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ORIGINAL ARTICLE / KLİNİK ÇALIŞMA

Short-Term Mortality in Adult Patients With Seizures Admitted to the Emergency Department and a Comparison of the First and Recurrent Seizure

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Acil Servise Nöbet Nedeniyle Başvuran Hastalarda Erken Dönem Mortalite ve İlk Nöbet-Tekrar Nöbetlerin Karşılaştırıma

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Summary

Objectives: Patients with seizures constitute 1%–2% of all emergency department (ED) admissions. The purpose of this study was to compare demographic and clinical characteristics and short-term mortality in patients with unprovoked first and recurrent seizures, admitted to the ED.

Methods: This prospectively planned study was conducted in a university hospital ED between January and December, 2015, and included patients with unprovoked seizures. Demographic characteristics, neurological examination findings, etiological risk factors, seizure type, and frequency, electroencephalography and neuroimaging findings, hospitalization rate, duration of hospitalization, short-term mortality, and medical and family history data were recorded.

Results: A total of 125 patients (62.4% male, n=78) with a mean age of 40.10±17.09 years (range, 18–86) were included in the study. The level of patients presenting due to first lifetime seizure was 23.2%. The short-term mortality rate in patients with status epilepticus (SE) was 7.69%. The most common finding at electroencephalography was interictal epileptic discharges.

Conclusion: A careful evaluation of cases presenting due to first lifetime seizure and initiation of antiepileptic drug therapy in the early period will significantly reduce the risk of seizure recurrence and also prevent complications, such as SE that can even result in death.

Keywords: Electroencephalography; emergency; first-seizure; mortality; status epilepticus; unprovoked seizure.

Özet

Amaç: Acil servis başvurularının %1–2'si nöbet geçirme nedeniyle başvuran hastalardan oluşmaktadır. Bu çalışmada acil servise ilk nöbet ya da rekürren nöbet nedeniyle başvuran hastalarda klinik ve demografik özelliklerin karşılaştırılması ve bu hastalarda kısa dönem mortalitenin belirlenmesi amaçlanmıştır.

Gereç ve Yöntem: İleriye yönelik olarak planlanan bu çalışmaya bir üniversite hastanesinin acil servisine Ocak 2015–Aralık 2015 arasında non-provoke nöbet nedeniyle başvuran hastalar alınmıştır. Başvuru nöbet sıklığına göre hastalar tek nöbet, sık nöbet ve status epileptikus olarak üç gruba ayrıldı. Demografik özellikler, özgeçmiş ve soygeçmiş özellikleri, nörolojik muayene, epilepsi risk faktörleri, nöbet tipi ve sıklığı, elektroensefalografi, nörogörüntüleme, hastaneye yatış oranı, ortalama yatış süresi ve kısa dönem mortalite veri formuna kaydedildi.

Bulgular: Çalışmaya yaş ortalaması 40.10±17.09 (18–86) olan toplam 125 hasta (%62.4'ü erkek, n=78) alındı. Hastaların %23.2'si (n=29) ilk nöbet nedeniyle başvurdu. Status epileptikus olgularında kısa dönem mortalite oranı %7.69 idi. En sık elektroensefalografi bulgusu interiktal epileptik boşalımlar olarak dikkati çekti.

Sonuç: Acil servise nöbet nedeniyle başvuran hastalarda doğru ve hızlı tanı konulmalı, gerekirse yatış yapılarak nöbet gözlemlenmeye çalışılmalıdır. İlk nöbet ile başvuran hastalarda dikkatli bir değerlendirme ve erken dönemde antiepileptik tedavi başlanması hem nöbet tekrarını hem de status epileptikus ve onun yıkıcı bir komplikasyonu olan mortalite riskini azaltacaktır.

Anahtar sözcükler: Elektroensefalografi; acil servis; ilk nöbet; mortalite non-provoke nöbet; status epileptikus.

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Introduction

Approximately 8%–10% of the population undergoes at least one seizure during the afebrile period.[1] Patients with seizures are generally first evaluated in the emergency department (ED). Approximately 1%–2% of ED patients are reported to have epileptic seizures.[2]

Not all attacks described as seizures by patients or relatives are epileptic seizures. They can also be provoked seizures, syncope, or non-epileptic psychogenic attacks. Provoked seizures are acute transient seizures occurring in the central nervous system for metabolic, toxic, structural, infectious, or inflammatory reasons, and therefore with a temporal relation between them (generally the first 7 days).[3] Provoked seizures recur very rarely and do not generally require antiepileptic drug (AED) therapy.[4,5]

In addition, some patients may experience a first lifetime seizure. The incidence of seizure recurrence in first-seizure patients is reported to range between 3% and 10% in acute symptomatic or provoked seizures, and between 23% and 71% in unprovoked seizures.[6–8] Seizure symptomatology and electroencephalography (EEG) and neuroimaging findings must not be overlooked in terms of early and accurate diagnosis and early initiation of AEI therapy, especially in patients presenting to the ED with first-seizure. However, EEG is not always available in the early period of the disease, especially in the ED. It is frequently performed in outpatient clinics in the following days, although some patients are not referred to the outpatient clinic, so epilepsy may be either diagnosed late or not at all.

Status epilepticus (SE) is defined in the 2015 International League Against Epilepsy guideline as recurring seizures exceeding 5 min (generalized convulsive SE) or 10 min (focal SE) in duration or not permitting a return to baseline status.[9] SE is the second most common neurological emergency, and it has high mortality and morbidity risk.[10] Seven percent of these patients are referred to the ED with SE.[11] The management of SE in the ED is particularly important in terms of clinical course and prognosis. The mortality rate in the first month after SE was reported to be 31.7% by Hocker et al.,[12] 21% by Classen,[13] 16.9% by Moghaddasi et al.,[10] and 3.45% by Koubeissi.[14]

The purpose of this prospective study was to determine demographic and clinical features, electroencephalographic and neuroimaging findings and mortality in the acute period of patients admitted to the ED with seizure, and to compare the first unprovoked seizures and recurrent seizures.

Materials and Methods

This single-center, prospective observational study was conducted between January and December, 2015, in a university hospital. Unprovoked and provoked seizures, syncope, and non-epileptic psychogenic attacks were diagnosed by a neurologist specializing in epilepsy. Informed consent forms were obtained from patients or their relatives. The study was approved by the University Ethics Committee.

Participants

Consecutive patients aged 18 years or older who provided informed consent forms (either personally or from first-degree relatives) were included in the study. Patients with recurrent ED admissions were included only once in the study, represented by the first presentation. Since seizures in the first 7 days associated with alcohol dependence, medication discontinuation, metabolic disease (such as hyponatremia, hypocalcemia, uremia, and advance stage live disease), and acute cerebral lesions (such as acute stroke) were regarded as provoked seizures, these were not included in the study. Additionally, patients diagnosed with syncope or non-epileptic psychogenic attack were excluded from the study.

Following emergency measures and clinical stabilization, patients and their relatives were asked about the history of seizures. Patients were also divided into three groups, depending on the frequency of seizures on admission: a single-seizure group, a frequent seizure group, and a SE group. Patients who had two or more seizures on the admission day, but were not diagnosed as SE, were considered to constitute the frequent seizure group. Demographics, etiological risk factors, seizure type and frequency, hospitalization, AEDs, and medical and family history data were recorded. Etiological risk factors investigated included head trauma, febrile convulsions, interventional or difficult birth, a family history of epilepsy, parental consanguinity, central nervous system infection, cerebrovascular disease, and tumor. In addition, cases presenting to the ED due to first lifetime seizure and patients with a previous history of seizures were identified. Patients with first-seizure were referred to

the epilepsy outpatient clinic and evaluated for appropriate antiepileptic therapy on the basis of a detailed seizure history, neurological examination, and laboratory findings. Focal and generalized seizures were classified depending on the seizure type.

Examinations

EEG

All patients underwent EEG within the first 24 h after admission. This was performed using the international 10–20 system with a 16-channel, 21-electrode digital EEG device. Thirty-minute routine EEG recordings, including hyperventilation and photic stimulation, were performed by certified EEG technicians. Cases were classified as normal, interictal epileptic discharges, and focal or generalized slowing, depending on the EEG traces.

Neuroimaging

Magnetic resonance imaging (MRI) of the brain was performed in all patients in the first 7 days after admission. MRI findings were evaluated by a radiologist blinded to the patient's clinical status. Patients were divided into two groups, based on the neuroimaging results: Group 1, normal; Group 2, abnormal.

Statistical analysis

A statistical analysis was performed using the Statistical Package for the Social Sciences version 16.0 software (SSPS Inc., Chicago, IL, USA). Normal distribution of data was assessed using the Kolmogorov–Smirnov test. Parametric tests were applied in the analysis of normally distributed data, and non-parametric tests were applied for non-normal distribution. Descriptive statistics (number–percentage, mean, standard deviation, and minimum–maximum) were used in the evaluation of continuous and censored variables. The chi-squared and Fisher's exact tests were used to compare categorical variables between groups. Statistical significance was set at $p<0.05$.

Results

A total of 253 consecutive patients were evaluated in the ED due to seizure. One hundred and three patients diagnosed with provoked seizure, non-epileptic psychogenic attack, or syncope, and 25 cases assessed as non-provoked seizures, but in which investigations could not be completed, were excluded from the study. One hundred and twenty-five patients diagnosed with unprovoked seizures, 62.4% male (n=78), with a mean age of 40.10±17.09 years (range, 17–86), were finally included in the study. The mean age at the onset of seizure was 30.86±22.54 years (range, 1–85) (Table 1). In terms of seizure frequency on admission, 49.6% (n=50) of patients were in the single-seizure group, 40% (n=62) in the frequent seizure group, and 10.4% (n=13) in the SE group. In this study, non-convulsive SE was diagnosed with EEG findings in two cases of consciousness impairment after a generalized tonic-clonic seizure. A previous history of seizures before presentation to the ED was present in 76.8% (n=96) of patients, while 23.2% (n=29) of cases presented to the ED due to first lifetime seizure. Fifty-four percent (n=27) of patients in the single-seizure group described at least one previous unprovoked seizure, while 46% (n=23) presented with the first lifetime seizure. In addition, 23.1% (n=3) of the patients in the SE group presented due to first-seizure and described no previous history of seizures.

Head injury (15.2%), febrile convulsions (13.6%), and parental consanguinity (14.4%) were the three most common etiological risk factors for epilepsy. In terms of prevalence of presentation seizures, a history of febrile convulsion was more common in the frequent seizure and status group compared to the single-seizure group (p=0.05) (Table 2).

Partial and generalized seizures were similar in frequency (44% vs. 56%) compared to referral seizure types. Generalized seizures were more common than partial seizures in all three groups, although there was no statistically sig-

Table 1. Demographic characteristics

	Single seizure	Frequent seizure	Status epilepticus	Total	p
n (%)	50 (40)	62 (49.6)	13 (10.4)	125	
Sex, n (%)					
Female	22 (44)	22 (35.5)	3 (23.1)	47 (37.6)	0.34
Male	28 (56)	40 (64.5)	10 (76.9)	78 (62.4)	
Mean age	44.66±18.95	34.77±13.31	47.92±18.73	40.1±17.09	0.02
Mean age at onset of seizure	37.98±24.03	22.9±17.49	41.46±26.01	30.86±22.54	<0.01

Table 2. Comparison of clinical features in terms of seizure frequency on admission

	Single seizure	Frequent seizure	Status epilepticus	Total	p
Risk factors for epilepsy n (%)					
Head trauma	1 (7.7)	12 (19.4)	6 (46.2)	19 (15.2)	NS
Febril convulsion	1 (7.7)	13 (21)	3 (23.1)	17 (13.6)	0.05
Brain tumor	6 (12)	5 (8.1)	3 (23.1)	14 (11.2)	NS
Stroke	3 (6)	5 (8.1)	2 (15.4)	10 (8)	NS
Difficult delivery	2 (4)	8 (12.9)	1 (7.7)	11 (8.8)	NS
CNS infection	6 (12)	6 (9.7)	2 (15.4)	14 (11.2)	NS
Family history of epilepsy	5 (10)	7 (11.3)	0	12 (9.6)	NS
Parental consanguinity	9 (18)	9 (14.5)	0	18 (14.4	NS
Seizure type					
Focal	20 (40)	29 (46.8)	6 (46.2)	55 (44)	
Generalized	30 (60)	33 (53.2)	7 (53.8)	70 (56)	NS
EEG (%)					
Normal	16 (32)	15 (22.6)	1 (7.6)	32 (25.6)	
Interictal epileptic discharges	25 (50)	34 (54.8)	6 (46.2)	65 (52)	
Focal slowing	3 (6)	5 (8)	0	28 (6.4)	
Generalized slowing	6 (12)	8 (13)	6 (46.2)	20 (16)	0.01
Neuroimaging (MRI/CT) n (%)					
Normal	20 (40)	27 (43.5)	3 (23.1)	50 (39.2)	
Abnormal	30 (60)	35 (56.5)	10 (76.9)	75 (60.8)	NS
Cerebral infarction, ischemic changes, gliosis	13 (26)	16 (25.8)	5 (38.4)	34 (27.6)	
Cerebral-cerebellar atrophy	1 (2)	3 (4.8)	2 (15.3)	6 (4.9)	
Tissue defect, postoperative changes, leukomalasia	7 (14)	10 (16.1)	3 (23)	20 (16.2)	
Intracranial tumor, arachnoid cyst	6 (12)	4 (6.4)	0	10 (8.1)	
Developmental anomaly	3 (6)	2 (3.2)	0	5 (4)	
AED treatment status					
Patients declared regular treatment	22 (44)	49 (79)	7 (53.8)	78 (62.4)	
Untreated or irregular treatment	28 (56)	13 (21)	6 (46.2)	47 (37.6)	0.001

CNS: Central nervous system; CT: Computerized tomography; EEG: Electroencephalography; AED: Antiepileptic drug; MRI: Magnetic resonance imagination; NS: Not significant.

nificant difference between the groups in terms of seizure types (p>0.05). Interictal epileptic discharges was the most common (52%) EEG finding among all groups. Interictal epileptiform discharges were not related to MRI findings. Generalized seizures were seen in the majority of patients with interictal epileptiform discharges. Cerebral MRI results were compared between the groups according to the seizure frequency on admission, and 60.8% of patients had abnormal findings at MRI. The EEG findings in the majority of patients with abnormal MR findings were also abnormal, although there was no correlation between MRI findings and seizure types. There was no difference between the groups in terms of frequency of seizures on admission at neuroimaging (p=0.39). In terms of treatment status, 46.2% (n=6) of the SE group, 21% (n=13) of the frequent seizure group and 56% (n=28) of the single-seizure group received no or irregular treatment. Since 79% (n=49) of the patients in the frequent seizure group were referred due to frequent seizures while declared regular treatment, this suggests that treatments should be further reviewed for effective AED therapy. The incidence of untreated patients or non-compliant patients was greater in the single-seizure or status group compared to the frequent seizure group (p=0.001) (Table 2).

Women constituted 62.1% (n=16) of the patients presenting with first lifetime seizure and 31.3% (n=31) of the recurrent seizure group (p=0.005). The mean age and age at the onset of seizure were higher in the first lifetime seizure group compared to the recurrent seizure group (p=0.006

Table 3. Comparison of clinical and demographic features in patients presenting with first-seizure and recurrent seizures

	Recurrent seizure	First seizure	p
Sex, n (%)			
Male	29 (30.2)	18 (62.1)	
Female	67 (69.8)	11 (37.9)	0.005
Mean age	37.52±15.33	49.88±20.04	0.006
Mean age at onset of seizure	26.39±20.59	49.88±20.04	<0.001
Risk factors for epilepsy, n (%)			
Head trauma	17 (17.2)	2 (7.7)	NS
Febrile convulsion	16 (16.2)	1 (3.8)	0.06
Brain tumor	11 (11.1)	3 (11.5)	NS
Stroke	8 (8.1)	2 (7.7)	NS
Difficult delivery	11 (11.1)	0	0.07
CNS infection	10 (10.1)	4 (15.4)	NS
Family history of epilepsy	11 (11.1)	1 (3.8)	NS
Parental consanguinity	13 (13.1)	5 (19.2)	NS
Neurological exam			
Normal	63 (65.3)	17 (59.7)	
Abnormal	33 (34.7)	12 (41.3)	NS
Seizure type, n (%)			
Focal	43 (44.7)	12 (41.3)	
Generalized	53 (55.3)	17 (59.7)	NS
Electoencephalography, n (%)			
Normal	24 (25)	8 (27.7)	
Interictal epileptic discharges	53 (55.2)	12 (41.3)	
Focal slowing	5 (4.7)	4 (13.7)	
Generalized slowing	14 (15.1)	5 (17.3)	NS
Neuroimaging, n (%)			
Normal	39 (40.6)	11 (37.9)	
Abnormal	57 (59.4)	18 (62.1)	NS
Cerebral infarction, ischemic changes, gliosis	28 (29.1)	7 (24.1)	
Cerebral-cerebellar atrophy	4 (4.2)	3 (10.3)	
Tissue defect, postoperative changes, leukomalasia	18 (18.7)	3 (10.3)	
Intracranial tumor, arachnoid cyst	5 (5.2)	4 (13.8)	
Developmental anomaly	2 (2.1)	1 (3.7)	

NS: Not significant.

and p<0.001, respectively). When the two groups were evaluated in terms of epilepsy risk factors, histories of febrile convulsions, and of difficult birth were higher in the recurrent seizure group (p=0.06 and p=0.07, respectively). No statistically significant difference was observed between the recurrent- and first-seizure groups in terms of seizure type, EEG, or neuroimaging findings (p>0.05) (Table 3).

In this study, 10.4% of patients had SE, one of whom died. The mortality rate among our SE patients was 7.69%. Ischemic stroke and subsequent pneumonic sepsis were regarded as the cause of death in a 76-year-old patient.

Discussion

The number of patients admitted to the ED with seizure symptoms is very high. Seizures account for 1% of all ED admissions in the United States.[2] However, the number of cases evaluated as unprovoked seizures is much lower. Approximately, 6% of these patients are SE, whereas 24% of them are first seizures.[15] In our study, 10.3% of the patients had SE, and 23.2% had the first-seizure, in agreement with the previous literature. It was also noteworthy that the three patients presenting with first-seizure presented with a manifestation of SE.

Epilepsy risk factors vary depending on age. Head trauma, central nervous system infections, and brain tumors are antagonistic as risk factors for all age groups.[16] Cerebrovascular diseases are the most common risk factor in patients over 60.[17] Annegers et al.[18] reported that the most common seizure etiologies were head trauma (16%), cerebrovascular diseases (16%), and infections (15%). The most common risk factors for epilepsy identified in our study were head trauma, febrile convulsion history, and parental consanguinity.

Paliwal et al.[19] reported 29.4% abnormal EEG in 136 first-seizure patients, and focal epileptiform abnormality is the most seen abnormal EEG finding. They reported abnormal neuroimaging in 14.7% of patients. In our study, abnormal EEG was found in 72.3% of the first-seizure patients, and the most common abnormal EEG finding is interictal epileptic discharges. We found abnormal neuroimaging in 62.1% of first-seizure patients. Paliwal et al. used MRI as neuroimaging in 33.6% of patients, although we used MRI in all of our patients. This can be explained by the fact that abnormal MRI findings are more common in our patients. The presence of abnormal EEG and neuroimaging in patients undergoing first unprovoked seizures are important factors indicating a high risk of recurrence.[8]

Some studies have reported rates of epileptiform activity changes between 20% and 50% at EEG performed within the first 24–48 h among ED patients with first-seizure symptoms.[5,20–22] In this study, the presence of interictal epileptic discharges at EEG was 42.3% in patients with first seizures. In first-seizure patients, early EEG is more likely to be epileptic than late EEG (50% vs. 34%).[20] In our study, EEG was performed in the early period. Successful seizure control is achieved with initial monotherapy in 47% of patients referred for first epileptic seizures and diagnosed with epilepsy.[23] Wyman et al.[24] reported that 24% (n=17) of 71 patients presenting with first-seizure were started on AEDs and that epilepsy was diagnosed in 88% of patients receiving AED therapy based on EEG findings. Abnormal but non-epileptic EEG findings were detected in 25% of patients. In our study, EEG was normal in 26.9% of first-seizure patients, while in 30.8% of cases, EEG was not epileptic, but focal, or subcortical slowing was detected.

It has been reported that the risk of recurrence is high in the first-seizure patients with EEG abnormalities, a prior brain lesion, a significant brain imaging abnormality, and a nocturnal seizure.[3] The 1-year risk of seizure recurrence has been reported to decrease between 35% and 57% with AED therapy in patients identified as undergoing non-provoked seizures, while the 3-year risk of seizure recurrence decreased between 50% and 72%.[25] The most important issue to be decided in the ED in patients with seizures is whether or not the subject is provoked for seizure. In addition, whether the patient is undergoing a first episode, and whether this first episode is unprovoked, require careful neurological evaluation in terms of epilepsy. In our study, AED therapy was initiated in 55.1% of the first-seizure group. Unfortunately, our patients with first-seizure did not have long-term follow-ups.

The risk of life-long acute symptomatic seizures has been reported at 5.0% in men and 2.7% in women in the United States, and it is 1.85-fold higher in men than women.[18] However, the risk of epileptic seizures is only slightly higher in men than in women.[26] In this study, the male-to-female ratio was 1.65 in patients presenting to the ED due to an epileptic seizure.

First 30-day mortality rates ranging between 2.7% and 32% have been reported in SE cases.[27] A mortality rate for refractory SE is three times greater than for non-refractory SE.[28] In this study, the mortality rate was 7.69% among SE patients, and the patient who died was diagnosed with refractory SE.

Our study limitations were the number of patients and the lack of long-term follow-ups of first-seizure patients.

Conclusions

A careful and detailed evaluation of patients with first seizures is important for diagnosis of epilepsy. A detailed history of seizures, completion of examinations with hospitalization if necessary, observation of the seizure for a sufficient length of time for diagnosis in this patient group, and immediate initiation of AED therapy in subjects diagnosed with epilepsy are most important in terms of the course and prognosis of the disease. The next presentation by a patient with inadequate treatment or not receiving AED therapy may be due to frequent seizures or SE, sometimes resulting in long-term hospitalization, and even worse, in mortality and morbidity.

Ethics Committee Approval

Ethics committee approved.

Peer-review

Externally peer-reviewed.

Conflict of interest

The authors declare that they have no conflict of interest.

Authorship Contributions

Concept: T.D., K.A., H.B.; Design: T.D., K.A.; Supervision: H.B., Z.K.; Materials: T.D., G.K.Ş.; Data collection &/or processing: T.D., G.K.Ş.; Analysis and/or interpretation: T.D., K.A., G.K.Ş.; Literature search: T.D., K.A.; Writing: T.D., K.A.; Critical review: H.B., Z.K.

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