RECTAL ADMINISTRATION OF DIAZEPAM

Sir,—The study by Sonander, Arnold and Nilsson (1985) claims to demonstrate the superiority of a rectal solution of diazepam over suppository for rectal premedication. Their results, however, do not necessarily support this conclusion. The suppository produced a higher serum concentration of diazepam than the rectal solution at 2 h and the median value for suppositories was consistently higher after 1.5 h. Clearly, in relation to the majority of clinical practice, the suppository represents a more usual situation where premedication is administered approximately 2 h before operation and will produce favourable blood concentrations at the time of induction. However, it is not apparent how many estimations are represented by each data point in figure 4 and, in view of the statement that an incomplete number of samples was obtained, it is questionable that a valid conclusion can be drawn.

The distribution of children’s ages in the groups is not given. It is important to know if the two groups were comparable in respect of children younger or older than 5 years of age, since it has been shown that serum concentrations of diazepam after oral administration are greater in older children than in those younger than 5 yr (Lindgren, Saarnivaara and Himberg, 1980).

The suggested sedative value for serum diazepam of 150 ng ml\(^{-1}\) exceeded by both regimens at 8 h and by the suppository groups at 24 h and the rectal solution might appear to offer some advantages in this respect. However, Fell and colleagues (1985) measured plasma diazepam concentrations in children at 24 h after oral premedication and the concentrations obtained in that study, of the order of 600–800 ng ml\(^{-1}\) exceed those of Sonander, Arnold and Nilsson at 24 h. The patients in that study were discharged from hospital immediately following blood sampling and no clinically important side effects were reported at that time. It may not be expected, therefore, that there is any clinical benefit at this time as a result of the lower serum concentration associated with the use of the rectal solution.

It would have been interesting to know if the two groups differed in their clinical response to the premedication for, although plasma concentrations do not correlate with clinical effects (Kanto et al., 1979), the differing rates of achievement of the maximum serum concentrations in Sonander’s patients might have produced some relevant clinical differences.

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REFERENCES


Sir,—Thank you for giving us the opportunity to reply to Dr Fell’s letter. Each data point in the figure in our study is the median of 5–7 plasma diazepam estimations. This number is sufficient for the statistics used (Wilcoxon rank sum test) to discriminate between the two groups. We usually do not administer premedication as early as 2 h before operation, 30–60 min is more common, in which case our opinion is that pharmacokinetic data favour the use of rectal solution of diazepam. The period around 30 min is supported by a study of Ellinwood and co-workers (1983). They found maximal behavioural impairment after oral diazepam administration in adults after 20–60 min in spite of higher plasma concentrations at 2 h and later. They also found that the slope of the response to dose at each time period was significant from 20 to 120 min.

Richardson and Manford (1979) found amnesia for induction at 240 ng ml\(^{-1}\) compared with no amnesia at 148 ng ml\(^{-1}\) (P < 0.01) so there is at least one report in favour of a positive correlation between plasma concentration and clinical effect in children.

In our study there were four children younger than 5 yr in both groups. Pooled data at 3 ± 0.5 h showed a higher, but not significant, plasma diazepam concentration in the six children older than 5 yr, which agrees with what Lindgren, Saarnivaara and Himberg (1980) found. Pooled data at 30 min, however, showed a higher median plasma concentration in children less than 5 yr (528 v. 288 ng ml\(^{-1}\)); this difference is not significant.

The plasma concentrations found by Fell and colleagues (1985) are remarkably high, since their mean (± SEM) value before operation (= 90 min) seems to be around 950 ± 70 ng ml\(^{-1}\) in the 0.25-mg kg\(^{-1}\) group, compared with 164 ± 14 ng ml\(^{-1}\) found by Lindgren, Saarnivaara and Himberg (1980) after the same oral dose. Diazepam concentrations in the order of 600–800 ng ml\(^{-1}\) at 24 h after premedication are probably without side effects unless they are accompanied by high levels of the metabolite N-desmethyldiazepam, which seem to cause drowsiness and prolonged sedation (Langslet et al., 1978).

One of our aims was to study the plasma concentrations in children in the 4–24 h interval, since this period seemed poorly documented when we started our study. Fell and colleagues have made a valuable contribution to this knowledge.

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REFERENCES


SUCCESSFUL RESUSCITATION AFTER CARDIAC ARREST FOLLOWING I.V. REGIONAL ANAESTHESIA (IVRA)

Sir,—There has been much recent correspondence about the hazards of IVRA using bupivacaine. We would like to report our own experience in this connection.

A 67-y-old lady with a right-sided Colles Fracture was seen in the Accident Department. She was found to be in good health and there was no medical history of any significance, nor was she on any medication. Her arterial pressure was recorded at 160/90 mm Hg. As is the policy of the department, it was decided to manipulate the fracture under IVRA.

An automatic tourniquet which included a sphygmomanometer cuff was used. A “Butterfly” needle was inserted to the dorsum of the hand on the affected side and the cuff was inflated to 220 mm Hg. After elevating the arm, 0.25% bupivacaine 40 ml was injected. At the end of the injection the patient complained of severe headache, screwed up her eyes and had an episode of convulsions similar to a Grand-Mal seizure lasting several seconds. She soon became apnoeic, cyanosed and had a second attack of convulsions, followed by cardiac arrest.

The trachea was intubated, the lungs ventilated and closed chest cardiac compression was commenced. Two doses of diazepam 10 mg were given i.v. between seizures through a “Venflon” inserted to the uninjured limb.

Cardiac output returned within 30 s and the patient commenced spontaneous breathing within 2 min. The trachea was extubated within 15 min of the episode and the patient had regained consciousness within 30 min, albeit somewhat drowsy as a result of diazepam. We estimate the total anoxic state to have lasted less than 2 min. The fracture was manipulated and the patient was admitted for observation. We are happy to report that she made an uneventful recovery.

The cardiovascular system is considered more resistant than the central nervous system to local anaesthetic agents (Albright, 1979; Scott, 1981). Several cases of convulsions whilst the cuffs were still inflated during IVRA have been reported in recent years. This may be the result of inadequate compression of the arm despite the manometer registering a reading well above the recorded systolic pressure. This, we feel, highlights the problems encountered with certain types of equipment (Heath, 1982).

In the light of our experience we have discontinued the use of the automatic tourniquet. We have recently acquired tourniquets with bicycle pump attachments, and find them more accurate and reliable.

We would like to stress that, as a departmental policy, all our manipulations are carried out in fully equipped theatres and a “Venflon” is inserted to the unaffected limb as routine. Above all we have a comprehensive training programme for our Accident and Emergency Staff in Cardio Pulmonary Resuscitation.

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