely to increased age couldnt be excluded.

Medication requirements: 44% of patients were continued on their discharge anticonvulsant medication without any modification. 30% were changed to another anticonvulsant. This was because of poor efficacy in 50%, side effects in 19% (cholestatic jaundice in one patient, rash or drowsiness in remainder) and undocumented reasons in 31%. In 17% of patients, the dosage was increased after discharge, while 2% had dosage decreased (Table 3). 8% of patients initially commenced on anticonvulsant medication were able to discontinue therapy without any relapse of seizures. Only 8% of patients still taking anticonvulsants at follow-up required combination therapy to control seizures (one of these still had poor control).

Discussion

We wish to acknowledge the deficiencies of a study that identifies patients retrospectively from HIPE details. Some patients with atypical seizures may have been inadvertently excluded due to incorrect diagnosis or coding. Notwithstanding this, some interesting points have emerged in this study.

The reported frequency of intracranial tumours in elderly patients with new onset seizures is 11-25%3,8. However, in the 96% of our patients who had cerebral imaging performed, none had an intracranial space-occupying lesion. It is unlikely that any lesions were missed because our hospital is the tertiary referral centre of the region for neurology and neurosurgery and to our knowledge, no patient has subsequently presented with a space-occupying lesion.

38% of patients had CT evidence of cerebrovascular disease. Some of these had diffuse small vessel ischaemia. This has been reported to be associated with seizures, if not confined to subcortical areas5. Some authors[6,7] advocate the performing of MRI scans in all elderly patients with seizures, as the sensitivity for vascular lesions is higher than CT scans. (Our value is therefore likely to be an underestimate as only one of our patients had MRI of brain performed). However, many physicians do not perform MRI scans routinely. A CT scan is usually sufficient to rule out a potentially treatable space-occupying lesion and the demonstration of a small vascular lesion, not visible on CT, may not influence treatment. From the perspective of our study, MRI would obviously have been preferable to CT to determine absence or presence of structural brain disease, but was not routinely used. Furthermore, only autopsy examination can fully exclude structural brain disease, particularly early neurodegeneration, and this was not performed on any patient.

EEG was infrequently performed in our patients (44%). The role of EEG in diagnosing seizures in the elderly is controversial. Many inter-ictal EEGs will be normal[9] or show non-specific abnormalities such as slow waves. Thus a single normal EEG is not helpful. However, some seizures in elderly patients can be difficult to differentiate from posterior cerebral circulation events or arrhythmias. In these cases, video-telemetry with simultaneous EEG and cardiac rhythm monitoring might be useful.

Due to the small number of patients in our follow-up group (55 patients), it was not possible to identify statistically significant clinical parameters at the time of diagnosis that predicted mortality, apart from atrial fibrillation. Patients with atrial fibrillation were older than those without, and we did find (not unexpectedly) increased mortality in older patients, so the presence of atrial fibrillation itself was not clearly the cause of increased mortality. Atrial fibrillation may be a marker for structural cerebrovascular disease, yet there was only a trend towards greater mortality in those with visible cerebral infarction, and improved prognosis in those with small vessel ischaemic changes. Obviously, a larger cohort of patients would be required to fully determine prognostically important clinical parameters.

80% of our patients with a single seizure were treated with anticonvulsants. In contrast to younger patients (in whom a single seizure is rarely treated), in elderly patients each seizure carries a significant morbidity risk, such as fractures and sub-dural haematomas. Older patients with a single seizure are more likely to have a second seizure than younger patients[9]. In cases with a documented structural brain lesion or a focal EEG discharge, it may be prudent not to delay treatment unless there was a clear and reversible precipitating event.

Despite the array of new anticonvulsant agents on the market that have fewer interactions with other medications and potentially less neurotoxicity, our patients were almost universally prescribed older agents. This may be because there is a relative lack of randomised controlled trials specifically in elderly patients for these drugs. Notwithstanding this, only one patient had a serious adverse reaction (cholestatic jaundice) and there were no documented drug interactions during follow-up.

Based on this study, we would recommend that seizures be borne in mind in all cases of loss of consciousness and unexplained confusion in elderly patients. This study demonstrates that not all seizures in the elderly involve obvious convulsive movements and physicians have to have a high threshold of suspicion if a prompt diagnosis is to be made. We have shown that seizures in the elderly are not a benign entity 5.5% of our follow-up group died as a direct result of seizures.

Furthermore, we have shown that elderly patients tolerate anticonvulsant therapy well and achieve good seizure control with monotherapy, strengthening the case for treatment after a single seizure. Finally, alcohol abuse and alcohol withdrawal must be specifically enquired about these are not uncommon problems in elderly patients, but were very poorly documented in the case notes.

Correspondence:

Suzanne Timmons
Dept. of Neurology, Cork University Hospital, Wilton, Cork.
Telephone: 021 4385337
Fax: 021 4501477
Email: suzannea@eircom.net

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