

# **Efficacy of buccal midazolam for emergency treatment of seizures in children**

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# General

- Tonic-clonic seizures: common problem in children
- A drug: easy to give, effective, and safe, and would have a long-lasting antiseizure action
- Rectal diazepam and buccal midazolam are used for emergency treatment
- Intravenous access is not always possible

# No intravenous

- Rectal diazepam
- Intranasalmidazolam
- Buccal midazolam

# Rectal diazepam

- Rapid initial response in 60–80%
- Risk of early recurrence of seizures: 30%
- Difficult to arrange in schools and respite care facilities or other out-of-hospital environments, and absorption is variable

# Intranasal midazolam

- Effective, but it can be less reliable in the presence of concurrent upper respiratory tract infection.

# 2005 July,UK

- Safety and efficacy of buccal midazolam versus rectal diazepam for emergency treatment of seizures in children

# Methods

- Multicentre, randomised controlled trial
- Children aged  $\geq 6$  months presenting to hospital with active seizures and without intravenous access
- Children who had chronic epilepsy or given prehospital emergency or rescue treatment were not excluded from the trial
- Most seizures would be generalised tonicclonic

# Buccal midazolam



# Dose

- Buccal midazolam or rectal diazepam:

**0.5mg/kg**

**2.5mg for 6–12months**

**5mg for 1–4years,**

**7.5mg for 5–9years**

**10mg  $\geq$  10years**

# Evaluation parameters

- Therapeutic success
- Time (mins) to stop seizing
- Given intravenous lorazepam
- Respiratory depression

# Therapeutic success

- Cessation of visible signs of seizure activity within 10 min
- Without another seizure within the hour.
- Without respiratory depression

# Results

- From October, 2000, to February, 2004, in the four participating hospitals: 219 separate episodes involving 177 patients
- 110 rectal diazepam treatment episodes
- 109 buccal midazolam treatment episodes

Characteristics  
of the sample  
2 study groups  
did not differ

	Buccal midazolam (109 episodes, 92 initial episodes)	Rectal diazepam (110 episodes, 85 initial episodes)
<b>Male</b>		
All episodes	59 (54%)	64 (58%)
Initial episodes	52 (57%)	46 (54%)
<b>Admission temperature (°C)</b>		
All episodes	37.3 (36.2–38.5)	37.1 (36.3–38.1)
Initial episodes	37.3 (36.3–38.2)	37.6 (36.3–38.5)
<b>Age (years)</b>		
All episodes	2 (1–5)	3 (1–6)
Initial episodes	2 (1–5)	3 (1–6)
<b>Previous seizures</b>		
All episodes	78 (72%)	79 (72%)
Initial episodes	61 (66%)	55 (65%)
<b>Receiving antiepileptic drugs</b>		
All episodes	52 (48%)	63 (57%)
Initial episodes	37 (40%)	42 (49%)
<b>Episodes with prehospital emergency treatment</b>		
All episodes	35 (32%)	33 (30%)
Initial episodes	28 (30%)	22 (26%)
<b>Seizure duration before treatment (mins)</b>		
All episodes	30 (10–49)	41 (10–61)
Initial episodes	30 (14–45)	37 (10–60)

Data are number (%) or median (IQR).

**Table 2: Baseline characteristics**

	Buccal midazolam (109 episodes)	Rectal diazepam (110 episodes)	Percentage difference (95% CI)
<b>Therapeutic success (%)</b>			
All episodes	61 (56%)	30 (27%)	29% (16 to 41)
Initial episodes	49 (53%)	24 (28%)	25% (11 to 39)
<b>Time (mins) to stop seizing after treatment (median, IQR)</b>			
All episodes	8 (5-20)*	15 (5-31)*	
Initial episodes	10 (5-22)†	15 (6-32)†	
<b>Stopped seizing within 10 min (%)</b>			
All episodes	71 (65%)	45 (41%)	24% (11 to 37)
Initial episodes	56 (60%)	36 (42%)	18% (4 to 33)
<b>Given intravenous lorazepam (%)</b>			
All episodes	36 (33%)	63 (57%)	24% (12 to 37)
Initial episodes	33 (36%)	47 (55%)	19% (5 to 35)
<b>Seizure stopped, then further seizure‡</b>			
All episodes	10 (14%) (n=71)	15 (33%) (n=45)	19% (4 to 36)
Initial episodes	7 (13%) (n=56)	12 (34%) (n=31)	22% (4 to 40)
<b>Respiratory depression (%)</b>			
All episodes	5 (5%)	7 (6%)	2 (-4 to 8)
Initial episodes	4 (4%)	6 (7%)	3% (-4 to 10)

Data are number (%) unless otherwise indicated. \* $p=0.01$ , hazard ratio 0.7 (95% CI 0.5-0.9). † $p=0.03$ , hazard ratio 0.7 (0.5-0.96). ‡Seizure stopped within 10 min, but further seizure within 1 h requiring treatment.

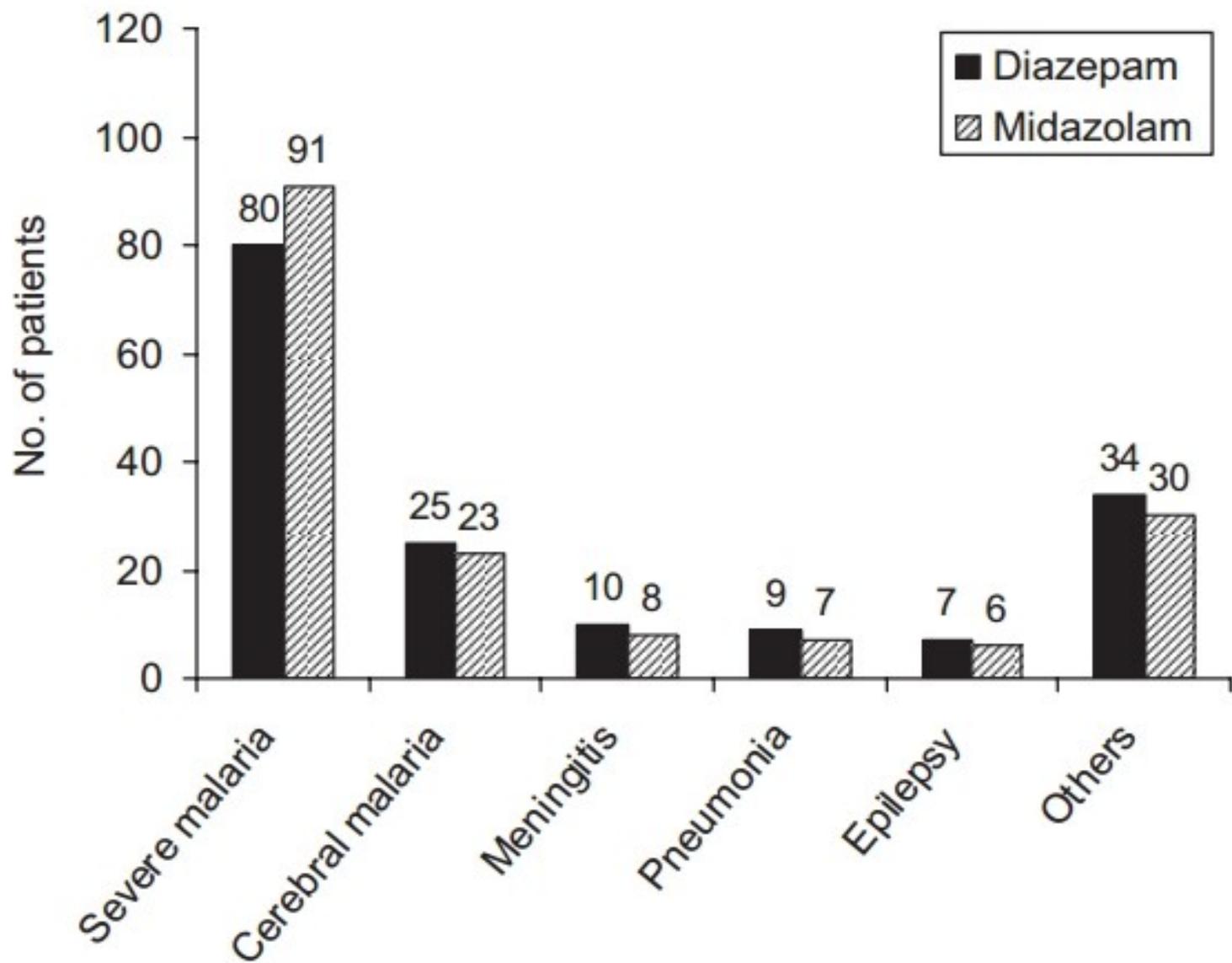
**Table 3: Outcome after treatment**

# Buccal midazolam

- Therapeutic success more rectal diazepam
- Stopped seizures within 10min in more children
- Does not appear to increase the risk of respiratory depression
- Few have given intravenous lorazepam

# 2008 Jan, Uganda

- Single-blind, randomized clinical trial in which 330 patients
- 3 months to 12 years
- Cessation of seizures within 10mins, without recurrence in 1hr.



# Results

- 114 (69.1%) seizures terminated within 10 minutes in the diazepam arm compared with 125 (75.8%) in the midazolam arm
- No statistical difference in malaria-related seizure.
- For children without malaria, buccal midazolam was superior (d=55.9% vs m=26.5%) (P=.002)

# Safety

- Only 4 (1.2%) children experienced respiratory depression. These patients included 2 in the diazepam group and 2 patients in the buccal midazolam arm



# trust clinical guideline

<b>Guideline ID</b>	<b>CG15</b>
Version	1.0
Title	Midazolam: Administration of the Patient's Supply for Seizures
Approved by	Clinical Effectiveness Group
Date Issued	01/01/2013
Review Date	31/12/2016
Directorate	Clinical
Authorised Staff	<input type="checkbox"/> Ambulance Care Assistant <input type="checkbox"/> Emergency Care Assistant <input checked="" type="checkbox"/> Student Paramedic <input checked="" type="checkbox"/> Advanced Technician <input checked="" type="checkbox"/> Paramedic (non-ECP) <input checked="" type="checkbox"/> Nurse (non-ECP) <input checked="" type="checkbox"/> ECP <input checked="" type="checkbox"/> Doctor
Clinical Publication Category	Guidance (Green) - Deviation permissible; Apply clinical judgement

## 1. Scope

- 1.1 This guideline aims to provide advice for ambulance clinicians on the administration of a patient's own supply of buccal or intranasal midazolam, which has been previously prescribed for the patient by an independent prescriber.

## 2. Background and Definitions

- 2.1 Prolonged seizures demand prompt medical assistance. The longer a seizure persists the more difficult they can be to stop, and on occasions can lead to Convulsive Status Epilepticus (a potentially life-threatening condition were seizures do not stop and brain damage may occur).
- 2.2 Parents and carers can be trained by medical staff to administer buccal or intranasal midazolam to a patient. Carers are trained to only administer one dose. If the seizure has not stopped within 10 minutes of giving midazolam, they are trained to call 999 for an ambulance.

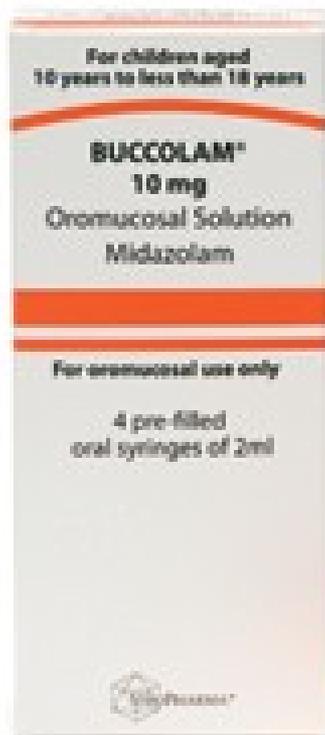
## 3. Guidance

### 3.1 Treatment Options

- 3.1.1 An ambulance clinician may arrive on scene to find that a patient has already been given one dose of their own midazolam by a carer or parent. In the event

# Conclusion

- Buccal midazolam recommended alongside rectal diazepam as the first-line treatment for prolonged seizure in children
- More effective than rectal diazepam for treatment of children with seizures in a hospital emergency department



# References

1. John McIntyre, Safety and efficacy of buccal midazolam versus rectal diazepam for emergency treatment of seizures in children: a randomised controlled trial, *The Lancet*, vol 366, **July 16, 2005**.
2. Knudsen FU. Rectal administration of diazepam in solution in the acute treatment of convulsions in infants and children. *Arch Dis Child* 1979; **54: 855-57**.
3. Dieckmann RA. Rectal diazepam for prehospital pediatric status epilepticus. *Ann Emerg Med* 1994; **23: 216-24**.

**THANK YOU**