



Review Articles

Epilepsy: A Review

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Abstract

Epilepsy is a neurological problem which is a cause of sufferings for the common people because of lack of proper scientific knowledge. The incidence of epilepsy is about 0.3 to 0.5% while the prevalence is about 5 to 10 people per 1000. Newer concepts about aetiopathogenesis, classification and treatment modalities are described in brief in this review article.

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Introduction

Epilepsy describes the condition in which a person has a tendency to have seizures and a seizure is a paroxysmal event due to abnormal, excessive hyper synchronous electrical discharges from the brain.^{1, 2} In a single Generalized Tonic Clonic Seizure (GTCS) with normal physical examination and normal investigation the chance of recurrence is 30% and for partial seizure it is about 80%.³ The incidence of Epilepsy is about 0.3 to 0.5% while the prevalence is about 5 to 10 people per 1000.⁴

Pathogenesis

In the normally functioning cortex synchronous discharge amongst neighboring groups of neurons are limited by recurrent and collateral inhibitory circuits. Inhibitory neurotransmitter GABA is important in this role.¹ Epileptic cerebral cortex exhibits hypersynchronous repetitive discharge involving large groups of neurons. Both reductions in inhibitory system and excessive excitation play a part in the genesis of seizure activity. Epileptogenesis refers to transformation of a

normal neuronal network into one that is chronically hyperexcitable. For example, there is often a delay of months to years between an initial CNS injury (trauma, stroke, infection) and the first seizure. The injury appears to initiate a process of gradual lowering of seizure threshold.²

Classification

(Modified International Classification of ILAE – International League against Epilepsy)

A. Partial Seizures:

1. Simple Partial Seizure (with motor, sensory, autonomic or psychic signs).
2. Complex Partial Seizures.
3. Partial Seizures with Secondary Generalization.
4. Tonic clonic (grand mal).
5. Tonic.
6. Atonic.
7. Myoclonic.
8. Clonic.

B. Primary Generalized Seizures:

1. Absence (Petit mal).

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2. Atypical absence seizure.
- C. Unclassified seizure:
 1. Neonatal seizure.
 2. Infantile spasms.

PARTIAL SEIZURE:³

Motor : Epileptic activity arises in the precentral gyrus affecting contra lateral face, arms, trunk or leg.

Jacksonian epilepsy – attacks of epilepsy begin in one part (e.g. mouth, thumb) and spread gradually. Duration – few seconds to several hours.

Todd's palsy – paresis of involved limb lasting for several hours after the seizure ceases.

Sensory : arise in the sensory cortex. Unpleasant tingling or electric sensations in contra lateral face and limbs.

Versive : Frontal epileptic focus involving the frontal eye field. Forced deviation of the eyes to the opposite side. Often becomes generalized to a tonic-clonic seizure.

Visual seizures : Occipital epileptic foci. Balls of light/patterns of color. Faces/scenes (in temporal lobe).

Complex Partial Seizure

- * Episodes of altered consciousness without the patient collapsing to the ground.
- * Stops activity, stares blankly and usually accompanied by some automatism.
- * Frequently begins with an aura (i.e. a simple partial seizure) like alteration of mood, memory and perception.
- * Marked by post-ictal confusion. To be distinguished from absence seizure when CPS occurs without any aura.

Absence Seizure

- * Sudden brief lapses of consciousness without loss of postural control.
- * Lasts only for seconds, no post-ictal confusion.
- * Usually accompanied by subtle, bilateral motor signs such as blinking of the eyes,

chewing, clonic movement (small amplitude) of hands.

- * Almost always begin in childhood (4 to 8 years) or early adolescence.
- * Can occur hundreds of times per day. The patient is not aware that anything is wrong.

Partial Seizure with Secondary Generalisation

- * Often difficult to distinguish from a primarily generalized tonic-clonic seizure, since bystanders tend to emphasize the more dramatic, generalized convulsive phase and overlook the more subtle focal symptoms present at onset. When marked by an aura then the distinction is clear.
- * When clinically not evident, careful EEG analysis is required.

Generalised Tonic – Clonic Seizure

- * Begins abruptly without any warning (patient may describe vague premonitory symptoms in the preceding hours of seizure but stereotypic auras are absent which if present denotes partial seizure with secondary generalization).
- * Tonic phase – patient goes rigid and unconscious with a loud cry, secretions pool in oropharynx, cyanosis, and tongue biting, urinary and bowel incontinence.
- * Clonic phase – starts after 10 to 20 seconds of the onset of tonic phase and it is due to periods of muscle relaxation on the tonic muscle contraction, usually lasts no more than 1 min.
- * Post ictal phase – gradually regains consciousness but is in a confused and disoriented state for half an hour or so, maybe for hours in prolonged seizures.

Atonic Seizures

- * Sudden loss of postural muscle tone lasting 1 to 2 seconds, with fall to ground.
- * Brief impairment of consciousness. Usually no post-ictal confusion.

Myoclonic Seizure

- * Sudden and brief muscle contraction involving one part of the body or the entire body.

Differentiation of epileptic seizures and non-epileptic attack disorder (NEAD).

	<u>Epileptic attack</u>	<u>NEAD</u>
Precipitating cause	Rare	Common, emotional o& stress related
When alone or asleep	Common	Maybe reported
Onset	Usually short	Maybe short or over several minutes.
Aura	Various, usually stereotyped	Fear, panic, altered mental state
Speech	Cry, grunt at onset, muttering words in automatism.	Semi-voluntary, often unintelligible
Movement	Atonic: tonic: if clonic synchronous small-amplitude jerks	Asynchronous thrashing of limbs pelvic thrusting, episthotonus
Injury	Tongue-biting, fall; Direct violence rare	May bite tongue, cheeks, lip, hands, throw self to ground. Direct violence not uncommon.
Consciousness	Complete loss may occur.	Variable, often inconsistent with seizure type
Response to stimulation	none in generalized tonic-clonic;	often reacts and this may terminate episode.
May respond in complex partial and postictally	Incontinence Sometimes	Common
Duration	Few minutes	Few minutes, may be prolonged
Recovery	Depends on seizure type. Few minutes	Maybe rapid or very prolonged And more prolonged confusion

Important points in the history when establishing the aetiology of seizures⁶ History of birth injury. Family history of seizure or neurological disease. History of CNS infection. Drug history. History of complicated febrile convulsion. History of head injury with skull fracture or loss of consciousness.

Investigations

- A. To diagnose and classify – EEG, serum Prolactin, serum CPK.
- B. To establish cause.
 1. EEG – Standard EEG, sleep EEG, Ambulatory EEG, Video telemetry.
 2. Serum Prolactin- rises immediately after a seizure (immediate 30 minutes of post-ictal period), but not in psychological seizure helps to differentiate between seizure and pseudoseizure.²
 3. Serum CPK – serum Creatine Kinase measured about 3 hours after the event is generally normal after syncopal episodes or pseudoseizures but markedly elevated after tonic-clonic seizures.¹
 4. To rule out common metabolic disorders in suspected cases; Blood urea, serum

5. Suspected inflammatory / infective disorder; Full blood count, ESR, CRP, Chest radiograph. Serology for syphilis, HIV, Collagen disease, and Lumbar puncture to study CSF, etc.
6. CT Scan / MRI. MRI is superior to CT.⁶ (Hippocampal sclerosis, cortical dysgenesis and small foreign tissue lesion in CNS – not detected in CT).

Not required if a confident diagnosis of Primary Generalized Epilepsy can be made with an EEG.

Indications are – onset after age 20 years, partial seizures, EEG showing focal seizure source, control of seizure is difficult or deteriorates.

7. Special consideration: Special blood (e.g. for Wilson's disease) and histological tests in congenital metabolic and infective causes of epilepsy.

Treatment

- A. Treatment of underlying conditions: e.g.
 1. Correction of metabolic problem causing an abnormality of electrolytes or glucose.
 2. If the apparent cause of seizure was medication (e.g. theophylline) or illicit drug abuse (e.g. cocaine – then avoid the drug.

3. Seizure in structural CNS lesions such as a brain tumor, vascular malformation or brain abscess may not recur after appropriate treatment of underlying lesion.²
- B Avoidance of precipitating factors:
1. Sleep deprivation.
 2. Alcohol (particularly withdrawal).
 3. Recreational drug abuse.
 4. Physical and mental exhaustion.
 5. Flickering lights, including TV and computer screen.
 6. Intercurrent infections and metabolic disturbance.
 7. Uncommonly – loud noise, music, reading, hot baths.
- C. Restrictions: Until good control of seizures has been established restriction to be put on -
1. Work or recreation above ground level, with dangerous machinery, near open fires or water.
 2. Cycling, swimming and driving.
- Anti – Epileptic Drug (AED) Therapy**
- i) Should be started in any patient in recurrent seizures of unknown aetiology.
 - ii) In recurrent seizure of known cause that cannot be reversed.
 - iii) In single seizure from an identified lesion like CNS tumor, infarction or trauma, which are strongly epileptogenic.
- iv) AED therapy is controversial in patients with a single seizure. But patients with single seizure with one or more than one of the following risk factors should be treated –
- An abnormal neurological examination.
 - Seizures presenting as Status Epilepticus.
 - Post-ictal Todd's palsy.
 - A strong family history of seizure.
 - An abnormal EEG.
- v) A single seizure in a patient with a particular job (e.g. driving) may prefer taking AED rather than risking seizure recurrence.
- Withdrawal of AED**
1. About 70% of children and 60% of adults can eventually discontinue therapy.
 2. AED withdrawal is considered only after 2 to 4 years of complete seizure free period.
 3. Greatest chance of remaining seizure free is in patients with single seizure type with normal neurological examination including intelligence and a normal EEG.
 4. Withdrawal should be undertaken slowly reducing the dose gradually over 6 to 12 months.
- Treatment Failure – may occur due to**
1. Wrong drug and dose.
 2. Poor compliance.
 3. Wrong diagnosis.
 4. Underlying structural disease.
 5. Psychological problem present.

AED of Choice: 1,2,6

<u>Epilepsy type</u>	<u>First Line</u>	<u>Second line</u>	<u>Third line</u>
Partial Seizure	(i) Carbamazepine (Tegretol)	Lamotrigine	Gabapentine
With or Without	200 to 2000 mg/day	(Lamictal)	Clobazam
Secondary	15 to 35 mg/kg/day	Topiramite	Primidone
Generalization	(ii) Valproate	Phenobarbitone	
	400 – 2500 mg/day, 20 to 60 mg/kg/day		60 to 180 mg/day, 3-6mg/kg/day
Primary GTCS	Valproate	Carbamazepine	Phenytoin
	Lamotrigine		Gabapentin
Absence	Ethosuximide		Carbamazepine
	Lamotrigine		500 to 1500 mg/day, 20-40mg/kg/day
	Clonazepam	Myoclonic	Valproate
	Clonazepam	Phenobarbitone	1 to 8 mg/day
Atonic	Valproate	Clonazepam	

Special Situations

Refractory Epilepsy:

- 30% of patients are non-responder to a single agent.
 - Focal epilepsy with an underlying structural lesion.
 - Multiple seizure types and developmental delay.
- Management
- Check compliance, monitoring of AED blood level.
 - Combination therapy with two of three first line drugs (Carbamazepine, Phenytoin, Valproate).
 - If no response a third agent may be added while first two maintained and if there is response the least effective of the first two drugs should be gradually withdrawn.
 - Failure of medical therapy (~20%) points towards surgical intervention in some cases. Surgery usually involves resection of a selective part of the brain.

Epilepsy, Pregnancy, Oral Contraception, Breast Feeding.

- Sodium valproate has little interaction with oral contraceptives.
- Carbamazepine, Phenytoin and barbiturates are hepatic enzyme inducer.
- All the major anticonvulsants are teratogenic (cleft lip, spina bifida, cardiac defects). Risk is more in first trimester and on multidrug therapy.
- Lamotrigine may be less teratogenic.
- Folic acid (5 mg daily) taken 2 months before conception may reduce the risk of some fetal abnormalities.
- Considering risk versus benefit ratio pregnant women with epilepsy should be on effective AED.
- Breast-feeding should be continued. However, the decision should be reconsidered if any evidence of drug effect on the infant such as lethargy or poor feeding.²

Status Epilepticus

- Definition – status epilepticus exists when a series of seizures occurs without the patient regaining consciousness between attacks.
 - Most commonly this refers to recurrent tonic-clonic seizure.
 - Status is never the presenting feature of idiopathic epilepsy.
 - When seizure lasts beyond 5 minutes, demand for acute use of parenteral anticonvulsant therapy arises.
- Treatment:
- * Inj. Diazepam: 10 mg IV – repeat once only 15 minutes. Or, Lorazepam – 4 mg IV.
 - * Sodium Valproate – 10 mg /kg IV over 3 to 5 minutes.
 - * Phenytoin – loading dose of 15 mg/kg at < 50 mg/min.
 - * Chlormethiazole – IV.
 - * Thiopentone with artificial respiration.

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