A COMPARATIVE STUDY BETWEEN EARLY-ONSET AND LATE-ONSET EPILEPSY IN ELDERLY PATIENTS

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ABSTRACT: Elderly people are a unique subgroup of population with high prevalence and incidence of epilepsies and seizures. Due to demographic trend, elderly people with epilepsy will continue to rise over next decades. In the present study, we aimed at comparison of the etiology, seizure semiology, epilepsy types and antiepileptic drug therapy in early onset and late-onset elderly patients with epilepsy.

SUBJECTS AND METHODS: Prospective study was conducted in a tertiary care centre in Eastern India from January 2012 to April 2013 in consecutive patients who is having seizure disorder and age more than 60 years. Recruited patients were subdivided into young-onset group (Group A: Elderly patient with epilepsy who had first unprovoked seizure before 50 years of age) and late-onset group (Group B: Elderly patient with epilepsy who had first unprovoked seizure after 50 years of age). Clinical data with respect to etiology, seizure and epilepsy types and anti-epileptic drug therapy were assessed using a structured questionnaire.

RESULTS: A total of 194 patients aged 60 or more were included in the study, out of which 112 (57.74%) patients started having seizures after 60 years of age (group B) and remaining patients (42.26%) had seizure onset before 50 years (group A). Mean duration of epilepsy in group A was 46.3 years and 6.3 years in group B ($p < 0.01$). In group B, localization-related symptomatic epilepsies were dominating in frequency as compared to group A ($p < 0.01$). Cerebrovascular diseases were the most common causes of epilepsies in group B patients as compared to group A ($p < 0.01$) and hippocampal sclerosis is extremely rare in group B patients ($p < 0.01$). Postictal neurodeficit was most commonly seen in group B than group A ($p < 0.01$). EEG and brain CT or MRI abnormalities were common in group B than group A ($p < 0.01$). Prolonged higher dosage and polytherapy with antiepileptic drugs were mostly seen in group A as compared to group B ($p < 0.01$).

CONCLUSION: The clinical profile with regard to etiology, epilepsy types, postictal conditions clearly depends on age of the patients and age of onset of epilepsy. Patients with an epilepsy onset after 60 years need lower doses of AEDs gain better seizure control than elderly patients with early-onset epilepsy.

KEYWORDS: Elderly, Seizures, Epilepsy, Symptomatic, AEDs.

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INTRODUCTION: The most rapidly expanding segment of world population is over the age of 65. Due to increased life expectancy, the elderly have become the population segment with the highest growth over the last few years. After stroke and dementia, epileptic seizures and epilepsies constitute the 3rd most frequent neurologic disorders encountered in elderly in developed countries.

Several epidemiologic studies in developed countries have revealed highest incidence and prevalence of seizure disorders in elderly.^{1,2,3} Epilepsy in elderly, compared with the younger adult population differs in etiology, clinical presentation, and prognosis. Additionally, 30% of acute seizures in elderly people present as status epilepticus, which carries a sizeable mortality of about 40%.⁴

Studies have shown that approximately 1 to 2% of aging population has epilepsy and as many as 9.2% of nursing home residents are taking AED medications for the control of seizures. The incidence of epilepsy in patients over 75 years is two to three-fold as compared to younger population.^{5,6} In India, incidence rate of epilepsy in the elderly age group is 23.2/100,000/year.⁷

There is considerable variability in the causes and risk factors for seizures in young and in elderly.^{8,9} Seizures in elderly may have onset at 60 years or above, or onset before 60 years of age.

There is considerable difference in etiology and types of seizures and epilepsies in young and in elderly individuals. Idiopathic epilepsy and primary generalized seizures are rare in elderly who have seizure onset after 60 years of age. Stroke, primary and secondary brain tumors, metabolic and toxic disorders constitute the major causes of seizures and epilepsy in late-onset elderly epilepsy.

On the other hand, idiopathic epilepsies are common in young onset epilepsy. Infections, drugs and toxins, head trauma are the most common causes of seizures and epilepsies in this age group. Mixed etiologies are not uncommon in elderly patients with epilepsy.⁸

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In this paper we are trying to compare etiology, seizure and epilepsy types, different EEG and neuroimaging findings and antiepileptic drug therapy in early-onset and late-onset epilepsy in elderly.

SUBJECTS AND METHODS: This prospective study was conducted in a tertiary care centre in Eastern India from January 2012 to April 2013 in consecutive patients who is having seizure disorder and age more than 60 years. All recruited patients and their caregivers were interviewed and relevant records relating to the illness were reviewed.

The following data was obtained in a structured questionnaire, age of onset of seizure, seizure type and epilepsy type, risk factors of seizure and epilepsy, current and past antiepileptic drug therapy and drug related side effects. Electroencephalogram(EEG), computed tomography(CT) and MRI brain with epilepsy protocol was performed in all cases. Classification of seizure and epilepsy was done as per ILAE

classification 1981/1989. Recruited patients were divided into two groups.

Group A (Early-onset elderly epilepsy) - Elderly patient with epilepsy who had first unprovoked seizure before 50 years of age.

Group B (Late-onset elderly epilepsy) - Elderly patient with epilepsy who had first unprovoked seizure after 50 years of age.

Finally, a comparison was made between early-onset and late-onset elderly epilepsy. Ethical clearance was taken from institutional ethical committee and study was conducted after taking written informed consent from all patients.

RESULTS: In total, 194 patients age more than 60 years were included in the study. Eighty-two patients (42.26%) were elderly patient with early-onset epilepsy (Group A) and 112 patients (57.74%) were elderly patients with late-onset epilepsy (Group B).

Characteristics	Elderly patients with early-onset epilepsy (n=82) Group A	Elderly patients with late-onset epilepsy (n=112) Group B
Age (years) (mean±SD, range)	67.2±5.4 60-75	76.2±9.1 61-82
Age at epilepsy onset (years) (meanSD, range)	29± 19.2 8-49	69± 7.5 50-79
Epilepsy duration (years) (mean±SD, range)	46.3±12.2 11-74	6.3±3.1 0-14
Table 1: Demographic data, age at epilepsy onset and duration of epilepsy in elderly patients with late or early-onset epilepsy.		

Epilepsy Syndromes	Elderly patients with early-onset epilepsy (n=82) Group A (%)	Elderly patients with late-onset epilepsy (n=112) Group B	P-value
Localization related	58 (70.73)	107 (95.53)	p<0.001
Idiopathic	0	0	
Symptomatic	48 (58.53)	91 (81.25)	
Cryptogenic	10 (12.9)	16 (14.28)	
Generalized	22 (26.82)	4 (3.57)	p<0.001
Idiopathic	14 (17.07)	0	
Symptomatic	2 (2.4)	0	
Cryptogenic	6 (7.3)	4 (3.57)	
Not classifiable	2 (2.4)	1 (0.8)	ns
Etiology of Epilepsy	Group A	Group B	P-value
Cerebrovascular diseases	8 (9.7)	66 (58.9)	p<0.0001
Head trauma	10 (12.9)	5 (4.4)	ns
CNS infections	14 (17.07)	8 (7.14)	p<0.03
Tumors	2 (2.4)	8 (7.14)	ns
Vascular malformation	1(1.2)	0	ns
Hippocampal sclerosis	14 (17.07)	0	p<0.0001
Dementia	0	4(3.57)	ns
Tuberous sclerosis	1 (1.2)	0	ns
Cryptogenic	16 (19.5)	20 (17.8)	p<0.001
Idiopathic	14 (17.07)	0	p<0.0001
Table 2: Epilepsy syndromes and etiology in elderly patients with late-onset and early-onset epilepsy.			

Age of patients and duration of epilepsy Table 1 shows the differences in age and duration of epilepsy in Group A and Group B. Patients in group B were 9 years older than patients in group A. Mean duration of epilepsy in group A 46.3 years

and 6.3 years in group B. This difference in mean duration of epilepsy in two groups is statistically significant (p<0.01).

Two groups differed significantly with respect to etiology, type of seizures and epilepsies ($p<0.01$). Table 2 and 3 shows difference in etiology, type of seizures and epilepsy between group A and group B. In group B, localization-related symptomatic epilepsies were dominating in frequency as compared to group A ($p<0.01$). On the other hand, generalized seizures and idiopathic epilepsies were rare in group B ($p<0.01$).

Cerebrovascular diseases were the most common causes of epilepsies in group B patients as compared to group A ($p<0.01$) and hippocampal sclerosis is extremely rare in group B patients ($p<0.0001$). Partial seizures were dominating seizure type in both the groups, but percentage was much more higher in group B ($p<0.01$) and generalized seizures is less common in group B as compared to group A ($p<0.01$).

	Elderly patients with early-onset epilepsy (n=82) Group A (%)	Elderly patients with late-onset epilepsy (n=112) Group B (%)	P-value
Partial seizure	52 (63.4)	104 (92.85)	$p<0.0001$
Simple partial	12 (14.6)	37 (33.03)	
Complex partial	14 (17.07)	12 (10.71)	
Secondarily generalized	26 (13.7)	55 (49.1)	
Generalized seizure	28 (34.14)	8 (7.1)	$p<0.0001$
Tonic-clonic	22 (26.8)	6 (5.3)	
Tonic	2 (2.4)	1 (0.8)	
Absences	1 (1.2)	0	
Myoclonic	4 (4.8)	0	
Unclassifiable	2 (2.4)	1 (0.8)	Ns

Table 3: Seizure types in elderly patients with late and early-onset epilepsy

Postictal Stage:

Neurodeficit reported by patients more often in group B than group A ($p<0.01$) and there was no significant difference

in postictal confusion, headache, memory disturbance, aphasia in two groups (Table 4).

	Elderly patients with early-onset epilepsy (n=82) Group A	Elderly patients with late-onset epilepsy (n=112) Group B	P-value
Postictal confusion	42 (51.21)	66 (58.9)	ns
Neurodeficit	26 (31.7)	58 (51.7)	$p<0.0001$
Headache	19 (23.1)	32 (28.5)	ns
Memory disturbance	4 (4.8)	9 (8.0)	ns
Aphasia	5 (6.09)	12 (10.7)	ns
Psychosis	3 (3.6)	7 (6.1)	ns
Others	4 (4.8)	8 (7.1)	Ns

Table 4: Postictal state in elderly patients with late and early-onset epilepsy.

	Elderly patients with early-onset epilepsy (n=82) Group A	Elderly patients with late-onset epilepsy (n=112) Group B	P-value
Abnormal EEG	23(28.04%)	50(44.64%)	$p<0.01$
Abnormal CT or MRI brain	42(51.21%)	86(76.79%)	$p<0.01$

Table 5: Electroencephalography and CT/MRI brain in elderly patients with late-onset and early-onset epilepsy

EEG and neuroimaging findings Table 5. shows difference in EEG and neuroimaging abnormalities in two groups. EEG abnormalities were most frequently seen among group B than group A patients ($p<0.01$). Brain CT or MRI was abnormal frequently in group B than group A ($p<0.01$).

Anti-Epileptic Drugs:

Within the two groups, there was a clear difference with respect to the applied AED. Number of patients receiving more than one AEDs (polytherapy) at higher dosage was significantly higher in group A ($p<0.01$) and phenytoin was the most common AED received by both groups. Reported incidence of adverse effects related to AEDs were higher in group A as compared to group B. Table 6 shows antiepileptic drugs profiles in both the groups.

	Elderly patients with early-onset epilepsy(n=82) Group A		Elderly patients with late-onset epilepsy(n=112) Group B		P-value
	Total Recipient (%)	Dosage mean±SD,range	Total Recipient (%)	Dosage mean±SD,range	
Phenytoin	36 (43.9)	350±26(200-400)	67 (59.8)	250±52.6(200-400)	p<0.01
Phenobarbitone	14 (17.07)	102±32.2(60-180)	2 (1.7)	60(60)	p<0.01
Carbamazepine	21 (25.6)	670±45.2(400-1200)	30 (26.7)	550±22.8(400-1000)	p<0.01
Sod. valproate	20 (24.3)	1400±52.6(1000-2000)	10 (8.9)	740±52.2(600-1500)	p<0.01
Levetiracetum	22 (26.8)	2050±12.8(1000-3000)	21 (18.7)	1450±42.2(1000-2000)	p<0.01
Clobazam	41 (50)	18±4.3(5-30)	35 (31.2)	14.1±2.2(5-20)	p<0.01
Oxcarbazepine	9 (10.9)	1200±72.5(900-1800)	6 (5.3)	1050±42.8(900-1200)	p<0.01
Lamotrigine	9 (10.9)	110±35.2(50-200)	0	0	p<0.0001
	Group A		Group B		p-value
Monotherapy	25 (30.4)		78 (69.6)		p<0.001
Polytherapy	57 (69.5)		34 (31.3)		p<0.0001
Adverse effects of AEDs	42 (51.2)		37 (33.03)		p<0.05
Table 6: Antiepileptic drug profiles of elderly patients with late-onset and early-onset epilepsy					

DISCUSSION: The study indicates that late-onset epilepsies differ in several aspects from early-onset epilepsies in elderly patients. In late-onset epilepsies in elderly localization related symptomatic epilepsies were the predominant epilepsy type, also described by Stefan et al.¹⁰ Cerebrovascular diseases constituted major cause of epilepsy in late-onset epilepsies in elderly as previously described by Loiseau et al.¹¹ On the other hand hippocampal sclerosis and idiopathic epilepsies are rare in late-onset epilepsies seen in our study, was also described by Stefan et al. Due to frequently encountered structural pathology in elderly patients, partial seizures were the most common seizure type in elderly-onset epilepsies.

As far as semiology of seizure is concerned, partial seizure with secondary generalization were the most common seizure type found in late-onset epilepsy in elderly followed by simple partial seizure, which was similar to previous study done by Sundaram. Sundaram in his study of 67 patients with epilepsy found partial seizures in 45 (67%) and generalized seizures in 22 (33%) elderly patients.¹²

There is significant difference in postictal manifestations of elderly patients with epilepsy from younger patients with epilepsy. Patients with late-onset epilepsy may be less handicapped by the ictal manifestation than by prolonged postictal paresis, which occur in our comparison more frequently than younger patients. Higher incidences of abnormal EEG in elderly-onset patients than early-onset group was due to presence of greater proportion of patients with symptomatic epilepsies or presence of greater proportion of patients with vascular diseases and structural abnormalities in the brain.¹³

There was higher proportion of patients with abnormal MRI and CT brain in elderly onset group, which is likely to be due to increased proportion of patients with symptomatic epilepsies in this age group. With respect to treatment of elderly patients, anticonvulsant dosage and number of AEDs often lower in elderly-onset epilepsies as compared to younger-onset epilepsies as previously described by Besocke et al.¹⁴ and Arain et al.¹⁵ In the present study, patients who

were having epilepsy from younger age required multiple antiepileptic drugs with increase in dosage than elderly onset group. Similarly Hiyoshi et al.,¹⁶ reported that mean number of antiepileptics used in the early onset group (<20 yrs) was 2.3, intermediate onset (20-49yrs) was 1.5 and 1.1 in late onset group, which clearly demonstrated that early onset group required more polytherapy.¹⁶ Though incidence of adverse effects of AEDs are more common in elderly patients, in this study higher percentage of adverse effects in early onset group was due to prolonged use and higher dosage of antiepileptic drugs in this group.

CONCLUSION: Epilepsy in the elderly is an important and growing problem. The clinical manifestations, etiology, investigation findings and treatment are different from those in younger patients. This study may stimulate further systemic comparisons of clinical characteristics of epilepsies in different ages, which may lead to further developments of age-related understanding of epileptogenesis and consecutive elaborated treatment strategies.

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