Benzodiazepines were as safe as and more effective than placebo for out-of-hospital status epilepticus


QUESTION: In patients with out-of-hospital status epilepticus, are benzodiazepines safer and more effective than placebo when given by paramedics for terminating the condition?

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Outcome Comparisons Event rates RBI (95% CI) NNT (CI)
Termination of status epilepticus
Lor v Dia 59% v 43% 37% (–13 to 80) Not significant
Lor v Plac 59% v 21% 166% (60 to 268) 3 (2 to 8)
Dia v Plac 43% v 21% 80% (0 to 190) Borderline significance

COMMENTARY

Convulsive status epilepticus (CSE) is a neurologic emergency. Prolonged CSE leads to brain damage and neurological morbidity and could also increase the risk for death. Furthermore, delaying treatment could result in CSE becoming more difficult to control. The study by Alldredge et al shows that out-of-hospital, intravenous administration of lorazepam and diazepam by paramedics is as safe as and more effective than placebo. Such early, out-of-hospital treatment is particularly important if the time to arrival at the emergency department is prolonged—a common scenario in clinical practice. The study by Alldredge et al should help alleviate doubts about the safety of these intravenous drugs at commonly recommended dosages. Fewer cardiopulmonary complications occurred with benzodiazepines than with placebo, but groups did not differ statistically. Lorazepam, commonly preferred by clinicians because of its longer anticonvulsant effect, had more CSE terminations than diazepam, but groups did not differ statistically.

Finally, the intervention was ineffective in about 40% of patients, a higher failure rate than previously reported. However, the definition of success in this study, termination of CSE at arrival in the emergency department, differs from previous studies. In the study findings, 3 conditions should be met. First, patients should have good respiratory and haemodynamic function. A higher frequency of cardiorespiratory complications may occur in patients who are sicker than those in this study. Second, paramedics require training. Third, clinicians at participating emergency departments must actively support this out-of-hospital intervention.

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Patients

205 patients (258 enrollments) who were ≥ 18 years of age (mean age 51 y, 63% men, 50% white) and had an out-of-hospital diagnosis of status epilepticus. Exclusion criteria included pulse < 60 beats/minute, systolic blood pressure < 100 mm Hg, and a history of long-term use of or sensitivity to benzodiazepines. Only data from the first enrollment of each patient was reported. [Follow-up was 100%].

Intervention

Patients were allocated to intravenous injection of lorazepam, 2 mg (n=66); diazepam, 5 mg (n=68); or placebo (n=71), given over a 1 to 2 minute period and only during generalised tonic clonic seizure activity. If seizures recurred or continued ≥ 4 minutes after the first injection, an identical second injection was given. Open label diazepam was immediately available for a difficult or unsafe extrication of a patient or if a patient was at high risk for a life threatening complication.

Main outcome measures

Termination of status epilepticus and out-of-hospital complications.

Main results

[Analysis was by intention to treat.†] Lorazepam and diazepam groups did not differ, but each were more effective than placebo for terminating status epilepticus (diazepam v placebo comparison was of borderline statistical significance) (table). An out-of-hospital complication occurred in 11%, 10%, and 23% of patients who received lorazepam, diazepam, and placebo (p=0.08), respectively.

Conclusion

In patients with status epilepticus, both lorazepam and diazepam were as safe and more effective than placebo when given by paramedics for terminating the condition.