### APPROACH TO A CHILD WITH STATUS EPILEPTICUS

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## **OBJECTIVES:-**

- Definition
- Epidemiology
- To understand the pathophysiologic events...
- Role of optimum investigation.
- To know the algorithm approach.
- To learn principles of management of child presenting with seizure in emergency room.

# **Definition: Status epilepticus**

- Status epilepticus (SE) is the most common childhood neurological emergency.
- Practically, SE is defined as any child presenting convulsing to a healthcare facility or having repeated seizures without regaining of consciousness in between.

# STATUS EPILEPTICUS IN TIME POINT (t1,t2)

TYPE OF SE:	TIME BEYOND WHICH IF SEIZURE PERSIST, PATIENT IS CONSIDERED IN SE (t1)	TIME AFTER WHICH PERSISTANT SEIZURES HAVE LONG TERM CONSEQUENSES(t2)
GENERALISED CONVULSIVE SE	5 MINUTES	30 MINUTES
FOCAL STATUS WITH IMPAIRED CONSIOUSNESS	10 MINUTES	60 MINUTES

## Status epilepticus – operational definition

 Generalized, convulsive status epilepticus refers ≥5 min of

1.Continous seizure or

2. Two or more discrete seizures between which there is incomplete recovery of consciousness.

## Why 5 min??

 Defining convulsive SE as a convulsive seizure that last for a period of at least 5 min is not only practical but is supported by the finding that the probability of a seizure stopping spontaneously without intervention is quite low after this.

# **Etiology:**

#### ☐ Known (symptomatic):

- Acute (stroke, toxicity, derangements in serum electrolytes and blood glucose, trauma, hypoxia, febrile seizures, neuroinfections, and inborn errors of metabolism)
- Remote (brain scars due to above causes, genetic, brain malformations, etc.)
- Progressive (neurodegenerative disorders and tumors)
- Known cases of epilepsy: Poor drug compliance or by nature drug-resistant epilepsies such as Lennox—Gastaut syndrome and Dravet syndrome;

## **Etiology- (cont.)**

#### □Unknown cause:

 Entities like new-onset refractory status epilepticus (NORSE), a subset of which is febrile infection-related epilepsy syndrome (FIRES)

## **NORSE**-new onset refractory status epilepticus ??

•Any of the causes of status epilepticus in a patient without prior epilepsy.

•It is often unknown etiology, presumed to be encephalitis or post encephalitis, can last for a week or longer, has poor prognosis.

## FIRES OR DESC??

- Is a syndrome of refractory status epilepticus that is associated with acute febrile infections, appears to be postinfectious in nature.
- Highly drug resistant.
- Responsive to ketogenic diet.

# **EPIDEMIOLOGY**

- Convulsive status epilepticus (children) 10-27/100000 per year.
- Febrile seizure -25-40%.
- Major proportion of morbidity and mortality associated with status epilepticus during episodes of refractory convulsive status epilepticus.

## **HISTORY AND EXAMINATION**

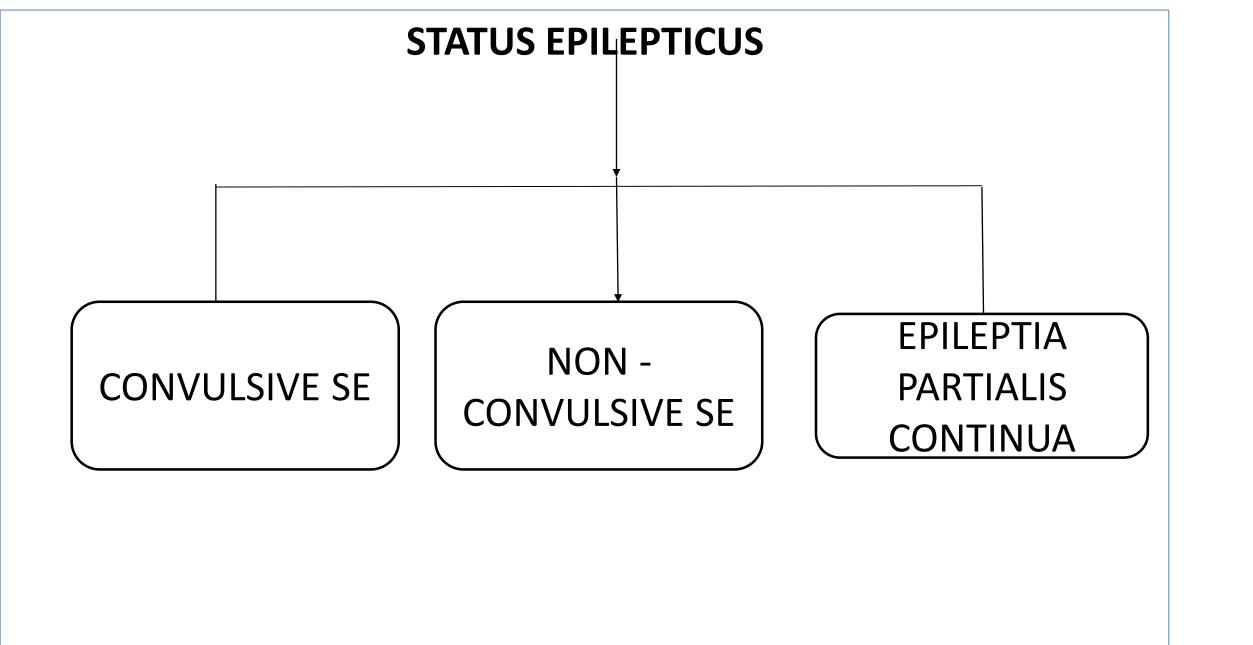
- Past History:
- Developmental Delay
- Neurodeficits
- Abnormal Birth History

- Seizure Precipitating Event:
- AED: Drug And Compliance
- Sleep Deprivation
- Stress
- Missed AED/ Underdosing
- Fever

### **ASSESS RISK FOR MENINGITIS**

- History:
- Drowsy ,vomiting
- >3 Days Duration Of Illness
- 6-12 Month Infant
   Unvaccinated For Hib ,
   Pneumococcus
- Complex Febrile Seizure

- Examination
- Neck Stiffness
- Neurodeficit
- Ear Discharge ,sinusitis
- Bulging AF



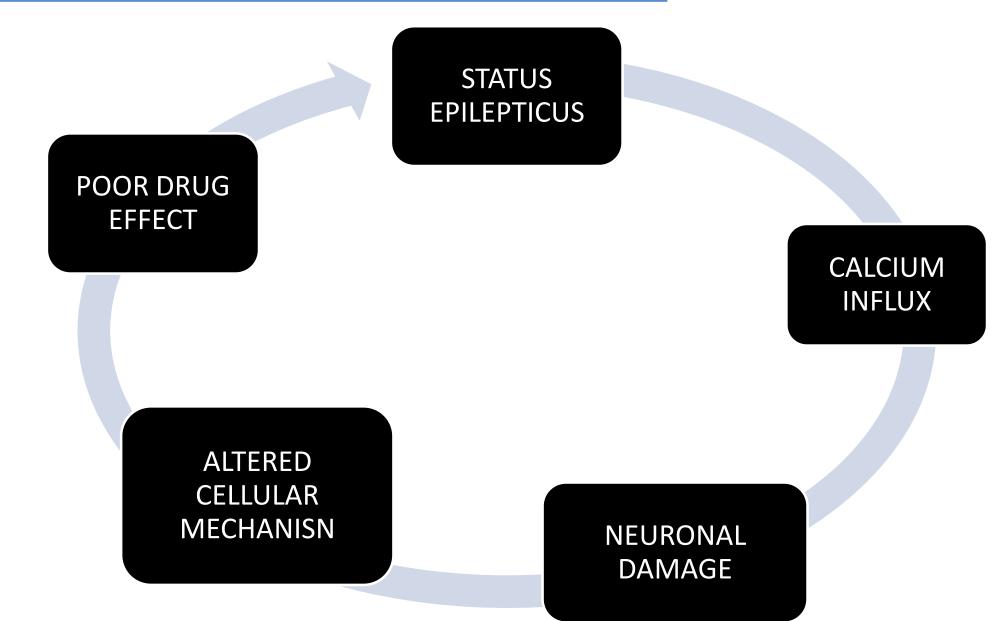
# ■ NCSE( Nonconvulsive Status Epilepticus)

- Focal SE with impaired consciousness
- Absence SE

#### **■ NCSE** manifest as:

- Confusional state
- Hyperactivity with behavioral problem
- Fluctuating impairment of consciousness
- With a time unsteady sitting or walking
- Fluctuating mental status, hallucination, paranoia, and or psychotic symptoms.

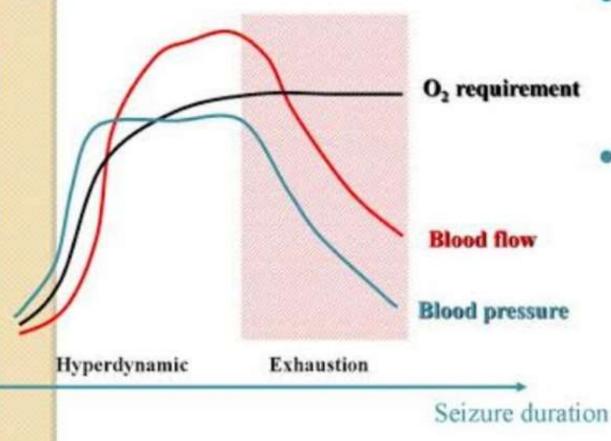
#### • STATUS EPILEPTICUS IS A VICIOUS CYCLE



## **HEMODYNAMIC CHANGES OF SE**

- 1. Hyperdynamic phase- CBF meets metabolic requirement
- 2.Exhaustion phase-
- Cerebral blood flow drop as hypotension sets in.
- Autoregulation exhausted.
- Neuronal damage ensues.

#### Cerebral blood flow - Cerebral O2 requirement



- Hyperdynamic phase
  - CBF meets CMRO<sub>2</sub>
- Exhaustion phase
  - CBF drops as hypotension sets in
  - Autoregulation exhausted
  - Neuronal damage ensues

## **GLYCEMIC CONTROL**

Hyperdynamic phase-hyperglycemia

 Exhaustion phase-hypoglycemia develops and neuronal damage ensues.

## PATHOPHYSIOLOGY OF STATUS EPILEPTICUS

- Cell death may result from –
- Excessive release of glutamate / excessive stimulation of glutamate receptors ,a process is known as excitotoxicity.
- The most vulnerable areas of brain include the hippocampus, amygdala ,cerebellum ,middle cortical area, and thalamus.

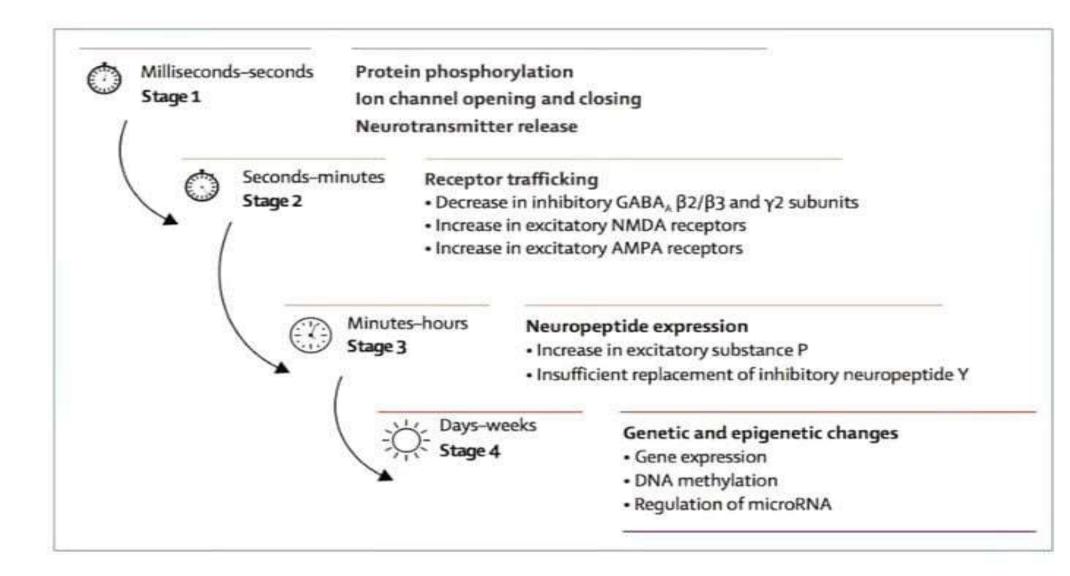
 Acute changes-venous congestion ,small petechial hemorrhages ,and edema.

• Ischemic cellular changes are the earliest histologic finding ,followed by neuronophagia, microglial proliferation ,cell loss ,and increased number of reactive astrocytes.

 Neuronal concentration of calcium, arachidonic acid and prostaglandins increase and may promote cell death.

Autonomic dysfunction - hypotension and shock as well as lactic acidosis.

#### Seizure to Status - Mechanism



#### **SEIZURE TO STATUS MECHANISM**

Stage 1- protein phosphorylation and neurotransmitter release.



stage 2- receptor trafficking



stage 3- neuropeptide expression.

stage 4- genetic and epigenetic changes gene expression and DNA methylation.

• Status epilepticus is a life-threatening emergency. To improve outcomes, each unit should have a fixed protocol.

Diagnosis and management should proceed together.

A quick history and examination help to search for etiology

## **MANAGEMENT GOALS**

1. Stabilization — maintain vital functions.

2. Abolish seizure.

3. Eliminate /treat precipitating cause.

#### 4. Rational investigations:-

- Routine investigations
- CSF
- Neuroimaging
- EEG

5. Manage complications

6.Prevent recurrence

# STEP 1-ACTIVELY SEIZING CHILD: INITIAL STABLIZATION(0 -5 MINUTES)

- Position child to avoid injuries.
- Ensure airway patency.
- Oxygen by nasal canula /mask.
- Prepare to assist with bag and mask ventilation.
- Assess and maintain vitals.
- Cardio-respiratory and saturation monitoring.
- Start timing seizure.
- Iv- line placement.

#### INDICATIONS FOR ENDOTRACHEAL INTUBATION.

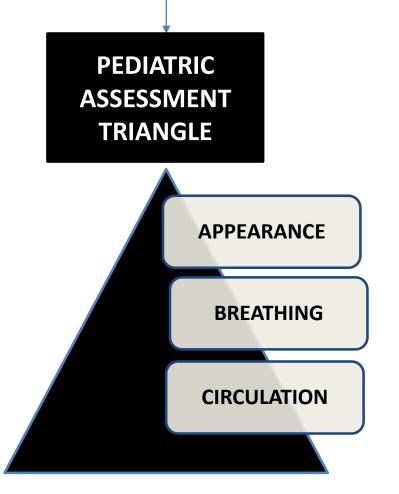
- Severe hypoxia (bradycardia, hypotension, poor perfusion)
- Failure or prolonged requirement of bag and mask ventilation.
- Children with features of raised intracranial pressure.
- Refractory status epilepticus.

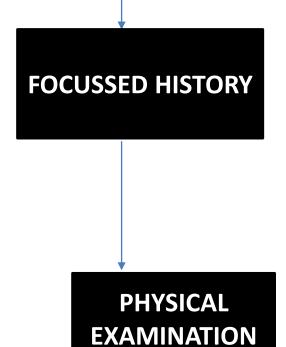
#### **TEAM APPROACH TO SEIZING CHILD**

 DESIGNATE TEAM MEMBER TO PROCEED TO ACHIEVE EACH OBJECTIVES.

INTRAVENOUS ACCESS

PROCEED WITH
SEIZURE
MANAGEMENT
ALGORITHM





## **STEP- 1(0-5MIN)**

# A benzodiazepines is the initial therapy of choice (level A)

- iv access established (level A)
- First AED: iv Lorazepam -0.1mg/kg,(max 4mg/dose), may repeat dose once or

- iv Midazolam- 0.15-0.2mg/kg,(max 5 mg), or
- iv Diazepam-0.2-0.3 mg/kg, (max 10 mg/dose), may repeat dose once

## **STEP-1(0-5MIN)**

If iv access not available ( level B)

Rectal diazepam 0.2-0.5mg/kg, max 20mg/dose, single dose. Or

Intranasal midazolam/ buccal midazolam.

#### •If benzodiazepine not available:

Intravenous phenobarbitone 15mg/kg/dose, single dose.

# **STEP-1(0-5MIN)**

 Take blood samples for CBC, sugar ,calcium, magnesium, sodium,potassium,and ABG/VBG

Treat if abnormal. Blood culture if fever.

## **STEP-2 (5-20 MIN) SECOND THERAPY PHASE**

- No evidence based preferred second therapy of choice (level U)
- General measures:
  - -Shift to picu if unstable.
  - -Watch for raised ICP-treat with mannitol/3%Nacl
- Choose one of the following.
- IV phenytoin 20mg/kg in NS@1mg/kg/min
- iv phosphenytoin 20pe/kg, phenytoin @3mg/kg/min with HR monitoring(level U)
- Can repeat IV phenytoin10mg/kg or IV phosphenytoin 10mgPE/kg

## STEP-3 (30-60MIN)THIRD THERAPY PHASE

- General measures watch for raised ICP, rhabdomyolysis, cardiac arrythmia, sepsis and hypersensitivity to AED. Monitor for organ function.
- Management : if seizure persists :
  - 1. Iv valproate 20-40 mg/kg
  - 2. Iv phenobarbitone 20mg/kg in NS@2mg/kg/min
  - 3. Iv levetiracetam 20-60mg/kg @5mg/kg/min
- → Start maintenance dose after 8-12hr

#### **REFRACTORY STATUS EPILEPTICUS**

- Refractory SE-failure of first line + second line anticonvulsant drugs, such as an initial benzodiazepine followed by another AED
- The second therapy appears less effective(marginal benefit with each additional AED-5% with second AED)
- Additional benefit of 23% move fast to HDST.

## **Step 4 - (1-24hours)**

- General measures Refractory status epilepticus: shift to PICU, start bedside EEG.
- <u>Investigations</u>: screen for neuroinfection, MRI brain +/-contrast and CT-brain if unstable. Autoimmune pannel, metabolic and genetic studies based on clinical suspicion.
- Management :
- A. General anaesthesia to achieve burst supression.

**B. Midazolam**: 0.2mg/kg iv bolus followed by infusion @ 1mcg/kg/min, increasing 1mcg/kg/min every 5 to 10 min till seizure stops, upto max 30mcg/kg/min, tappering initiated after 24hr of seizure controll @ 1mcg/kg/min every 3hr.

OR

**High dose Phenobarbitone** – 5 – 10 mg/kg boluses every 30 min upto 120mg/kg over 24hr, target seizure control and burst supression, maintainence upto 40mg/kg/day.

#### OR

**Propofol**: Loading dose of 1-2mg/kg, followed by continuous infusion of 1-2mg/kg/hr, max 5mg/kg/hr.

#### OR

**Thiopentone**: Loading dose 5mg/kg bolus followed by 3-5mg/kg/hr infusion to achieve burst supression followed by tapering after 24 hr seizure free period.

**Topiramate** through OG/NG tube (2-5mg/kg enteral loading, increase by 5-10mg/kg/day upto max of 25mg/kg/day) while tappering anaesthetic agents. **Ketamine** can also be tried.

#### **SUPER REFRACTORY STATUS EPILEPTICUS**

 Persistent seizure activity or seizure recurrence despite
 24 hour of general anesthesia with medications such as midazolam, pentobarbital, and/or propofol.

## Step 5 – after 24 hr (super refractory SE)

- **General measure**: shift to higher center with neurocritical care unit.
- Therapeutic options (on case to case basis )
- 1. Ketogenic diet
- 2. Immunotherapy IV methylprednisolone/ IV IG/Others
- 3. Vagal nerve stimulation, therapeutic hypothermia
- 4. Epilepsy surgery in selected cases

## IF THE CHILD IS ALREADY ON ANTI EPILEPTIC DRUG AND CAME IN STATUS EPILEPTICUS ?

For phenytoin ≤6mg/kg/day, phenobarbitone≤5mg/kg/day,valporate≤30mgkg/day, levetiracetam≤30mg/kg/day or if the child has missed few doses of aed or child has vomiting /diarrhea

GIVE HALF THE LOADING DOSE OF RESPECTIVE AED

 If the child is receiving AED at dose higher than mentioned in previous slide.

# AVOID LOADING WITH THAT AED, AND MOVED TO NEXT STEP

#### STATUS EPILEPTICUS PROTOCOL

- COMORBIDITY RX
- HYPOXIA
- HYPERTHERMIA
- HYPOGLYEMIA
- CEREBRL EDEMA

FIRST AED: IV Lorazepam/Midazolam/Diazepam If No iv , Diazepam per rectal/ im Midazolam

Second Aed: iv Phosphenytoin/ Phenytoin

Third Aed :iv Valproate / Levetira/Phenobarbitone

Burst Suppression
Midazolam/Thiopentone/Propofol/Pentobarbital

LAB INVESTIGATION ECG

EEG MONITORING: BURST SUPPRESSION NCSE

#### **Laboratory investigation**

- Complete blood count.
- Serum electrolyte.
- •Blood urea nitrogen, creatinine.
- •Glucose, calcium.
- •Should be considered based on individual clinical circumstances (vomiting, diarrhea, dehydration, failure to return to baseline alertness)
- •Blood sugar in all prolonged seizure and neonate.

#### INDICATION OF LUMBAR PUNCTURE

- < 6month:Lumber puncture Warranted For Any Child With Fever and Seizures.
- 6-12 Month: If Child Has Seizures And Is Non Vaccinated For Hib, Pneumococcus.
- >12 Month :any Child With Fever And Meningeal Sign( Concern About Meningitis Or Encephalitis)
- Immunocompromised Patients.

#### **ROLE OF NEUROIMAGING**

- CT scan is the imaging of choice in emergency room.
- → It Should Be Done If:
- 1. Acute Onset Neurodeficits/ Focal Seizure
- 2. Prolonged Seizure
- 3. Features of raised ICP.

- 3. HDST(High dose supressive therapy)
- 4. Refractory status epilepticus
- 5. H/O head trauma / VP shunt
- Should be done only after the child is stabilized

#### **ROLE OF EEG IN EMERGENCY ROOM**

 Persistent altered sensorium after clinical seizures have stopped for detection of NCSE.

Suspected herpes encephalitis.

 For assessment and monitoring of the efficacy of therapy for seizure and status epilepticus.

#### **ANTI-EPILEPTIC DRUG LEVEL**

 It should be considered when a child with epilepsy on AED prophylaxis develops prolonged seizure.

#### **PROGNOSIS**

- Prolonged status epilepticus is associated with high mortality and morbidity.
- Mortality of 28% -2 hour.
- Mortality of 50% > 24 hour.
- Long term sequelae- epilepsy , focal neurologic deficits , cognitive decline.

## **TAKE HOME MESSAGE**

1. ABC first and AED next.

2. Intubate SOS at any time

3. Mortality is due to poor airway management

4. Midazolam = lorazepam = diazepam

5. Phosphenytoin = levetiracetam = valproate.

6.Refractory status – midazolam infusion widely used.

7.EEG monitoring – NCSE, burst suppression.

8.immunotherapy

