Management of Acute Generalized Seizures

UHN Toronto Western Hospital

Step 1

Initial Management: aim to quickly terminate seizures (<15 min.)

- **Lorazepam** 0.1mg/kg up to 4mg slow **IV push** ; may repeat X1 in 5 minutes
- **Midazolam** 0.2mg/kg up to 10mg **IM**
- Anti-epileptic drug (AED)
  - Start loading AED (**Levetiracetam** 60mg/kg to max 4.5g OR **Phenytoin** 20mg/kg to max 2g)
- STAT capillary glucose, serum sodium, calcium, magnesium
- Check home medication drug levels if applicable

Seizures terminated and patient waking?

YES

Seizure Workup & Determine etiology
- Consult Neurology
- CT brain
- Order routine EEG
- CSF Examination if applicable

NO

Step 2

Refractory Status Epilepticus: Terminate Seizures

Start sedative infusion and titrate up until seizures terminated OR maximum recommended dose
Consider subhairline EEG monitoring & titration to EEG burst-suppression

Seizures terminated?

NO

Increase infusion OR Start additional infusion OR Inhaled Isoflurane

YES

Sedative / Anesthetic Infusions
See over for dosing regimens and breakthrough seizure management

First choices:
- Midazolam
- Propofol

Other choices:
- Inhaled Isoflurane via AnaConDa
- Ketamine (high dose – see over)

- Consult neurology
- Intermittent EEG to rule out non-convulsive seizures
- If non-convulsive seizures documented consider neurocritical care consult or EMU staff consultation for long-term / frequent EEG monitoring

Anti-Epileptic Drugs Include But Not Limited To:

Phenytoin	Phenobarbital
Levetiracetam	Clobazam
Lacosamide	Topiramate
Valproic Acid	

Optimize Anti-Epileptic Drugs
Neurology Consult Service and Pharmacy can assist in selection and monitoring of antiepileptic drugs

Start workup for Etiology / Precipitant of Seizures
- Imaging
- CSF examination
- Investigations for toxic, metabolic and autoimmune / paraneoplastic causes

Step 3

Wait 24-24 hrs
Allow time for AEDs to reach therapeutic level

Wean Sedative Infusions
- After 24 hours seizure-free on sedation, and AEDs optimized, begin reducing sedative infusions by approximately 20% every hour and allow patient to emerge from coma

Recurrent Seizures?

NO

Patient waking up?

YES

Neurology to prescribe:
- Frequency of follow-up EEG(s)
- Ongoing workup and management

YES

NO

Return to STEP 2
(1) Increase sedative infusions until seizures terminated **AND**
(2) Add Additional AED

Routine EEG r/o non-convulsive Seizures
- Return to STEP 2 ONLY if non-convulsive seizures documented

NO seizures

Ver. 7 17/01/2023 JM Singh

Medication List

Sedative Infusions

- Midazolam
  - 0.1-0.2 mg/kg slow bolus followed by infusion at 0.05-0.2mg/kg/hr
  - Breakthrough: 0.1-0.2mg/kg IV bolus and increase infusion by 5-10 mg/hr (max 2mg/kg/hr)
- Propofol
  - 1-2mg/kg IV bolus followed by continuous infusion at 25-75 mcg/kg/min
  - Breakthrough: 1 mg/kg IV bolus and increase infusion rate by 10-20 mcg/kg/min

Other agents:

- Isoflurane
  - Administered through the AnaConDa device with MAC monitoring. Please see UHN RT policy guide
- Ketamine
  - 1-2mg/kg IV bolus (max 4.5mg/kg) followed by continuous infusion 0.5-7.0 mg/kg/hr
- Phenobarbital
  - 20 mg/kg (max 2g) IV loading dose (consider 10mg/kg loading if patient has already received loading dose of phenytoin) no faster than 50 mg/min with EKG monitoring
- Thiopental
  - 5 mg/kg IV bolus followed by continuous infusion at 1-5 mg/kg/hr
  - Breakthrough: 1/mg/kg IV bolus and increase infusion rate by 0.5-1.0 mg/kg/hr
  - Note: requires Health Canada SAP approval prior to administration.
    Consult pharmacy and see http://www.hc-sc.gc.ca/dhp-mps/acces/drugs-drogues/index-eng.php for forms.

Anti-Epileptic Drugs

- Levetiracetam (SV2A binding)
  - Load: 60mg/kg to max 4.5g IV
  - Maintenance: 1000-1500 mg enteral tube BID
- Phenytoin (Na^+ channel)
  - Load: 20mg/kg (max 2g) IV loading dose no faster than 50mg/min, EKG monitoring required,
  - Maintenance: 100mg IV q8h (~70kg patient) beginning 12 hours after initial load
- Lacosamide (Na+ channel – distinct from PHT)
  - Load: 400mg PO/enteral tube/IV
  - Maintenance: 200-400mg PO/enteral tube BID
  - *IV formulation available*
- Valproic Acid (Ca^{++} channel)
  - Load: 40mg/kg divided PO/enteral tube BID X 2 days followed by initial maintenance of 1000 mg PO/enteral tube BID
  - *IV formulation available* through Health Canada SAP only for intolerance of enteral preparation
- Phenobarbital (GABA, Glutamate, Na^+, K^+ & Ca^{++} channels)
  - Load: See sedative agents
  - Maintenance: 5mg/kg/day IV/PO/enteral tube in divided doses beginning 24 hours after initial load
- Clobazam (GABAa Agonist)
  - Load/Maintenance: 10-20mg PO/enteral tube BID
- Topiramate (GABA, AMPA / Glutamate, Na^+)
  - Load: 200-400mg PO/enteral tube followed by initial maintenance of 400-800mg PO/enteral tube in divided doses
- Perampanel (AMPA)
  - Load: 24mg on day 1, followed by 12 mg/day
  - LONG half-life (4 days)
  - Requires dose reduction with hepatic failure

Note: Consultation with a pharmacist and therapeutic drug monitoring (e.g. phenytoin, phenobarbital, and valproic acid) is recommended due to numerous drug and pharmacokinetic interactions

Experimental / Alternative Agents For Super-Refractory Status Epilepticus

Therapies that have been administered in case reports/series of super-refractory status epilepticus include:

Induced Hypothermia	Ketogenic Diet **
Immunomodulation (steroids, IVIG, PLEX, etc)	Acute Surgical Management

Consultation between Epilepsy Neurology, Neurocritical Care and Anesthesia required.

** - *Carbohydrate restriction in the context of ketogenic diet may increase the risk of Propofol Infusion Syndrome (PRIS).* It is recommended that Propofol should be reduced or discontinued with initiation of ketogenic diet.

Brophy et al. *Guidelines for the Evaluation and Management of Status Epilepticus*. Neurocrit Care (2012) 17:3.
Gerstner T. et al. *Oral rapid loading of valproic acid—An alternative to the usual saturation scheme*? Seizure. (2006) 15:8.
Koubeissi M. et a.. *Tolerability and efficacy of oral loading of levetiracetam*. Neurology. (2008) 70 (22 pt 2).
Shorvon et al. *The treatment of super-refractory status epilepticus: a critical review of available therapies and a clinical treatment protocol*. Brain (2011) 134:10 .
Silbergleit et al. *Intramuscular versus Intravenous Therapy for Prehospital Status Epilepticus*. N Engl J Med (2012) 366:591-600.

UHN Toronto Western Hospital

Ver. 6 08/2021 JM Singh