Chapter 43

Epilepsy and seizures in geriatric practice

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Introduction

Epilepsy is the third most common neurological disorder in old age after dementia and stroke. With the elderly population (particularly those over 75 years) rapidly increasing, epilepsy in old age should be regarded as a significant public health issue as well as an important clinical problem.

Epidemiology

The incidence of epilepsy follows a bi-modal distribution. The first peak is in the first few years of life whilst a second and more pronounced peak is in those over 60 years old. Indeed, the elderly are now the group with the highest incidence of epilepsy in the general population[1]. Incidence rates of over 100 per 100,000 for epilepsy in people over 60 years old have been reported[2]. The incidence of acute symptomatic or provoked seizures also rises significantly in older persons[3] and the prevalence of epilepsy increases with advancing age, although to a lesser degree.

Aetiology and risk factors

A number of studies show considerable variability in the causes and risk factors for epilepsy[4-6]. The most frequently reported risk factor is cerebrovascular disease (30–68%), though stroke is responsible for an even higher proportion of cases (around 75%) in which a definite risk factor is identified[7]. In elderly people with epilepsy, clinically unsuspected cerebral infarcts are often demonstrable on scanning[8].

Tumours are a less frequent cause of seizures (around 10–15%)[5,7] and are usually metastatic or aggressive gliomas, though the epidemiological data are inadequate. Meningiomas may mimic transient cerebral ischaemia. Metabolic and toxic causes (e.g. drugs or alcohol) and cerebral hypoxia secondary to the many causes of syncope in old age account for around 10% of all seizures, and a higher proportion of acute symptomatic seizures, in old age. Seizures often have a mixed aetiology, and a minor metabolic insult may trigger epileptic discharges from a pre-existent focus of injury. Other causes of seizures include head injury, infection, subdural haematoma and non-vascular dementia.

Seizure types and syndrome classification

Focal seizures occur more frequently than generalised seizures (of any type) in old age[5] but generalised seizure disorders do occasionally first manifest themselves in this age group[9]. Thus EEG recording in this age group may be required to classify seizure type, particularly if there is the possibility of a generalised seizure disorder. EEG may also be required at times if focal onset is suspected when secondary generalisation is the only clinical manifestation.

To date, most studies in the elderly have not used a syndromic classification. Epileptic syndromes that occur commonly in the elderly are:

- Remote symptomatic seizures, usually due to precedent stroke or cerebro-vascular disease. Seizures are usually easy to control.
- Acute symptomatic or provoked seizures, possibly due to acute stroke, toxic or metabolic causes or secondary to syncope or cerebral systemic infection. Some people have repeated intercurrent seizures, each related to a recurrent acute situation (e.g. alcohol or hypoglycaemia).
- Progressive symptomatic seizures, usually caused by a tumour or non-vascular dementia (though the latter is controversial).
- Cryptogenic cases in which a cause cannot be identified but which are presumed to be symptomatic. Many such cases are believed to be due to occult cerebro-vascular disease.
- Late onset idiopathic generalised seizures are relatively rare in the elderly; the seizures are usually easy to control. People may be misdiagnosed as having non-lesional partial epilepsy. Sleep deprivation EEG studies are indicated.

Diagnostic pitfalls

As in younger people, the diagnosis of epilepsy in the elderly is entirely clinical. Eyewitness accounts are often lacking and differentiating hypoglycaemia, syncope or impairment of cerebral circulation from other causes may be difficult. Persistent headache or confusion after an episode of loss of consciousness is suggestive of a seizure. Recurrent partial seizures are often misdiagnosed as transient cerebral ischaemia if the stereotypical nature of the epileptic symptoms is not recognised.

Concurrent disorders that predispose to syncope, e.g. carotid sinus syncope, micturition syncope, and postural hypotension, are common in the elderly. Focal jerking of one arm may occur in tight carotid stenosis. The elderly brain may be more sensitive to a number of external insults. Cardiac arrhythmias frequently present with seizures in the elderly. Conversely seizures of temporal lobe origin may present with autonomic disturbance and cardiac dysrhythmia. Even after intensive investigation with EEG and 24-hour ECG, diagnostic uncertainty may persist in a considerable proportion of people.

Post-ictal states in the elderly may be prolonged; Todd's paresis may persist for days and is often misinterpreted as a new stroke. Post-ictal confusion with disorientation, hyperactivity, wandering and incontinence may persist for up to one week.

Diagnostic difficulties may also arise with neuropsychiatric presentations, e.g. epilepsia partialis continua may be confused with an involuntary movement disorder, and the rare paroxysmal sensory epilepsy is often labelled as recurrent transient cerebral ischaemia.

Prognosis in elderly with seizures and epilepsy

The National General Practice Study of Epilepsy[7] reported an 80% risk of seizure recurrence in older people at 52 weeks. Remote symptomatic seizures carried a higher risk of recurrence (85%) at three years than acute symptomatic seizures (46%). Other studies have not found older age to be a significant predictor of recurrence[10,11]. The presence of Todd's paresis or previous acute symptomatic seizures relating to the original insult appears to increase the risk of recurrence[11]. A classic study examined prognosis in a large group of elderly admitted to hospital following a seizure[12]. Of those not previously treated and observed for at least 12 months, 62% remained seizure free and 26% had less than three seizures per year; 72% of the whole group entered remission within the first year. No controlled clinical trials exist but

most studies report that the vast majority of older people with seizures are readily controlled with a low dose of a single antiepileptic drug (AED). A Veterans Administration trial of AEDs in adults showed that a higher proportion of older adults achieved control than did younger adults[13].

Management

As with younger people, accurate diagnosis is crucial. A trial of an AED is rarely appropriate and a brief period of hospital admission for observation may be useful if the history is unclear.

Identification of the underlying aetiology of seizures is necessary for counselling and may be relevant in deciding future management plans. General management, including reassurance and education for both the person and carer, is crucial. A multidisciplinary approach is helpful: nursing staff are vital in counselling and monitoring the person and an occupational therapist can advise on safety aspects, which may include a home visit and provision of a personal alarm where appropriate.

There is a lack of relevant data allowing rational therapeutic policies to be made for the treatment of seizures in old age. Information regarding seizure recurrence after an incident seizure and response to AEDs is scant. Such data are necessary to weigh the risks of treatment against the risks of epilepsy and its complications.

Acute symptomatic seizures are most appropriately managed by treating the underlying precipitant (e.g. treatment of infection, correction of metabolic upset, or withdrawal of drug precipitant). AED therapy may be necessary in some circumstances on a temporary basis to suppress seizures while control of the underlying illness is achieved. Advanced age appears to be an independent risk factor for increased mortality in status epilepticus, and this should therefore be treated vigorously.

The approach to treatment of a first unprovoked seizure in an older person is more contentious. Such people are often classifiable as having remote symptomatic seizures secondary to a cerebral infarct. Treatment to prevent serious injury and the dangers of prolonged post-ictal states may well be justified after a first generalised seizure on the basis of a persisting, epileptogenic focus. However, some such seizures may be erroneously classified as remote symptomatic if a concurrent acute vascular event is clinically silent. For people with simple partial seizures and in whom investigation is unremarkable, a ‘wait and see’ policy may be more appropriate.

Recurrent unprovoked seizures clearly require treatment. Potential first-line broad-spectrum AEDs that may be used in the elderly include lamotrigine, levetiracetam and sodium valproate; comparative trials in older persons are, however, few. A multicentre trial comparing sodium valproate and phenytoin suggested both agents were useful first-line drugs[14]. More failure occurred for people receiving phenytoin (poor control 6%, adverse events 14%) than sodium valproate (poor control 1%, adverse events 9%) although the differences were not significant. A study assessing the impact of sodium valproate and phenytoin on cognitive function found no difference between the drugs in a group of elders[15,16]. Frequent non-cognitive side effects were, however, reported. Trials have also shown no difference of efficacy between lamotrigine, carbamazepine and gabapentin[16–18].

AED pharmacokinetics may be altered by age. It should be emphasised that inter-individual variability may be much more important than changes associated with age alone[19,20]. Tailoring of the dose with regard to concurrent illness and drug treatment is paramount to avoid toxicity.

Which AED?

Phenytoin is the AED still used by many geriatricians as first-line treatment. Its advantages include once-daily dosing, low cost and ready availability in parenteral form. Disadvantages, however, outweigh advantages and these include non-linear kinetics, such that small alterations of dosage may produce plasma concentrations associated with toxicity or inefficacy. Increased free concentration of phenytoin with neurotoxicity may occur when plasma albumin falls, particularly during acute illness. As in younger people, seizure control is frequently achieved in people with plasma concentrations below the quoted range. Concentration-dependent neurotoxicity may be experienced more frequently and at more modest plasma concentrations in older people. Phenytoin may cause metabolic bone disease and folate deficiency that may be particularly problematic in this age group.

Carbamazepine, an enzyme inducer is an option in the treatment of epilepsy in the older person particularly if there is no associated co-morbidity. Sedative effects may limit tolerability but can be minimised by starting with a very low dose and slow upward titration. Intra-dosage variation in concentrations of carbamazepine, which are related to the extent of autoinduction of metabolism[21–23], appears to be rather less in the frail elderly. Once or twice-daily dosing with conventional carbamazepine tablets is sufficient for most. While the overall risk of bone marrow suppression and hepatitis is small the incidence may be increased by age. Carbamazepine has an antidiuretic hormone-like effect, and this may produce fluid retention and precipitate cardiac failure. Mild hyponatraemia is usually asymptomatic but profound reductions in serum sodium may occur during intercurrent illness or during concomitant treatment with thiazide diuretics. Carbamazepine may precipitate problems with cardiac conduction in elderly people with pre-existent cardiac disease. There are also concerns about its potential effects on bone health. Oxcarbazepine, a carbamazepine like pro-drug that avoids epoxidation would be an alternative but there is no definitive data regarding its use in this age group and there are concerns particularly with its propensity to cause hyponatraemia.

Sodium valproate is usually very well-tolerated and effective in older people. Unlike phenytoin and carbamazepine it is not an enzyme-inducing drug and is less susceptible to involvement in drug interactions. Sedation, cognitive slowing, tremor and gastrointestinal disturbances are the most frequent limiting adverse effects. Cognitive slowing usually improves on dose reduction but it can be so severe in some older people that the drug may have to be withdrawn.

Lamotrigine is a first-line drug in this age group particularly in view of its overall good tolerability. It does not exhibit auto-induction, is not an enzyme inducer and has little cognitive effect. It does, however, have the potential to cause idiosyncratic skin reactions and, very occasionally, more severe reactions. Another problem in this age group is its propensity to cause insomnia and tremor. If insomnia becomes a problem switching drug intake to an earlier time may be helpful.

Levetiracetam is also a first-line drug in this age group, particularly in view of its overall good tolerability and clean pharmacokinetic profile. It has, however, the potential to cause lethargy and irritability which may be more pronounced in some older people.

Overall, the current treatment choice for chronic treatment of older people with epilepsy probably rests with low-dose monotherapy with lamotrigine, levetiracetam or sodium valproate. Phenytoin is cheap and can be given once a day in standard formulation, it is difficult to use because of non-linear kinetics. Adverse effects of unsteadiness and dizziness can occur even at low serum concentrations. In addition, there are concerns about its chronic

effects, particularly its effects on bone health (see Chapter 40). Carbamazepine, an enzyme inducer, is also best avoided as a first option, particularly due to concerns about its potential effects on bone health.

Whichever drug is used the introductory dose should be low and dose titration should be slow and cautious. Monitoring for potential side effects should be intensive and due consideration should be given to the presentation of non-specific side effects of AEDs, e.g. falls, confusion, incontinence. Therapeutic ranges are less helpful in elderly people.

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