

# Epilepsy In Elderly

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## Introduction

Epilepsy is characterized by recurrent seizures of cerebral origin, presenting with episodes of sensory, motor or autonomic phenomenon with or without loss of consciousness. After cerebrovascular disorders and dementias, epilepsy is the commonest neurological problem in elderly. Traditionally, it has been considered a disease of the young and much interest was not paid to elderly as a special subgroup. Current evidences suggest that epilepsy in the elderly requires a greater attention regarding aetiology, clinical presentation, diagnosis, antiepileptic drug (AED) selection and prognosis. Diagnosis is often delayed due to lack of knowledge amongst primary care clinicians and emergency room physicians. Its optimal management requires rapid investigation, accurate diagnosis, effective therapy, education and assured support. Epilepsy can have a profound psychological impact in old age. Stigma associated with this disease, social withdrawal, loss of confidence and reduced independence has profound effect on quality of life.<sup>1</sup>

The elderly are the most rapidly growing segment of the population and the incidence of epilepsy is higher in the elderly than in any other age group. Antiepileptic drugs (AEDs) are the mainstay of treatment and complete control can be achieved in around 70% of patients. There are special problems related to altered pharmacokinetics, drug toxicity, and presence of co-morbid conditions requiring multiple medications (i.e. more chances of drug interaction). Moreover, specific trials of anticonvulsants in the aged population are scarce. General guidelines for treatment include starting

at lower doses, slowing the titration schedule, individualising the choice of anticonvulsant to the characteristics of the patient, avoiding anticonvulsants with important cognitive or sedative adverse effects, and where possible, treating with monotherapy. Newer AEDs offer some advantages in this respect over older agents.

## Epidemiology

Prevalence of epilepsy steadily increases with advancing age and it is higher by 1.5 to 2 times at the age of 70 years compare to that in children and young adults.<sup>2</sup> The incidence of new onset epilepsy is also higher among the elderly than in any other age group. It is approximately 45 per 100,000 at 40 years of age and rises to 90 per 100,000 at 65 years and to 140 per 100,000 at the age of 80 years (Fig 1).<sup>3-5</sup> The risk of recurrence after first seizure is also higher in elderly (upto 80%) compared to young people. Upto 30% of new onset acute seizures may present as status epilepticus which carries a high mortality.

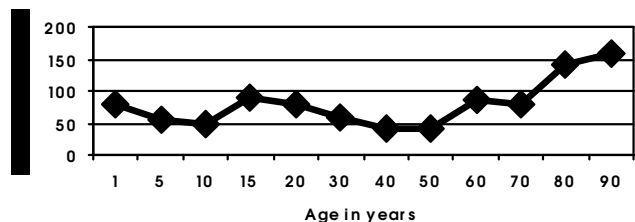


Fig 1: Incidence of epilepsy in relation to age

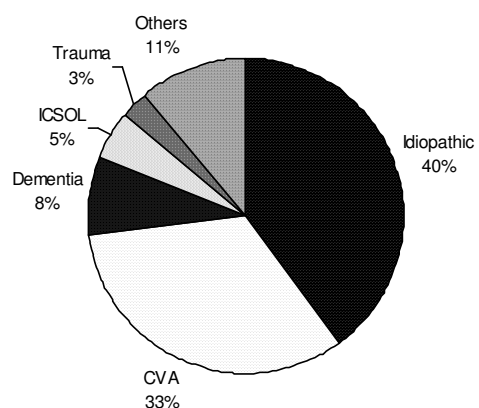


Fig 2: Causes of epilepsy in elderly

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**Table 1:** Metabolism, protein binding, half-life and common side effects of AEDs

AED	Protein binding	Metabolism/ Elimination	Half-life (hrs)	Disadvantages	Drug-specific adverse effects
Phenobarbital	50%	·Hepatic ·Induces CYP2C, CYP3A, UGT	100	Drug interactions	Sedation, difficulty in concentrating, impaired cognition, dizziness, impaired coordination
Phenytoin	90%	·Hepatic ·Induces CYP2C, CYP3A, UGT; inhibits CYP2C9	13-69	Drug interactions, nonlinear kinetics	Dizziness, impaired coordination, ataxia, cognitive impairment, gingival hyperplasia
Carbamazepine	80%	·Hepatic ·Induces CYP2C, CYP3A, UGT	12-17	Drug interactions, autoinduction, and short half-life	Ataxia, dizziness, diplopia, hyponatremia, cardiac conduction disturbances
Valproate	95%	·Hepatic ·Inhibits epoxide hydrolase, CYP2C9, UGT	9-16	Drug interactions	Ataxia, drowsiness, weight gain, hair loss, tremor
Felbamate	25	·Renal/hepatic ·Induces CYP3A4; inhibits CYP2C19	20	Toxic, Drug interactions	Somnolence, dizziness, anorexia, nausea, headache, aplastic anemia, hepatic dysfunction
Gabapentin	<10%	·Renal ·No induction/ inhibition	5-7	Dose limited absorption	Somnolence, dizziness, ataxia, headache, pedal edema
Lamotrigine	55%	·Hepatic	25	Slow titration	Somnolence, dizziness, ataxia, diplopia, rash
Levetiracetam	<10%	·Renal ·No induction/ inhibition	7	Short half-life	Somnolence, lack of energy, dizziness, Behavioral changes
Oxcarbazepine	50%	·Hepatic/renal ·Induces CYP3A4/5; inhibits CYP2C19	8-10	Limited clinical experience	Somnolence, dizziness, diplopia, nausea, ataxia, hyponatremia
Tiagabine	95%	·Hepatic ·No induction/ inhibition	7-9	Multiple (2-4) daily doses	Somnolence, dizziness, impaired coordination, tremor, difficulty in concentrating, weakness
Topiramate	15%	·Hepatic/renal ·Induces oxidation and inhibits CYP2C19	23	Slow titration	Dizziness, ataxia, difficulty in concentrating, tremor, weight loss word-finding difficulty, nephrolithiasis
Zonisamide	40%	·Renal/hepatic	60	Slow titration	Somnolence, dizziness, ataxia, anorexia, weight loss, skin rash, nephrolithiasis

**Table 2: Dosing and titration of antiepileptic drugs in elderly patients**

Drug	Indications	Starting dose (mg/d)	Titration by	Adult maintenance dose (mg/d)	Recommended regimen
Phenobarbital	PS, GTC	60-90	30-60 mg/d every 1-2 weeks	90-240	Lower doses may be required
Phenytoin	PS, GTC	300	30-100 mg/d every 10-21 days	300-400	Start 3 mg/kg/d
Carbamazepine	PS, GTC	200-400	200 mg/d every week	600-1,600	Start 3 mg/kg/d
Valproic acid	PS, GTC, Abs, Myo	250-750	5-10 mg/kg/d every week		Start 10 mg/kg/d
Felbamate	PS LGS	1,200	1,200 mg/d every 2 weeks	2,400-3,600	Usual adult regimen
Gabapentin	PS	300-900	300-900 mg/d every 3 to 7 days	900-2,400	Reduce if CrCl < 60 mL/min
Lamotrigine	PS, GTC, Abs, LGS	50	50 mg/d every 2 weeks	300-500	Usual adult regimen
Topiramate	PS, GTC, Abs, LGS	25-50	50 mg/d every week	400	Start 25 mg/d; reduce for CrCl < 70 mL/min
Tiagabine	PS	4	4 mg/d every week	32-56	Lower doses recommended
Levetiracetam	PS, GTS LGS	1,000	1,000 mg/d every weeks	3,000	Reduce for CrCl < 80 mL/min
Oxcarbazepine	PS, GTC	150-300	150 mg/d every 2 weeks	600-1,200	Reduce for CrCl < 30 mL/min
Zonisamide	PS, GTC	100	100 mg/d every 2 weeks	200-400	Usual adult regimen; reduction for severe renal dysfunction

GTC: Generalised tonic clonic; PS: Partial seizures; Abs: Absence seizures, Myo: Myoclonic; LGS: Lennox-Gastaut Syndrome

Approximately 25% to 50% of cases of epilepsy in elderly have no identifiable (idiopathic or cryptogenic) cause and many of them have concomitant neurodegenerative or neoplastic disease (Fig 2). Cerebrovascular disease is the leading cause (up to 40% of cases) of epilepsy in the elderly.<sup>6-7</sup> In most cases, epilepsy occurs within 3 months to 1 year after the stroke. It occurs more frequently after primary

intracerebral hemorrhage then after an infarct (25% vs 9.5%). Major risk factors for development of post-stroke epilepsy are cortical involvement, occurrence of seizures within two weeks of stroke and lobar haematoma.<sup>8</sup> Other common causes of epilepsy in elderly are dementia or degenerative diseases (10-15%), primary brain tumors or metastases (5%), trauma (3%) and CNS infections.<sup>9</sup> Meningiomas, astrocytomas,

**Table 3:** Points to be considered while selecting individual AED.

1. Effectiveness in a particular type and syndrome of epilepsy
2. Various dosage forms available including parenteral one
3. Once or twice daily dosing
4. Low cost and availability
5. Low protein binding and linear pharmacokinetics
6. Few or no drug-drug interactions
7. Little or no allergic and idiosyncratic potential
8. Interchangeability with other AEDs
9. Minimal to no side effects or major organ toxicity

oligodendrogliomas, glioblastomas, malignant gliomas, and brain metastases have higher propensity to develop seizures.<sup>7</sup> Seizures in these patients can be precipitated with acute metabolic disturbances (uremia, hypothyroidism, hyperglycemia, hypoglycemia, and hyponatremia), central nervous system infections, subdural haematoma, drugs (e.g. antipsychotics, antidepressants, antibiotics, theophylline, levodopa, thiazide diuretics, herbal remedy ginkgo biloba, bupropion, clomipramine, selective serotonin re-uptake inhibitors such as fluoxetine and phenothiazines) and alcohol withdrawal.<sup>10</sup> Seizures secondary to acute central nervous system infections occur more commonly in developing countries than in developed countries.

### Pathophysiology

Diagnosis of new onset seizures is based on identification and classification of brain function pathology and seizure manifestations. Increased seizure susceptibility in elderly remains a major challenge for research workers.<sup>11</sup> A number of investigators have shown that elderly animals are more susceptible to seizures than younger animals. These results suggest that genomic alterations in early adulthood initiate decreased signaling and synaptic plasticity in neurons, extracellular changes, increased myelin turnover and inflammation in the glia.

### Pharmacokinetics

Pharmacotherapy is the mainstay of treatment with the primary aim to provide a good seizure control with least adverse effects. Elderly needs special consideration in view of polypharmacotherapy, drug-drug interactions and concomitant medical problems (e.g. cardiovascular, neurological, metabolic, cerebrovascular, neurodegenerative or neoplastic). For

**Table 4:** Differential diagnosis for patients presenting with epilepsy

**Neurological:** Transient ischemic attacks, Transient global amnesia, Dementia, Cardioembolic stroke, Migraine, Huntington's disease, Parkinson's disease, Episodic microsleep, Narcolepsy, Obstructive sleep apnoea, Restless leg syndrome, Hypnic jerks, Rapid eye movement sleep disorders and others episodic events (confusion, disorientation, memory disturbance, impaired consciousness, motor or sensory symptoms, vertigo, chorea, essential tremor, blackout spells, dizziness)

**Cardiovascular:** Vasovagal syncope, Orthostatic hypotension, Conduction block (Stokes-Adams attacks) and Cardiac arrhythmias

**Metabolic:** Hypoglycemia, Hypokalaemia, Hyperglycemia, Hyponatremia, Alcohol, Drug-related episodes, pseudoseizures

a rational prescribing, major pharmacokinetic changes that occur with aging need to be taken into consideration (Table 1). In general, elderly have decrease in lean body mass, serum albumin concentrations and total body water effecting drug distribution and dosing of most of the AEDs. Gastric acidity and gastrointestinal motility decreases in old age. However, these changes do not affect AEDs significantly. Both hepatic metabolism and creatinine clearance decrease by 10% per decade in patients older than the age of 40. Kidney size, glomerular filtration rate and renal blood flow also decrease with age. Similarly content of enzyme cytochrome P450 within the liver also decrease with advancing age. Other age related changes not well understood are alterations in brain neurotransmitters, receptor functions, autonomic pharmacology and homeostatic mechanisms.

The concentration of anticonvulsants in the nervous system correlate with free or unbound concentration in the plasma rather than that bound to protein. Albumin levels also decrease in old age or in chronically ill elderly individuals resulting in higher free concentrations of many protein bound drugs (e.g. phenytoin, carbamazepine, and valproic acid). In view of reduced clearance of AEDs in old age, titration for optimal effects should be done with smaller increments.

### Drug-drug interactions

Monotherapy diminishes side effects and drug-

**Table 5: Diverse clinical manifestations of epilepsy in elderly**

Manifestations of Epilepsy	Young	Old
Number of seizure types	Many	Single
Common seizure type	Generalized tonic clonic	Partial complex
Aura & ictal automatism	Common	Less common
Seizure frequency	High	Low
Postictal state	Brief	Prolonged
Injury potential	Low	High

**Table 6: Essential elements in management**

1. Accurate diagnosis of type of epilepsy e.g. epilepsy syndrome, seizure type
2. Aetiology and precipitating factors
3. Appropriate pharmacological interventions considering spectrum of activity, concomitant medical conditions, side effect and interaction profile, and long term effects.
4. Start with a low dose, titrate slowly upward observing efficacy and toxicity. Monotherapy is adequate in most of the patients.
5. If first agent does not adequately control seizures or causes unacceptable adverse effects, consider alternate drug as monotherapy. Polytherapy to be considered after failure with two or more agents.
6. Monitor treatment response and side effects
7. Compliance can be increased with clear written instructions, explanation of the regimen, and provision of dosing.
8. Reassurance and explanation to patient and caregiver, patient's anxieties and misconceptions to be identified and addressed

drug interactions. Phenobarbital, phenytoin, and carbamazepine are inducers of hepatic monooxygenase enzymes. They interact with many lipid soluble drugs commonly e.g. warfarin, cardiac antiarrhythmics, theophylline, corticosteroids, antidepressants, cytotoxics, and macrolide antibiotics. Enzyme induction also accelerates the catabolism of vitamin D leading to decreased calcium absorption, secondary hyperparathyroidism, and increased bone loss. Several commonly used drugs e.g. propoxyphene, erythromycin, cimetidine, diltiazem, fluoxetine, paroxetine, verapamil, valproate and alcohol inhibit AED metabolism by the P450 hepatic system.

Certain side effects e.g. osteoporosis, ataxia and falls, cognitive disorders, dizziness, ataxia, tremor, blurred vision, sedation, impaired cognition and weight increase need careful attention while prescribing AEDs (Table 2). Choice of AED will depend more on their pharmacokinetics and their potential to trigger certain side effects than on their effectiveness (Table 3). The ones with the most favorable pharmacokinetic profile are levetiracetam and pregabalin, followed by oxcarbazepine and lamotrigine. Drugs with minimal effect on cognition e.g. valproate, gabapentin, lamotrigine, levetiracetam should be considered as first line option.

Phenytoin, primidone, and phenobarbital cause altered bone metabolism (osteoporosis/ osteopenia, osteomalacia, and fractures) and should be avoided in these patients. In view of adverse pharmacokinetic profile in elderly, therapeutic drug monitoring has a bigger role. However, newer AEDs do not have established serum concentration therapeutic range. Large interindividual pharmacokinetic variability contributes to the need for individualised dosage (Table 1, 2). Measurement of serum drug concentrations can be useful as an aid to dosage individualization in these age groups but interpretation of therapeutic drug monitoring data should also take into account the possibility of age related changes in pharmacodynamic sensitivity and, for neonates and the elderly, alterations in drug binding to serum proteins.<sup>12</sup>

**Phenytoin** has been used extensively in elderly patients. Its positive features are low cost, once daily dosing, oral and intravenous formulation. There is a predictable relationship of blood levels of phenytoin with efficacy and side effects. However, it is highly protein bound (upto 90%) with nonlinear pharmacokinetics and has hepatic metabolism associated enzyme induction. It is associated with extensive acute and chronic adverse events like gait disturbances, osteoporosis and

fractures, and allergic reactions. Serum concentrations should be routinely monitored to avoid potential toxicity. A lower dose of 3 mg/kg/day should be initiated instead of 5 mg/kg/day in young adults. In emergency situation, intravenous fosphenytoin is a better option than usual intravenous phenytoin.

**Carbamazepine** is an effective drug and is available in oral formulation only. It requires 2-3 weeks of titration. It is an enzyme inducing agent with significant auto induction requiring frequent monitoring and dose adjustments during initial months of therapy. It has moderate protein binding and is metabolized extensively in the liver. Relationship between blood levels of drug and efficacy is less predictable. It has a high potential for drug-drug interactions with other AEDs. Because of serious adverse effects such as CNS and gastrointestinal adverse events, cardiac conduction problems, allergic potential, acute dermatologic reactions, hyponatremia, and hematological changes, its use in elderly is recommended with caution.

**Oxcarbazepine** is similar to carbamazepine in action and efficacy but with better tolerability and lesser side effects.

**Phenobarbital** is a low cost, effective AED that can be administered once in a day. It has linear pharmacokinetics, acceptable degree of protein binding, and has oral as well as parenteral formulation. Major organ toxicities are rare. However, it is a potent enzyme inducer with few unacceptable side effects e.g. drug-drug interactions, sedation, impaired cognition, behavioral changes. Thus, phenobarbital has a limited role in treating epilepsy in older adults.

**Valproate** is available in oral as well as in intravenous formulations. Though moderately expensive, its advantages are efficacy, quick titration and low allergic potential. It has nonlinear pharmacokinetics and is associated with many drug-drug interactions. It is highly protein bound and major side effects are weight gain, liver toxicity, pancreatitis and thrombocytopenia. Its blood levels do not predict efficacy or side effects. It is effective in associated mania and migraine also.

**Lamotrigine** is a broad spectrum AED with good safety profile. It has low protein binding and linear pharmacokinetics. It is expensive and not available in a parenteral formulation. It causes skin rash in up to 10% of patients and may result in life threatening Stevens Johnson syndrome. It is exacerbated by

coadministration and rapid titration with sodium valproate.

**Topiramate** is also a broad spectrum agent with low protein binding, linear pharmacokinetics and an acceptable profile of drug interactions. However, it is expensive and not available for parenteral administration. Cognitive side effects are frequent and often accentuated in the elderly. Serious adverse effects are uncommon and include weight loss, metabolic acidosis, kidney stones and elevated intraocular pressure.

**Gabapentin** is a moderately effective, well tolerated, and safe AED. It has a linear pharmacokinetic profile and does not interact with other drugs. It has dose dependent absorption with no appreciable hepatic metabolism. It is expensive and requires multiple daily dosing. Adverse effects are modest and include weight gain and ataxia.

**Levetiracetam** is a broad spectrum AED with linear pharmacokinetics and good tolerability. It is not protein bound and is not metabolized through the CYP3A4 pathway. Drug-drug interactions are negligible. It is expensive and moderately effective. Common side effects are behavioral problems, irritability, somnolence and asthenia.

**Zonisamide** is also a broad spectrum AED that needs gradual titration. Drug-drug interactions are uncommon. Common side effects are weight loss, hypersensitivity (e.g., Stevens-Johnson syndrome), renal stones and hematological abnormalities. Its use in elderly is still evolving.

**Tiagabine** has not been tried extensively in elderly patients. It requires 2 to 4 dosing per day with titration period of 6 weeks or more. Adverse effects include effects on cognition as well as somnolence and fatigue.

**Felbamate** is not tolerated well in elderly subjects due to age related pharmacokinetic differences. In addition, serious side effects such as aplastic anemia and hepatic failure preclude its use in elderly subjects.

## Diagnosis

Correct diagnosis of epilepsy in the older individual is often a challenging one as several transient episodes mimic it (Table 4).<sup>2</sup> The assessment of the elderly person, like any other patient in practice, begins when he enters the clinic and continues till this encounter is complete. Presentation of epilepsy in elderly patients is often non specific and differs from those of the younger population.<sup>2</sup> First symptoms of epilepsy is

often mild and nonspecific e.g. dizziness, confusion, gaps in conversation, altered state of awareness, blank stares, minor automatisms, syncope, and memory lapses. There are few differences in clinical presentation compared to younger patients as has been tabulated in Table 5. Seizure frequency, aura, and automatisms tend to be less common in the elderly than in younger population. In view of these factors, underdiagnosis and misdiagnosis are common. Initial assessment often relies on an accurate and detailed patient history. Diagnosis of epilepsy is often delayed in old age because of memory loss and preoccupation, social isolation, inadequacies in history and eye witness account, associated medical and psychiatric illnesses, large number of differential diagnoses and seizure imitators, and difficulties in convincing patients about disease and medications.<sup>13</sup> Comprehensive neurological and cardiovascular systems examination is the next step in the diagnosis. In young patients (< 40 years) proportion of partial onset and generalized onset is almost equal. However, proportion of partial epilepsy rises in elderly patients and it is approximately 75% at the age of 75 (Fig 3).<sup>14</sup> Temporal lobe or complex partial seizures are the most common (48%) type. However, its non motor manifestations e.g. memory lapses, confusion, dizziness, spells of black out, periods of inattention and staring, apparent syncope, decreased mentation, and unresponsiveness are more common. Complex partial seizures in the elderly are more likely to be extratemporal than temporal origin. Status epilepticus, either convulsive or non-convulsive, is quite common in patients older than 60 years of age, tends to be more prolonged, and associated with higher mortality (upto 40%).<sup>15</sup>

Laboratory parameters for evaluation include full blood count, metabolic screenings for hypoglycemia, drug intoxications, electrolyte disorders, renal functions and hepatic functions. A routine 12 lead electrocardiogram must be done in all cases. A computed tomography (CT) or magnetic resonance imaging (MRI) scan is mandatory in all new onset unprovoked seizures in elderly. In general, MRI is more sensitive than CT in detecting relevant abnormalities. Age related changes such as diffuse atrophy, periventricular hyperintensities, and lacunar infarction is common and should be interpreted accordingly. As such, extensive reliance on neuroimaging over clinical evaluation is to be deterred. A detailed cardiovascular evaluation (24 hour ambulatory ECG monitoring and tilt table testing) is needed when cardiac cause is

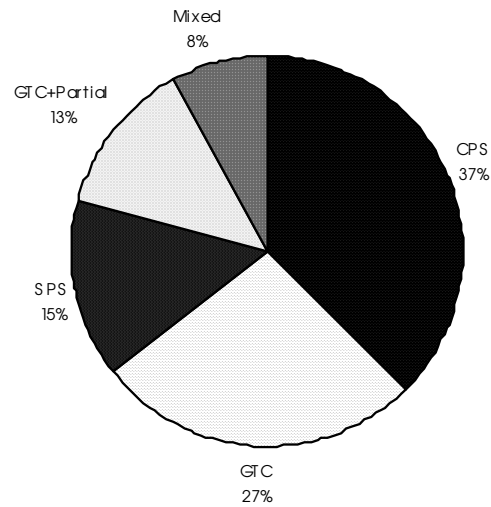


Fig 3: Seizure types in elderly

suspected.

Routine scalp EEG is neither sensitive nor specific for the diagnosis of epilepsy in elderly people.<sup>14</sup> It should always be interpreted in the clinical context. Extended-duration EEGs may significantly increase the yield of epileptiform activity. Though presence of paroxysmal abnormal discharges support clinical diagnosis, its absence does not rule out the diagnosis. As non-convulsive seizures and status epilepticus are quite common in elderly and may present atypically, EEG studies allows for the confirmation of the diagnosis.<sup>15</sup>

**Treatment**

The primary goal of management is to achieve a complete (or near complete) control of seizures with minimal or no side effects. Brighter side of management is that elderly patients responds well to treatment and up to 80% of them can be well controlled. Intractability is related mostly to the presence of neoplasm, complex partial seizures, or medication noncompliance rather than to true pharmacoresistance. However, darker side is that majority of elderly patients do not receive adequate treatment and are more susceptible to the adverse effects of drugs than their younger counterparts. Moreover, there is a great unpredictability about safe withdrawal of treatment once seizure freedom has been achieved for 2-3 years. Essential elements in management are as in Table 6.

**Starting AED therapy:** A key management issue in the elderly patient with epilepsy is whether to treat the first onset seizure as opposed to waiting for a

recurrence.<sup>16</sup> Recent studies have shown that the recurrence rate is twice higher (> 60% by one year) in older patients compared to young individuals.<sup>17,18</sup> The risk for seizure recurrence, physical and psychological consequences, related increased morbidity must be weighed against the malice of treatment e.g. increased side effect profile, drug-drug interactions and high cost. Thus we should discuss thoroughly with the patient and consider AED therapy after first attack. Treatment of first attack can be deferred in presence of an avoidable precipitant such as sleep deprivation, concurrent illness, physical or mental stress, drugs related seizures.

Perhaps more difficult question is that when can AED be stopped or reduced once satisfactory control is achieved for 2-5 years. Recurrence after stopping AED is higher in elderly patients particularly those with partial onset.

**Selection of AED:** Although first generation AEDs (i.e., carbamazepine, phenytoin, phenobarbital, and sodium valproate) have historically been the mainstay of therapy, they are fraught with drug-drug interactions, poor tolerability and substantial adverse effects. Newer AEDs (i.e. felbamate, gabapentin, lamotrigine, levetiracetam, oxcarbazepine, tiagabine, topiramate, and zonisamide) are efficacious and offer favorable characteristics with regard to administration, monitoring, drug interactions, and adverse-effect profiles (Table 5). Reluctance on part of clinicians to use newer AEDs is due to unfamiliarity with the drug, increased cost and absence of long term data. Pharmacologic interventions for epilepsy depend on the type of seizure (i.e., partial or primary generalized) and epilepsy syndrome (e.g., Lennox-Gastaut syndrome or juvenile myoclonic epilepsy) (Table 5). Based on available information, carbamazepine, oxcarbamazepine, valproate, gabapentin, lamotrigine, tiagabine and zonisamide are good options in elderly patients.

**Adverse events:** Elderly patients are more susceptible to side effects of AEDs. Advanced age is a risk factor for bone loss, which may be exacerbated by older AEDs, such as phenobarbital, phenytoin, and primidone. Polytherapy appears worse than monotherapy in terms of increasing risk of osteoporosis and osteomalacia. Fractures associated with bone disease may lead to loss of independence, hospitalization, and death. Patients being treated with carbamazepine or oxcarbazepine should be monitored for development of hyponatremia. This problem is compounded in elderly

patients because of poor intake and concomitant diuretic administration.

Risk of cognitive impairment is of great concern in the elderly who are being treated with AEDs. Phenobarbitone and primidone are not preferred because of their effect on cognition and sedation. Cognitive impairment is further effected in presence of Alzheimer's disease, Parkinson's disease, multiple cerebral infarcts, chronic alcoholism and other related conditions. Valproate, gabapentin, lamotrigine, and levetiracetam have minimal effect on cognition and are preferred in such situations. It must be appreciated that AEDs effective for one seizure type may worsen other types of seizures. Gabapentin and tiagabine are known to aggravate absence seizures, and gabapentin and lamotrigine may aggravate myoclonic seizures.

**Status Epilepticus:** Compared with younger patients, the elderly are more likely to have status epilepticus of prolonged duration (e.g., longer than 24 hours) and higher mortality. Initial treatment consists of lorazepam (0.1 mg/kg at 2 mg/minute) followed by fosphenytoin (20 mg/kg phenytoin equivalents at 150 mg/minute). Elderly patients are more susceptible to the pharmacodynamic alterations of benzodiazepines and phenytoin. A close monitoring for respiration (ventilator assistance), supplemental oxygenation, and blood pressure support is recommended.

#### **Vagus Nerve Stimulation (VNS)**

VNS is generally reserved for patients with refractory partial or generalized seizures, Lennox-Gastaut syndrome, and for multiple seizure types who are suboptimal candidates for open brain surgery. It is a costly but well tolerated procedure with no drug related side effects. It consists of a pacemaker-like device implanted in the chest with an electrode wrapped around the left vagus nerve. The mechanism of action is unknown, but metabolic changes have been observed in the brainstem, basal ganglia, cerebral and insular cortices, cerebellum, limbic structures, and thalamus. Though there is no complete remission, seizure frequency is decreased by 25% to 30% in majority of the patients.

#### **Surgery**

Though a good option in patients with difficult to treat epilepsy, surgery is neither popular nor accepted by elderly patients. Anterior temporal lobe resection for mesial temporal sclerosis is the commonest successful

surgery. Other conditions that may respond to surgery are low-grade gliomas, cavernous angioma, and malformations of cortical development (e.g. focal cortical dysplasia and heterotopia). Partial resections of the frontal, parietal, and occipital lobes; hemispherectomy, corpus callosotomy, and multilobar resection are less favored options in these patients

### **Avenues for Improving Patient Care**

Despite many challenges, there are numerous avenues through which we can improve care for elderly patients suffering from epilepsy.

1. Majority of these patients are managed and handled at primary health care level and explicit guidelines are needed for referral to a neurologists or epileptologists at an epilepsy clinic. There is need to disseminate clinical research to primary care physicians.
2. **Educate** public, family members and primary health workers about recognition of seizures and its differential diagnosis in elderly.
3. **Proper recording** of ictus and related events, indications related to investigations and treatment, maintenance of seizure diary and side effects, and instructions related to emergency treatment in all patients.
4. Development of cost effective **drug level monitoring** of first generation as well as second generation AEDs.
5. **Research** need to be undertaken to assess quality of life with special attention to injuries and falls, economic and psychological impacts, whether single unprovoked tonic clonic seizure be treated, specific dosage schedule for various AEDs and long term effects of newer AEDs.
6. **Development of newer drugs** with better drug profile and elaborate trials with existing second generation AEDs.

### **Conclusion**

There is a growing interest in this subset of epilepsy because of rapidly increasing elderly population, challenges in diagnosis and treatment, favorable outcome, and improvement in quality of life with appropriate treatment. Early and accurate diagnosis are crucial for prompt and appropriate drug treatment. Cerebrovascular and neurodegenerative diseases are the most common

causes of new onset seizures in these patients. Partial (simple or complex) seizures are the commonest. In view of diverse and different presentations, seizures are often misdiagnosed or mismanaged in the elderly. Alterations in protein binding, distribution, elimination, and increased sensitivity to the pharmacodynamic effects of AEDs are frequent, and must be considered while formulating a treatment plan. Drug-drug interaction is an important issue in elderly patients because of polytherapy and multiple comorbid conditions. Seizure management in this group is a challenge and it must eliminate seizures without producing adverse effects and ultimately improve quality of life. Newer AEDs offer some favorable drug properties and tolerability and require further evaluation in elderly. Paucity of data precludes us from giving specific recommendation at this stage.

### **Summary points**

1. Around 1-2% of elderly people have epilepsy, often secondary to cerebrovascular disease.
2. Clinical presentation is often non-specific, and many other conditions can mimic an epileptic seizure.
3. With appropriate pharmacological treatment, 80% of elderly people will remain seizure free.
4. When choosing an antiepileptic drug, particular attention should be paid to side effects and potential for drug-drug interactions.
5. Randomized clinical trials suggest that lamotrigine and gabapentin are better tolerated than carbamazepine in elderly people.
6. Epilepsy can have a profound physical and psychological impact in old age, with a substantial negative effect on quality of life.

### **References**

1. Stephen LJ, Brodie MJ. Epilepsy in elderly people. *Lancet* 2000; 355:1441-1446.
2. Brodie MJ, Kwan P. Epilepsy in elderly people. *BMJ* 2005;331:1317-1322.
3. Bergey GK. Initial treatment of epilepsy: special issues in treating the elderly. *Neurology* 2004; 63(suppl 4):S40-S48.
4. Hauser A, Kurland LT. The epidemiology of epilepsy in Rochester, Minnesota, 1935 through 1967. *Epilepsia* 1975; 16: 1-66.
5. Hussain SA, Haut SR, Lipton RB, et al. Incidence of epilepsy in a racially diverse, community dwelling, elderly cohort: results from the Einstein aging study. *Epilepsy Res* 2006;

- 71:195-205.
6. Sung CY, Chu NS. Epileptic seizures in elderly people: aetiology and seizure type. *Age Ageing* 1990; 19: 25-30.
  7. Nikanfar M, Arami MA, Mansourpoor L, et al. Common etiologies of adult onset epilepsies in northwest of Iran. *Acta Medica Iranica* 2005; 43: 223-226.
  8. Loiseau P. Pathological processes in the elderly and their association with seizures. In: Rowan A, Ransay R, (eds). *Seizures and Epilepsy in the Elderly*. Butterworth-Heinemann, Boston, 1997; 63-85.
  9. Luhdorf K, Jensen LK, Plesner A. Etiology of seizures in the elderly. *Epilepsia* 1986; 27:458-463.
  10. Kramer G. Epilepsy in the elderly: some clinical and pharmacotherapeutic aspects. *Epilepsia* 2001; 42 (Suppl 3):55-59.
  11. Blalock EM, Patrylo PR, Kelly KM. Models of epilepsy in aging. *Epilepsia* 2004; 45(suppl7):1.
  12. Perucca E. Clinical pharmacokinetics of new generation antiepileptic drugs at the extremes of age. *Clin Pharmacokinet* 2006; 45:351-363.
  13. Tallis R, Boon P, Perucca E, et al. Epilepsy in elderly people: Management issues. *Epileptic Disord* 2002; 4: S33-S39.
  14. Anne C, Van Cott. Epilepsy and EEG in the Elderly. *Epilepsia* 2002; 43: S94-S102.
  15. Sheth RJ, Draskowski JF, Sirven JL et al. Protracted ictal confusion in elderly patients. *Archives of Neurology* 2006;63: 529-532.
  16. Leppik, Ilo E. Epilepsy in the Elderly. *Epilepsia* 2006; 47: S65-S70.
  17. Elwes RD, Johnson AL, Shorvon SD, et al. The prognosis for seizure control in newly diagnosed epilepsy. *N Engl J Med* 1984; 311: 944-947.
  18. Hopkins A, Garmon A, Clark C. The first seizure in adult life: value of clinical features, electroencephalographs, and computerised tomographic screening in prediction of seizure recurrence. *Lancet* 1988; 1: 721-726.

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