REVIEW ON CLINICAL MANIFESTATIONS, PATHOLOGICAL CONDITIONS, DIAGNOSIS AND MANAGEMENT OF STATUS EPILEPTICUS

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ABSTRACT

Generalized, convulsive status epilepticus in adults and older children (>5years old) refers to >5min of (a) continuous seizures (b) two or more discrete seizures between which there is incomplete recovery of consciousness. Clinical manifestations depend on the type of seizure. Seizures widely classified as partial seizures, absence seizures and clonic tonic seizures. The overall incidence of status epilepticus is 9.9 to 41 per 1 lakh per year with peaks in children and elderly with febrile seizures young strokes as its main etiologies. Epilepsy treated by AED effective against GTC and partial seizures probably work by delaying recovery of sodium channels from activation.

INTRODUCTION

Status epilepticus is characterized by abnormally prolonged seizure activity. Although there are numerous forms of status epilepticus. This epitome is directed toward generalized convulsive status epilepticus (GCSE) in adults and older children.[1] The overall incidence of status epilepticus is 9.9to 41 per 1 lakh per year with peaks in children and elderly with febrile seizures young strokes as its main etiologies.[2] Seizures results from excessive excitation or from disordered inhibition of neurons. Initially small number of neurons fire abnormally. Normal membrane conductance and inhibitory synaptic currents then breakdown and excitability spreads locally [focal seizures] or more widely generalized seizures.

Symptoms depend on seizures type. Partial seizures manifests as alterations in motor functions, sensory or somatosensory symptoms. People may have memory loss or aberrations of behavior. In complex partial seizures, there is impairment of consciousness. Absence seizures exhibit a sudden onset, interruption of ongoing activities, blank stare and possibly brief upward rotation of the eyes. tonic clonic seizures begin with a short tonic contraction of muscles followed by a period of rigidity and clonic movements. The patient may loss sphincter control, bite the tongue or become cyanotic. The episode is frequently followed by a deep sleep. Diagnosis is mainly through EEG and treated with AED's.

CLASSIFICATION & CLINICAL MANIFESTATIONS[3]

GENERALISED SEIZURES: These happen when nerve cells on both side of your brain misfire, which leads to muscle spasm. Subclassifies as: -

- Tonic-clonic (or grandmal) seizures – noticeable

1. Body stiffness
2. Shakes
3. Loss consciousness
4. Some times loss control of your bladder or bowel
   They usually lag 1-3 mins. If they go longer that can leads to breathing problem and tongue bite

- Clonic seizures:
  Muscles have spasm which often make your face neck, and arm muscles jerk rhythmically. They may last several minutes.
- Tonic seizures:
  Muscles in legs arms and trunk tense up these lasts less then 20 sec and often happen in sleep but if you standing up at the time you lose your balance and fall.
- Atonic seizure:
  Muscles suddenly go stiff and your head may lean forward. Its hard to hold anything. These usually lasts for less than 15 seconds.
- Myoclonic seizures:
  Muscle has sudden jerks. They might start in the same part of the brain as an atonic seizure and some people have both myoclonic and atonic seizures.
- Absence (or Petitmal) seizures
  They seem disconnected from other around you and not respond to others. And also stares blankly into space. It usually lasts only few seconds. It is most common in children under age 14.

FOCAL SEIZURES:

- Simple focal seizures:
  its features are twitches in fingers, arms, legs twitch. loss of consciousness associated with sweating.
- Complex focal seizures:
  Usually happen in the part of brain that controls emotions and memory. May loss consciousness but still look like awake. Symptoms common like gag, smack your lips, laugh or cry. It takes several minutes to come out of it.
- Secondary generalized seizures:
  They are similar to generalized seizures.

PATHOPHYSIOLOGICAL CONDITIONS

Seizure's activity is characterized by paroxysmal discharges occurring synchronously in large population of cortical neurons. This is characterized on EEG as a sharp wave or spike.

The basic physiology of seizures episodes is traceable to an unstable cell membrane or its surrounding supportive cell the seizure originates from the grey matter of any cortical or perhaps subcortical area initially a small number of neurons fire abnormally normal membrane conductance and inhibitory synaptic currents break down and excess excitability spreads , either locally to produce a focal seizure or more widely to produce a generalized seizures this onset propagates by physiologic pathways to involve adjacent or remote areas

An abnormality of potassium conductance defect in the voltage sensitive ion channels, or a deficiency in the membrane ATPase linked to ion transport may result in neuronal membrane instability and seizures.

A relative deficiency of inhibitory neurotransmitters such as GABA or an increase in excitatory neurotransmitters such as glutamate would promote abnormal neuronal activity.

DIAGNOSIS[4]

The diagnosis of convulsive status epilepticus is made clinically but requires emergent neuroimaging and laboratory studies to identify the potential etiology. A head computed tomography (CT) scan is appropriating most situations and most easily obtained. Magnetic imaging resonance (MRI) of the brain is more sensitive for identifying malformations in pediatric patients but may be difficult to obtain and may require sedation. Laboratory study should include bedside blood glucose level, serum electrolytes (sodium, potassium, calcium, magnesium) BUN, creatinine, serum bicarbonate, complete blood count, and a lumbar puncture with cerebrospinal fluid (CSF) evaluation if the patient has a known seizure disorder antiepileptic drug levels should be obtained, suspicion of toxic ingestion mandates toxicology studies (urine toxicology screen, serum levels of specific toxins such as theophylline or lithium). Other studies may be considered based on the presentation (LFT in borne errors of metabolism, and coagulation studies). A pregnancy test should be obtained in all women child bearing age. And EEG should be obtained. Non convulsive status epilepticus requires all of the previously mentioned imaging and laboratory studies for the identification of underlying etiology but also requires EEG monitoring for diagnosis.

MANAGEMENT[5]

NON- PHARMACOLOGICAL THERAPY

Vagal nerve stimulation: which is implantation of a vagal nerve stimulator. The device consists of an implantable, programmable pulse generator connected to av helical lead.

Surgery is the most widespread and most useful non pharmacologic therapy. A focus in the temporal lobe has the best chance for a positive outcome.

Protein and calorie intake are set at level that will meet requirements for growth.

PHARMACOLOGICAL THERAPY[6]

Begin with monotherapy about 65% patients can be maintained on one antiepileptic drug the mechanism of action of most AEDs includes effects on ion channel (sodium, calcium) kinetics, augmentation of inhibitory neuro transmission (increase in CNS GABA), and modulation of excitatory neuro transmission (decreasing or antagonizing glutamate and aspartate). AED effective against GTC and partial seizures probably work by delaying recovery of sodium channels from activation.

	1ST LINE	2nd LINE	FDA Approved
PARTIAL SEIZURES	• Carbamazepine • Gabapentin • Oxcarbazepine • Phenobarbital	Lamotrigine Levetiracetam Oxcarbazepine Valproic acid	• Carbamazepine • Phenobarbital • Phenytoin

	• Phenytoin • Valproic acid • Topiramate		• Valproic acid • Topiramate • lacosamide
GENERALISED SEIZURE Absence Tonic-clonic	• Lamotrigine • Topiramate	Clobazam Clonazepam Levetiracetam Topiramate	• Ethosuximide • Valproic acid • Lamotrigine • Levetiracetam • Topiramate
JUVENILE MYCLONIC SEIZURE	• Ethosuximide • Lamotrigine • Valproic acid	Clobazam Clonazepam Levetiracetam Topiramate	

CARBAMAZEPINE

Food may enhance the bioavailability of carbamazepine. Rashes may occur in 10% of patient's other side effects includes nausea, hepatitis, cardiac conduction defects.

Carbamazepine may interact with other drugs by inducing their metabolism. Valproic acid increases the concentration of 10,11-epoxide metabolite without effecting the concentration of carbamazepine.

The interaction of erythromycin and clarithromycin with carbamazepine is particularly significant.

CLOBAZAM

Abrupt discontinuation can cause the withdrawal syndrome (e.g., behavioral disorder, tremor, anxiety, dysphoria, insomnia, convulsions, psychosis).

GABAPENTINE

Gabapentin is a second line agent for patients with partial seizures who have failed initial treatment. It may also have a role in patients with less severe seizure disorder.

FELBAMATE

Felbamate is approved for atonic seizures and is effective for partial seizures

LACOSAMIDE

Lacosamide is schedule 5 controlled substance. There is a linear relationship between daily doses and serum concentrations up to 800mg/day. The starting dose is 100mg/day in 2 divided doses with dose increased by 100mg/day, every week until a daily dose of 200mg to 400mg.

LAMOTRIGINE

Lamotrigine is useful as both adjunctive therapy for partial seizures and monotherapy. It may also be useful alternative for primary generalized seizures such as absence and has adjunctive therapy for primary GTC seizures.

LEVETIRACETAM

It is effective in the adjunctive treatment of partial seizures in adults who have failed initial therapy. Adverse effects include sedation, fatigue and agitation. The recommended initial dose is 500mg orally twice daily.

PHENYTOIN

Phenytoin is the first line AED for primary generalized convulsive seizures and for partial seizures. Absorption may be saturable at higher doses. Fosphenytoin can be safely administered IV and IM. Phenytoin may be initiated in adults at oral doses of 5mg/kg/day.

VIGABATRIN

Vigabatrin is first line for infantile spasms and third line adjunctive agent for refractory partial epilepsy.

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