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How to recognize treat and epilepsy in the elderly

Abstract

The Increase in life expectancy has led to a progressive growth in chronic degenerative diseases and neurological disorders such as epilepsy, defined the brain by Caused disorder Persistent predisposition of the brain to generate epileptic seizures, with neurobiological, cognitive and psycho-social policies, que Affects Approximately 1% of the world's population. It is of multifactorial origin, and has the cerebrovascular disease of the most common etiology in this specific cohort. Thus, it is Necessary to know the peculiarities of the aging process and to identify the particular presentations of early these seizures in the elderly, and qualified through the broad approach.

Diagnosis in this population can be hampered by atypical presentation and comorbidities. The focal crises are more frequent, with less prominent auras and automatisms and with longer duration of the post-ictal confusion. Status epilepticus is common, with high mortality rate.

Treatment at this age group is challenging because of drug pharmacokinetic and pharmacodynamic changes, polypharmacy, drug interactions, low compliance, and cognitive problems. It must be stipulated carefully considering the safety, tolerability and effectiveness of the medication, are que there are no Consequences que lead to deterioration of the quality of life, loss of functionality and autonomy.

Seizures can be commonly controlled with low doses of a single antiepileptic medication (AEM). Drug-resistant epilepsy is uncommon. The aim of this review was to understand the clinical manifestations, etiology and the best therapeutic options available for epilepsy in the elderly population.

It is concluded que, despite the existence of a collection of papers related to epilepsy, there is still little scientific data on this subject in this population, especially in extreme frail elderly. Therefore, there is a need for more studies in this area with the greater inclusion of the elderly in clinical trials, as well as the development of models for the comprehensive care of care these patients.

Keywords: signs and symptoms, diagnosis, epilepsy, therapeutic, anticonvulsivants, aged

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Introduction

Population aging is a global phenomenon and Brazil already accounts for 13% of the population, average life expectancy of 75.8 years. THEs projections indicate that by 2060 the population of people aged 65 or over will reach 26.7% of total population.[1]

The elderly are affected more often by Geriatric syndromes and chronic degenerative diseases of great impact on quality of life.

Neurological disorders such as epilepsy, which will be addressed in this article, is a disorder with major repercussions on the overall health of the individual, whose definition extends beyond the occurrence of at least one spontaneous seizure with neurological manifestations, but also includes the behavioural, psychiatric and cognitivas[2–5] demonstrations.

Its incidence is higher in the elderly than in other age group, exceeding 100 cases per 100,000 inhabitants / year. Approximately 25% of new cases occur in individuals 65 years or older, due mainly to degenerative neurological diseases and injuries cerebrovasculares.[3,6–8]

Clinical and epidemiological analysis of epilepsy in the elderly is hampered by several factors: lack of epidemiological studies in this age group, heterogeneous characteristics, complexity of distinction between senescence and senility, co morbidities and sub diagnostics.

Therefore, with the suspicion of a seizure in the elderly, a careful semiotic analysis is needed, with proper diagnosis and treatment, as the crises increase the risk of falls, injuries, functional impairment and rebound biopsicossocial.[7,9]

Treatment directed to the elderly must respect the pharmacokinetics and pharmacodynamics of aging, seizure type, patient profile, adverse effects, interactions, comorbidities and polifarmácia.[9]

So perform the workup of this disorder in clinical practice is challenging, as few studies have emphasized the neurobiological and clinical aspects of epilepsy in this age group, making it difficult to definition, preventive and therapeutic strategies that could modify the prognosis clinico.[10]

The purpose of the article was to review the literature, the clinical features of epilepsy in the elderly; approach, identification and treatment that should be applied in this population. In addition to spark interest in better understanding the subject.

Material and methods

This is a review, the past two decades, with searches of journal articles available in the databases PubMed/ Medline, SciELO and LILACS, in English and Portuguese.

Also Ministry of Health data were analyzed (MS), Brazilian

Institute of Geography and Statistics (IBGE) and other scientific sources (books, magazines, websites) that addressed the issue. Descriptors were used in the Health Sciences (MeSH): signs and symptoms (Signs and Symptoms), diagnosis (diagnosis), epilepsy (epilepsy), seizures (epilepsy), treatment (therapy); antiepileptic (anticonvulsants), old (aged).[11]

As inclusion criteria, the selected articles addressed the epidemiology, demographics, workup, features, available and appropriate therapy for epilepsy in the elderly population. They were analyzed and summarized in a table in order to facilitate identification of the studies.

Results and discussion

The lack of studies on the features and epilepsy therapy in the elderly may be related to lack of screening, identifying difficulties and cases studied age group that most often does not include the large elderly or is not principal[5,12] sample.

However, some studies of epilepsy in the elderly population were found, analyzed and the content of that review will be addressed and discussed below.

The elderly may be affected by neurological disorders such as epilepsy and seizures related to anatomical changes and brain biochemistry altering neuronal response to insults with increasing epileptogenic seizures, especially in older patients with multiple comorbidades.[6,9]

Epilepsy was already a known disease in ancient Egypt, and only Hippocrates (460-377 BC), in his work "On the Sacred Disease", referred to the seizure of more rational and established scientific principles to his fisiopatologia.[9]

The term epilepsy, according to Avicenna (980 AD) meant "being seized or possessed". In 1980, with the ratings of the International League of Epilepsy (ILAE), the term, epileptic syndrome was introduced. The Brazilian Association of Epilepsy, based on terminology revised in 2010, defines epilepsy as a brain disorder caused by persistent predisposition of the brain to generate seizures, with neurobiological consequences, cognitive and psicossociais.[2,4,9,13]

The seizure stems from excessive and synchronous neuronal electrical activity with different manifestations (sensory, autonomic, motor, cognitive or behavioural), as the area affected. And seizure, is motor manifestation resulting from this crise.[3,13]

Symptomatic acute crisis (or caused) is derived from an identified immediate cause (metabolic disorder, exogenous intoxication, withdrawal from sedatives, acute neuronal injury, trauma, infection and neoplasia) 3.6.

Since the only crisis (isolated) is defined as emergency or crisis using the 24-hour period corresponding to the symptomatic acute attack or the first manifestation of epilepsy, if recorrente.[3,14]

The epileptics status is determined by crisis lasting more than 30 minutes or the presence of two or more seizures without return of consciousness between elas.[3,9]

According to the World Health Organization (WHO), epilepsy is the most common brain disease, affecting 1% of the world population, with incidence and prevalence increasing with age. The estimated incidence in the western population is 1 case per 2,000 people / year. The overall probability of being affected by epilepsy throughout life is 3%.[7,15]

The incidence of epilepsy is higher in the first year of life and increases again after age 60, and It relates to the comorbidities and twice in the presence of one and seven times higher in those with three or more comorbidades.[16,17]

The prevalence rates of active epilepsy in the elderly in Brazil is 11.9/1,000 in São Paulo, 16.5/1000 in Porto Alegre and 8.5/1000 the study covering Campinas and São José do Rio Preto.[7,18] The prevalence in the US was 10.8 per 1,000 individuals. It is estimated that between 60-69 years there are 76-100 cases per 100,000 inhabitants and more than 70 years ago the dobro.[6] In long-term care facilities is a prevalence of seizures five times higher than in Community.[9]

Epilepsy the age of 65 may be idiopathic (49.7%), Cerebrovascular disease (30-49%), neurodegenerative disorders (9-17%), tumors (4.5 to 11%), trauma (3%) infection (0.6%), Toxic-metabolic disorders, neuropsychiatric disorders (depression, anxiety).[6,9,17,19,20]

Since the causes of acute symptomatic seizures in elderly are metabolic encephalopathy (10-30%), trauma (4-17%), intoxication or withdrawal from alcohol or drugs (10%) cancers (8.8%) and infections (2 %) 9,20,21.

The classification of epileptic seizures, are based on the clinical description, in EEG findings and topography. They are divided into: partial seizures (CP) at first located (focused) or generalized seizures (CG), involving both hemispheres simultaneously. CP are subdivided into simple partial seizures (CPS), with no change of consciousness, and complex partial seizures (CPS), with alteration of consciousness.[5,7,9,10]

Among the crises in the elderly, there are the CPS, CPC and status epilepticos. The CG are less frequentes.[9,22]

THE study VACS (Veterans Administration Cooperative Study # 428) of epilepsy in elderly showed that only 27% of patients had GC (50% immediately identified) and more than 60%were CPS and CPC, whose clinical manifestations are more difficult to be determined (only 21% of cases detected early) with generalization in 26% of the evaluated elderly patients; 13% of secondary generalized seizures and partial seizures mistas.[23] Given these, corroborated by other estudos.[9,21]

The PSC, in general, originate in the temporal lobe, but in the elderly are generally in the frontal region, which occur most cerebrovascular accidents (stroke), the major causes of epilepsy in geriatric[6,24] population.

Clinical manifestations in the elderly are often atypical and vague complaints, resulting in under diagnosis or misdiagnosis, especially in women, older people living alone, people with cognitive impairment, long-term care facility residents, fragile, with comorbidities and poly medicated. In addition, there are great semiotic difficulties in obtaining information from patients and witnesses as the episódio[10,24,25] characteristics.

It is reported that the manifestation of classical a urea's is less common in the elderly, and the preceded crises, most commonly by paresthesias poorly located, muscle cramps, dizziness and stare. Crises can manifest as syncope, falls and confusional states. Drowsiness is more common that the motor manifestations (automatic), repetitive motor acts; and post-ictal state and cognitive deficits are more prolongados.[6,9, 23–26]

The status epilepticus, which often occurs in the elderly, is presented as acute confusional frame, able to come to eat. It can occur

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in 70% of elderly people with no previous history of seizure and be confused with Delirium. The etiologic agents are: Stroke, hypoxia, metabolic disorders, exogenous intoxication (alcohol), anoxia, trauma, bleeding and withdrawal of sedative drugs, tumors or infection of the central nervous system (CNS), exacerbation of crises by irregular use of anti-epileptic drugs (MAE). It is a neurological emergency, whose mortality reaches 30%.[3,9]

Early detection, as well as the differential diagnosis of epilepsy in the elderly is a challenge. When you have preserved awareness, differentiate movement disorders, Benign paroxysmal vertigo, transient ischemic episodes; if it occurs impaired consciousness: not psychogenic seizures, syncope, acute confusional state; and events during sleep, differentiate: physiological myoclonus, behavioural disorders of REM sleep, restless legs syndrome, apnea sono.[9,27]

In the VACS study, 72% of patients had an initial diagnosis of epilepsy, only 26% were confirmed, and the rest were: altered mental status (40%), confusion (39%) and syncope/blackout (27%).[23] In Long Term Institution elderly analyzed in one study, it was found that 7.7% of the admitted elderly MAE using only 60% had indicated by epilépticas9 seizures.

Therefore, seniors who have a first episode of seizure must have a thorough clinical evaluation in an attempt to confirm the diagnosis before instituting treatment. Risk of recurrence in two years, if changes in the electroencephalogram and neuro imaging, early brain insult and noturnas[9,14] crises.

In essentially the clinical diagnosis of epilepsy, additional tests are advisable: electroencephalogram (EEG), which assists in identifying the epileptogenic region, etiology, prognosis and therapy in decision; electrocardiogram (ECG), laboratory tests and imaging studies (computed tomography -TC- skull or MRI brain -RNM-) are useful to rule out heart conditions, metabolic and structural respectivamente.[7,9,17,26]

One study showed that 31% of patients who had normal EEG, when monitored by video-EEG examination revealed paroxysmal events, 50% of seizures and 45% of non-epileptic seizures, mainly psychogenic events, syncope, transient ischemia and tremors, noting that the normal EEG does not rule out the diagnosis of epilepsy in the elderly.[3,6]

The brain CT scan and MRI were normal in only 18% of patients. The changes were detected: stroke (43%), small vessel disorders (41%), diffuse atrophy (35%), encefalomalácea (9%) and benign tumors (1.5%). Neuro imaging tests are important in the first crisis in the elderly to remove structural brain lesions, which may be present in 66% of casos.[3,23]

In the course of the disease, the elderly person is subject to complications: related to epilepsy itself, the trauma (TBI vertebral fractures), risk of aspiration pneumonia, psychiatric co morbidity (depression and anxiety) and unexplained sudden death. In addition to acute and chronic adverse effects of MAE, bio psychosocial complications and increased risk of mortality in recurrent crises and evil state epiléptico.[26,28]

The seizure does not always mean epilepsy and needs medical treatment. However, one should consider the presence of a risk factor (focal neurological deficit, brain injury, mental retardation and epileptiform EEG), whose presence increases by 80% the chances of a new episódio.[9,29]

In epilepsy newly diagnosed with risk of recurrence (especially if partial seizure), it is argued early treatment at the first crisis. In elderly patients with single episode without pathology or structural CNS change, no family history, no post-ictal paralysis and normal EEG, it should be further research to non-epileptic paroxysmal events and delaying initiation of therapy, since a large percentage will not present a second convulsão.[9,14,20,26,30]

The acute symptomatic seizures (or secondary), in turn, should be promptly treated with MSA for a given time, and should not be maintained after acute treatment (maximum 30 days) and the correction priority base[9,29] disease.

The basic goal to start treatment is to avoid new crises. The control is achieved in 70% of cases, while 20-30% of patients develop symptomatic chronic epilepsy and of these, 5% present intractable epilepsy with impairment and dependência.[9]

For therapeutic decision are considered some criteria: etiology of crises, risks and consequences of recurrent crises, peculiarities of pharmacokinetics and pharmacodynamics in the elderly, properties, efficacy and adverse effects of MAE.[9,19,22,30]

Historically, antiepileptic drugs can be classified into three generations. The first includes potassium bromide, phenobarbital, phenytoin (PTH), primidone, ethosuximide, and trimethadione. The second includes carbamazepine (CBZ), sodium valproate (VPA) and benzodiazepines (BZD). After 1980 appeared the third generation, progabide, gabapentin (GBP), vigabatrin, tiagabine, lamotrigine (LTG) and topiramate (TPM) later, developed molecules with more suitable properties: fosphenytoin, oxcarbazepine (OXC), levetiracetam (LEV) and pregabalin (PGB).[30]

The principles for prescribing MAE follow the same pharmacology in this age group: start with monotherapy, low dose use of short half-life MAE, slow titration, not abruptly discontinue use (unless present allergic reaction).[9,30]

Despite the therapeutic options, there is no established consensus on the clinical use of MAE in the elderly, but the experience of experts, studies and guidelines make recommendations that assist in therapeutic decision. (Annex 1) [31–45] Also, knowing the adverse reactions and the occurrence of potential elderly, also assists in that decision (Annex 2).[46]

Before the survey data, it is recommended for the elderly, MAE not induce hepatic metabolism, with better tolerability profile, less drug interactions, dosing convenience, less ataxia and cognitive impairment, as the most modern agents that may have advantages with respect to these effects, however does not have intravenous formulations and the cost is high. And despite the drawbacks, traditional drugs are still widely used, and have efficacy in partial crisis, typical in idoso.[9,26]

In specific cases, such as dementia with epilepsy, using MAE with safer profile (LTG, GBP and OXC). In advanced stages, however, where the myoclonic seizures are more common, it is chosen to VPA or Divalproex of sódio.[10,23]

consider the recommendations of the American Geriatrics Society should be (AGS) about some inappropriate medications for the elderly: as phenol barbital should be avoided by the high rate of dependency and intoxication; benzodiazepines (inappropriate for insomnia, agitation and delirium) may be used for controlling some seizures;

CBZ avoid association with antidepressants and OXC (fencing inhibitors of serotonin, norepinephrine, tricyclic) and diuretics, the risk of hyponatremia and syndrome of inappropriate secretion of anti diuretic hormone; using LEV, PGB and GBP at reduced doses in patients with glomerular filtration less than 60 ml/min.[9]

Annex 1 Brief presentation of the articles analyzed on AEDs for seniors

Author/year name of study	Design and methodology	Goals	Results/recommendations for elderly
Brazil. Ministry of Health. Department of Health Care (2013) 7	Protocol prepared from meta-analysis of studies, randomized clinical trials, systematic reviews and controlled; Search in database, Neurology textbooks and articles not indexed;	Update parameters on epilepsy in Brazil and national guidelines for diagnosis, treatment and monitoring of patients with epilepsy;	Prefer not inducing antiepileptic hepatic metabolism (GBP and LTG);Avoid classical antiepileptic enzyme inducing drugs (CBZ PTH and phenobarbital); Slow dose escalation; maximum dose to be achieved must be less than the currently recommended for drugs;Avoid the use of anticonvulsant polytherapy.
Clinical Protocol and Therapeutic Guidelines Epilepsy	Included in the protocol, special cases such as Elderly (over 60 years)		
Rowan et al.[23] Study VACS (Cooperative Study of Veterans Affairs) # 428	Randomized studies of 18 centers, double-blind with 593 elderly subjects (mean age 72 years) with newly diagnosed seizures;	To determine the relative efficacy and tolerability of LTG and GBP compared to CBZ in the elderly;The primary outcome measure was in retention trial is 12 months. Patients taking lamotrigine (LTG) or gabapentin (GBP) did better than Those taking carbamazepine.	Interruptions due to adverse events: LTG 12.1%, 21.6% GBP, CBZ 31%;seizure control was similar between groups; Improvement relative to GBP compared to the LTG or CBZ; Seizure control was similar among groups. LTG and GBP Should be Considered the initial therapy for older Patients with newly diagnosed seizures.LTG and GBP should be considered initial therapy for elderly patients with newly diagnosed epilepsy and focal seizure
Brodie[31]	clinical trial, randomized, multicenter, double-blind, with 150 elderly patients (mean age 77 years)	Compare with LTG elderly groups and CBZThe hazard ratio for withdrawal was 2.4 (95% CI 1.4-4.0) indicating That the patient was treated with CBZ more than twice as Likely to come off taking medication than one LTG.	LTG: high medication maintenance rate until the end of the observation period (71% x 42% CBZ), increased percent free of seizures for 16 weeks (39 vs. 21%) and fewer side effects (N = 102 x 48); The main difference between the groups was the dropout rate due to adverse events (18% vs. CBZ LTG 42%). LTG: initial treatment of choice for older with epilepsy newly diagnosticada.This was in part the consequence of the lower rate rash with LTG (LTG 3%, CBZ 19%; 95% CI 7-25%).
Brodie et al.[32]	randomized, double-blind, 309 patients. During 2- and 6-week titration periods, respectivamente, GBP dosage Reached 1,800 mg / day, and LTG 150 mg / day.	Compare GBP and LTG as monotherapy in newly diagnosed epilepsy.	Monotherapy with GBP and LTG was equally effective and well tolerated in patients with partial seizures (with or without secondary generalization) or tonic-clonic seizures primary. PMID: 12199724
Brodie[33]	3 randomized, double-blind, placebo-controlled trials with 1052 patients over 12 years (without specifying age limit) Patients (> or = 12 years of age) participating in the Trials Were highly refractory to treatment, experiencing at least six seizures and in 4-week seizure-free period During the eight-week baseline phase, even though 73% received at least two antiepileptic drugs and three received 23%.	To evaluate the efficacy and safety of PGB as adjuvant therapy for patients with partial epilepsy with or without secondary generalization	Few patients (<or = 5% in any treatment group) were discontinued for lack of efficacy;These results Indicate That the pregabalin is highly effective adjunctive therapy in the treatment of Patients with partial seizures with or without secondary generalization.BPG is highly effective as adjunctive therapy

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Annexs Continues...

Author/year name of study	Design and methodology	Goals	Results/recommendations for elderly
T May et al.[34]	Research samples of 167 adult patients using drug combination (PGB and other MAE)	Analyze the samples and investigate the influence of the age of the patient and comedication in serum PGB. In all, 198 samples of 167 (adult) inpatients who fulfilled the inclusion criteria (eg trough concentration, body weight available) Were investigated.	In contrast to other studies which showed no interactions, it was found that the interaction of PGB with enzyme-inducing mothers (PTH CBZ OXC) can moderately decrease the serum concentrations of PGB (about 20% to 30%), probably due to Further studies also by shouldnt clarify the effect of acts and interactions on PGB concentrations.idade; It is recommended a 50% reduction in the daily dose of PGB for patients with creatinine clearance between 30 and 60 ml / min.
Marson et al.[35] Sanad study	Study registered as a randomized controlled trial International Standard; controlled trial randomized unblinded in hospital clinics in the UK, with 1721 patients with epilepsy using CBZ	Compare patients using CBZ who continued with CBZ with those who had replacement for GBP, LTG, OXC or TPM	LTG is more effective than CBZ, GBP and TPM as a first-line monotherapy for Focal epilepsy; It is recommended to continue to assess the cost-effectiveness of the newly available medications.
Glauser et al.[36,37] International League Report Epilepsy (ILAE)	previous analysis methodology (July 2005 evidence review to March 2012)	Update the 2006 ILAE report and identify the level of long-term efficacy or effectiveness evidence donates MAEs as initial monotherapy for patients with newly diagnosed epilepsy or untreated	LTG and GBP were more effective than CBZ in the elderly; Elderly with focal epilepsy: - LTG and GBP (level of evidence A) New efficacy findings included: LEV and zonisamide for adults with partial onset seizures (level of evidence A); No major changes in the level of evidence to another subgroup.
Saetre et al.[38]	multicenter, randomized, double-blind, controlled trial for 40 weeks; 185 aged 65 or more; 185 aged 65 or more.	To evaluate the comparative effectiveness, efficacy and tolerability of LTG and CBZ prolonged release in the treatment of newly diagnosed epilepsy in the elderly.	Demonstrated comparable efficacy between LGT and prolonged release CBZ for partial tonic-clonic seizures and / or generalized not caused; Better tolerability LTG (14%) compared to CBZ (25%); The differences in results compared to earlier tests may be related to different dosage rates and the use of a sustained release formulation for CBZ.
Fields et al.[39]	A systematic review of 65 studies and meta-analysis, comprising 16,025 patients.	To compare the relative tolerability of the new MAEs * available for monotherapy of all types of epilepsy; CBZ compare with other mothers to monotherapy of focal epilepsy *New MAE: LEV, LTG, OXC, TPM Former MAE:VPA, CBZ, Clobazam	New MAE: no significant differences between them; greater efficiency compared to the old; suitable for monotherapy; no evidence of superiority or inferiority compared to CBZ; CBZ: therapy discontinuation intolerable adverse reactions; LEV: more tolerable therapy; more subjects free of seizures; worst profile compared to Clobazam and LTG; LTG: better tolerability and safety profile; New mothers (more effective and more tolerable) recommended for monotherapy focal epilepsy

Annexs Continues...

Author/year name of study	Design and methodology	Goals	Results/recommendations for elderly
National Clinical Guideline Center - UK[17]	Members of the Guideline Development Group (GDG) conducted a partial update of "The epilepsies: diagnosis and management of epilepsy in adults and children in primary and secondary care" (NICE, 2004). It updates the pharmacological management sections of the 2004 guideline and Also includes the use of the ketogenic diet.	Update the pharmacological management sections of the 2004 guidance; Address new mothers and compare them to older	CBZ: significant higher incidence of premature death and somnolence as compared to the LTG; increased risk of side effects; no significant difference was CBZ when the sustained-release formulation; First choice: MAEs non-enzymatic inductors; It is recommended to use lower doses of mothers (to have equivalent reduction crises and less adverse effects); if using CBZ, prefer controlled release; Provide elderly people with epilepsy, the same services, investigations and therapies as the general population; Attention the pharmacokinetics and pharmacodynamics of idososIt is better to use non-enzyme inducing the AEDs this population are Likely to be taking other medications. At the time the reviews were: OXC: fewer side effects; greater tolerability;Divalproex: option for the elderly and depression; Divalproex, and VPA LTG: Selected for the elderly at risk of cognitive impairment; symptomatic focal epilepsy and secondarily generalized: CBZ and OXC idiopathic generalized epilepsy: Divalproex, VPA and LTG
Betting et al.[40] Consensus Brazilian experts	method of study that gathers the opinion of several experts in the field and epilepsy therapy approach in 2002; Type of study with great value in clinical practice;	Gather expert opinions and experiences with epilepsy treatments;	At the time the reviews were: OXC: fewer side effects; greater tolerability;Divalproex: option for the elderly and depression; Divalproex, and VPA LTG: Selected for the elderly at risk of cognitive impairment; symptomatic focal epilepsy and secondarily generalized: CBZ and OXC idiopathic generalized epilepsy: Divalproex, VPA and LTG
Bruun et al.[41,42]	Retrospective study of records of MAEs prescription patterns between 2000 and 2013 to 529 elderly aged 65 years or older and 201 younger adults (16-64 years) - Kuopio University Hospital (KUH) - Finland; Furthermore, nationwide register data from the Social Insurance Institution of Finland Were included in the analysis, from the years 2004 and 2012. DadosDaData (2011-2012) 1081 elderly - Facility national register of Social Security Finland Furthermore, register data of the Social Insurance Institution of Finland Were used for Assessing potential interactions in a nationwide cohort of elderly subjects with newly diagnosed epilepsy.	Assess the choice of initial MAE for the elderly and adult patients younger with newly diagnosed epilepsy monotherapy MAE; Identify potential pharmacological drug interactions in elderly patients;	MAE most prescribed: VPA-49%; CBZ 31%Interactions: 63% CBZ, VPA and -2% with no OXC;High risk of clinically relevant pharmacokinetic interactions with other drugs, especially CBZ; It is suggested prediction of possible drug interactions on the patient's profile.
Pohlmann-Eden B et al.[29] KOMET study	Post-hoc analysis of subgroups of data from a randomized study with 308 patients ≥ 60 years;	To evaluate the efficacy and tolerability of MAEs as initial monotherapy for elderly patients. Compare the efficacy of LEV, VPA extended release (ER) and CBZ controlled release (CR) alone;	LEV: more favorable tolerability profile; suitable option as initial monotherapy for patients ≥ 60 years with newly diagnosed epilepsy; withdrawal time of treatment was higher with LEV compared to standard MSA.
Theitler et al. [43]	observational and retrospective study of 115 patients aged 60-90 years, epilepsy clinic at the Assaf Harofeh Medical Center Zerifin, Israel (4-year period - from February 2012 to 2016)	Evaluate the use of MAE and the rate of adverse events related in an outpatient cohort of elderly patients with epilepsy general MAEs evaluated: Old: PTH, VPA, CBZ, Phenobarbital, Clobazam, clonazepam New generation: GBP, LEV, LTG, TPM, OXC, Lacosamide, Perampanel	New MAE: administered in 44.5% and used in combination in 18.2% of the elderly; Comorbidities present in 98.3% of patients; MAE most used PTH, GBP, LEV and LTG. common adverse reactions fatigue and related to more frequent CNS among the new generation of MAE *;* Featured in the LEV (though its use is recommended since it makes slow titration and lower maximum dosage)

Annexs Continues...

Author/year name of study	Design and methodology	Goals	Results/recommendations for elderly
Krumholz et al.[14] Evidence-based guidelines	A systematic review of published studies evidence in accordance with the classification criteria of the American Academy of Neurology and the American Epilepsy Society.	Provide evidence-based recommendations for treatment (with MAEs) of adults with a first unprovoked seizure	After first unprovoked seizure report that the risk of seizure recurrence is higher in the first two years (21% -45%) (Level A); Risk factors: previous cerebral insult (Level A), EEG epileptiform (Level A), brain abnormality (Level B) and nocturnal seizures (Level B); MAE therapy immediately after the second seizure, is likely to reduce the risk of recurrence in the first 2 years (Level B), but may not improve quality of life (Level C); Over a longer term (> 3 years), immediate AED treatment is unlikely to Improve the prognosis seizure measured by sustained remission (Level B).The long-term (> 3 years), it is unlikely that immediate treatment with MAE improve the prognosis (level B); Patients That Should be advised risk of AED adverse events (AEs) may range from 7% to 31% (Level B) and Likely That These AEs are predominantly mild and reversible. Notify that the risk of adverse events for mothers can vary from 7% to 31% (Level B) and are predominantly mild and reversible; IClinicians' recommendations Whether to initiate immediate AED treatment after the first seizure Should be based on individualized assessments That weigh the risk of recurrence against the NAs of AED therapy, considerable educated patient preferences, and advise That immediate treatment will not Improve the long-term prognosis for seizure remission but will reduce seizure risk over the subsequent two years.Get started on treatment immediately after MAE first crisis will depend on individual ratings
Cumbo et al.[44]	A prospective, randomized study of 93 patients with Alzheimer's disease (AD) and seizures were randomized to receive LEV, Phenobarbital, and LTG compared to a group of 68 control patients (without AD without seizures and without AEDs)	To evaluate the efficacy, tolerability and cognitive effects of LEV and seizures in patients with Alzheimer's disease (AD); Compare the three groups to a control group to evaluate the cognitive effects of MAEs	We examined drug effects cross-sectionally at baseline, 6 months, and 12 months.There were no significant differences in efficacy between the three mothers; PB produced persistent negative cognitive side effects.Phenobarbital produced negative persistent cognitive side effects; LEV was associated with improved cognitive performance, attention Specifically level and oral fluency items. LTG had a better effect on mood; LEV Caused fewer adverse events than the other AEDs.LEV: caused fewer adverse events than other mothers; It was associated with enhanced cognitive performance, the level of attention and fluency; LTG had a better effect on neuropsychological mood.LEV had a benign side effect profile, making it a cognitively safe drug to use for controlling seizures established in Elderly Patients with Alzheimer's disease. So cognitively safe drug to control seizures in elderly patients with Alzheimer's disease.
Arif et al.[45] Columbia Comprehensive Epilepsy Center, New York.	retrospective non-randomized study with 417 patients over 55 years with epilepsy	Compare the effectiveness of MAE for use in older adults	Higher compliance rates at 12 months were obtained with LTG and LEV (79% and 73%, respectively) compared CBZ, PTH, GBP and TPM (48% to 59%); Seizure remission at 12 months was also higher in patients with LTG and LEV (54% and 43%, respectively); OXC was less effective than most other mothers.

Annex 2 Characteristics of antiepileptic drugs (mothers)

medications	Benefits	Disadvantages	Adverse effects
phenobarbital	affordable cost	neurotoxic potential	Dizziness, sedation, depression, behavioral disorders, cognitive impairment
Phenytoin (PTH)	affordable; intravenous presentation; rapid titration; Broad spectrum for focal and generalized seizures	Inductor liver, many interactions (verapamil, metoprolol, tricyclic)	cognitive impairment, ataxia, somnolence, encephalopathy, osteoporosis, gingival hyperplasia, changes in atrioventricular conduction, Stevens-Johnson Syndrome
Sodium valproate (VPA) Valproic acid	intravenous presentation; rapid titration; Broad spectrum and effective for focal and generalized seizures Mood stabilizer	Inductor liver; High protein binding; many interactions (Warfarin, Sertraline, Paroxetine) neurotoxic potential	Somnolence, parkinsonism, cognitive disorders, liver failure, thrombocytopenia, weight gain, osteoporosis, Stevens-Johnson (combination of VPA and LTG)
Carbamazepine (CBZ)	Minimal sedation and lighter cognitive effects; Broad spectrum for focal and generalized seizures; mood stabilizer	Inductor liver, many interactions (warfarin, statins, verapamil, metoprolol, tricyclic risperidone)	diarrhea, nausea, vomiting, mood swings, tremor, memory disorder, sedation, ataxia, diplopia, skin rash, hyponatraemia, weight gain, changes in atrioventricular conduction, osteoporosis and Stevens-Johnson syndrome
Oxcarbazepine (OXC)	Favorable pharmacokinetic profile for the elderly; Profile favorable for patients with dementia; It can be used in polytherapy; It has lower liver induction and fewer drug interactions than CBZ;Effectively to crises focal and generalized	Hyponatremia more often	Dizziness, nausea, vomiting, ataxia, diplopia, lethargy, tremor, hyponatremia, rash
Lamotrigine (LTG)	Favorable pharmacokinetic profile for the elderly; linear kinetics; discreetly induce its own metabolism; absence of interactions between the LTG and drugs metabolized by cytochrome P450 enzymes; No cognitive effects (Profile favorable for patients with dementia); Mood stabilizer; VPA half-life increased (positive synergy); Efficacy focal seizures	Set in moderate to severe liver disease; Half-life decreases with CBZ (favors neurotoxic effects); Start with low doses / Slower titration (to avoid rash) Higher cost	Skin rash, nausea, dizziness, headache, diplopia, ataxia, tremor, anxiety, osteoporosis, Stevens-Johnson (interaction between VPA and LTG)
Topiramate (TPM)	No hepatic inductor; Little interaction (only with phenytoin); Effectiveness for focal and generalized seizures	Titration should be very slow, which delays the target therapeutic dose;Weight loss; Set in kidney disease; neurotoxic potential; Higher cost	Sleepiness, anorexia, weight loss, nervousness, lethargy, cognitive effects, paresthesia, acidosis, nephrolithiasis, closed angle glaucoma.
Gabapentin (GBP)	hepatic metabolism of absence; little interaction; easy dosage Profile favorable for patients with dementia; renal excretion Efficacy focal seizures	Set in kidney disease Effectiveness limited antiepileptic Multiple daily doses High cost	Weight gain, dizziness, ataxia, nystagmus, headache, tremor, fatigue, nausea, loss of bone mass in men
Pregabalin (PGB)	Favorable pharmacokinetic profile for the elderly; generalized anxiety disorder; hepatic metabolism of absence;You can start with therapeutic dose; little interaction; Easy to dose; renal excretion; Efficacy focal seizures;	----------	Drowsiness, ataxia, fatigue, dizziness, weight gain
Levetiracetam (LEV)	Profile favorable pharmacokinetic; absence of hepatic metabolism;You can start with therapeutic dose;They can be used in patients with comorbidities and the elderly;without significant interactions; suitable for monotherapy or in adjunctive andgeneral pilepsia and newly diagnosed	High cost	asthenia, ataxia, drowsiness, headache, weight gain, psychiatric disorders particularly in people with prior psychomotor retardation, depression, insomnia, irritability, personality disorders, restlessness, rash, eczema, pruritus.

It is important to mention that the state epilepticus affects 10 times more in elderly and 0.5% admitted to the Intensive Care Unit (ICU) suffer this crisis, whose mortality rate is 18-52%, depending on the cause, with cognitive sequelae. Therapy should be early, but cautious, as aggressive therapy MAE is controversial and without satisfactory results. Start with intravenous BZD (Diazepam and Lorazepam), if the situation persists, ndovenoso MAE (phenytoin), treat the cause and monitor in UTI.[3,6,9]

is not recommended polytherapy with MAE, the drug interactions, adverse effects and idiosyncratic reactions; but in 10-15% of patients refractory after 3 months of monotherapy, it is necessary to conduct associations for seizure control.[2,7,9,47]

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In epilepsy therapy, 50% of patients will not relapse after cessation of drug treatment. On the other hand, Suitable drugs using the same type of seizure, 20-30% are refractory and 15% is unsatisfactory control in focal epilepsy (partial) being candidates for treatment cirúrgico.[7]

The neurosurgery for epilepsy correction is made less frequently in elderly, because: seizures are easily controlled with MAE, there is a higher prevalence of cardiovascular diseases and comorbidities that increase surgical risks, some patients do not meet clinical criteria for surgery or when operated not completely remit of crises. Patients aged 50 years or more with intractable seizures of hippocampal sclerosis showed positive results after temporal lobectomy that are comparable to young patients long prazo. Older Patients should not be denied treatment on the basis of age. However, lobectomy or hemispherectomy has been successfully performed in this population, and this type of treatment should not be denied based on age. Hitherto, it has been reported that the older patient undergoing the surgery was 76 anos.[19,48–50]

And for starting to discontinuation of treatment, it is necessary to consider risk/benefit It should happen by: lack of response after 3 months with treatment at maximum doses; seizure remission (after 2 years of treatment); acute neurological injury (suspended for 12 weeks).[7,30]

Nevertheless, slow reductions were suggested, according to previously established criteria for each MAE. And an intermediate position defined "conservative", suggesting reductions of 25% of the dosage of the drug every three meses.[26,30]

The latest definitions, it is considered more epilepsy when, in the period of 10 years or more, there is the presence of seizures and no use of MAE. However there are no guarantees about futures 4 crises.

The drugs can prevent seizures without altering the natural history of epilepsy, as 50% -70% of patients come into lasting remission and 40% go into remission even without the use of MSA. Delay or stop treatment for any reason, does not imply change of course prognosis once considered certain kindness that surrounds the global prognosis of most epilepsias30apud.[51,52]

To encourage the initiation and maintenance of long-term treatment, it is necessary to expose the treatment performed in an individualized manner, respecting the specificities, has great chances of complete control of seizures. And consequently, there will be a satisfactory outcome, while maintaining the functionality and independencepatient.[2,6,9,10,19]

Conclusion

Epilepsy is a common neurological condition in the geriatric population, and like all chronic diseases in this age group, requires professional skills with thorough and timely diagnostic workup, given the atypical presentations and aging characteristics.

It is important to follow the International League of Epilepsy, which periodically makes updates. The classification of epilepsies of the International League against Epilepsy (ILAE) is to aid in the diagnosis of patients in research, development and antiepileptic therapies for communication around the world. It was updated in 2017 according to the new knowledge of epilepsy and scientific development, and incorporates the etiology and comorbidities such as steps required for diagnosis, for promoting therapeutic implications significantes.[53] Within this new perspective, the elderly population, which significantly, has pluripatologias and comorbidities may have a more precise classification of epilepsy before the epileptic seizures.

The treatment applied must be careful not to compromise the adhesion, present minor adverse reactions, considering comorbidities, degree of dependence and need for third party monitoring.

The choice of MAE depends on the type of crisis, tolerability, cost/benefit, possible effects associated with altered pharmacokinetics and pharmacodynamics. Therefore, appropriate adjustments to MAE for the elderly include prescription with lower starting dose, slower titration and a lower target dose than for younger adults.

In this article, we describe the particular characteristics and peculiarities for the treatment of epilepsy in the elderly. The recommendations were based on the studies analyzed, cautiously drew a parallel between the characteristics of the elderly and pharmacological profiles. Thus, a careful and individualized approach will always be useful in clinical practice in order to make a good therapeutic decision.

Despite the new generation of medications, there is need to develop new treatments for epilepsy, with effective drugs for resistant cases, with fewer side effects and to modify the natural history of the disease, protecting the brain damage. In addition to more studies related to therapeutic behaviour and response of epilepsy in the elderly.

It is known that elderly patients with newly diagnosed epilepsy have a good prognosis and a good chance of successfully MAE alone.

It is essential to clarify that uncontrolled epilepsy has important implications for the independence, security and quality of life of the elderly. And the goal of treatment is to achieve seizure control with minimal side effects and preservation of functional status.

Finally, it is expected that, given the new classification of the ILAE, there is an improvement in research and care in epilepsy, considering the age of the elderly, especially the large elderly over 80 years, so that we have emplacements for a treatment more safety.

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Conflicts of interests

The authors of this manuscript have no competing interests.

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