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Diagnostic and therapeutic approach to patients with first seizure episode

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Abstract

Seizures are transient episodes of signs and/or symptoms resulting from abnormal, excessive or synchronous neuronal activity in the brain. About 8% to 10% of people will experience a seizure at some point in their lives, and of that group, about 2% to 3% will develop epilepsy. Given the impact that epilepsy can have on a person's quality of life and related medical, cognitive, or psychiatric conditions, it is crucial to perform a detailed evaluation when a patient presents an unprovoked first seizure episode. A seizure crisis must be distinguished from other events with a similar presentation, as the possible causes must be determined, to establish the need for adequate treatment, and establish a long-term prognosis.

Keywords: Seizure; Epilepsy; Seizure Physiology; Anticonvulsants; Seizure Treatment

1. Introduction

Seizures and epilepsy are neurological problems that affect a significant proportion of the general population, becoming one of the most common neurological conditions. To effectively address these conditions, a meticulous diagnostic approach is crucial. The detailed clinical history is the most relevant aspect to begin the diagnostic approach. When faced with a first episode of crisis, one should inquire about the onset, duration, and all the characteristics, in addition, ask about alcohol and psychoactive substance intake, and family history. It is important to establish a differential diagnosis with other paroxysmal events that can mimic it, such as migraine, transient ischemic attacks or syncope [1], [2]. Therefore, the comprehensive approach in a patient with their first seizure not only seeks diagnostic confirmation, but also establishes the need to start or not to an early antiepileptic treatment.

2. Definitions

A seizure is the temporary appearance of signs and/or symptoms due to excessive or synchronous abnormal neuronal activity in the brain. The variety of symptoms depends on the area of the brain involved. Seizures can range from a loss of consciousness with body tremors, confusion, and difficulty responding; visual symptoms, isolated postures or movements of a single limb; or brief loss of consciousness, among other symptoms [3].

Epilepsy is defined as at least two unprovoked seizures more than 24 hours apart or one unprovoked seizure with a probability of a recurrence risk of subsequent seizures of approximately 60% (similar to the 10-year risk of recurrence after two unprovoked seizures) [4].

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Immediate provoked seizures usually have clear identifiable causes such as toxins, medications or metabolic alterations. Frequently, people who experience these crises present previous symptoms such as confusion or behavioral changes, which may continue after the crisis; and these tend to be generalized seizures and generally do not need preventive antiepileptic treatment [1]. Among the common causes are alcohol or benzodiazepine intoxication, hydro electrolytic alterations (hyponatremia, hypocalcemia, hypomagnesemia, hypoglycemia or hyperglycemia) or drugs of abuse [4].

Acute symptomatic seizures, representing 40-50% of all cases of seizures, are a manifestation of an acute event (36% infectious, 30% vascular, 13% metabolic and 11% toxicological) and may not reappear when the underlying cause has been eliminated or the hyperacute phase has passed [4]. Specific treatment targeting the underlying brain process may be necessary; however, patients may additionally require short-term anticonvulsant medication [1].

Unprovoked seizures, including *remote symptomatic seizures*, *occur due to pre-existing brain injury, with seizure manifestation after 7 days*, seizures associated with epileptic syndromes and without apparent cause [4].

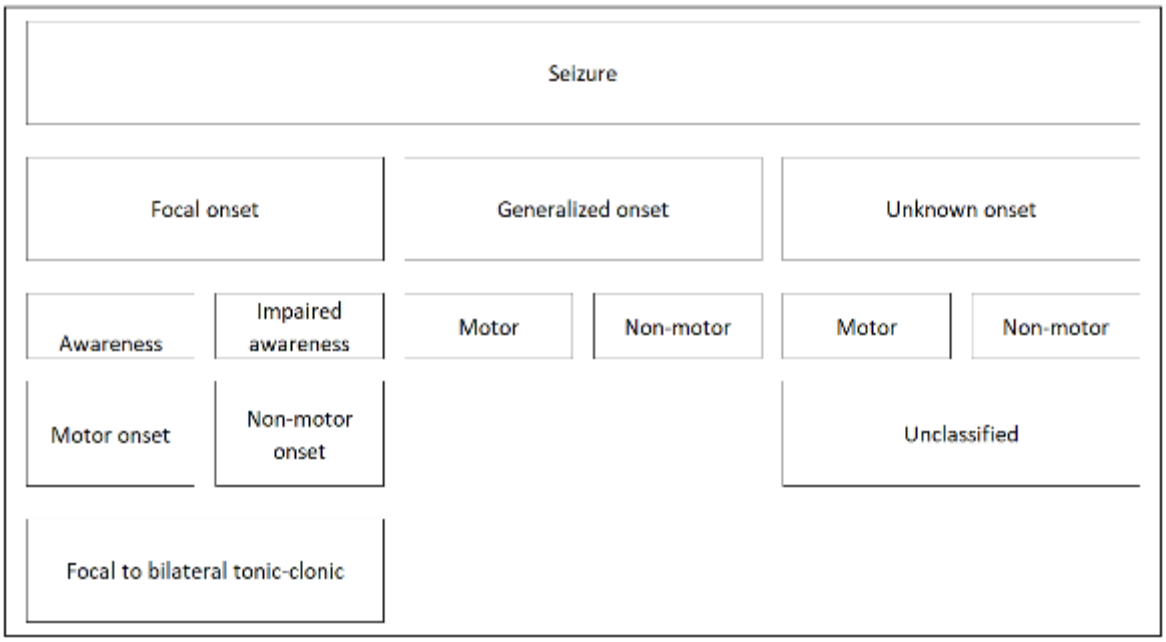

Figure 1 Classification of crises. Adapted from ILAE 2017 [5]

2.1. Types of seizures

Seizures are classified according to their onset as focal, generalized and unknown. When they have a generalized onset, it means that their origin involves neurons from both cerebral hemispheres, while focal onset implies an onset from one region or hemisphere [1].

2.1.1. Focal seizures

Focal seizures originate from a neural network, whether localized and limited to a brain region or with a broader distribution but within the same hemisphere. The terms "simple focal seizures" and "complex focal seizures" were eliminated in the new 2017 classification [5]. According to the new ILAE classification, focal seizures are divided according to whether consciousness is preserved or altered and according to the presence of motor and non-motor symptoms. Furthermore, it must be remembered that a focal seizure can evolve into bilateral seizure activity [1], [5].

2.1.2. Focal seizures without alteration of consciousness

Focal seizures can have motor manifestations (such as tonic, clonic or myoclonic movements) or they can be non-motor manifestations (such as sensory, autonomic or emotional symptoms) and very importantly without alteration of consciousness [5].

2.1.3. Focal seizures with altered consciousness

Focal seizures may also be accompanied by a temporary alteration in the ability to maintain normal contact with the environment. Clinically they manifest with the patient being unable to respond to visual or verbal commands during the

course of the seizure. Crises usually begin with an aura. The ictal phase consists of a sudden interruption of the patient's activity, who remains immobile and with his gaze lost, which marks the beginning of a period of decreased state of consciousness. It could be accompanied by automatisms (chewing movements, sucking with the lips, swallowing). After the crisis, the patient presents a characteristic state of confusion that gradually recovers completely, the alteration of consciousness can last from seconds to 1 hour or more, and may also present anterograde amnesia, or transient neurological deficiencies (such as aphasia or vision loss) caused by postictal inhibition of the cortical regions most affected in the seizure itself [5].

2.1.4. Generalized crises

Generalized seizures originate somewhere in the brain but connect immediately and quickly with neural networks in both cerebral hemispheres. They are classified as motor and non-motor. Various types of generalized seizures have characteristics that place them in distinctive categories and facilitate their clinical diagnosis [1].

2.1.5. Tonic-clonic seizures

This type of seizure can affect 10% of individuals with epilepsy. They can arise in various clinical contexts. It generally begins suddenly, although some patients experience mild symptoms that anticipate the crisis. The initial phase is characterized by a tonic contraction of all the muscles of the body, and can lead to a sound like a grunt or an "ictal scream" due to the contraction of the expiratory muscles and the larynx. Tension of the jaw muscles can cause tongue biting. There is an increase in sympathetic activity that leads to an increase in heart rate, blood pressure and change in pupil size. After approximately 10 to 20 seconds, the tonic phase gives way to a clonic phase. In this stage, muscle contractions alternate with moments of relaxation. Relaxation intervals become more frequent until the ictal phase concludes, which typically lasts less than a minute. The postictal phase is characterized by unresponsiveness, muscle weakness, and excessive salivation, which can lead to noisy breathing and partial airway obstruction. There may also be loss of sphincter control [5].

2.1.6. Atonic seizures

Atonic seizures are characterized by a sudden loss, for 1 to 2 seconds, of postural muscle tone. The state of consciousness is briefly altered, but there is usually no post-ictal period.

2.1.7. Myoclonic seizures

Myoclonus is a sudden, brief muscle contraction of a part of the body or the entire body. The characteristic form of myoclonus is the sudden jerking movement that appears when someone is falling asleep. Pathological myoclonus appears associated with metabolic disorders, degenerative CNS diseases or anoxic brain lesions [6].

Epilepsy is defined according to the ILAE when any of the following exists:

- Patient who presented two or more unprovoked seizures, separated by at least 24 hours.
- Patients with a single seizure, but with a risk of future seizures of at least 60% (based on medical history or electroencephalogram).
- Diagnosis of an epilepsy syndrome [5)

2.2. Epidemiology

The epileptic seizure is a common condition affecting approximately 8 – 10% of the population throughout their life [7], it represents 1.2% of all visits to the emergency department and 24% of them, corresponds to a first episode of crisis [8]. About 170,000 people in the United States experience their first seizure episode each year. Of that number of patients, 50% never have any new crises in their lives [3]. The incidence of unprovoked seizures varies from 50 to 70 per 100,000 inhabitants, and of epilepsy from 30 to 50 per 100,000 inhabitants [9]. The incidence continues to increase with age and rates of new-onset epilepsy in the elderly are higher than in any other age group. There is an estimated cumulative incidence of 4.4% at age 85 years [3]. In Colombia in 2015, the prevalence was estimated at 10.3 per 1,000 inhabitants and it was concluded that each year 5.25 years of healthy life are lost per 1,000 Colombians [10].

3. Pathophysiology

Neurons generate electrical signals through the action potential, which propagates along the axon from the soma, and synaptic transmission, which allows communication between neurons through chemical impulses converted into electrical ones. The action potential induces the release of neurotransmitters that bind to postsynaptic receptors,

generating excitatory or inhibitory postsynaptic potentials. The synchronized sum of these postsynaptic potentials produces the electrical activity recorded in the electroencephalogram. The main excitatory neurotransmitters are glutamate and aspartate, and the main inhibitor is gamma-aminobutyric acid (GABA) [6].

4. Anamnesis and physical examination

When faced with a first epileptic seizure, the primary objective is to recognize if the episode is really a seizure, therefore it is important to take a detailed anamnesis, a complete physical examination and request paraclinical tests to confirm the event [11]. The history questions should be oriented towards the symptoms that occurred before (premonitory symptoms such as aura), during and after the episode, to rule out seizure simulators.

Table 1 Epileptic seizure simulators. Adapted from: Rao VR. 2022 [6]

Epileptic seizure simulators	
Syncope	Migraine
Cardiac arrhythmia	Narcolepsy
Heart disease	Paroxysmal choreoathetosis
Psychogenic crises	Benign paroxysmal vertigo
Hypoglycemia	Apnea
Hypoxia	Night terrors
Panic attack	Psychoactive drugs

Family history plays a fundamental role, since a positive history of seizures increases the risk of epilepsy, mainly if it is related to absence seizures or myoclonic seizures.

Inquire about precipitating factors such as sleep deprivation, stress, intense emotions, alcohol consumption, or high-intensity flashing lights. Causative factors (of acute symptomatic crises) such as the consumption of toxic substances, alcohol or drugs. In unwitnessed epileptic seizures, the physical examination should look for the presence of some signs and symptoms that increase the probability that a seizure episode has actually occurred, for example: evidence of tongue biting, urinary incontinence or characteristic patterns of self-harm [11].

The second step, once the crisis is confirmed, is to investigate whether we are really facing a first episode, since up to 40% of the patients admitted with a first crisis have actually already had a previous episode and therefore questions should be made about the presence of an aura, the presence of blood on the pillow, whether waking up with a bitten tongue or even urinary incontinence [12].

The third step is to try to determine whether it is a provoked or unprovoked seizure and a complete physical examination must be performed, looking for signs of pathologies that can generate epileptic seizures, such as, for example, examining the skin may reveal signs of neurocutaneous disorders. such as tuberous sclerosis or neurofibromatosis, or even chronic liver or kidney disease. Presence of congenital asymmetry of the limbs that raises suspicion of a brain injury that occurred in the early stages of childhood development. Signs of head trauma and alcohol or drug use should be looked for. Auscultation of the heart and carotid arteries allows the identification of abnormalities predisposing to suffering a stroke [11], [12].

5. Differential diagnosis

An extensive interrogation should always be carried out aimed at mainly ruling out pathologies like syncope, which mainly occurs in older people with cardiovascular disease. For this purpose, the Sheldon score can be used.

Another condition to be considered as part of the differential diagnosis must be the psychogenic non-epileptic seizures; these often arise in a particular context in response to external or internal triggers (also called atypical events). When the seizure occurs with numerous concomitant symptoms it usually suggests somatization. Also, it's important to

consider sleep disorders, mainly when the crisis takes place during the night, in this case the first diagnostic considerations could be an awakening disorder such as: night terrors, sleepwalking and confusional arousals [11].

Table 2 Sheldon scale

Item	Points
Tongue bite	2
Feeling of deja vu or presence of aura	1
Emotional stress is associated with loss of consciousness?	1
Ocurrance of head rotation?	1
Has anyone ever noticed that you are unresponsive, have unusual postures or shake your limbs during your seizures or do not remember your seizures afterwards? (Rate yes for any positive answers)	1
Post-crisis confusion	1
Dizziness prior to the episode?	-2
Sweating prior to the episode?	-2
Is sitting or standing for a long time associated with your attacks?	-2
The patient has seizures if the score is ≥1 and syncope if the score is <1.	

Questions to determine if the loss of consciousness is due to seizures or syncope. Adapted from Sheldon R. 2002 [13].

6. Complementary studies

Initial lab tests to identify the possible causes of the seizure, or pre-existing conditions, Complete blood count, Serum electrolytes (including calcium and magnesium), Blood glucose, Kidney and liver function, Electrocardiogram (mainly in adults) and urinalysis [14].

Other lab tests depending on the findings of the examination and interrogation.

- Thyroid and liver profile
- Alcohol and drug testing
- Lumbar puncture

6.1. Electroencephalogram

It should be performed preferably in the inter-ictal period or within the first 24 hours of the post-ictal period. Anomalies have been identified in 51% in the post-ictal period and in 34% in patients who underwent encephalogram hours later. However, the diagnostic performance of the test performed in ambulatory or sleep-deprived patients further increases the diagnostic performance compared to those who are performed in the inter-ictal period with normal EEG results.

Abnormal EEG findings increase the likelihood of a second seizure within the next 2 years.

It must always be kept in mind that a normal electroencephalogram does not exclude the diagnosis of epilepsy [14].

Detection of spike and wave discharges on EEG was associated with a 50% risk of recurrence at 18 months if seizures are considered idiopathic [15].

6.2. Neuroimaging

In every first episode, a neuroimaging study must be performed to rule out structural pathology, except in those patients with metabolic or hydro electrolyte disorders that justify the crisis. Given availability, simple skull tomography is initially preferred. In the case of seizures with focal onset, persistently altered mental status, or in which alterations not

evident in the tomography are suspected, nuclear magnetic resonance is recommended because it has greater sensitivity and specificity than head CT scan[12].

MRI abnormalities were found more frequently in patients with focal-onset seizures (53%) than in the first-seizure group (28%). The most common types of lesions in patients with focal seizures were gliosis or encephalomalacia (49%) [15].

6.3. Treatment

Every patient with an epileptic seizure, whether or not it is the first episode, should begin general support measures (ABCDE), take seizure duration, oxygen, monitoring, and blood sugar level test and use of benzodiazepines as first-line medication because they are potent anticonvulsant drugs. Its mechanism of action is related to a BZD receptor that increases GABAergic transmission. Higher concentrations also limit repetitive neuronal firing similar to carbamazepine and phenytoin. Its adverse effects include respiratory depression (3-10%), hypotension (< 2%) and worsening level of consciousness (20-60%) [16], [17].

- Diazepam
- Midazolam
- Clonazepam
- Lorazepam

Most patients in their first crisis enter the emergency department/room in the postictal period or already with recovery of their baseline state, therefore decisions about whether or not to start therapy are based on the risk of recurrence (alterations in electroencephalogram and/or in neuroimaging studies, presence of provoking factors, among others).

Anticonvulsant therapy in the first epileptic seizure is indicated in those patients who have a risk of new unprovoked seizures that is estimated to exceed 60% in the next 10 years [14].

The Medical Research Council Multicenter Trial for Early Epilepsy and Single Seizures showed that the risk of seizure recurrence was lower in the first 2 years after a first seizure in those who received medication early (mainly carbamazepine or sodium valproate) than in those in whom it was delayed until a new episode (32% vs 39%). However, it did not increase remission early and generated a greater presence of adverse effects [14], [18].

Table 3 Probability of a new seizure after an epileptic episode and recommendations on the use of antiepileptic medication. adapted from Smith 2021 [14]

Risk level and number of attacks	**Neurological alterations or abnormalities in the electroencephalogram**	**Indications for the use of antiepileptic drugs**
Low risk		
1 crisis	None	No
Medium risk		
1 crisis	Some	Evaluate
2 to 3 crises	None	
High risk		
1 crisis	Both	
2 to 3 crises	Some	Yes
More than 3 crises	None	

Medication should be based on the type of crisis, taking into account the effectiveness, adverse effects and characteristics of its pharmacokinetics and pharmacodynamics and mainly on the patient's profile, starting as monotherapy and gradually increasing the dose until the minimum effective dose is reached.

The initiation of treatment in patients with recovery from their baseline state and without new episodes, but with high risk, should begin before leaving the emergency department or as soon as the first outpatient check-up is performed, preferably with a neurologist.

If there is an identified reversible provoking factor, the risk of recurrence is likely to be lower than if it did not exist and antiepileptic treatment is generally not indicated [14].

There are a limited number of randomized trials that used anticonvulsant medications as initial monotherapy with similar efficacy, without demonstrating significant differences between anticonvulsants to date. The recommended medications during the first epileptic episode in those with focal onset seizures are: lamotrigine or levetiracetam. For patients with generalized onset seizures, the first option is sodium valproate, as long as they are not breastfeeding women or likely to be pregnant; in that case, the treatment recommendation is levetiracetam [14].

7. Antiepileptic medication

7.1. Lamotrigine

Intended use: Preferred in focal onset seizures, effective in generalized onset, but with risk of the appearance of myoclonus and absence.

Initial dose: 25 mg orally daily for 4 to 6 weeks to avoid skin rash, during this time it can be combined with other antiepileptics (avoiding the use of carbamazepine and sodium valproate due to the risk of drug interactions)

Maintenance dose: 100 to 200 mg orally daily in 1 to 2 doses [14].

7.2. Levetiracetam

Intended use: Crisis of focal or generalized onset.

Initial dose: 250 mg orally daily

Maintenance dose: 1000 to 2000 mg daily divided into 2 doses [14].

7.3. Sodium valproate

Intended use: mainly for generalized seizures.

Initial dose: 200 to 500 mg orally daily

Maintenance dose: 500 to 1500 mg orally daily, divided into 1 to 2 doses

Other medications that can be considered in partial seizures are: phenobarbital, phenytoin, lamotrigine; the latter can also be used as an alternative in generalized crises [17], [19].

7.4. Treatment flow chart

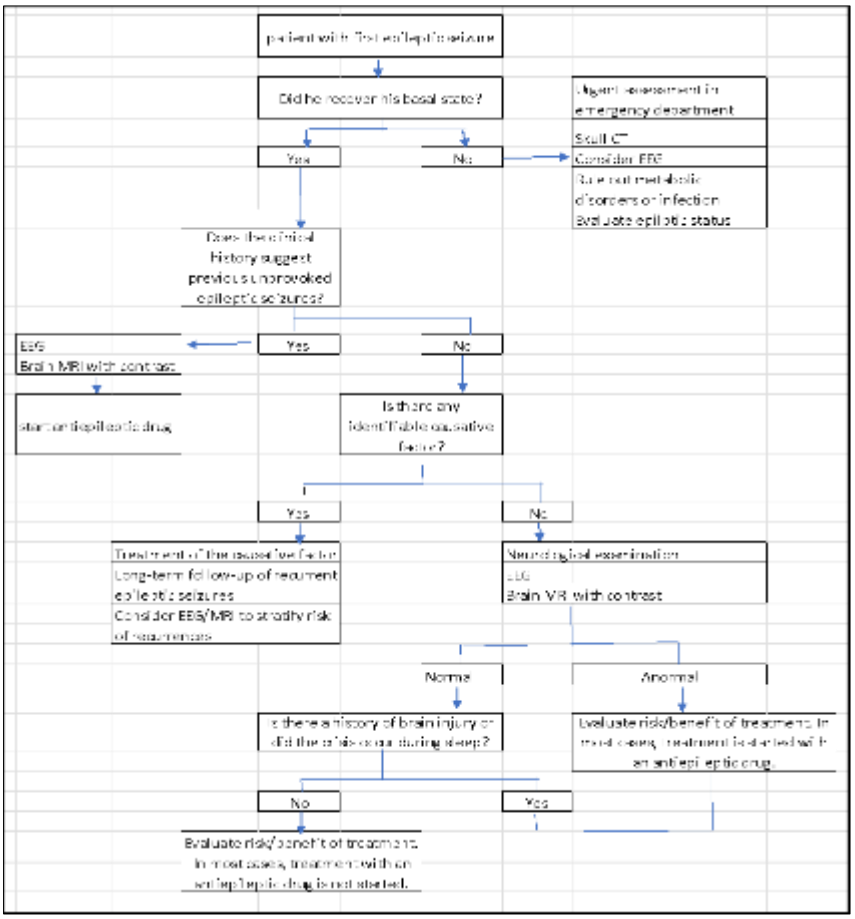

Figure 2 Flowchart for management of the patient with the first epileptic seizure. Adapted from Gelfand M. 2022. [20]

7.5. Other actions

Before discharge, patients should be educated about their illness (causes, risk of recurrence, limitations in examinations, and prognosis). Recommend changes in lifestyle: such as safety measures at home and in your work area, restrictions when driving and performing risky sports, and prevention of factors that cause epilepsy; as well as stress management and referral for comprehensive management in case of reporting stress or depression [9].

8. Conclusion

The evaluation of a patient during their first epileptic seizure should focus mainly on identifying those patients with a higher risk of recurrence, based on a detailed clinical history seeking to identify provoking factors, aided by paraclinical studies, mainly electroencephalogram and neuroimaging studies, in order to define patients who can benefit from an early antiepileptic therapy and education as pillars of good adherence and prevention of new seizures.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] Wirrell E. Evaluation of first seizure and newly diagnosed epilepsy. Continuum (Minneap Minn). 2022;28(2):230–60.

[2] Gavvala JR, Schuele SU. New-onset seizure in adults and adolescents: A review. JAMA. 2016;316(24):2657.

[3] Johnson EL. Seizures and epilepsy. Med Clin North Am 2019; 103: 309–324.

[4] Gunawardane N, Fields M. Acute symptomatic seizures and provoked seizures: To treat or not to treat? Curr Treat Options Neurol 2018; 20: 41

[5] Brodie MJ, Zuberi SM, Scheffer IE, Fisher RS. The 2017 ILAE classification of seizure types and the epilepsies: what do people with epilepsy and their caregivers need to know? Epileptic Disord. 2018;20(2):77–87.

[6] Rao VR, Lowenstein DH. Seizures and Epilepsy. In: Loscalzo J, Fauci A, Kasper D, Hauser S, Longo D, Jameson J. eds. Harrison's Principles of Internal Medicine, 21e. McGraw-Hill Education; 2022.

[7] Bergey GK. Management of a first seizure. Continuum (Minneap Minn) 2016; 22: 38–50.

[8] Wyman AJ, Mayes BN, Hernandez-Nino J, Rozario N, Beverly SK, Asimos AW. The first-time seizure emergency department electroencephalogram study. Ann Emerg Med. 2017;69(2):184-191.e1.

[9] Krumholz A, Wiebe S, Gronseth GS, Gloss DS, Sanchez AM, Kabir AA, et al. Evidence-based guideline: Management of an unprovoked first seizure in adults: Report of the Guideline Development Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Neurology. 2015;84(16):1705–13.

[10] Méndez-Ayala A, Nariño D, Rosselli D. Burden of epilepsy in Colombia. Neuroepidemiology. 2015;44(3):144–8.

[11] Nowacki TA, Jirsch JD. Evaluation of the first seizure patient: Key points in the history and physical examination. Seizure. 2017;49:54–63.

[12] Foster E, Carney P, Liew D, Ademi Z, O'Brien T, Kwan P. First seizure presentations in adults: Beyond assessment and treatment. J Neurol Neurosurg Psychiatry. 2019;90(9):1039–45.

[13] Sheldon R, Rose S, Ritchie D, Connolly SJ, Koshman M Lou, Lee MA, et al. Historical criteria that distinguish syncope from seizures. J Am Coll Cardiol 2002;40(1):142–8

[14] Smith PEM. Initial management of seizure in adults. N Engl J Med 2021; 385: 251–263.

[15] Kunze A, Reuber M. The first seizure as an indicator of epilepsy. Curr Opin Neurol 2018; 31: 156–161.

[16] Rodríguez Moreno C, Donado Budiño E, Tarragó Bofarull J, Durán Parrondo C, Tato Herrero F, Pato Pato A, et al. el estado epiléptico. Med Integr. 2002;40(8):358–64.

[17] Olmos-López A, Ibarra-Aguilar J, Cornelio-Nieto JO, Ocaña-Hernández LA, Márquez-Amaya MA, Luna-López NA, et al. Guía clínica. Estado epiléptico en niños y adultos. Revista Mexicana de Neurociencia. 2023;20(2).

[18] Bonnett LJ, Tudur-Smith C, Williamson PR, Marson AG. Risk of recurrence after a first seizure and implications for driving: further analysis of the Multicentre study of early Epilepsy and Single Seizures. BMJ. 2010;341:c6477.

[19] Nevitt SJ, Sudell M, Cividini S, Marson AG, Tudur Smith C. Antiepileptic drug monotherapy for epilepsy: a network meta-analysis of individual participant data. Cochrane Libr. 2022;2022(4).

[20] Gelfand M. 70 - Valoración de una primera crisis epiléptica en un paciente adulto. Toma de decisiones en neurología. Elsevier España, S.L.U.; 2022. 144–145