UNM Neonatal & Pediatric Status Epilepticus Pathway

Indication: neonates - 18 years with:
- seizure > 5 minutes in duration OR
- recurrence of seizure without return to baseline

### Stabilization Phase

- **POC Glucose**

Order if applicable:
- iStat (VBG and electrolytes)
- Chem10
- CBC
- Calcium (total and ionized)
- Magnesium
- Head CT or MRI

- Oxygen
- Utox
- LP (especially if <2 years, immune suppressed, or recent antibiotics)
- Blood cx, UA, Urine cx
- AED Levels – valproic acid, phenytoin, phenobarbital, levetiracetam

### First Line Therapy

<table>
<thead>
<tr>
<th>Route</th>
<th>Drug</th>
<th>Dose</th>
<th>Maximum</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>IntraVENOUS</td>
<td>lorazepam</td>
<td>0.1 mg/kg</td>
<td>4 mg</td>
<td></td>
</tr>
<tr>
<td>IntraNASAL</td>
<td>midazolam</td>
<td>0.2 mg/kg</td>
<td>10 mg</td>
<td></td>
</tr>
<tr>
<td>IntraMUSCULAR</td>
<td>midazolam</td>
<td>• 5 mg if 13-40 kg • 10 mg if &gt; 40 kg</td>
<td>10 mg</td>
<td></td>
</tr>
</tbody>
</table>

If seizure continues give 2nd benzodiazepine 5 minutes from 1st dose

**NOTIFY NURSE TO DRAW UP 2ND LINE MEDS FROM PIXIS**

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<tr>
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<th>Dose</th>
<th>Maximum</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>IntraVENOUS/IntraOSSEOUS *preferred agent</td>
<td>lorazepam</td>
<td>0.1 mg/kg</td>
<td>4 mg</td>
<td></td>
</tr>
<tr>
<td>IntraMUSCULAR *risk for stacking</td>
<td>midazolam</td>
<td>• 5 mg if 13-40 kg • 10 mg if &gt; 40 kg</td>
<td>10 mg</td>
<td></td>
</tr>
</tbody>
</table>

### Second Line Therapy

<table>
<thead>
<tr>
<th>Route</th>
<th>Drug</th>
<th>Dose</th>
<th>Maximum</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>IntraVENOUS</td>
<td>Levetiracetam</td>
<td>60 mg/kg</td>
<td>4500 mg</td>
<td>N/A</td>
</tr>
<tr>
<td>IntraVENOUS</td>
<td>Fosphenytoin</td>
<td>20 mg/kg</td>
<td>1500 mg</td>
<td>2 hours after Load</td>
</tr>
<tr>
<td>IntraVENOUS</td>
<td>Valproic Acid</td>
<td>40 mg/kg</td>
<td>3000 mg</td>
<td>2 hours after Load</td>
</tr>
<tr>
<td>IntraVENOUS</td>
<td>Phenobarbital</td>
<td>20 mg/kg</td>
<td>1000 mg</td>
<td>2 hours after Load</td>
</tr>
</tbody>
</table>

### If clinical seizure continues

- Consult Pediatric Neurology
- Consult PICU
- Order STAT continuous EEG
- Proceed to Refractory Pathway
UNM Neonatal & Pediatric Status Epilepticus Pathway
Refractory Status Epilepticus

**MIDAZOLAM INFUSION**

- **Bolus:** 0.2 mg/kg
  - Max 10 mg
  - Start infusion at 0.1 mg/kg/h

  **If seizure continues**

- **Bolus:** 0.15 mg/kg AND Increase infusion rate by 0.05-0.1 mg/kg/h [Repeat bolus and rate-increase q 15 minutes until seizure cessation]

  **Notes:**
  - If a rate of 1 mg/kg/h fails to control seizures for >30 minutes, advance to next agent
  - No max rate reported; note that rates above 50 mg/h OR 2 mg/kg/h have been used in adults

  **Seizure cessation**

  **Continue infusion until 24-48 hours seizure-free**

- **WEAN:**
  - Decrease rate by 0.05 mg/kg/h q 6 hours

- **Transfer to PICU if seizure continues**
  - Start midazolam infusion

- **IF SEIZURE CONTINUES**

  **PENTOBARBITAL INFUSION**

- **Bolus:** 5 mg/kg over 30 minutes
  - Repeat as needed to burst suppression IBI 10 seconds, up to 30 mg/kg (6 boluses total)

  **ONCE BURST SUPPRESSION IS ACHIEVED:**
  - Start infusion at 1.0 mg/kg/h
  - Stop midazolam infusion

  **If seizure continues**

- **Increase infusion by 0.5 mg/kg/h as needed to maintain BS**

  **Notes:**
  - Monitor serum levels
  - Max rate: 5 mg/kg/h
  - If IBI becomes prolonged, hold infusion until IBI < 20 seconds, then resume infusion at dose 0.5 mg/kg/h less than previous dose

  **Seizure cessation**

  **Continue infusion until 48 hours seizure-free**

- **WEAN:**
  - Decrease rate by 0.5 mg/kg/h q 6 hours
### KETAMINE INFUSION
(Continue midazolam infusion, see below)

- **IV Bolus**: 2.5 mg/kg x 2 q 5 minutes
- **Start IV infusion at 0.5 mg/kg/h**
- **Decrease midazolam infusion to 0.05 mg/kg/h q 6 h**

- **Increase rate by 0.5 mg/kg/h every 15 minutes as needed to achieve resolution of clinical and/or electrographic seizures**
- **Continue Ketamine infusion until 48 hours seizure-free**
- **Wean by 0.5 mg/kg/h q 6 h**

**Notes**
- Max rate: 3.5 mg/kg/h
- Doses as high as 10 mg/kg/h have been used in adults

**Reference:**

### LACOSAMIDE BOLUS

**Weight <40 kg**
- **IV Bolus**: 10 mg/kg
- **Maintenance**: 10 mg/kg/day div BID (start 12 hours later)

**Weight >40 kg**
- **IV Bolus**: 400 mg
- **Maintenance**: 200 mg bid

**Notes**
- Max maintenance dose: 14 mg/kg/day
- Max infusion rate: 60 mg/min

**Reference:**
4. Hofler I, Intravenous lacosamide in status epilepticus and seizure clusters, Epilepsy (2011)

### PROPOFOL INFUSION

- **IV Bolus**: 3 mg/kg
- **Start infusion at 50 mcg/kg/min**
- **Stop midazolam infusion**

- **Increase rate by 8 mcg/kg/min every 15 minutes as needed to achieve burst suppression (goal IBI 10 seconds)**
- **Once burst suppression is achieved → continue infusion for 24 hours → wean to 50% max rate for 6-12 hours → wean to 25% max rate for 6-12 hours → stop**

- **Monitor ABG, LFTs, CK q 6 x24 hours, then q12**

**Notes**
- Max duration: 48 hours
- Max dose: 300 mcg/kg/min
- **Contraindications**: ketogenic diet, metabolic disorder, egg allergy

**Reference:**
1. Phelps S, Pediatric Injectable Drugs, 2013

### VALPROIC ACID INFUSION

- **IV Bolus**: 20-40 mg/kg, then start infusion
  - **Obtain level 2 hours after rate increase**

- **Start infusion**
  - **Rate**: 1 mg/kg/h
  - **With PHENObarbital or phenytoin, rate**: 2 mg/kg/h
  - **With PENTObarbital, rate**: 4 mg/kg/h

- **Increase rate by 1 mg/kg/h as needed to achieve serum concentration (80-100 mg/L)**
  - **Obtain level 2 hours after rate increase**

**Notes**
- Max rate: 6 mg/kg/h
- Wean: 1 mg/kg/h q 2 hours
- Contraindicated if suspected or known metabolic disease, caution in children <2 years

- **Monitor CBC, CMP daily**

**Reference:**
2. Hovinga CA, Use of intravenous valproate in three pediatric patients with nonconvulsive or convulsive status epilepticus, Ann Pharmacother (1999)
3. Phelps S, Pediatric Injectable Drugs, 2013

### TOPIRAMATE BOLUS

- **Enteral Bolus**: 5 mg/kg
- **Maintenance**: 5 mg/kg/day div BID (start 12 hours later)

**Notes**
- **CAUTION** if patient has acidosis
- Seizure-free after 24 hours: Continue 5 mg/kg/day div BID
- Seizures continue after 24 hours: Increase dose by 5 mg/kg/day q day
- Max dose reported in children: 25 mg/kg/day
- Max dose reported in adults: 1600 mg/day

- **Monitor BMP daily**

**Reference:**
UNM Pediatric Status Epilepticus Pathway
Super refractory status epilepticus treatment options

IMMUNOTHERAPY

METHYLPREDNISONE
- 30 mg/kg/day IV x 3 days

Notes:
- Max: 1 gram/day
- Consider antiviral/antibiotic agents if infectious studies pending

IMMUNOGLOBULINS
- 1 gm/kg x 2 days

Notes:
- Ensure all auto-antibody/infectious titers are drawn prior to administration

PLASMA EXCHANGE
- 5 exchanges
- Frequency: every other day

Notes:
- Ensure all auto-antibody/infectious titers are drawn prior to administration

If an autoimmune or paraneoplastic etiology is confirmed and patient is not responding to above treatments, consider rituximab or cyclophosphamide.

Reference:
Abend N, et al. Status epilepticus and refractory status epilepticus management, Semin Ped Neurol (2014)

KETOGENIC DIET

Step 1: Draw Screening Labs
- CBC
- CMP
- Mg and Phos
- Plasma acyl/carnitine profile
- Urine organic acids
- Plasma amino acids
- Free and total carnitine
- 25-hydroxy vitamin D3
- Zn and Se

Step 2: Develop a Feeding Plan
- Estimate calorie needs:
  - For intubated patients: Use the BMR (see below)
  - For extubated patients: Use the BMR x 1.2-1.4
- Estimate fluid needs:
  - 0-10 kg: 100 mL/kg/day
  - 10-20 kg: 1000 mL + 50 mL/kg/day
  - 20-40 kg: 1500 mL + 20 mL/kg/day
  - >40 kg: use adult fluid needs
- Determine starting ratio:
  - <18 months: Initiate at 3:1 ratio and adjust as needed
  - >18 months: Initiate at 4:1 ratio and adjust as needed
- Determine formula recipe:
  - Ketocal 4:1 liquid is 1.5 kcal/mL
  - Ketocal 4:1 or 3:1 powder is 7 kcal/g
  - (Displacement: 1 mL/g)

Step 3: Diet Initiation
- Remove all dextrose from fluids
- Change all medications to low-carbohydrate forms
- Slowly advance continuous feeds to goal and condense feeds further as tolerated

Step 4: Diet Monitoring
- BMP, Mg, Phos daily
- UA q8hrs until 4+ ketones then q12hrs
- Blood glucose q4hrs until 4+ ketones then q8hrs
- CO2 level
- If on carbonic anhydrase inhibitor
  - 16
  - 1 mEq/kg
  - 13-15
  - 2 mEq/kg
  - <12
  - 3 mEq/kg

Step 5: Discharge Planning
- If weaning diet, can decrease by 0.5:1 ratio every week until negative urine ketones then resume a regular diet
- If continuing diet, family needs a gram scale, urine ketone strips, glucometer, extensive dietitian education, and close follow-up as an outpatient

Reference:

Last Updated August 4, 2020 by Danny Rogers MD (Department of Neurology) and Julie Tuccillo PharmD (Department of Pharmacy)
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