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Evaluation of Epilipsy and Seizure

Anil Balasaheb Golande
Aditya Pharmacy college, Beed, maharashtra

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ABSTRACT:-In this project work we speak about different types of epilepsy. Epilepsy is 4th most common neurological disorder affecting 65 million peoples worldwide. According to epilepsy foundation of America, he found that approximately 45000 People are dead due to epilepsy. It is categorized into two main types i.e. partial seizure (affecting small portion of brain) generalized seizures (covering all portion of brain). Several etiological factors responsible for causing epilepsy such genetic, CNS infection, metabolic disorders, miscellaneous. Epilepsy is caused due to imbalance between glutamate and GABA neurotransmitters. Abnormal jerking movement, confusion, fatigue repetitive blinking are some common symptom soft epilepsy. While diagnostic test such as EEG, CT scan, PET scan, MRI and other treatment such ketogenic diet, vague nerve stimulation, help to many people o fall age who live with epilepsy. Today's several anti epileptic drugs are available such, carbamazepine, ethosuximide, Phenobarbital, may help to treat all types of epileptic seizures. So, there is need to continue research on it to treat all epileptic problems worldwide.

I. INTRODUCTION:-

Epilepsy is a chronic disorder of the brain that affects people worldwide. Epilepsy is a chronic noncommunicable disorder of the brain that affects people of all ages.

It is characterized by recurrent seizures, which are brief episodes of involuntary movement that may involve a part of the body (partial) or the entire body (generalized), and are sometimes accompanied by loss of consciousness. There are over 2.5million people diagnosed with epilepsy every year.

Epilepsy is one of 4th most common serious neurological disorder affecting about 65 million people globally. It affects 1% of the population by age 20 and 3% of the population by age 75. Nearly 80% of the people with epilepsy live in low and middle- income countries.

According to Epilepsy Foundation of America, he found that approximately 45,000 peoples are dead due to epilepsy. These timed proportion is between 4 to10 people/1000 is suffering from epilepsy.

During the 20th century, the invention of EEG, the advance in neurosurgery, the discovery of anti epileptic drugs, and the delineation of underlying pathophysiological mechanisms, were them significant advances in the field of research in epilepsy. Now a day's different antiepileptic drugs are available to treat seizure.

Definition

o Epilepsy is a disease due to central nervous system disorder which is characterized by seizures and convulsion or other abnormal body movements with loss ofconsciousness.

- A seizure is defined by release of excessive and uncontrolled electrical activity in the brain. **OR** it is hyper excitation of neurons in the brain leading to altered behavior with or without violent motor activity.

Types of epilepsy/seizures:-

Classification of seizures is as either focal or generalized, based on how the abnormal brain activity begins.

1) Focal/ partialseizures
   I. Simple focalseizures
   II. Dyscognitive focalseizures

2) Generalizedseizures
   I. Tonic-Clonic seizures/Convulsive seizures
   II. Absenceseizures
   III. Tonicseizures
   IV. Clonicseizures
   V. Atonicseizures
   VI. Myclonicseizures

1] Focal seizures:-

Focal seizures (previously called partial seizures) start in one part of the brain and affect he part of the body controlled by that part of the brain or generally produced in a small area of the brain (fig no1). The symptoms the person experiences will depend on the function that the focal point is

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associated with or controls.
Depending on where they start and which parts of the brain they involve, focal

Fig1: Represent focal seizure

Seizures may or may not alter consciousness or awareness;they can classified into two types.

1. Simple focalseizures:-

These seizures do not result in loss of consciousness. They may alter Emotion or change the way things look, smell, feel, taste or sound. They may also result in involuntary jerking of the body parts, such as an armor legs, and spontaneous sensory symptoms such as tingling, dizziness, and flashing lights.

2. Dyscognitive focal seizures:-

These seizures alter consciousness or awareness and may cause to lose awareness for a longer period of time. Dyscognitive focal seizures often result in starting and purposeless movements such as hand rubbing, chewing, swallowing, or walking in circles.

1) Generalizedseizures:-

- Seizures that appear to involve all areas of the brain are called generalized seizures. Generalized epilepsy, also known as primary generalized epilepsy or idiopathic epilepsy, is a form of epilepsy characterized by generalized seizures with no apparent cause
- Bite your cheek or tongue
- Lick your jaw
- Lose control of your bladder or bowels
- Turn blue in the face

Many generalized seizures start and spread so quickly it is impossible to identify the source. If the source of a seizure is unidentifiable, surgery is not available as a treatment option.

Generalized seizures follow a basic pattern. First, your muscles stiffen and become rigid. Then, you experience violent muscle contractions in which the muscles move in quick, random spasms.

Fig2:- Represent generalized seizures

You lose consciousness, or black out, so that you're no longer aware of what's happening. The different types of generalized seizures are

Tonic-clonic seizures:-

Tonic means stiffening, and clonic means rhythmical jerking Tonic–clonic seizures (formerly known as grandma seizures) are a type of generalized seizure that affects the entire brain. Atonic-clonic seizure usually begins on both sides of the brain, but can start in one side and spread to the whole brain.

Absence seizures:-

Most commonly seen children's. Absence seizures are characterized by a brief loss of awareness, impairment of consciousness, blank stare, brief up ward rotation of eyes. These type seizures from few second to half of minutes.

Tonic seizures:-

These are the type of generalized seizures which causes stiffening of muscles. This seizure usually affects the muscles of arms and legs and may cause to fall to the ground. These types of seizures usually last 1to3 minutes and take longer for a person to recover.

Clonic seizures:-

Clonic seizures reassociated with rhythmic, jerking muscles movements. These seizures usually affects the neck,face,and legs.

Atonic seizures:-

These are the type of generalized seizures which causes a loss of muscle control or tone, which may result in suddenly collapse or fallow. Atomic seizures can be begin in on eerier side of the brain (focal on set) or both sides of the brain (generalized onset). These seizures typically last less than 15second

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Myoclonic seizure:-

These are the type of generalized seizures usually appear as sudden brief jerks or twitches of arm and legs. During a my clonic seizure, the person is usually awake and able to think clearly. Myoclonic twitches or jerks usually are cause by sudden muscle contractions, called positive my clonus, or by muscle are laxation, called negative my clonus.

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Etiology / Causes:-

Many times the seizure are idiopathic in nature where exact cause is not found. It may varying peoples. Some people within clear cause of epilepsy, but may have a some following causes which are responsible for epilepsy.

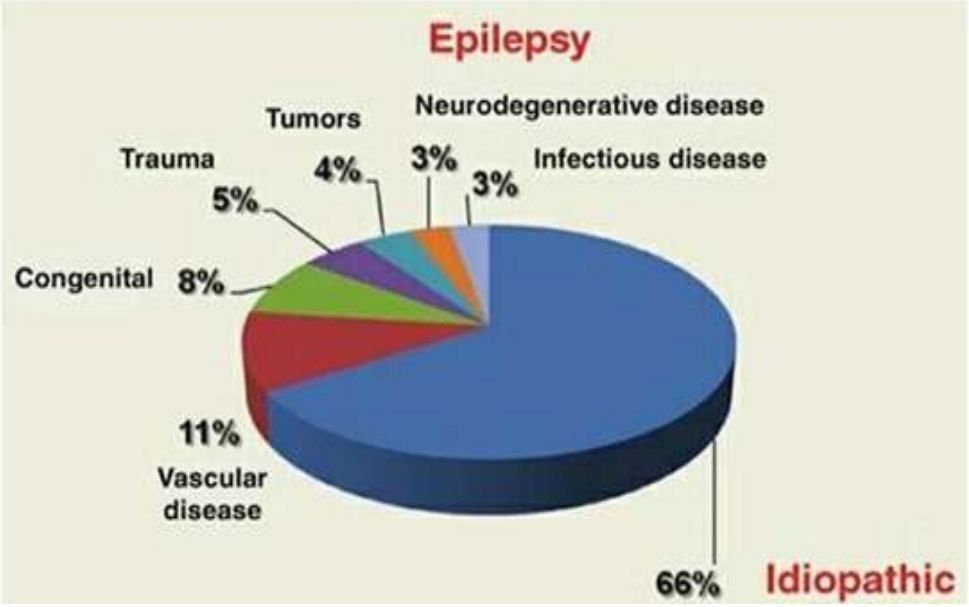

Fig3:-Etiological causes of epilepsy

Table no1: common causative factors for causing epilepsy

Genetics	Mitochondrial disorder, gene disorder
Metabolic Disorder	Alkalosis ,hyperparathyroidism, hypocalcemia, hyponatremia, hypoglycemia, uremia, fever, phenyl-ketonuria
CNS infection	Meningitis,encephalitis,neurosyphilis,toxoplasmosis.
Cardiovascular disorders	Hypertension,hypertensiveencephalopathy
Cerebral vascular disease	Hemorrhage, thrombosis, cysts, an Eyes is, migraine, hypoxia,stroke.

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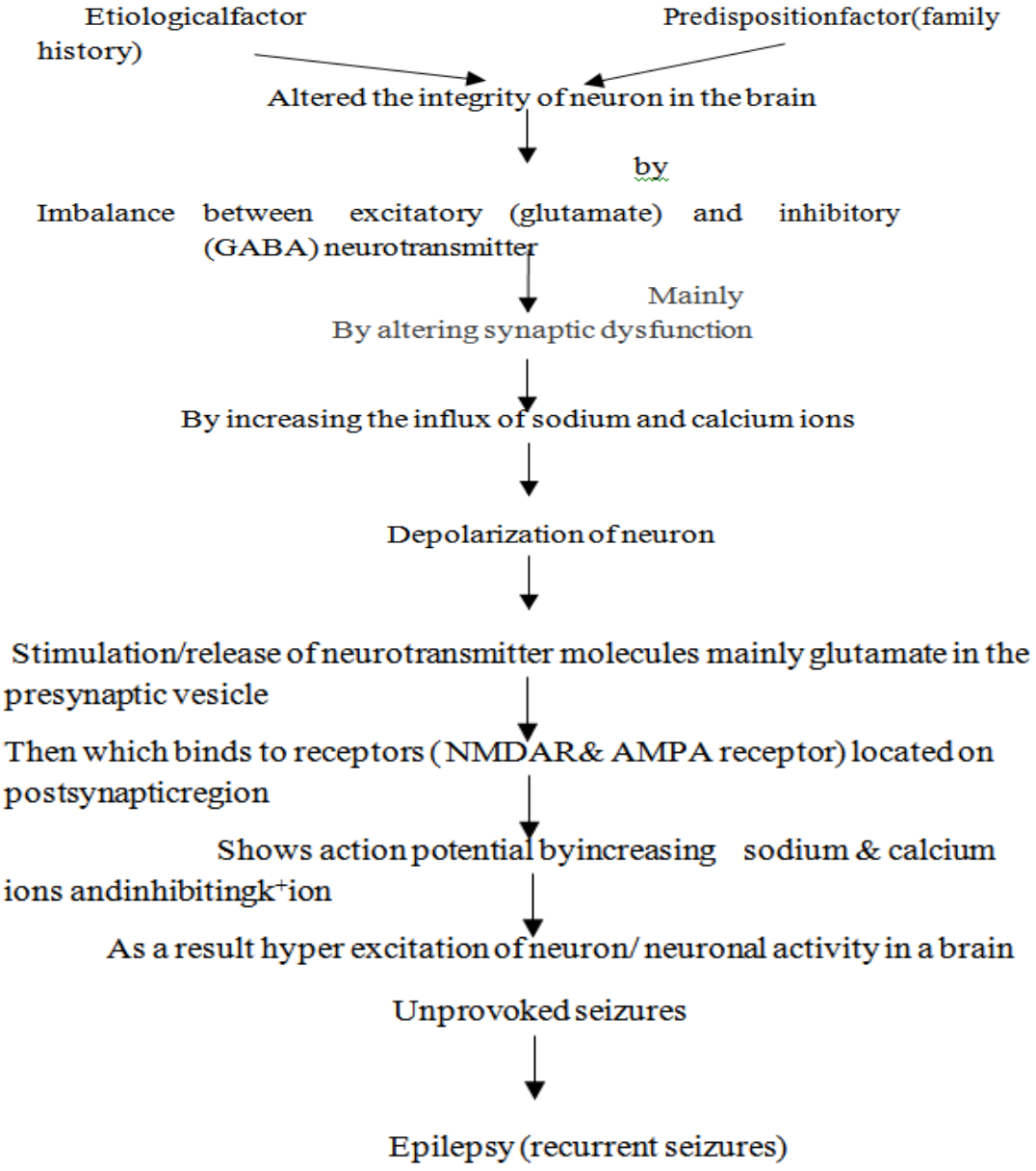
Degenerative diseases	Alzheimer's disease, multiples sclerosis.
Head injury	Trauma, increased intracranial pressure, birth trauma.
Drugs and chemicals	Amphetamines, camphor, epinephrine, carbon monoxide, amitriptyline, lead, lidocaine.
Miscellaneous	Hot water, physical and mental exertion, emotional stress, sleep deprivation, flickering lights

Pathogenesis of epilepsy:



Flow chart 1:- Pathogenesis of epilepsy

Pathogenesis of epilepsy So, currently, there is no universally

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accepted definition for epileptogenesis. The term epileptogenesis is defined as a process that leads to the occurrence of the first spontaneous seizure and recurring epileptic form events after the brain insult. OR Epileptogenesis is the process by which the previously normal brain is functionally altered and biased towards the generation of the abnormal electrical activity that sub serves chronic seizures. Latency period refers to seizure-free or pre-epileptic periods between the brain insult and the occurrence of the first spontaneousseizure.

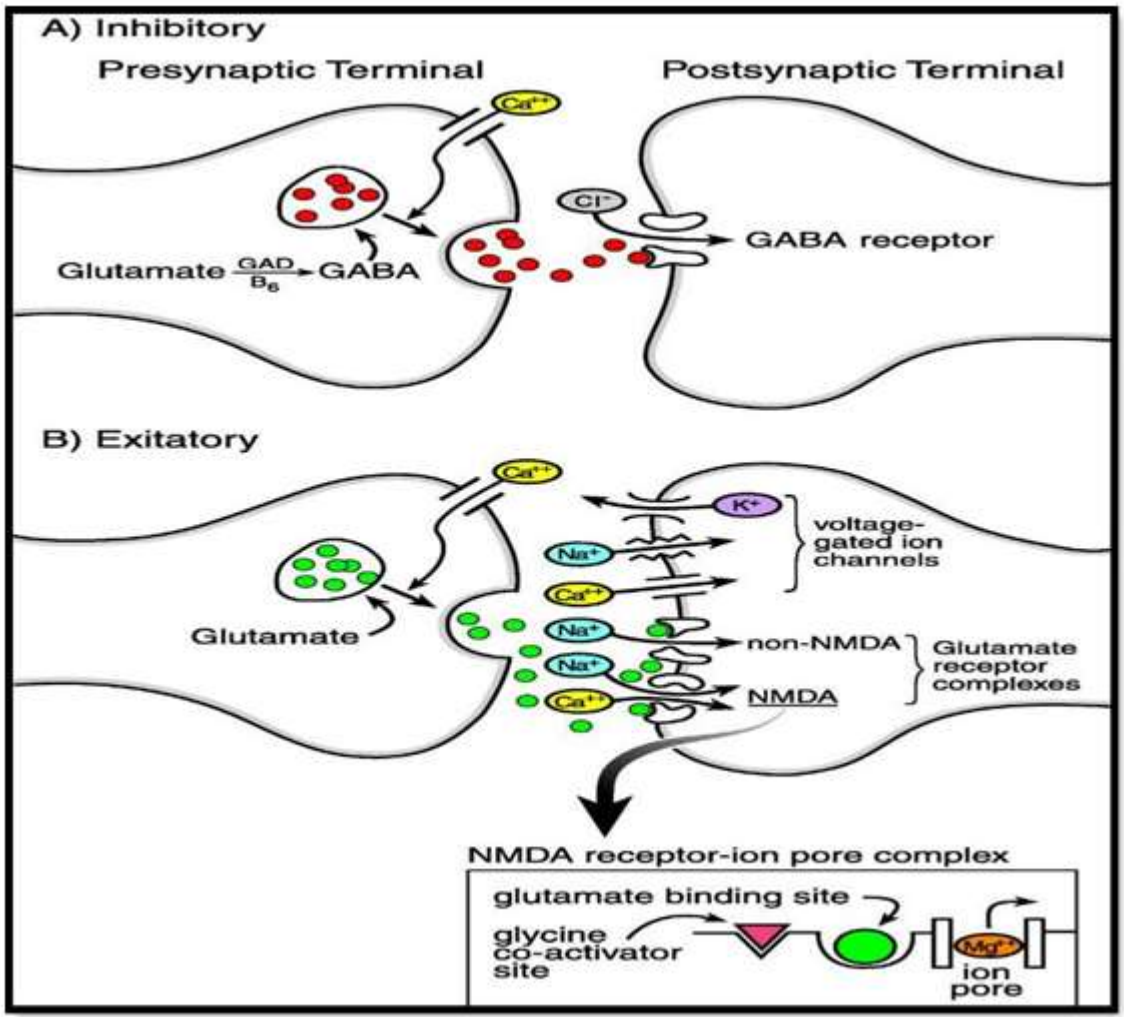

Fig4:-Excitatory and inhibitory neurotransmitter involved in Pathogenesis of epilepsy by binding to their specific receptor.

Sign and symptoms:-

Following signs and symptoms are observed, if patients suffering from epilepsy.

- Loss of consciousness or awareness
- Uncontrollable/involuntary jerking movements of arms and legs
- Visual hallucination
- Temporary confusion
- Alteration to sense of taste, smell, slight, hearing, and touch
- Performing repetitive movements
- Speech arrest, vocalizations
- Shaking
- Loss of bladder or bowel control
- Muscle stiffness, stiffening of body
- Episodes of staring
- Illusions
- Pupillary dilation/ eyerolling
- Repetitive movements of lips making and blinking
- Sometimes person goes in dreamy state
- Unusual fatigue

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- Headache, nausea, vomiting
- Rapid heart beats
- Sweating, excessive salivation
- Musclespasms.
- Repetitive blinking of eyelids
- Altered mood

Table no 2:-Different epileptic seizures shows different sign and symptoms, they classified as following.

Sr.No	Type	Symptoms
A	Partial/ focal seizures	Involuntary movement, unpleasant smell,taste,stiffeningoflimbs,alteredemotion, nauseaseizurelessthan2min
a	Simple partial seizures	Change in way of things, odd sound, smell, taste, dizziness, rising feeling in tummy, involuntary movements of body parts such as arms &legs, flashing lights.
b	Complex partial seizures	Loss of consciousness, picking at cloths, smacking your lips, hand rubbing, chewing, swallowing, walking in circles
B	Generalized seizures	Loss of consciousness or awareness, involuntary jerking movements of arms and legs, stiffening of body muscles, altered smell, taste, sound, seizures last less than 3 min.
a	Tonic-clonic seizures	Stiffening or rhythmical jerking movements of arms and legs, shaking, increase heartbeats, loss of consciousness, biting tongue, difficulty in breathing, loss of bladder
		control, lips may turn blue, seizures at least1-3min.
b	Absence seizures	Blank stare, brief loss of consciousness or awareness,repetitive blinking,seizures at least
		few sec to half of min.
c	Tonic seizures	Stiffening of muscles may cause to fall down, seizures at least 1-3min.
d	Clonic seizures	Mainly affect on neck, face or legs.
e	Atonic seizures	Loss of muscle control or tone, results collapse or fall down, droop attack, seizures less than 15sec.
f	Myoclonic seizures	Sudden brief jerks or twitches of arms and legs, muscles contraction.

Diagnosis of epilepsy:- Epilepsy can be diagnosed by performing different

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test, they are given below. Your doctor may order several tests to diagnose epilepsy and determine the cause of seizures, they are given below

1) Neurological examination
2) Electrons holograms (EEG)test
3) Computerized axial tomography (CT scan CAT scan)
4) Magnetic reason once imaging (MRI scan)
5) Functional magnetic resonance imaging(f MRI scan)
6) Positron emission tomography (PETscan)
7) Complete blood count (CBC)test
8) Chemistrypanel
9) Spinal taptest
10) Single photo emission computerized tomography (SPECT scan)
11) Magnetic resonances spectroscopy (MRS scan)

Complications:-

Epileptic seizures create many complications, sometimes it is dangerous to human beings, they are given below.

1) Injuries andaccidents:-

Injuries from falls:-Because many people with seizures fall, injuries are common. Although such injuries are usually minor, people with epilepsy have a higher incidence of fractures than those without the disorder. Patients who take the drug phenytoin have an even higher risk, since the drug can cause osteoporosis.

House hold accidents:-House hold environments, such as the kitchen and bathroom can be dangerous places for children with epilepsy. Parents should take precautions to prevent burning accidents from stoves and other heat sources. Children with epilepsy should never be left alone when bathing.

Driving and the risk for accidents:-Being unable to drive is an extremely distressing and severe component of epilepsy. Drivers with well-controlled epilepsy are not at a high run acceptable risk for automobile accidents. Uncontrolled epilepsy, however, poses a high risk. Needless to say, seizures can be very dangerous if they occur while après on is driving and result in injuries to the patient or others. **Accidents while swimming**:-Swimming poses another danger for people with epilepsy, particularly those with tonic seizures, which can cause the diaphragm to expel air quite suddenly. People with epilepsy who swim should avoid deep and cloudy water (a clear swimming pool is best), and always swim with acknowledgeable, competent, and experienced companion or have a life guard on site.

2] Status epileptics:-

Status epileptics is a medical emergency in which seizures recur without the patient regaining consciousness between events. This condition can develop in any type of seizure but is most common in tonic-clonic seizures. Status epileptics may cause brain damage or cognitive dyes' function and may be fatal. Subsequent seizures become briefer; more localized, and may be reduced to my o clonic activity.

2) Sudden Unexplained Death in Epilepsy (SUDEP):-

Sudden unexplained death in epilepsy (SUDEP) occurs in a small percentage of persons with epilepsy. For reasons that are poorly understood, an otherwise. Healthy person with epilepsy can die suddenly. Which is also happens within the general population, persons with symptomatic epilepsy have a much greater risk. Autopsies have not uncovered a physical cause of SUDEP. It is possible that pulmonary edema (fluid build- up in the lungs), suffocation, or cardiac arrhythmias (irregular heart beat) may be responsible. Some people appear to be at a higher risk than others, such as young adults with generalized tonic-clonic seizures that are not fully controlled with medication and those who abuse alcohol and illicit drugs. Patients using two or more anticonvulsants may be at increased risk for sudip.

3) Effect of epilepsy on children's:-

- **Long-term general effects**:-In general, the long-term effects of seizures vary widely depending on the seizure's cause. The long-term outlook for children with idiopathic epilepsy (epilepsy of unknown causes) is very favorable.

Children whose epilepsy is a result of a specific condition (for example, a head injury or neurologic disorder) have higher mortality rates than the normal population, but their lower survival rates are most often due to the underlying condition, not the epilepsy itself.

- **Effect on memory and learning:-**The studies on the effects of seizures on memory and learning vary widely and depend on many factors. In general, the earlier a child has seizures and the more extensive the area of the brain affected, the poorer the outcome. Children with seizures that are not well-controlled are at higher risk for intellectual decline.
- **Social and Behavioral Consequences**:-

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Learning and language problems, and emotional and behavioral disorders, can occur in some children. Whether these problems are caused by the seizure disorder and anti- seizure medications or are simply part of the seizure disorder remains unclear.

4) Effect of epilepsy in adults:-

Psychological Health:-Many adults with epilepsy show signs of depression .People with epilepsy have a high risk for suicide, particularly in the first 6 months following diagnosis. The risk for suicide is highest among people who have epilepsy and an accompanying psychiatric condition such as depression, anxiety disorder, schizophrenia, or chronic alcohol use. Antiepileptic drugs (such as carbamazepine, gabapentin, to piramate, valproate, and many others) can increase the risk of suicidal thoughts and behavior.

- **Overall Health**.

Patients with epilepsy of ten describe their overall health as "fair "or" poor, "compared to those who do not have epilepsy. People with epilepsy also report a higher frequency of pain, depression, anxiety, and sleep problems. In fact, their overall health state is comparable to people with other chronic diseases, including arthritis, heart problems, diabetes, and cancer. Treatment scan cause considerable physical effects, such as osteoporosis and weight changes.

5) EFFECT ON SEXUAL AND REPRODUCTIVE HEALTH

- **Effects on Sexual Function**. Some patients with epilepsy experience sexual disturbances, including erectile dysfunction. Causes of these problems may be emotional; medications induced, or are salt of changes in hormone levels.
- **Effects on Reproductive Health**. A woman's hormonal fluctuation can affect the course of her seizures. Estrogen appears to increase seizure activity, and progesterone. Anti seizure medications may reduce the effectiveness of oral contraceptives. Epilepsy can pose risks both to a pregnant woman and her fetus. Some types of anti-epileptic drugs should not be taken during the first trimester as they can cause birth defects. Women with epilepsy who are thinking of becoming pregnant should talk to their doctors in advance to plan changes in their medication regimen. Women should learn about the risks associated with epilepsy and pregnancy, and precautions that can be taken to reduce them.

6) Effects of epilepsy on pregnant women:-

If the pregnant women suffering from tonic-clonic seizure, there is a temporary interruption of breathing; although this interruption rarely affects the mother, it can lead to oxygen deprivation in your baby. Additionally your baby's heart rate can slow for as long as 30 minutes after a tonic-clonic seizure. This form of seizure also increases the risk of trauma to the baby. Tonic-clonic seizures present the greatest risk during the last trimester, when the baby's brain is larger and needs more oxygen. Epilepsy can affect pregnancy in a verity of ways. If seizures occur during pregnancy, a number of complications can occur affecting the baby including:

- Fetal heart rate deceleration Fetal injury
- Premature separation of the placenta a from the uterus
- Miscarriage due to trauma experienced during seizures
- Preterm labor
- Premature birth

Anticonvulsant drugs:

Epileptic women have a 4-6 % chance of having a baby born with a birth defect as a result of taking anticonvulsant drugs. Some are mild defects such as small fingers and toenails. However, there are more major birth defects such as spinal bifida, cleft lip, neural tube defects, and heart abnormalities. You should consult your doctor about your anticonvulsant medication when trying to become pregnant. They may recommend changing your medication or lowering the dosage of your current medication.

Non-pharmacological treatment:-

Different non pharmacological treatment available to control epileptic seizures or also treat them.

1) **Ketogenic diet:-**

The ketogenic diet is a special high-fat, low-carbohydrate diet that helps to control seizures in some people with epilepsy. It is prescribed by a physician and carefully monitored by a dietitian. It is more strict, with calorie, fluid, and protein measurement and occasional restriction than the modified Atkins diet, which is also used today.

2) **Vagus nerve stimulation:-**

Vagus nerve stimulation (VNS) is designed to

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prevent seizures by sending regular, mild pulses of electrical energy to the brain via the vagus nerve. These pulses are supplied by a device something like a pacemaker.

***3)* Ayurvedic treatment for epilepsy:**

In Ayurveda Epilepsy is known as A pasmara and the epileptic attacks are known as Akshpaka.

There are some herbs that are used in treatment of epilepsy. These are as following:

***a)* Brahmi (Bacopamonnieri):-**

- It nourishes brain and helps in bringing coordination between nervous system and dailyactivity.
- It acts as braintonic.
- It is also help full in treatment of epilepsy, insomnia
- It is helpful in all type of mood disorders. It is also helpful in relieving anxiety, stress and mental fatigue

***b)* Ashwagandha (Withaniasomnifera):-**

- It is best anxiolytic herb in Ayurveda.
- It manages stress andanxiety.
- It is nerve tonic,it has claiming effect on nerves.
- It is very beneficial for the nervous system.
- This herb possesses anti-inflammatory, anti-stress, immune modulatory, anti oxidant properties.
- It is use full in increase mental and physical performance.

***b)* Jatamansi (Nardo stachysja tamansi):-**

- It is CNSrelaxant.
- It is best her b with tranquillizing effect on brain.

***c)* Tagar (Valerianawallichii):-**

- It helps to calming down nervous system.
- It help store live stress, depression and anxiety which are the underlying causes of epilepsy**.**

***d)* Shankhpushpi (Convolvuluspluricaulis):-**

- It has mild anti-epileptic/anticonvulsant property.
- It help to reduce stress, depression, anxiety, dementia which are underlying causes of epilepsy.

***4)* Others:**

***a)* Asan**

***b)* Yoga**

Animal models of epilepsy: use and limitations

Chemoconvulsants:

Rodents with spontaneous recurrent seizures have been generated by using chemoconvulsants, primarily pilocarpine and kainic acid.3 Usually, these models intend to mimic TLE, and therefore rodents must display a similar "clinical history" as the human counterpart, including an initial precipitant injury afflicting the hippocampus and/or the temporal lobe (e.g., status epilepticus [SE]), a latent period between the injury and the occurrence of spontaneous seizures, chronic manifestation of spontaneous seizures (usually partial and tonic-clonic seizures), and histopathological changes deemed characteristic of TLE.2,4,5 Unfortunately, animal models of chronic epilepsy are not widely used because of time constraints and costs.

Kainic acid was one of the first compounds used to model TLE in rodents.6 It is an L-glutamate analog, the systemic or intracerebral administration of which causes neuronal depolarization and seizures, preferentially targeting the hippocampus.7 Injected rodents show recurrent seizures, usually secondarily generalized and of variable frequency, with remarkable histopathological correlates of hippocampal sclerosis.8 Kainic acid has the advantage of causing habitually hippocampus-restricted injuries, unlike pilocarpine, which can also produce lesions in neocortical areas.6 Nevertheless, extrahippocampal areas are also significantly compromised in human TLE,9 making pilocarpine another useful chemoconvulsant.

Pilocarpine is a muscarinic acetylcholine receptor agonist. Systemic or intracerebral injection of pilocarpine causes seizures that build up into a limbic SE.10,11 Structural damages and subsequent development of spontaneous recurrent seizures resemble those of human complex partial seizures.12 In fact, antiepileptic drugs (AEDs) that are effective against complex partial seizures in humans can also halt spontaneous seizures in the pilocarpine model.13

In addition, there are several network and neurochemical similarities between human TLE and the pilocarpine model. For instance, the subiculum can generate interictal activity in both the human TLE14 and the pilocarpine model.15 Neurotrophins are upregulated in the hippocampus of mesial TLE patients,16 as well as in the hippocampus and neocortex of pilocarpine-treated rats.17 Cognitive and memory deficits commonly found in TLE patients18,19 are also present in pilocarpine-injected rats.20,21

Other compounds such as pentylenetetrazol (PTZ), strychnine, N-methyl-D,L- aspartate, tetanus toxin, and penicillin are widely used as acute seizure models, and not as

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animal models of epilepsy. The difference is that seizure models may be useful for rapid screening of AED action, but they do not necessarily result in chronic epilepsy, with the exception of tetanus toxin,22 and probably of repeated penicillin injections.23 Crude extract of the star fruit and its active compound caramboxin are also potent chemoconvulsants and are capable of inducing SE,24 but it remains to be described whether they also result in later spontaneous recurrent seizures, as in chronic models. Compounds that trigger seizures can be used on testing different AEDs that would act on different seizure types. For instance, strychnine and N-methyl-D,L-aspartate produce generalized tonic-clonic seizures, as well as PTZ nonconvulsive absence or myoclonic seizures.25 Ethosuximide, trimethadione, valproate, and other clinically efficacious drugs have been discovered by using seizure models.26 However, drugs such as levetiracetam, vigabatrin, and tiagabine, which act on mechanisms other than sodium channel blockade, were discovered in models that predict drug efficacy against partial seizures27 (eg, those seen in chronic TLE models or full electrical kindling).

Chemoconvulsants in the immature brain:

SE has a special propensity to develop in the immature brain, with about 50% of the cases occurring in children younger than 2 years old.5,28 Clinical studies point out that 13%–74% of children who suffered a convulsive SE developed epilepsy.29 Furthermore, SE during development is often associated with hippocampal injury and mesial temporal sclerosis, as well neurological, cognitive, and behavioral impairments. Thus, animal models of SE are important for investigating whether SE can result in maladaptive neuronal reorganization, epileptogenesis, and cognitive impairment.30

SE in the developing brain is modeled in immature rodents (younger than 21 postnatal days [<P21]) mainly by kainic acid and pilocarpine administration. Administration protocol is similar to that used in adult rodents, except that young ones have enhanced susceptibility to seizure induction, thus requiring smaller doses.31,32 In both models, seizure manifestation becomes more evident with age progression.31 In addition, kainic acid excitotoxicity is higher in older animals,33 as are severity and duration of SE.30 In rats older than P7, SE induced by pilocarpine or kainic acid ceases exploratory activity, and animals develop scratching, body tremors, chewing, clonic movements of the forelimbs, and head bobbing before progressing into tonic and clonic activity.

Electrical stimulation:

Animal models of seizures induced byelectrical stimulation convey the advantage of reproducing epileptogenic features in the intact brain with low mortality and high reproducibility. Moreover, unlike chemical-induced seizures, postictal alterations from electrical stimulation can be investigated when the epileptogenic cause is no longer present. However, seizure modeling by electrical stimulation does not provide cell-type specificity in the brain. In addition, stimulation protocols can be costly and laborious when used for chronic studies **Electroshock-induced seizures:**

Electroshock-induced seizures (ES) are among the most studied models of electrical stimulation. Electroshock is conveniently applied a single time and does not require the stereotaxic implant of electrodes.

It involves whole-brain stimulation protocols (e.g., 6 Hz in mice and 50–60 Hz in rats) and may be divided into minimal ES and maximal ES.

Minimal ES are a putative model of myoclonic seizures and can be induced with current stimulation through corneal electrodes. In this case, the epileptiform activity is usually more prominent in the forebrain and is associated with minimal clonic behavioral seizures.47 Minimal ES may become generalized if stimulation intensity is increased.48 In turn, maximal ES induction has been useful when modeling generalized tonic-clonic seizures. It is mostly associated with hindbrain seizures and can be generated by auricular stimulation at threshold current intensities.49 Maximal ES and PTZ seizure models have been largely employed for AED screening. However, AEDs that protect against partial and non convulsive seizures in epileptic patients failed to do so in the maximal ES and PTZ models, respectively.

Kindling:

- At this time, kindling is the most studied model of electrical stimulation. Kindling refers to a seizure-induced plasticity phenomenon that occurs when repeated AD induction by electrical stimulation in a specific brain region evokes a progressive enhancement of seizure susceptibility.
- Ultimately, it culminates in emergence of spontaneous seizures and the establishment of a permanent epileptic state.65 Initially, behavioral alterations during ADs resemble

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partial seizures (classes 1–3),66 which evolve into secondary generalization (classes 4–5).

- Although a fully kindled state is established after 90–100 class 5 seizures,68 it is also possible to induce spontaneous behavioral seizures and focal hippocampal injury by milder protocols, as demonstrate…

Brain pathology:

- The developing human brain is at higher risk of developing seizures, particularly during the first month of life.
- In addition to possible insults associated with the birthing process, the immature brain has a predominance of excitation over inhibition, which, on the one hand, is important for synaptogenesis but, on the other hand, increases seizure susceptibility.
- Animal models of seizures in the developing brain provide a unique opportunity to study this enhanced excitability during development. The main question is whether seizures in this critical period disturb neuronal circuit development and whether such disturbances promote epileptogenesis and cognitive deficits later in life

Antiepileptic drugs:

- Antiepileptic (also commonly known as Anticonvulsant drugs or as Anti seizure drugs) are a diverse group of pharmacological agents used in the treatment of epileptic seizures.
- Anticonvulsants are also increasingly being used in the treatment of bipolar disorder and borderline personality disorder, since many seem to act as mood stabilizers, and for the treatment of neuropathic pain.
- Anticonvulsants suppress the excessive rapid firing of neurons during seizures. Anticonvulsants also prevent the spread of the seizure within the brain. Anti epileptic drugs may block sodium channels or enhance γ-aminobutyric acid (GABA) function.
- Antiepileptic drugs reduce the release of excitatory glutamate, whose release is considered to be elevated in epilepsy, they also act on voltage gated calcium channel.

Classification of antiepileptic drug:-

Anticonvulsant drug may be classified according to their chemical structure, they are given below.

- Barbiturate: Eg: phenobarbital, mephobarbital, pentobarbital
- Benzodiazepine: Eg: diazepam, clonazepam, nitrazepam
- Hydantoin:-Eg:phenytoin,ethotoin, mephenytoin.
- Succinimide:-Eg:ethosuximide, phensuximide, methsuximide.
- Oxazlidinedione:Eg:trimethadione,paramethadione.
- Iminostilbine:- Eg: carbamazepine
- Valproic acid derivative:- Eg: Valproic acid, valproate sodium, divalproex sodium.
- Chemically unrelated anticonvulsant:-Eg: acetazolamide, primidone.

Phenytoin:

Phenytoin (diphenylhydantoin) is a hydantoin compound related to the barbiturates that are used for the treatment of seizures. It is an effective anticonvulsant for the chronic treatment of tonic-clonic (grand mal) or partial seizures and the acute treatment of generalized status epilepticus.

MOA:

phenytoin binds to a voltage-dependent sodium channel and prevent the high frequency repetitive firing of action potential. This can be done by prolong inactivation state of sodium channel. Each sodium channel dynamically exists in the following 3 states:

- A resting state, during which the channel allows passage of sodium into the cell
- An active state, in which the channel allows increased influx of sodium into the cell
- An inactive state, in which the channel does not allow into the cell passage of sodium

Phenytoin that target the sodium channels prevent the return of these channels to the active state by stabilizing them in the inactive state so, they prevent repetitive firing of the neuron.

Uses:

Highly effective in

- Tonic-clonic seizures
- Partial seizures (simple, complex)
- Status epilepticus
- Arrhythmia
- Trigeminal neurological
- Common phenytoin side effects may include:
- dizziness, drowsiness, confusion, nervousness
- nausea, vomiting, constipation;
- tremors, slurred speech, loss of balance or co-ordination
- prorate, trimethadione.

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Vigabatrin:

- Vigabatrin is an antiepileptic drug that inhibits the breakdown of γ- aminobutyric acid (GABA) by acting as a suicide inhibitor of the enzyme GABA transaminase (GABA-T).
- OR vigabatrin prevent the catabolism of GABA by irreversibly inhibiting the enzyme GABA transaminase, but does not bind to a receptor.
- vigabatrin inhibit GABA transaminase enzymes and prevent the conversion of GABA to succinic semialdehyde .

Use:

It is used for treatment of adult refractory Complex partial seizure. Good first choice for infantile spasm from tuberous sclerosis.

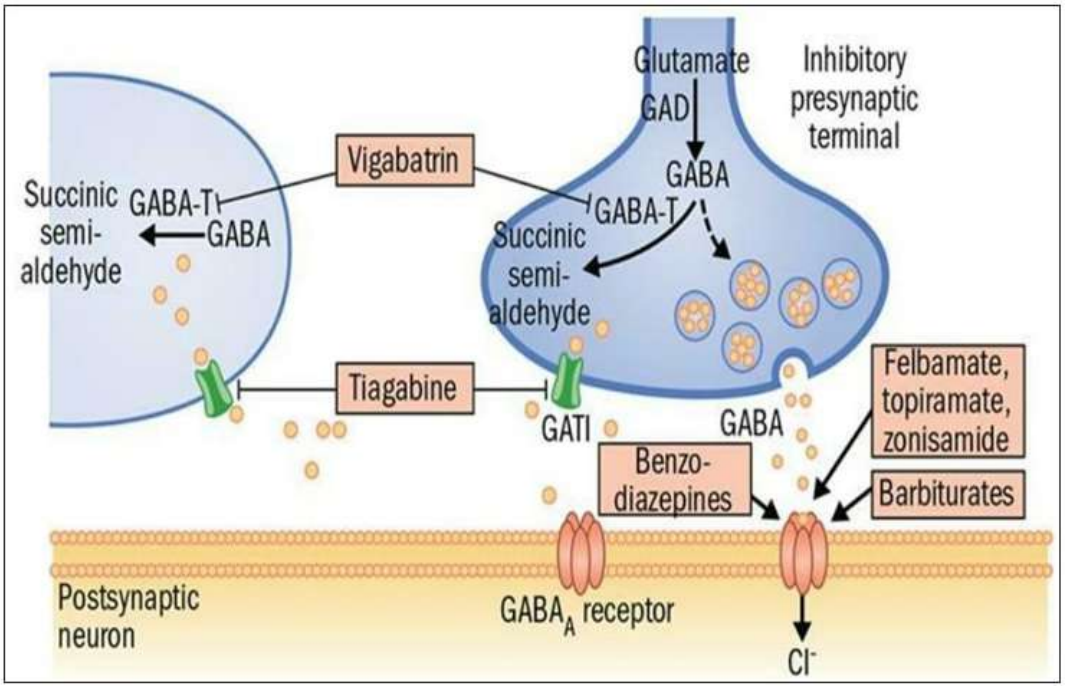

Fig5: vigabatrin inhibit GABA transaminase enzymes and prevent the conversion of GABA to succinic semialdehyde .

Side effects

Central nervous system: headache, dizziness, nervousness, memory disturbance, in so mania, confusion.

Gastrointestinal tract: headache nausea abdominal pain constipati

II. CONCLUSION:-

The treatment of epilepsy has been transformed since the serendipitous discovery of Phenobarbital in1912, both in the spectrum of medication available and improved knowledge of how best to use AEDs.

Improving access to special is t information, as provided by the PwSI epilepsy service in primary care, encouraging adherence to medication combined with a rational combination of AED and concomitant medication, minimizing side- effects and addressing any modifiable risk factors and addressing psychosocial issues can serve to optimize care for the patients with epilepsy.

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