

Clinical Features of Late-Onset Seizures

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Abstract

Introduction: We aimed to evaluate the types of seizures, etiologic factors, effectiveness and adverse effects of antiepileptic treatment in the elderly.

Method: We evaluated the medical data of the 138 patients, who had their first seizure above the age of 65, and admitted to our clinic between years 2011-2013. We determined the type of seizure, etiologic factors, seizure recurrence, antiepileptic treatment, adverse effects of the treatment and the rate of patients who were seizure free at the last visit.

Results: In the 138 patients, whose mean age was 75.6 ± 7.2 years at the time of first seizure, we found the most common seizure type was generalized seizure and the most common etiologic factor was cerebrovascular diseases. Levetiracetam was the most used antiepileptic drug, and for the overall group, the rate of adverse effect of the antiepileptic drugs were 20.3%. At the last visit, 89.9% of the patients were seizure free with a mean time of 17.8 ± 22.7 months.

Conclusion: In conclusion, symptomatic seizures were common in elderly with better response to antiepileptic drugs and usually monotherapy was sufficient for maintenance of the seizure free period. The side effects and drug interactions must be taken into account while choosing the antiepileptic treatment, since the comorbid diseases and multiple drug usage is common in elderly.

Key words: Epilepsy, elderly, seizure, etiology.

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Introduction

Elderly population is gradually increasing not only in Turkey but also worldwide, and according to year 2013 data, approximately 7.7% of the population (n=5 878 603) consists of people at the age of 65 and above (according to the data from the Turkish Statistical Institute). In epidemiological studies, incidence of epilepsy is higher in the individuals older than 65 years of age in comparison with the other age groups, and the incidence is increasing in age-dependent manner (1). Epilepsy incidence is reported as 80.8/100,000 in all age groups, but this rate rises up to 85.9/100,000 in the age group of 65-69 years and to 135/100,000 in age group of over 80 (1). On the other hand, etiology, clinical findings and response to treatment in elderly patients with epilepsy demonstrate variations in comparison with the young patients (2). Moreover, presence of comorbidity and use of multi-drugs are more frequent and therefore, diagnosis of epilepsy and selection of medical treatment are challenging (1).

The purpose of this study is to determine types of epileptic seizures and etiologic factors in elderly population and to find out efficacy of anti-epileptic medications and likely side effects related to age.

Materials and Method

The patients over the age of 65, who were assessed in Neurology Department from 2011 to 2013 and diagnosed with epileptic seizure, were retrospectively evaluated. Diagnosis of epilepsy was based on classification made by International League Against Epilepsy (ILEA) (3, 4).

Age, gender, comorbidity, medications, seizure type, electroencephalography (EEG) results, magnetic resonance imaging (MRI) and/or computed tomography of brain (CT of brain), antiepileptic drugs (AED) and drug side effects are derived from medical records of patients. In addition, likely etiologic factors are identified in the light of workup.

Etiologic factors are classified as follows; the patient who had history of intracerebral hemorrhage and infarction are included in group of cerebrovascular disease; patients with dementia in group of degenerative disease; primary and metastatic mass lesions in tumor group; and the patients with no epileptic focus on imaging studies in idiopathic group.

Basal EEGs and brain imaging studies of the patients were recorded. EEG data was classified as normal, disorder in background activity, paroxysmal disorder



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and epileptiform activity. Brain imaging studies were also assessed regarding presence of mass lesion, atrophy, lesion related to small vessel disease, vascular lesion consistent with clinical presentation and malformations that could be an epileptic focus.

Long-term seizure-free rates were determined for patients. In addition, presence of status epilepticus, injury secondary to seizure and death were also recorded.

This study was approved by Research Committee and Ethics Committee of Baskent University (project No: KA 14/70).

Statistical analysis

Data from the study were imported into statistical package for the social sciences (SPSS) 11.0 (SPSS Inc., Chicago, IL) for analysis. Categorical changes were expressed in frequencies and percentages. Mean and standard deviations were calculated for continuous variables.

Results

We evaluated the data of 138 patients followed up in Neurology Clinic, who were ≥ 65 at the time of first seizure. Of patients, 50.8% were female (n=70) and mean age at first seizure was 75.62 ± 7.2 years (65-95 year). Average duration of disease was 33.3 ± 36.1 (1-197) months and duration of clinical follow-up was 27.5 ± 34 (1-197) months.

Cerebrovascular disease, the most common etiological factor, was found in 34.8% of patients. Ischemic lesions were detected in 85.1% of these patients. Degenerative diseases were the most common second etiology, whereas idiopathic group includes 31.2% of patients. Hypocalcaemia was found in one patient, who was considered having seizure secondary to metabolic disorders, and hypoglycemia was determined in another one. Other etiological causes and their distributions are summarized in Table 1.

Table 1. Distribution of etiologic factors.

Etiology	n (%)
Cerebrovascular disease	48 (34.8%)
Degenerative disease	28(20.3%)
Tumor	13(9.4%)
Trauma	2(1.4%)
Metabolic disturbance	2(1.4%)
Hypoxic-Ischemic Encephalopathy	2(1.4%)
Undetermined	43(31.2%)

The most common type of seizure was generalized seizure that was found in 63.8% of patients (n=88). Generalized myoclonic seizure was observed in two (1.4%) patients who developed hypoxic ischemic encephalopathy following cardiac arrest. Other types of seizures are summarized in Table 2.

Table 2. Type of Seizure

Type of seizure	n (%)
Generalized	88(63.8%)
Focal	50 (36.2%)
*With impairment of consciousness or awareness	25 (18.1%)
*Without impairment of consciousness or awareness	21 (15.2%)
*Evolving to a bilateral. convulsive seizure	4 (2.9%)

Of patients, 20.3% (n=23) and 79.7% (n=110) had medical history of single seizure and two or more seizures, respectively. In the last follow up examination, 89.9% (n=124) of patients were seizure-free, and average seizure-free period was 17.8 ± 22.7 months. Status epilepticus was observed at rate of 3.6% (n=5), 4 of them experienced at the first seizure. All of the patients with status epilepticus had underlying structural lesions.

Antiepileptic drugs (AED) were used by 96.4% of patients. Two out of five patients who did not use AEDs had seizures secondary to metabolic etiology, while other three patients had no etiological factor and they were considered having low risk for recurrent seizure in the light of investigations. The most frequently preferred AED was levetiracetam and 64.5% of patients were first started on this drug. Other AEDs are summarized in Table 3. In 75.9% (n=110) of patients, treatment was maintained with the initial medication, whereas switch to other drugs was required in 24.1% (n=32). Medication shift was secondary to side effect in 8 of 32 patients (25%) and recurrent seizure in 24 patients (75%).

Table 3. Distribution of initial antiepileptic drug.

Antiepileptic drug	n (%)
Levetiracetam	89 (%64.5)
Diphenylhydantoin	19 (%13.8)
Carbamazepine	10 (%7.2)
Oxcarbazepine	9 (%6.5)
Valproic acid	5 (%3.6)
Lamotrigine	1 (%0.7)
Without medication	5 (%3.6)

Drug-emergent side effects were observed in 27 of 133 patients (20.3%) who took antiepileptic

drugs. When rate of side effects was reviewed by medications, side effects were observed in 18% (n=16) of the patients who used levetiracetam, although medication switch was required in only one patient. Most frequent side effect was somnolence that was seen in 12 patients. Itching, forgetfulness, agitation and anxiety were the other reported side effects and each symptom was observed in one patient. Hepatic function tests elevated in 3 patients (15.8%) who used diphenylhydantoin, and medication switch was required in 2 patients for this reason. Elevated levels of gamma glutamyltransferase (GGT) were determined in 3 (30%) patients who used Carbamazepine, resulting with medication switch in 2 patients. Medication switch was required due to hyponatremia (n=1) and elevated GGT (n=1) in totally 2 patients (22.2%) of oxcarbazepine group. Parkinsonism (n=2) and somnolence (n=1) were observed in patients who used valproic acid, and two patients required medication switch in this group. No side effect was observed in the patient who used lamotrigine.

Seizure-related injury was observed in 5.1% (n=7) of patients. Those injuries included proximal humerus fracture (n=1), minor head trauma (n=2), subdural hemorrhage (n=1), tarsal fracture secondary to fall (n=1), thoracic vertebra fracture (n=1) and multiple rib fractures (n=1). Death, related to etiology of seizure developed in 7.2% (n=10) of patients.

All patients had at least one of the systemic diseases, such as hypertension, hyperlipidemia, diabetes mellitus, hypothyroidism, coronary artery disease, peripheral artery disease and cerebrovascular disease. Additionally, 19.6% of patients (n= 27) had past medical history of malignancy that was independent from etiological factor. Only one patient was not using medical treatment for comorbidity(ies).

Electrophysiological data showed epileptiform findings in only 4.3% of patients (n=6), slow background activity in 5.1% (n=7), bilateral or generalized paroxysmal discharges in 9.4% (n=13) and normal EEG in 49.3% (n=68). No EEG recording was available for 31.9% of patients (n=44).

Brain imaging studies showed at least one of the following changes; atrophy, ischemic lesions suggestive of small vessel disease or cerebrovascular accident, in 97.8% of patients. Mass lesions, suggesting metastasis or primary brain tumor, were observed in thirteen patients (9.4%). Three patients had normal brain imaging results (2.2%).

Discussion

We found the most common type of seizure as generalized seizures and our results suggested seizure free period easily can be obtained by monotherapy.

Incidence of seizures in elderly patients is increasing as number of elderly people increases in the population. Therefore, better understanding of additional problems in those patients such as characteristics of seizure, underlying etiological causes and drug interactions is necessary for effective patient management.

Cerebrovascular disease is reported to be the most common etiological factor, as the case in this study (2, 5-8). On the other hand, no etiology can be determined in approximately 50% of patients (9, 10). Although degenerative disease takes the second place in our study, we saw that this group of patients were not included in many studies (2, 5, 9). However, studies reported that seizure increases by 5 to 10 folds in patients with degenerative disease in comparison with population, and it is expected that patients with dementia accounts for 10-20% of late-onset epilepsy cases (5, 11). Moreover, in some diseases such as Creutzfeldt-Jakob disease and autoimmune encephalitis, it should be kept in mind for differential diagnosis that cognitive loss and seizure can be observed as a part of the clinical picture (11). In addition, seizures may lead to cognitive decline, fall and injury in patients with dementia, and moreover, these patients may be more sensitive to side effects of AEDs (11). In this study, all patients were already diagnosed with dementia, and they had their first seizures after this diagnosis was made. Since this is a retrospective study, effects of seizures and medications on cognitive status of patients could not be evaluated in detail.

When types of seizures in elderly people are evaluated, variations may be observed in comparison with young subjects and in different studies (6, 12). In our study, most common ones were generalized seizures, whereas on the contrary to our data, focal seizures were reported to be the most frequent ones in the literature (6). Tanaka et al. (10) reported incidence of generalized seizures and secondary generalized seizures as 7.1% and 40%, respectively. Another study reported similar figures (2). When retrospective feature is taken into consideration and etiological factors are considered, high dementia rates are secondary to the fact that focal component is overlooked and especially the secondary generalized seizures may be classified as generalized seizure.

Symptomatic seizures are common in elderly patients and recurrent seizures are frequently observed after first seizure (5, 6). It's reported that prevalence of seizure after diagnosis is 53% in first year and this figure rises to 75% in year 5 (6). An epidemiological study reported that ratio of elderly patients, who had two or more seizures, is 76.8% (8). This study reported ratio of patients, who had two or more seizures, as 79.7%, a figure consistent with the literature.

Since seizure relapses at frequent intervals, use of AEDs after the first seizure is more frequent in elderly people in comparison with young patients (6). It is considered that frequent recurrence of seizure is dependent to etiological factors, rather than age (6, 12). However, comorbidity and multi-agent medication should be taken into consideration when appropriate drug is selected. In addition, response to medications is better in elderly patients, therefore seizures can be controlled with less medication at lower doses (2, 8-10, 13). Our observations also prove this data, whereas monotherapy is sufficient in more than 75% of patients.

Side effects of medications should be considered in selection of anti-epileptic medications. Particularly, conventional antiepileptic medications (such as diphenylhydantoin, carbamazepine, valproic acid, phenobarbital, primidone) should not be preferred in elderly patients due to side effect profiles (11). Besocke et al. (9) found side effects in 30% of the patients and reported a linear correlation between use of four or more AEDs and emergence of side effects. Rate of side effect was reported as 27% in a retrospective study, in which conventional anti-epileptic medications were used. Since side effects were observed in approximately 20% of patients in this study, medication switch was required in approximately 30% of these patients due to side effects.

It is reported that clinical picture of status epilepticus is 5 or 10 folds more likely in elderly patients in comparison with young people (14). Incidence of status epilepticus is reported as up to 40% in the literature, whereas the figure was 3.6% in this study – a ratio significantly lower than the literature (8, 12, 15). As clinical details of patients, who developed clinical picture of status epilepticus, are not present in studies, we had no opportunity to make comparison. However, differences between study centers may influence distribution of the patients; therefore, this difference might be also secondary to difference in inter-group etiology variations, other comorbidities and other factors, such as medications that may influence clinical picture of seizure.

Several types of injuries had been reported due to seizures and seizure dependent traumas might affect patients' quality of life (16-18). Fracture risk increases due to both negative effects of some medications on bone metabolism and low bone densities, especially in elderly patients (14). Fractures account for approximately 10-35% of injuries that develop secondary to seizures (16, 17, 19). Among all injuries, fracture appears more prevalent in this study – 57.1%, a figure higher than the literature. However, soft tissue traumas were also classified as injury in other reports and there may be some deficiencies in data as our study is a retrospective one and we think that particularly simple injuries were not recorded.

In conclusion, seizures in elderly patients are mostly symptomatic. Although tendency of seizure recurrence is high, response to AED is good, and seizure-free status can be frequently be achieved with low dose single medication. Since comorbidities and use of multi-agent therapy are high in elderly patients, both drug interactions and side effect profiles must be considered while selecting AEDs. Seizures, drugs used and potential injuries may affect the patients' and their relatives' quality of life.

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