

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

Allredge BK, Gelb AM, Isaacs SM, et al. A comparison of lorazepam, diazepam, and placebo for the treatment of out-of-hospital status epilepticus. *N Engl J Med*. 2001 Aug 30;345:631-7.

## 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?

## DESIGN

Randomized {allocation concealed\*}†, blinded {patients, clinicians, data collectors, and outcome assessors}†,\* placebo-controlled trial with follow-up to time of arrival at the emergency department.

## SETTING

San Francisco, California, USA.

## PATIENTS

205 patients (258 enrollments) who were  $\geq 18$  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/min, 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 generalized tonic-clonic seizure activity. If seizures recurred or continued  $\geq 4$  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 vs 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 as and more effective than placebo when given by paramedics for terminating the condition.

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\*See Glossary.

†Information provided by author.

### Lorazepam (Lor) vs diazepam (Dia) vs placebo (Plac) for out-of-hospital status epilepticus until arrival at the emergency department‡

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

‡Abbreviations defined in Glossary; RBI, NNT, and CI calculated from adjusted data in article.

## COMMENTARY

Convulsive status epilepticus (CSE) is a neurologic emergency. Prolonged CSE leads to brain damage and neurologic morbidity and could also increase the risk for death. Furthermore, delaying treatment could result in CSE becoming more difficult to control (1). The study by Allredge and colleagues 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 therapy is particularly important if the time to arrival at the emergency department is prolonged—a common scenario in clinical practice (2).

The study by Allredge and colleagues should help alleviate doubts about the safety of these intravenous drugs at commonly recommended doses. 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 did diazepam, but groups did not differ statistically.

Finally, the intervention was ineffective in about 40% of patients, a higher failure rate than previously reported (2, 3). However, the defini-

tion of success in this study, termination of CSE at arrival in the emergency department, differs from previous studies.

In applying the study findings, 3 conditions should be met. First, patients should have good respiratory and hemodynamic 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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## References

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