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REVIEW

New-onset epilepsy in the elderly

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People who are 60 years old and older have the highest incidence of developing new-onset epilepsy. The increase of the ageing population has resulted in a greater number of patients with new-onset epilepsy or at risk of developing the condition. Previously published review articles regarding epilepsy in older patients have had a broad focus, including people who were diagnosed with epilepsy in their childhood or middle age. The present review focuses on the causes, treatment, prognosis and psychosocial impact of *new-onset* epilepsy in people aged ≥60 years. Following a search of the medical electronic databases and relevant references, we identified 22 studies overall that met the inclusion criteria. Only four randomized clinical trials (RCTs) were identified that compared different antiepileptic drug treatments in this population, demonstrating that newer-generation antiepileptic drugs (e.g. lamotrigine and levetiracetam) were generally better tolerated. One uncontrolled study provided promising evidence of good outcomes and safety for surgical resection as a treatment for people with uncontrolled seizures. Five studies reported that people ≥60 years with new-onset epilepsy have significant cognitive impairments (e.g. memory loss) and psychological issues including depression, anxiety and fatigue. We found that there is limited evidence to guide treatment in people with Alzheimer's disease and epilepsy. The specific features of new-onset epilepsy in this target population significantly influences the choice of treatment. Cognitive and psychiatric screening before treatment may be useful for management. Two studies with proposed guidelines were identified but no formal clinical practice guidelines exist for this special population to assist with appropriate management. There is a need for more RCTs that investigate effective treatments with limited side effects. More research studies on the psychosocial effects of new-onset epilepsy, and long-term outcomes, for people aged ≥60 years are also required.

Introduction

By the end of 2015, half of new-onset seizures in Australia were estimated to be in older patients or people 60 years old and older [1]. With the ageing population, the number of people aged ≥60 years in the community who are diagnosed with new-onset epilepsy has increased significantly. A pivotal early study from the USA (Rochester, MN) reported that the incidence of new-onset epilepsy increases with age from 28 per 100 000 at 50 years old, to 40 per 100 000 at 60 years old and 139 per 100 000 at 70 years old [2]. Another recent large study from Finland demonstrated the increasing incidence of new-onset epilepsy in people aged ≥60 years with time, from 57 per 100 000 in 1973 to 217 per 100 000 in 2013, an almost fivefold increase [3]. The likelihood of developing epilepsy in people older than 80 years old is three times higher than that in children [4]. Rates of hospitalization of people aged ≥60 years with new-onset epilepsy is three times higher in comparison with people with chronic established epilepsy (52% *vs.* 15%) [5]. Not only is the hospitalization rate high, but also mortality, with a recent population-based study that reported a standardized mortality ratio of 3–20 among those with the condition [6]. This indicates not only an important issue for the clinical setting, but also a significant public health issue, particularly with more people living longer owing to advancements in medical treatments and greater knowledge relating to health and wellbeing [7].

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The most common risk factors for the development of new-onset epilepsy in people aged ≥60 years include increasing age, metabolic or toxic factors (e.g. drugs or excessive amounts of alcohol) and depression. The increased prevalence of new-onset seizures in people aged ≥60 years is due to several factors associated with this special population (apart from the increase in the ageing population), including coexisting conditions (or comorbidities) such as cerebrovascular diseases (e.g. stroke), high blood pressure, diabetes and dementia [8]. These comorbidities are frequent in people aged ≥60 years, and for this reason are an important consideration when managing those with new-onset epilepsy.

In comparison with younger age groups, the type of new-onset epilepsy experienced in people aged ≥60 years are most commonly *focal seizures with impaired awareness* (previously called complex partial seizures), with or without secondary evolution to generalized bilateral tonic–clonic seizures [7]. Seizures in older people compared to younger people are shorter in time duration, with less overt clinical features and symptoms, which may be masked by cognitive impairments or other neurological conditions. Therefore they can be more difficult to identify and diagnose (Table 1). The diagnosis may take some time before it is considered, let alone confirmed, which in many cases, means that appropriate treatment initiation is delayed. However, there is a high possibility of seizure remission in older people who have earlier detection and response to treatment, facilitating better long-term outcomes.

Treatment can also be challenging in these individuals as they generally: (i) have a decreased capacity to metabolize drugs; (ii) have an increasing sensitivity to the cognitive and neurological effects of drugs; and (iii) take multiple medications [8]. Newer-generation antiepileptic drugs (AEDs), such as lamotrigine, levetiracetam and gabapentin, may be better tolerated and have fewer drug interactions, and hence are more commonly used for new-onset epilepsy in people ≥60 years than older-generation AEDs, such as carbamazepine or phenytoin [9, 10]. However, there is a lack of well-conducted clinical trials for effective AEDs for treating new-onset epilepsy in this population to act as a guide for health professionals.

Over the past 5–10 years, there have been several reviews published on epilepsy in people aged ≥60 years (incorporating those who developed the condition in childhood or middle age); however, only a small number of these have focused specifically on *new-onset epilepsy* in the elderly [11–13]. Although one of these reviews was published only a couple of years ago, its focus was just on causes, without consideration of treatment and the psychosocial impact. Therefore, the objective of the present review was to update the limited existing evidence for the causes, treatment and psychosocial impact of new-onset epilepsy in people aged ≥60 years.

Methods

We searched the electronic medical databases MEDLINE, EMBASE and the Cochrane Library from 1 January 1990 to 1 September 2017, using the following search terms: 'new-onset', 'newly diagnosed', 'epilepsy', 'causes', 'prognosis', 'EEG', 'imaging', 'psychosocial', 'psychological' and 'elderly'.

Eligibility criteria

People aged ≥60 years with a diagnosis of new-onset epilepsy were included. If the study did not specify that it included new-onset epilepsy or the age at diagnosis, we excluded it. We excluded people aged ≥60 years who developed the epilepsy at a younger age, as this does not meet the definition of being new onset. We also excluded studies that primarily involved veterans who were 60 years of age and over, as this is a specific population which may be skewed towards males, and therefore not generalizable to other populations or contexts, such as all people in the community. All study types (both qualitative and quantitative) were included, except for

Table 1

Differential diagnosis: common symptoms whose clinical presentation is similar to that of new-onset seizures or postictal confusion [12, 13]

Clinical presentation	Differential diagnosis
Confusion/delirium/psychiatric illnesses	• Electrolyte disturbance – e.g. hypocalcaemia, hyponatraemia, hypokalaemia etc. • Side effects from common medications in the elderly ◦*Antidepressant*: amantadine, amisulpride, amitriptyline ◦*Antipsychotic agents*: olanzapine, clozapine, quetiapine, risperidone ◦*Cholinesterase inhibitor for Alzheimers*: donepezil, galantamine, rivastigmine
Faint/weakness/dizziness/loss of consciousness/'funny turn'	• Cardiovascular: cardiac arrhythmias, carotid sinus syndrome, postural hypotension, vasovagal syncope • Cerebrovascular: stroke, transient ischaemic attack • Endocrinology: hypoglycaemia, hyperglycaemia, uraemia • Sleep disorders: obstructive sleep apnoea, rapid eye movement sleep disorders
Attack including tremors	• Psychiatry: psychogenic non-epileptic seizure • Neurology: parkinsonism, neuropathic tremor, Holmes tremor • Drug-induced toxic tremor ◦Antiarrhythmic agents: amiodarone, mexiletine, procainamide ◦Drugs of misuse: cocaine, nicotine, MDMA ◦Toxins: ammonia, copper, lead, mercury

MDMA, 4-methylenedioxymethamphetamine

reviews. Only studies that looked at the causes, prognosis (outcomes), treatment and psychosocial impact were included. The language of the articles was restricted to English. The searches were also supplemented with manual searches of the reference lists of all included studies, and references provided by experts in the topic area.

All titles and abstracts of studies were screened using the predetermined eligibility criteria by authors L.V. and L.P. Data were extracted from the studies according to the study design, number of participants, type of epilepsy, main findings and type of treatment studied. Following extraction, the data were analysed and summarized narratively.

Results

Overall, we identified 22 studies that met the inclusion criteria. We identified two possible guidelines for the treatment of epilepsy in people aged ≥60 years [14, 15] and one systematic review looking at the treatment of epilepsy for people with Alzheimer's disease (AD) [16]. We also identified a protocol for a systematic review and meta-analysis of the pharmacological treatments for elderly with epilepsy [16].

One of the guidelines identified was based on the results from a consensus meeting of epileptologists held in Belgium in 2004 in relation to the management and treatment of epilepsy in older people. The guideline proposed three key recommendations [14]:

1. 'We propose to do a sleep or a nap [electroencephalogram] EEG recording if the awake EEG is negative.' (page 111)
2. 'We propose to treat after a first unprovoked seizure in the presence of a brain lesion or epileptiform abnormalities. For a first unprovoked seizure of unknown origin, the decision to treat should be individualised, after the evaluation of the vital risk induced by comorbidities, the increased risk of status epilepticus in elderly population, the risk of serious injuries especially bone fracture in osteoporotic patients, and the potential adverse events of antiepileptic drugs.' (page 112)
3. 'In first line treatment and due to the adverse events of previously described old AEDs we recommend the use of valproate if a rapid titration or an intravenous use is necessary.' (page 114)

The proposed guideline provided an algorithm for helping clinicians to decide whether it is appropriate to treat after a first seizure, and how to choose the most appropriate AED for treatment. The authors also reported that: 'there is [*sic*] very few evidence based data on the use of these drugs in older patients, especially in the very old and in elderly with co-disease(s)' (page 112) [14].

The second guideline identified was an operational 'good practice guide', produced by a guideline development group in Scotland using evidence from the literature, expert opinion and consultation with clinicians and patients [15]. The guide provided recommendations for obtaining a witness history, options for identifying suspected epilepsy, a referral algorithm, recommendations for starting treatment and choosing the right one, and key considerations for other aspects of patient care, including psychosocial impacts, driving and models of care.

A systematic review looking at the treatment of epilepsy in people with AD identified only one randomized controlled trial (RCT), involving a small group of 95 people [16]. The trial involved a comparison of three AEDs (levetiracetam, lamotrigine and phenobarbital) but no significant difference in seizure freedom was found for any of the treatments. Levetiracetam was found to improve cognition in people with epilepsy and AD but lamotrigine and phenobarbital had the opposite effect. Lamotrigine was found to improve depression but phenobarbital and levetiracetam worsened mood. The authors reported that the evidence identified was of low level and should not be generalized to the target population warranting further research studies.

A protocol for a systematic review and meta-analysis on the safety and effectiveness of the medical treatment of epilepsy in older patients was identified [17]. Preliminary results have been reported at a national annual meeting in America [18] but the full results are not yet available. The review found 10 studies for inclusion in their analysis, involving 938 patients. The authors concluded that lamotrigine and levetiracetam were as effective as other AEDs and were better tolerated. Levetiracetam was found to be more effective than lamotrigine but had a greater risk of side effects. There is also some evidence to support the effectiveness of brivaracetam, perampanel and topiramate in this population. Topiramate was also found to be effective and well tolerated in older people with uncontrolled seizures. Further studies are required to provide evidence for the best possible treatment in new-onset epilepsy in people aged ≥60 years.

Clinical assessment and prognosis of new-onset epilepsy in older people

Four studies were identified that assessed the clinical characteristics of older people presenting with new-onset epilepsy [19–22]. The number of patients in each study ranged from 70 to 1848 (one study did not provide any details). The type of epilepsy provided as a diagnosis was mostly similar across studies, with the most common type being focal seizures, although one of the studies reported mixed types, including status epilepticus and structural epilepsy, especially in the late-onset group [19]. The main cause identified by two of the studies was stroke, ranging in prevalence from 16% to 38% of participants [19, 20], and AD in one study, with a prevalence of 10–22% [23]. Dementia was reported as the second highest cause in one study, with a prevalence of 10% [20]. Four studies were identified which reported on the prognosis of new-onset epilepsy in older people [24–27]. The length of follow up for all of the studies ranged from 2.7 years to >20 years. Seizure freedom with the use of AEDs was achieved by most patients in all four studies (range 60–92%) [24–27].

AEDs for new-onset epilepsy in older adults

Table 2 provides an overview of the RCTs that were identified to compare the effectiveness and tolerability of different AEDs as monotherapy in older patients [9, 10, 28, 29]. They all showed that the effectiveness in controlling seizures was comparable between new AEDs, such as lamotrigine,

Table 2

Overview of randomized clinical trial studies identified investigating pharmacological treatment for new-onset epilepsy in the elderly

Study/country	No. of participants/ type of epilepsy	Intervention	Main findings
Wernhahn *et al* (2015) [29] **47 ambulatory or hospital sites in Germany, Austria and Switzerland**	359 elderly patients (aged ≥60 years), all with new-onset focal epilepsy	Group 1: 380 mg day^{-1} CR-CBZ Group 2: 950 mg day^{-1} LEV Group 3: 95 mg day^{-1} lamotrigine LTG Duration of follow-up: 58 weeks (6 weeks of dose adjustment)	Rate of discontinuation due to adverse effects: LEV (17.2%) < LTG (26.3%) < CR-CBZ (32.2%) No difference was found for seizure freedom across the groups: CR-CBZ 33.3%, LTG 38.5%, LEV 42.6%; $P = 0.33$. New antiepileptic drug LEV is preferred for initial monotherapy compared with LTG and CBZ for newly diagnosed focal epilepsy in the elderly because of better tolerability
Saetre E *et al*. (2007) [28] **29 centres from Croatia, Finland, France, Italy and Norway**	184 people with new-onset epilepsy idiopathic/cryptogenic epilepsy ($n = 70$) Symptomatic epilepsy ($n = 114$)	Group 1: LTG Group 2: sustained-release CBZ • Initial dose: LTG 25 mg *vs*. CBZ 100 mg • Maintenance: LTG 100 mg *vs*. CBZ 400 mg • Maximum dose: LTG 500 mg *vs*. CBZ 2000 mg per day Duration of follow-up: 40 weeks (4 weeks of dose adjustment)	No significant difference between LTG (52%) and CBZ (57%) for seizure freedom New antiepileptic drug LTG is better for initial monotherapy of newly diagnosed epilepsy in the elderly
Rowan AJ *et al*. (2005) [9] **18 Veterans Affairs Medical Centers in the USA**	593 elderly patients (aged ≥65 years) Patients had epilepsy of any type	Group 1: LTG treatment dose - 2.87 + 1.60 μg ml^{-1} Group 2: GBP treatment dose - 8.67 + 4.83 μg ml^{-1} Group 3: CBZ treatment dose - 6.79 Duration of follow-up: 12 months	Rate of discontinuation due to adverse events: LTG (12.1%) < GBP (21.6%) < CBZ (31%) No significant difference between LTG (61.3%) and GBP (60.0%) for seizure freedom. However, they were less effective than in the CBZ group (71.4%) New antiepileptic drugs (LTG and GBP) are preferred initial monotherapy to CBZ for newly diagnosed epilepsy in the elderly because of better tolerability
Brodie MJ *et al*. (1999) [10] **Country not reported**	150 elderly patients (mean age 77 years) Type of epilepsy was not reported	75–100 mg LTG *vs*. 300–600 mg CBZ Duration of follow-up: 24 weeks of observation after dose adjustment	Rate of discontinuation due to adverse events: LTG (18%) < CBZ (42%). LTG (39%) > CBZ (21%) New antiepileptic drug LTG is better initial monotherapy than CBZ for newly diagnosed epilepsy in the elderly because of better tolerability

CBZ, carbamazepine; CR, controlled-release; GBP, gabapentin; LEV, levetiracetam ; LTG, lamotrigine

topiramate and levetiracetam, and older AEDs, such as carbamazepine. However, the newer drugs resulted in fewer adverse effects and had higher tolerability and retention rates than older-generation drugs, such as carbamazepine.

Surgery for new-onset epilepsy in the older patients

Resective surgery is also another treatment option for epilepsy in older patients, particularly for drug-resistant, or

difficult to treat seizures that are due to drug interactions for coexisting conditions. We identified a retrospective study of patients over 60 years of age with new-onset focal epilepsy using the surgical database at the University of California (UCLA) from 1998 to 2013 [30]. These authors showed that a good postsurgical outcome (Engel class I–II) was achieved for 11 out of 12 patients (91.7%), and half of the patients (six of 12 patients) were completely seizure free (Engel class IA) at the end of the follow-up period (mean 3.1 ± 2.1 years). All patients had at least one medical comorbidity in addition to epilepsy. The authors reported that resective surgery for epilepsy in patients aged ≥60 years is safe and effective in most cases.

Neuropsychological and psychiatric comorbidities

We identified five studies that investigated the neuropsychological and psychiatric comorbidities of new-onset epilepsy in the elderly [31–34]. Two of these looked at cognitive functioning in people aged ≥60 years with new-onset epilepsy [31, 32]. An early case–control study involved people in this age group with new-onset focal epilepsy who were on AED treatment (40 participants) and compared their cognitive functioning with that of healthy controls of a similar age, using a battery of neuropsychological tests [31]. The authors reported that these older people with new-onset focal epilepsy had significantly impaired cognitive functioning in comparison with controls, indicated by poorer scores on neuropsychological testing. Further analysis revealed that the use of polytherapy was associated with impaired cognitive functioning. The other study identified investigated cognition (primarily) and quality of life (QoL) in a large cohort of people in this age group with new-onset epilepsy, before treatment (n = 257) [32]. Following neuropsychological testing (using the diagnostic program EpiTrack), over half of the cohort (58%) had cognitive impairments, with 43% of people found to have marked impairment. Factors that were associated with cognitive impairment included cerebrovascular causes (e.g. infarction and vascular stroke), neurological comorbidities and a higher body mass index. Subjective reporting from people with cognitive impairment revealed that forgetfulness and memory were the most frequent issues. In terms of QoL, the mean overall score was 74 out of a possible 100, with the highest mean score for social functioning (82.7) and the lowest for energy–fatigue (63.5). A better QoL was associated with not having any neurological comorbidities and being male. Based on the findings of the study, the authors recommended that people in this age group with new-onset epilepsy should undergo cognitive behavioural screening before treatment.

One identified study investigated psychiatric and neurological conditions that may be risk factors for the development of new-onset epilepsy in people aged ≥60 years using a population cohort obtained from the US national Medicare beneficiaries database and prior history [33]. The authors reported an incidence rate of 2.9 per 1000 beneficiaries, with higher incidences found for older age groups (75–84 years and 85+ years). Overall, there were significantly higher comorbidity burdens in people aged ≥60 years, with associations found for five psychiatric diseases, including substance abuse, psychosis, bipolar disorder, schizophrenia and depression. Cerebrovascular disease and depression were found to be significantly associated with new-onset epilepsy. The incidence of psychiatric comorbidities and new-onset epilepsy ranged between 8.8 and 29.2 per 1000 and this was higher than for neurological conditions, at 9.4 to 18.6 per 1000. In terms of adjusted rates, the association of substance abuse/dependence was significantly lower in women, and psychiatric conditions were associated with new-onset epilepsy with no history of neurological conditions.

We identified only two studies that explored the psychosocial impact relating to QoL in new-onset epilepsy in the elderly [34, 35]. One study from the UK utilized a community-based cohort of people with new-onset epilepsy in four different age groups: (i) men <60 years old; (ii) women <65 years old; (iii) men aged ≥65 years diagnosed before the age of 65 years, and women aged ≥60 years diagnosed before the age of 60 years; and (iv) men aged ≥65 years diagnosed at the age of ≥65 years and women aged ≥60 years diagnosed at ≥60 years. Their QoL was assessed through a postal survey, using validated measures of health-related QoL [34]. People aged ≥65 years with new-onset epilepsy did not have a poorer QoL; rather, they perceived their overall QoL as more likely to be negative, particularly if they were post-retirement. This group was also reported to have more anxiety and depression compared with the younger age groups [34].

Another study investigated whether there was a difference in psychosocial impact between people aged ≥60 years with new-onset epilepsy (incident group) and those diagnosed with epilepsy before 65 years of age (prevalent group) [35]. This study was qualitative, using in-depth face-to-face interviews. Following analysis, eight themes of importance were identified relating to the psychosocial impact of new-onset epilepsy, including comorbidities, significant life changes, emotional and physical impact (e.g. depression, anxiety, fatigue, trouble with memory and injuries due to fragile bones), information gathering, AED side effects, stigma, changes in relationships and attitude towards diagnosis. The authors concluded that new-onset epilepsy in people aged ≥60 years had a negative correlation with health-related QoL in comparison with people with chronic epilepsy (the prevalent group).

Discussion

We found that the most common type of epilepsy in people aged ≥60 years with new-onset epilepsy was focal seizures. There were key differences in the clinical characteristics from the identified studies in comparison with studies in younger patients (Table 3) [36]. Firstly, seizures were generally briefer, with less overt clinical features, compared with those in younger age groups, making diagnosis more challenging. Generalized-onset seizures and simple partial seizures accounted for only 7.1% and 5.7%, respectively, in older patients [37]. Furthermore, postictal (the period following a seizure) confusion could last much longer in the elderly, even up to 2 weeks, compared with a few minutes or a few hours in younger patients. This could make an epilepsy diagnosis more complicated owing to misdiagnosis as delirium from other causes.

Table 3

Comparison of new-onset epilepsy in the elderly with chronic epilepsy in the elderly and in young people

	New-onset epilepsy in the elderly (aged ≥60 years)	Chronic epilepsy in the elderly (onset in childhood or middle age)	Epilepsy in young age groups (<18 years)
Most common type	Focal epilepsy or status epilepticus[a]	Generalized and focal epilepsies	All types but in particular epilepsy syndromes, developmental and epileptic encephalopathies
Most common characteristic of seizures	Short duration focal seizures (30 s to 2–3 min) with *subtle* clinical features: • Blank stare • Loss of awareness • Confusion • Memory problems	• Tonic–clonic seizures (jerking and muscle stiffening) with loss of awareness • Short duration focal seizures (30 s to 2–3 min)	• Tonic–clonic seizures (jerking and muscle stiffening) with loss of awareness • Cluster seizures (repetitive seizures which start and stop but occur in groups) • In severe developmental encephalopathies, seizures can last longer than 5 min • Seizure duration of approximately 10 s (focal epilepsy with loss of awareness) to 2–3 min (generalized) with clearer clinical features
Features of the postictal period	Long postictal confusion period (up to 2 weeks) Easily misdiagnosed as delirium or patient experiencing a 'funny turn'	Both short and long postictal confusion period Fatigue	Short postictal confusion period(up to a few hours) Fatigue

[a]Status epilepticus can present as confusion without clear generalized tonic–clonic activity (a seizure lasting longer than 5 min and seizures closely follow one another without recovery of awareness between them for at least 30 min)

Diagnosing new-onset epilepsy in the elderly is very challenging. Common medical issues in older adults, such as stroke and AD, are the frequent causes of new-onset epilepsy [8, 38–40]. After considering the specific features discussed above, selecting appropriate AEDs for older adults with new-onset epilepsy can be different from the selection of these drugs for older patients *with pre-existing epilepsy*. The aim of prescribing medication is to achieve seizure freedom and reduce the consequence of injury, while minimizing adverse effects.

Generally, people aged ≥60 years with new-onset epilepsy have a good prognosis for seizure control when using appropriate AED treatment. The percentage of patients who achieve seizure freedom can range from 84% to 92%, which is higher than in newly treated epilepsy in younger patients [22, 41]. However, there is an increased risk of medical and neurological comorbidities, and mortality, with new-onset epilepsy. In a retrospective study of older patients with new-onset seizures over a 4-year period, 38% had evidence of cerebrovascular disease, such as computed tomography-visualized focal infarction or haemorrhage in small-vessel ischaemia [41]. Furthermore, 45% had died 1.9 years after the epilepsy diagnosis, even though treatment with AEDs had been effective in maintaining 92% of patients as seizure free [41]. Copeland *et al*. [5] showed that the subset of older patients with new-onset epilepsy had a 52% hospitalization rate, compared with 15% in older patients without epilepsy. In patients whose seizures could not be controlled with AEDs, surgery and vagus nerve stimulation (VNS) was found to have similar outcomes in terms of seizure control and complications in younger patients [42].

Drug selection

Almost all the available AEDs, except for ethosuximide, are effective in treating older patients with new-onset epilepsy [43]. Furthermore, as discussed above, it is generally easier to achieve seizure-free status in older patients compared with younger age groups. However, older patients with new-onset epilepsy often have poor adherence to AED treatment, probably because of adverse effects. A study found that 42–63% of older patients with new-onset epilepsy had poor adherence to AEDs [44]. The rate is worse for AEDs that induce weight gain or cognitive difficulties [44].

Older patients have undergone physiological changes, often have multiple comorbid conditions and take multiple medications. Thus, it is important to consider drug pharmacokinetics and pharmacodynamics carefully when treating older patients with new-onset epilepsy [45]. Hepatic and renal drug clearance is decreased in older people. These changes lead to higher serum AED concentrations than in younger adults for the same administered dose [46]. Thus, the AED dose must be carefully chosen and titrated to achieve a desirable serum concentration in older adults. Moreover, AEDs that induce cytochrome P450 enzymes, such as phenytoin, carbamazepine and phenobarbital, have most commonly been associated with osteoporosis, possibly due to the higher metabolism of vitamin D [46, 47]. However, decreased bone mineral density is also seen in AEDs that are not enzyme inducers, and recent evidence suggested that newer AEDs are not necessarily safer regarding their effects on bone [47]. Patients taking AEDs have an increased risk of falls and fractures, which can lead to serious consequences in older people [48–50].

Furthermore, as older patients often take multiple drugs for multiple conditions, such as cardiovascular disease, diabetes and arthritis, it is ideal for AEDs to have few or no pharmacological interactions [38]. Many of the older-generation AEDs either induce (e.g. carbamazepine phenytoin and phenobarbital) or inhibit (e.g. valproate) the metabolism of many other drugs, including antihypertensive agents, anticoagulants and antidepressants [51]. The newer AEDs, such as lamotrigine, levetiracetam, lacosamide and gabapentin, have fewer effects on the pharmacokinetics of other medications that older patients often take [37].

Monotherapy or polytherapy as an approach to treatment

Monotherapy is the preferred choice for older patients, in order to minimize side effects and drug interactions, with seizure freedom achieved in more than 60% of patients [52]. Drug-resistant epilepsy is less common in older patients, particularly those with newly diagnosed epilepsy. However, AED polytherapy is required if resistance to monotherapy occurs. Polytherapy is associated with poorer drug adherence, a reduction in QoL and a decline in bone density in older patients with epilepsy [53]. Therefore, before prescribing polytherapy and subjecting patients to potentially more adverse reactions and increased cost, it is important to carry out additional investigations to rule out other conditions that may mimic epilepsy [12].

Side effect considerations

Dose adjustment and appropriate titration are very important as the hepatic and renal capacity of older patients is often decreased. Treatment with AEDs should be started at a low dose and then gradually titrated to the target dose [54]. This will help to maximize a patient's tolerability and avoid adverse side effects, such as visual problems, drowsiness, dizziness and gait unsteadiness. For patients who need the introduction of AED polytherapy, if there are adverse effects, the baseline AED can be reduced to allow continued titration of the added therapy. Moreover, dose-related adverse effects may be due to the interaction of multiple AEDs, not just solely to the newly added AED [55].

Duration of treatment

The risk of recurrent seizures after withdrawing medication is higher in older compared with younger people [56]. Thus, stopping medication is less often achieved in older patients with new-onset epilepsy compared with those with chronic pre-existing epilepsy [56]. There are limited data about when to stop medication in older patients who have been seizure free for many years [43]. If there is doubt about the diagnosis of epilepsy after starting medication, stopping it is a reasonable option. This is a common scenario as dementia, syncope, sleep deprivation, drugs or the consumption of excess alcohol may have been the causes of the new-onset seizures in older people [56].

For patients who are ≥60 years of age, there are many concerns when considering resective epilepsy surgery. There is often a higher rate of comorbid medical conditions and postsurgical cognitive decline in older patients. Therefore, clinicians often worry about the lower safety profile for surgery, lower likelihood of seizure freedom after surgery and lower impact on improving QoL. The study by Dewar *et al*. [30] provided promising evidence for the safety and effectiveness of surgical treatment for patients aged ≥60 years with pharmacoresistant epilepsy. The latter study was the only one to identify surgical treatment for new-onset epilepsy in people aged ≥60 years. Although these results are promising, further studies are required to confirm the safety and effectiveness of surgery in this special population.

The current review found conflicting evidence about people aged ≥60 years with new-onset epilepsy in relation to QoL. One study [32] reported that overall QoL was good, whilst two other studies [34, 35] concluded that there were negative correlations or perceptions with health-related QoL. However, within QoL, components including depression, anxiety and fatigue were reported to be at higher levels in comparison with younger age groups. Unfortunately, a limitation of the studies looking at neuropsychological and psychiatric comorbidities [31–35] was that the length of time since onset and diagnosis was not documented, so it was difficult to determine the point at which people may have been studied, which might have affected the results. One study reported that older adults with new-onset epilepsy had better scores on mental and social health scales but lower scores on physical function, general health and emotional health scales in comparison with young or middle-aged adults [57]. The latter study was the only one to report better scores on mental and social health scales. The data were obtained from the US Veterans Health Administration databases, whereas other studies have used outpatient and population-based samples. The current review did not include studies involving veterans, which may have been a potential limitation. Further studies are required to understand the experience of new-onset epilepsy in people aged ≥60 years, to facilitate more appropriate management and ensure better long-term outcomes.

Recommendations for future research

Given the considerable difference between people aged ≥60 years new-onset epilepsy and those with chronic (or an established diagnosis of) epilepsy, there is a need for greater differentiation of patient cohorts in research studies. As the diagnosis of new-onset epilepsy in people aged ≥60 years is challenging, further information obtained through research studies specific to this population may assist health professionals in managing them. In addition, the development of standard clinical measurements specific to the older adult population (people aged ≥60 years) is warranted to reflect accurately this special population (e.g. health-related QoL) [58].

Over the past decade, there has been a large increase in the number of research studies in the ageing population, given that more people now have longer lifespans. For this reason, it is imperative that more research efforts are invested into neurological conditions such as new-onset epilepsy, which

is the third most common diagnosis in people aged ≥60 years. The higher incidence of other conditions, including stroke and dementia, which are established risk factors for new-onset epilepsy in people ≥60 years of age, calls for interdisciplinary collaborations to establish ways of improving QoL in this age group and further reduce the incidence of these neurological conditions. The current review found one systematic review of people with AD and epilepsy, which identified one RCT; however, of the three treatments documented, there was no significant difference in effectiveness. Identifying the prevalence and incidence of seizures and epilepsy in people with AD, and understanding the possible risk factors for developing preventive strategies, would be of great value. Furthermore, it would also be helpful to design and conduct larger, high-quality studies of pharmacological treatments in people with AD and epilepsy.

Implications for clinical practice

A recent systematic review identified that there are currently no clinical practice guidelines for epilepsy in the older population [59]. However, we identified two publications that reported potential guidelines for the management of epilepsy in people aged ≥60 years. Given that these publications are over a decade old, and the significant increase in evidence identified by the present review and others since that time, we propose that it would be beneficial as a next step to develop clinical practice guidelines for people aged ≥60 years with new-onset epilepsy to improve current management.

The hospitalization rate for new-onset epilepsy in people aged ≥60 years is three times higher than in people with chronic established epilepsy [5]. Another study also highlighted the importance of studying people aged ≥60 years who present to hospital with seizures [60]. These authors concluded that, based on a national audit of seizure management from hospitals in the UK, people aged ≥60 years who are admitted should be referred to a specialist epilepsy clinic/service upon their discharge.

A well-known concept of significant importance in current clinical practice is patient-centred care. This is informed by the patient's views of their own experience. Early evidence suggests that problems and needs experienced by people aged ≥60 years with new-onset epilepsy can be grouped into six categories: information; physical and emotional symptoms; memory and concentration; medications; commitments; and relationships [61]. Outcomes have also been studied, and reported with themes, including maintaining normalcy; we want to be involved; well-equipped; seizure freedom; fitting epilepsy in with other conditions; and incongruence with provider goals. These findings provide evidence to enable health professionals to develop a framework for future interventions, and to use in counselling and educating people aged ≥60 years with new-onset epilepsy [62].

Conclusion

New-onset epilepsy in people aged ≥60 years is a common condition, which is often difficult to diagnose and presents different therapeutic challenges to those associated with chronic established epilepsies in older adults or with epilepsies in younger patients. The current review was able to identify a number of published studies on the causes, prognosis, treatment and psychosocial impact of new-onset epilepsy in this age group. The most common identifiable causes of new-onset epilepsy in this population are stroke and AD. Our findings showed that it is important to choose suitable AEDs, titrate carefully and use monotherapy whenever possible, to limit adverse side effects and drug interactions. As people who are aged ≥60 years have undergone significant emotional and life changes, it is important to consider these as a part of their treatment and long-term management. Further, high-quality clinical trials are needed to determine more effective treatments that do not have adverse side effects. Although the prognosis for most people aged ≥60 years with new-onset epilepsy is good, it is also important to note the high mortality that can occur as a result of other neurological comorbidities, physiological changes with age and psychological issues. More investment in research studies that focus on developing clinical measurements that are specific to this population, clearer reporting of length of time since diagnosis, surgical intervention for uncontrolled epilepsy, strategies aimed towards reducing and/or preventing the incidence of new-onset epilepsy in people with AD and stroke, and management incorporating patient-centred care and outcomes are needed. Unless preventive therapy can be developed, it is expected that the incidence of new-onset epilepsy in people aged ≥60 years will continue to increase.

Competing Interests

T.J.O. is a member of the Reviews Board for the *BJCP* but has no competing interests to declare. All co-authors have no competing interests to declare.

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