Status Epilepticus: Refractory Management

Associated Power Plans: PICU Status Epilepticus

Children's Mercy KANSAS CITY | Evidence Based Practice

Inclusion criteria:
- Patients > 1 month of age with:
  - Continuous or recurrent seizures lasting > 60 minutes **-AND-**
  - Located in ICU or ED care setting

Exclusion criteria:
- Patients presenting after a seizure that is now resolved (refer to other clinical pathway, if applicable):
  - Seizure: First, Non-Febrile
  - Seizure: Febrile

Appropriate initial management:
- Includes treatment with at least three adequately dosed anti-seizure medications:
  - At least one benzodiazepine **-AND-**
  - Loading doses of two additional anti-seizure medications

Seizure first aid / stabilization:
- Monitor airway, breathing, circulation
- Anticipate need for additional support
  - Intubation
  - Vasopressors
- Initiate continuous EEG
- Continue timing and observation of seizure

Labs for consideration:
- CBC, BMP, ionized calcium, magnesium, POC glucose
- Hepatic function
- AED levels
- Complete toxicology screen
- Infectious workup:
  - Cultures (blood, urine, respiratory if indicated)
  - Respiratory panel (RP) PCR
  - Urinalysis - *for screening criteria, refer to UTI Clinical Pathway*
  - LP (cell count, culture, glucose, protein, HSV 1/2 PCR) *especially if < 2 years, immunosuppressed, or recent antibiotic use*

Imaging for consideration:
- MRI (seizure protocol)
- Non-contrast head CT *if MRI not available or concern for bleed*

Communication strategies:
- Ongoing conversation between ICU, Neurology and Epilepsy is required throughout dose escalation
- Attending to attending conversation should occur each morning after 1000 to discuss goals for the day
  - Primary attending to page Epilepsy Consult via web on call
- Provide frequent updates to parent/caregiver regarding treatment plan

Patient meeting inclusion criteria

Did patient receive appropriate initial management?

No → Refer to Status Epilepticus: Initial Management Clinical Pathway AND Contact Neurology to discuss rapid escalation of therapy

Yes

- Continue seizure first aid / stabilization while initiating next-line treatment
- Consider additional labwork and/or imaging if not previously obtained

Special Considerations

Initiate IV Midazolam Bolus/Infusion
(diluted in NS if patient on ketogenic diet)

Loading dose: 0.2 mg/kg (max 10 mg)
Continuous IV infusion: 0.2 mg/kg/hr
Titration: Increase infusion by 0.1 mg/kg/hr every **15 - 20 minutes**. *Each increase should be preceded by a bolus of 0.1 - 0.2 mg/kg.*
- Communication strategies
- Continue to escalate midazolam infusion until goals of therapy have been achieved or a secondary agent is initiated

Consider adding second agent when:
- Time: 4 hours and still escalating midazolam without adequate response
- Dose: 0.8 mg/kg/hr and still escalating midazolam without adequate response
- Usual upper dose threshold is 2 mg/kg/hr
- Increasing adverse effects of midazolam (e.g., hypotension)

Are you adding a second agent?

No →
- Maintain seizure control or burst suppression for 24-72 hours in consultation with general neurology / epilepsy
- Continue continuous EEG monitoring
- Discuss maintenance therapy and timing of weaning with General Neurology / Epilepsy

Weaning considerations

Yes

Pentobarbital | Ketamine

Does patient continue to seize?

No → (same as above)

Yes

Contact Epilepsy for additional recommendations

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Inclusion criteria:
- Patients > 1 month of age with:
  - Continuous or recurrent seizures lasting > 60 minutes
  - **-AND-**
  - Located in ICU or ED care setting

Exclusion criteria:
- Patients with liver failure
- Patients presenting after a seizure that is now resolved (refer to other clinical pathway, if applicable):
  - Seizure: First, Non-Febrile
  - Seizure: Febrile

Special considerations:
- Use with caution in patients < 1 year of age due to immaturity of liver and kidneys
- Use with caution in patients with renal dysfunction, as this may increase the risk of propylene glycol toxicity
- Avoid use in patients with liver failure; use with caution in patients with liver dysfunction
- Closely monitor for extravasation as drug may be irritant

Communication strategies:
- Ongoing conversation between ICU, Neurology and Epilepsy is required throughout dose escalation
- Attending to attending conversation should occur each morning after 1000 to discuss goals for the day
  - Primary attending to page Epilepsy Consult via web on call
- Provide frequent updates to parent/caregiver regarding treatment plan

Side effects:
- Hypotension
- Bradycardia
- Hypoventilation
- Respiratory depression
- Ileus

Signs of propylene glycol toxicity:
- Lactic acidosis
- Acute renal failure
- Osmolar gap
- Arrhythmias
- Hemolysis
- Refractory hypotension

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Pentobarbital

Special Considerations

- **Loading dose:** 5 mg/kg
- **Continuous IV infusion:** 1 mg/kg/hr
- Remain on midazolam, may begin weaning midazolam once burst suppression achieved

Has burst suppression been achieved within 30 min?

Yes

No

- **Bolus:** 2 - 3 mg/kg **every 15 - 30 min**
- **Titration:** Increase pentobarbital infusion: 0.5 mg/kg/hr **every 60 min** *(every other bolus to avoid over-suppression)*
- Reassess every 30 minutes
- Communication strategies

Have goals of therapy been achieved?

Yes

- Maintain burst suppression for 36-72 hours in consultation with General Neurology / Epilepsy
- Monitor for side effects and signs of propylene glycol toxicity
- Discuss maintenance therapy and timing of weaning with General Neurology / Epilepsy

No

Has rate of 5 mg/kg/hr been reached?

No

Yes

Contact Epilepsy for additional recommendations

Weaning considerations

Status Epilepticus: Refractory Management Clinical Pathway

Additional References

Almohaish, S., Tesoro, E. P., & Brophy, G. M. (2024). Status epilepticus: An update on pharmacological management. *Semin Neurol*, *44*(3), 324-332. https://doi.org/10.1055/s-0044-1785503

Vasquez, A., Farias-Moeller, R., & Tatum, W. (2019). Pediatric refractory and super-refractory status epilepticus. *Seizure*, *68*, 62-71. https://doi.org/10.1016/j.seizure.2018.05.012

Contact: EvidenceBasedPractice @cmh.edu

Link to synopsis and references

Last Updated: 03/14/2025

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Inclusion criteria:
- Patients > 1 month of age with:
  - Continuous or recurrent seizures lasting > 60 minutes
  -AND-
  - Located in ICU or ED care setting

Exclusion criteria:
- Patients presenting after a seizure that is now resolved (refer to other clinical pathway, if applicable):
  - Seizure: First, Non-Febrile
  - Seizure: Febrile

Special considerations:
- Use with caution in patients with known or suspected heart failure
- Use with caution in patients with increased intracranial pressures

Communication strategies:
- Ongoing conversation between ICU, Neurology and Epilepsy is required throughout dose escalation
- Attending to attending conversation should occur each morning after 1000 to discuss goals for the day
  - Primary attending to page Epilepsy Consult via web on call
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Side effects:
- Increased or decreased BP, HR
- Arrhythmia
- Respiratory depression
- Increased secretions
- Laryngospasm

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Ketamine

Special Considerations

- **Loading dose:** 2 - 3 mg/kg
- **Continuous IV infusion:** 15 mcg/kg/min
- Remain on midazolam, may consider weaning midazolam once adequate control achieved and maintained for a minimum of 12 hours
  - Consider remaining on low dose midazolam to prevent emergence delirium

Does seizure continue 30 min after intervention?

No

Yes

Bolus and titrate every 30 minutes
- **Bolus:** 2 mg/kg **every 30 min**
- **Titration:** Increase ketamine infusion: 10 mcg/kg/min **every 30 min**
- Reassess every 30 minutes
- Communication strategies

Have goals of therapy been achieved?

Yes

- Maintain seizure control for 36-72 hours in consultation with General Neurology / Epilepsy
- Monitor for side effects
- Discuss maintenance therapy and timing of weaning with General Neurology / Epilepsy

Weaning considerations

No

Has rate of 60 mcg/kg/min been reached?

No

Yes

Contact Epilepsy for additional recommendations

Status Epilepticus: Refractory Management Clinical Pathway

Additional References

Fang, Y., & Wang, X. (2015). Ketamine for the treatment of refractory status epilepticus. *Seizure*, *30*, 14-20. https://doi.org/10.1016/j.seizure.2015.05.010

Jacobwitz, M., Mulvihill, C., Kaufman, M. C., Gonzalez, A. K., Resendiz, K., MacDonald, J. M., Francoeur, C., Helbig, I., Topjian, A. A., & Abend, N. S. (2022). Ketamine for management of neonatal and pediatric refractory status epilepticus. *Neurology*, *99*(12), e1227-e1238. https://doi.org/10.1212/wnl.0000000000200889

Rosati, A., Ilvento, L., L'Erario, M., De Masi, S., Biggeri, A., Fabbro, G., Bianchi, R., Stoppa, F., Fusco, L., Pulitanò, S., Battaglia, D., Pettenazzo, A., Sartori, S., Biban, P., Fontana, E., Cesaroni, E., Mora, D., Costa, P., Meleleo, R.,...Guerrini, R. (2016). Efficacy of ketamine in refractory convulsive status epilepticus in children: A protocol for a sequential design, multicentre, randomised, controlled, open-label, non-profit trial (KETASER01). *BMJ Open*, *6*(6), e011565.

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Link to synopsis and references

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