Status Epilepticus

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Disclosures

I have no relevant disclosures with respect to this presentation

Status Epilepticus (SE)

- neurologic emergency
- incidence of 10- 61 cases/100,000 pop/yr
- worldwide incidence of 3 million cases
- significant morbidity and mortality
- important factors: age and etiology

Guidelines for the Evaluation and Management of Status Epilepticus Neurocrit Care (2012) 17:3–23

Status Epilepticus: definition

- continuous clinical and/or EEG seizure activity that lasts 5 minutes or more (other sources cite 30 minutes)
- recurrent seizure activity without recovery, defined, as returning to baseline between seizures

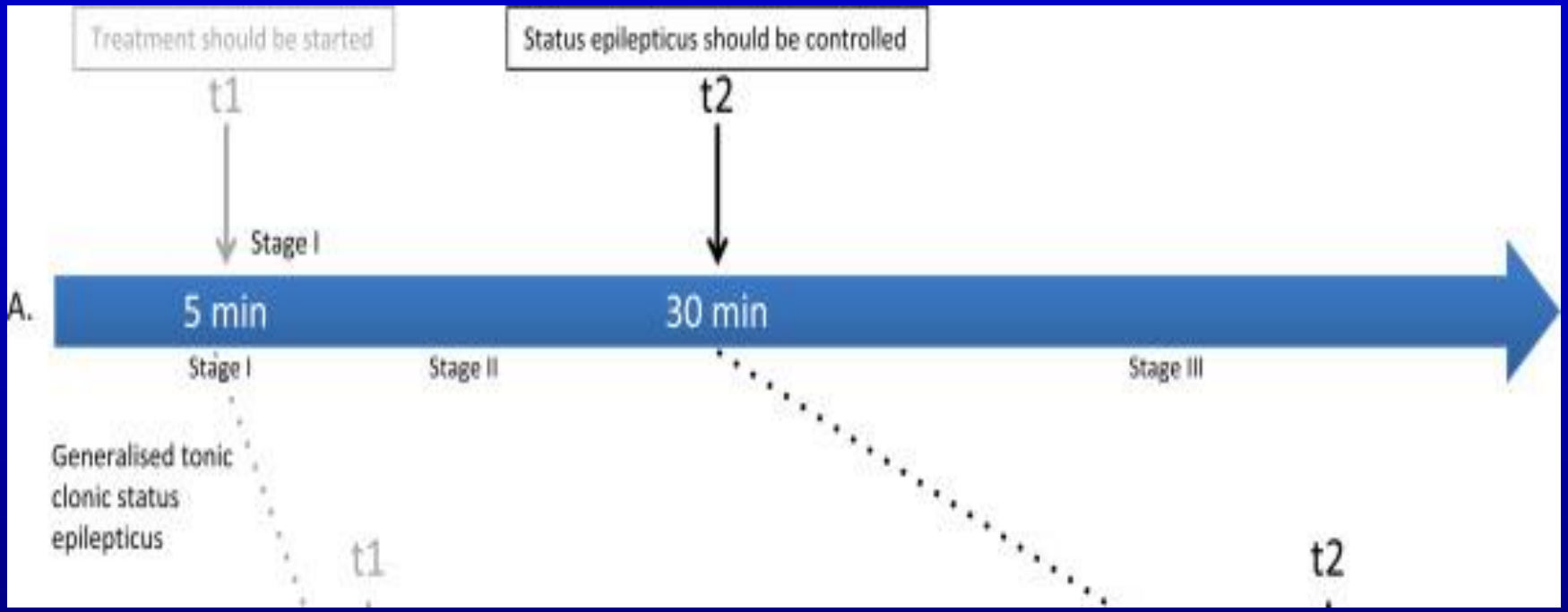
Guidelines for the Evaluation and Management of Status Epilepticus Neurocrit Care (2012) 17:3–23

Status Epilepticus: definition

Status epilepticus is a condition resulting either from the failure of the mechanisms responsible for seizure termination or from the initiation of mechanisms, which lead to abnormally prolonged seizures. (after time point t1).

It is a condition, which can have long-term consequences (after time point t2) including neuronal death, neuronal injury, and alteration of neuronal networks, depending on the type and duration of seizures

25 years of advances in the definition, classification and treatment of status epilepticus. Seizure. 2017 Jan;44:65-73



25 years of advances in the definition, classification and treatment of status epilepticus. Seizure. 2017 Jan;44:65-73

Status Epilepticus

- convulsive status epilepticus
- non-convulsive epilepticus
- refractory status epilepticus

Guidelines for the Evaluation and Management of Status Epilepticus Neurocrit Care (2012) 17:3–23

Convulsive Status Epilepticus

- convulsions associated with rhythmic jerking of the extremities (tonic-clonic)
- altered mental status
- may have post-ictal neuro deficits (Todd's Paralysis)
- focal motor SE and epilepsia partialis continua are not included

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Todd's Paralysis

- AKA post-ictal paresis
- brief period of temporary paralysis
- may be partial or complete but usually occurs on just one side of the body
- can last from ½ hour to 36 hours, (average 15 hours)
- may also affect speech and vision
- complete recovery

Nonconvulsive Status Epilepticus

- seizure activity seen on (EEG) without motor symptoms
- associated with coma (subtle status)
- not associated with coma
  - e.g. absence SE

Guidelines for the Evaluation and Management of Status Epilepticus Neurocrit Care (2012) 17:3–23

Refractory Status Epilepticus

- patients who have not responded to standard treatment regimens
- failure of 2 or 3 antiepileptic drugs
- duration of seizure activity no longer part of the definition
- may occur in 10-70% of adult patients
- morbidity and mortality

Guidelines for the Evaluation and Management of Status Epilepticus Neurocrit Care (2012) 17:3–23

Underlying Etiology of SE

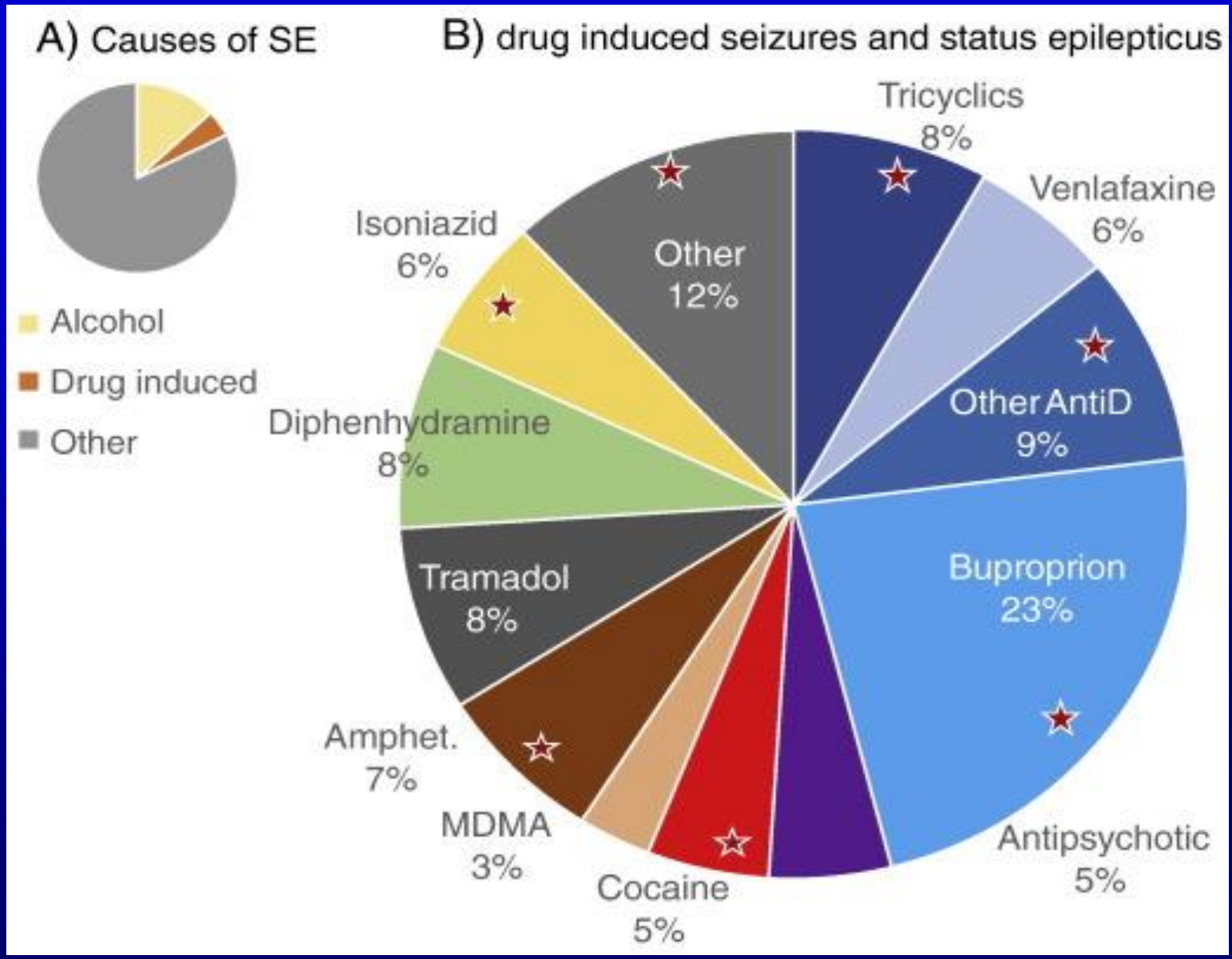
- sub-therapeutic antiepileptic drug levels
- alcohol + other substance use/abuse
- metabolic disorders
- CVA
- acute cerebral anoxia/hypoxia
- CNS infection
- brain tumour
- traumatic brain injury
- cryptogenic

Subtherapeutic Drug levels

- most common cause of SE
- non-compliance
- drug metabolism (e.g. phenytoin)
- usually more favourable outcome
- often responds to standard 1st line treatment

Alcohol + Substance Abuse/Overdose

- alcohol abuse and withdrawal generally associated with a more favourable outcome
- mortality of < 10%
- toxin related SE may have a higher mortality
- phenytoin is not useful in toxin related seizures



Drug-induced status epilepticus. **Epilepsy & Behavior Volume 49, August 2015, Pages 76-82**

Isoniazid (INH) Overdose

- pyridoxine is a necessary cofactor for production of (GABA).
- INH combines with pyridoxine, inactivates it → depletion of brain GABA
- antidote: pyridoxine
  - dose: gram per gram of ingestion
  - if unknown ingestion 5 gm empirically

Metabolic Disorders

- electrolyte imbalance, hypoglycemia, hypocalcemia, hyperglycemia
- incidence varies from 5-35%
- cause of refractory SE (20-25%)
- significant morbidity and mortality (10-35%)

Cerebrovascular Disease

- especially in the elderly
- cause of refractory SE: up to 20%
- associated with worse prognosis

Severe Acute Cerebral Anoxia/Hypoxia

- 8-13% of SE cases
- very poor prognosis
- high mortality rates: 60-80%

CNS Infection

- important cause of SE in children
- 1-2% of SE in resource poor countries
- very poor prognosis
- SE induced by encephalitis
  - often refractory to treatment
  - predictor of long-term epilepsy

Uncommon Causes of SE

- brain tumour: 2-5%
- traumatic brain injury: 0-10%
- cryptogenic: 5-15%

- more favourable outcome
- lower mortality

Other Factors Affecting Outcome

- duration of SE
  - > 1 hour: mortality 32-39.4%
  - < 1 hour: mortality 2.7-3%
- LOC on admission
- age
- extremes of age → higher mortality
  - < 1 yr
  - > 60 (45? 65?)
  - underlying etiology

Complications of Status Epilepticus

- hypoxia
- aspiration
- rhabdomyolysis
- renal failure
- pulmonary edema
- myocardial injury including Takatsubo cardiomyopathy

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Office Management of SE

- ABCs
- avoid patient injury
- check glucose!
- 1st line drugs if available
- route of administration
  - IV preferable
  - other routes (buccal, nasal, rectal)
- call 911

No IV Access

- lorazepam: 0.1 mg/kg max 4 mg
- midazolam:
  - IM: 0.2 mg/kg or 10 mg
  - Nasal/buccal: 0.2 mg/kg or 10 mg
- diazepam:
  - nasal (adult): 10 mg
  - rectal: (Peds)
    - 2-5 yr: 0.5 mg/kg
    - 6-11 yr: 0.3 mg/kg
    - > 12 yr: 0.2 mg/kg

ED Management of SE

- ABCs
- bedside glucose
- diagnostic workup
- administration of anti-seizure meds
  - emergent initial therapy
  - second-line therapy
  - treatment of refractory SE

Diagnostic Workup of SE

- CBC, Chem 7, Ca, Mg, EtOH
- anti-epileptic drug levels (if applicable)
- head CT

Further testing based on clinical presentation

- MRI
- lumbar puncture
- other blood work: INR, LFTs, VBG, inborn errors of metabolism testing

Emergent Initial Therapy

- benzodiazepines
- enhance neurotransmission of GABA at the GABA receptor
- major adverse effect: respiratory depression
  - lorazepam (IV, IM, IO)
  - midazolam (IV, IM, IO, nasal, buccal)
  - diazepam (IV, PR, IO)

Second-line Therapy

- maintenance therapy
- escalation in tx for ongoing seizures
- phenytoin or fosphenytoin
- valproate*
- levetiracetam (Keppra)*
- * special access program
  - neurology OK required
- phenobarbital

Phenytoin and Fosphenytoin

- block voltage-gated sodium channels
- not useful for toxin induced SE
- dose: 18-20 mg/kg IV (not IM)
- infusion rate:
  - phenytoin 50 mg/min
  - fosphenytoin: 150 mg/min
- adverse effects:
  - heart block with too rapid infusion
    extravasation→ tissue necrosis

Valproate

- special access program
- prolongs sodium channel inactivation and augments GABA
- equal in efficacy to phenytoin
- dose: 20-40 mg/kg
- contraindicated in pregnancy, mitochondrial disease, liver dysfunction, porphyria

Levetiracetam (Keppra)

- special access program
- binds to synaptic glycoprotein SV2A, reducing neurotransmitter release
- dose: 1500-4000 mg
- effective as phenytoin
- also been used as first line treatment

Phenobarbital

- long-acting barbiturate → binds to GABA receptor
- dose: 20mg/kg
- respiratory depression
- hypotension
- long half-life (53-118 hr)

Refractory SE

- anesthetic therapy
- inhaled anesthetics in the past
- intravenous agents
  - midazolam
  - propofol
  - pentobarbital or thiopental
  - ketamine?

Midazolam

- repeat 0.2 mg/kg bolus (up to 10)

  or

- infusion:
- 0.1 mg/kg/h to 2.9 mg/kg/h
- respiratory depression

Propofol

- activates $GABA_A$ receptors
- inhibits N-methyl-D-aspartate (NMDA) receptors
- dose:
  - 1-2 mg/kg Q 5 min until seizures stop (max 10 mg/kg)
  - initial infusion of 1.98 mg/kg/hr infusion
  - maintenance dose: 1-15 mg/kg/hr
- respiratory depression + hypotension
- propofol infusion syndrome

Propofol Infusion Syndrome

- more common in children
- prolonged infusions
- circulatory collapse
- lactic acidosis
- hypertriglyceridemia
- rhabdomyolysis

Pentobarbital or Thiopental

- short or ultra short acting barbiturates
- same adverse effects as phenobarbital
- Thiopental
  - loading dose: 1-2 mg/kg
  - maintenance dose: 1-5 mg/kg/hr
- Pentobarbital
  - loading dose: 5 mg/kg
  - maintenance dose: 1-5 mg/kg/hr

Ketamine

- N-methyl-D-asparate (NMDA) receptor antagonist
- tachycardia and hypertension
- Emergent reaction?
- Dose: 1.5 mg/kg Q 5min until seizures stop (max 4.5 mg/kg)
- Initial infusion: 1.2 mg/kg/hr, maintenance 0.3-7.5 mg/kg/hr

SE in Pregnancy

- consider eclampsia
- magnesium sulfate
- benzodiazepines
- Keppra not teratogenic

Questions