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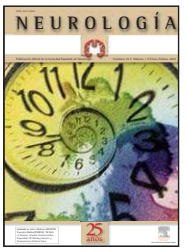

ORIGINAL ARTICLE

Convulsive status epilepticus: clinico-epidemiologic characteristics and risk factors in Peru

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KEYWORDS
Epilepsy;
Status epilepticus;
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Abstract
Introduction: Convulsive status epilepticus constitutes a medical emergency that requires a fast and aggressive management with the objective to prevent neuronal damage and systemic complications. The objective is to determine clinico-epidemiologic characteristics and risk factors associated with convulsive status epilepticus in adults attended in a National Hospital from Lima-Peru in a period of four years.
Methods: Case-control study. Cases were constituted by patients admitted for convulsive status epilepticus in the Adult Emergency Service of National Hospital Dos de Mayo between January 2003 and December 2007. Controls were patients with diagnoses of epilepsy that received treatment in outpatient service of neurology, couplet by age and sex with the group of cases. Medical histories were reviewed and patients were interviewed obtaining clinical, epidemiologic and possible risk factors to convulsive status epilepticus that were registered in an instrument of data recorded.
Results: 41 cases of convulsive status epilepticus were presented. 68.3% were male, 28.6% had age between 20 and 29 years old and 15.5% resided in endemic areas of neurocysticercosis. The more frequent aetiologies were remote symptomatic secondary crisis to cranio encephalic trauma and neurocysticercosis and idiopathic; 26.8% showed some intercurrent infection; while, mortality was of 7.3% Factors associated with a convulsive status epilepticus were the abrupt interruption or suspension of drugs used for the control of convulsions (p=0.038), chronic intake of alcohol (p=0.030) and irregular antiepileptic treatment (p=0.006).
Conclusions: Aetiologies more frequent in the hospital studied from Lima-Peru are remote symptomatic secondary crisis to cranio encephalic trauma, neurocysticercosis and

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idiopathic. The irregular antiepilepticus treatment constitutes a risk factor to convulsive status epilepticus.

PALABRAS CLAVE
Epilepsia;
Estado epiléptico;
Etiología;
Factores asociados

Estado epiléptico convulsivo: características clínico-epidemiológicas y factores de riesgo en Perú

Resumen
Introducción: El estado epiléptico convulsivo constituye una emergencia médica que requiere un manejo rápido y agresivo con la finalidad de prevenir el daño neuronal y complicaciones sistémicas. El objetivo es determinar las características epidemiológicas, clínicas y los factores de riesgo para estado epiléptico convulsivo en adultos en un hospital nacional de Lima-Perú en un período de cuatro años.
Métodos: Estudio casos y controles. Los casos estuvieron constituidos por pacientes atendidos en consultorios externos de Neurología y admitidos por estado epiléptico convulsivo entre enero de 2003 y diciembre de 2007. Los controles fueron pacientes con diagnóstico de epilepsia que recibían tratamiento en consultorios de Neurología, pareados por edad y sexo con el grupo de casos. Se revisó las historias clínicas y se realizó una entrevista a los pacientes obteniéndose datos epidemiológicos, clínicos y posibles factores de riesgo para estado epiléptico convulsivo los cuales fueron registrados en un instrumento de recolección de datos.
Resultados: Se presentaron 41 casos de estado epiléptico convulsivo. El 68,3%correspondió al sexo masculino; el 28,6%tenía una edad entre los 20 y 29 años y el 15,5%residía en áreas endémicas de neurocisticercosis. Las etiologías más frecuentes fueron las crisis sintomáticas remotas secundarias a traumatismo craneoencefálico, neurocisticercosis y la idiopática; el 26,8%presentaba alguna infección intercurrente; mientras que la mortalidad fue del 7,3% Los factores de riesgo para estado epiléptico convulsivo fueron la interrupción brusca o suspensión del fármaco usado para el control de las convulsiones ($p = 0,038$), ingesta crónica de alcohol ($p = 0,030$) y el tratamiento antiepiléptico irregular ($p = 0,006$).
Conclusiones: Las etiologías más frecuentes en el hospital estudiado de Lima-Perú son las crisis sintomáticas remotas secundarias a traumatismo craneoencefálico y neurocisticercosis así como la idiopática. El tratamiento antiepiléptico irregular constituye un factor de riesgo para estado epiléptico convulsivo.

Introduction

The definition of convulsive status epilepticus is the occurrence of two or more successive seizures, without a full recovery of consciousness between episodes, or a single seizure lasting over 30 minutes. It constitutes a true medical emergency that requires rapid, aggressive treatment to prevent neuronal damage and systemic complications.[1-9] The mortality rate increases from 2.6% to 19% when the seizure activity lasts more than 30 minutes and is very high when it lasts for longer than 60 minutes.[10-13]

Convulsive status epilepticus is a dynamic condition during which a progressive sequence of events occur whose pathophysiology is mostly unknown. Various changes have been observed during prolonged seizures, such as inadequate blood flow, decreased glucose use and lowered mitochondrial oxygen consumption, as well as glutamate-mediated excitotoxicity. Convulsive status epilepticus therefore involves a complex cascade of changes, which intensify and perpetuate the seizures, making them more difficult to control.[7,14]

In adults, the most common type of convulsive status epilepticus is the secondarily generalised form. Factors associated with convulsive status epilepticus include the irregular use of antiepileptic drugs, a decrease in serum levels of antiepileptic drugs, intercurrent infections, sleep deprivation in the days leading up to the status epilepticus and prior neurological abnormalities.[13,14] The most commonly reported aetiologies are a history of central nervous system damage, stroke, alcohol consumption, metabolic abnormalities and tumours.[6,10-19]

The present study aimed to determine the clinical and epidemiological characteristics and risk factors for status epilepticus in patients at a national hospital in Lima (Peru). Another aim was to present the epidemiological and clinical characteristics of this group of patients in a developing country.

Patients and methods

Design

Case and control study

The case group comprised all the patients with epilepsy attended at the outpatient clinic of the Neurology Department of the Hospital Nacional Dos de Mayo (Lima, Peru) who presented convulsive status epilepticus (generalised and secondarily generalised) between January 2003 and December 2007. The controls were patients diagnosed with epilepsy who had never experienced status epilepticus but were also admitted at the Neurology outpatient clinic for a control examination. They were matched with cases by age and gender in a 1:1 ratio. Patients who did not agree to participate in the study were excluded.

Technique and working method

A review was made of the medical records of patients with status epilepticus admitted at the adult Emergency Department of the Hospital Nacional Dos de Mayo, and of the medical records of the controls. Personal details and medical and family history were obtained, as were factors associated with convulsive status epilepticus such as irregular treatment, interruption or discontinuation of anticonvulsive medication, intercurrent infections, acute and chronic consumption of alcohol, drug abuse, drug addiction, ingestion of neurotoxic substances and sleep deprivation in days leading up to the episode. These data were supplemented with an interview conducted by a neurologist during the hospitalisation of the case group and the outpatient consultation of the control group. The data were recorded with an instrument for data collection and added to a computer database.

Data processing and analysis

To begin with, univariate and bivariate statistics were calculated with Pearson's chi-square test. The variables that resulted significant in the bivariate analysis were entered in the multivariate analysis. The conditional logistic regression model was used and the odds ratio (OR) and confidence intervals were estimated for this analysis. The variables of each block that presented a statistically significant and positive association with status epilepticus during the first stage remained part of the model in the subsequent stages, except for the non-associated ones from the 3 respective blocks (step by step inclusion, forward method). The final model was composed of variables selected at each stage of the analysis, with their respective statistical significance. The calculations were carried out with a confidence level of 95%

Ethical aspects

The rights of the patients were respected, as were the ethical principles stated by the Helsinki Declaration of the World Medical Association. The project was approved by the Ethics Committee of the Medicine School of the Universidad Nacional Mayor de San Marcos.

Table 1 Breakdown by age group of patients with convulsive status epilepticus at Hospital Dos de Mayo in Lima (Peru)*

Age group	Frequency	%
15-19 years	7	17.1
20-29 years	11	26.8
30-39 years	7	17.1
40-49 years	7	17.1
50-59 years	5	12.2
60-69 years	1	2.4
70-79 years	2	4.9
80-89 years	1	2.4
Total	**41**	**100.0**

*The controls maintain the same distribution by age because they were matched with the study cases.

Results

Epidemiology

During a period of 4 years, a total of 41 cases of convulsive status epilepticus were admitted to the adult Emergency Department of the Hospital Nacional Dos de Mayo. The average age of patients was 36.7±18.2 years, the most affected age group was 20 to 29 years (26.8%) (table 1) and the most frequently affected gender was male (68.3%). A total of 84.5% of patients came from urban areas in the Lima region, whereas the remaining 15.5% had permanent residences in the Huánuco, Cerro de Pasco, Puno and Junin regions, near the Peruvian Andes, which are recognised as endemic areas for neurocysticercosis in our country. A total of 34.1% of patients reported frequent consumption of pork and 12.2% kept pigs at home.

Clinical characteristics

Of the patients who attended the emergency department, 22% had suffered at least one previous episode of convulsive status epilepticus. For the current episode, they attended the hospital after a mean period of 3 hours had elapsed from the start of the first convulsive episode (range, 1-144 hours), and had suffered a mean of 5 successive crises (range, 2-20) from the onset of the status until they reached the hospital. The main aetiologies of status epilepticus are described in table 2.

An anamnesis conducted among the patients revealed that 56.1% had abruptly interrupted or discontinued their antiepileptic medication, 53.7% were not taking their medication regularly and 14.6% were not taking the correct medication to control epileptic seizures. The antiepileptic drug most frequently taken before suffering status epilepticus, in a total of 41.5% of cases, was phenytoin, while 39% were not taking any medication. This is illustrated in table 3. In addition, 26.8% presented intercurrent infection: community-acquired pneumonia (44.4%), urinary tract infection (33.3%), acute gastroenteritis (11.1%) and

Table 2 Aetiologies of convulsive status epilepticus (cases) and epilepsy (controls) at the Hospital Nacional Dos de Mayo

Aetiology	Frequency - cases	%	Frequency - controls	%
Symptomatic epilepsy	34	83.0		
Remote symptomatic crisis secondary to TBI	9	22.1	6	14.6
Remote symptomatic crisis secondary to neurocysticercosis	4	9.8	5	12.2
Remote symptomatic crisis secondary to ischemic cerebrovascular disease	3	7.3	5	12.2
Meningoencephalitis tuberculosa under treatment	2	4.8		
Remote symptomatic crisis secondary to meningoencephalitis tuberculosa	2	4.8	1	2.4
Remote symptomatic crisis secondary to post neurosurgery	2	4.8	4	9.8
Viral encephalitis	2	4.8	3	7.3
Mental retardation from Down syndrome	1	2.4		
Primary cerebral vasculitis	1	2.4		
Arteriovenous malformation	1	2.4	1	2.4
Intracerebral expansive process	1	2.4	4	9.8
Cerebral paralysis	1	2.4		
Hepatic encephalopathy	1	2.4	1	2.4
Mental retardation from Down syndrome +TBI	1	2.4		
Remote symptomatic crisis secondary to TBI + alcoholism	1	2.4		
Remote symptomatic crisis secondary to TBI + cerebral abscess	1	2.4		
Sequel of vascular cerebral hemorrhagic disease + hyperosmolar coma	1	2.4	1	2.4
Idiopathic epilepsy	6	14.6	4	9.8
Cryptogenic epilepsy	1	2.4	6	14.6
Total	**41**	**100.0**	**41**	**100.0**

TBI: traumatic brain injury.

lower limb cellulitis (11.1%). In the case of one patient, convulsive status epilepticus was the first manifestation of the disorder, and in another case, the status occurred in a woman who was 34 weeks pregnant. With regard to bad habits and lifestyles, it was observed that 34.1% of patients had experienced sleep deprivation in the 24 hours prior to the convulsive status epilepticus, 31.7% suffered from alcoholism and 9.8% used illicit drugs. A cerebral computed tomography (CT) scan showed pathological findings in 70.7% of patients. Mortality resulting from the status epilepticus or from related complications was 7.3%.

Risk factors for convulsive status epilepticus

Bivariate analysis showed that the risk factors associated with convulsive status epilepticus were the abrupt interruption or suspension of the drug treatment used to control seizures (P=.038), chronic alcohol consumption

Table 3 Antiepileptic drugs used by patients with convulsive status epilepticus and controls with epilepsy

Drug	Frequency cases	%	Frequency controls	%
Phenytoin	17	41.5	25	61.0
Carbamazepine	2	4.9	4	9.8
Valproic acid	2	4.9	5	12.2
Oxcarbazepine	1	2.4	0	0
Phenobarbital	0	0	1	2.4
Phenytoin + phenobarbital	2	4.9	4	9.8
Phenytoin + valproic acid	0	0	1	2.4
Phenobarbital + carbamazepine	1	2.4	0	0
Phenobarbital + carbamazepine	0	0	1	2.4
Did not receive treatment	16	39.0	0	0
Total	**41**	**100.0**	**41**	**100.0**

Table 4 Statistical analysis of potential risk factors for convulsive status epilepticus

Evaluated factor	*P* value	Odds ratio	Confidence interval
Bivariate analysis			
Sudden interruption or suspension of antiepileptic drug	0.038	2.5*	1.01-6.02
Chronic alcohol intake	0.030	3.3*	1.07-10.49
Irregular antiepileptic treatment	0.006	3.6*	1.40-9.20
Multivariate analysis			
Irregular antiepileptic treatment	0.035	2.9**	1.078-7.818

*Unadjusted odds ratio (OR).
**Adjusted OR.

(*P*=.030) and irregular antiepileptic treatment (*P*=.006), the latter with stronger association compared to the other factors. Multivariate analysis with conditional logistic regression showed that irregular antiepileptic treatment was the only independent risk factor associated with status epilepticus (*P*=.035).

The use of inadequate medication for the type of crisis, intercurrent infection, sleep deprivation in the 24 hours prior to the status, acute alcohol intake, drug addiction, frequent consumption of pork, home breeding of pigs and male gender did not constitute risk factors. The statistical analysis of risk factors can be observed in table 4.

Discussion

Status epilepticus is a neurological medical emergency resulting from diverse aetiologies. Factors that directly influence its manifestation and prognosis have been observed. These factors vary depending on the geographic region. Generalised tonic-clonic seizures are the most common type (convulsive status epilepticus), but there are at least another 12 types of status epilepticus, which are less frequent yet still pose a diagnostic challenge.[20-25]

The present research shows that convulsive status epilepticus is a condition frequently treated at a national hospital in Lima (Peru), often in males under 30 years, and who frequently also suffer infectious aetiologies. This has national significance and also extends to an international level given that tourist activity in Peru has increased exponentially in recent years, as has the migration of Peruvians towards Europe, where Spain is the most common destination. Due to the fact that bacterial (tuberculosis) or parasitic (neurocysticercosis) diseases are aetiologies of symptomatic epilepsy, the epidemiological history of travel or migration is relevant to the diagnosis.

Clinical characteristics have shown that patients seek hospital help 15 hours after the start of the first episode of convulsive status epilepticus. This delay may be due to the following factors: economic (generally the most common), social and cultural. It is difficult to attribute this phenomenon to the accessibility of health services because most patients are from districts close to the hospital.

Within acute symptomatic epilepsy, the most common aetiologies were remote symptomatic seizures secondary to traumatic brain injury (TBI) and neurocysticercosis. The former constitute a recurrent seizure disorder that can occur several years after severe TBI. Little is known about the mechanisms by which TBI can cause a convulsive disorder; however, the presence of cortical lesions could be important in the genesis of epileptogenic foci in genetically susceptible patients. Oxidative stress has been implicated in the pathogenesis of the disease, mainly by way of primary excitotoxicity via hydroxyl radicals. Early treatment does not alter its incidence, and prophylactic treatment with anticonvulsants is not advised.[26,27] Neurocysticercosis accounts for 10% of cases of symptomatic epilepsy, which correlates with the presence of epidemiological risk factors such as frequent consumption of pork (34%), coming from endemic areas within the country (14.6%) and having bred pigs at home (12.2%).

Another common aetiology was idiopathic epilepsy (14.7%), often with an early onset and good prognosis with the correct treatment. The problem lies in the precarious economic and cultural conditions of the patients, which leads to irregular treatment and the interruption or discontinuation of antiepileptic treatment.

The analysis of the aetiology and clinical characteristics of patients at the Hospital Nacional Dos de Mayo showed they were similar to those reported by Murthy et al (2007), who studied a series of 85 patients treated at a hospital in India. In their series, it was observed that the mean age of the patients was 33 years and the time elapsed from the onset of the seizure to the start of hospital treatment was 18 hours. The most commonly reported aetiologies were: cryptogenic, vascular, neurocysticercosis, tuberculous meningitis and encephalitis, among others (remote symptomatic seizures secondary to TBI were not included).

The similarity between the profiles of patients in Peru and India can be attributed to their condition as developing countries.[28] In contrast, there is a noticeable difference in aetiologies compared with those reported by Hui[29] (2003) in Hong Kong (China), where there were frequent cases of cerebrovascular disease, idiopathic and metabolic disorders, and a low prevalence of status epilepticus related to alcohol abuse (less than 3%) was observed.

It was noted in the results presented that the only risk factor associated with convulsive status epilepticus at the Hospital Nacional Dos de Mayo was irregular antiepileptic treatment. It was observed that patients were 2.9 times

more likely than controls to suffer status epilepticus, a finding similar to that of Garzón (2003) in adult patients in Brazil.[19]

The abrupt interruption or suspension of the antiepileptic treatment was significantly associated with the decompensation of epilepsy, a finding which is consistent with that reported by Karasalhoglu (Turkey, 2003) in paediatric patients.[17] Chronic alcohol consumption was also associated with status epilepticus, which is consistent with the results found by Scholtes[6] in a study involving 346 patients. Alcoholism is a known risk factor, and it has been observed that status epilepticus is a relatively frequently observed manifestation in developed countries. Among patients at the Hospital Nacional Dos de Mayo, there was a high prevalence of alcoholism, reaching 31.7%, in contrast to that reported in countries like the United States, where Alldredge (1993) found that in a series of 249 patients with status epilepticus (observed between 1977 and 1989), 10.8% showed symptoms of alcohol abuse.[30]

Some researchers include both adults and paediatric patients in their research series. Patients under the age of 18 have been excluded from this study, because the aetiologies of this group differ greatly from those of adults.

The mortality found in adults with convulsive status epilepticus at the Hospital Nacional Dos de Mayo was 7.3%, falling within the range reported at an international level. The international level ranges between 4% and 21% for patients admitted to a hospital[10,18,19] in both developed and developing countries.

The main obstacle encountered when carrying out this study was the lack of updated information related to status epilepticus in its various forms in our country, as well as the associated risk factors. Another limitation was the lack of measurement of the serum levels of medication used for epileptic control because the study was not performed at our hospital and patients did not usually have money to pay for such measurements.

Irregular antiepileptic treatment, chronic alcohol consumption and the sudden interruption or discontinuation of antiepileptic therapy are factors associated with convulsive status epilepticus. The most common aetiologies in the hospital studied in Lima (Peru) were post-TBI, idiopathic and neurocysticercosis-related epilepsies.

In conclusion, the most common aetiologies at the hospital studied in Lima (Peru) were remote symptomatic seizures secondary to TBI and neurocysticercosis, and idiopathic causes. Irregular antiepileptic treatment was a risk factor associated with convulsive status epilepticus.

Conflict of interest

The authors declare no conflict of interest.

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