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A Study on Etiological Pathophysiology and Management of Epilepsy

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ABSTRACT

Hippocrates was the among the earliest who discovered epilepsy and suggest that is hereditary rather than contagious. Epilepsy is a disorder of the brain characterized by repeated seizures. It is usually defined as a sudden alteration of behaviour due to a temporary change in the electrical functioning of the brain. Epilepsy, a disorder of unprovoked seizures is a multifaceted disease affecting individuals of all ages with a particular predilection for the very young and old. In addition to seizures, many patients often report cognitive and psychiatric problems associated with both the seizures themselves and its therapy. Epilepsy has numerous etiologies both idiopathic and acquired with a wide range of therapeutic responses. Despite numerous neuromodulatory devices, a large treatments available to control repetitive seizures including medications, diets, immunotherapy, surgery, and percentage of patients continue to suffer the consequences of uncontrolled seizures, which include psychosocial stigma and death.

KEYWORDS: Hippocrates, Epilepsy, seizures, immunotherapy, surgery etc.

ARTICLE DETAILS

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INTRODUCTION

There are millions of brain nerve cells in our cerebral cortex, and under normal circumstances, each cell carries a very small current. The electric waves transmit neural information and make us produce thoughts, feelings and activities, and coordinate functions such as breathing or heartbeat. Epilepsy is a problem with brain function (electric waves), which causes paroxysmal transient brain dysfunction (seizures). In addition to epilepsy, patients have a higher chance of having other problems (such as intellectual disability, cognitive problems, and emotional problems). Different parts of the brain are responsible for different functions. Depends on the location of seizure onset and propagation, patients with epilepsy can have different symptoms and different manifestations of seizures. Epilepsy is usually diagnosed when someone has had more than one seizure. Seizures can affect your feelings, awareness or movement. Different types of seizures involve different things. These may include confusion, strange feelings, repetitive movements, 'blank' moments (where you are briefly unresponsive), muscle jerks, sudden falls, or jerking movements (while unconscious). The human cerebral cortex consists of 3 to 6 layers of neurons. The phylogenetically oldest part of the cortex (archipallium) has 3 distinct neuronal layers, and is exemplified by the hippocampus, which is found in the medial temporal lobe. The majority of the cortex (neocortex or neopallium) has 6 distinct cell layers and covers most of the surface of the cerebral hemispheres. A particularly important cortical structure in the pathophysiology of one of the more common epilepsy syndromes is the hippocampus.

TYPES

Fig: classification of epilepsy

EPIDEMIOLOGY

In a systematic review and meta-analysis of incidence studies, the pooled incidence rate of epilepsy was 61.4 per 100,000 person-years (95% CI 50.7–74.4) [**1**]. The incidence was higher in low/middle-income countries (LMIC) than in high-income countries (HIC), 139.0 (95% CI 69.4–278.2) vs. 48.9 (95% CI 39.0–61.1). This can be explained by the different structure of populations at risk and a greater exposure to perinatal risk factors, higher rates of CNS infections, and TBI in LMIC. The incidence of epilepsy is also higher in the lowest socioeconomic classes in HIC and, within the same population, people of differing ethnic origin [**2**]. Differences can be also explained by methodological issues, such as more stringent case verification and the exclusion of isolated and acute symptomatic seizures in some studies.

ETIOLOGY

1.IDIOPATHIC EPILEPSY: benign famililal neonatal convulsions ,autosomal dominant nocturnal frontal lobe epilepsy [3][6]

2**. SYMPTOMATIC EPILEPSY:**

PREDOMINANTLY GENETIC OR DEVELOPMENTAL CAUSATION :west syndrome;Lennox-Gastuat syndrome, neuronal ceroid lipofuscinosis ,mitochondrial cytopathy PREDOMINANTLY AQUIRED CAUSATION: hippocampal sclerosis , cerebral palsy, open head injury, closed head injury [4]

PROVOKED EPILEPSY: ,menstrual cycle and catamenial epilepsy ;sleep-wake cycle ;alcohol and toxin induced seizures [5]

3. **COMMON SEIZURES CAUSED BY**

- Birth trauma
- Congenital problems
- Fever/infection
- Metabolic and chemical imbalances in the body
- Genetic factors
- Brain tumor
- Neurological problems
- Drug withdrawl
- Medications
- Use of illict drugs

RISK FACTORS

- Bleeding in the brain
- Serious brain injury or lack of confusion
- Blockage of arteries
- Alzheimers disease
- Illict drug use
- Children with small age

PATHOPYSIOLOGY

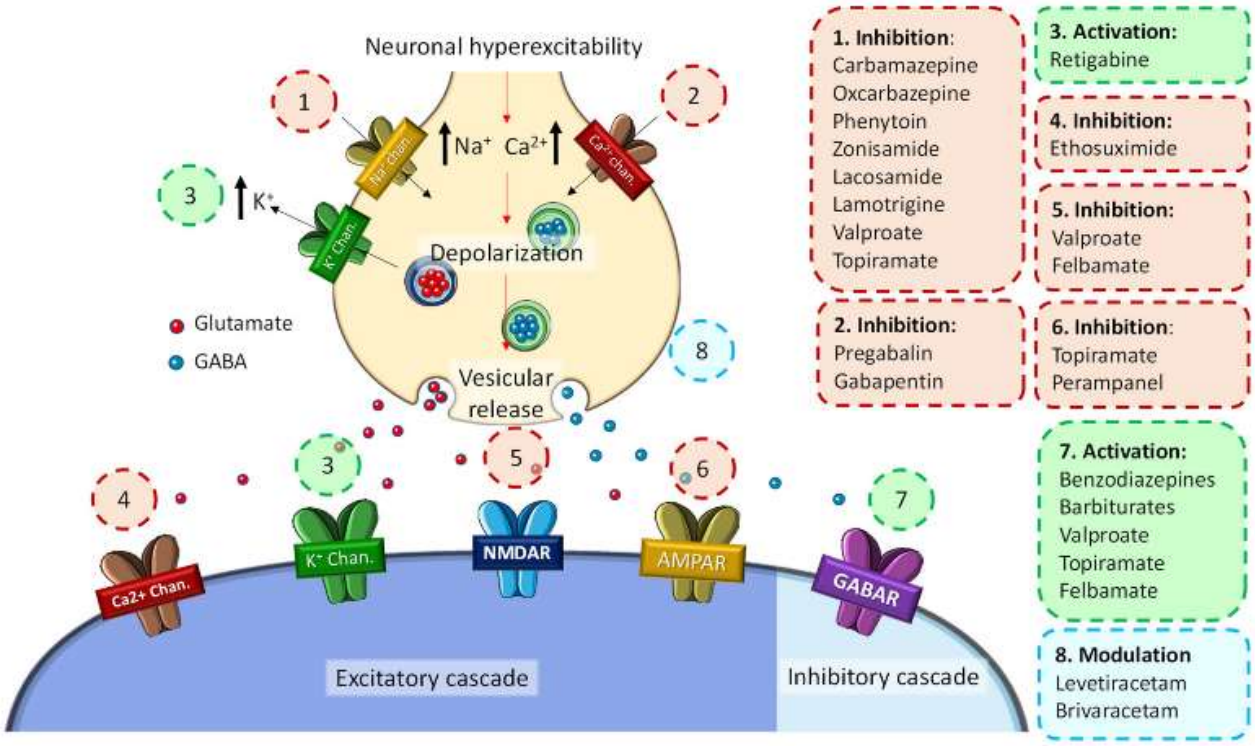

Fig.2 A diagrammatic representation on pathophysiology of the epilepsy

CLINICAL MANIFESTATIONS

SYMPTOMS BASED ON THR TYPE OF SEIZURES:

1.**SIMPLE PARTIAL SEIZURES** : unusual smell or taste

- Tingling in the arms and legs
- Stiffness or twitching in part of your body

2.**COMPLEX PARTAL SEIZURES**: making random noises

- Rubbing your hands
- Moving your arms around

3.**TONIC CLONIC SEIZURES**: loss of consciousness

- Falling to the floor
- Tongue biting
- Difficulty in breathing

4.**ABSENCE SEIZURES** :stay blankly into space
Fluttering eyes, day dreaming

5.**MYOCLONIC SEIZURES** : electric shock
Sudden twitches or jerks

DIAGNOSIS

DIFFERENT TESTS TO DETECT EPILPESY:

1. **EEG [ELECTROENCEPHALOGRAM**]:In this test small sensors are attached to scalp which checks the unsual activity in which we seen in people with epilepsy

2**. BRAIN SCAN**:

MRI[MAGNETIC RESONANCE IMAGING]:in this it uses the magnetic field which checks for the tumor in the brain ,and also the brain damage caused by the stroke or any scars present in the brain

3.**PET SCAN [POSITRON EMISSION TOMOGRAPHY]:**It is a nuclear medicine procedure which detects changes in the brain metabolism .

4.**SPECT SCAN[SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY]**:It is also called" ICTAL SPECT" which detects or check changes in the blood flow, transmission between the cells

5**. INTRACRANIAL MONITORING:** To detect the characteristics of pateints seizures physicians use this technology and correlate these finding with EEG .This test include

Depth electrodes: These are small, multi-contact probes that are inserted through small holes made in the skull and the coverings of the brain.

Strip and grid electrodes: These small platinum disks are set in a sheet of plastic and inserted underneath the covering of the brain called the dura.

Depth, strip and grid electrodes record brain wave activity in between and during seizures for planning epilepsy surgery.

6. **WADA TESTS**: helps determine the type of surgery that will best treat seizures while preserving areas of the brain associated with speech, memory and thinking functions.

PREVENTIONS OF EPILPESY

- 1.By improving the maternal health[7]
- 2.Avoiding early teenage pregnancies which prevent epilepsy
- 3.By taking immunizations
- 4.Mandatory use of helmet for sports and traffic
- 5.Banning sports who have a increased risk of traumatic encephalopathies[8]

MANAGEMENT OF EPILEPSY

NON PHARMACOLOGICAL TREATMENT: patients choose for alternative therapies because they may be dissatisfied with antiepileptic druga due to unpleasant side effects ,long duration of seizures ,failure to control seizures.the non pharmacological therapy includes

1.ketogenic diet :The diet induces ketosis which help in the control of seizures[9]

MOA:The harmone called leptin which is generated by taking ketogenic diet .which help in controlling seizures .

2.ALTERNATIVE /COMPLEMENTARY THERAPIES :

YOGA: Which relaxes body and mind reduce stress ,and helps in the control of seizures

AYURVEDA:the Ayurveda used to treat epilepsy by unblocking the channels of the heart and mind that may be clogged by excess of doshas and tumors .[11]

ASANAS OR POSTURES:Which help in maintaining the control of metabolic systems and the body functions .which calms nervous systems by increasing the stamina.[10]

3.ELECTROENCEPHALOGRAPHY

4.TRANSCRANIAL MAGNETIC STIMULATION

5.HERBAL MEDICINE

PHARMACOLOGICAL TREATMENT OF EPILPESY: [12][13][14][15]

DRUG	**BRAND NAMR**	**INITIAL/STARTING DOSE**	**MAXIMUM DOSE**	**COMMENTS TARGET SERUM CONCENTRATION RANGE**
BARBITURATES **Phenobarbitone**	Various	1-3mg/kg/day (10-20mg/kgLD)	180–300 mg	10–40 mcg/mL (43–172 μmol/L)
Primidone	Mysoline	100-125mg/kg	750–2,000 mg	5–10 mcg/mL (23-46 μmol/L)
BENZODAIZEPINES Clobazam	Onfi	≤30 kg 5 mg/day; >30 kg 10 mg/day	≤30 kg up to 20 mg; >30 kg up to 40 mg	0.03–0.3 ng/mL (0.1–1.0 nmol/L)
Clonazepam	Klonopin	1.5mg/kg	20mg	20–70 ng/mL (0.06–0.22 μmol/L)
Diazepam	Valium	PO: 4–40 mg IV: 5–10 mg	PO: 4–40 mg IV: 5–30 mg	100–1,000 ng/mL (0.4–3.5 μmol/L)
Lorazepam	Ativan	PO: 2–6 mg IV: 0.05 mg/kg IM: 0.05 mg/kg	PO: 10 mg IV: 0.05 mg/kg	10–30 ng/mL (31–93 nmol/L)
HYDANTOIN Phenytoin	Dilantin	PO: 3–5 mg/kg (200–400 mg) (15–20 mg/kg LD)	PO: 500–600 mg	Total: 10–20 mcg/mL (40–79 μmol/L) Unbound: 0.5–3 mcg/mL (2–12 μmol/L)
SUCCINAMIDE Ethosuxmide	Zarotin	500mg/day	500–2,000 mg	40–100 mcg/mL (282–708 μmol/L)
OTHER Carbamazepine	Tegretol	400mg/day	400–2,400 mg	4–12 mcg/mL (17–51 μmol/L)
Ezogabine	Potiga	300mg/day	1200mg	Not defined
Felbamate	Felbatol	1200mg/day	3600mg	30–60 mcg/mL (126–252 μmol/L)
Gabapentin	Neurotin	300-900mg/day	4800mg	2–20 mcg/mL (12–117 μmol/L)
Locasamide	Vimpat	100mg/day	400mg	Not defined
Lamotrigine	Lamictal	25 mg every other day if on VPA; 25–50 mg/day if not on VPA	100–150 mg if on VPA; 300–500 mg if not on VPA	4–20 mcg/mL (16–78 μmol/L)
Levetriacetum	Keppra Keppra xr	500-1000mg/day	3000-4000mg	12–46 mcg/mL (70–270 μmol/L)

Oxcarbazepine	Trileptal	300-600mg/day	2400-3000mg	3–35 mcg/mL (MHD) (12–139 μmol/L)
Pregabalin	Lyrica	150mg/day	600mg	Not defined
Rufinamide	Banzel	400-800mg/day	3200mg	Not defined
Tiagabine	Gabitril	4-8mg/day	80mg	0.02–0.2 mcg/mL (0.05–0.5 μmol/L)
Topiramate	Topamax	25-50mg/day	200-1000mg	5–20 mcg/mL (15–59 μmol/L)
Valproic acid	Depakene Depakene SR Depakote Depakote ER Depacon	15mg/kg(500-1000mg)	60 mg/kg (3,000–5,000 mg)	50–100 mcg/mL (347–693 μmol/L)
Vigabatrin	Sabril	100mg/day	3000m	0.8–36 mcg/mL (6–279 μmol/L)
Zonisamide	zonegran	100-200mg/day	600mg	0.8–36 mcg/mL (6–279 μmol/L)

NEW DRUG FOR EPILEPSY

The U.S Food and Drug Administartion today approved XCOPRI(cenobamate tablet) to treat partial –onset seizures in adults .cenobamate is under the class of medications called anticonvulsants .it works by decreasing abnormal electrical activity in the brain .[16]

NEW TECHNOLOGY TO TREAT EPILEPSY

The machine called ROSA allows surgeons to more precisely target parts of the brain responsible for epileptic seizures[17].

BEST VITAMNIN TO TREAT EPILPESY

Vitamin D may help to control seizures

Some anti-seizure medications interfere with how vitamin D is processed in the body .supplemental vitamin D may be necessary for people who have these risk factors to maintain normal blood levels.

REFERENCES

I. Fiest KM, Sauro KM, Wiebe S, Patten SB, Kwon CS, Dykeman J, et al. Prevalence and incidence of epilepsy: A systematic review and meta-analysis of international studies. *Neurology*

II. Beghi E, Hesdorffer D. Prevalence of epilepsy – an unknown quantity. *Epilepsia*. 2014 Jul;55(7):963–7.2017 Jan;88(3):296–303.

III. Aird RB. (1983) The importance of seizure-inducing factors in the control of refractory forms of epilepsy. Epilepsia 24:567–583.

IV. Beghi E. (2004) Etiology of epilepsy. In Shorvon SD, Perucca E, Engel J(Eds) The treatment of epilepsy. 2nd ed. Blackwell Science, Oxford, pp. 50–64.

V. Berg A, Berkovic S, Brodie M, Buchhalter J, Cross J, van Emde Boas W, Engel J, French J, Glauser T, Mathern G, Mosh S, Nordli D, Plouin P, Scheffer I. (2010) Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005–2009. Epilepsia 51:676–685.

VI. This list is derived from the book Causes of Epilepsy (Shorvon et al., 2011b).

VII. Dreifuss FE. Prevention as it pertains to epilepsy. Arch Neurol. 1995;52(4):363–6.

VIII. Sillanpää M, Gissler M, Schmidt D. Efforts in epilepsy prevention in the last 40 years: lessons from a large nationwide study. JAMA Neurol. 2016;73(4):390–5. An important article showing that we failed to prevent epilepsy in people below age 65 and a massive increase in epilepsy in the elderly.

IX. Freeman JM, Kossoff EH, Hartman AL. Ketogenic diet: One decade later. *Pediatrics.* 2007;119:535–43.

X. Rajesh B, Jaychandran D, Mohandas G, Radhakrishnan K. A pilot study of yoga meditation protocol for patients with medically refractory epilepsy. *J Altern Compliment Med.* 2006;12:367–71.

XI. Moharana D, Moharana S. A clinical trial of mentat in patients with various types of epilepsy. *Probe.* 1994;33:160–2.

XII. Barbara G. Wells, PharmD, FASHP, FCCP Dean Emeritus and Professor Emeritus Executive Director Emeritus, Research Institute of Pharmaceutical

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XVI. https://www.fda.gov/news-events/press-announcements/fda-approves-new-treatment-adults-partial-onset-seizures.

XVII. https://www.npr.org/2023/01/19/1149993707/new-tech-gives-hope-for-a-million-people-with-epilepsy