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Impact of a rapid systemic guide on pediatric patients with suspicion of epilepsy



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Epilepsy;
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Abstract

Objectives: Increase the percentage of etiological diagnosis of epilepsy (according to the classification by the 2010 ILAE) using a systematic quick guide for pediatric patients with suspected epilepsy.

Methods: Ambispective cohort study. Patients under 16 years old with suspected epilepsy were studied, and a systematic quick guide was applied to the prospective group, and later the two groups were compared. It was a convenience sample, with a study period of one year for both groups.

Results: The prospective group was 120 patients and the retrospective group 71 patients. Comparing the epileptic diagnosis by etiology groups, in the prospective group (only outpatient patients), 3.3% had epilepsy of an unknown cause, 55% had epilepsy of a genetic cause, 36.7% had epilepsy of a structural/metabolic cause, and 5% had conditions that are not epilepsy itself. Meanwhile in the retrospective group, 52.1% had epilepsy of an unknown cause, 11.3% had epilepsy of a genetic cause, and 36.6% had epilepsy of a structural/metabolic cause ($p < 0.001$). **Conclusions:** Compared to other similar studies, the etiological percentages of epilepsy increased. Using the systematic quick guide proposed, the percentage of etiological definitions of epilepsy was increased in pediatric patients.

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Introduction

Seizure, according to the International League Against Epilepsy (ILAE), is the transitory occurrence of signs and/or symptoms due to abnormal excessive synchronous neuronal activity in the brain.¹ Epilepsy is a disorder of the brain defined as the presence of hyper synchronous neuronal activity, which is clinically expressed by any of the following circumstances²:

- At least two unprovoked or reflex seizures occurring more than 24 hours apart.
- An unprovoked or reflex seizure, and a probability of presenting further seizures over the next 10 years, similar to the general recurrence risk (at least 60%) subsequent to the onset of two unprovoked seizures.
- As an integral part of an epileptic syndrome.

An epilepsy syndrome is a group of signs and symptoms which define a unique epileptic condition, made up of convulsive crises with specific characteristics, onset age, gender predominance, etiology, cognitive or behavioral comorbidity, daily variation or its link to sleep and family history. Some triggering factors are: sleep deprivation, photic stimulation, hyperventilation, etc., which has direct implications in its management, evolution and prognosis within neurodevelopment and the result of the epilepsy, genetic tests and inheritance.³

In Mexico, the prevalence in the Priority Programs for Epilepsy centers is 11–15/1000, thus this numbers suggest that in our country the number of patients with epilepsy is around 1.5 million.⁴ In 2010, the ILAE redesigned the classification of seizures and epilepsy crises; dividing them into generalized, focal and unknown crisis (epileptic spasms).⁵ Regarding to electro-clinical syndromes and other epilepsies, they were classified according to the age of onset and specific etiology as follows: genetic, structural/metabolic, of unknown causes, and in conditions which are not actual epilepsy.⁵

The objective of this paper was to increase the percentage of epilepsies etiologic diagnoses in pediatric patients (according to the classification by the 2010 ILAE) using a systematic quick guide in pediatric patients with suspected epilepsy.

Materials and methods

An ambi-directional cohort study was conducted, with interventionism in the prospective group (with the application of the proposed systematic quick guide). The sample size was at convenience, all patients who arrived during one year in both groups.

The first group studied was the prospective group, a systematic quick guide was used in this group (see [annex 1](#)). *Inclusion criteria*: patients under 16 years of age who attended the "Dr. José E. González" University Hospital in Monterrey, Nuevo León, México (at its hospital admission area or outpatient clinic) for the first time with suspicion of epilepsy, and who have been assessed by the Pediatric Neurology Service between June 18, 2014 and June 17, 2015. *Exclusion criteria*: Those patients who were 16 years old

or older. *Elimination criteria*: Patients with an incomplete systematic quick guide, patients with an incomplete clinical file, patients who were ruled out of having epilepsy, and epileptic patients who did not complete the minimum studies (EEG and/or imaging studies) in order to classify them etiologically.

After finishing the prospective group, the retrospective group began. We searched for the registries of every patient who attended the Pediatric Neurology Outpatient Clinic for the first time. All the files from those patients were reviewed, obtaining epidemiological data and etiological diagnoses of all patients with epilepsy. *Inclusion criteria*: Patients under 16 years of age, with suspicion of epilepsy. *Exclusion criteria*: Patients who were 16 years of age or older. *Elimination criteria*: Patients who were ruled out of having epilepsy and patients with incomplete clinical files.

Databases for both groups were set up using Microsoft Excel 2010. Subsequently, a statistical analysis was performed using SPSS version 20, where a descriptive statistical analysis of the prospective and retrospective groups was completed, then the comparison between both groups was conducted using Pearson's chi square test (for the variables: gender and etiological diagnosis of epilepsy) and the Student *T*-test (for the age variable). A $p < 0.05$ value was determined as a statistically significant result. This work was approved by the Ethics Committee of the School of Medicine at the Autonomous University of Nuevo Leon on April 20th, 2015, with the registry code NR15-003.

Results

The proposed systematic quick guide was conducted on 137 patients with suspicion of epilepsy. Eight patients were ruled out of having epilepsy, and thus were eliminated, and another 9 patients with epilepsy were eliminated as well because they did not comply with the minimum tests (EEG and/or imaging studies) in order to classify them etiologically. The prospective group included 120 patients, while the retrospective group included 71 patients.

First, a description of the prospective group was done ([Tables 1 and 2](#)), and the Denver II tool was used to evaluate the patients' psychomotor capability. Subsequently, an age comparison between prospective groups (patients admitted plus outpatients, and only outpatients) and the retrospective group was conducted ([Table 3](#)). Lastly, a comparison of epilepsy diagnosis by etiological groups was done between prospective groups (patients admitted plus outpatients, and only outpatients) and the retrospective group ([Table 4](#)).

Discussion

A total of 120 patients were included in the prospective group and 71 patients in the retrospective group. Average age was 6.3 years for the first group and 7.7 for the second group, compared to a study conducted in Spain where the average age was 5.2 years.⁶ Gender distribution in the prospective group was 66.7% male and 33.3% female, whereas for the retrospective group the distribution was 66.2% male and 33.8% female, compared to a study conducted in Turkey where 59.3% of the patients

Table 1 Description of the prospective group (in-hospital and ambulatory patients).

Variant	Number	Percentage
<i>Hereditary or family history of epilepsy</i>		
Negative	88	73.3%
Positive	32	26.7%
<i>Psychomotor development</i>		
Normal	85	70.8%
Abnormal	35	29.2%
<i>Presentation of seizures</i>		
Awake	93	77.5%
Asleep	12	10
Awake and asleep	15	12.5%
<i>Seizure type</i>		
Generalized	100	83.3%
Focal	17	14.2%
Unknown (epileptic spasms)	3	2.5%
<i>Type of generalized seizure</i>		
Tonic-clonic	35	35%
Tonic	34	34%
Absence	12	12%
Clonic	8	8%
Atonic	6	6%
Myoclonic	4	4%
Clonic + Myoclonic	1	1%
<i>Type of focal seizure</i>		
Motor	15	88.2%
Autonomic	1	5.9%
Psychic phenomena	1	5.9%
Sensitive	0	0%
<i>Performance of electroencephalogram</i>		
Performed	117	97.5%
Not performed	3	2.5%
<i>Electroencephalogram result</i>		
Abnormal	101	86.3%
Normal	16	13.7%
<i>Performance of imaging study</i>		
Performed	96	80%
Not performed	24	20%
<i>Type of imaging study performed</i>		
MRI	71	74%
Computed axial tomography	25	26%
<i>Result of the imaging study</i>		
Abnormal	65	67.7%
Normal	31	32.3%
<i>Physical neurological examination</i>		
Abnormal	85	70.8%
Normal	35	29.2%

Table 2 Prospective group (in-hospital and ambulatory patients).

Variant	Average	±SD
Age at first seizure (in years)	4.4	4.5
Duration of seizures (in min)	8.1	19
Duration of postictal period (in min)	74.6	155.9

SD: Standard deviation.

presented a focal and 2.5% presented an unknown (epileptic spasms), in comparison to a study conducted in Iceland⁹ where 58% of patients presented a generalized seizure crisis, 40% presented a focal and 2% presented an unknown; furthermore, a study conducted in the US¹⁰ showed 40% of patients with a generalized seizure crisis, 57% with a focal and 3% with an unknown seizure crisis. This gap in percentages can be attributed to the difficulty to express clinical characteristics of the crisis by people who witness them (they might have started focally and later become generalized). Regarding the prospective group, 70.8% of patients presented some anomaly in the neurological physical examination, while a study in Turkey reported only a 25.8% of patients presenting neurological anomalies.⁷ This could be due to the fact that any neurological abnormality, including abnormalities in the higher brain functions, were considered anomalies in this study. If we change the nomenclature of the epileptic etiology from the symptomatic epilepsy, idiopathic epilepsy and cryptogenic epilepsy of the old ILAE 1989 classification, to the structural/metabolic epilepsy, genetic epilepsy and epilepsy with an unknown cause, respectively, from the new classification from the ILAE 2010, the prospective group (inpatient and ambulatory) had 2.5% unknown cause, 31.7% genetic cause (electro-clinical syndromes), 61.7% structural/metabolic causes, and 4.2% which were not epilepsy, strictly speaking. In the retrospective group, we found that 52.1% of the patients had epilepsy of an unknown origin, 11.3% had epilepsy of a genetic origin, 36.6% had epilepsy of a structural/metabolic origin, and 0% had conditions which were not epilepsy, strictly speaking. We can compare our results to those of a study in Iceland,⁹ where 53% of the patients had epilepsy of an unknown origin, 14% had epilepsy of a genetic origin, 32% had epilepsy of a structural/metabolic origin, and 1% had conditions which were not epilepsy, strictly speaking. Another study in Switzerland¹¹ concluded that 35% of the patients had epilepsy of an unknown origin, 10.3% had epilepsy of a genetic origin, 54% had epilepsy of a structural/metabolic origin, and 1% had conditions which were not epilepsy, strictly speaking.

The positive aspects of this study include the following: it is a cohort, ambi-perspective study in a third level hospital, which is a reference center for the northeast of Mexico. It includes an important number of patients with epilepsy in both groups (prospective and retrospective), and the genders and ages within both groups were homogenous and therefore comparable. Other points in favor of this study are: the inclusion of clinical, demographic, epidemiological and therapeutic characteristics, creating a database for these patients. With the systematic rapid guide proposed in this study for pediatric patients under suspicion of epilepsy, this study showed, with statistical importance,

were male and 40.7% were female.⁷ In the prospective group, 26.7% had family history of epilepsy, compared to the 22.2% and 22.5% of studies conducted in Germany⁸ and Turkey,⁷ respectively. In the prospective group, 83% of patients presented a generalized seizure crisis, 14.2%

Table 3 Age comparison between the prospective groups (in-hospital and ambulatory patients, and only ambulatory patients) and the retrospective group.

Group	Average (in years)	±SD	p
Age			
Prospective (in-hospital and ambulatory patients)	6.3	5	0.076
Retrospective	7.7	5	
Prospective (ambulatory patients)	8.2	4.6	0.509
Retrospective	7.7	5	

SD: Standard deviation.

Table 4 Comparison of the epilepsy diagnosis by etiological groups between the prospective groups (in-hospital and ambulatory patients, and only ambulatory patients) and the retrospective group.

Group	Diagnosis of epilepsy by etiological group	Number	Percentage	p
Prospective (in-hospital and ambulatory patients)	Epilepsy of an unknown cause	3	2.5%	<0.001
	Epilepsy of a genetic cause	38	31.7%	
	Epilepsy of a structural/metabolic cause	74	61.7%	
	Conditions that are not epilepsy, strictly speaking	5	4.1%	
	Epilepsy of an unknown cause	37	52.1%	
Retrospective	Epilepsy of a genetic cause	8	11.3%	<0.001
	Epilepsy of a structural/metabolic cause	26	36.6%	
	Conditions that are not epilepsy, strictly speaking	0	0%	
	Epilepsy of an unknown cause	2	3.3%	
Prospective (ambulatory patients)	Epilepsy of a genetic cause	33	55%	<0.001
	Epilepsy of a structural/metabolic cause	22	36.7%	
	Conditions that are not epilepsy, strictly speaking	3	5%	
	Epilepsy of an unknown cause	37	52.1%	
Retrospective	Epilepsy of a genetic cause	8	11.3%	<0.001
	Epilepsy of a structural/metabolic cause	26	36.6%	
	Conditions that are not epilepsy, strictly speaking	0	0%	

that this guide decreases the “unknown cause” diagnoses of epilepsy and it increases the diagnoses of genetic and structural/metabolic epilepsy for our pediatric patients.

Both study groups were evaluated over the course of a year, and it would be important to extend the follow-up time for these patients. This study has aspects which could be improved: 2.5% of the patients in the prospective group did not received an electroencephalogram, due to death or surgical or medical complications, or they were discharged before an electroencephalogram could be performed. 20% of the patients did not received any brain imaging studies, some of them due to a lack of economic resources and some due to contraindications from the sedative drugs during the study, due to which some patients may have been subdiagnosed with epilepsy of a structural origin. The genetic studies were no performed on patients from both groups; it will be important for some patients to corroborate their epileptic diagnosis in the future, for which they will have to be cheaper, as they currently cost around 20,000 MXN, which is quite inaccessible for the population at our hospital. This study did not document the frequency of convulsive crises before and after the epilepsy diagnosis, and if there was some electric or clinical improvement after having made the etiological diagnosis using the proposed systematic quick guide, and treating them accordingly. Because of this, we recommend a follow-up study to corroborate clinical or

electric improvement in these patients. Some patients in the genetic epilepsy category may also have been “over-diagnosed” when we used the guide to determine their etiology.

Another negative aspect of this study is that we were unable to document all the variables in the retrospective group that we were able to do with the prospective group.

In this study, we can conclude that the rapid systemic guide we used can be corroborated with statistical significance with the increase in the etiological definition of epilepsy in pediatric patients, both in-hospital and ambulatory. This guide can be used by first contact doctors or pediatric neurologists to create a proper diagnostic approach oriented toward all patients under suspicion of epilepsy, to find an etiology diagnosis in accordance with the 2010 ILAE classification. This determination of the specific etiology, as well as the electro-clinical syndromes, will allow us to provide a complete management, oriented on and recommended by the international guides for each patient, which will help us to predict the clinical prognosis of our patients with greater exactitude.

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Conflict of interest

The authors have no conflicts of interest to declare.

Appendix A.

Annex 1: Rapid Systematic Guide (1st version)

“Dr. José E. González” University Hospital

Pediatric Neurology Service



Date: _____ Register: _____ Age: _____

Name: _____

Address and telephone number: _____

Sex: _____ Weight (in kg): _____ Height (in cm): _____

Head circumference (in cm): _____ Department: _____

Family history of seizures/epilepsy, psychiatric or neurological abnormalities:

No _____ Yes (specify) _____

Other family history: _____

Pregnancy: _____ Prenatal control: _____ Course: _____

Type of birth: _____ Motive: _____

Gestational age: _____ Apgar score: _____

Weight at birth: _____ Height at birth: _____ Head

circumference at birth: _____

Complications at birth: _____

Previous diseases, surgeries or hospitalizations: No _____ Yes _____

Specify: _____

Psychomotor development (in months or years)

Cephalic Hold: _____ Sedestation: _____ Bipedestation: _____

Walking: _____ Jumping: _____ Potty training: _____

First word: _____

Age at first seizure: _____

Date of latest seizure: _____

Seizure happens when: Awake _____ Asleep _____ Both (awake and asleep) _____

Types of seizures

Generalized (specify if tonic-clonic, absence, myoclonic, tonic, clonic, atonic)

Epileptic spasms _____

Focal (specify if motor, sensory, autonomic or psychic)

Discognitive data: No _____ Yes (specify) _____

Duration of seizures: _____

Gaze deviation: Yes (specify direction) _____ No _____

Postictal period: No _____ Yes (specify duration) _____

Frequency of seizures (specify number of seizures):

Per day: _____ Per week: _____

Per month: _____ Per year: _____

Conventional or invasive electroencephalogram, polysomnography or EEG video (specify date and interpretation):

Imaging study (structural or functional, specify date and interpretation):

Paraclinical diagnostic studies (specify if genetic, biopsy or metabolic):

Current treatment used (to specify the reason, if a medication was changed or added):

Specify the anomalies found in the physical, neurological examination:

Etiological suspicion of epilepsy, according to the ILAE (2010)

I- Genetic (electroclinical syndrome) by age of onset

1- Neonatal period (<44 weeks gestation)

a) Benign neonatal familial epilepsy _____

b) Early myoclonic encephalopathy _____

c) Ohtahara syndrome _____

2- Lactation (<1 **years**)

a) Childhood epilepsy with migrant focal seizures _____

b) West syndrome _____

- c) Myoclonic epilepsy in infancy _____
- d) Benign childhood epilepsy _____
- e) Benign childhood familial epilepsy _____
- f) Dravet syndrome _____
- g) Myoclonic encephalopathy in non-progressive disorders _____
- 3- Childhood (1 to 12 years)
 - a) Febrile seizures _____
 - b) Panayiotopoulos syndrome _____
 - c) Myoclonic epilepsy with atonic crises _____
 - d) Benign epilepsy with centrotemporal spikes _____
 - e) Autosomal nocturnal frontal lobe epilepsy _____
 - f) Late childhood occipital epilepsy _____
 - g) Epilepsy with myoclonic absences _____
 - h) Lennox-Gastaut syndrome _____
 - i) Epileptic encephalopathy with continuous spiked waves during sleep _____
 - j) Landau-Kleffner syndrome _____
 - k) Childhood absence epilepsy _____
- 4- Adolescent-Adult (>12 years)
 - a) Juvenile epilepsy with absences _____
 - b) Juvenile myoclonic epilepsy _____
 - c) Epilepsy with only tonic-clonic seizures _____
 - d) Progressive myoclonic epilepsies _____
 - e) Autosomal dominant epilepsy with auditory symptoms _____

- f) Other hereditary temporal lobe epilepsies _____
- 5- Not related to age
- a) Familiar focal epilepsy with diverse foci (childhood adulthood) _____
- b) Reflexive epilepsies _____

II- Structural/Metabolic

- 1- Distinctive constellations
 - a) Mesial temporal lobe epilepsy with hippocampal sclerosis _____
 - b) Rasmussen syndrome _____
 - c) Gelastic crisis with hypothalamic hamartoma _____
 - d) Hemiconvulsion-hemiplegia epilepsy _____
 - e) Epilepsies that don't fall into these diagnostic categories can be distinguished first by the presence or absence of some known structural or metabolic condition (a suspected cause) and also on the basis of the type of the first crisis (focal or generalized)
- 2- Attributed epilepsies organized by structural-metabolic causes
 - a) Malformations of cortical development _____
 - b) Neurocutaneous syndromes _____
 - c) Tumor _____
 - d) Infection _____
 - e) Trauma _____
- 3- Angioma
 - a) Perinatal injuries _____
 - b) Apoplexy _____

III- Unknown and conditions that are not epilepsy, strictly speaking

- 1- Unknown _____
- 2- Benign neonatal seizures _____
- 3- Febrile seizures _____

Definitive diagnosis of epilepsy (date at which the diagnosis was made):

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