UNM Neonatal & Pediatric Status Epilepticus Pathway

Indication: neonates - 18 years with:

- seizure > 5 minutes in duration OR
- recurrence of seizure without return to baseline

REFERENCES:

[1]Glauser T, et al. Treatment of Convulsive Status Epilepticus in Children and Adults, *Epilepsy Currents* (2016)

[2]Alford E, et al. Treatment of Generalized Convulsive Status Epilepticus in Pediatric Patients, *J Pediatr Pharmacol Ther* (2015)

Time from seizure onset 0-5 minutes

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

5-20 minutes

First Line Therapy

Did patient already receive appropriate 1st dose of benzodiazepine?

No / Yes

Route	Drug	Dose	Maximum
IntraVENOUS	lorazepam	0.1 mg/kg	4 mg
IntraNASAL	midazolam	0.2 mg/kg	10 mg
IntraMUSCULAR	midazolam	• 5 mg if 13-40 kg • 10 mg if > 40 kg	10 mg

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

NOTIFY NURSE TO DRAW UP 2ND LINE MEDS FROM PIXIS

Route	Drug	Dose	Maximum
IntraVENOUS/ IntraOSSEOUS *preferred agent	lorazepam	0.1 mg/kg	4 mg
IntraMUSCULAR *risk for stacking	midazolam	• 5 mg if 13-40 kg • 10 mg if > 40 kg	10 mg

20-40 minutes

Second Line Therapy

If clinical seizure continues

Route	Drug	Dose	Maximum	Level
IntraVENOUS	Levetiracetam	60 mg/kg	4500 mg	N/A
IntraVENOUS	Fosphenytoin	20 mg/kg	1500 mg	2 hours after Load
IntraVENOUS	Valproic Acid **NOT if metabolic disease** **Caution < 2 years of age**	40 mg/kg	3000 mg	2 hours after Load
IntraVENOUS	Phenobarbital **1st line for 0-1 month old**	20 mg/kg	1000 mg	2 hours after Load

>40 minutes

If clinical seizure continues

- ❑ Consult Pediatric Neurology
- ❑ Consult PICU
- ❑ Order STAT continuous EEG
- ❑ Proceed to Refractory Pathway

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Refractory Status Epilepticus

REFERENCES:

1. Brophy GM, et al. Guidelines for the evaluation and management of status epilepticus *Neurocritical Care* (2012)
2. Morrison G, et al. High-dose midazolam therapy for refractory status epilepticus in children. *Intens Care Med* (2006)
3. Abend NS and Loddenkemper T. Pediatric Status Epilepticus Management. *Current Opinion in Pediatrics* (2014)
4. Phelps S, Pediatric Injectable Drugs, 2013

40 minutes from seizure onset

TRANSFER TO PICU if seizure continues
Start midazolam infusion

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

WEAN:

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

If seizure recurs

Seizure cessation

Continue infusion until 24-48 hours seizure-free

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

WEAN:

- Decrease rate by 0.5 mg/kg/h q 6 hours

Seizure cessation

Continue infusion until 48 hours seizure-free

UNM Pediatric Status Epilepticus Pathway

Super refractory status epilepticus treatment options

KETAMINE INFUSION

(Continue midazolam infusion, see below)

- IV Bolus 2.5 mg/kg x2 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:
- Ilvento L, et al. Ketamine in refractory convulsive status epilepticus in children avoids endotracheal intubation *Epilepsy and Behavior* (2015)
- Gaspard N, et al. Intravenous ketamine for the treatment of refractory status epilepticus: a retrospective multicenter study, *Epilepsia* (2013)

LACOSAMIDE BOLUS

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

Weight >40 kg[5]
- IV Bolus: 400 mg
- Maintenance: 200mg bid

Notes
- Max maintenance dose: 14 mg/kg/day[2-4]
- Max infusion rate: 60 mg/min[6]

Reference:
- [2]Grosso S, et al. Lacosamide in children with refractory status epilepticus. A multicenter Italian Experience, *European Journal of Paediatric Neurology* (2014)
- [3]Poddar K, et al. Intravenous Lacosamide in Pediatric Status Epilepticus: An Open-Label Efficacy and Safety Study. *Pediatric Neurology* (2016)
- [4]Arkilo D, et al. Clinical experience of intravenous lacosamide in infants and young children. *European Journal of Paediatric Neurology* (2016)
- [5]Phelps S, Pediatric Injectable Drugs, 2013
- [6]Hofler J, Intravenous lacosamide in status epilepticus and seizure clusters, *Epilepsia* (2011)

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:
- Akyildiz BN, et al. Treatment of pediatric refractory status epilepticus with topiramate, *Childs Nerv Syst* (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:
- Phelps S, Pediatric Injectable Drugs, 2013
- Rossetti AO, et al. Propofol treatment of refractory status epilepticus: a study of 31 episodes, *Epilepsia* (2004)
- Van Gestel JP, et al. Propofol and thiopental for refractory status epilepticus in children, *Neurology* (2005)

VALPROIC ACID INFUSION

- IV Bolus: 20-40 mg/kg, then start infusion
  - ❑ Obtain level 1 hour after bolus
- 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:
- Uberall R, et al. Intravenous valproate in pediatric epilepsy patients with refractory status epilepticus *Neurology* (2000)
- Hovinga CA, Use of intravenous valproate in three pediatric patients with nonconvulsive or convulsive status epilepticus, *Ann Pharmacother* (1999)
- Phelps S, Pediatric Injectable Drugs, 2013

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 Neur* (2014)

KETOGENIC DIET

Step 1: Draw Screening Labs	Step 2: Develop a Feeding Plan	Step 3: Diet Initiation	Step 4: Diet Monitoring	Step 5: Discharge Planning
-CBC -CMP -Mg and Phos -Plasma acylcarnitine profile -Urine organic acids -Plasma amino acids -Free and total carnitine -25-hydroxy vitamin D3 -Zn and Se	Estimate caloric 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: 1000mL + 50mL/kg/day 20-40 kg: 1500mL + 20mL/kg/day >40kg: 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: 1mL/g)	Remove all dextrose from fluids Change all medications to low-carbohydrate forms Slowly advance continuous feeds to goal and condense feeds further as tolerated	BMP, Mg, Phos daily UA q8hrs until 4+ ketones then q12hrs Blood glucose q4hrs until 4+ ketones then q8hrs CO2 level / Bicitra dosing (split BID): If on carbonic anhydrase inhibitor — 1 mEq/kg 16 — 1 mEq/kg 13-15 — 2 mEq/kg <12 — 3 mEq/kg Blood sugar / Intervention: < 40 mg/dL (with autonomic instability, jitteriness, sweating, dizziness or pallor) — 1. Give 15-30 mL of juice PO (or 3-5 oz unflavored Pedialyte via tube) 2. Wait 15 min & recheck blood sugar levels. If <40 mg/dL give an additional 15 mL juice (or 3 oz Pedialyte) & recheck blood sugar until >40 mg/dL	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:
Farias-Moeller R, et al. A practical approach to ketogenic diet in the pediatric intensive care unit for super-refractory status epilepticus, *Neurocrit Care* (2017)

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