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Epilepsy in older adults

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Abstract

Epilepsy, a chronic neurological disorder characterized by recurrent seizures, is not limited to any specific age group. While often associated with children and younger adults, epilepsy also presents unique challenges in older adults. This review aims to explore the epidemiology, aetiology, clinical presentation, diagnosis, and management of epilepsy in older adults. The review discusses the complexities of diagnosing epilepsy in this population, considering comorbidities, medication interactions, and age-related changes in the central nervous system. Furthermore, the importance of a multidisciplinary approach to the management of epilepsy in older adults, encompassing pharmacological interventions, lifestyle modifications, and psychosocial support is highlighted. By understanding the specific needs and challenges faced by older adults with epilepsy, healthcare professionals can optimize their care and improve their quality of life.

Key words: epilepsy in elderly, epilepsy in older adults, pharmacotherapy in epilepsy, seizures in older adults

Introduction

Epilepsy is a neurological disorder characterized by recurrent seizures, affecting individuals of all ages. While the prevalence of epilepsy tends to peak in childhood and early adulthood, it remains a significant health concern in the elderly population. Despite advances in diagnosis and treatment, management of epilepsy in older adults poses unique challenges due to age-related changes in physiology, comorbidities, and polypharmacy.

Epilepsy has a bimodal distribution according to age with peaks in the youngest individuals and in the elderly. The prevalence of epilepsy in older adults varies across different studies and populations. According to recent epidemiological data, the incidence and prevalence of epilepsy tend to increase with age, with a notable rise in individuals aged 60 and above.[1] The prevalence rate of epilepsy in persons 65 years or older is approximately 1.5%.[1] In a study that included individuals aged 55 years or older, the overall prevalence of active epilepsy was 9 per 1,000, with an increase with age from 7 per 1,000 for people aged 55-64 years to 12 per 1,000 for those aged 85-94 years.[2]

Elderly people with epilepsy have 2-3 times greater mortality than the general population. Additionally, 30% of acute seizures in elderly people present as status epilepticus, which carries a sizeable mortality of about 40%.[3]

The increased incidence in the elderly can be attributed to the increase of age-related and aging-related epileptogenic conditions. Hence the aetiology of epilepsy in older adults differs from that in younger populations, with cerebrovascular disease, neurodegenerative disorders, traumatic brain injury, and brain tumours being common underlying causes (Table 1).[4] For example both ischemic and hemorrhagic stroke which is commonly associated with older adults are associated with a high risk of seizures and epilepsy. In patients with ischemic stroke, the cumulative incidence is 2-33% for acute symptomatic seizures, 3-67% for unprovoked seizures, and 2-4% for recurrent unprovoked seizures.[5] One in ten individuals aged ≥65 years has Alzheimer dementia (AD) and its prevalence continues to increase with increasing age. Compared to non-demented individuals matched for age and sex,

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patients with AD have a sixfold risk of unprovoked seizures and people with other types of dementia have even an eightfold risk.[6] Additionally, age-related structural changes in the brain, such as hippocampal sclerosis and cortical atrophy, may predispose older adults to epileptic seizures. Furthermore, metabolic disturbances, including electrolyte imbalances and renal dysfunction, can contribute to seizure susceptibility in this age group.[4]

Table 1. Differences in aetiology between older and young adults

Older adults	*Young adults*
Cerebrovascular disease	Genetic
Neurodegenerative disease	Perinatal injuries
Traumatic brain injury	Congenital brain malformations
Tumours	Infections

Epilepsy in older adults is often underdiagnosed or misdiagnosed due to atypical clinical manifestations and overlapping symptoms with other age-related conditions.

Clinical features

Epilepsy in older adults presents with some unique clinical features compared to patients who are younger. Focal onset seizures with impaired awareness are more common in older adults compared to generalized seizures.[7] This also true for focal to bilateral tonic-clonic seizures (formerly known as secondary generalized seizures) which were found to occur in only 26% of elderly patients, as opposed to 65% of younger adults.[8] Extratemporal lobe epilepsies are more common than in the younger population.[9] This is likely due to the fact that the most common aetiology for epilepsy in this population is stroke.[10]

Patients in this age category may have atypical semiology of seizures compared to their younger counterparts (Table 2). A typical temporal aura is rarely described. This may be due to the fact that most seizures in older patients begin in the frontal lobe.[8] Therefore, auras, are described as a nonspecific vague sensation or dizziness, and are of little help in the differential diagnosis.[9] Automatisms often observed with temporal onset seizures also occur less frequently. Thus, the entire seizure may be characterized by confusion, which can persist for a prolonged period following a seizure.[11] This may ultimately render it difficult or impossible to make a clear distinction between individual seizures. These symptoms may be mistaken for other conditions which are commonly observed in older adults such as delirium, dementia, transient ischaemic attack or psychiatric disorders.

Diagnosis

Diagnosing epilepsy in older adults can be more challenging due to various factors such as age-related changes in symptoms, comorbidities, and the presence of other neurological conditions. Obtaining a thorough clinical history is essential. However, in older adults, memory impairment or cognitive decline may complicate the history-taking process. Caregivers or family members may provide valuable information about the individual's symptoms and episodes, including descriptions of any witnessed events. It's important to obtain a detailed description of the events from both the patient and witnesses.

Given the diverse clinical presentations of seizures in older adults, it's crucial to consider other conditions that can mimic epileptic seizures, such as transient ischemic attacks, syncope, transient global amnesia, migraine, metabolic disturbances, and transient neurological deficits due to other causes.[12]

A comprehensive neurological examination should be performed to assess focal deficits, signs of cognitive impairment, or other neurological abnormalities.

Table 2. Differences in semiology of seizures between older and young adults

Feature	*Older adults*	*Young adults*
Aura	Infrequent, non-specific	More common
Automatisms	Less common	More common
Focal to bilateral tonic clonic seizures	Less common	More common
Psot-ictal confusion	Hours to days	5-15 minutes

Once a seizure or seizures are deemed a likely diagnosis a decision needs to be made if the seizures are provoked or unprovoked (Information box 1). The incidence of provoked seizures in patients older than 60 years is ~100 per 100,000 and increases with each decade of advancing age.[10] If the seizure or seizures are unprovoked a diagnosis of epilepsy needs to be considered if criteria are fulfilled (Information box 1).

EEG is a key diagnostic tool for epilepsy. However, it may be less sensitive in older adults due to age-related changes in brain function.[13] Neuroimaging studies such as CT or magnetic resonance imaging (MRI) are essential to identify structural brain abnormalities that may be associated with seizures, such as strokes, tumours or vascular malformations.[14] MR imaging is more sensitive in detecting lesions and is the preferred imaging modality when available.[14] Routine blood tests may be performed to assess for metabolic abnormalities or underlying medical conditions that could contribute to provoked seizures, such as electrolyte imbalances, renal or hepatic dysfunction, or infections.[12] Electrocardiography or Holter monitors should be considered in appropriate cases as cardiac disease, such as atrioventricular block or ventricular tachycardia, may frequently mimic seizures, particularly events with loss of consciousness.[15] Lumbar puncture for cell count, protein, glucose, stains, and cultures should be performed whenever meningitis or encephalitis is suspected as a cause for provoked seizure/s.

In some cases, a neuropsychological assessment may be helpful to evaluate cognitive function, memory, and other aspects of cognitive health.[15] This can assist in identifying any underlying neurodegenerative disorders or cognitive impairment that may impact the diagnosis and management of epilepsy.

Overall, diagnosing epilepsy in older adults requires a careful and comprehensive evaluation, taking into account the unique clinical features, potential comorbidities, and age-related considerations.

Management

Managing epilepsy in older adults requires a comprehensive approach tailored to the individual's clinical needs, comorbidities, and potential medication interactions.

Anti-seizure medication selection (ASM)

A careful consideration of ASMs is crucial, taking into account 4 factors.[16] First is the efficacy of the ASM to prevent seizures. For this, seizure type needs to be considered. Second is the potential of the ASM to cause adverse effects involving memory, cognition, mood, coordination, balance, sedation, and other factors that affect quality of life. The third consideration is drug-drug interactions, not only with other ASMs, but also with other drugs used by older adults due to a higher prevalence of multimorbidity in this population. Fourth, one must consider additional economic and practical factors such as cost and availability.

Information box 1 – Definitions

Epilepsy	Epilepsy is defined by any one of the following three criteria. 1. At least two unprovoked (or reflex) seizures occurring >24 hours apart 2. One unprovoked (or reflex) seizure with >60% risk of further occurring over seizures 10 years. 3. Diagnosis of an epilepsy syndrome (characteristic seizure, cluster of clinical features and specific EEG findings)
Epilepsy syndrome	Seizures occurring with a cluster of clinical features, typical age of seizure onset, specific seizure type/s and specific findings on EEG and or brain imaging.
Acute symptomatic seizure (provoked or reactive)	A seizure that occurs in close temporal association with a brain insult-occurring within one week of a stroke, traumatic brain injury, CNS infection, anoxic encephalopathy etc. They may also occur following a systemic insult, eg; severe metabolic derangements with specific biochemical abnormalities within 24 hours of hypoglycaemia, hyponatraemia, hypocalcaemia, drug, alcohol intoxication.
Remote symptomatic seizure (unprovoked)	A seizure, occurring in a patient with a pre-existing brain injury, beyond the interval estimated for an acute symptomatic seizure. Eg; a seizure occurring 6 months after a stroke, traumatic brain injury or CNS infection etc.

The ideal ASM for an elderly population would be one that has a long half-life to permit once-a-day dosing, stable serum drug level with a low peak but long absorption, no drug interactions, and very good antiseizure properties with minimal side effects on other functions.[16] Though almost all ASMs do not possess all of the said characteristics, the newer ASMs would possess most of the above compared to older ASMs. In a meta-analysis which studied 12 ASMs and included only randomized control trials or quasi-randomized studies, levetiracetam was found to have a higher probability in achieving seizure freedom when compared to lamotrigine (risk ratio [RR]=0.83, 95% confidence interval [CI]=0.68-0.97), and lamotrigine was better tolerated than carbamazepine (RR=1.83, 95% CI=1.23-2.43).[17] In another metanalysis the newer generation ASMs – lacosamide, lamotrigine, and levetiracetam were the most effective treatments, in that order, to achieve 6-or 12-month seizure freedom, and no significant differences were found in efficacy across the three.[18] Thus, recommended ASMs in older adults include: levetiracetam, lamotrigine, and lacosamide due to their favourable side effect profiles and minimal drug interactions.[16] The newer ASMs (lacosamide, lamotrigine, levetiracetam) while offering a clear advantage, can have specific disadvantages compared to older ASMs (ie phenytoin, carbamazepine, valproate). These include higher costs, less long-term data, potential adherence issues, and a less well-characterized risk profile (due to lack of data in this age group). Specific advantages and disadvantages of each drug are highlighted in Table 3.

Table 3. Advantage and disadvantages of commonly used ASMs in older adults
(adopted from Brodie at el.[3])

ASM	*Advantages*	*Disadvantages*
Older ASM		
Phenytoin	Once daily No titration Cheap	Sedation Allergic reactions Saturation kinetics Enzyme induction Bone loss
Carbamazepine	Gold standard for focal seizures Studied in elderly Relatively cheap	Neurotoxicity Allergic reactions Enzyme induction Hyponatraemia Bone loss
Valproate	Gold standard for generalised seizures Broad spectrum Rapid titration Few interactions Relatively cheap	Tremor Weight gain Enzyme inhibition Parkinsonism Bone loss
Newer ASMs		
Lamotrigine	Broad spectrum Good tolerability Few interactions Studied in elderly	Slow titration Dose-associated rash Insomnia
Levetiracetam	No allergic reactions No interactions Fast titration Studied in elderly	Sedation Behavioural problems
Lacosamide	Effective for focal seizures minimal cognitive side effects	Can prolong the PR interval More costly

ASM dose titration

Older adults may be more sensitive to medication side effects and have altered pharmacokinetics due to age-related changes in metabolism and organ function. For instance, gastric secretion, blood flow, and gastrointestinal motility are lower in the elderly, and these may affect absorption of ASMs. Reduction in serum albumin levels in elderly leads to reduction in protein binding and increase in free fraction of the drug, which is particularly significant for highly protein bound drugs such as phenytoin, carbamazepine, and valproic acid.[16] Aging is often accompanied by decreased renal and hepatic function, which can affect drug clearance. Common drugs to be affected due to reduce hepatic metabolism include phenytoin, carbamazepine, valproate and lamotrigine. Drugs affected due to reduced renal clearance include levetiracetam and topiramate.[16]

Thus, due to medication sensitivity a "start low and go slow" strategy is adopted for older patients. It is reasonable to start lamotrigine at a dose of 25mg daily and levetiracetam at a dose of 250mg bid with slow titration to an initial maintenance of lamotrigine 50mg twice daily or levetiracetam 500mg twice daily, as seizures will be controlled with modest dosing in most older people.[16]

Seizure control monitoring

Regular monitoring of seizure frequency and medication adherence is essential to assess treatment efficacy and safety. Utilization of seizure diaries or electronic monitoring devices may aid in tracking seizure activity. Clinicians should be vigilant for potential triggers of breakthrough seizures, such as medication nonadherence, sleep disturbances, or intercurrent illnesses.

Comorbidity management

Older adults with epilepsy often have multiple comorbidities such as hypertension, diabetes, or cognitive impairment, requiring coordinated management. Collaboration between specialists, such as geriatricians, cardiologists, neurologists specializing in cognitive disorders, or psychiatrists may be necessary to address comorbid conditions effectively.

Fall risk assessment and prevention

Older adults with epilepsy are at increased risk of falls, which can lead to serious injuries. This can be due to multiple reasons and include seizure related falls, post-ictal confusion and weakness, side effects of anti-seizure medication, other comorbidities that can affect mobility and balance such as osteoporosis, arthritis, and cardiovascular disease, cognitive impairment and ploypharmacy.[19] Osteoporosis is a major risk factor for fractures following falls in the elderly. Enzyme-inducing ASMs (see below), as well as valproate have been shown to increase the rate of bone loss, leading to osteoporosis and increased risk of fractures and other bone injuries. Bone density should be measured, and preservation strategies put in place when epilepsy is diagnosed and treatment begun. Non-pharmacological (e.g., regular physical activity, balanced diet, smoking cessation and measured, in alcohol intake) and pharmacological treatments (e.g., integration of calcium and vitamin D, the use of bisphosphonates, selective estrogen receptor modulators, hormone replacement therapy, recombinant forms of PTH and calcitonin) could be recommended for the said patient population though there is no clear consensus in guidelines.

Comprehensive fall risk assessments should be conducted, including evaluation of gait, balance, vision, and environmental hazards. Implementation of fall prevention strategies, such as home modifications, physical therapy, and medication review, can reduce the risk of falls.

Medication management

Polypharmacy is common in older adults with epilepsy, increasing the risk of medication interactions and adverse effects. Regular medication reviews should be performed to minimize polypharmacy and optimize therapeutic regimens. Clinicians should be cautious when prescribing medications with potential interactions with ASMs, such as anticoagulants, statins, or benzodiazepines. Such interactions are common with older ASMs such as carbamazepine, phenytoin (enzyme inducers) and sodium valproate (enzyme inhibitor).[20]

Psychosocial support

Older adults with epilepsy may experience psychosocial challenges, including stigma, anxiety, depression, and social isolation.[21] Access to psychosocial support services including counseling can improve quality of life and treatment adherence.

Life style modification

Lifestyle modifications play a vital role in managing epilepsy in older adults. By adhering to medication

schedules, maintaining good sleep hygiene, following a balanced diet, engaging in regular exercise, managing stress, preventing falls, adhering to safety guidelines (especially with regards to driving in which restriction are imposed for one year following the last seizure in the case of private vehicles), attending regular medical check-ups, and addressing mental health needs, older adults can improve seizure control and overall quality of life.

Gaps in knowledge in the management of epilepsy

Older adults are underrepresented in clinical trials for ASMs, leading to a lack of evidence on the efficacy and safety of these drugs in this population. Most dosing recommendations are extrapolated from younger populations and based on expert consensus. Furthermore, the side effect profiles of these drugs in this population, who often have multiple comorbidities and encounter polypharmacy, are not well-characterized. Dedicated trials are required to address this gap in knowledge.

Conclusion

Effective management of epilepsy in older adults requires a multidisciplinary approach, integrating pharmacotherapy, comorbidity management, lifestyle modifications, and patient education. By considering age-related changes and individualized treatment goals, clinicians can optimize seizure control and improve the quality of life for older adults living with epilepsy.

Author declaration

No conflicts of interest declared.

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Key points

- Common aetiologies for epilepsy in older adults include cerebrovascular disease, neurodegenerative disorders, traumatic brain injury, and brain tumours.
- Epilepsy in older adults presents with unique clinical features and diagnosis can be a challenge. Focal onset seizures are common, and seizures may be characterized by confusion, which can persist for a prolonged period.
- Older adults may be more sensitive to medication side effects and have altered pharmacokinetics due to age-related changes in metabolism and organ function.
- Comorbidities and polypharmacy are common in older adults with epilepsy, increasing the risk of medication interactions and adverse effects.
- Older adults with epilepsy are at increased risk of falls and risk for fractures thus necessitating fall risk assessment.

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