


Review: lorazepam provides the best control for status epilepticus

Prasad K, Al-Roomi K, Krishnan P, *et al.* Anticonvulsant therapy for status epilepticus. *Cochrane Database Syst Rev* 2005;(4):CD003723.


Clinical impact ratings GP/FP/Primary care ★★★★★☆ IM/Ambulatory care ★★★★★★ Internal medicine ★★★★★★
Emergency medicine ★★★★★★ Neurology ★★★★★★

Q In patients with status epilepticus (SE), which anticonvulsant drugs are most effective?


METHODS



Data sources Cochrane Epilepsy Group Specialised Register, Cochrane Central Database of Controlled Trials, Medline, EMBASE/Excerpta Medica, and reference lists.



Study selection and assessment randomised or quasi-randomised controlled trials (RCTs) that compared any anticonvulsant drug with placebo or another anticonvulsant drug in patients with premonitory, early stage, established, or refractory SE. Quality assessment of individual studies included randomisation method, baseline comparability of groups, blinding, and intention to treat analysis.



Outcomes outcomes included development of SE, death, continuation of seizures, continuation of SE requiring use of a different drug or general anaesthesia for control, long term disabling sequelae, and need for ventilatory support.

MAIN RESULTS

11 RCTs (n=2017) met the selection criteria. Patients had premonitory (5 RCTs), established (1 RCT), refractory (1 RCT), and mixed SE (2 RCTs), and 2 RCTs did not define the status. Superior results were seen with intravenous (IV) lorazepam for cessation of seizures and reducing risk of SE that required a second drug (table). IV diazepam was better than placebo for reducing death, continuation of seizures, SE, and ventilatory support (table). Diazepam gel was better than placebo, and 30 mg of diazepam gel was superior to 20 mg for reducing continuation of seizures (table). No differences were seen for comparisons of lorazepam with diazepam plus phenytoin, phenobarbital, or midazolam; diazepam with midazolam (IV or intramuscular); diazepam plus phenytoin with phenobarbital or phenytoin alone; or phenobarbital with phenytoin.

CONCLUSIONS

In patients with status epilepticus, lorazepam is better than diazepam, phenytoin, or placebo for cessation of seizures, and diazepam is better than placebo. Lorazepam is better than placebo or

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diazepam for preventing status epilepticus requiring a different drug or general anaesthesia, and diazepam is better than placebo.

Abstract and commentary also appear in ACP Journal Club and a modified version of the abstract appears in Evidence-Based Nursing.

Commentary

SE is a neurological emergency with a 30 day mortality rate of about 22%, contingent on duration before treatment, underlying cause, and patient age.¹ Prasad *et al* have attempted to determine which initial pharmacological treatment for SE is best in terms of rapidity of action, maintenance of efficacy, and incidence of adverse events. Most of the studies enrolled patients with “premonitory SE,” which, while not meeting the criteria for “established SE,” is generally thought to be a condition best addressed early and aggressively.

Their results affirm the consensus of standard clinical practice, but underscore the diversity that exists among investigator definitions of SE and outcome measures. Their strongest conclusion, that lorazepam is more effective than diazepam or phenytoin, reinforces guidelines published >10 years ago,² matches the preferences of surveyed neurologists,³ and is in turn buttressed by the theoretical pharmacokinetic advantages of lorazepam.

The review shows that any of the agents investigated perform better than placebo regardless of administration route, although routes were not a focus of study. Despite this lack of comparative data, we recommend IV formulations when available, and rectal formulations when IV is not feasible—reserving the intramuscular route as a last resort. This review also does not address what to do when initial treatments fail, but a related review concludes that continuous IV pentobarbital, titrated to electroencephalographic background suppression, produces the most favourable results.⁴

Prasad *et al* highlight the need for further RCTs that use a standardised approach to the classification of SE, the dosing and route of compared agents, and common outcome measures.

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- 1 DeLorenzo RJ, Hauser WA, *et al.* *Neurology* 1996;**46**:1029–35.
- 2 Treatment of convulsive status epilepticus. Recommendations of the Epilepsy Foundation of America's Working Group on Status Epilepticus. *JAMA* 1993;**270**:854–9.
- 3 Claassen J, Hirsch LJ, Mayer SA. *J Neural Sci* 2003;**211**:37–41.
- 4 Claassen J, Hirsch LJ, Emerson RG, *et al.* *Epilepsia* 2002;**43**:146–53.

Anticonvulsant drugs for status epilepticus to hospital discharge*

Outcomes	Number of trials (n)	Comparisons	Event rates	RRR (95% CI)	NNT (CI)
Non-cessation of seizures	3 (264)	Lorazepam v diazepam	24% v 38%	36% (10 to 55)	8 (5 to 25)
	1 (137)	Lorazepam v placebo	41% v 79%	48% (29 to 62)	3 (2 to 5)
	1 (198)	Lorazepam v phenytoin	35% v 56%	38% (14 to 55)	5 (3 to 13)
	1 (139)	Diazepam v placebo	57% v 79%	27% (8 to 43)	5 (3 to 17)
	2 (165)	Intrarectal diazepam gel v placebo	32% v 72%	57% (38 to 70)	3 (2 to 4)
	1 (39)	Intrarectal diazepam gel 30 mg v 20 mg	28% v 71%	61% (14 to 82)	3 (2 to 7)
Continuation of status epilepticus requiring a different drug	3 (264)	Lorazepam v diazepam	24% v 39%	37% (12 to 55)	7 (4 to 25)
	1 (137)	Lorazepam v placebo	41% v 79%	48% (29 to 62)	3 (2 to 5)
	1 (139)	Diazepam v placebo	57% v 79%	27% (8 to 43)	5 (3 to 17)
Death	1 (139)	Diazepam v placebo	4.4% v 15%	72% (2 to 92)	10 (5 to 100)
Ventilatory support	1 (139)	Diazepam v placebo	8.8% v 23%	61% (6 to 84)	8 (4 to 50)

*Abbreviations defined in glossary; weighted event rates, RRR, NNT, and CI calculated from data in article using a fixed effects model. All drugs given intravenously unless otherwise noted. Event rates with 1 trial are unweighted.