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Review Article

To Study the Epilepsy Disease

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ABSTRACT

Today, people experience many kinds of stress in their fast-paced lives, and many individuals worldwide struggle with different brain disorders. Epilepsy is one of the most widespread brain disorders, affecting about 50 million people globally, with 90% of those affected coming from developing countries. Genetic issues, brain infections, strokes, tumours, and high fevers can lead to epilepsy. This condition creates a significant financial strain on healthcare systems and is linked with stigma and discrimination against the patient and their family in the community, at work, in school, and at home. Many individuals with epilepsy deal with intense emotional stress, behavioural problems, and severe social isolation. There are many different kinds of seizures and ways that the brain can cause seizures. The two main features that lead to seizures are overly excited neurons and tightly synchronized groups of nerve cells. Various mechanisms change the balance between excitement and calmness in specific areas of the brain, leading to localized or widespread hyperexcitability and hypersynchrony. This review aims to cover the history, prevalence, causes, how epilepsy affects the body, classification of epilepsy, symptoms, diagnosis, treatment, and future directions.

INTRODUCTION

About 1% of the global population has epilepsy, making it the second most common brain disorder after stroke.[1] An estimated 50 million people around the world have epilepsy, with 90% of these cases found in developing countries.[2] In recent years, our understanding and view of epilepsy have greatly improved. This ongoing brain

problem comes from an imbalance between brain activity and control, causing uncontrolled activity and leading to repeated, unexpected seizures. [3,4,5] Research has shown clear differences in how young and mature brains function, as well as the effects of strokes. Epilepsy includes many types of seizures that vary widely in how often they happen, how they show up, their causes, and how to treat them. Seizures involve strange

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neuronal activity that can be too much or too synchronized in the brain. These episodes often lead to a short loss of consciousness, risk of injury, and can affect education and work.[6] While epilepsy is more common in young children and people over 65, it can occur at any age. It's important to remember that epilepsy is not just one illness but a syndrome with various symptoms, arising from sudden abnormal electrical activity in the brain.[7] Not all types of epilepsy last a lifetime; some are only present during certain childhood years. The usual treatment for epilepsy mainly involves seizure-controlling medications.[9] However, over 30% of people with epilepsy do not gain control over their seizures, even with the best medication.[10,11] Although these drugs can often help manage or reduce the number of seizures, some patients see little or no improvement, leading to considering surgery in tough cases. While there are treatments to help control seizures, there are currently no effective prevention methods or cures available.[12] Sticking to medication schedules is a major challenge because of the long-term nature of treatment.

History of Epilepsy:

The term epilepsy comes from the Greek word 'Epilepsia,' which means 'to seize.' This term has evolved from 'epi,' meaning 'above,' and 'lambanein,' which was thought to be significant. In the past, epilepsy was often connected to weak religious beliefs or seen as caused by a demon.[13] Long ago, many believed that those with epilepsy were taken over by demons or that their visions were messages from a god. According to Potnis et al. in the *Journal of Drug Delivery & Therapeutics* (2020), epilepsy was viewed as a holy sickness, with the idea that these visions were signs from the gods. For instance, in Hmong animist

communities, epilepsy was seen as an attack by an evil spirit, but the person affected could become a shaman because of their unique experiences. In various cultures, people with epilepsy have often faced disrespect and, in some cases, were locked away. In modern neurology, Jean-Martin Charcot described those with epilepsy as having a mental disability, chronic syphilis, or as being criminally insane. In places like Tanzania, people still believe that epilepsy is linked to evil spirits, witchcraft, poisoning, or illness.[14] The Romans called epilepsy *Morbus comitialis*, or the disease of the assembly hall, thinking it was caused by divine curses. Even though the negative perception of epilepsy still exists, it is gradually improving over time, especially in less developed countries. Hippocrates believed that the fear of epilepsy would soon disappear, as it is not a punishment from the gods.[15]

Epidemiology:

Epilepsy is one of the most important neurological disorders that are common today.[16] In India, it is estimated that there are 55 people with epilepsy who are not accounted for, while the United States has 20 missing cases, and the United Kingdom has 3.[17] Each year, about 120 people per 100,000 in the United States seek help for a newly discovered seizure. Importantly, at least 8% of the general population will have at least one seizure but will not be diagnosed with epilepsy. The chance of having another uncaused first seizure within five years ranges from 23% to 80%. The age-adjusted rate of epilepsy is 44 cases per 100,000 people every year. Each year, around 125,000 new cases of epilepsy are diagnosed, with 30% occurring in people under 18 at the time of their diagnosis. The occurrence of epilepsy among older adults is becoming more recognized, with at least 10% of patients in long-term care facilities taking at least



one antiepileptic drug (AED). A national audit about epilepsy-related deaths, done by 'Bereaved Epilepsy,' pointed out this serious concern, showing that about 1,000 deaths happen each year in the UK due to epilepsy, with many of these related to seizures, and 42% of these deaths considered possibly preventable.[18]

Causes of epilepsy: -

1. In newborns and young kids, the most common reasons include brain damage from lack of oxygen, infections in the central nervous system, injuries, birth defects in the brain, and metabolic issues.
2. In late childhood, fever-related seizures and infections, along with injuries to the central nervous system, are often seen.
3. Epileptic syndromes are usually identified during childhood.
4. In teenagers and adults, the causes are more often linked to problems in the central nervous system.
5. In older people, brain blood vessel diseases are the main cause, with other contributing factors like brain tumors, head injuries, and degenerative diseases such as dementia.[19]

Pathophysiology of epilepsy: -

Seizures are sudden and brief events that come from the brain's outer layer. They happen when there is a quick disturbance between excitatory and inhibitory forces within the network of brain cells. Factors like unusual potassium flow, problems in voltage-sensitive ion channels, or lack of membrane ATPases needed for ion movement can disrupt the brain cell membrane and start a seizure. Different neurotransmitters, such as glutamate, aspartate, acetylcholine, norepinephrine, histamine, corticotropin-releasing factor, purines,

peptides, cytokines, and steroid hormones, can increase brain cell activity and help spread the signal. On the other hand, neurotransmitters like gamma-aminobutyric acid (GABA) and dopamine work to reduce brain cell activity and its spread. During a seizure, there is a higher need for blood flow to the brain to provide oxygen and nutrients important for brain cell function. However, if the seizure continues, the brain may face more low blood supply, which can lead to brain cell damage and injury.[6] Moreover, changes in different genes have been connected to certain types of epilepsy. Genes that code for protein parts of voltage-gated ion channels have been linked to general epilepsy and seizure problems in children.[23] It has been suggested that some inherited forms of epilepsy may come from changes in genes for sodium channel proteins, which can stay open too long, causing excessive brain cell activity due to too much glutamate.[16]

Partial seizures

In simple partial seizures, also known as focal cortical epilepsy, the seizure begins in a certain part of the motor cortex, causing episodes that affect specific muscle groups. During these seizures, patients lose voluntary control over the affected areas but remain aware. On the other hand, complex partial seizures start with localized electrical activity that usually stays in one area. Symptoms can include uncontrolled muscle movements, unusual sensory experiences, automatic body reactions, or changes in mood and behavior, which is often called psychomotor epilepsy.[26] The seizure focus is typically located in the temporal lobe. Additionally, a secondary generalized seizure may occur after a partial seizure and just before a generalized tonic-clonic seizure (grand mal).



Generalized seizures

Generalized seizures affect the entire brain, including the reticular system, leading to unusual electrical activity on both sides of the brain. A sudden loss of awareness is a key characteristic of generalized epileptic seizures.[27] Absence seizures, also known as petit mal, are commonly seen in children and involve brief moments of lost consciousness without muscle activity or convulsions, which can range from slight eyelid flickering to more noticeable clonic movements.[28] These episodes usually last from 3 to 30 seconds, resulting in either unconsciousness or reduced awareness.[29] Myoclonic seizures are defined by quick muscle jerks as the main motor sign. Clonic seizures involve a loss of awareness, automatic body symptoms, and rhythmic clonic movements that affect all muscle groups. Tonic seizures are marked by loss of consciousness and automatic symptoms, along with strong contractions of the limbs. During this phase, lasting about a minute, the person may stop breathing and experience involuntary bowel movements, urination, and drooling, followed by severe, simultaneous convulsions.[27] The patient remains unconscious for several minutes before slowly becoming aware again, which includes losing consciousness and muscle relaxation due to strong inhibitory signals, possibly causing the person to fall.[30] Infantile spasms, or hypsarrhythmia, are characterized by sporadic muscle spasms and are associated with learning difficulties and worsening neurological issues.

Unclassified category

The third group consists of unclassified and unknown epilepsy, along with various epilepsy syndromes. Notable syndromes include cases like

febrile convulsions, where seizures happen because of specific conditions. About 2-4% of children are affected by problems related to tissue diseases. In recent times, only 2 to 3% of these children have developed epilepsy, which is six times more common than in the general population. Several factors increase the chances of having existing brain issues or growth delays, including a family history of febrile convulsions or complex epilepsy. For children considered high-risk for repeated febrile convulsions and epilepsy, giving rectal diazepam during fever episodes can help prevent future seizures and reduce the negative effects of long-term treatment.[12]

Status epilepticus

Status epilepticus is defined by a long seizure or a series of seizures mixed with periods of normal awareness, lasting more than 30 minutes, as described by Potnis et al. However, seizure activity lasting more than 5 to 10 minutes can also indicate the start of status epilepticus and requires medical assistance. While any type of seizure can lead to this condition, generalized tonic-clonic status is the most common and poses serious risks. The first step is to ensure proper breathing and maintain stable blood pressure. Then, antiepileptic treatment may start with intravenous or rectal diazepam, followed by phenytoin (or other options like phenobarbital, clomethearate, or paraldehyde) to stop more seizures. Once seizure activity is under control, intravenous sodium phenytoin can be administered while closely watching blood pressure and ECG. If seizures persist, anesthetics like short-acting barbiturates such as thiopental may be necessary, and the patient should be carefully observed. It is important to note that children might show actions that look like seizures but are not due to epilepsy. These behaviors include:



1. The watchful eye.
2. Benign tremors (common in children under 2 years, usually occurring when tired or excited).
3. Self-soothing actions (like nodding, swaying, or banging their heads).
4. Conversion disorder (characterized by shaking or head movements).

Conversion disorder can be identified as the episodes do not occur during sleep and are not associated with loss of bladder control or self-harm.

Symptoms of seizures: -

A seizure is a sign of epilepsy, marked by bursts of high-frequency signals coming from a group of neurons in the brain. The signs and symptoms of a seizure depend on where the epileptic signals are in the cortex, as well as how they spread through the brain. For example, shaking or convulsions are linked to activity in the motor cortex, while the hypothalamus is related to involuntary body responses, and involvement of the reticular formation in the upper brainstem can cause a loss of consciousness.[27]

Medical History:-

A detailed medical history, which includes information about the symptoms and length of seizures, is crucial for diagnosing epilepsy and identifying the specific types of seizures the person has.

Blood Tests:-

Seizures can sometimes be caused by severe toxic or metabolic issues, requiring specific treatment for conditions like low calcium levels. Blood samples are regularly checked for genetic or metabolic disorders that might be related to

seizures. Additionally, these samples are tested for problems such as infections, lead poisoning, anemia, and diabetes, which can either cause or trigger seizures.[31]

Management of epilepsy:

Anticonvulsant and antiepileptic are words that are often used interchangeably. An anticonvulsant is a substance that stops seizures caused in lab settings, while an antiepileptic is a drug used in medical treatment to handle epilepsy.[32]

Management Principles

1. It is important to address any underlying issues that may cause epilepsy, like brain tumors.
2. Patients should be informed about their condition, how long treatment may last, and the need to stick to the prescribed plan.
3. Individuals should avoid triggers, such as drinking alcohol, not getting enough sleep, and high levels of emotional stress.
4. It is key to expect natural changes; for example, seizures may mostly happen or only occur during the menstrual cycle in women.
5. Antiepileptic medication should only be given when the type and frequency of seizures justify it, especially if changes are required more than once every 6 to 12 months.

Mechanism of action of antiepileptic drugs:

Antiepileptic medications mainly work through one of three main ways:

1. They lower the excitability of electrical cell membranes, especially by blocking voltage-dependent sodium channels that allow the inward flow of current needed to create action potentials;



2. They increase synaptic inhibition through GABA by either blocking GABA transaminase or acting as direct GABA activators. This results in a rise in chloride ion movement across the membrane, which reduces cell excitability;
3. They block T-type calcium channels, which are important for controlling seizures, or they reduce the action of excitatory neurotransmitters like glutamate.[27,33]

Some common contraindications include the following:

Epilepsy and oral contraceptive:

Certain antiepileptic medications, such as carbamazepine, phenytoin, barbiturates, topiramate, and oxcarbazepine, are known to increase enzymes that break down steroids, which may cause hormonal contraceptives to stop working. As a result, people using these antiepileptic drugs might need to raise their dosage of oral contraceptives that contain estrogen to 50 mg per day.[33]

Breastfeeding:

Antiepileptic medications are usually found in breast milk at different levels, and breastfeeding is generally considered safe when these drugs are taken at regular doses, except for barbiturates and ethosuximide. Using benzodiazepines and barbiturates may cause sedation problems in newborns, while ethosuximide is present in high amounts in human milk, so it is best to avoid breastfeeding during its use.[30]

Epilepsy in children:

Adjustments for young patients are handled the same way as for adults; however, children may

show different and more upset reactions, especially when using medications like sodium valproate or phenobarbital. For cases of febrile seizures, an antiepileptic drug may be given continuously, like phenobarbital at a dose of 3-4 mg/kg/day, until the child turns five. Nevertheless, long-term use of drugs like phenytoin or phenobarbital may negatively affect brain development, making it necessary to stop the drug.[33]

Treatment of epilepsy:

- People aged 60 or 65 and older, commonly called the elderly, make up the fastest growing group in the overall population.
- The elderly population with epilepsy is a special clinical group when compared to younger age groups.
- The number and rate of new epilepsy cases are significantly higher among the elderly.
- The main causes of epilepsy in this age group include brain blood vessel problems, brain degeneration diseases, and tumors, while idiopathic epilepsy is usually considered to have no known cause.
- Genetic factors are the most common cause of epilepsy in younger people.
- In contrast, the rate of status epilepticus in older adults is almost double that seen in younger people, leading to a higher death rate.
- Older patients with epilepsy are at a higher risk for different medical and mental health issues, such as depression, weak bones, and memory loss.
- Managing epilepsy in older adults is made more difficult by age-related issues, such as having multiple health conditions and changes in how drugs are processed in the body.
- Older individuals who have memory problems or difficulty swallowing need extra



considerations, such as having specific drug options (like liquid or crushable medicines) and how often to give medication.

- The use of many medications at once, known as polypharmacy, is common in this group and is connected to a greater risk of interactions between antiepileptic drugs (AEDs).
- Many AEDs stimulate liver enzymes.
- These different factors increase the risk of negative effects and raise concerns about whether elderly patients will take their medications as prescribed.
- Therefore, it is important for doctors to be careful when choosing AEDs and adjusting doses for older patients with epilepsy, aiming to effectively control seizures while minimizing potential risks.

CONCLUSION

The choice of an anti-seizure medication mainly depends on how well it works for treating certain types of epileptic seizures and epilepsy. While handling seizures generally works well for most patients, a large number of people with epilepsy have severe or treatment-resistant forms of the condition, even when they take the right medication regularly and at the right dose from the beginning. As a result, there is a strong need for new drugs that provide better results regarding side effects and how well patients can handle them, even if that means they might not work as well as current epilepsy medications. Even though there are many treatment choices available, there is a big focus on finding new methods. Many of these methods aim to understand the genetic, cellular, and molecular processes that cause excessive excitability, which could point to specific targets for new treatment options.

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