McMaster Children's Hospital

Guidelines for the Pharmacological Management of Convulsive Status Epilepticus

This guideline is applicable to the emergency room (ER), in-patient wards and the critical care units within the Children's Hospital.

Measures to maintain adequate airway, breathing & circulation and, appropriate investigations depend on the individual situation.

When to initiate pharmacological treatment for ongoing convulsive seizures:

1. Convulsive seizure lasting more than 5 minutes or the onset of convulsion is unclear (in special situations like acute brain injury where seizure are likely to cause additional brain insult, immediate attention is needed)
2. Two or more seizures within a short period time without patient returning to baseline neurobehavioral stage.
3. Strong clinical suspicion of non-convulsive seizures following a convulsive seizure

Time from onset

Onset	Blood glucose, electrolytes
	First episode of seizure and/or etiology unclear: consider serum calcium, phosphorous, magnesium, toxicology screen, ammonia, blood gas, CBC, blood culture, LFTs
5 minutes	Intravenous Lorazepam 0.1 mg /kg (maximum 4 mg) IV over 1 minute
10 minutes	Intravenous Lorazepam 0.1 mg /kg (maximum 4 mg)IV over 1 minute
	If IV access is not established, the options include the following
	(a) Per rectal Lorazepam 0.1 mg/kg(Max 4 mg) (use the IV preparation)*
	(b) Intranasal Midazolam 0.2 mg/kg (maximum 10 mg) (Use the IV preparation))**
15 minutes	If seizure continues despite 2 doses of benzodiazepines (including pre-hospital doses), please proceed to Phenytoin
	Phenytoin 20 mg/kg (maximum 1g) IV in normal saline over 20 minutes
	If no IV access: Phenytoin IO 20 mg /Kg (maximum 1 g)***
	If patient is already on oral Phenytoin, consider IV Phenobarbital
	If the patient has seizures while phenytoin is being infused, continue additional doses of Benzodiazepines.
35 minutes	Phenobarbital 20mg/kg IV over 20 minutes (maximum 1 g)

55 minutes Refractory Status Epilepticus

Points to remember

1. Waiting 5 minutes before initiating treatment of convulsive seizures in high risk patients could potentially cause additional brain insult (Eg Brain injury patients).
2. *Diazepam 0.5 mg/kg PR (maximum 20mg) is another option
3. **Intranasal midazolam: Divide dose between nares. Atomizers for intranasal delivery are available (http://www.wolfetory.com/Products/MAD/), but drug should be administered with a syringe if atomizer is not immediately available.
4. Pre-hospital doses of benzodiazepine should be counted towards the total number of doses.
5. Prepare Phenytoin if you need to administer the second dose of Benzodiazepine. This avoids further delay.
6. In neonates, phenobarbital is preferred to phenytoin
7. ***If no IV access: Another option is IM Fosphenytoin 20 mg PE/Kg (maximum 1 g) **(if available).**
8. Consider Pyridoxine 100 mg IV in children <18 months with history of unexplained developmental delay.

Refractory Status Epilepticus (RSE)

Defined as ongoing convulsive seizures despite 2 doses of Benzodiazepines, 20 mg/kg each of phenytoin and Phenobarbital.

First line

Intravenous Midazolam IV 0.15 mg/kg bolus then 2 µg/kg/min infusion [Use of IV Midazoalm should prompt immediate consultation with PCCU]

End point is absence of electrographic seizures (not burst suppression) in the EEG and clinical seizures.

Rapid titration: Increase as needed by 2 µg/kg/min q5 minutes

Bolus 0.15 mg/kg with each increase in infusion rate

Maximum infusion rate: 24 µg/kg/min (maximum 40 mg/hour)

Maintain phenobarbital and phenytoin at therapeutic serum levels

Goal is to maintain seizure free status for 24-48 hours.

Tapering Midazolam: Decrease by 1 µg/kg/min q15 minutes (not slow tapering unless indicated for sedation or withdrawal management purposes)

If seizures recur while/after tapering Midzolam, maintain midazolam infusion for another 24 - 48 hours.

Points to remember

1. Midazolam can cause hypotension and accumulate in fat tissue
2. Midazolam is very short acting. Rapid titration (with intermittent boluses) is essential.
3. Maintenance dose of phenytoin and phenobarbital is continued.
4. EEG end point for Midazolam titration is absence of EEG seizures and not burst suppression

Second Line (if seizures persist despite midazolam infusion)

Intravenous Pentobarbital

Load: 5 mg/kg IV (maximum rate up to 50 mg/min); repeat 5 mg/kg boluses until seizures stop.

Initial rate: 1 mg/kg/hour

Maintenance: Repeat bolus and increase infusion if needed. Usual maximum infusion is 3 mg/kg/hour, traditionally titrated to suppression-burst on EEG but titrating to seizure suppression is reasonable as well (discuss the target with neurology). Higher doses may be required.

Continue Phenytoin

If no seizures for 48 hours: taper off Pentobarbital over 12 hours. Before tapering Pentobarbital, restart the maintenance dose of Phenobarbital.

Points to remember:

1. Discontinue Phenobarbital and midazolam once Pentobarbital is started, but continue Phenytoin
2. Pentobarbital use is associated with the risk of hypotension and acidosis. Concomitant use of Topiramate and Propofol augments the risk of acidosis.
3. Therapeutic end point is usually burst suppression pattern in the EEG with an interburst interval of 8-20 seconds.
4. Restart the maintenance dose of Phenobarbital before tapering pentobarbital.
5. Other antiseizure medications may be considered only in conjunction with pediatric neurology consultation.

Foot note

1. *S/L Lorazepam is not listed here. In convulsive seizure, protection of the airway could include clearing oral secretions which could reduce the effect of S/L medication.*
2. *Paraldehyde is not freely available (discuss with pharmacy). Dose is 200-400 mg /kg (per rectal) mixed with equal volume of olive (mineral) oil.*
3. *Thiopentone is not freely available*

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