

Buccal midazolam may be a useful alternative to rectal diazepam for treating acute seizures in refractory epilepsy

Scott RC, Besag FM, Neville BG. Buccal midazolam and rectal diazepam for treatment of prolonged seizures in childhood and adolescence: a randomised trial. *Lancet*. 1999 Feb 20; 353:623-6.

QUESTION

In children and adolescents with refractory epilepsy, is buccal midazolam in solution as effective and safe as rectal diazepam in solution for treating acute seizures?

DESIGN

Randomized (allocation concealed*), unblinded,* controlled trial with follow-up to end of seizure.

SETTING

A residential center for children and young people with severe epilepsy and other needs in Lingfield, Surrey, England, United Kingdom.

PATIENTS

18 of 42 enrolled students with refractory epilepsy (mean age 15 y, 50% girls) who had previously received rectal diazepam for acute seizures and who had a seizure that lasted ≥ 3 minutes during the study period. Follow-up was complete.

INTERVENTION

When a seizure occurred, the student was allocated to receive either midazolam, 2

mL (10 mg) in a 2-mL syringe given buccally ($n = 40$ seizures in 14 patients), or diazepam, 10 mg given rectally ($n = 39$ seizures in 14 patients).

MAIN OUTCOME MEASURES

Clinical response (seizure stopped within 10 min), time taken for nurse to give medication, time to clinical response, and incidence of adverse events.

MAIN RESULTS

In the midazolam group, 24 seizures were generalized tonic-clonic, 8 were complex partial, 6 were myoclonic, and 2 were tonic. In the diazepam group, 22 seizures were tonic-clonic, 9 were complex partial, 4 were myoclonic, and 4 were tonic. The treatment groups did not differ for clinical response ($P = 0.16$) (Table), time required for nurse to give medication (median time 2 min in each group, $P = 0.81$), time to

clinical response (median time 6 min for midazolam vs 8 min for diazepam, $P = 0.31$), and incidence of adverse events (none occurred in either group). When patients rather than seizures were the units of analysis, the groups did not differ for any of the outcomes.

CONCLUSION

In children and adolescents with refractory epilepsy, buccal midazolam was as effective and safe as rectal diazepam for treating acute seizures.

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*See Glossary.

Buccal midazolam vs rectal diazepam for acute seizures in children and adolescents with refractory epilepsy†

Outcome at 10 min	Midazolam	Diazepam	RBI (95% CI)	NNT
End of seizure	75%	59%	27% (-7 to 79)	Not significant

†Abbreviations defined in Glossary; RBI, NNT, and CI calculated from data in article. Results refer to proportions of seizures (not patients).

COMMENTARY

Although rectal diazepam is effective in prolonged acute seizures (1), it has practical problems. Scott and colleagues' promising evidence of the effectiveness of buccal midazolam is welcome. However, clinicians should consider some issues before adopting it.

Study patients had severe epilepsy and had received diazepam. Would patients receiving a benzodiazepine for the first time respond similarly? A nurse gave midazolam, and medical care was available. Neither of these is normally present in the community. Efficacy, safety, and the optimal doses for young children and elderly persons remain to be determined. Finally, patients with prolonged seizures, not status epilepticus, were treated.

The study methods deserve comment. Seizures (not patients) were randomized, and 50% of seizures occurred in 2 of 18 patients. Data from more patients would reassure clinicians. Blinding would

have required concurrent buccal and rectal administration. I believe, however, that it is feasible in this context, and it would have strengthened the findings.

Buccal midazolam offers definitive advantages over rectal diazepam and may be used as an alternative for young persons with prolonged, complex partial, and generalized motor seizures. However, its safety and efficacy in the community require further exploration.

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Reference

1. Dreifuss FE, Rosman ND, Cloyd JC, et al. A comparison of rectal diazepam gel and placebo for acute, repetitive seizures. *N Engl J Med*. 1998; 338:1869-75.