

Overview of Epilepsy and It's Management

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ABSTRACT

Now a days peoples are facing various types of stress in their life due to their hectic lifestyle and commonly peoples in the world suffering from many types of neurological disorder Epilepsy is one of the most common neurologic disorders of the brain which is growing now a days. Epilepsy is class of non-communicable neurological disorder diagnosed by recurrent epileptic seizures. Various factors like genetic factors as well as infection in brain, stroke, cancer, high fever can cause epilepsy. In a seizure, person may experience abnormal behavior, symptoms and sensation that includes loss of consciousness. There are various types of seizure and their different mechanisms by which brain generate seizures. Purpose of the review is to discuss history, etiology, pathophysiology, classification of epilepsy, symptoms, causes, diagnosis and management of epilepsy.

Keywords: Antiepileptic drug, Seizure, Pathophysiology, Brain.

INTRODUCTION

The term epilepsy is derived from the Greek word '*epilam-banein*', it means to attack or seize. Hippocrates explained that epilepsy was a disorder of the brain. [1] Epilepsy is a chronic medical disease, which is unpredictable, unprovoked, recurrent seizures that affect various types of mental and physical functions. It is affecting more than 3 million people in the U.S. [2] and about 50 million people worldwide. [3] "Epilepsy can be defined as recurrent seizure disorder characterized by abnormal electrical discharge from brain, often in the cerebral cortex". [4]

Epilepsy is a chronic disease that causes repeated seizures because of irregular electrical signal produced by damaged brain cells. Seizures involved changes your awareness, muscle control, emotions, sensation and behavior. Epilepsy is known as seizure disorder. Epilepsy is a neurological condition in which person have two or unprovoked seizures that cause more than 24 hours apart. A seizure is a sudden increase of electrical activity in the brain that cause various symptoms, depending on parts of brain are involved seizures which can be genetic or a brain injury, but often their cause is unknown. [5] Epilepsy is commonly occurred in young children or people above 60 years of age; however, it can occur at any time.[6] All epilepsy syndromes are not lifetime-some forms are confined to specific stages of childhood. Generally, management of epilepsy consists Primarily of anticonvulsant medications. [7-8] Although these medications often control or reduce the frequency of seizures, some patients show little or no improvement

and therefore surgery may be their treatment in difficult cases.[9] The objective of this review is to provide general considerations and management of epilepsy.

HISTORY

The history of epilepsy can be traced back to a 4000-year-old Akkadian tablet found in Mesopotamia; inscribed on it is a description of a person with “his neck turning left, hands and feet are tense, and his eyes wide open, and from his mouth froth is flowing without him having any consciousness” [10] Proof of epilepsy has also been found in ancient Egypt, as explained by the Edwin Smith Surgical Papyrus written circa 1700 BC. Egyptians proved that seizures can be occur by cortical disruption. Hippocrates was also one of the first to explain the concept of post-traumatic epilepsy; through his study and observations of head trauma, he observed convulsions which were always contralateral to the head wound. [11]

ETIOLOGY:

Seizures causes from a condition in the normal imbalance of excitation and inhibition within CNS as well as abnormal brain function. Due to so many properties control neuronal excitability, it is usual that this normal balance can disturbed in very different ways; thus, there are many reasons of seizures and epilepsy. [12]

- 1) Seizures may be occurring in children by very high fever, even if they are healthy, they have a structure defect or genetic risk factors.
- 2) A person having trauma or injury, connected with up to 50% risk of epilepsy.
- 3) In aged patients, Alzheimer’s disease and also stroke can cause epilepsy.[13]

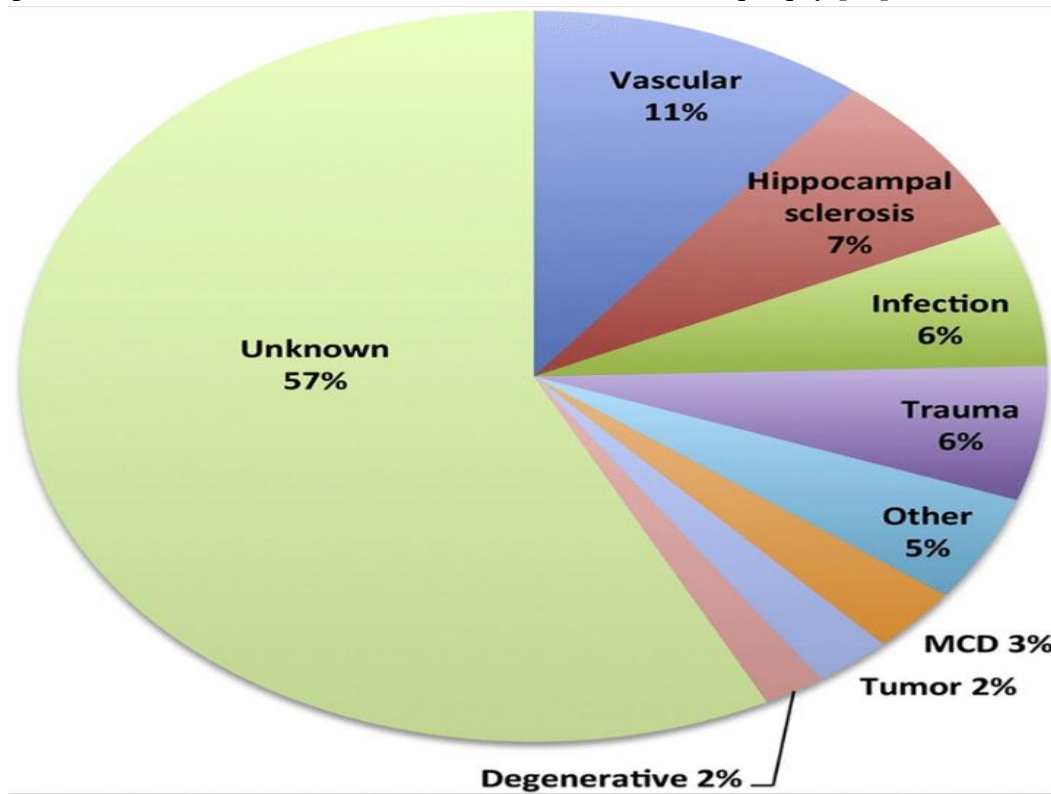


Fig.no. 01

PATHOPHYSIOLOGY

The brain coordinates the functions of the body by keeping the control on the activities of the neurons which are specialized nerves that conduct electrical impulses throughout the central nervous and peripheral systems. We use electro-encephalogram (EEG) to count the electrical function of the brain. EEG recording is helpful for the diagnosis of epilepsy.

A seizure occurs due to undisciplined depolarization of neurons resulting in irregular motor or sensory activity with or without loss of consciousness.[14] Seizure occurs due to disparity between neuronal excitation & inhibition which causes from hyper excitation & hypersynchronisation of a neuronal network.[15] Change in the property of neuronal membrane may occur due to hypoxia, alkalosis, hypoglycemia and irregular neurotransmitter properties, which may cause the release of huge amounts of neurotransmitters at the synapse and ultimately promote seizure. The irregular neuronal discharge causes clinical indication with change in sensation, motor function, autonomic function, behavior & consciousness.[16] The neurons in the epileptogenic focus are hyper excitable because of their lower threshold for stimulation. Some physiological changes & certain conditions like fatigue or lack of sleep, fever, constipation, stress, are reasons for activation of irritable neurons & hence lowers the threshold for seizures. Some other factors like loud noise, bright light or biochemical stimuli like excessive fluid retention, change in medication, hypoglycemia, sudden withdrawal from sedatives & alcohol may trigger epilepsy in some people.[14] The immediate period in which epileptic seizure occurs, is termed as postictal state. This state may include signs of headache, confusion, memory loss, short term paralysis, dysphasia, and deep sleep.[16]

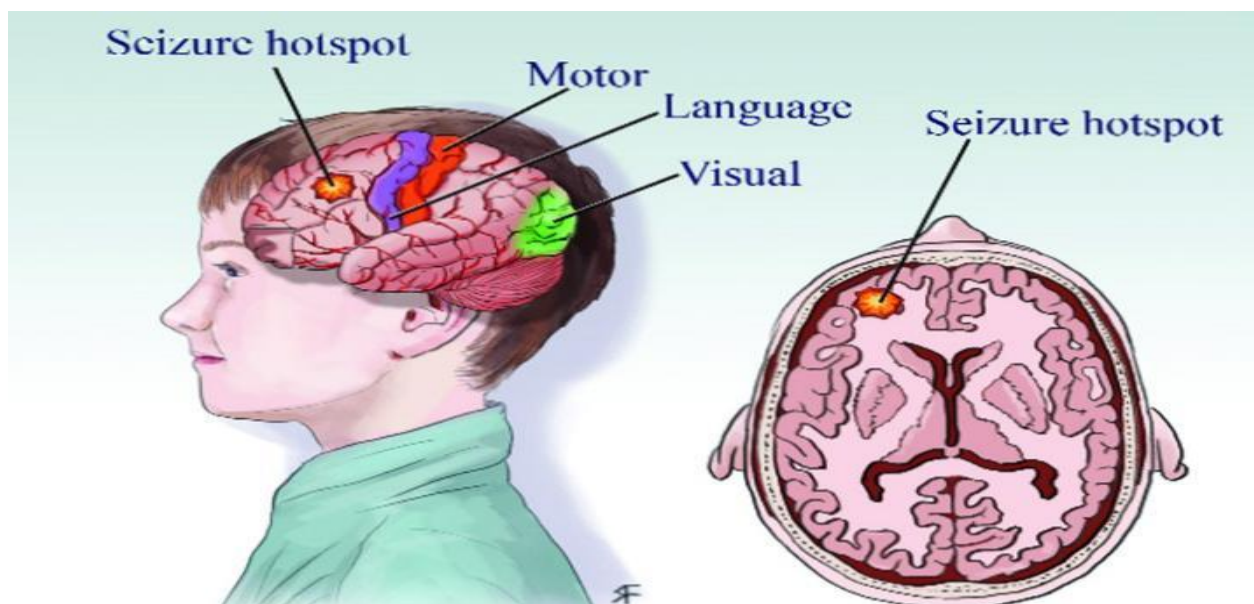


Fig.2

Stages of a Seizure

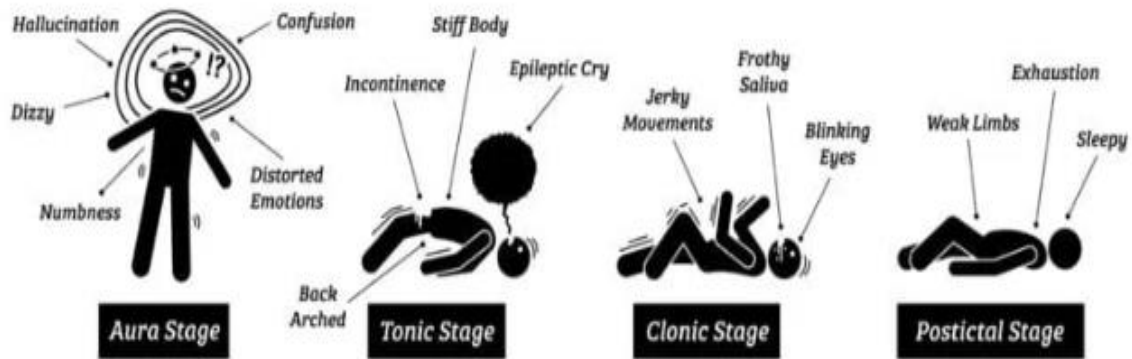


Fig.3

CAUSES OF EPILEPSY

- 1) Brain injuries
- 2) Meningitis
- 3) Tumors
- 4) Deficiency of blood supply to the brain
- 5) Habit of drug for depression and mental disorder.
- 6) Regular and excessive use of chemical drugs
- 7) Damage to the CNS
- 8) Anti phospholipid syndrome.
- 9) Genetically (30% to 40% chances) [17]

causes of EPILEPSY



Fig.4

SIGN & SYMPTOMS

- 1) Unconsciousness
- 2) Anxiety and depression
- 3) Disturbance in sensation like vision and test
- 4) More chances of psychological problems [5]
- 5) Disturbance of mood
- 6) Short term confusion
- 7) Harshening of the body
- 8) Problem in breathing
- 9) Not any response to noise
- 10) Eyes blinking rapidly. [18]



Fig.5

CLASSIFICATION OF EPILEPSY

Epilepsy is classified mainly in two classes as follows

- 1) Primary epilepsy / idiopathic Epilepsy
- 2) Secondary epilepsy /symptomatic epilepsy

1. Primary Epilepsy / Idiopathic Epilepsy

Idiopathic epilepsy is most usual form of Epilepsy which may accounts for 50-60% of peoples with the medical condition. In this type of epilepsy there is no confirm fundamental cause. Although there is no fixed known reason for seizures in many patients, a genetic susceptibility to hypersensitivity of the neurons is considered as reason behind this.[14]

2. Secondary Epilepsy/ Symptomatic epilepsy

On the contrary of primary epilepsy, in secondary epilepsy there are some fixed reasons behind the seizures. The causes include infection, head injury, hereditary syndrome, brain cancer, stroke, congenital abnormalities.[18] Some other reasons behind the symptomatic seizure may include, primary neurological disorder or anatomical deformity of brain, hemorrhage, infection to CNS, metabolic disorder, electrolyte imbalance, alcohol, abuse. [19]

MANAGEMENT OF ANTIEPILEPTIC DRUG

Mainly in management of Epilepsy Anti-epileptic drugs are used to control the epilepsy

CLASSIFICATION OF ANTIEPILEPTIC DRUG

1. Hydantoin: Phenytoin, Phos phenytoin
2. Barbiturates: Phenobarbitone
3. Iminostilbenes: Carbamazepine, Oxcarbazepine.
4. Succinimides: Ethosuximide
5. Aliphatic Carboxylic Acid: Valproic acid
6. Benzodiazepines: Clonazepam, Diazepam
7. New Compounds: Gabapentin, lamotrigine, Tiagabin [20]

Some widely used drugs are explained below

1) PHENYTOIN

Structure:

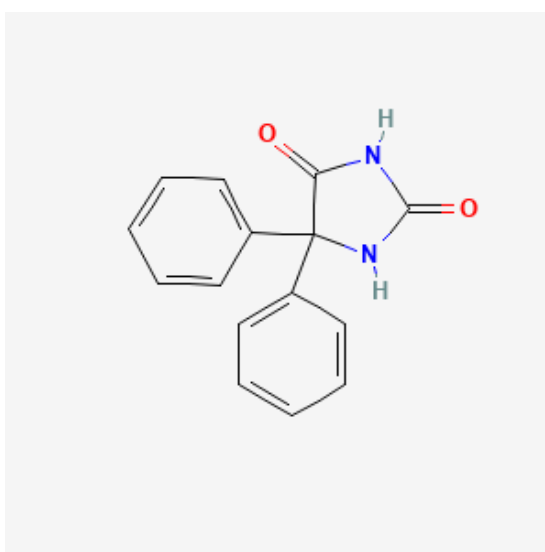


Fig no.06

Molecular formula: C₁₅H₁₂N₂O₂

IUPAC Name: 5,5-diphenylimidazolidine-2,4-dione

MOA:

- It firstly blocks sodium channels of neurons
- Inhibition of release of excitatory transmitter
- It shortens the duration of action potential
- Decrease the synaptic release of glutamate & e enhance the release of GABA

COMMON SIDE EFFECTS

- Drowsiness, headaches, nausea, ataxia
- Diplopia or nystagmus,
- Slurring of speech,
- Gingival hyperplasia,
- Rash and hirsutism. etc.

Uses:

1. Treatment of Epilepsy
2. Control irregular heartbeat
3. Trigeminal neuralgia
4. In generalized tonic-clonic seizures
5. Anxiety
6. Neuropathic pain

Dose: 100 mg 3 times a day or 300 mg once a day [21]

Administration Route: Oral and IV

Brand name: Dilantin, Epanutin, Phenytek

Contraindication: Avoid in pregnancy.

2) PHENOBARBITONE

Structure:

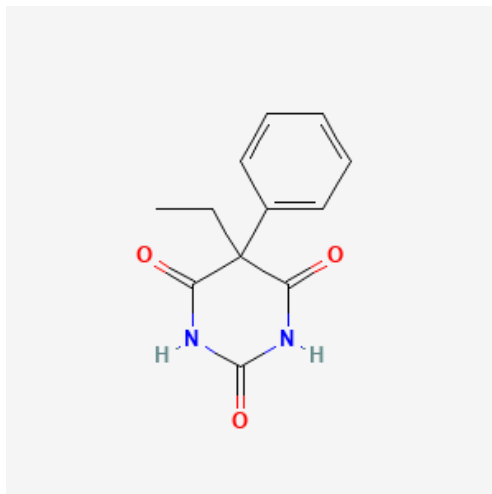


Fig no 07.

Molecular formula: C₁₂H₁₂N₂O₃

IUPAC Name :5-ethyl-5-phenyl-2,4,6(1H,3H,5H)-pyrimidinetrione

MOA:

- Phenobarbital gets binds to the GABA receptor at different allosteric sites
- Facilitate the GABA action
- It increases the duration of opening of Chloride channels
- Hyper polarization
- CNS gets depressed

COMMON SIDE EFFECTS

- Rashes, drowsiness.
- mental slowing,
- aggressiveness, depression.
- Withdrawal seizures may cause if stopped abruptly after prolonged use.

Uses:

1. Use in treatment of seizure
2. In insomnia
3. Used in sleep disorder
4. Use as analgesic
5. Use in neurological problems like migraine

Dose: 50 to 100 mg two to three times a day.

Administration route: Oral

Brand name: Phenobarbitone, Phenobarb

Contraindications: Can't give in known barbiturates sensitivity patients.

3) CARBAMIZAPINE

Structure:

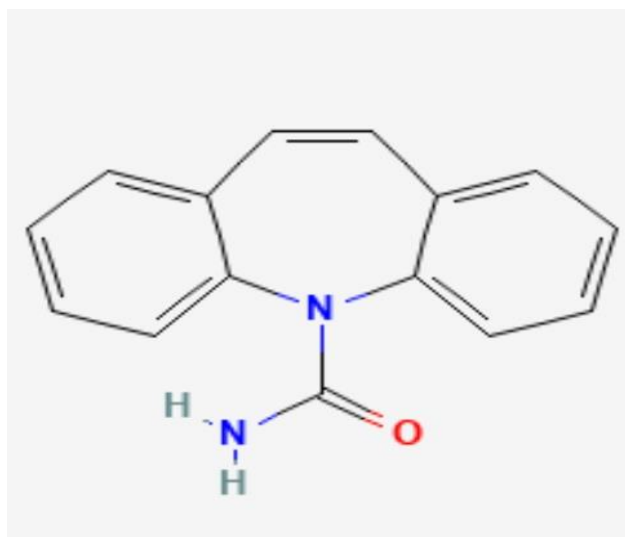


Fig no.08

Molecular formula: C₁₅H₁₂N₂O₂

IUPAC Name: 5H-dibenzo [b, f] azepine-5-carboxamide

MOA:

- Blockage of sodium channels reduce propagation of irregular impulses in the brain
- Inhibits repetitive action potential.
- Inhibits the release of glutamate

COMMON SIDE EFFECTS

- Oedema, rash,
- Fatigue.
- blood disorder and drowsiness.

Uses:

1. Used as Antiepileptic drug
2. To treat migraine
3. In nerve pain
4. Act as antipsychotic drug
5. Used in partial seizure

Dose: In (Adult 100 mg or o teaspoon 4 times a day)

In (Children 6 to 12 years 50 mg tow times a day)

Administration Route: Oral

Brand name: Tegretol, Curatil.

Contraindications: Strictly contraindicated in the patient having bone marrow depression

4) VALPROIC ACID

Structure:

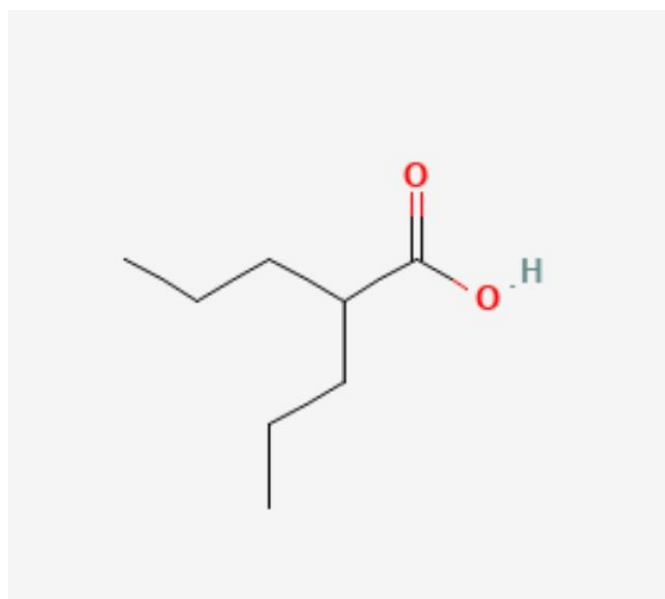


Fig.no.09 [22]

Molecular formula:C8H16O2

IUPAC Name:2-propylpentanoic acid

MOA

- Inactivation of voltage activated sodium channel
- Stimulate the activity of GABA enzyme
- Inhibit GABA Degradative enzyme, GABA transaminase
- Blocked NMDA receptor mediated excitation (glutamate)
- Reduction of T type Ca²⁺ channels in thalamus

COMMON SIDE EFFECTS

- Aggression,
- anemia,
- confusion,
- diarrhea, deafness.
- risk of congenital malformations and developmental delay if used during pregnancy.

Uses:

- 1) In bipolar disorder
- 2) Mood and anxiety
- 3) To treat migraine prophylaxis
- 4) Sleep disorder
- 5) As anticonvulsant drug

Dose: In pediatrics <10 mg /kg / day

Adult <400 mg / day

Administration route: Oral and Iv

Brand name: Belva, Depakote, Syonell, Convulex, Dyzantil

Contraindications: Avoid in pregnancy

CONCLUSION

Therefore, the choice of anticonvulsant medication is often based on its effectiveness against specific types of seizures and convulsions. While seizure control is generally good for most patients, the majority of people with epilepsy have refractory or drug-resistant epilepsy despite early disease treatment and adequate antibiotic use to take daily medication Representatives. For this reason, despite the cost, new drugs that are more effective in terms of side effects and tolerance compared to existing antiepileptic drugs are needed.

Although many treatment options are available, we are committed to exploring new techniques. Many of these studies are expressing the genetic and molecular mechanisms of hyper excitability and promise to provide specific targets for new treatments.

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