“Triphasic Waves” In Encephalopathy: BIDMC Guideline for Trials of Anti-Seizure Therapy (TOAST)

Background and Rationale

In-hospital EEG’s are often ordered to clarify the cause of encephalopathy. Generalized Periodic Discharges (GPDs) with triphasic morphology (“Triphasic Waves”, TW) are a common finding in this setting. TW have traditionally been interpreted as a sign of toxic-metabolic encephalopathy to be managed without anti-seizure medications (ASMs). However, in some cases short-term use of ASM provides clinical benefit; such ASM-responsive cases are considered a form of nonconvulsive seizures (NCS) or nonconvulsive status epilepticus (NCSE). No features alone or in combination have been shown to reliably identify cases that are responsive ASMs (Neurology 2003; 61:1035-6, Can. J. Neurol. Sci. 2006; 33:175-180). Consequently, in cases of TW with features concerning for NCSE we recommend a time-limited trial of empirical trial of ASM (Clin. Neurophys. 118 (2007) 1660–1670). We recommend the following as a default approach to evaluating patients with TW patterns in the setting of unexplained or incompletely explained encephalopathy. This approach is meant as general guideline, should be modified as clinically indicated, and may not apply to all patients.

Recommended Protocol

Inclusion: GPDs with triphasic morphology at >1Hz, with prevalence >30%, in the setting of acute encephalopathy
Exclusion: Anoxic brain injury
EEG: Continuous EEG monitoring for 48 hours, to cover the duration of the following test(s).

Initial evaluation: Benzodiazepine trial

Required monitoring: Continuous EEG, pulse oximetry, blood pressure, ECG, respiratory rate. A neurologist should be at the bedside during the trial to monitor and perform a neurologic exam before and after ASM administration.

Procedure: Give sequential small doses of Lorazepam (Ativan), 0.5-1 mg/dose, up to 4 mg total. Before the first dose and between doses, perform repeated clinical and EEG assessment.
Trial is stopped after any of the following: (1) Persistent resolution of the EEG pattern; (2) definite clinical improvement; (3) respiratory depression, hypotension, or any adverse event; (4) maximum recommended dose of Lorazepam is reached.

Interpretation: The trial is positive (+) or “successful” if there is:
(1) Resolution of the EEG pattern
AND
(2) Unequivocal improvement in encephalopathy
The test is inconclusive if the EEG improves but the patient’s encephalopathy does not (e.g. patient simply falls asleep).

For inconclusive results or when unable to do benzodiazepine trial: Levetiracetam (LEV) or Lacosamide (LCM) trial

Procedure: Loading dose: LEV 20 mg/kg IV x 1 or LCM 200 mg IV x 1
Maintenance dose: Levetiracetam 1500 mg BID (oral or IV) or LCM 200 mg BID
Trial continues for 48 hours.
Note: check renal function and ECG before administering LEV or LCM, respectively.
Positive response: Defined in the same way as for benzodiazepine trial.
Stop ASM if the result is not clearly positive.
Note: A LEV or LCM trial may also be appropriate in cases where a benzodiazepine trial is considered unsafe.

Disclaimer

Clinical situations and considerations may vary. This guideline has been developed for use by our team at BIDMC for use in clinically appropriate circumstances. Changes in our practice may occur without notice. We make no statements or warranties about appropriateness or utility of this working guideline in other clinical environments. This guideline has not been evaluated in a randomized clinical trial. Note that positive results of an ASM trial do not constitute a diagnosis of epilepsy, and should not be considered an indication for long-term ASM therapy.

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