

Acute seizure epidemiology in a neurological emergency department

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Introduction. Acute seizures in patients with epilepsy are a potential source of neurological damage; their causes must be researched.

Aim. To explore the epidemiology of acute seizure exacerbations in patients with epilepsy in a neurological emergency department in Mexico City.

Patients and methods. Descriptive prospective study of patients with a previous diagnosis of epilepsy that receive medical care in an emergency department due to acute seizures.

Results. 100 patients were analyzed between August 2016 and January 2017. 86 patients presented with focal seizures, of which 76 were focal to bilateral tonic-clonic, 2 with impaired awareness and motor onset, 3 with impaired awareness and non-motor onset, 1 without impaired awareness and motor onset, and 4 without impaired awareness and non-motor onset. 14 patients had generalized seizures with motor onset. The causes of exacerbation were as follows: 26 patients due to antiepileptic dose omission, 21 due to a unknown cause, 19 due to infection, 13 due to sleep deprivation, 3 due to stress, 3 were catamenial, 2 due to alcohol abuse and 3 due to other reasons. Of the 26 patients with dose omission, 10 were due to forgetfulness, 7 refused to comply with their prescription, 6 could not afford to buy their prescription and 3 had their prescription changed by another doctor.

Conclusions. In Mexico, antiepileptic drug dose omission represents up to 25% of patients with acute seizure exacerbations; increased patient education on epilepsy hygiene measures may be an area of opportunity for reducing its frequency.

Key words. Emergency department. Epidemiology. Exacerbation. Non-adherence. Seizures.

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Introduction

Epilepsy is one of the most common non-transmittable neurological diseases in the world with a prevalence of approximately 70 million patients [1]. In Mexico, epilepsy has a prevalence between 10.8 to 20 cases/1,000 persons, which means approximately 2% of the population has epilepsy [2]. Mexico city has a population of 8,851,000, implying that there are 95,000 to 177,000 patients with epilepsy [3].

Patients with epilepsy have thrice as much mortality as healthy controls; key to this risk is the lack of seizure control, which are associated with trauma, fractures, burns, and increased social burden, such as depression and anxiety disorder [4].

Acute seizure exacerbation is defined as an abrupt increase in seizure frequency. Such seizures represent an increase in disease severity, have a low chance of remitting without treatment, and may lead to status epilepticus and neuronal damage [5]. Thus, one way to reduce epilepsy morbidity is preventing acute seizure exacerbations.

Factors that cause seizure exacerbations are defined as those that are associated with an increased

risk of seizures in a relatively brief and defined time period. Most common causes of seizure exacerbation include emotional stress or anxiety, sleep deprivation, dosage omission or treatment non-adherence, menses-related and alcohol use [6]. Other less common causes of acute seizure exacerbation include olfactory, tactile or auditive stimuli, dehydration, contact with hot water and prolonged fasting [7].

In most patients with epilepsy, seizures do not occur in isolation randomly; they are clustered in up to 50% of cases with a well-defined temporal pattern in up to 35% of women. When such patient is coincident with menses, it is defined as catamenial epilepsy [8].

To the best of our knowledge, there are no previous studies that explore the epidemiology and causes of acute seizure exacerbations in Mexican adults. The aim of this study is to carry out the first epidemiological description in Mexico of patients with acute seizure exacerbation that are received in a neurological emergency department, in order to collect information that guides further epilepsy hygiene education.

Table. Demographics of acute seizure exacerbation ($n = 100$).

	%/mean (median) ^a	Range	SD
Mean age (years)	38.5	16-92	15.6
< 65 years	91%		
≥ 65 years	9%		
Years with epilepsy	14.2	0-57	13.2
Focal seizures	86%		
Focal to bilateral tonic-clonic	88.7%		
With impaired awareness and motor onset	0.02%		
With impaired awareness and non motor onset	0.03%		
Without impaired awareness and motor onset	0.01%		
Without impaired awareness and non motor onset	0.04%		
Generalized seizures	14%		
With motor onset	100%		
Monthly seizure frequencies	3.67 (0.62)	0-90	12.04
0 monthly seizures	22%		
0-1 monthly seizures	50%		
> 1 monthly seizure	28%		
Time from last seizure (days)	449 (60)	1-7.665	1.035
1-30 days	36%		
31-365 days	42%		
> 365 days	22%		
Number of seizures in 24 hours	7.59 (2)	0-180	25.9
≤ 1 seizure	30%		
2 seizures	26%		
≥ 3 seizures	44%		
Time from episode start to arrival at hospital (h)	85.5 (12)	1-1.440	218
< 24 h	58%		
24-72 h	24%		
> 72 h	18%		
Patient-provided information	59%		

SD: standard deviation. ^a If there is high data dispersion.

Patients and methods

We carried out the study in the National Institute of Neurology and Neurosurgery of México City. Our hospital's emergency department is exclusively

for neurological disorders. A mean of 15 monthly patients (180 yearly) with acute seizure exacerbations were attended the year before the study. We calculated a required sample of 100 patients with a confidence level of 90%. Beginning on August 28 2016, we sequentially included the first 100 patients that met the inclusion criteria:

- Patients with at least 16 years old.
- A previous diagnosis of epilepsy by a neurologist in the hospital's clinical records.
- Patients with acute seizure exacerbation, defined as two or more seizures in less than 24 hours, an increase of at least 50% in the number of seizures in the last week according to a patients daily seizure estimate, or a patient with at least a single seizure after two months of seizure absence.

Exclusion criteria:

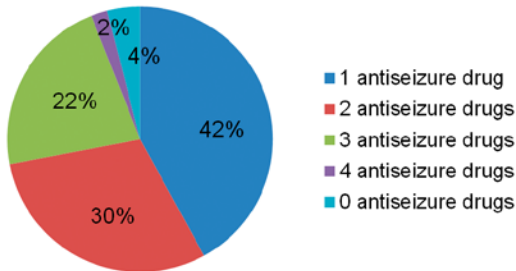
- Patients with a diagnosis of non-epileptic seizures.
- Patients whose epilepsy has not been diagnosed or confirmed by a neurologist in our hospital.
- Patients with more than one visit to the emergency department due to persistent acute seizures (only the first episode is analyzed).
- Patients who declined participation in the study.
- Patients with diagnosis of convulsive or non-convulsive status epilepticus.

Each patient was evaluated by one of the investigators, or, by a resident or staff member, with subsequent validation by one of the investigators.

We classified each patient according to the classification scheme proposed in 2017 by the International League Against Epilepsy (ILAE) [9,10].

- *Seizure type*:
 - a) Focal onset: aware or with impaired awareness; motor or non-motor onset; focal to bilateral tonic-clonic.
 - b) Generalized onset: motor; non-motor.
 - c) Unknown onset: motor; non-motor.
- *Etiology*: genetic, structural, metabolic, infectious, autoimmune or unknown.

We analyzed the following variables: age, gender, epilepsy's evolution time, monthly seizure frequency, date of last seizure before exacerbation, number of seizures in the last 24 hours, hours of seizure exacerbation, hospitalization rate, number and type of antiepileptic drugs used by the patient before the acute episode, most probable cause of the exacerbation, and whether the patient was able to relate his current issue or not. If the cause was due to lack of treatment adherence, we looked into the specific reason behind it. If the cause was an infection, we

Figure 1. Number of antiepileptic drugs used before seizure exacerbation.

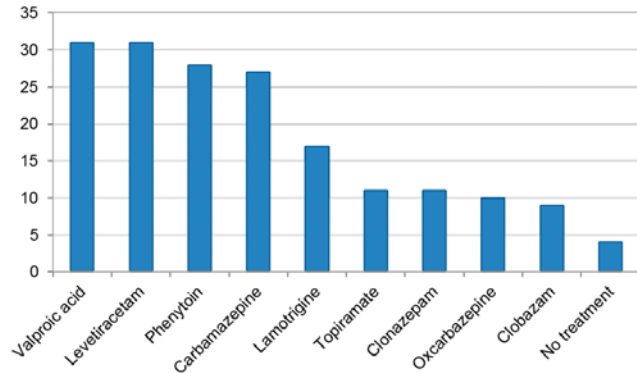
describe the most probable foci. If it was menses-related, we described the day of the cycle in which it occurred. In order to assign stress as the cause of the acute seizure exacerbation, a clear, acute objective event had to be mentioned by the patient.

We described the demographics of the obtained information. For qualitative data, we explored frequencies and percentages. For quantitative data, we explored the mean (median if required) and the standard deviation. We used Microsoft Excel's (2007, v. 12.0) worksheet statistic package.

Results

We analyzed 100 patients between August 2016 and January 2017. 52 patients were male and 48 female. More than 90% of our patients had an age less than 65 years old. There is a great heterogeneity in the epilepsy duration, from 0 to 57 years, although with a mean of 14.2. Most (86%) were focal seizures, with a clear predominance of focal to bilateral tonic-clonic (88.7%). All generalized seizures were classified as generalized motor onset. The seizure frequency was variable, from 0 to 90; half of the patients had a monthly frequency of 0-1 seizure. Time from last seizure was also variable; we found patients with seizure freedom of more than 10 years, although most were in the range between 1 month and 1 year. 44% patients had at least 3 seizures during the day they presented to the hospital. The rest of the demographics are described in the table.

Forty-two patients were on monotherapy by the time they were attended (Fig. 1). The most used antiepileptic drug (Fig. 2) was both valproic acid and levetiracetam (31 patients each). The most frequent cause of acute seizure exacerbation was treatment non-adherence (Fig. 3). However, 20% of the patients had no identifiable cause of seizure exacerbation.

Figure 2. Antiepileptic drugs used before seizure exacerbation.

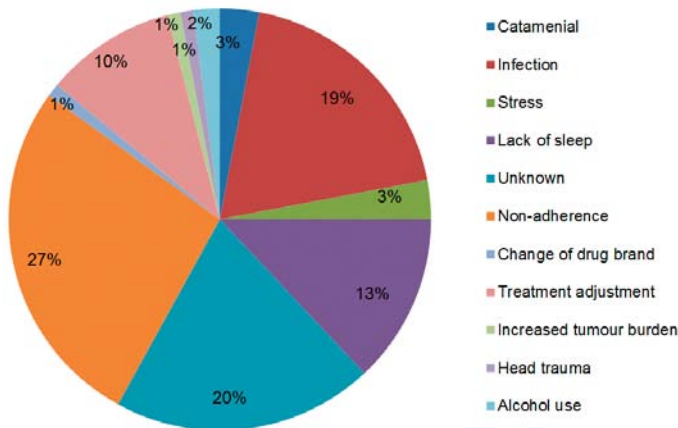
The most frequent cause of treatment non-adherence was dose omission (Fig. 4), which was more frequent than refusal to take the drug, or lack of economical resources. Out of 19 patients with an infectious cause of their seizure exacerbation, 13 were due to respiratory foci, four due to gastrointestinal foci and two due to genitourinary foci. All three patients with catamenial seizure exacerbation started on the third day of their menses. The most common seizure etiology was structural (63 patients), followed by unknown ($n = 22$), genetic ($n = 8$), infectious ($n = 4$) and metabolic ($n = 3$).

Discussion

The patients are mostly young with an epilepsy evolution of more than 10 years. There is a clear predominance of focal seizures with progression to bilateral tonic-clonic. This is probably due to a high number of patients with a structural cause of epilepsy. Acute seizure exacerbation may happen even in patients that have daily seizure. Some patients had not have seizures for more than 10 years. This reinforces the concept that even when epilepsy is considered in remission, appropriate epilepsy hygiene is required for life.

It is noteworthy that a high number of patients delayed more than three days (18%) in attending our Hospital; this could be explained by the lack of centers with the capacity of treating epilepsy in the neighboring states of Mexico City. Unlike other studies, stress is not the first cause of exacerbations, but treatment non-adherence. In Mexico, public healthcare is not exhaustive; an important number of patients must buy their own treatments; 10% of

Figure 3. Causes of seizure exacerbation.

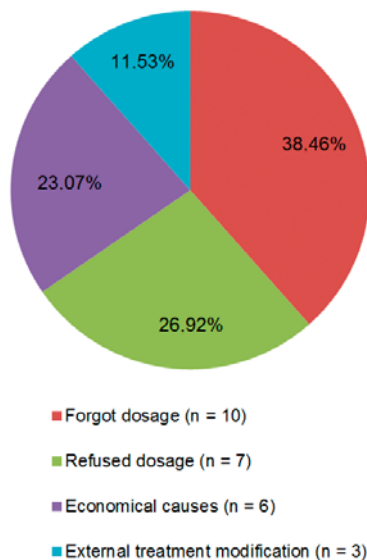


all seizure exacerbations were due to insufficient resources for buying antiepileptic drugs. On the other hand, up to 25% of patients used more than two antiepileptic drugs, elevating treatment cost without a clear benefit. Even so, the most common cause overall is treatment non-adherence due to involuntary dose omission; patient education must emphasize the consequences of having uncontrolled seizures. Remarkably, we did not identify a seizure exacerbation etiology in an important number of patients. These patients could represent clustering seizures without an identifiable trigger.

Our study has the following limitations: Our Institute is a concentration center for cases that are not treatable at regional Hospitals or health care centers. Thus, many patients have a structural cause of their epilepsy due to the brain tumors. Lastly, a number of our patients could have gone to a different health system hospital for treatment of acute seizures.

These results could form the basis for adequate patient education in the follow-up visit, particularly in reminding patients about the consequences of omitting doses of antiseizure drugs, while encouraging them to use methods to avoid this, such as alarm reminders or through assistance of a family member. Some patients may voluntarily and consciously omit dosages because they haven't had seizures for a long time; they must be reminded that dose-reduction is only advised with the close su-

Figure 4. Causes of treatment non-adherence (n = 26).



pervision of an expert. Preventing epilepsy complications is a task of both the doctor and the patient, the only effective way of diminishing the risks is with a good communication between them.

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Epidemiología del descontrol de la epilepsia en un servicio de urgencias neurológicas

Introducción. El descontrol de la epilepsia representa un potencial daño neurológico, por lo que deben investigarse sus causas.

Objetivo. Explorar la epidemiología de pacientes mexicanos con descontrol agudo de epilepsia en un servicio de urgencias neurológicas.

Pacientes y métodos. Análisis prospectivo descriptivo de pacientes con diagnóstico previo de epilepsia que acuden a un servicio de urgencias por descontrol de las crisis.

Resultados. Se analizó a 100 pacientes entre agosto de 2016 y enero de 2017. Ochenta y seis fueron crisis focales, de las cuales 76 fueron focales a bilaterales tonicoclónicas, dos fueron con alteración de la consciencia de inicio motor y tres de inicio no motor, una sin alteración de la consciencia de inicio motor y cuatro de inicio no motor. Catorce fueron generalizadas de inicio generalizado motor. Las causas de descontrol fueron: 26 pacientes por falta de adhesión al tratamiento antiepiléptico, 21 de causa desconocida, 19 por infección, 13 por privación de sueño, 10 por ajuste de tratamiento, tres por estrés, tres por menstruación, dos por uso de alcohol y tres por otras razones. En los 26 pacientes con falta de adhesión, 10 fueron por olvido de dosis, siete por negarse a tomar el medicamento, seis por causas económicas y tres por indicación de médico ajeno a la institución.

Conclusiones. En México, la falta de adhesión al tratamiento representa un 25% de los casos de descontrol de la epilepsia, lo que es un área de oportunidad para incrementar la educación de higiene de crisis y disminuir la frecuencia de éstas.

Palabras clave. Crisis epilépticas. Descontrol. Epidemiología. Falta de adhesión. Urgencias.