

TREATMENT OF OUT-OF-HOSPITAL STATUS EPILEPTICUS

A Comparison of Lorazepam, Diazepam, and Placebo for the Treatment of Out-of-Hospital Status Epilepticus

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BACKGROUND: It is uncertain whether the administration of benzodiazepines by paramedics is an effective and safe treatment for out-of-hospital status epilepticus.

METHODS: We conducted a randomized, double-blind trial to evaluate intravenous benzodiazepines administered by paramedics for the treatment of out-of-hospital status epilepticus. Adults with prolonged (lasting five minutes or more) or repetitive generalized convulsive seizures received intravenous diazepam (5 mg), lorazepam (2 mg), or placebo. An identical second injection was given if needed.

RESULTS: Of the 205 patients enrolled, 66 received lorazepam, 68 received diazepam, and 71 received placebo. Status epilepticus had been terminated on arrival at the emergency department in more patients treated with lorazepam (59.1 percent) or diazepam (42.6 percent) than patients given placebo (21.1 percent) ($P=0.001$). After adjustment for covariates, the odds ratio for termination of status epilepticus by the time of arrival in the lorazepam group as compared with the placebo group was 4.8 (95 percent confidence interval, 1.9 to 13.0). The odds ratio was 1.9 (95 percent confidence interval, 0.8 to 4.4) in the lorazepam group as compared with the diazepam group and 2.3 (95 percent confidence interval, 1.0 to 5.9) in the diazepam group as compared with the placebo group. The rates of respiratory or circulatory complications (indicated by bag valve-mask ventilation or an attempt at intubation, hypotension, or cardiac dysrhythmia) after the study treatment was administered were 10.6 percent for the lorazepam group, 10.3 percent for the diazepam group, and 22.5 percent for the placebo group ($P=0.08$).

CONCLUSIONS: Benzodiazepines are safe and effective when administered by paramedics for out-of-hospital status epilepticus in adults. Lorazepam is likely to be a better therapy than diazepam.

COMMENTARY

It is obvious that rapid treatment of status epilepticus (SE) before arrival at the emergency room is desirable. Treatment of this condition by emergency medical personnel represents a significant intervention, potentially limiting the duration of SE, the occurrence of refractory SE, and the morbidity and mortality of SE. There is, however, limited objective information on out-of-hospital treatment. This study, published by Allredge et al., definitively settles this point with a well-designed, placebo-controlled trial. Patients with generalized convulsive SE, diagnosed by paramedics after a radio review by a physician, were randomized to receive intravenous injections of 5 mg of diazepam, 2 mg of lorazepam, or placebo. Injections could be repeated once if seizure activity continued. The study was considered ethical because at the time there was no set policy determining which of these treatments a patient would receive.

The primary outcome variable was termination of SE upon arrival at the hospital. This occurred in 59% of the patients given lorazepam, 43% given diazepam, and 21% given placebo. These results were highly significant for both drugs versus placebo, but a comparison of lorazepam versus diazepam showed a trend favoring only lorazepam. Not surprisingly, the overall duration of SE following treatment was also shorter in the treated patients, as measured by the log-rank test.

Perhaps most important is that the paramedics' administration of diazepam or lorazepam was safe. Out-of-hospital complications, including hypotension, cardiac dysrhythmia, or respiratory compromise, were actually more common in the placebo group, although this was not significant. Interestingly, outcome measures, including the number of patients going to intensive care, neurologic deficit, and death, were not different between groups, although there was a trend toward increased mortality in the placebo group.



The study should end any hesitancy about giving intravenous lorazepam or diazepam by paramedics for SE, and all paramedics should be trained in its use. The use of these agents is clearly safe and effective compared with placebo. When intravenous access is not possible, rectal or (perhaps in the future) intranasal administration, which is not addressed in this article, should be an option. The study does not solve the debate of whether lorazepam or diazepam is better. Although the trend favored lorazepam, this may be partly because of the dose (a comparison of 2 mg of lorazepam with 10 mg rather than 5 mg of diazepam might have been more reasonable). In any case, practical storage issues may dictate the continued use of diazepam. As seen in other studies in and out

of the hospital, rapid administration is probably more important than the actual agent. The potential for misdiagnosis by paramedics remains a nagging concern, as this can occur by even highly trained neurologists in more controlled settings. It is not clear from this study whether misdiagnosis occurred and, if so, how often. It is probably impossible to know this for patients whose episodes resolved. Regardless, however, the documented safety of out-of-hospital administration means that rare use in other diagnoses will probably not be detrimental to these patients.

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