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Characterizing antiseizure medication in patients with diagnosis of epilepsy in San Jose Infantil and San Jose Centro Hospitals: A retrospective cohort study in Colombia, 2019-2022

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Abstract

Introduction: Epilepsy is one of the most common neurological diseases in the world that affects millions of people. We aimed to characterize antiseizure medications (ASM) and to evaluate their clinical behavior in terms of treatment adherence and seizure control of patients treated for epilepsy in two hospitals in Bogotá, Colombia: San José Centro and San José Infantil, between 2019 and 2022.

Methods: We performed a retrospective review of patients treated for epilepsy in two hospitals in Bogota, Colombia: San José Centro and San José Infantil. The study was approved by the faculty and ethics committee of Fundación Universitaria de Ciencias de la Salud (FUCS). We surveyed patients who met the International League Against Epilepsy (ILAE) criteria for epilepsy. The survey included demographic, social impact, clinical, and treatment data. Statistical analysis was done with Stata v.17 and Jamovi V2.3.26.

Results: The study included 797 patients who met the criteria for epilepsy diagnosis. A total of 44.1% of the patients needed only one medication to control their seizures adequately. We found that patients who used the new generation of antiseizure medications had better control of epilepsy, primarily due to greater adherence in this study population.

Discussion: New-generation antiseizure medications demonstrate similar efficacy to older drugs but with better adherence, fewer adverse effects, and lower treatment abandonment. No additional benefit was observed with polytherapy, emphasizing the importance of a rational treatment approach. Reduced drug interactions make these medications particularly beneficial for vulnerable populations. Additionally, failure to achieve seizure control with the first medication increases the risk of pharmacoresistance, highlighting the need for individualized management.

Conclusion: The new generation of antiseizure medications shows a clinical response comparable to that of older drugs, with a better adherence rate, fewer adverse effects, and a lower rate of treatment abandonment.

Keywords: Epilepsy, Antiseizure Medication, Hospitals, Vulnerable Populations, Diagnosis, Drug Interactions.

Comportamiento de medicamentos anticrisis en pacientes con diagnóstico de epilepsia del Hospital de San José y del Hospital Infantil Universitario de San José: un estudio de cohortes retrospectivo en Colombia, 2019-2022

Resumen

Introducción: la epilepsia es una de las enfermedades neurológicas más comunes en el mundo que afecta a millones de personas. Nuestro objetivo fue caracterizar los medicamentos anticrisis y evaluar su comportamiento clínico en términos de adherencia al tratamiento y control de crisis en pacientes que fueron tratados por epilepsia en dos hospitales de Bogotá, Colombia: San José Centro y San José Infantil entre 2019 y 2022.

Métodos: realizamos una revisión retrospectiva de pacientes que fueron tratados por epilepsia en dos hospitales de Bogotá, Colombia: San José Centro y San José Infantil. El estudio fue aprobado por el cuerpo docente y el comité de ética de la Fundación Universitaria de Ciencias de la Salud (FUCS). Realizamos una encuesta a aquellos pacientes que cumplían con los criterios de epilepsia de la ILAE (Liga Internacional Contra la Epilepsia). La encuesta incluyó datos demográficos, de impacto social, clínicos y de tratamiento. El análisis estadístico se realizó con Stata v.17 y Jamovi V2.3.26.

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Resultados: se incluyeron en el estudio 797 pacientes que cumplían con los criterios para el diagnóstico de epilepsia. El 44,1 % de los pacientes necesitó un solo medicamento para tener un control adecuado de las crisis epilépticas. Encontramos que los pacientes que utilizaron medicamentos anticrisis de nueva generación tuvieron un mejor control de la epilepsia, debido a una mayor adherencia en esta población de estudio.

Discusión: los medicamentos anticrisis de nueva generación muestran una eficacia similar a los tradicionales, pero con mejor adherencia, menos efectos adversos y menor abandono del tratamiento. No se observó un beneficio adicional con la politerapia, lo que resalta la importancia de una selección racional del tratamiento. Una menor interacción medicamentosa hace que estos fármacos sean especialmente beneficiosos para poblaciones vulnerables. Además, la falta de control de crisis con el primer medicamento aumenta el riesgo de farmacorresistencia, enfatizando la importancia de un manejo individualizado para cada paciente.

Conclusión: la nueva generación de medicamentos anticrisis tiene una respuesta clínica similar a los más antiguos, con mejor tasa de adherencia, disminución de efectos adversos y menor abandono del tratamiento.

Palabras clave: epilepsia, medicamentos anticrisis, hospitales, población vulnerable, diagnóstico, interacciones farmacológicas.

Introduction

Epilepsy has been a well-known disease for many decades. However, it continues to be stigmatized, even though approximately 70% of people with epilepsy can lead a normal life (1). This does not avoid the fear and labels of the diagnosis, which in turn leads to a greater probability of misinformation about the disease, with consequences that affect the patient's work, social, and emotional environments (2,3). According to statistics from the World Health Organization, fifty million people have epilepsy in the world, and almost 80% of these patients live in low-income countries, which affects the behavior of the disease, prognosis, and possible treatment, both medical and surgical. In Colombia, approximately 1.3% of the population suffers from this disease. By 2017, it accounted for 0.8% of the mortality in our country. The prevalence of epilepsy is 586 per 100,000 inhabitants, with the Esencia study reporting a predominance in men between 40 and 49 years (4).

Its association with psychiatric pathologies and intellectual disability should not be underestimated, since individuals who present both epilepsy and a disability have a higher mortality rate, particularly those with recent epileptic seizures. Our study did not directly address these comorbidities, but they remain crucial in tailoring treatment and prognosis. These two conditions have been linked to up to 33% of the population (3,5), thus generating a more significant impact at a biopsychosocial level. In an observational study carried out in Ireland, 50.3% of the patients were exposed to polytherapy with antiseizure medications (ASM), 13.7% had an associated psychotropic drug, and antipsychotics with epileptogenic potential represented 80% of these medications.

That is why it is essential to individualize the therapeutic option for each patient (6). In the last few years, the therapeutic options have expanded, increasing their availability and offering a more complete alternative for the specific management of each type of epilepsy (7,8). At least one systematic review of recent literature has made it possible to obtain high-quality evidence that supports the use of medications such as lamotrigine as the first line for focal epilepsy and levetiracetam as an alternative, thus controlling adverse effects, which leads to better adherence (9). Different studies, including a cohort from Ethiopia, have provided data about the reasons why some patients are unsatisfied with treatment, including side effects, low effectiveness of the medication, comfort in the use of the medication, impact on daily activities, and also if the medicines were complimentary or were paid by the patient, in addition to culture, beliefs, and education (10).

Currently, we don't have studies that allow us to understand the behavior of ASMs in our population, including some elements like adherence and treatment abandonment (11). Even though there has been an increase in the availability of ASMs worldwide due to their excellent tolerability and the fact that adherence reduces the frequency of seizures (12,13), this has become a challenge for the treating physician when choosing the best therapeutic option.

Some factors become essential when selecting treatment, especially potential drug interactions, patient preferences on the schedule of treatment, and the increased risk of worsening in certain types of

epilepsy with specific medications (14). These considerations are especially important given that there is a lack of data available to compare effectiveness between drugs (15,16).

This study aimed to characterize the use of ASMs and to describe the behavior and clinical response of ASMs in terms of adherence and seizure control in patients diagnosed with epilepsy treated in our hospitals.

Methods

This study was approved by the Fundación Universitaria de Ciencias de la Salud faculty and the Ethics Committee of the Fundación Universitaria de Ciencias de la Salud (SIDI 5414). We performed a retrospective review of patients treated for epilepsy in two major hospitals in Bogota, Colombia: San José Centro and San José Infantil, between 2019 and 2022. We included those patients over 18 years of age with an epilepsy diagnosis according to ILAE criteria. Patients with incomplete data, those who did not meet ILAE criteria, and those who disagreed to be included in the research were excluded.

The research was carried out on patients in the database from the two previously mentioned hospitals, selecting individuals with CIE-10 codes (G400, G401, G402, G403, G404, G408, G409, Z820) to include patients who met ILAE criteria. These patients were subsequently asked to answer a telephone survey with prior consent. All calls were placed by trained research coordinators (neurology residents) under the supervision of the principal investigator, using a standardized script to ensure consistency.

The survey included demographic, social impact, clinical, and treatment data. These results were used to estimate the impact of adherence and treatment on the Colombian population. ASMs were grouped according to their historical development and pharmacological profiles. First-generation ASMs included phenobarbital, phenytoin, carbamazepine, and sodium valproate; second-generation agents comprised lamotrigine, topiramate, oxcarbazepine, and valproic acid; and third-generation ASMs encompassed levetiracetam, lacosamide, and brivaracetam.

Treatment adherence was assessed by patient- or caregiver-reported telephone interviews. We defined a patient as adherent if they self-reported taking ≥ 80% of prescribed ASM doses over the previous month. We recognize that the use of a non-validated, self-report method, rather than using an objective pill count or a validated scale such as the MMAS-8, may have led to an overestimation of adherence compared with other studies. In accordance with the recommendations of the ILAE, we defined seizure control or seizure freedom as the absence of any epileptic seizure for at least 12 months, or for a period equal to three times the longest interseizure interval prior to treatment initiation, whichever is longer (17).

The data was analyzed using descriptive statistics. The qualitative variables were assessed using absolute and relative measures, and the quantitative variables were assessed using measures of trend and dispersion. Statistical analysis was done with Stata v.17 and Jamovi V2.3.26.

Results

An initial population of 847 patients was obtained, of which 50 patients gave up continuing in the study for different reasons, for a total of 797 patients. The average age was 38,4 ± 2,0; 50.1% were male. By socioeconomic status, the highest frequency was status 3, with 66.5% (Table 1).

A family history of epilepsy in the first degree of consanguinity was reported in 28.7% of individuals. The past medical history of febrile seizures only represented 9.6%; regarding the type of epilepsy, focal represented 69.8%, generalized 13.3%, and unknown etiology 16.8%. According to monthly ictal frequency, 48.4% of the total population did not have seizures with treatment adherence. On the other hand, 128 patients (16.1%) reported having just one episode monthly. Just three patients (0.4%) reported having more than one episode. One case had up to 300 episodes monthly. According to the number of medications, 16 ASMs were included. A total of 51.6% of patients were treated with one drug, while 23.8% were treated with two medications. The most frequently used were levetiracetam (41.7%) and lacosamide (31.6%), while the least used were brivaracetam (6.1%), phenytoin (5.2%), and vigabatrin (2.0%) (Table 2).

In terms of monthly ictal frequency, 44.2% of patients were managed with a single medication, 20.7% required two, and 4.0% needed three. Seizure freedom was attained in 30.7% of those on one medication, 8.0% on two, and 3.2% on three medications.

Table 1. Clinical and demographic characteristics of the patients

Characteristic	Participants: 797
Age (years)	38.4
Median	33
Interquartile range	
Gender	
Female n (%)	398 (49.9 %)
Male n (%)	399 (50.1 %)
Socioeconomic status*	
1	44 (5.5%)
2	198 (24.9 %)
3	531 (66.5%)
4	17 (2.1 %)
5	7 (0.9%)
Origin	
Urban	724 (90.9%)
Rural	73 (9.1%)
Type of affiliation ¥	
Contributive	647 (81.1%)
Subsidiary	149 (18.6%)
Family history of epilepsy	
Yes	229 (28.7%)
No	568 (71.2 %)
Febrile seizure	
Yes	77 (9.6%)
No	720 (90.3 %)
Epilepsy type	
Focal	557 (69.8%)
Generalized	106 (13.3%)
Unknown etiology	134 (16.2 %)

Note. *A socio-economic status refers to Colombia's official residential strata (1=low, 2=lower-middle, 3=middle, 4=upper-middle, 5=high).

¥ Type of affiliation refers to the patient's health-insurance regime (contributive=worker-funded, Subsidiary=state-subsidized).

Source: Own elaboration.

Treatment adherence was assessed through a survey, which indicated that 91% of patients adhered to their treatment, with the most frequently used combination being levetiracetam and lacosamide (Table 2).

Table 2. Results

Medications	
Levetiracetam	332 (41.7%)
Lacosamide	251 (31.6 %)
Valproic acid	204 (25.6)
Lamotrigine	151 (19%)
Carbamazepine	112 (14.8%)
Clobazam	69 (8.7%)
Topiramate	60 (7.6%)
Oxcarbazepine	58 (7.4 %)
Brivaracetam	49 (6.1%)
Phenytoin	41 (5.2%)
Clonazepam	27 (3.3%)
Sodium Divalproate	22 (2.8%)
Phenobarbital	18 (2.3%)
Vigabatrin	16 (2%)
Cannabidiol	2 (0.3%)
Gabapentin	1 0.1%)
Monthly ictal frequency control	
One medication	352 (44.1%)
Two medications	165 (20.7%)
Three or more medications	26 (3.2%)

Source: Own elaboration.

Discussion

This study describes the results obtained from the research and interpretation of the behavior of anti-seizure medications in patients with a diagnosis of epilepsy who were treated in two high-complexity hospitals in Bogota for 4 years, with three epileptologists who led the epilepsy program.

Furthermore, it was evident that, independently of the number of ASMs used and the new generation of drugs, the highest percentage of the population adhered to treatment and controlled their seizures. However, polytherapy did not provide additional benefits or a better clinical response (18,19). While extended-release formulations of ASMs have been shown to improve adherence in other settings, it remains unclear whether these delivery systems are readily available to our patient population within Colombia's public and private health networks.

As previously mentioned, the rational use and behavior of the new generation of ASMs reduced the risk of drug interactions, the leading cause of which is related to drug metabolism through inhibition/induction of CYP 450 (20–22).

Most of these medications are metabolized oxidatively. Therefore, interactions with other medications affect their metabolism. This is especially important in pediatric patients, older adults, and women of childbearing age (23,24). Additionally, major congenital malformations can be reduced with the appropriate medication selection. These are related to polytherapy and the type of ASM used. Levetiracetam, lamotrigine, and carbamazepine, frequently used in our emergency services, have demonstrated a lower frequency of teratogenicity (25,26).

This translated into an improvement in the patient's quality of care and a reduction in the risk of sudden unexpected death in epilepsy (SUDEP), which is associated with a recent history of epilepsy, a high frequency of generalized tonic–clonic seizures, and the reappearance of seizures after a long period of control (23,27,28). Likewise, it can influence the decrease of public health costs (29).

In comparison with the study published by Brodie et al. (16), we found that the most frequently diagnosed type of epilepsy was focal epilepsy, with 78.5%, which correlates with our findings: 69.8% was associated with poor pharmacological response. Like our premises, the present analysis demonstrates that not achieving seizure control with a first medication increased the risk of refractoriness, while adding a second medication only provided a possibility of absence of seizure of 8.0%, and 4.0% with a third medication.

In this study, it is observed that the use of new antiseizure generation medication (such as lamotrigine, levetiracetam, and lacosamide) had a similar response to old medications according to the control of ictal frequency (18), including phenobarbital, phenytoin, and carbamazepine, which are widely used in our media with a high potential of drug interactions, already reported in previous studies, and loss of efficacy of medications that are used in the patients with concomitant diseases (renal disease, HIV, and/or liver disease) (30).

Treatment decisions tend to be more complex in older adults with a diagnosis of refractory epilepsy. They typically require dose adjustment due to renal or hepatic dysfunction, which may go beyond correcting glomerular filtration rate (GFR) and even require measuring free drug levels (31,32). This impacts patients' perceptions of satisfaction with treatment efficacy and satisfaction with medical care. Additionally, previous studies also showed that being seizure–free for over a year was associated with better patient adherence rates (10).

As a limitation, patients with pharmacological and nonpharmacological combined therapies, such as a neurostimulator or ketogenic diet, were not included (33,34). Bias was controlled by collecting information from patients admitted to the neurology service database in the two hospitals. The survey used was standardized and answered by the patient or caregiver.

An important limitation of this study is the potential underrepresentation of patients from rural areas or those without affiliation to the national health system. Since the hospitals involved are tertiary referral centers located in urban settings, most patients had access to specialized care and newer-generation ASMs. In contrast, individuals in rural regions are more likely to be treated with traditional or first-generation medications and often face significant geographic or financial barriers to accessing specialized epilepsy care. This selection bias may influence the observed patterns of ASM use and limit the generalizability of our findings to broader or underserved populations.

It remains unclear whether these newer ASMs are uniformly available throughout Colombia's public and private systems, particularly outside Bogotá and in rural areas, where even some first-generation drugs may be in short supply or subject to stockouts.

The predominance of second- and third-generation ASMs observed in this cohort likely reflects the treatment practices of specialized urban epilepsy centers. These medications may not be readily available in non-specialized or rural healthcare settings, where traditional ASMs are still commonly prescribed. Therefore, the treatment profiles identified in this study must be interpreted within the context of a referral-based population with greater access to updated pharmacological therapies.

Although treatment response in terms of seizure control was evaluated, adverse effects or tolerability profiles for specific ASMs were not systematically

recorded in this study. This limits our ability to compare safety or efficacy across different drug classes. Furthermore, while seizure control outcomes were stratified by monotherapy and polytherapy, future studies should examine ASM performance by epilepsy type (focal vs. generalized), as pharmacological response may vary across syndromic classifications.

Moreover, our cohort did not include pregnant women or patients under 18 years of age, whose ASM pharmacokinetics, safety profiles, and treatment goals differ substantially hence, our findings cannot be extrapolated to these vulnerable subgroups. Additionally, although the general principles of ASM polytherapy, such as selecting combinations with complementary mechanisms of action, non-overlapping toxicity, and minimal pharmacokinetic interactions, are well established in clinical practice, we did not have sufficient data to evaluate whether these strategies were systematically applied in our patients.

Finally, it is essential to consider that although ASM does not impact the underlying pathophysiological mechanisms, it does affect seizure control (35). It was discovered that there are many causes why there was not any seizure control, like the presence of side effects in polytherapy and the use of the same therapeutic targets, as well as other situations that hinder adherence, produce abandonment, and modify the course and prognosis of the disease.

Conclusion

Based on the data obtained from this study, rationality is essential for ASM. Most patients in this study were controlled with one medication, considering that they received the new generation of drugs that allow better management, adherence, and tolerance. We always suggest that in clinical practice, it is crucial to continuously review the diagnosis of the seizure type or epileptic syndrome before starting the medication, which has a direct impact on the adequate control of ictal frequency.

Authors' contribution. Lorena Horta: Conceptualization, supervision, methodology, and original draft preparation; Gregory David Corena: Conceptualization, supervision, methodology, and original draft preparation; Jean Paul Vergara: Data curation; Valentina Galvis: Formal analysis and visualization; All authors: Writing – review and editing.

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