ORIGINAL ARTICLE

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

L.R. Morales-Mancías, S. Vázquez-Fuentes*, A.C. Cantú-Salinas, L. de León-Flores, B.E. Chávez-Luévanos, H. Villarreal-Velázquez

Pediatric Neurology Service at the "Dr. José Eleuterio González" University Hospital of at the Autonomous University of Nuevo León, Monterrey, Mexico

Received 3 December 2015; accepted 23 February 2016
Available online 22 June 2016

KEYWORDS
Epilepsy; Pediatrics; Guide; ILAE

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.

© 2016 Universidad Autónoma de Nuevo León. Published by Masson Doyma México S.A. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

* Corresponding author at: Servicio de Neurología Pediátrica del Hospital Universitario "Dr. José Eleuterio González" de la Universidad Autónoma de Nuevo León, Av. Francisco I. Madero pte y Ave. Gonzalitos s/n, Col. Mitras Centro, CP 64460 Monterrey, NL, Mexico.
E-mail address: svfuentes03@yahoo.com.mx (S. Vázquez-Fuentes).

http://dx.doi.org/10.1016/j.rmu.2016.02.001
1665-5796/© 2016 Universidad Autónoma de Nuevo León. Published by Masson Doyma México S.A. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
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 circumstances:2

- 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 convalusci 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 these numbers suggest that in our country the number of patients with epilepsy is around 1.5 million.4 In 2010, the ILAE redesigns 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 ambidirectional 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 León 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).

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

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

<table>
<thead>
<tr>
<th>Variant</th>
<th>Average</th>
<th>±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at first seizure (in years)</td>
<td>4.4</td>
<td>4.5</td>
</tr>
<tr>
<td>Duration of seizures (in min)</td>
<td>8.1</td>
<td>19</td>
</tr>
<tr>
<td>Duration of postictal period (in min)</td>
<td>74.6</td>
<td>155.9</td>
</tr>
</tbody>
</table>

SD: Standard deviation.

were male and 40.7% were female. In the prospective group, 26.7% had family history of epilepsy, compared to the 22.2% and 22.5% of studies conducted in Germany and Turkey, respectively. In the prospective group, 83% of patients presented a generalized seizure crisis, 14.2% presented a focal and 2.5% presented an unknown (epileptic spasms), in comparison to a study conducted in Iceland where 58% of patients presented a generalized seizure crisis, 40% presented a focal and 2% presented an unknown; furthermore, a study conducted in the US 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 examination, while a study in Turkey reported only a 25.8% of patients presenting neurological anomalies. This could be due to the fact that any neurological abnormality, including abnormalities in the higher brain functions, were considered abnormalities 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, 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 Switzerland 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, ambispective 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,
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 receive 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 receive 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 systematic 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.

**Funding**

No financial support was provided.
Impact of a rapid systemic guide on pediatric patients with suspicion of epilepsy

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: _______________________


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

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 ______

Documento descargado de http://www.elsevier.es el 25-08-2016
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 _______
Impact of a rapid systemic guide on pediatric patients with suspicion of epilepsy

f) Other hereditary temporal lobe epilepsies

5- Not related to age
a) Familial 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):
References