NASAL RATHER THAN RECTAL BENZODIAZEPINES IN THE MANAGEMENT OF ACUTE CHILDHOOD SEIZURES?

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A recent report by Latson *et al.* (1991) recommended intranasal midazolam sedation for children undergoing outpatient echocardiography. The ages of the 15 children studied ranged from 4 to 30 months, and satisfactory sedation was achieved in 13 of them.

Benzodiazepines are routinely used by the rectal route for the treatment of acute epileptic seizures. Teachers are reluctant to use this method in schools, and older children find the procedure very embarrassing.

We felt that if benzodiazepine was absorbed from nasal instillation this could provide a more acceptable alternative to rectal administration.

We have previously described the use of EEG monitoring to assess the use of benzodiazepines given intravenously and it was felt that a similar method could be used to assess the effectiveness of nasal midazolam (Livingston *et al.* 1987).

Patients and method

PATIENTS

A series of 19 consecutive children (one child was assessed twice) was chosen from those attending the Department of Neurophysiology, Royal Hospital for Sick Children, Edinburgh.

All the children were known to suffer from epilepsy (Table I). All had seizures that were difficult to control and all had an EEG that showed unequivocal activity of seizure type (*i.e.* paroxysmal slow activity, usually associated with spike and/or polyspike component). This abnormal paroxysmal activity persisted throughout a normal 20 minute recording. Two 20 second epochs were chosen pre- and post-medication and the spike rate was quantified. The post-medication epoch was always chosen when benzodiazepine-induced fast activity, if present, was at its maximum. The children were being considered for benzodiazepine medication as part of their clinical management. It is routine in this Department to assess sensitivity, habituation or a paradoxical response to benzodiazepines by monitoring the effects of an acute dose under EEG control.

MIDAZOLAM

To ensure correct dosage all the children were weighed before the procedure. The dosage of midazolam was 0.2 mg/kg of the intravenous solution (5 mg/ml). It was dripped slowly into the nose. If a patient did not respond in 10 minutes the dose was repeated. The patient's oxygen saturation and ECG were continuously monitored in addition to EEG.

Full resuscitation equipment was available, and a doctor was present during the administration of the drugs. The procedure was explained in detail to the parents, who in most cases were present throughout the procedure, and a full explanation was made to the child when appropriate.

Developmental Medicine and Child Neurology, 1996, 38, 1037–1045

TABLE 1
Summary of patient details

Case	*Age (yrs)*	*Sex*	*Diagnosis*	*Seizure types*	*Medication*
1 JMH	3.7	M	Rasmussen syndrome	Generalized tonic clonic	Phenytoin, phenobarbitone
2 CF	5.0	M	Mental retardation, epilepsy, autistic spectrum disorder	Polymorphic	Sodium valproate, phenytoin
3 DC	8.0	M	Lissencephaly	Tonic	Lamotrigine, clobazam pre-test
4 AF	6.5	M	Sturge--Weber syndrome	First presentation in status	Phenytoin
5 JC	5.0	M	Cerebral palsy secondary to HSV[1] encephalitis	Polymorphic	Lamotrigine, sodium valproate, clobazam post-test
6 SR	6.6	M	Intracerebral fungal abscess, shunted hydrocephalus, cyanotic heart disease	Generalized tonic clonic	Phenytoin
7 HMD	1.16	F	Shunted hydrocephalus, epilepsy	Generalized tonic clonic	Sodium valproate
8 DA[2]	5.0	M	Myoclonic epilepsy	Myoclonic	Carbamazepine and clobazam post-test
9 LL	3.0	F	Lennox–Gastaut syndrome	Polymorphic	Sodium valproate, phenytoin
10 RB	5.5	M	Cortical dysplasia, epileptic dysphasia	Atonic	ACTH, clobazam
11 LS	3.0	M	Lennox–Gastaut syndrome	Polymorphic	Phenytoin, sodium valproate, nitrazepam
12 TR	8.0	F	Cerebral palsy, microcephaly, epilepsy	Tonic	Carbamazepine
13 HA	1.0	F	Cryptogenic infantile spasms	Salaam attacks	Nitrazepam post-test
14 CB	0.5	M	Cerebral palsy, microcephaly	Generalized tonic clonic	Phenytoin, phenobarbitone
15 DH	14.0	M	Tuberous sclerosis	Generalized tonic clonic	Phenytoin, clobazam pre-test, lamotrigine
16 CF[3] see case 2					
17 BC	3.0	F	Epileptic aphasia	Aphasia, behavioural problems	Nitrazepam, ACTH
18 CMG[4]	3.0	M	Lennox–Gastaut syndrome	Polymorphic	Lamotrigine, clobazam post-test
19 WI	10	M	Primary epilepsy	Generalized tonic clonic	Carbamazepine
20 JB	7	M	Cervical meningocele with shunted hydrocephalus, cortical dysplasia and cerebral palsy	Generalized tonic clonic	Carbamazepine

[1]HSV = herpes simplex virus. [2]See Fig.1. [3]Cases 2 and 16 are same patient. [4]See Fig. 2.

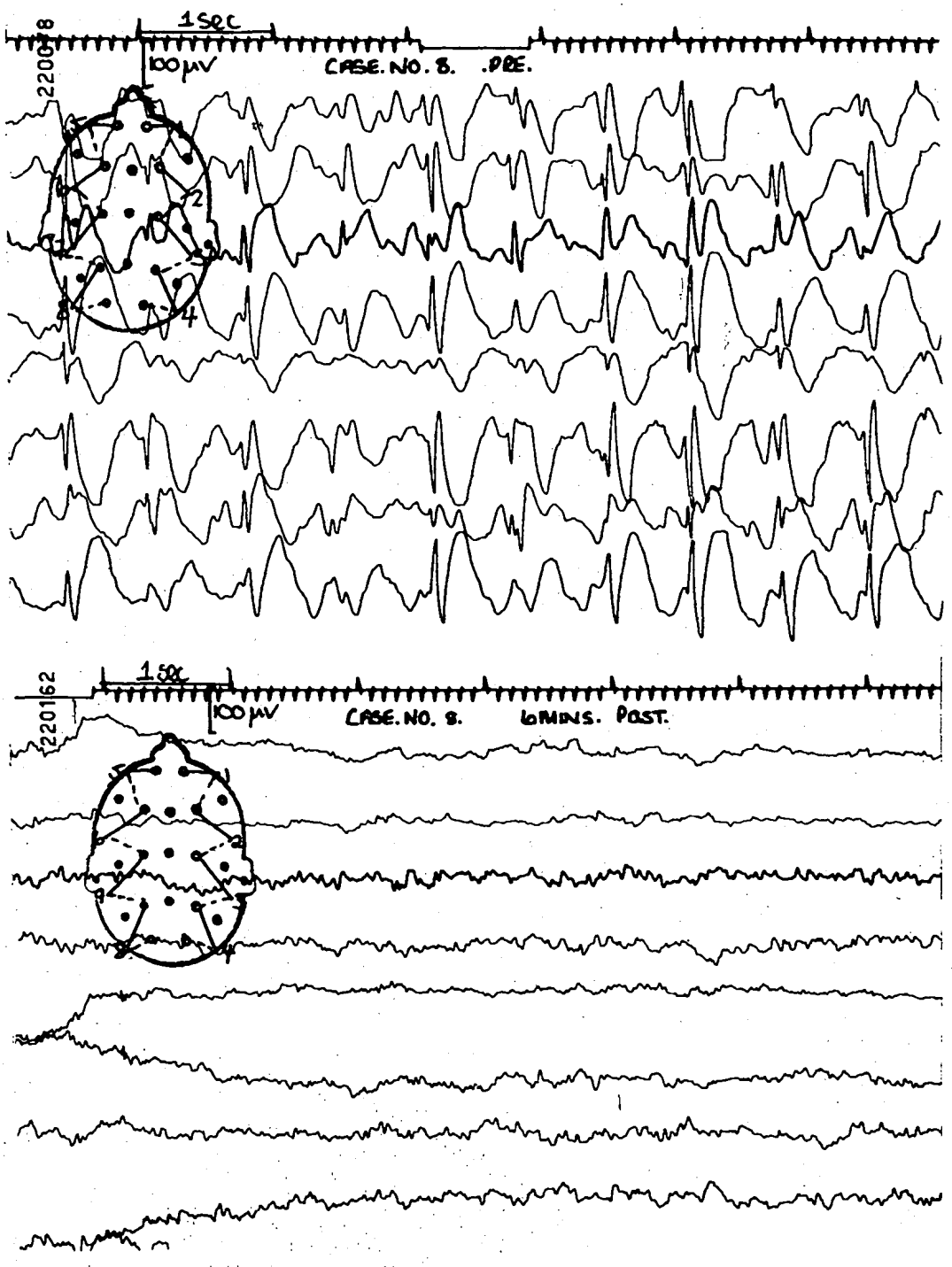

Fig. 1. A 5-year-old boy (case 8) in myoclonic status had a positive clinical response to intranasal midazolam.

EEG

Silver/silver chloride electrodes were applied by paste using the conventional 10–20 system and a routine baseline recording was made using a standard 16 channel EEG machine.

ANALYSIS

The following factors were assessed:

1) Sedative effects as seen clinically or with appropriate EEG changes.

2) Any changes noted in the heart rate or oxygen saturation.

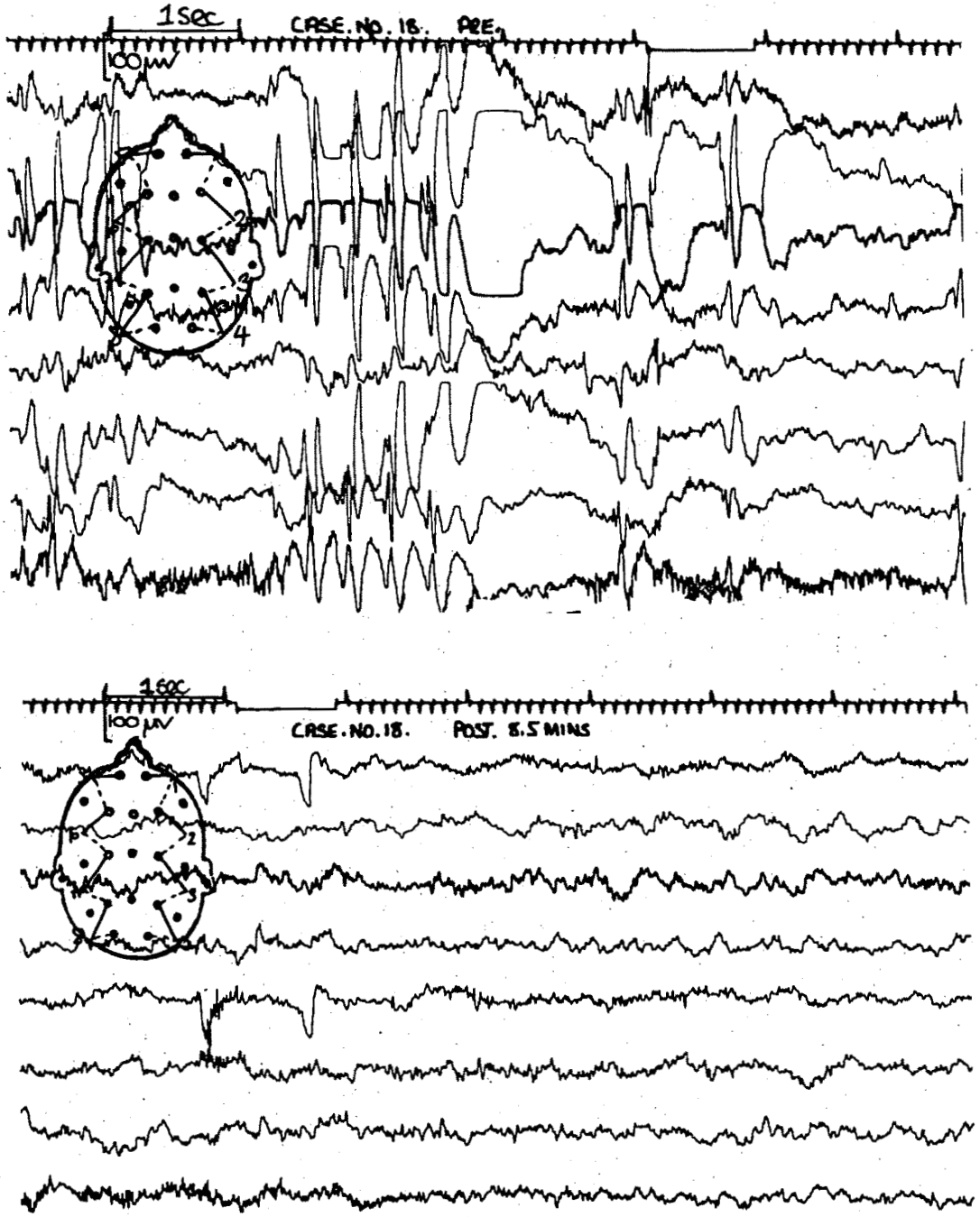

Fig. 2. *A 3-year-old boy (case no 18) with Lennox–Gastaut syndrome demonstrated a positive response to intranasal midazolam with abolition of the spike and wave complexes.*

3) Appearance of beta activity in the EEG.

4) Time of appearance of beta activity following medication.

5) Number of spikes seen before medication. The number of spikes per minute was counted in a representative part of the EEG. As soon as the count reached 100 it was terminated.

6) Number of spikes after medication. This was counted in exactly the same way as for before medication.

7) Effects on background EEG. Background abnormalities were divided

of EEG results before and after intranasal midazolam (MDZ)

normal EEG	*Spike count/ min pre-MDZ*	*Spike count/ min post-MDZ*	*Background pre-MDZ*				*Background post-MDZ*			
			Normal background	*Slow waves (ind)*	*Slow waves with Spike*	*Beta activity*	*Normal background*	*Slow waves (ind)*	*Slow waves with spikes*	*Drug-ind beta acti*
Yes	100	3	0	3	0	0	1	0	0	1
Yes	100	50	0	3	2	1	0	3	2	1
Yes	100	100	0	0	0	1	0	0	0	1
Yes	100	10	0	3	3	0	1	1	0	0
Yes	65	61	0	3	2	0	0	3	2	0
Yes	100	66	0	3	0	0	1	0	1	1
Yes	41	6	1	0	3	0	1	0	1	1
Yes	60	5	0	2	3	0	1	0	0	0
Yes	25	0	1	0	3	0	1	1	2	0
Yes	50	24	0	2	3	0	1	1	2	0
Yes	24	16	0	3	3	0	0	2	2	0
Yes	5	2	0	2	2	0	0	1	1	1
Yes	34	14	0	3	2	0	0	0	1	1
Yes	22	25	0	1	3	0	0	1	3	1
Yes	21	3	0	2	1	0	0	1	0	0
Yes	53	27	0	0	3	0	1	0	2	1
Yes	46	0	1	3	0	0	0	0	0	1
Yes	42	0	1	1	2	1	0	0	0	1
Yes	30	21	1	0	1	0	1	0	1	1
Yes	46	6	1	1	2	0	1	0	0	1
	53.2	21.95	0.2	1.75	1.9	0.15	0.5	0.75	0.85	0.7
	31.13	27.15	0.47	1.25	1.16	0.36	0.51	1.01	0.98	0.47
		3.8						2.77	4.3	4.12
		<0.01 Spike count pre and post-MDZ						<0.02 Slow wave independent	<0.01 Slow wave and spike	<0.001 for the appearan of beta p MDZ

the same patient as case 2.

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