

MGH STATUS EPILEPTICUS TREATMENT PROTOCOL

DIAGNOSIS OF STATUS EPILEPTICUS:

1) Generalized convulsive status epilepticus

Continuous convulsive seizure activity lasting > 5 mins
OR, ≥ 2 convulsive seizures without full return to baseline between seizures

2) Non-convulsive status epilepticus (NCSE)

2a) NCSE by strict electrographic criteria (adapted from *J Clin Neurophysiol* 2005; 22:79-91)

An EEG pattern lasting ≥ 10 secs and satisfying either of the following, qualifies as an electrographic seizure*:

- 1) Repetitive generalized or focal spikes, sharp-waves, spike-&-wave, or sharp-&-slow wave complexes at ≥3 Hz.
- 2) Sequential rhythmic, periodic, or quasiperiodic waves at ≥ 1 Hz & unequivocal *evolution* in frequency (gradually increases/decreases by ≥ 1 Hz), morphology, or location (gradual spread into or out of a region involving ≥ two electrodes). Evolution in amplitude alone or in sharpness without other change in morphology is not enough to satisfy evolution in morphology.

* Intracranial EEG may increase sensitivity of detecting electrographic seizures (*AnnNeurol* 2014;75(5):771-8).

2b) NCSE by electroclinical or electroradiologic criteria

Rhythmic/periodic EEG activity without evolution and with at least one of the following, qualifies as NCSE:

- 1) Benzodiazepine trial (see below) demonstrating electrographic or clinical improvement
- 2) Clear correlation between rhythmic/periodic EEG activity and clinical symptoms
- 3) CT-PET or MRI neuroimaging showing a pattern of hypermetabolism or diffusion restriction not clinically explained by another inflammatory or ischemic processes.

Benzodiazepine Trial (adapted from *Clin Neurophys* 2007;118:1660-1670)

Indication: rhythmic or periodic epileptiform discharges on EEG with concurrent neurological impairment

Monitoring required: EEG, pulse ox, blood pressure, EKG, respiratory rate with dedicated nurse

Give sequential small doses of rapidly acting, short-duration benzodiazepine (e.g., midazolam at 1mg/dose), or a non-sedating IV anticonvulsant (e.g., levetiracetam, valproic acid, fosphenytoin, or lacosamide). Between doses, repeat clinical & EEG assessment. Trial is stopped for any of the following:

- 1) Persistent resolution of the EEG pattern (and examination repeated).
- 2) Definite clinical improvement.
- 3) Respiratory depression, hypotension, or other adverse effect.
- 4) Maximum allowed dose is reached (e.g., 0.2 mg/kg midazolam)

Interpretation: POSITIVE test (i.e., seizure) if the ictal EEG pattern resolves and there is improvement in the patient's clinical state and/or appearance of previously absent normal EEG patterns (e.g., return of posterior dominant rhythm). EQUIVOCAL test if the ictal EEG pattern improves but the patient does not.

TREATMENT OF STATUS EPILEPTICUS:

1) Generalized convulsive status epilepticus: Use protocol on next page

2) Non-convulsive status epilepticus by electrographic, electroclinical, or electroradiologic criteria: No strong evidence to guide treatment; decision must be made on a case-by-case basis, weighing potential benefits of aggressive treatment (e.g. intubation and high dose anesthetics) vs potential risks. Benefits: rapid termination of seizures, prevention of seizure-induced secondary brain injury. Risks: side effects of anesthetics (e.g. hypotension, propofol infusion syndrome), prolonged mechanical ventilation and ICU course, with attendant risks of infection.

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MGH STATUS EPILEPTICUS TREATMENT PROTOCOL

ANTI-CONVULSANT THERAPY

CONCURRENT MANAGEMENT

1st line (seizures ongoing for 5-10 mins) STATUS EPILEPTICUS

Lorazepam 4mg IV (push over 2mins),
If szs not controlled within 5mins, repeat 4mg IV x 1
If no IV access:
Diazepam 20mg rectally (using IV sol'n)
or, **Midazolam** 10mg intranasal/buccal/IM (using IV sol'n).

If seizures persist

2nd line (10-30 mins)

Choose from the following (may be used in combination):

- 1) **Valproic acid** 40mg/kg IV (max rate 6mg/kg/min)
- 2) **Levetiracetam** 20mg/kg IV (max rate 100mg/min)
- 3) **Phenobarbital** 20mg/kg IV (max rate 50-75mg/min)
- 4) **Fosphenytoin** 20mg PE/kg IV (max rate 150mg PE/min)
or, **Phenytoin** 20 mg/kg IV (max rate 25-50mg/min)
If no effect, can give additional dose:
Fosphenytoin 10mg PE/kg IV or **Phenytoin** 10 mg/kg IV
- 5) **Lacosamide** 400mg IV over 5 min (need EKG pre/post)

If seizures persist

3rd line (30 - 60 mins)

REFRACTORY STATUS EPILEPTICUS

Choose from the following (may be used in combination):

- 1) **Midazolam** (good choice if BP unstable)
Load 0.2mg/kg IV.
Repeat q5mins until szs stop (max load 2mg/kg)
Maint. infusion 0.1- 2 mg/kg/hr
- 2) **Propofol**
Load 2mg/kg IV.
Repeat q5mins until szs stop (max load 10mg/kg)
Maint. infusion 1-10mg/kg/hr (< 5 if tx > 48hrs)

Titrate infusion to stop seizures or induce burst suppression (currently no evidence to guide best depth / duration of suppression).

Use IV fluids and pressors to support BP (anesthetic doses required to tx refractory SE are much higher than doses used for routine sedation).

Once sz-free for >24-48hrs, start slow taper of 3rd line meds over 24hrs, while maintaining high therapeutic levels of AEDs to avoid recurrent szs. Continue EEG monitoring until sz-free off 3rd line meds for >24 hrs, to monitor for recurrence of non-convulsive szs or NCSE.

4th line (> 72 hrs)

SUPER-REFRACTORY STATUS EPILEPTICUS

Choose from the following (may be used in combination):

- 1) Repeat burst suppression for 24-48hrs
- 2) Add other AEDs (consider CBZ, TOP, not listed above)
- 3) IV magnesium (bolus 4g, then infuse 2-6g/hr)
- 4) Ketamine
Load w/ 1.5mg/kg IV
Repeat q5mins until szs stop (max load 4.5mg/kg)
Maint. infusion at 1.2-7.5mg/kg/hr
- 5) Pentobarbital (titrate to burst suppression)
Load 5mg/kg IV (max rate 50mg/min).
Repeat q5mins until szs stop (max load 15mg/kg)
Maint. infusion 1-10 mg/kg/hr
- 6) IV pyridoxine (200mg/day)
- 7) Immune modulation
Steroids (methylprednisolone 1g IV qd x 3-5 days)
and/or IVIG (0.4g/kg/day x 5 days)
and/or plasma exchange (every other day x 5-7 days)
- 7) Ketogenic diet
- 8) Therapeutic hypothermia
- 9) Electroconvulsive therapy (ECT)

- 1) Airway, Breathing, Circulation
- 2) Vital signs (cont. monitoring): HR, BP, O2, EKG
- 3) Finger stick blood glucose
If glucose low/unk: give thiamine 100mg IV, then D50 (50mL IV)
- 4) Obtain IV access (≥ 2 IVs)
- 5) If febrile, tx w/ anti-pyretics, cooling, consider Abx
- 6) Labs: CBC, BMP, Ca, Mg, Phos, LFTs, troponin, ABG, tox screen (blood & urine), blood cxs (esp if febrile), AED levels (in pts w/ prior hx of epilepsy), HCG (females)

Check anti-convulsant levels post-load and re-bolus if needed (see box below for therapeutic levels):

PHT, VPA, PHB - send level 1hr after load
FOS-PHT - send level 2hrs after load

INTUBATE.
Start continuous EEG monitoring

Continue maintenance anticonvulsants and adjust doses for therapeutic level:

MAINTENANCE DOSES & THERAPEUTIC LEVELS

- 1) **Valproic acid** 30-60 mg/kg/day (BID) 70-120 ug/mL
- 2) **Levetiracetam** 2-4 g/day (BID) 25-60 mg/L
- 3) **Phenobarbital** 1-4mg/kg/day (BID) 20-50 mg/mL
- 4) **Fosphenytoin** 5-7 PE/kg/day (TID) 15-25 ug/mL* (total),
1.5-2.5 ug/mL (free)
or, **Phenytoin** 5-7 mg/kg/day (TID) "
- 5) **Lacosamide** 400-600mg/day (BID) Unknown

* Total dilantin level should be corrected for patient's renal function and albumin:
<http://www.mdcalc.com/phenytoin-dilantin-correction-for-albumin-or-renal-failure/>
If there is significant renal dysfunction or hypoalbuminemia, check a free dilantin level.

Continue workup to determine underlying cause of SE
1) Neuroimaging - brain MRI (preferred) or head CT
2) Lumbar puncture - evaluate for infection, inflammatory, autoimmune causes

Treat underlying cause of status epilepticus.

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10) Neurosurgical treatment (eg, resection of focal lesion)

11) TMS

No strong evidence to guide best treatment here.