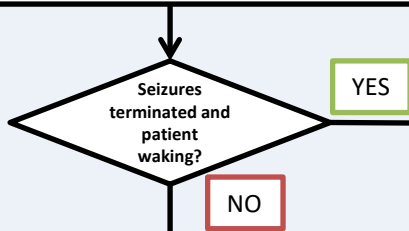


Management of Acute Generalized Seizures

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

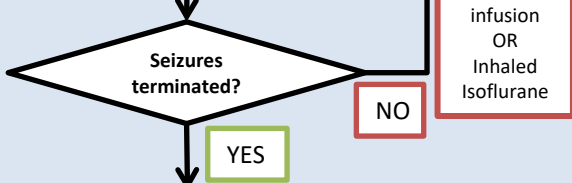
- Lorazepam 0.1mg/kg up to 4mg slow IV push ; may repeat X1 in 5 minutes
- Midazolam 0.2mg/kg up to 10mg IM
- Anti-epileptic drug (AED)
 - Start loading AED (**Levetiracetam 60mg/kg** to max 4.5g OR **Phenytoin 20mg/kg** to max 2g)
- STAT capillary glucose, serum sodium, calcium, magnesium
- Check home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



Seizure Workup & Determine etiology

- Consult Neurology
- CT brain
- Order routine EEG
- CSF Examination if applicable

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



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

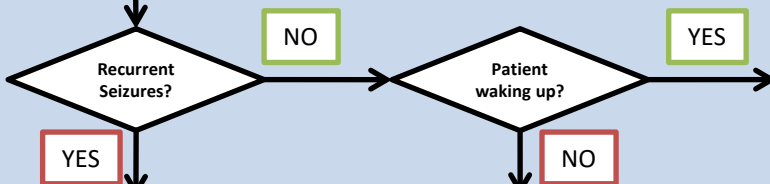
Start workup for Etiology / Precipitant of Seizures

- Imaging
- CSF examination
- Investigations for toxic, metabolic and autoimmune / paraneoplastic causes

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



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

Neurology to prescribe:

- Frequency of follow-up EEG(s)
- Ongoing workup and management

Step 1

Step 2

Step 3

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 (GABA_A 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 al. *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.

