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A Comprehensive Overview And Diagnostic Approaches For Seizure

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ABSTRACT:

Seizure, acknowledged as one of the most prevalent neurological disorders, continues to present challenges in comprehending fully, leading to difficulties in precisely diagnosing and selecting appropriate treatments. This all-inclusive article aims to provide a comprehensive overview of seizures, with a particular emphasis on their classification, causes, and underlying mechanisms. Seizures, sudden and abnormal electrical disruptions in the brain, manifest in various ways, complicating their identification and categorization. To achieve accurate diagnoses, a series of extensive diagnostic tests are employed, including Electroencephalography (EEG), Furthermore, neuroimaging techniques, such as MRI and CT scans, aid in identifying structural abnormalities in the brain, while blood tests are essential for detecting metabolic or infectious triggers. Treatment options are selected carefully based on the type of seizure, frequency, and individual patient characteristics, with antiepileptic drugs (AEDs) being the primary choice, though surgery or alternative therapies may be considered for drug-resistant cases.

KEYWORDS: Seizure, GABA, dopamine, Electroencephalography, Antiepileptic drug therapy, intraparenchymal haemorrhages.

INTRODUCTION:

Seizure is one of the most prevalent neurological disorder, with an incidence of about 50 new cases per 1,00,000 people annually. One third of seizure patients develop refractory seizure, which 1% of the population overall. 75% of seizure cases start in childhood, which is indicate of the developing brain's increased propensity for seizures.[1] A seizure represents the uncontrolled, abnormal electrical activity of the brain that may cause changes in the level of consciousness, behaviour, memory or feelings.[2] There are two types of seizure provoked and unprovoked. Acute symptomatic seizure can have a variety of reasons, including electrolyte imbalance, toxin,

head trauma, viral disease, vascular abnormalities, tumours or other mass lesion, among others. There is a long list of triggered causes of seizure, which includes issues with practically any medical process. Some common causes are electrolyte disturbance, acute toxic effects, sepsis, CNS infections, hypoxic brain injury, stroke ischemic or hemorrhagic, neoplasm, sleep deprivation.[3] In the diagnosis of seizure, history is the key, because in most adults, the physical examination is relatively nondefinitive.[4] The examination of newborns and children is more important since the identification of some very recognisable neurological illnesses that cause seizure is made possible by the presence of dysmorphic and cutaneous abnormalities.[5] Several laboratory tests, such as a complete blood count, blood chemistry profiles, liver and thyroid function tests, an EEG, and a brain examination, preferably with magnetic resonance imaging, are typically included in the initial diagnostic diagnosis(MRI). In a emergency or for extremely young children, computed tomography (CT) scanning may be the only practical examination. Later on, some patients could need video/EEG or prolonged EEG monitoring, either in the hospital or at home using portable equipment.[4] Other procedures that might be used include cardiac stress tests, Halter monitoring, tilt-table testing, long-term patient activated cardiac monitors, and sleep studies. Any patient who may have a seizure problem should get an EEG evaluation as away. Nearly all patients with newly developing seizures ought to undergo a brain imaging examination to look for underlying structural issues. For the detection of brain lesions related to epilepsy, MRI is more effective than CT.[5] Numerous children seizure disorders, such as absence epilepsy with 3-second spike-and-wave discharges and benign childhood epilepsy with centrotemporal spikes, have also been linked to a more complex genetic component. Both of these illnesses are inherited as incompletely penetrant autosomal dominant features, possibly in a more complex way.[4]Gene changes linked to symptomatic epilepsy seem to be connected to processes that influence the development of the central nervous system or neuronal homeostasis. Other neurological abnormalities, like cognitive impairment, coexist with seizures in patients with symptomatic epilepsy. Finding the several susceptibility genes that underlie the more prevalent types of idiopathic seizures is the difficult task.[5]

EPIDEMIOLOGY:

A lifetime risk of 8% to 10% for spontaneous or acute symptomatic seizures and a 2% to 3% chance of actually developing epilepsy were reported in population-based studies conducted in the 1980s and 1990s.[6,7] Acute symptomatic seizures occur between 29 and 39 times per 1,00,000 people annually, single unprovoked seizures occur between 23 and 61 times per 1,00,000 people annually, and epilepsy affects 50.4 people worldwide per 1,00,000 people annually, according to more recent studies.[8] This led to an estimated 1.6 million visits to emergency departments (ED) for seizure examination in 2011 and about 4,00,000 patients presenting with newly-onset seizures.[9]

CLASSIFICATION:

To focus the diagnostic approach on a specific etiologic component, choose the best medication therapy, undertake scientific studies that call for defining clinical and EEG phenotypes, and offer crucial information regarding the prognosis, it is required to identify the kind of seizure.[36,37] The International Classification of Epileptic Seizures (ICES), which was amended and published by the International League against Epilepsy (ILAE) in 1981, has remained a highly helpful classification system.[37] It is based on the clinical characteristics of seizures and the related EEG results. The cellular substrate or aetiology are not taken into account.

Partial, generalised, and unclassified seizures are the three basic categories of seizures.[37]

Types of seizure
Partial seizure • Simple seizure • Complex partial • Partial seizures
Primarily generalized seizure • Absence • Clonic • Myoclonic • Tonic • Tonic-clonic • Atonic
Unclassified seizure • Neonatal seizure • Infantile spasms

ETIOLOGY:

Seizure's root cause is absolutely unknown. Although some occurrences of seizure are caused by genetic factors, it can also result from head traumas from blows to the head, stroke, infections, high fever, or tumours. The term "epilepsy" says nothing about the source or severity of the person's seizures.[10] Although it can affect persons of any age, it has been shown that inheritance (genetics) plays a significant part in many causes of epilepsy in very young children. For example, not everyone who sustains a severe head injury clearly a cause of seizures will go on to acquire epilepsy.[11] Reflex epilepsy refers to certain epilepsy syndromes that require specific precipitants or triggers for seizures to occur, such as reading or flashing lights. Patients with epilepsy may also identify emotional stress, sleep deprivation, heat stress, alcohol, and feverish illness as precipitants. Notably, the effect of

different precipitants changes depending on the epilepsy syndrome.[12] When a woman has epilepsy, her menstrual cycle can affect her seizure recurrence patterns and catamenial epilepsy, which is a seizure that is associated with the menstrual cycle.[13] Different causes of epilepsy are prevalent in various age groups;

1. Most frequent causes of hypoxic-ischemic encephalopathy in the neonatal period and early infancy are CNS infections, trauma, congenital CNS abnormalities, and metabolic disorders.

2. Most frequent febrile seizures in late infancy and early childhood may be brought on by CNS illnesses and trauma.

3. Well-defined epilepsy syndromes are typically seen in children.

4. The causes are more likely to be secondary to any CNS damage in adolescence and adulthood.

5. The most frequent cause of dementia in older people is cerebrovascular illness; additional reasons include CNS tumors, head trauma, and other degenerative disorders like dementia.[14]

PATHOPHYSIOLOGY:

Paroxysmal manifestations of the cerebral cortex are seizures. When the excitatory and inhibitory forces within the network of cortical neurons suddenly become unbalanced, seizures follow. A cell membrane that is unstable, or one that is close to or around an unstable cell membrane, is where the basic physiology of a seizure episode is found. Any cortical or subcortical location in the grey matter is where the seizure starts. At first, only a few neurons fire improperly. A focal seizure is caused by the breakdown of inhibitory synaptic current, normal membrane conductance, and excess excitability spreading locally or more broadly to cause a generalised seizure. This onset spreads through physiological pathways to affect nearby and far-off locations. Unstable neuronal membranes can result in seizures due to abnormalities in potassium conductance, voltage-activated ion channel defects, or deficiencies in membrane ATPases involved in ion transport. Glutamate, aspartate, acetyl choline, norepinephrine, histamine, corticotropin releasing factor, purines, peptides, cytokines, and steroid hormones are just a few neurotransmitters that increase the excitability and propagation of neuronal activity, while GABA and dopamine decrease it. The demand for blood flow to the brain increases during a seizure in order to remove CO and provide substrate for the metabolic activity of the two neurons. As the seizure lasts longer, the brain experiences greater ischemia, which may cause neuronal death and brain damage.[15]

Some kinds of epilepsy may be caused by mutations in various genes.Generalized epilepsy and infantile seizure disorders have been linked to genes that produce voltage-sensitive and ligand-activated ion channel protein subunits.[16]

One proposed mechanism for some types of inherited epilepsy is mutation of the genes encoding for sodium channel proteins; these defective sodium channels remain open for long periods of time and cause the neurons to be overly excitable as a result; glutamate, an excitatory neurotransmitter, may be released in large amounts from the neurons; this excessive glutamate release, when it binds with nearby glutamanergic neurons, causes excessive calcium (Ca^{2}+) release in the post synaptic cells.[17]

DIAGNOSIS:

The history and physical examination serve as a reference for further clinical evaluations. The first consideration is whether the seizure was induced or unprovoked if the clinician thinks it was. Typically, electrolytes are collected through laboratory testing. Patients with fever, a history of immunosuppression, or other signs that point to a probable central nervous system infection should be given lumbar puncture consideration.

Based on historical circumstances or focal findings on the neurologic examination, neuroimaging is frequently acquired and has a greater yield. In patients with a history of acute head trauma, a history of malignancy, immunocompromise, fever, a persistent headache, usage of anticoagulants, age greater than 40, or the beginning of focal seizures, imaging is advised if there is a suspicion of an acute intracranial process.[18, 19]

Determining serum sodium and glucose levels is advised for a healthy adult patient who has recovered to baseline normal neurologic function and appears to have experienced a first seizure. A guideline for women of childbearing age is pregnancy testing.[20] Neuroimaging and other lab work are frequently required.

Additional testing, such as neuroimaging and other serologic studies, will be required if there is a persistent disturbance in consciousness or if seizures are still occurring. Making appointments for a neurology consultation and an EEG is necessary if nonconvulsive status epilepticus is a factor.[20]

Electroencephalography:

All patients who have had their first unprovoked seizure are required to obtain an electroencephalogram (EEG), and 29% of these patients exhibit substantial abnormalities.[26] It also aids in identifying the seizure focus involved, classifying the seizure subtype, and classifying the seizure type (epileptic vs. nonepileptic, focal vs. generalised). As a result, EEG has implications for determining recurrence risk and potential treatments for each patient.[23,25,26,27]

In patients with epilepsy, a single routine record has a sensitivity of only about 50% for epileptiform discharges.[23] The diagnostic yield, however, can be increased by taking three or more serial records (up to 80%-90%), taking records within the first 24 hours following an epileptic seizure, and by using stimulation procedures including hyperventilation, photostimulation, and sleep deprivation (up to 80%).[21,23,26] The anterior temporal lobe spikes, vertex spikes, generalised paroxysmal rapid activity, generalised slow spike and wave, and

hypsarrhythmia are a few paroxysmal discharges with significant epileptogenic potential (>90%).[23] When there are epileptiform discharges, the likelihood of another seizure is thought to be roughly 77%.[28]

Recent research on patients who had their first unprovoked seizure in an emergency room found that the EEG had a higher diagnostic yield if it was performed prior to discharge (24% and 29.4% of them had abnormal records), which was important for both the diagnosis of epilepsy and the start of AED treatment.[29,30] In patients who had their first unprovoked seizures, a 24hour videoelectroencephalogram was done during the first seven days; epileptiform abnormalities were discovered in nearly 42% of them and were a risk factor for seizure recurrence.[31]

Its key drawbacks are the fact that it does not rule out the diagnosis of epilepsy, the fact that emergency rooms do not have access to it, the fact that it is expensive, and the fact that records can be interpreted incorrectly.[23,25]

EEG applications in epilepsy diagnosis:

EEG assists patients with epilepsy in identifying the kind of seizure and epilepsy syndrome, which helps with antiepileptic drug selection and prognosis prediction. In order to determine whether the seizure condition is focal or generalised, idiopathic or symptomatic, or a component of a particular epilepsy syndrome, EEG results are important to the multi-axial diagnosis of epilepsy.

Brain imaging:

All individuals with their first unprovoked seizure require a neuroimaging scan (CT or MRI).[26] 10% of patients with this illness had significant changes on a cranial tomography (CT) scan.[26] Due to its widespread use in emergency rooms and ability to expedite diagnostic testing for patients exhibiting an acute neurological deficit, it is regarded as the first line imaging modality. This is especially true when excluding vascular causes or any conditions that call for neurosurgical intervention. As a result, every patient who has had their first seizure needs to get a CT scan. [21,22,24,32]

All patients who experience their first unprovoked seizure should undergo magnetic resonance imaging (MRI), unless there are medical reasons not to do so. [23, 26]

Because it makes it easier to spot important lesions including intraparenchymal haemorrhages, brain tumours, vascular malformations, posttraumatic alterations, mesial temporal sclerosis, and anomalies of cortical development, MRI is more sensitive than CT scanning.[23]

Nearly 30% of the individuals in these studies were found to have a possibly epileptogenic change[32,33] and of these patients, roughly 12% had a particular pathological abnormality despite having a normal CT scan.[32] When patients undergo an epilepsy protocol-specific brain MRI and have their first focal or provoked seizure, the diagnostic yield of MRI is higher (about 50%). [34,35]

General laboratory studies :[serum electrolytes, blood cytometry, glucose]

In these studies, changes are present in 0% to 15% of the patients, but they are rarely clinically significant (5%).[48,49] As a result, they ought to be used sparingly and only when specifically requested.[26] However, we advise testing serum electrolytes (sodium, calcium, and magnesium) as well as glucose in every patient who has had a first seizure.

Lumbar puncture

Patients with a clinical suspicion of a CNS infection, subarachnoid haemorrhage, persistent mental impairment, or immunocompromised individuals should think about having this operation (even if they are afebrile).[25,50]

Hyperproteinorrachia (30%) and pleocytosis (10% of cases, mean 10.2 cells/mm3) are two abnormalities that have been seen in the cerebrospinal fluid of patients who have had their first unprovoked seizure. They are most likely caused by the blood-brain barrier temporarily being disrupted following the seizure.[51]

Other tests

Electrocardiogram, prolactin levels, pregnancy test, Toxicological profile.

When there is a significant degree of clinical suspicion, such as in individuals with toxicosis, known substance use, or changed mental status on evaluation, a toxicological profile may be conducted. However, the evidence is insufficient to execute it frequently.[26,27]

Prolactin levels have been shown to be higher than normal in people who have had epileptic seizures, and they have been used to distinguish between psychogenic non-epileptic seizures and seizures with altered awareness (PNES). The aforementioned is applicable if baseline measurements of them (6 hours prior to the event) are made, and these measurements are contrasted with new measurements made 10–20 minutes after the episode, which is challenging to implement in clinical practise. Additionally, because they might be raised in both conditions, they cannot differentiate between syncope and seizures.[52]

A 12-lead ECG and a pregnancy test for women of childbearing age should also be done on all patients in this situation. The first is to check for any heart abnormality associated with syncope, and the second is because eclampsia and pregnancy itself are linked to epilepsy.[9,47] Depending on the circumstances surrounding each patient, it might be appropriate to ask for an echocardiography, Holter study, HIV test, etc.[47,54]

Differential Diagnosis:

Spells that resemble seizures can result from a variety of causes. An important distinction to make is between a seizure and a syncopal occurrence. Both episodes start abruptly, but syncopal events frequently have a provoking origin, the loss of consciousness lasts just a short time, and full consciousness is quickly regained without a

confused state. With either kind of incident, incontinence could be present. Sometimes syncope is accompanied by motor movements that resemble seizures.[25]

MANAGEMENT:

The optimum course of treatment must be chosen when a neurologist or doctor has diagnosed seizures or epilepsy. If epilepsy (a persistent propensity to have seizures) is identified, the neurologist will typically prescribe drugs that prevent seizures. Surgery, a specific diet, complementary therapies, or vagus nerve stimulation may be tried if medications are unsuccessful. Treatment aims to stop new seizures, avoid side effects, and restore patients' ability to lead active lifestyles.[37]

Antiepileptic drug (AED) therapy, the mainstay of treatment for the majority of patients, has four objectives: to completely eliminate seizures or reduce their frequency to the lowest possible level, to avoid the negative effects associated with long-term treatment, to help patients maintain or resume their typical psychosocial and vocational activities, and to support patients in maintaining a normal lifestyle.[36]

The choice to begin AED

Medication should be based on a thorough evaluation of the risk of seizure recurrence, the patient consequences of ongoing seizures, and the advantages and disadvantages of the selected pharmacological agent.[38]

A single seizure brought on by a known lesion, such as a CNS tumour, an infection, or trauma, in which there is sufficient evidence that the lesion is epileptogenic, should be treated.[37] However, whether to start medication in a patient with a single seizure is debatable. The primary objective of AED therapy is to entirely eliminate seizures.

Depending on the type or spectrum of seizures, the relative risk of epilepsy recurrence can change.[39] Patients who have congenital neurological abnormalities or epileptic form discharges on an EEG are at a significant probability of recurrence (almost 90%).[38] When starting AED therapy, the patient's and their family's perspectives should also be taken into account.[40]

SELECTION OF ANTIEPILEPTIC THERAPY:

Unfortunately, currently available AEDs not only frequently produce negative side effects that range in severity from minor CNS impairment to death from aplastic anaemia or hepatic failure, but also frequently fail to control seizure activity in some patients. The treating physician or practitioner must select the right AED or combination of medications that best controls seizures with a satisfactory level of control. It is generally acknowledged that up to 50% of patients can obtain total seizure control, and another 25% experience significant improvement.[44]The success rate of treatment varies depending on the type of seizure, family history, and severity of the underlying neurological abnormalities, and it is higher in people with newly diagnosed epilepsy.[41] The possibility of a seizure recurrence, the repercussions of ongoing seizures, and the positive and negative effects of

the agent in avoiding a recurrence can all be taken into consideration before starting AED treatment.[42] Depending on the seizure type or syndrome, there may be a range in the relative likelihood of recurrence.[39] Patients who have congenital neurological abnormalities or epileptiform discharges on an EEG are at a significant risk (up to 90%) of recurrence.[42] Patients with brain lesions, Todd's paralysis, prior symptomatic seizures, and these conditions all carry an increased chance of recurrence (a brief, temporary paralysis following a seizure).[43]

Surgical therapy:

For certain patients with drug-resistant epilepsy, epilepsy surgery—which involves resection or, less frequently, disconnection or destruction of epileptic tissue—is the most successful form of treatment. A series of tests, including structural MRI, fluorodeoxyglucose positron emission tomography, ictal and interictal single-photon emission computed tomography, functional MRI, and neuropsychological testing, are used to establish a patient's suitability for surgery. These investigations seek to define the "epileptogenic zone" (i.e., the smallest area of cortex that, if removed, severed, or destroyed, would prevent seizures) and the likelihood of post-operative morbidity. To better localization of the epileptogenic zone, some patients also require intracranial EEG, either as intra-operative electrocorticography or chronic extra-operative recordings.[45]

CONCLUSION:

Seizure is predominantly one of the most common neurological disorder which can affect the quality of life of a person.The most frequent test to identify epilepsy is the Electroencephalogram (EEG).A lumbar puncture is performed to look for any abnormalities. Anticonvulsant drug like carbamazepine are used to treat the seizure now a days. Patients with seizures can benefit from antiepileptic medication therapy by having a better quality of life. Thus, compared to the current antiepileptic therapies, there is a need for newer drugs with better adverse effect and tolerance profiles, Although there are many therapies available, a huge effort is put into developing new methods for treat seizure.

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