Intravenous lorazepam reduced alcohol related seizures in patients with chronic alcohol abuse

D'Onofrio G, Rathlev NK, Ulrich AS, et al. *Lorazepam for the prevention of recurrent seizures related to alcohol*. *N Engl J Med* 1999 Mar 25;340:915-9.

Question

In patients with alcohol abuse who present with a seizure, does lorazepam prevent recurrent alcohol related seizures?

Design

Randomised, double blind, placebo controlled trial with follow up for 6 hours.

Setting

2 hospital emergency departments in Boston, Massachusetts, USA.

Patients

229 patients were enrolled but 43 met the initial exclusion criteria, including another possible cause of the seizure, currently taking drugs that caused or protected against recurrent seizures, or required treatment for symptoms of moderate to severe alcohol withdrawal other than seizures. 186 patients who were ≥ 21 years of age (mean age 45 y, 96% men) with chronic alcohol abuse who presented after a witnessed, generalised seizure and who had had ≥ 1 drinks within the previous 72 hours were included in the intention to treat analysis.

Intervention

100 patients were allocated to receive 2 mg of lorazepam in 2 ml of normal saline intravenously, and 86 were allocated to receive 4 ml of normal saline intravenously.

Main outcome measures

The primary endpoint was the occurrence of a second seizure during the 6 hour observation period. Secondary endpoints included admission to hospital.

Main results

In an intention to treat analysis, fewer patients in the lorazepam group had a second seizure within 6 hours than did those in the control group ($p < 0.001$) (table). Hospital admission rates were not statistically significantly higher in the placebo group compared with the lorazepam group {odds ratio 1.76, 95% CI 0.96 to 3.23}^{*}. Of the 50 patients in the control group who were discharged from the emergency department after the study, 7 (14%) were transported to an emergency department in Boston within 48 hours with a second seizure; the number in the lorazepam group was 1 of 67 {1.5%, absolute difference 13%, CI 4% to 25%}[†].

Conclusion

Intravenous lorazepam reduced recurrent seizures in patients with chronic alcohol abuse who presented after a witnessed, generalised, alcohol related seizure.

^{*}Numbers calculated from data in the article using the intention to treat sample ($n = 186$).

[†]Numbers calculated from data supplied by the author.

Intravenous lorazepam v placebo in patients with chronic alcohol abuse presenting after a witnessed, generalised, alcohol related seizure[‡]

Outcome at 6 hours	Intravenous lorazepam	Placebo	RRR (95% CI)	NNT (CI)
Second seizure	3%	24%	88% (63 to 96)	5 (4 to 9)

[‡]Abbreviations defined in glossary; RRR, NNT, and CI calculated from data in article.

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Abstract and modified version of the commentary also published in ACP Journal Club.

Commentary

The excessive consumption of alcohol, acute or chronic, is one of the everyday reasons for admission to emergency medical services. The prevalence in emergency services of patients in difficulty with alcohol is approximately 30%. Seizures are a clinical manifestation of alcohol withdrawal but can also occur outside withdrawal periods. Many reasons exist for seizures. 50% of seizures admitted to emergency services are associated with excessive alcohol consumption,¹ but almost all other causes can be aggravated by alcohol consumption of > 50 g/day.

The study by D'Onofrio *et al* used rigorous methodology, but only included patients whose seizures were directly related to alcohol. Alcoholic patients with other causes of seizures (hypoglycaemia, hypomagnesaemia, cranial trauma, pre-delirium tremens, etc) were excluded, although these are substantial clinical problems.

A key clinical message of this study is that secondary prevention of recurrent seizures by lorazepam is useful for these patients and should be used systematically in emergency services. In a wider context, the authors succeeded in showing that emergency services can successfully treat patients with problems secondary to excessive alcohol consumption. The reduced rate of readmission for recurrent seizures within 48 hours of treatment underlines the importance of the findings. It is hoped that these results will help to change negative attitudes related to people in difficulty with alcohol and the scepticism about the effectiveness of treatment that is often encountered with emergency service teams. Clearly, alternative pharmacotherapeutic treatments and psychotherapies remain to be developed for other somatic and psychological problems arising at various stages in the illness of alcohol abuse. In this study, the low rate of patients

who finally benefited from being treated specifically for their alcoholic problem highlights this need. At present, some emergency service teams have already received specific training that is reinforced by the routine and daily support of an alcohol specialist. The effectiveness of this support remains to be proved.

Further research is required to develop a specific, flexible response and to make valid protocols for the various clinical situations available to emergency teams. This study provides evidence of one intervention that could be included in such a protocol.

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¹ Bouget J, David C, Saussey E. Accident de sevrage alcoolique. Le problème des crises convulsives. *Alcoologie* 1999;21:178-83.