PROFILE AND SHORT-TERM OUTCOME IN ADULT PATIENTS WITH NEW-ONSET SEIZURES

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ABSTRACT

BACKGROUND

The annual incidence is 85 per 1,00,000 for people aged 65-69 years and 135 per 1,00,000 for those aged over 80 years. Epilepsy in older patients poses several additional problems for the provision of services compared with the rest of the population as diagnostic difficulties and polypharmacy.

The aim of the study is to-

1. Know the various causes of seizures, clinical profile and correlation between neurological imaging and VEEG characteristics.
2. Know the differences between the aetiologies of seizures in young age and elderly >65 years.

MATERIALS AND METHODS

This was a prospective, hospital-based case control study conducted on 75 patients older than 65 years with new-onset seizures at KGH Neurology OP and IP Services from September 2014 - November 2016 using EEG, MRI or CT brain and relevant laboratory tests.

RESULTS

75 patients (46 males, 29 females) with a mean age of 73.72 ± 8.72 years were enrolled in the study. Overall, the seizures were classified as generalised onset in 7 (9.4%), focal onset in 52 (70.1%) and uncertain onset in 15 (20.5%) patients. The aetiology was acute symptomatic in 29 (39.2%), remote symptomatic in 24 (31.7%), progressive symptomatic in 14 (19.1%) and unknown in 8 (10.1%) patients.

CONCLUSION

Most of the new-onset seizures in our elderly patients were focal onset as a consequence of vascular brain lesion. The recurrence was high. The major risk factors for recurrent seizures were acute, remote and progressive symptomatic aetiologies, epileptiform discharges and nonspecific abnormalities on EEG. Elderly patients maybe at a higher risk of recurrence following an initial stroke than younger people.

KEYWORDS

New-Onset Seizures, Elderly, Recurrent Seizure, Short-Term Outcome.

HOW TO CITE THIS ARTICLE: Gopi S, Chowdary S. Profile and short-term outcome in adult patients with new-onset seizures. J. Evid. Based Med. Healthc. 2018; 5(2), 115-120. DOI: 10.18410/jebmh/2018/26

BACKGROUND

Elderly people are the most rapidly growing segment of the population. The incidence and prevalence of epilepsy are higher in this age group than in younger people. Old age stage is a peak period for developing epilepsy and seizures.[1] The incidence of epilepsy and seizures is higher in the elderly (60 years old) than in other age groups.[2,3] It has been estimated that the annual incidence is 85 per 1,00,000 for people aged 65-69 years, 159 per 1,00,000 for people aged over 80 years and 80.8 per 1,00,000 people over all age groups.[4] A recent epidemiological study shows that the average annual incidence of epilepsy in the elderly aged 65 years and older is up to 240 per 1,00,000. Nearly, 25% of new-onset epilepsy occurs in the elderly.

Some scholars predict that the elderly will account for half of all new-onset epilepsy people by 2020.[5] Elderly individuals with epilepsy are a unique subpopulation of patients with several important differences from younger people with epilepsy.[6] The literature indicates that epileptic seizures are often difficult to diagnose in the elderly for various reasons such as difficulty in obtaining an accurate clinical history, a frequently atypical ictal presentation and difficulty in diagnostically distinguishing between an epileptic and nonepileptic event.[7] Recurrent seizure appears to be common in this population, but the data are largely inconclusive.

There also appear to be differences in this patient group in the epidemiology, aetiology and treatment with antiepileptic drugs in developing countries compared to developed countries.[6] Data on epilepsy in the elderly from developing countries are sparse. With the rapid increase in the elderly population in our societies, more attention must be paid to this group of patients when planning future medical services for epilepsy. In this study, we aimed to

Financial or Other, Competing Interest: None.
Submission 15-12-2017, Peer Review 21-12-2017,
Acceptance 01-01-2018, Published 03-01-2018.
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DOI: 10.18410/jebmh/2018/26

elucidate the aetiology, clinical and EEG profile seizure and describe comorbidities in older adults who presented with first seizure to a tertiary care hospital in and around Visakhapatnam.

Aims and Objectives

- To know the various causes of seizures in adult people.
- To know their clinical profile.
- To study the correlation between neurological imaging and VEEG characteristics and their comorbidities.
- To know the different causes and the differences between the aetiologies of seizures in young age and elderly >65 years.

MATERIALS AND METHODS

Study Design- Prospective study.
Study Period- March 2015 - March 2016.
Study Subjects- The present study was done in the Department of Neurology, Andhra Medical College, King George Hospital, Visakhapatnam.

75 patients who presented to the Neurology OPD and wards and Neurosurgery and allied branches with seizures after age 65 years were recruited into the study.

Inclusion Criteria- All patients aged above 65 years presenting to OPD and wards of Neurology Department, KGH, Neurosurgery and allied branches with new-onset seizures after age 65 years were recruited into the study.

Exclusion Criteria- Seizure mimics like-

1. Syncope.
2. TIA hypoglycaemia.
3. Migraine attacks.

Study Tools- The types of seizure were classified based on the International Classification Epileptic Seizures.[3]

Study Procedures- Patients fulfilling inclusion and exclusion criteria were subjected to detailed case pro forma, questionnaires followed by ILAE seizure classification, demographic characteristics, the cliniconeurological examination findings, initial diagnosis, clinical features including seizure type, duration of epilepsy before adequate treatment, antiepileptic drugs prescribed, recurrent seizure, VEEG, later MRI/CT brain was done.

MRI- 750 wide bore 1.5 Tesla GE made model with diffusion weighted imaging in 25 directions was used.

CT brain- A 64-slice CT GE made was performed with 1 mm thickness.

VEEG 32 channel Nicolet, Natus Software v2.1.01 with video recording.

Laboratory and other investigations done included electrolytes, blood glucose, urea and creatinine levels and Electrocardiography (ECG).

Video Electroencephalogram (VEEG) and brain imaging (MRI/CT brain) were obtained for all patients.

An MRI scan 52 for patients, CT scan for 10 patients and both for 13 total of 75. The aetiology of seizure was classified as-

1. Acute symptomatic seizure occurred within a week of acute Central Nervous System (CNS) or systemic insult;
2. Remote symptomatic seizure in the presence of history of CNS insult presumed to result in a static encephalopathy associated with an increased risk for epilepsy;
3. Progressive symptomatic seizure in the occurrence of non-static conditions; and
4. Unknown seizure owing to conditions presumed to be symptomatic, but cause unclear.

We evaluated seizure recurrence and comorbidities at one to one-and-a-half years.

Statistical Analysis

- Data was entered in excel 2007, analysis of data was done using SPSS-16 version.
- Group comparisons between seizure-free and recurrent seizure were made using a two sample.
- T-test or the Wilcoxon rank sum test.
- The correlates of recurrent variables were determined using logistic regression models.
- Each demographic and clinical variable was analysed for marginal association with seizure recurrence using univariate logistic regression based on the P-value.
- Descriptive data was presented as frequencies and percentages.
- Unpaired t-test was applied to find the statistical difference between means.
- Data representation was done by appropriate pie charts, bar diagram and box plots for median.
- Data was tabulated as per the content appropriate.

Ethical Considerations- Written informed consent was obtained from the patients. Confidentiality of the patients was maintained by blinding the case report forms and not mentioning their personal details.

RESULTS

Baseline characteristics of cases were matched for age and gender.

Variable	Total	Seizure Free	Seizure Recurrence	P-value
	n=75	n=41	n=34	
Age at Onset (Years)	73.32 ± 8.72	71.75 ± 7.61	73.07 ± 9.97	0.212
Sex				
M	46	21	18	0.343
F	29	20	16	0.285

Duration (Number in Days)	13.02 ± 24.29	14.38 ± 24.39	11.23 ± 24.14	0.285
Seizure Type; n (%)				
Focal onset	52 (70.1)	24 (59)	17 (41.0)	0.526
Generalised onset	26 (9.4)	22 (53.8)	15 (46.2)	
Uncertain	15 (20.5)	21 (50.9)	16 (49.1)	
Aetiology; n (%)				
Acute symptomatic	29 (39.2)	24 (58.7)	14 (41.3)	<0.000
Remote symptomatic	24 (31.7)	31 (76.1)	8 (23.9)	
Progressive symptomatic	14 (19.1)	4 (9.4)	31 (90.6)	
Unknown	8 (10.1)	32 (78.6)	7 (21.4)	
Electroencephalography; n				
Normal	23 (29.9)	29 (71.1)	10 (28.9)	<0.000
Nonspecific abnormality	31 (41.4)	27 (67)	12 (33)	
Epileptiform discharge	22 (28.8)	11 (27.5)	25 (7.5)	
S.E. at First Presentation; n (%)				
Yes	16 (21.6)	16 (38.3)	21 (61.7)	0.001
No	59 (78.4)	25 (61.9)	13 (38.1)	
Misdiagnosis of Non-Seizure Activity; n (%)				
Yes	18 (24.1)	27 (64.5)	12 (35.8)	0.164
No	57 (75.9)	14 (35.5)	22 (64.2)	
Comorbidity; n (%)				
Stroke	27 (36)	12 (29)	15 (44.1)	0.076
Diabetes	31 (42)	17 (41.4)	15 (44.1)	0.279
Hypertension	40 (54)	30 (73.1)	20 (58.8)	0.625
CAD	8 (12)	5 (12.2)	4 (11.7)	0.401
Antiepileptic Drug; n (%)				
Phenytoin	43 (57.6)	24 (57.5)	14 (42.5)	0.989
Carbamazepine	6 (7.2)	22 (55.0)	15 (45.0)	
Valproate	15 (19.4)	24 (57.4)	14 (42.6)	
Phenobarbital	2 (2.9)	3 (62.5)	1 (37.5)	
Topiramate	4 (5.0)	2 (57.1)	1 (42.9)	
Levetiracetam	6 (7.9)	2 (50.0)	2 (50.0)	
Death; n (%)				
Yes	2 (16.2)	1 (42.2)	1 (51.8)	0.031
No	73 (83.8)	40 (59.7)	3 (40.3)	

Table 1. Basic Clinical Characteristics, Clinical Data and Comorbidities of Study Patients

DISCUSSION

The present prospective study was done in a tertiary health care setting among 75 patients with objectives of understanding the clinical profile of patients presenting with seizure symptoms in elder adults and role of VEEG and neuroimaging in understanding seizure and epilepsy syndromes.

The results were compared with the available literature and presented in line with the objectives. In the present study, the notable risk factors of recurrent seizure were acute symptomatic aetiology, remote symptomatic aetiology, progressive symptomatic aetiology, epileptiform discharge on EEG and nonspecific abnormality on EEG and the most common comorbidities were depression and anxiety.

The incidence of seizures in the elderly is at least as high as in the first decade of life. With increasing age, secondary causes of seizure become more frequent and consequently seizures are more likely to be focal onset. In our study, 70.1% of the patients presented with focal onset seizure, most due to ischaemic stroke.

In a study from India, Thomas et al found that 12 of 23 patients had focal onset seizure and 56.5% had an identifiable aetiology.[8] However, all of the patients in this study were investigated before MRI scanning was available, which would have probably led to a diagnosis of 'unknown aetiology' in several of those cases.

In a more recent study from Canada, Holt-Seitz et al found that 88% of their cases presented with focal onset epilepsy and only 55% had an identifiable aetiology (acute symptomatic in 49% and remote symptomatic in 6%).[3] In contrast, in our study, all of our patients had neuroimaging (MRI or CT of the brain) and we identified the aetiology in 89.9%. Cerebrovascular disease is the single most common pathology underlying epilepsy in elderly people, and in our study, similar to the study of Paradowski and Zagrajek,[4] the most common aetiology was ischaemic stroke (16.2%) followed by haemorrhagic stroke (14.7%). The majority of our patients were treated with long-term antiepileptic drugs, even after the first seizure. Unacceptable side effects from the antiepileptic drugs were seen in 43% of cases receiving the standard dosage regimen. Two patients died over the one to one-and-a-half year follow up period of the study, but this is not excessive given that this was an elderly population. Of the one to one-and-a-half year survivors in our study, 34% had had recurrent seizure, which is a little

higher than other studies, which have reported recurrent seizures ranging from 11% to 28% in one to one-and-a-half years follow up.[4,9] Of those patients with a previous history of stroke in our study, recurrent seizures recurred in more than 72% similar to the rate as reported by Luhdorf, et al[10] in which there was seizure recurrence in more than 80% of elderly patients with a history of stroke. Status epilepticus de novo frequently occurs in the elderly with no prior history of epilepsy and represents a considerable risk for the subsequent development of epilepsy.[5] Our study found that status epilepticus presented as a first seizure in elderly patients in 21.6% of cases, and among those, 61.7% had recurrent seizure.[11,12] Our study found, as other studies, that epileptiform activity on an EEG was a risk factor for recurrent seizure,[11] and nonspecific abnormality on EEG were the main risk factors of recurrent seizure.

Stroke is the most important risk factor for the development of subsequent epilepsy in the elderly and there seems to be a bidirectional association between epilepsy and cerebrovascular disease in older people with the risk of stroke increased by nearly three-fold in those who develop late-onset seizures.

Depression maybe the most common psychiatric illness in older adults with epilepsy, although some authors have emphasised the potential importance of anxiety disorders.[13] When combined, depression and epilepsy have a greater negative impact on socioeconomic indices than either illness alone.[13] Not only, the sleep and sleep deprivation cause seizures, but epilepsy can also alter the patterns of sleep and contribute to sleep disruption. In our study, we found that depression and anxiety, sleep disorder and stroke were the most common comorbidities associated with late-onset epilepsy. In conclusion, most of the new-onset seizures in our elderly patients were focal onset in nature. This was usually the consequence of a vascular brain lesion, the recurrence was high. The major risk factors for recurrent seizure were acute symptomatic aetiology, remote symptomatic aetiology and progressive symptomatic aetiology, epileptiform discharge on EEG and nonspecific abnormality on EEG.[14] Hypertension, diabetes mellitus and stroke were the most common comorbidities.[15] Based on our results, the implications are firstly, elderly patients maybe at a higher risk of recurrence following an initial stroke than younger people and treatment following a first seizure should be considered, especially in patients who show a structural lesion on MRI of the brain and/or an abnormal EEG.

Secondly, psychological problems, especially depression and anxiety are common comorbidities and elderly patients should receive psychological counselling following a first episode of seizure. Two patients presented with dementia and generalised seizure one had AD and other FTD-CBS. Using data from both CHS and CMS, they found that epilepsy in older adults was common, prevalent in 3.7% of individuals at baseline and affecting 5.7% of the cohort by the end of 14 years of follow-up.[16] The overall incidence of epilepsy in this cohort was 2.47 per 1,000 person-years making it 1.5 times more common than what has been reported for Parkinson disease in older adults.[17] They confirmed that independent predictors of developing epilepsy after age 65 included advanced age, black race and history of both prevalent and incident stroke.[18] Prevalent coronary heart disease, obesity at baseline and incident congestive heart failure diagnosed during the CHS follow-up were independently associated with a reduced risk of incident epilepsy.[19]

Their estimated point prevalence of epilepsy at baseline was higher than previously reported for community-dwelling older adults, possibly reflecting differences in methods of case ascertainment. However, there incidence rate was nearly identical to that in a study that used CMS outpatient diagnosis codes. A review of methods for identifying epilepsy with administrative and claims data showed that positive predictive values can vary across studies. A prior study examining the validity of different algorithms for identifying cases with epilepsy in administrative data found that the probability of detecting epilepsy increased with increasing numbers of ICD-9 codes. The ability to detect cases with epilepsy increased even further when prescription data were combined with ICD-9 codes. Their criteria required multiple diagnosis codes and took into account whether they were submitted by neurologists or non-neurologists. Additionally, their criteria required other sources of data such as hospitalisation discharge ICD-9 codes, use of antiepileptic medications, and self-report, likely further improving the detection of participants with epilepsy. A recent study examining all sectors of the US population found a prevalence estimate of 8.5 cases per 1,000 persons and documented age-specific estimates of epilepsy incidence similar to those of other studies with higher rates in persons 5 or 6 years of age.[20] Disparity in risk by race was the most salient finding in our study.

Blacks had a greater likelihood of having prevalent epilepsy and increased risk of developing incident epilepsy after age 65.[21,22] Both population-based and tertiary care center studies have shown that older black persons have nearly double the incidence rate of epilepsy compared to whites, a finding consistent with their estimates. Stroke is the most common known cause of epilepsy in the older adult population and blacks have a 2-fold increased risk of stroke compared with whites living in the same community. Emerging data from genetic studies suggest that ethnicity may have a role in genetic causes of epilepsy in specific populations.

In contrast to previous studies in which the incidence rate of epilepsy among older adults increased linearly with age. We found that the risk was nonlinear being highest in the 75- to 79-year-old group compared to other 5-year groups ranging from 65 to 80 years of age. The incidence rate for the 80-year-old group actually decreased similar to other studies that found the lowest risk among the oldest age group (85 years old). These findings raise the question of the specific age range in which susceptibility to incident epilepsy maybe higher or lower. On the other hand, lower risk in the oldest age groups maybe an effect of survivor bias, a selection bias whereby healthy people are selectively

retained, while unhealthy people say those with epilepsy die. A number of sociodemographic and clinical factors were significantly associated with incident epilepsy. Participants with a highest level of education (graduate/professional) had the lowest incidence of epilepsy in the unadjusted analysis. We do not believe that this is a result of reverse causality, in which epilepsy leads to lower educational attainment, because participants' education was completed long before enrolment in CHS or age 65.[22]

This particular finding raises the question of socioeconomic status serving as an independent risk factor or a proxy for some other risk factor for epilepsy in older adults, not confounded by other risk factors such as cerebrovascular disease.

We also found no sex differences similar to what others have reported in the past. In another study of epilepsy in older adults, women were slightly more likely to have incident epilepsy than men. However, this finding was confounded by women living longer than men, when adjusted for age difference, the incidence rates for women were in fact slightly lower than for men.

Study Name	Most Common Seizure Type (Focal) and Frequency
Our study	70.1%
Thomas et al	56.5%
Paradowski and Zagrajek et al	62.5%
Hoh-Seitz et al	88%

Table 2. Comparison of Our Studies with Other Studies

Studies	Patients with Post-Stroke Epilepsy at 1 Year
Bladin et al[18]	3.8% (9 months)
Burn et al[19]	4.2%
So et al[20]	3.0%
Lamy et al[21]	3.1%
Lossius et al[22]	2.5%
Roivainen et al[23]	6.9%
Hsu et al[24]	15%

Table 3. Studies in which the Risk of Developing Epilepsy within the First Year has been Described Regarding Cerebrovascular Diseases

CONCLUSION

- In conclusion, most of the new-onset seizures in our elderly patients were focal onset in nature.
- This was usually the consequence of a vascular brain lesion, the recurrence was high.
- The major risk factors for recurrent seizure were acute symptomatic aetiology, remote symptomatic aetiology and progressive symptomatic aetiology, epileptiform discharge on EEG and nonspecific abnormality on EEG.
- Stroke, hypertension, diabetes mellitus and CAD are the most common risk factors.
- Based on our results, the implications are- firstly, elderly patients maybe at a higher risk of recurrence following an initial stroke than younger people and treatment following a first seizure should be considered, especially in patients who show a structural lesion on MRI of the brain and/or an abnormal EEG.

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