UNRAVELING THE COMPLEXITY OF SEIZURES AND EPILEPSIES: A MULTIFACETED APPROACH TO CLASSIFICATION, SYNDROMES, CAUSES, AND INTEGRATED THERAPIES

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ABSTRACT

Objective: To investigate the clinical diversity, genetic bases, diagnostic complexity, and therapeutic approaches of epileptic syndromes, highlighting recent advances in understanding these disorders.

Theoretical Framework: Epileptic syndromes are neurological disorders characterized by recurrent epileptic seizures, resulting from abnormal neuronal activity in the brain, whose classification has evolved towards clinical and genetic criteria.

Method: A systematic approach was employed for bibliographic review on epileptic syndromes, consulting biomedical databases and applying strict selection criteria. Studies addressing clinical diversity, genetic bases, and diagnostic complexity were included, followed by qualitative data analysis to identify patterns and gaps in the literature.

Results and Discussion: Results reveal evident genetic heterogeneity, with some syndromes exhibiting well-defined genetic bases. Advances in genomics and molecular neurobiology have provided insights into pathogenic mechanisms, despite persistent challenges, including resistance to conventional medications.

Implications of the Research: In-depth understanding is crucial for accurate diagnosis and effective therapeutic development, emphasizing the continuous need for research to improve clinical outcomes and quality of life for patients.

Originality/Value: Highlights recent advances in understanding epileptic syndromes, identifying key areas for future research, and contributing to better comprehension and quality of life for affected patients.

Keywords: Epileptic Syndromes, Epileptic Seizures, Neuronal Activity, Antiepileptic Medications, Scientific Advances.

DESVENDANDO A COMPLEXIDADE DAS CONVULSÕES E EPILEPSIA: UMA ABORDAGEM MULTIFACETADA À CLASSIFICAÇÃO, SÍNDROMES, CAUSAS E TERAPIAS INTEGRADAS

RESUMO

Objetivo: Investigar a diversidade clínica, bases genéticas, complexidade diagnóstica e terapêutica das síndromes epilépticas, além de destacar avanços recentes na compreensão desses distúrbios.

Referencial Teórico: As síndromes epilépticas são distúrbios neurológicos caracterizados por crises epilépticas recorrentes, resultantes de atividade neuronal anormal no cérebro. A classificação evoluiu para critérios clínicos e genéticos.

Método: Abordagem sistemática para revisão bibliográfica sobre síndromes epilépticas, utilizando bases de dados biomédicas e critérios de seleção rigorosos. Inclusão de estudos sobre diversidade clínica, bases genéticas e complexidade diagnóstica. Análise qualitativa dos dados para identificar padrões e lacunas na literatura.

Resultados e Discussão: Revelam uma heterogeneidade genética evidente, com algumas síndromes apresentando bases genéticas bem definidas. Avanços na genômica e neurobiologia molecular forneceram insights sobre mecanismos patogênicos. Desafios persistem, incluindo resistência a medicamentos convencionais.

Implicações da Pesquisa: Compreensão aprofundada é crucial para diagnóstico preciso e desenvolvimento terapêutico eficaz. Necessidade contínua de pesquisas para melhorar resultados clínicos e qualidade de vida.

Originalidade/Valor: Destaca avanços recentes na compreensão das síndromes epilépticas, identificando áreas-chave para futuras pesquisas e contribuindo para uma melhor compreensão e qualidade de vida dos pacientes.

Palavras-chave: Síndromes Epilépticas, Crises Epilépticas, Atividade Neuronal, Medicamentos Antiepilépticos, Avanços Científicos.
DESCIFRANDO LA COMPLEJIDAD DE LAS CRISIS Y EPILEPSIAS: UN ENFOQUE MULTIFACÉTICO PARA LA CLASIFICACIÓN, LOS SÍNDROMES, LAS CAUSAS Y LAS TERAPIAS INTEGRADAS

RESUMEN

Objetivo: Investigar la diversidad clínica, bases genéticas, complejidad diagnóstica y enfoques terapéuticos de los síndromes epilépticos, resaltando los avances recientes en la comprensión de estos trastornos.

Marco Teórico: Los síndromes epilépticos son trastornos neurológicos caracterizados por crisis epilépticas recurrentes, resultado de una actividad neuronal anormal en el cerebro, cuya clasificación ha evolucionado hacia criterios clínicos y genéticos.

Método: Se empleó un enfoque sistemático para la revisión bibliográfica de los síndromes epilépticos, consultando bases de datos biomédicas y aplicando criterios de selección estrictos. Se incluyeron estudios que abordaban la diversidad clínica, bases genéticas y complejidad diagnóstica, seguidos de un análisis cualitativo de los datos para identificar patrones y brechas en la literatura.

Resultados y Discusión: Los resultados revelan una evidente heterogeneidad genética, con algunos síndromes que presentan bases genéticas bien definidas. Los avances en genómica y neurobiología molecular han proporcionado conocimientos sobre los mecanismos patogénicos, a pesar de los desafíos persistentes, incluida la resistencia a los medicamentos convencionales.

Implicaciones de la investigación: La comprensión en profundidad es crucial para un diagnóstico preciso y el desarrollo terapéutico efectivo, enfatizando la necesidad continua de investigación para mejorar los resultados clínicos y la calidad de vida de los pacientes.

Originalidad/Valor: Destaca los avances recientes en la comprensión de los síndromes epilépticos, identificando áreas clave para futuras investigaciones y contribuyendo a una mejor comprensión y calidad de vida para los pacientes afectados.

Palabras clave: Síndromes Epilépticos, Crisis Epilépticas, Actividad Neuronal, Medicamentos Antiepilépticos, Avances Científicos.

1 INTRODUCTION

Epileptic syndromes represent a heterogeneous group of neurological disorders characterised by recurrent seizures resulting from abnormal neuronal activity in the brain\(^1\). These conditions affect millions of people worldwide, with a variety of clinical manifestations, from generalised seizures to more subtle forms of focal epileptic activity\(^7\). Understanding the diversity of these syndromes, their genetic bases and their clinical complexity is crucial for accurate diagnosis, proper clinical management and the development of targeted therapies\(^4\).

The classification of epileptic syndromes has evolved significantly over the years, moving from a purely symptomatic approach to one based on clinical criteria, and more recently on specific genetic substrates\(^12\). However, many syndromes still challenge precise...
categorisation due to overlapping clinical and genetic characteristics, highlighting the continuing need for in-depth investigation in this area\textsuperscript{13}.

The etiology of epileptic syndromes is multifaceted, involving a complex interaction between genetic, environmental and epigenetic factors\textsuperscript{10}. While some syndromes have a well-defined genetic basis, others remain poorly understood, reflecting the underlying complexity of these disorders. Recent advances in genomics and molecular neurobiology have provided important insights into the pathogenic mechanisms underlying various epileptic syndromes, promoting a deeper understanding of their pathophysiology and opening up new therapeutic perspectives\textsuperscript{2,5}.

This paper presents a comprehensive review of the current literature on epileptic syndromes, with an emphasis on clinical diversity, known genetic bases, and diagnostic and therapeutic complexity. By bringing together and synthesising the latest knowledge in this area, we seek to provide an up-to-date view of epileptic syndromes, highlighting recent advances and identifying key areas for future research. This review is expected to contribute to a better understanding of these disorders and ultimately to an improvement in the quality of life of affected patients.

2 THEORETICAL FRAME

A seizure is the transient onset of signs or symptoms due to abnormal, excessive, or synchronic neuronal activity, and can range from dramatic motor activity to subtle sensory phenomena\textsuperscript{7}. Its incidence and prevalence are influenced by several factors, being most common in early childhood and advanced adulthood\textsuperscript{9}. It is crucial to differentiate the term seizure from the term epilepsy: while seizure refers to isolated or recurrent occurrences due to correctable or avoidable circumstances, epilepsy describes a condition in which a person is at risk of recurrent seizures due to a chronic underlying process\textsuperscript{3}. Epilepsy covers various forms and causes, including different epileptic syndromes, each with distinctive clinical and pathological features that suggest a specific etiology\textsuperscript{1}. The classical definition of epilepsy as the occurrence of two or more unprovoked seizures results in an overall incidence of approximately 0.3 to 0.5\% in different populations, with an estimated prevalence between 5 to 30 people per 1,000 individuals\textsuperscript{8}. 
2.1 CLASSIFICATION OF SEIZURES: CLINICAL IMPLICATIONS

Seizure classification is crucial to guide diagnosis, treatment choice, and provide important prognoses. The International League Against Epilepsy (ILAE) introduced an updated approach in 2017 considering clinical and electroencephalographic manifestations. Seizures may be focal or generalised, originating in limited or distributed brain networks in the cerebral hemispheres, respectively. Focal seizures are often associated with structural brain abnormalities, while generalised seizures may result from more widespread abnormalities. ILAE classifies different subtypes of seizures, such as focals with perceptual or nonperceptual onset, and generalised motor and nonmotor. Although the current system is mainly based on clinical and electroencephalographic manifestations, it is possible that in the future there will be a greater consideration of the etiological characteristics or of the cellular substrate as we advance in the understanding of the associated physiopathological mechanisms.

2.1.1 Focal Seizures

Focal seizures, neurological disorders characterised by abnormal electrical activity in a specific area of the brain, have been the subject of intense study and classification. Recently, a review of the classification system has brought a more refined understanding of these events, considering not only their origin and nature, but also their impact on patient perception and awareness. Formerly simplified as "simple" or "complex", focal seizures are now differentiated based on the effect on perception and the nature of onset, recognising their complexity and ability to evolve into generalised forms.

In the diagnosis of focal seizures, electroencephalography (EEG) plays a key role. Although interictal EEG may be normal in many cases, it may reveal characteristic epileptiform discharges, aiding in the identification of epileptogenic focus. However, precise localisation of focus can be challenging, especially in seizures that originate in deep regions of the brain.

Focal perceptive seizures are characterised by motor or non-motor manifestations without impairment of patient consciousness. These symptoms may be accompanied by sensory, autonomic, or emotional sensations, adding complexity to the clinical picture. Disperceptive focal seizures have transient impairment of consciousness, which may include postictal manifestations and automatisms, reflecting the complexity of the cortical areas involved in the seizure.
Careful interpretation of symptoms is essential due to the wide variety of manifestations associated with focal seizures. In cases of atypical behaviour, additional detailed EEGs may be helpful in differentiating between seizure activity and other neurologic conditions\(^1\). This multidimensional approach is crucial for an accurate evaluation and effective management of focal seizures, recognising the ongoing evolution of knowledge in this field.

### 2.1.2 Generalised Seizures

Generalised-onset seizures encompass a variety of distinct types, each with specific clinical and electrophysiological features\(^12\). Typical absence seizures, for example, are brief lapses of consciousness often seen in children, marked by subtle signs such as chewing movements or rapid blinking of the eyes\(^6,9\). These seizures can occur hundreds of times a day and are often perceived as unexplained daydreams, which can delay diagnosis, especially in children without a previous history of seizures\(^1\).

Atypical absence crises, on the other hand, present longer duration of loss of consciousness and more evident motor signs, indicative of structural abnormalities in the brain\(^11\). In contrast to typical seizures, they respond less to conventional treatments with antiseizure drugs, making their management more challenging\(^5\).

Generalised tonic-clonic seizures are one of the most common types of seizures and are recognised by an initial tonic phase of muscle contraction followed by the clonic phase of rhythmic movements\(^5\). During this phase, marked features such as ictal moaning, respiratory and cardiovascular changes may occur, often resulting in postictal confusion, and physical symptoms such as headache and fatigue after seizure\(^1\).

Atonic seizures, characterised by sudden loss of muscle tone, represent another type of generalised-onset seizure\(^12\). Although short in duration, only a few seconds, they can result in dangerous falls, posing a significant risk of head injury\(^5\). In EEG, these seizures are marked by slow-wave discharges, reflecting abnormal activity in the brain during event\(^1\).

Myoclonic seizures, on the other hand, are characterised by sudden, brief muscle contractions that can affect a part or the whole body\(^12\). These events, considered true epileptic events, are identified by slow-wave bilateral synchronic discharges into the EEG, indicating cortical dysfunction during seizure\(^5\).

Finally, epileptic spasms are defined by brief periods of sustained muscle flexion or extension, often seen in infants and associated with hypsarhythmia in EEG\(^5\). These spasms may
result from differences in neuronal function in an immature central nervous system, requiring a differentiated approach to management and treatment\(^7\).

### 2.2 EPILEPTIC SYNDROMES

Epileptic syndromes represent disorders where epilepsy is the predominant feature, evidenced by clinical, electroencephalographic, radiological or genetic observations that suggest a common underlying mechanism\(^2\). For example, autosomal dominant frontal lobe epilepsy (ELFNAD), associated with mutations in the CHRNA4 gene, presents nocturnal seizures with prominent motor movements, often mistaken for primary sleep disorders\(^5\). This is just one example among many others of epileptic syndromes with known genetic bases, such as familial benign neonatal seizure (CNFB) and generalised epilepsy with febrile seizures plus (EGCF+), related to mutations in the KCNQ2 and SCN1A genes, respectively\(^5\).

Juvenile myoclonic epilepsy (JME), in turn, is a generalised seizure disorder of unknown cause, characterised by bilateral myoclonic shocks, often triggered by sleep deprivation, and often associated with generalised tonic-clonic seizures\(^2\). Although complete remission is rare, seizures usually respond well to anticonvulsant medication, with a possible genetic influence suggested by genetic binding studies\(^9\).

Lennox-Gastaut syndrome, on the other hand, is defined by a triad of features that include multiple types of seizures, EEG abnormalities, and cognitive dysfunction\(^5\). Associated with various etiologies, such as de novo mutations and acquired lesions, its prognosis is often poor, due to the severity of the seizures and their physical and psychosocial consequences\(^11\).

In addition, mesial temporal lobe epilepsy syndrome (MTLS) represents a common example of focal seizures with impaired consciousness, often associated with detectable hippocampal sclerosis in magnetic resonance imaging\(^5\). This syndrome, refractory to anticonvulsants, responds well to surgical intervention and provides valuable insights into the basic mechanisms of epilepsy, especially in experimental studies\(^10\).

### 2.3 CAUSES OF SEIZURES AND EPILEPSY

Seizures and epilepsy are triggered by an imbalance between excitation and inhibition in the central nervous system (CNS), resulting in a wide variety of causes\(^1\). Three key clinical observations highlight the diversity of factors that determine why certain conditions lead to the occurrence of these neurological disorders in a specific patient. First, the normal brain may have
seizures under appropriate circumstances, with individual differences in susceptibility or threshold for seizures, suggesting genetic and developmental influences on the brain. Then, certain conditions are highly likely to result in chronic seizure disorders, such as severe head trauma, indicating a persistent pathological change in the CNS after injury, known as epileptogenesis. Finally, seizures are episodic and triggered by factors such as psychological stress, sleep deprivation and exposure to toxic substances, highlighting the complexity of the causes of seizures and epilepsy.

Individualised patient assessment is crucial to determine proper conduct and provide specific interventions to prevent and treat these neurological disorders. The causes of seizures vary according to the patient's age, which is an important factor in determining the most likely causes. For example, during the neonatal period and early childhood, common causes include hypoxic-ischemic encephalopathy, traumatism, and CNS infection, while in early childhood, epileptic syndromes such as idiopathic generalised tonic-clonic seizures begin to manifest. In adolescence and early adulthood, epilepsy secondary to acquired CNS lesions predominate, while in older adults, cerebrovascular diseases, trauma, and degenerative disorders are common.

2.4 PATIENT APPROACH

When a patient is treated after a seizure, initial priorities include checking vital signs, providing respiratory and cardiovascular support, and treating seizures if they return. It is crucial to identify and treat potentially serious conditions, such as CNS infections, metabolic imbalances or substance poisoning. If the patient is not severely ill, initial assessment focuses on investigating the history of previous seizures. If this is the first seizure, it is important to determine if the episode described was indeed a seizure and then identify the cause by analysing risk factors and triggers. Deciding whether antiseizure therapy is needed beyond treatment of the underlying disease is critical at this time.

For patients with previous seizures or known history of epilepsy, the evaluation aims to identify the underlying cause and the triggers, as well as assess the effectiveness of the current therapy of the patient. This approach helps determine whether adjustments to therapy are needed to ensure adequate seizure control.
2.4.1 Anamnesis and Physical Examination

During the history and physical examination, the first goal is to determine whether the event was indeed a seizure. A detailed history is critical because often the diagnosis of seizure is based only on clinical criteria, with physical examinations and laboratory tests usually normal\(^5\). It is important to carefully question the witnesses of the event, since seizures often occur outside the hospital setting and the patient may not be aware of the immediate ictal and postictal phases\(^11\).

During history, it is crucial to focus on symptoms that occurred before, during, and after the episode to distinguish between seizure and other paroxysmal events\(^1\). Risk factors and predisposing events, such as history of febrile seizures, family history of seizures, and occurrence of previous unrecognised aurorae or brief seizures, should be investigated\(^5\). Epileptogenic factors such as head trauma, stroke, tumour, or CNS infection should also be identified, as should triggering factors such as sleep deprivation, systemic disorders, electrolyte or metabolic imbalances, acute infections, and use of certain drugs or substances\(^11\).

The general physical examination includes looking for signs of infection or systemic disease, as well as evaluating possible neurocutaneous disorders, chronic kidney or liver disorders, and abnormalities that may indicate brain damage\(^11\). All patients also require a complete neurologic examination, with special attention to signs of cerebral hemispheric disease, mental status assessment, motor function screening tests, and cortical sensitivity to detect possible lesions in the central nervous system\(^5\).

2.4.2 Laboratory and Electrophysiological Examinations

To investigate possible metabolic causes of seizures, routine blood tests to check electrolytes, glucose, calcium, magnesium, and liver and kidney function are indicated\(^1\). In addition, it is important to perform screening for toxins in the blood and urine, especially in patients without a clear trigger factor\(^13\). Lumbar puncture is indicated in cases of suspected meningitis or encephalitis, and is mandatory in patients with HIV, even in the absence of symptoms suggestive of\(^5\).

The electroencephalogram (EEG) is a valuable tool for recording the electrical activity of the brain\(^1\). In this procedure, electrodes are placed on the patient's scalp. The potential difference between these electrodes is amplified and displayed in different devices, such as computers, oscilloscopes or paper. The digital technology allows to reconstruct and visualise
the EEG in various formats, facilitating the analysis and allowing the detection of certain abnormalities.

The characteristics of normal EEG vary according to the age and waking state of the patient. In adults, during wakefulness and with eyes closed, it is common to observe an alpha rhythm of 8 to 13 Hz, especially in the posterior regions of the brain. When the eyes are opened, this alpha rhythm decreases. During states of somnolence and surface sleep, theta (4-7 Hz) and delta (< 4 Hz) activities become more evident.

All patients with suspected seizure disorder should undergo EEG as soon as possible. During a clinically evident episode, the presence of abnormal convulsive activity in the EEG, characterised by repetitive rhythmic patterns, can clearly establish the diagnosis. However, it is important to note that the absence of seizure activity in the EEG does not exclude a seizure disorder, as focal seizures may originate from regions not detected by the electrodes on the scalp.

In situations where EEG cannot be done during a clinical event, activating procedures such as hyperventilation, photic stimulation, sleep and sleep deprivation are often used. Continuous monitoring in telemetry units with EEG-video in hospitalised patients or the use of portable equipment to record EEG continuously for more than 24 hours in outpatient patients are useful for capturing electrophysiological findings associated with clinical events.

EEG may also be useful in the interictal period, showing abnormalities suggestive of epilepsy, such as abnormal discharge triggers. However, it is important to note that even patients with confirmed epilepsy may have normal interictal EEG in up to 60% of cases. Thus, EEG is not definitive for the diagnosis of epilepsy in many cases, but it can aid in the classification of seizure disorders and in the selection of antiseizure drugs.

2.4.3 Imaging and Genetic Testing

Brain imaging is critical for the evaluation of patients with recent seizures, with magnetic resonance imaging (MRI) being preferred to computed tomography (CT) because of its increased sensitivity in detecting brain lesions associated with epilepsy. Advanced MRI technology, such as the 3-Tesla scanner and structural imaging at submillimetre resolution, significantly increased sensitivity in detecting abnormalities, including hippocampal atrophy associated with mesial temporal sclerosis and abnormalities of cortical neuronal migration. In cases of suspected central nervous system (CNS) infection or expansive lesion, emergency CT may be obtained initially, followed by MRI if necessary. In addition, functional imaging tests,
such as PET and SPECT, are used in patients with seizures that are refractory to clinical treatment\textsuperscript{11}. Genetic testing is also becoming an integral part of diagnostic evaluation, especially in infants and children with epileptic syndromes of genetic origin, and can guide therapeutic options and help in early diagnosis and adequate choice of treatment\textsuperscript{9}.

2.5 INTEGRATED THERAPEUTIC APPROACH TO SEIZURES AND EPILEPSY

Management of patients with seizure disorders is complex and usually requires a multifaceted approach\textsuperscript{2}. This involves not only treating the underlying conditions that trigger or contribute to seizures, but also identifying and eliminating any triggers, as well as suppressing recurrent seizures through prophylactic therapies, such as the use of antiepileptics or surgery\textsuperscript{2, 3}. Moreover, psychological and social issues should be carefully considered and addressed\textsuperscript{7}. It is crucial to recognise the individuality of each patient, given the variety of types and causes of seizures, as well as the differences in the effectiveness and toxicity of antiepileptic drugs in each case\textsuperscript{7}. Therefore, it is recommended that a neurologist specialising in epilepsy leads the formulation and supervision of the therapeutic plan\textsuperscript{2}. Patients with refractory epilepsy or those requiring multiple antiepileptic drugs should receive regular follow-up from a neurologist to ensure proper management of the condition and adjustments as needed\textsuperscript{2}. This integrated approach aims not only to control seizures, but also to improve the quality of life and the overall well-being of the patient.

2.5.1 Specific Approaches to Dealing with Underlying Causes and Preventing Seizure Triggers**

Treatment of seizures varies considerably based on the underlying cause and the triggers involved\textsuperscript{2}. When seizures are caused by metabolic disorders, such as serum electrolyte imbalances or blood glucose, the primary focus is to immediately correct the metabolic problem to prevent recurrences\textsuperscript{11}. In such cases, antiepileptic therapy is usually not needed unless there is an imminent risk of new seizures due to the inability to rapidly correct the metabolic disorder\textsuperscript{5}.

In situations where seizures are triggered by substances such as drugs or illicit drugs, proper treatment involves avoiding the causative substance\textsuperscript{1}. Often, the use of antiepileptics is not necessary unless recurrent seizures occur in the absence of these triggers\textsuperscript{1}. Seizures due to structural damage to the central nervous system, such as brain tumours or vascular...
malformations, may not recur after effective treatment of the underlying lesion\textsuperscript{5}. However, most patients are kept on antiepileptics for at least one year after treatment, as there is still a risk of persistence of the seizure focus in the surrounding tissue\textsuperscript{5}.

The prevention of triggers plays a crucial role in the management of epilepsy\textsuperscript{1}. Sleep deprivation is a near-universal trigger, and patients should prioritise sleep quality\textsuperscript{4}. In addition, identifying and avoiding other situations that appear to lower the seizure threshold, such as alcohol consumption, is essential\textsuperscript{4}. In rare cases of reflex seizures, induced by specific stimuli, such as video game monitors, music, or voice, it is important to avoid these triggers\textsuperscript{11}. Stress reduction strategies, such as physical exercise, meditation, and psychotherapy, can also be helpful due to the association between stress and seizures\textsuperscript{2}.

\textbf{2.5.2 Antiepileptic Drug Therapy: Considerations in the Choice and Administration of Medicines}

The administration of antiepileptics is the basis of treatment for most patients with epilepsy\textsuperscript{2}: The overall goal is to completely prevent seizures without causing undesirable adverse effects, preferably with a single medication and a dosing schedule that the patient can easily follow\textsuperscript{1}. The classification of seizures is an important element in the design of the therapeutic plan, as some antiepileptics have different activities against the various types of seizures\textsuperscript{12}. However, there is considerable overlap among many antiepileptics, so the choice of treatment is often determined more by the specific needs of the patient, especially by his assessment of side effects\textsuperscript{5}.

When initiating antiepileptic pharmacotherapy: Drug therapy should be initiated in any patient with recurrent seizures of unknown aetiology, or with a known cause that is irreversible\textsuperscript{11}. The institution of treatment in patients after a single seizure is controversial. Patients with a single seizure due to identified lesions, such as a CNS tumour, infection, or trauma, in which there is strong evidence that the lesion is epileptogenic, should be treated\textsuperscript{5}. The risk of recurrence in a patient with seemingly unprovoked or idiopathic seizure is uncertain, and estimates range from 31 to 71\% in the first 12 months after the initial seizure\textsuperscript{5}. This uncertainty stems from differences in the underlying types of seizure and etiologies in the various published epidemiological studies. Risk factors generally accepted as associated with seizure recurrence include: (1) abnormal neurologic examination, (2) seizures manifesting as status epilepticus, (3) postictal Todd paralysis, (4) significant family history of seizures, or (5) abnormal EEGs\textsuperscript{1,3,5}. Most patients with one or more of these risk factors should be treated.
Issues such as work or driving may also influence the decision to start medication\(^5\). For example, a patient with a single idiopathic seizure whose job depends on driving may prefer to use antiepileptics rather than risk a new seizure and lose the right to drive.

Selection of antiepileptic drugs: In the world, older drugs, such as phenytoin, valproic acid, carbamazepine, phenobarbital, and ethosuximide, are often used as first-line treatment in most epileptic disorders because, overall, they are as effective as the more modern and significantly cheaper drugs\(^4,5\). Most of the new drugs that have become available in the past decade are used as additional or alternative therapy, but many are being used as first-line monotherapy\(^5\).

In addition to efficacy, factors influencing the choice of an initial medication include the convenience of dosing (eg, 1 vs. 3 or 4\(\times\)/day) and potential side effects\(^5\). In this respect, several of the newer drugs have the advantage of reduced drug interactions and easier dosing\(^1\). Almost all commonly employed antiepileptics cause similar and dose-related side effects, such as sedation, ataxia, and diplopia\(^13\). Long-term use of some agents in adults, particularly in the elderly, may lead to osteoporosis\(^5\). Careful follow-up is necessary to ensure that these side effects are readily recognised and reversed. Most older drugs and some newer drugs also cause idiosyncratic toxicity, such as rash, bone marrow suppression, or hepatotoxicity\(^5\). Although rare, these side effects can be fatal\(^5\).

Genetic testing: Genetic testing can help in choosing treatment and identifying an underlying cause for seizures\(^2\). Identifying a specific mutation may indicate that a specific therapy is preferable because the patient is more likely to respond to it or avoid the toxicity of alternative drugs\(^5\). Thus, the choice of treatment can be individualised for each patient, based on genetic information on the metabolism and response of the drug, as well as on the etiology of epilepsy\(^4\).

### 2.5.3 Initiation, Monitoring and Discontinuation of Antiepileptic Treatment

Anti-epileptic therapy requires a cautious approach from initiation to eventual discontinuation of treatment, with the goal of achieving seizure control and minimising side effects\(^2\). Gradual dosing titration over months is common, especially in cases of infrequent seizures, with careful monitoring of serum drug levels\(^5\). When initial therapy fails, a switch to another antiepileptic may be necessary, with gradual transition to avoid adverse reactions\(^11\). After a period of complete seizure control, discontinuation of drug treatment may be considered for some suitable patients, following specific criteria and a gradual discontinuation over...
months, with close monitoring for relapses in the first months after discontinuation of therapy. Common options for initial treatment of focal seizures include carbamazepine, oxcarbazepine, lamotrigine, phenytoin, and levetiracetam, with the choice of drug varying according to individual patient factors.

3 METHODOLOGY

A systematic approach was adopted to conduct a bibliographic review on epileptic syndromes, aiming to understand their diversity, genetic bases and clinical complexity. The research involved consulting various biomedical databases, including PubMed, Scopus, and Google Scholar. Relevant search terms, such as "epileptic syndromes", "genetic epilepsy", "etiology of seizures", among others, have been combined to ensure a comprehensive search. There was no restriction of language or date of publication during the selection of the studies.

Initially, relevant articles were identified through electronic databases and the analysis of specialised books on epilepsy and neurology. After the application of exclusion criteria, including duplicate studies and articles not directly related to epileptic syndromes, the articles were selected for analysis. Studies were included that addressed aspects related to the diversity of epileptic syndromes, their known genetic bases and the associated clinical complexity.

During the data collection, relevant information was extracted about the variety of epileptic syndromes, their known genetic bases and their clinical complexity. The data were analysed qualitatively to identify patterns, trends and gaps in the literature related to epileptic syndromes. The most relevant findings were highlighted and the key points were summarised to provide a comprehensive overview of the different aspects addressed.

It is important to note that this study is a bibliographic review and did not involve the collection of primary patient data, therefore, no ethical review was necessary. In addition, article selection and data analysis have been carried out systematically, but are still subject to possible selection bias.

4 RESULTS AND DISCUSSIONS

Classification and understanding of seizures and epilepsy are critical for accurate diagnosis, effective treatments, and improved prognosis. The multifaceted approach outlined in this article sheds light on the intricate nature of these neurological disorders, offering insights into their diverse manifestations, underlying causes and integrated therapeutic strategies.
One of the main discoveries highlighted in our exploration is the evolving classification system proposed by the International League against Epilepsy (ILAE). By considering both clinical manifestations and electroencephalographic findings, this updated classification provides a more refined understanding of seizures, paving the way for personalised diagnostic approaches and targeted treatments. However, it is important to recognise ongoing challenges in the precise categorisation of seizures, particularly in cases where the etiology is multifactorial or not fully understood.

In addition, our analysis highlights the complexity inherent in focal seizures. The transition from simplistic categorisations to more sophisticated differentiation based on perceptual effects and motor involvement reflects the intricately driven nature of these events. This subtle perspective not only enhances our understanding of focal seizures, but also highlights their potential to evolve into generalised forms, emphasising the need for comprehensive diagnostic assessments and personalised treatment plans.

By exploring generalised seizures, our analysis reveals the diverse clinical and electroencephalographic characteristics associated with the different subtypes. From typical absence seizures to tonic-clonic seizures and atonic seizures, each subtype presents unique challenges in diagnosis and management. In addition, the identification of genetic syndromes, such as juvenile myoclonic epilepsy, highlights the intricate interaction between genetic factors and seizure phenotypes, emphasising the importance of genetic testing in guiding treatment decisions.

Going beyond classification, our analysis enters the multifaceted etiology of seizures and epilepsy. While substance-induced metabolic disorders and seizures represent identifiable triggers, the complex interaction between genetic predisposition and environmental factors complicates our understanding of disease mechanisms. This highlights the need for comprehensive diagnostic evaluations, including laboratory testing, neuroimaging, and genetic screening, to elucidate underlying etiologies and inform personalised treatment strategies.

In light of these findings, our discussion emphasises the importance of an integrated therapeutic approach to seizures and epilepsy. From pharmacological interventions to lifestyle modifications and surgical interventions, effective management requires a holistic understanding of the individual patient’s clinical profile, underlying etiology, and treatment objectives. In addition, the recognition of epilepsy as a heterogeneous disorder highlights the need for personalised treatment regimens and continuous multidisciplinary care to optimise outcomes and improve the quality of life of patients living with seizures and epilepsy.
5 CONCLUSION

In short, the detailed investigation of convulsions and epilepsy reveals the intrinsic complexity of these neurological disorders. The multifaceted approach adopted in this study provides a comprehensive view of the various clinical manifestations, syndromes, causes and integrated therapies associated with these conditions. Through the analysis of the updated classifications, it is evident the importance of considering both clinical and electroencephalographic aspects in diagnostic evaluation and in the development of personalised therapeutic strategies.

In addition, deepening our understanding of focal and generalised seizures highlights the need for a differentiated approach for each subtype, recognising their distinctive characteristics and specific challenges in clinical diagnosis and management. The identification of epileptic syndromes with known genetic bases highlights the growing importance of genetics in guiding therapeutic decisions and patient prognosis.

When considering the multifactorial causes of seizures and epilepsy, comprehensive diagnostic evaluations are critical to identify triggers and contributors, including metabolic disorders, poisoning, and genetic predisposition. This deeper understanding of the underlying etiologies is essential to direct effective therapeutic interventions and improve clinical outcomes.

Ultimately, the conclusion of this study reinforces the importance of an integrated and multidisciplinary approach in the management of patients with seizures and epilepsy. Through close collaboration between neurologists, geneticists, radiologists and other health care professionals, we can optimise early diagnosis, personalised treatment and continuous follow-up, aiming not only to control seizures but also to improve the quality of life and overall well-being of patients affected by these challenging neurological conditions.

REFERENCES


