Resource-Limited ENLS
Status Epilepticus

Immediate stabilization: As in any setting, the first priorities for managing suspected status epilepticus in a resource-limited setting is to assess the patient's circulation, airway, and breathing (CABs). Patients with depressed mental status (GCS less than 9), impaired handling of oral secretions, witnessed aspiration, or hypoxemia should be intubated promptly. If intubation is unavailable, the patient should be emergently transferred to the nearest facility equipped with capacity for intubation and mechanical ventilation, with temporizing oxygen support from a bag-valve mask if available. Patients who are following commands, protecting their airway, and maintaining adequate oxygenation may be monitored closely without intubation. Oxygen saturation should be monitored with continuous pulse oximetry if available and supported with supplemental oxygen as needed until the airway can be secured. IV access should be established to provide hemodynamic support and antiseizure medications (ASMs). Finally, a finger stick blood glucose should be checked to exclude the reversible etiologies of hypo- or hyperglycemia.

Emergent initial therapy: Benzodiazepines are widely available, even in most resource-limited settings. If available in IV formulation, lorazepam 4mg or diazepam 10mg can be given as early emergent antiseizure therapy. These doses can be repeated after 5 minutes if seizure termination is not achieved after the first dose. Careful attention should be paid to the patient's airway status after loading with benzodiazepines, though undertreating with benzodiazepines has been shown to increase risk of airway compromise and the doses required for status epilepticus are higher than for many other indications.[1]

The choice of first-line ASM to administer alongside a benzodiazepine is likely to depend on local resource availability. Commonly used first-line ASMs in high-resource settings, including levetiracetam, phenytoin, and valproic acid,[2] may be unavailable in many resource-limited settings. If so, phenobarbital is on the World Health Organization's Essential Medications List and is available in most resource-limited settings.[3] For status epilepticus, it is given as a 20mg/kg IV loading dose, and can be equivalently dosed for enteral administration via nasogastric tube if IV formulation is unavailable. A starting maintenance dose of 2mg/kg/day divided into 2-3 doses can be titrated to clinical response and a desired serum level of 10-40mcg/mL. Carbamazepine is another widely available ASM, and can be loaded via nasogastric tube at 400-800mg, with a maintenance dose of 400-1600mg/day divided into 2 doses given every 12 hours.

Urgent control therapy and refractory SE: Patients whose seizures are aborted with first-line antiseizure therapy should be admitted for inpatient monitoring, initiation of maintenance ASMs, diagnostic workup, and supportive care (see below). Patients in refractory status epilepticus whose seizures do not respond to benzodiazepines and an ASM load should be admitted to an ICU or transported to the nearest facility with critical care capacity. They should be intubated and an anesthetic drip should be initiated; choices include propofol, midazolam, and ketamine depending on local availability. It is not safe to administer these medications without a secure airway. Their first-line ASM should be continued at a maintenance dose and serum levels checked as indicated to ensure therapeutic dosing if drug monitoring is available. If IV-loadable ASMs are unavailable, an enteral load of an oral ASM may be considered. Carbamazepine and oral phenobarbital are available in most resource-limited settings. Carbamazepine can be loaded with 400-800mg per nasogastric tube, and phenobarbital can be loaded with 15mg/kg per nasogastric tube. Consideration should also be given to additional ASMs as available to minimize the risk of recurrent seizures when weaning anesthetics. The patient should be connected to electroencephalography (EEG) if available and

monitored for as long as feasible, with the goal of 24 hours of seizure suppression before lifting anesthetics. EEG, however, is unavailable in most resource limited settings, necessitating close monitoring of the patient's clinical exam to detect recurrence of seizures, acknowledging the limited ability to detect and diagnose non-convulsive status epilepticus in this scenario.

Diagnostic workup: Concurrent with the critical care stabilization and implementation of initial and control therapies discussed above, a diagnostic workup should be performed to determine the underlying etiology and guide management for any reversible causes. An urgent non-contrast head CT should be performed for all patients with new-onset seizures, and an MRI brain with contrast should be performed as able for patients whose CT scan does not reveal a clear etiology. Lumbar puncture (LP) should be performed for patients with new-onset seizure in whom neuroimaging does not reveal a mass lesion that poses a risks for cerebral herniation. LP may be particularly informative in patients with a known or possible diagnosis of HIV (See ENLS module on "Meningitis and Encephalitis"). Patients known to be prescribed an ASM should have a serum drug level checked to assess for medication non-adherence as a possible trigger, though this testing may not be available in LMICs. A comprehensive laboratory evaluation for toxic, metabolic, or infectious etiologies should be performed, including comprehensive metabolic panel/electrolytes, glucose, complete blood count, urinalysis, HIV antibody test for patients with unknown HIV status, CD4 count for patients with known HIV, pregnancy test for women of child-bearing age, and toxicology screen if available.

Supportive care: High-quality supportive care is vital for this patient population and can be effectively delivered in resource-limited settings. The oral cavity should be assessed for evidence of tongue laceration or other oral injuries. Patients who were found down or presented after an unwitnessed fall should undergo a comprehensive trauma survey to assess for peripheral injuries sustained during the presenting seizure. Aspiration pneumonia is a common complication of status epilepticus and antibiotics and aggressive airway clearance therapy should be initiated promptly for patients with suspected or confirmed pneumonia. Fevers should be treated aggressively to minimize risk of secondary brain injury. Adequate hydration should be maintained with IV fluids to prevent a negative fluid balance. Chemoprophylaxis for deep venous thrombosis should be initiated for all patients without contraindications, and frequent turning should be performed for all intubated and/or comatose patients to minimize risk of pressure ulcers.

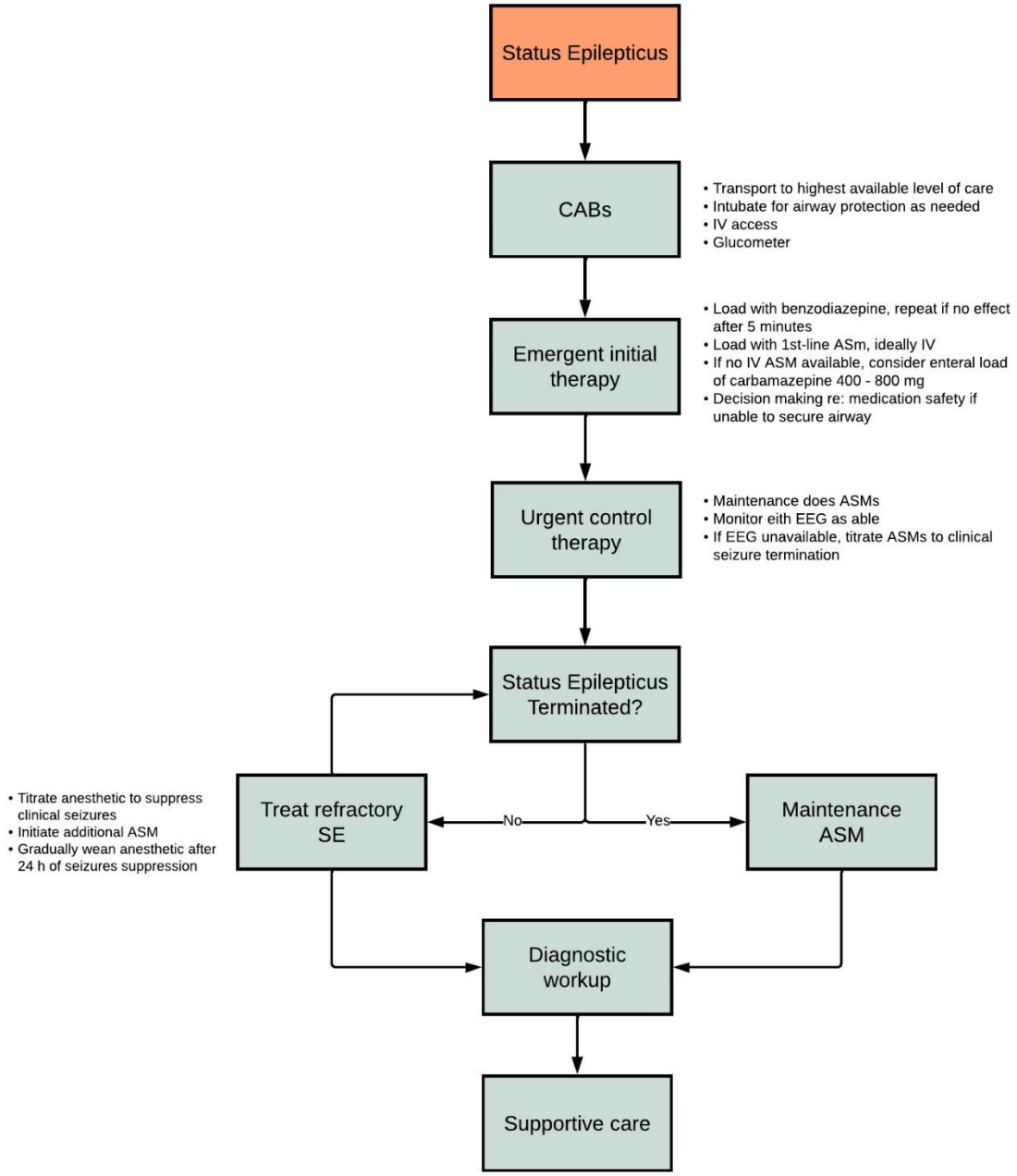

Figure 1

Algorithm for status epilepticus management in resource-limited settings

ABCs = airway, breathing, circulation; ASM = antiseizure medication; EEG = electroencephalogram; SE = status epilepticus.

References

1. Treiman DM, Meyers PD, Walton NY, Collins JF, Colling C, Rowan AJ, Handforth A, Faught E, Calabrese VP, Uthman BM, Ramsay RE, Mamdani MB, Yagnik P, Jones JC, Barry E, et al. A comparison of four treatments for generalized convulsive status epilepticus. Veterans Affairs Status Epilepticus Cooperative Study Group. *The New England journal of medicine*. 1998;339(12):792–798.

2. J K, J E, JM C, W B, J C, D L, S S, R C, C M, H C, N F, JT C, R S. Randomized Trial of Three Anticonvulsant Medications for Status Epilepticus. *The New England journal of medicine*. 2019;381(22):E211–E216.

3. World Health Organization. WHO Model List of Essential Medicines - 23rd list, 2023.

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