EPILEPSY:

المحاضر: أ.د. احمد هاشم عبد الغفور

Epilepsy is a brain disorder in which clusters of nerve cells, or neurons, in the brain can misfire. This in turn can lead to unusual sensations, emotions and behaviors; it can also cause convulsions, muscle spasms and loss of consciousness..

Seizures and epilepsy are not synonymous.

A seizure (convulsion) is defined as a paroxysmal involuntary discharge of cortical neurons that may be manifested clinically by an impairment or loss of consciousness, abnormal motor activity, behavioral and emotional abnormalities, sensory disturbances, or autonomic dysfunction. Some seizures are characterized by abnormal movements without loss of consciousness.

The term epilepsy refers to spontaneous recurrent seizures unrelated to fever. In other words, a patient who has a single nonfebrile seizure that does not recur over time would not merit the diagnosis of epilepsy. The ages of greatest risk for nonfebrile seizures are during infancy, childhood, and adolescence.

Nonepileptic Seizures

A seizure that looks like an epileptic seizure, but is **not** caused by an electrical change in the brain is called a nonepileptic seizure. According to the Epilepsy Foundation (EF), nonepileptic seizures often resemble epileptic seizures both in the way they look and in the way the person having the seizure feels. EF says sometimes even trained medical professionals who are witnessing the seizure cannot tell the difference between an epileptic and nonepileptic episode.

There are two types of nonepileptic seizures. According to EF, they are:

- physiologic
- psychogenic

A physiologic nonepileptic seizure may be caused by a number of conditions that can trigger seizures. According to EF, they include:

- changes in heart rhythm
- sudden drops in blood pressure
- very low blood sugar
- sleep disorders
- movement disorders
- vascular lesions

A psychogenic nonepileptic seizure appears to be caused by emotional trauma or excessive stress. (Read about "Stress")

Febrile Seizures

Convulsions brought on by a high fever in small children are called febrile seizures. According to NINDS, a child experiencing a febrile seizure will often lose consciousness, shake, move limbs, become rigid or twitch. Most febrile seizures last just a minute or two, but they can be shorter and longer than that. NINDS says that approximately one in 25 children will have at least one febrile seizure, and many of them will have more before they turn 5 years of age. Febrile seizures usually occur in children between 6 months and 5 years.

There are a few factors that can increase a child's risk for having recurrent febrile seizures. According to NINDS, they include:

- having the first seizure before 15 months of age
- frequent fevers
- having an immediate family member with a history of febrile seizures
- having a seizure shortly after a fever has started or when the temperature is low

Although febrile seizures may look frightening, NINDS says it is unlikely the child will be injured. According to NINDS, there is no evidence that this type of seizure causes brain damage. Here are some things a parent can do, according to NINDS that can help prevent injury or possible choking.

- remain calm
- place child on a protected surface, like the floor
- do not restrain the child during convulsion
- place child on stomach to prevent choking
- remove all items in the child's path
- never place anything in the child's mouth

NINDS also recommends that the child be taken to a doctor for evaluation as soon as possible, especially if he or she shows signs of a stiff neck, lethargy or vomiting.

Nonfebrile Seizures

Seizures that occur without a fever are called nonfebrile seizures. They are not uncommon, according to the American Academy of Pediatrics (AAP). Most nonfebrile seizures are a one-time event. AAP says they may be caused by a temporary interruption in normal brain functioning. If the seizures are recurrent, they may be epileptic seizures and could be a chronic problem.

AAP recommends that if your child has two or more seizures you should talk to your doctor. Tests can be performed to determine if epilepsy is present.

Partial or Focal Seizures

Partial or focal seizures occur in just one part of the brain. According to NINDS, about 60 percent of all people with epilepsy suffer from focal seizures. (Read about "Epilepsy") There are two types of focal seizures, simple and complex.

In a simple focal seizure, the person will remain conscious, but may experience a number of feelings like joy, anger or sadness. The senses may also be affected. According to NINDS the person may see, smell, taste, hear, or feel things that aren't even there.

In a complex focal seizure, there is a change in or loss of consciousness. People having such a seizure may act strangely. They may blink, twitch or even walk in circles. These seizures usually last just a few seconds.

Generalized Seizures

A generalized seizure is caused by abnormal neuronal activity on both sides of the brain. It may result in a number of physical symptoms like falls, muscle spasms and loss of consciousness. NINDS lists several types of generalized seizures and their symptoms. They include:

- absence seizure: staring and jerking or twitching muscles
- tonic seizures: stiffening of muscles in the back, legs and arms
- clonic seizures: repeated movement of the upper body, arms or legs
- atonic seizures: loss of normal muscle tone

- tonic-clonic seizures: stiffening of the body, repeated jerking of limbs, and loss of consciousness

ETIOLOGY of Epilepsy:

Congenital defects

Head injuries

Trauma

Hypoxia

Infections

Brain tumor

Drug withdrawal

Fever in children (febrile convulsion)

Hypoglycemia

Photo seizure due to watching TV

CLASSIFICATION of Epilepsy:

Partial seizures

a) Simple (Jacksonian)

b) Complex (Psychomotor)

Generalized seizures

a) Tonic-Clonic (Grand mal)

b) Tonic

c) Clonic

d) Atonic

e) Myoclonic

f) Absence (Petit mal)

g) Status epilepticus

h) Febrile

Diagnosis and treatment options

Other conditions may be confused with seizures and/or epilepsy, such as syncope and stroke .Therefore, if you are experiencing seizures , it's important to get an accurate diagnosis. Diagnosis can include a number of tests such as electroencephalography (EEG), which is a recording of your brain-wave activity. (Read about "EEG - Electroencephalograph") CT, MRI and PET can also be used. (Read about "CT Scan - Computerized Tomography" "MRI - Magnetic Resonance Imaging" "PET - Positron Emission Tomography")

— Diagnosing seizures can be done through special monitoring. EF says an electroencephalogram or EEG (Read about "EEG - Electroencephalograph") can test brain waves during an actual seizure. According to EF, it's the most accurate way to diagnose nonepileptic seizures. Certain blood tests (Read about "Laboratory Testing") may also help in determining whether the episode is epileptic or nonepileptic. Once the data is thoroughly evaluated, experts can work on a treatment plan. Medication and/or counseling are just some of the ways that may help eliminate these episodes. EF says the outcome of treatment is usually better than for that of people with epilepsy.

EEG AND NEUROIMAGING STUDIES

The EEG is a useful adjunct to the history and physical examination in establishing the diagnosis of epilepsy, but a routine interictal (between seizures) EEG will show an epileptiform abnormality in only approximately 60% of patients. EEG abnormalities are more likely to be recorded in the infant or child who has epilepsy than in the adolescent or adult who has epilepsy. Various procedures are employed during the EEG in an attempt to activate a seizure discharge in a child suspected of having epilepsy, including eye closure, hyperventilation, photic stimulation, and in specific circumstances, sleep deprivation and special electrode placement (eg, zygomatic leads).

—**Treatment for seizures:**

—Treatment for seizures depends upon the type of seizure the person is having. Sometimes, a person may have one seizure and never have another. In some cases of nonepileptic seizures, professional counseling

may be all the patient needs. If seizures continue to happen, anticonvulsant medications may be necessary. The specific medication used depends on the person's age, type of seizure and side effects. For some patients, a special diet called the ketogenic diet (low in carbohydrates and high in protein) may be indicated. Other treatment options include surgery and vagus nerve stimulation (in which small pulses of energy are sent to the brain from the vagus nerve in the neck). It's important that all treatment options be discussed with the patient's physician.

General rules for treatment of epilepsy

Accurate diagnosis

Antiepileptic drugs are given when two or more attacks occurred in short time (6 months)

Antiepileptic drugs are given to suppress not to cure the attacks,

Monotherapy is preferred

Drugs are usually given orally

Monitoring plasma drug level is useful ,but not a routine.

Avoid sudden withdrawal (causing status epilepticus)

Treatment must not be for life , most patients can be relieved within few years.

Withdrawal started :

more years from the last fit. After seizure –free period of 2-3 or

Normal neurological examination

Normal EEG

Antiepileptic Drugs

Phenobarbital

Phenobarbital, also known as **phenobarbitone** or **phenobarb**, is a medication recommended by the World Health Organization for the treatment of certain types of epilepsy in developing countries. In the

developed world it is commonly used to treat seizures in young children, while other medications are generally used in older children and adults. It may be used intravenously, injected into a muscle, or taken by mouth. The injectable form may be used to treat status epilepticus. Phenobarbital is occasionally used to treat trouble sleeping, anxiety, drug withdrawal, and to help with surgery. It usually begins working within five minutes when used intravenously and half an hour when administered orally. Its effects last for between four hours and two days.

Side effects include a decreased level of consciousness along with a decreased effort to breathe. There is concern about both abuse and withdrawal following long term use. It may also increase the risk of suicide. It is pregnancy category B or D in the United States and category D in Australia, meaning that it may cause harm when taken by pregnant women. If used during breastfeeding it may result in drowsiness in the baby. A lower dose is recommended in those with poor liver or kidney function, as well as elderly people. Phenobarbital is a barbiturate that works by increasing the activity of the inhibitory neurotransmitter GABA.

PHENYTOIN

Well absorbed orally, available in two forms rapid-release & extended - release

Highly bound to plasma proteins

Plasma half-life (20 hrs).

Metabolized in liver to inactive metabolites.

Enzyme inducer

Excreted in urine

MECHANISM OF ACTION

Blocks sodium channels & inhibit the generation of repetitive action potentials.

Enhancement of responses to GABA system & reduce the glutamate activity.

CLINICAL USES

Effective in generalized tonic-clonic & partial seizures (simple & complex) , status epilepticus.

Not effective in absence seizures.

ADVERSE EFFECTS

Dose related :

Diplopia , ataxia , nystagmus.

Sedation

Non –dose related

Gingival hyperplasia

Hirsutism , coarsened facial features.

Osteomalacia

Hypersensitivity reactions

Hyperglycemia &glycosuria.

Hepatitis (rare)

Teratogenic effect (cleft lip, cleft palate

Bleeding disorders in infants

Megaloblastic anemia (low folate level)

DRUG INTERACTIONS

Drugs that affect phenytoin metabolism (enzyme inducers or inhibitors)

Phenytoin increase the metabolism of other drugs by inducing P450 e.g. oral contraceptive & **Warfarin .**

CARBAMAZEPINE

Related to antidepressant drugs (TCA).

Given only orally.

Highly bound to plasma proteins

Potent enzyme inducer , including its own metabolism (its plasma half-life decrease with chronic use).

Completely metabolized , one of metabolites has anticonvulsant activity

Slow-release preparations can be used.

Excreted in urine .

MECHANISM OF ACTION

Blocks sodium channels, so inhibiting the generation of repetitive action potentials in the epileptic focus & prevent its spread .

Potentiates the action of GABA.

CLINICAL USES

Drug of choice for partial seizures (simple & complex type.

Used in generalized tonic-clonic seizures

Can be used with phenytoin in patients who are difficult to control

(It is not sedative in its usual therapeutic range)

ADVERSE EFFECTS

DOSE RELATED :

Hyponatremia &Water intoxication

GIT upset

Diplopia & ataxia

NON-DOSE RELATED

Blood dyscrasias (leucopenia, aplastic anemia)

Hepatotoxicity

PRECAUTIONS

Frequent blood & liver function tests are recommended.

Teratogenic effect (less than other antiepileptic drugs)

Avoid drinking grapefruit juice while on carbamazepine .

DRUG INTERACTIONS

As enzyme inducer

With grape fruit as it is enzyme inhibitor

VALPROIC ACID (Sodium Valproate)

Absorbed rapidly & completely after oral

Highly bound to plasma proteins

Metabolized in liver to inactive metabolites.

Plasma half-life (15 hrs)

Excreted in urine

Enzyme inhibitor

MECHANISM OF ACTION

Blocking sodium channels

Increase GABA content of the brain

CLINICAL USES

Broad spectrum anti-epileptic

Absence seizures

In patients has concomitant absence & generalized tonic –clonic seizures

Myoclonic seizures

Partial seizures

Atonic attack

Lennox-Gastaut syndrome

ADVERSE EFFECTS

GIT upset (Dose-related)

Sedation

Fine tremor

Weight gain

Hair loss

Hepatotoxicity (Should be used cautiously)

Teratogenic (spina bifida)

Enzyme inhibitor

LAMOTRIGINE (2nd generation)

Well absorbed orally

Metabolized in liver

Protein binding (55%)

Excreted in urine

No effect on hepatic enzymes

Half-life (24 hrs).

MECHANISM OF ACTION

Suppresses the rapid firing of neurons & blocks sodium channels.

Inhibits the release of excitatory neurotransmitters (glutamate)

Inhibitory action on voltage – activated Ca^{++} channels .

CLINICAL USES

As add-on therapy in generalized tonic-clonic seizures & in patients with resistant partial seizures.

Monotherapy for partial seizures.

Effective in absence seizure & myclonic seizure in children.

Lennox-Gastaut syndrome

ADVERSE EFFECTS

Life-threatening dermatitis in 5% of patients

May progress to Steven-Johnson syndrome .

Influenza like syndrome

Dizziness, ataxia.

Somnolence

Blurred vision

LEVETIRACETAM

Taken orally

Absorption not affected by food

Not metabolized by cytochrome P450 Two thirds of the drug is excreted unchanged in urine.

Minimal protein bound (less than 10%) Minimal drud- drug interactions

Half-life 6-8 hrs

Well tolerated

MECHANISM OF ACTION

Unknown

Has a brain specific binding sites

CLINICAL USES

Adjunctive (add-on) therapy in partial & generalized tonic-clonic epilepsy

It is effective as adjunctive therapy in refractory partial seizures

SIDE EFFECTS

Asthenia

Dizziness

Somnolence

Pin & needles sensation in extremities

Frequent attacks of severe forms of seizures.

Drugs used for treatment are :

Diazepam (I.V.)

Clonazepam (I.V.)

Phenytoin(I.V.)

Phenobarbital (I.V.)

TREATMENT OF FEBRILE SEIZURE

Diazepam(rectally, I.V.)

Sodium valproate I.V.

Phenobarbital (not commonly used now).

THE KETOGENIC DIET

The ketogenic diet was used frequently for the treatment of intractable epilepsy before the discovery of the newer antiepileptics—carbamazepine, the benzodiazepines, and vallproic acid. Interest has been renewed in this high-fat diet by television shows and videotapes sponsored by parent groups. The mode of action is unknown, but seizure control may be correlated directly with elevated levels of beta-hydroxybutyrate and acetoacetate that result from ketosis. Children who have complex myoclonic epilepsy associated with tonic-clonic convulsions are most likely to respond to the diet. For those who do respond, it often is possible to decrease or discontinue most, if not all, anticonvulsants, so that the child inevitably becomes brighter and more responsive. The use of valproic acid is contraindicated in conjunction with the ketogenic diet because the latter potentiates the hepatotoxicity of the former. The ketogenic diet may be appropriate for the child

who has recalcitrant seizures despited polytheraphy, in whom an underlying cause of the seizure is unknown. Because the diet is unpalatable and has a high fat content, some children beyond the age of 1 to 2 years will not tolerate it. The ketogenic diet usually is continued for a period of 2 years in children who have good seizure control.