Title: Patterns of Benzodiazepine Underdosing in the Established Status Epilepticus Treatment Trial

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Abstract

Objective

To describe patterns of benzodiazepine use as first-line treatment of status epilepticus (SE) and the association of benzodiazepine doses with response to second-line agents in patients enrolled in the Established Status Epilepticus Treatment Trial (ESETT).

Methods

Patients who failed adequate dose of benzodiazepines for the treatment of SE were enrolled in ESETT. Choice of benzodiazepine, doses given prior to administration of second-line agent, route of administration, setting, and patient weight were characterized. These were compared with guideline-recommended dosing. Logistic regression was used to determine the association of the first dose of benzodiazepine and the cumulative benzodiazepine dose with the response to second-line agent.

Results

Four-hundred-sixty patients were administered 1170 doses of benzodiazepines (669 lorazepam, 398 midazolam, 103 diazepam). Lorazepam was most frequently administered intravenously in the emergency department, midazolam intramuscularly or intravenously by the emergency medical services personnel, and diazepam rectally prior to ambulance arrival. The first dose of the first benzodiazepine (n=460) was lower than guideline recommendations in 76% of midazolam administrations and 81% lorazepam administrations. Among all administrations, > 85% of midazolam and > 76% of lorazepam were lower than recommended. Higher first or cumulative

benzodiazepine doses were not associated with better outcomes or clinical seizure cessation in response to second-line medications in these benzodiazepine-refractory seizures.

Significance

Benzodiazepines as first-line treatment of SE, particularly midazolam and lorazepam, are frequently under-dosed throughout the US. This broad and generalizable cohort confirms prior single site reports that underdosing is both pervasive and difficult to remediate.

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