Epilepsy in the emergency department: Who needs hospitalization?

Mirac Aysen Unsal1, Ahmet Senel2

1 Clinic of Neurology, Istanbul Sultan Abdulhamid Han Training Hospital, Istanbul, Turkey
2 Clinic of Emergency, Istanbul Sultan Abdulhamid Han Training Hospital, Istanbul, Turkey

Abstract
Aim: Epilepsy is one of the most common serious chronic neurological diseases, imposing a huge economic burden on the individual and the society. Hospital services have been shown to be the highest direct-cost source for epilepsy patients. Therefore, in our study, we planned to discern the indications of hospitalization and the factors affecting the decision to hospitalize.

Material and Methods: Patients admitted to our adult emergency department with epileptic seizures were included in the study between February 2017 and September 2018. A total of 111 patients were recorded in terms of demographic data, preferred transportation method when arriving at the emergency department, anti-epileptic drugs they used, seizure triggers, pre-hospital treatments, duration of seizures, and indication, and duration of hospitalization.

Results: The rate of status epilepticus was lower in patients receiving a single antiepileptic drug compared to patients receiving two antiepileptic drugs and those using three or more antiepileptic drugs. The duration of the hospital stay was longer in patients receiving three or more antiepileptic drugs. Single antiepileptic drug users had a lower rate of hospitalization and a lower rate of intensive care unit admission and pre-hospital ambulance medication.

Conclusion: The most significant variable affecting the study’s results was the number of antiepileptic drugs used by the patients. Patients receiving polytherapy should be considered as a special group, and the effects of this situation on both the individual and the health care system should be examined in more detail.

Keywords: Hospitalization; status epilepticus; status epilepticus in emergency department

INTRODUCTION

Epilepsy is one of the most common serious chronic neurological diseases, affecting 50 million people of all ages. Epilepsy affects people of every nation, sex, race, and income. Especially those living in low- and middle-income countries are subject to a disproportionate burden, both socially and financially (1).

As many studies have emphasized, the two most common causes of the direct cost of epilepsy are antiepileptic drug (AED) costs and hospitalization (2-4).

The basic questions that we expected to answer during this study were the following: How many epilepsy patients visit the emergency room per month? How many of these patients require hospitalization? What are the main factors affecting hospitalization? Do the patient-related factors, the transportation method chosen on arrival to hospital, and pre-hospital treatment methods affect the rate and duration of hospitalization?

For this reason, we collected evidence regarding all these variables by evaluating all records of epilepsy patients who came to the emergency room for 18 months.

MATERIAL and METHODS

Patients

This study was approved by the hospital’s local ethics committee. Patients admitted to our adult emergency department with seizures were included in the study between February 2017 and September 2018. These patients had one or more seizures prior to hospital admission and came to the emergency room by their own choice of transportation, while some of them were still having seizures and were brought to the hospital under the supervision and treatment of health professionals on an ambulance. Patients under 16 years of age were excluded from the study because they were followed up and treated by pediatricians.

A total of 111 patients with seizures were recorded in terms of demographic data, preferred transportation method...
when arriving at the emergency department, AEDs used, seizure triggers, pre-hospital treatments, duration of seizures, and indication and duration of hospitalization. To describe patients with status epilepticus, the definition proposed by Trinka et al. was used (5). Whether the patients were using AEDs or how many AEDs were used to control seizures was classified to emphasize the drug-refractory epilepsy (DRE) group. The indications of epilepsy patients who were hospitalized were divided into three groups: Group 1. Patients who had convulsions cannot be managed adequately in an emergency department. Group 2. Patients had concomitant non-neurological medical conditions (infection, electrolyte imbalance, acute renal failure, malnutrition). Group 3. Patients had accompanying surgical pathologies (trauma, fractures, and dislocations). The pre-hospital treatment method was not compared in the study, since the treatments given in ambulances were intravenous diazepam in all patients.

**Statistical analysis**
All analyses were performed using Statistical Packages for the Social Sciences (SPSS) software Version 24.0 (SPSS Inc. Chicago, USA). Quantitative variables were expressed as mean±SD and/or median (min–max) analyzed with the Kolmogorov–Smirnov test. The student’s t-test or the Mann-Whitney U test was used to compare variables with normal distribution and variables without normal distribution, respectively. Categorical variables were expressed as the number of patients. A chi-square test and Fisher’s exact test were used to compare categorical variables. A P value of less than 0.05 was regarded as statistically significant.

**RESULTS**
A total of 111 patients were included in the study. Demographic data were as follows: The mean age of the 44 female patients was 47.2 ± 15.8, and the mean age of 67 male patients was 43.9 ± 13.6. An average of six patients per month was admitted to the emergency department of our hospital for epilepsy.

There was no significant relationship between age and total hospitalization (n=28), or hospitalization and ICU admission (n=6) (p=0.252, p=0.445). Twenty-six of the patients were diagnosed with status epilepticus in the emergency room. The remaining 85 patients were admitted to the hospital after one or more seizures. There was no difference between status epilepticus and non-status epilepticus patients in terms of age (p=0.715). Moreover, there was no significant difference between age and mean duration of hospital stay between two groups (p=0.856).

Fourteen of 26 patients with status epilepticus were admitted to the hospital by ambulance. The rest were admitted to the hospital by their own transportation method. Status and non-status epilepticus patients were evaluated according to gender, age, whether they use medication for epilepsy, and the number of AEDs used (single AED, two AEDs, three and more AEDs), which transportation method they preferred, and whether treatment was performed in the ambulance.

The relationship between patients using and not using AEDs and hospitalization, ICU admission, ambulance delivery, AED administration in the ambulance, and status epilepticus was investigated and shown in Table 1. The rate of status epilepticus was higher in patients who had not previously used any AEDs (ratio: 4/6, p=0.026). The rate of AED administration in the ambulance was highly significant higher in status epilepticus patients (ratio: 24/28, p= <0.001). The rate of transportation with an ambulance was higher in patients with status epilepticus (ratio: 14/37, p=0.011). The rate of status epilepticus was lower in patients receiving a single AED compared to patients receiving two AEDs and those using three and more AEDs (ratio: 8/69 vs. 14/36, p=0.001). In addition, patients who did not use any AED received more hospitalizations (ratio: 5/6, p=0.004), and these patients were treated in the ambulance before their hospital admission more than AED user patients (ratio: 4/6, p=0.004).

<table>
<thead>
<tr>
<th>No AED users n=6</th>
<th>One AED user n=69</th>
<th>Two AED user n=29</th>
<th>Three and more AED user n=7</th>
<th>Total number:111</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with status epilepticus</td>
<td>Hospitalization</td>
<td>ICU admission</td>
<td>Transport with ambulance</td>
<td>Prehospital treatment</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>1</td>
<td>4</td>
<td>4</td>
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<td>8</td>
<td>9</td>
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<td>3</td>
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Table 1. The relationship between number of antiepileptic drugs (AEDs) used and status epilepticus rate, admission to ICU, transport with ambulance, pre-hospital treatment in ambulance and mean duration of hospital stay
The relationship between single AED users, two AED users, and patients using three and more AEDs, admission to an ICU, transport with an ambulance, AED treatment in an ambulance, and status epilepticus was investigated. Single antiepileptic AED users had a lower rate of hospitalization (n=9, p=0.004), ICU admission (n=1, p=0.002), and pre-hospital ambulance medication (n=8, p <0.001). To increase the number of the second group, the chi-square relationship between the use of a single AED and two and more AEDs and their relationship with hospitalization, admission, and transport with an ambulance, treatment in an ambulance, and the status epilepticus ratio was investigated. The rate of hospitalization, intensive care hospitalization rate, ambulance transportation rate, and ambulance treatment rate of patients using a single AED was found to be lower than those using two and more AEDs (p=0.002; p=0.046, p=0.001, p<0.001).

<table>
<thead>
<tr>
<th>Group</th>
<th>Hospitalization</th>
<th>ICU admission</th>
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<tbody>
<tr>
<td>Group 1. Uncontrolled seizures in emergency department</td>
<td>16</td>
<td>3</td>
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<tr>
<td>Group 2. Concomitant non-neurological medical conditions</td>
<td>11</td>
<td>2</td>
</tr>
<tr>
<td>Group 3. Accompanying surgical pathologies</td>
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<td>1</td>
</tr>
</tbody>
</table>

Three indication groups for hospitalization and ICU admission were compared with patient age and number of AEDs used (indication groups are shown in Table 2). However, no statistically significant difference was found. The relationship was investigated between single AED users, two AED users, and patients using three and more AEDs, medication used in the ambulance, and the mean of hospitalization duration. The duration of the hospital stay was significantly higher in patients using three and more AEDs (p=0.042). No significant relationship was found between the groups of indications for hospitalization and the duration of hospitalization (p=0.28).

Two of the patients included in the study were intubated during ICU hospitalization. Due to the lack of numbers, we could not evaluate them statistically.

**DISCUSSION**

Epilepsy is one of the costliest neurological diseases due to its high prevalence and long-term treatment (6). The cost of diagnostic research, AEDs, surgical treatments, outpatient appointments, routine blood tests and EEG controls, emergency admissions for seizures, surgical interventions due to accidents, and numerous hospitalizations contribute to this cost. Many distinctions in the cost studies of epilepsy are due to variations in methodological approaches. However, hospital services have been shown to be the highest direct cost source for epilepsy patients (7,8).

In our study, we wanted to examine epilepsy patient admissions to the emergency department of a state hospital in one of the biggest cities of our country. One of the outcomes of our study was to investigate whether the factors before the admission to the hospital affect the decision to hospitalize. Consequently, we evaluated demographic data, preferred transportation method when applying to the emergency department, AEDs used, seizure triggers, pre-hospital treatments, and indications and durations of hospitalization. We predicted that prolonged seizure duration, associated complications, and associated non-neurological conditions were the major causes of hospitalization in epilepsy patients. As the early intervention of status epilepticus is one of the most important factors, active treatments started in the ambulance may reduce the progression of the seizure and reduce the complications, hospitalizations, and ICU admission rates.

Drug-refractory epilepsy is the presence of uncontrolled seizures despite the use of two appropriately selected, tolerable AEDs (9,10). To evaluate this group more clearly, we assessed two groups receiving two AEDs and three or more AEDs. In our study, the rate of status epilepticus was lower in patients receiving a single AED than in patients receiving two or more AEDs. The duration of hospital stay was longer in patients receiving three or more AEDs. Single AED users had a lower rate of hospitalization, ICU admission, and pre-hospital ambulance medication. In particular, the most significant results in our study related to the variable number of AEDs used.

Besides all the financial burdens mentioned above, especially in DRE, this burden should be more seriously examined for both the patient and the health care system (11,12). Due to the polytherapy of AEDs, the patient meets several side effects earlier. In addition, morbidities such as depression, anxiety disorder, accidents, and injuries will occur more frequently in the patient’s life and will affect work and private life more prominently (13,14). Strzelczyk et al. noted that DRE patients treated with AED polytherapy were hospitalized more frequently in the three-year follow-up period than the general population and had higher morbidity levels and a sevenfold increase in mortality in three years (15).

The other results of our study are consistent with the general approach of status epilepticus. The rate of transportation with ambulance was higher in patients with status epilepticus, and the rate of AED administration in the ambulance was significantly higher in status epilepticus patients.
The most obvious limitation of our study is the shortness of the time interval. The main target here is to decide how to follow up the patients who are hospitalized more frequently. In the continuation of the study, the existing plans are to follow up with patients frequently who needed hospitalization and how this reflects on the morbidity and burden of the disease.

CONCLUSION
In conclusion, the most significant variable affecting the study’s results was the number of antiepileptic drugs used by the patients. Patients receiving polytherapy should be considered a special group, and the effects of this situation on both the patient and the health care system should be examined in more detail.

Competing interests: The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

Ethical approval: This study was approved by the Institutional Ethics Committee and conducted in compliance with the ethical principles according to the Declaration of Helsinki.

REFERENCES