

■ INITIAL TREATMENT OF GENERALIZED CONVULSIVE STATUS EPILEPTICUS

Treiman DM, Meyers PD, Walton NY, et al. A comparison of four treatments for generalized convulsive status epilepticus. *N Engl J Med* 1998; 339:792-8.

Clinical question What is the best initial treatment to use with generalized convulsive status epilepticus?

Background Status epilepticus is a life-threatening medical emergency. Commonly used intravenous anticonvulsant medications include lorazepam, diazepam followed by phenytoin, phenobarbital, or phenytoin. The efficacy of these drugs has not been directly compared, despite their widespread use.

Population studied Patients 18 years and older who presented to 16 Veterans Affairs medical centers and 6 affiliated university hospitals with generalized convulsive status epilepticus were enrolled over a 5-year period. Exclusion criteria included pregnancy, treatment prior to enrollment with an anticonvulsant and no further seizure activity, a neurologic event necessitating surgery, contraindication to treatment with study drugs, or status epilepticus of a type different from generalized convulsive status epilepticus.

Study design and validity This double-blind randomized multicenter trial compared the efficacy of 4 intravenous anticonvulsant medications in aborting and preventing recurrence of status epilepticus. Subjects were randomly assigned to receive 1 of the 4 study regimens: lorazepam 0.1 mg/kg; phenobarbital 15 mg/kg; phenytoin 18 mg/kg; or diazepam 0.15mg/kg followed by phenytoin 18 mg/kg. Prior to the infusion, serum levels were drawn to monitor concentrations of study drugs, and drawn again at 2 hours and 12 hours after initial infusion. Electroencephalogram (EEG) electrodes were placed as early as possible during infusion and monitored regularly for the total 12 hours of study. The study was designed to analyze overt and subtle generalized seizures separately. Overt generalized seizures were defined as 2 or more generalized convulsions, without full recovery of consciousness between seizures, or continuous seizure activity for more than 10 minutes. Subtle generalized seizures were defined as coma and ictal discharges on EEG with or without subtle convulsive movements. All 4 treatment groups were similar in baseline characteristics.

Outcomes measured The primary outcome was successful abolishment of seizure activity within 20 minutes of the initiation of drug infusion without recurrence in the next 40 minutes (1 hour total from beginning of infusion). Secondary outcomes included recurrence of seizure activity within 12 hours of drug infusion, side effects, and mortality at 30 days.

Results Of the 1750 patients eligible, 1135 patients were excluded, usually because they were not having generalized status epilepticus (868) or because the study team was not called (113). The remaining 570 subjects were included in an intention-to-treat analysis. Of this group, 52 were found to not have generalized convulsive status epilepticus at randomization in a post hoc evaluation; the remaining 518 made up the "verified diagnosis" group. These were divided into 2 subgroups according to type of generalized convulsive status epilepticus: 384 patients had the overt type and 134 had the subtle type. While a statistically significant difference in efficacy was found for patients with overt status epilepticus in the verified diagnosis group (with lorazepam being most effective and phenytoin least effective), this analysis is less valid and important, because it has the potential for introducing significant bias. The authors found no significant difference between the 4 treatments in the intention-to-treat analysis, although the trend was similar to that of the verified diagnosis group. No significant difference was noted between treatment groups for side effects or 30-day mortality in the verified diagnosis group.

Recommendations for clinical practice This trial compared the efficacy of lorazepam, diazepam followed by phenytoin, phenobarbital, or phenytoin in aborting and preventing recurrence of generalized convulsive status epilepticus. The intention-to-treat analysis found no difference in efficacy between any of the 4 drug regimens, although there was a nonsignificant trend in favor of lorazepam. Therefore, until further information is available from randomized controlled trials, the clinician can choose any of these regimens; they have equal efficacy and no difference in harm. Lorazepam may be preferred by physicians because it is easier to use and has a shorter infusion time.

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