

## **CLINICAL INVESTIGATION OF EPILEPSY DISEASE AND ITS PHARMACOLOGICAL TREATMENT**

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### **Summary**

These are the group of disorders of the C.N.S characterized by paroxysmal cerebral dysrhythmia and loss of consciousness with or without characteristic body movement. Most of medications are taken every day to prevent seizures and can significantly reduce seizure frequency or even eliminate seizures completely. Medication include valproic acid, lamotrigine, phenytoin, tigabine etc.

**KEY WORDS:** Epilepsy, seizure, neurons, GABA receptors, consciousness

### **INTRODUCTION**

Epilepsy is a common but serious brain disorder. It is universal, with no age, sex, geographical, social class or racial boundaries. There is also a hidden burden associated with stigma and discrimination against the patient and even his/her family in the community, workplace, school and home. Many patients with epilepsy suffer severe emotional distress, behavioural disorders and extreme social isolation. Thus, the regional Office for South-East Asia (**SEARO**) of the World Health Organization (**WHO**) has decided to give high priority to the control of epilepsy in the community.<sup>1</sup>

**CAUSES** Generalised seizures occur if the abnormal electrical activity affects all or most of the brain where as partial seizures occur when burst of electrical activity starts in, and stays in one part of the brain.<sup>2</sup>

## SYMPTOMS OF EPILEPSY

### GENERALISED SEIZURES

In generalized seizures, patients suddenly stop what they are doing, the eyes and head turn to one side and the body becomes stiff. This is usually followed by several jerks of the hands and legs, groaning and frothing from the mouth. During the episode, the tongue may be bitten or severe injury can result from a fall or an accident. Sometimes the patient may pass urine or stools. The group is quite heterogeneous.

**Atonic-clonic seizure** is the most common type of generalised seizure. With this type of seizure whole body stiffens, loss of consciousness, and then body shakes (convulses) due to uncontrollable muscle contractions.

**Absence seizure** With this type of seizure a brief loss of consciousness or awareness occurs. There is no convulsion, you do not fall over, and it usually lasts only seconds. Absence seizures mainly occur in children.

**Myoclonic seizure** is caused by a sudden contraction of the muscles which cause a jerk. These can affect the whole body but often occur in just one or both arms.

**Atonic seizure** causes a brief loss of consciousness, and patient may become stiff and fall to the ground. Tonic seizures cause stiffening and contraction of the muscles usually in the legs, arms and back

**An atonic seizure** causes to become limp and collapse, often with only a brief loss of consciousness.

### PARTIAL SEIZURES

Different parts of the brain control different functions and so symptoms depend on which part of the brain is affected.

**Simple partial seizures** muscular jerks or strange sensations in one arm or leg and development an odd taste, or pins and needles in one part of body. Loss of consciousness or awareness does not occur.

**Complex partial seizures** Depending on the part of the brain affected, patient may behave strangely for a few seconds or minutes. For example, you may fiddle with an object, or mumble, or wander aimlessly. In addition, patient may have odd emotions, fears, feelings, visions, or sensations.<sup>2</sup>

## TREATMENT OF EPILEPSY DISEASE

### **HYDANTOIN: Phenytoin**

Phenytoin (brand name: **Dilantin**) is indicated for controlling generalized tonic – clonic (grand mal) and complex partial (psychomotor, temporal lobe) seizures. The primary site of action appears to be the motor cortex, where the drug inhibits the spread of seizure activity by promoting sodium efflux from neurons.<sup>3</sup>

#### **Side effect of phenytoin**

Side effect of phenytoin is Ataxia, slurred speech, decreased coordination, confusion, gum hyperplasia.<sup>4</sup>

### **BARBITURATES: Phenobarbital**

Barbiturates (brand name: **Luminal**) are substituted pyrimidine derivatives. The drug potentiates inhibitory neurotransmission by increasing the duration of time that GABA-mediated chloride channels remain open and reduces neurotransmitter release from nerve terminals, probably through its effect on calcium channels.<sup>3</sup>

#### **Side effect of phenobarbital**

Side effect of Phenobarbital is Phenobarbital may cause hyperactivity, behavioral problems, sedation, and even dementia.<sup>5</sup>

### **IMINOSTILBENES: Carbamazepine**

Carbamazepine (brand name: **Carbatrol**) is related to the tricyclic antidepressants (TCAs). It acts on voltage activated sodium channel and stabilizes the inactivated state of sodium channels.<sup>3</sup>

#### **Side effect of carbamazepine**

Side effect of carbamazepine is Sedation, weight gain, irritability, impaired attention.<sup>4</sup>

### **SUCCINIMIDES: Ethosuximide**

Ethosuximide (brand name: **Zarontin**) is chemically designated as alpha-ethyl-alpha methyl-succinimide. The drug's activity is accomplished via modulation of thalamic T-type calcium currents, thereby blocking synchronized firing of neurons associated with spike-and-wave discharges.<sup>3</sup>

#### **Side effect of ethosuximide**

Side effect of ethosuximide is ataxia, somnolence, headache, sedation, depression, agitation, changes in skeletal muscular strength, or other neurological dysfunctions.<sup>6</sup>

**ALIPHATIC CARBOXYLIC ACID: Valproic acid**

Valproic acid (brand name: **Depakene**) is a carboxylic acid. It acts on sodium channel, GABA receptor and T-type calcium currents. Its principal mechanism of action is believed to be the inhibition of the transamination of GABA.<sup>7</sup>

**Side effect of valproic acid**

Side effect of valproic acid is Nausea, diarrhea, vomiting, dyspepsia, weight gain, tremor, drowsiness, dizziness.<sup>4</sup>

**BENZODIAZEPINES: Clonazepam, Lorazepam, Diazepam, Chlordiazepoxide**

The benzodiazepines are used primarily as sedative-antianxiety drugs but also have broad antiseizure properties. Benzodiazepines act at GABAA receptors and increase the frequency of openings at GABA-activated Cl<sup>-</sup> channels.<sup>3</sup>

**Side effect of benzodiazepines**

Side effect of benzodiazepines is dependence, rebound anxiety, memory impairment, and discontinuation syndrome.<sup>8</sup>

**OTHER ANTISEIZURE DRUGS**

**Gabapentin** (brand name: **Neurontin**) is specifically a GABA analogue. Gabapentin may promote release of GABA.<sup>3</sup>

**Side effect of Gabapentine**

Side effect of gabapentine is Somnolence, dizziness, ataxia, weight gain, peripheral edema.<sup>4</sup>

**Lamotrigine**

Lamotrigine (brand name: **Lamictal**) is an anticonvulsant drug used in the treatment of epilepsy and bipolar disorder. It acts on sodium channel.<sup>3</sup>

**Side effect of Lamotrigine**

Side effect of lamotrigine is Somnolence, dizziness, ataxia, confusion, nausea.<sup>4</sup>

**Tiagabine**

Tiagabine (brand name: **Gabitril**) is a derivative of nipecotic acid. Tiagabine is indicated as adjunctive therapy in adults and children 12 years of age and older with partial seizures. It act by enhancing the activity of GABA.<sup>3</sup>

### **Side effect of Tiagabine**

Side effect of tiagabine is Dizziness, asthenia, somnolence, nausea, nervousness/irritability, tremor, abdominal pain, impaired attention.<sup>4</sup>

### **Zonisamide**

Zonisamide (brand name: **Zonegran**) is an antiseizure sulfonamide, but it is not related to other AEDs. It acts on sodium and calcium channels.<sup>3</sup>

### **Side effect of zonisamide**

The side-effects of zonisamide is Somnolence, dizziness, anorexia, nausea, irritability.<sup>4</sup>

## **MULTIDISCIPLINARY APPROACH**

Multidisciplinary approach is helpful for improving service of epilepsy through studies, service demonstration grants, training grants, and educational and informational activities. Pharmacist, speech and language therapist, dietician, social worker, sex therapist, general physician etc affect directly epilepsy patients.

### **PHARMACIST**

A Pharmacist is qualified to prepare and dispense prescribed drugs, and plays a key role in the lives of persons with Epilepsy disease as they require a regularized supply of their medications.

### **SPEECH AND LANGUAGE THERAPIST (SLT)**

Speech and language therapists help people communicate to the best of their ability by assessing and treating speech, language and communication problems.

### **DIETICIAN**

A dietician advises on a healthy diet and specific dietary needs. They can offer advice on how diet can ease some symptoms, such as constipation, heart burn etc.

**SOCIAL WORKER** Social workers are trained to help with the social, emotional and financial needs of the person with Epilepsy disease, their caregiver and their family.

### **SEX THERAPIST**

Sex therapists are trained to provide advice and counseling on all aspects of sexual health and related concerns and can help persons with Epilepsy disease cope with any difficulties they may experience in this regard.

### **PRIMARY CARE PHYSICIAN OR A GENERAL PRACTITIONER**

Usually called family physicians or general physician, the primary care physician is aware of the patient's long term medical history, is able to advice the family on referrals to specialists, able to see the patient regularly and follow up the treatment closely.

### **PHYSIOTHERAPIST**

A physiotherapist is a healthcare professional who deals with physical weaknesses and difficulties. Physiotherapists are trained to manage mobility problems including gait, posture, balance, transfers (e.g. getting in and out of bed or a chair) and dexterity.

### **A NEUROLOGIST**

Neurologist is a doctor trained to diagnose, treat and manage patients with neurological disorders (disorders of the nervous system) such as Epilepsy disease and movement disorders.

### **NURSE**

Some countries may have Specialist Nurses for Epilepsy disease who can act as a 'bridge' between the patient and the doctor. They may be closely involved in certain aspects of care, such as medication.

### **OCCUPATIONAL THERAPIST (OT)**

Occupational therapy promotes good health and are trained to help one adapt to the motor, cognitive and other impairments associated with Epilepsy by providing special equipment and through the modification of the patient's environment.

## **PSYCHIATRIST**

A psychiatrist evaluates a person's mental health along with his or her physical health and can prescribe medications to treat mental and emotional disturbances.

## **PSYCHOLOGIST**

They play an important role in the lives of persons with Epilepsy disease and their families by helping to maintain their compliance to treatment, help motivate them to be involved in their self care, deal with cognitive difficulties and cope with demoralizing feelings.

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