EFFECTS OF THE RECTAL ADMINISTRATION OF DIAZEPAM

Diazepam Concentrations in Children Undergoing General Anaesthesia

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Pharmacokinetic studies have compared parenteral and various rectal preparations of diazepam in adults (Moolenaar et al., 1980; Magnusson et al., 1979) and children (Meberg et al., 1978) and indicated that systemic concentrations increase rapidly and are well maintained after rectal administration. Such a profile is of interest to the anaesthetist as it will provide a rapid increase to sedative concentrations for premedication and an effect which will last into the period after operation. We have studied serum concentrations of diazepam for 24 h after its rectal administration, in solution or by suppository, to children undergoing general anaesthesia.

PATIENTS AND METHODS

Following consent from the parents and the approval of the local Ethics Committee, 14 children (aged 1.5–8 yr) weighing 11–22.5 kg (mean 16.9 kg) were given diazepam before minor surgery (mainly squint operations). Seven were given a solution (solvent: propyleneglycol) through a rectal tube (Stesolid, AS Dumex) and seven received suppositories (Stesolid supp., AS Dumex). No special precautions were taken to keep the drug in the rectum. A dose of 1 mg/kg body weight, adjusted to the nearest 5 mg, was used. This resulted in a mean dose of 0.99 mg kg⁻¹ (range 0.8–1.2) of the rectal solution and 0.96 mg kg⁻¹ (range 0.8–1.1) of the suppositories.

Venous blood was withdrawn before administration and at the following intervals for measurement of serum diazepam concentration: for rectal solution—5, 10, 15, 20, 30, 40 min, 1, 1.5, 2, 4, 8, 24 h; for suppositories—10, 20, 40 min, 1, 1.5, 2, 2.5, 3, 4, 8 and 24 h. Slight deviations in sampling times occurred and all times are given with the range within which blood sampling was performed. Samples could not be obtained at all intervals in all children. Serum was deep frozen for later analysis of the concentration of diazepam using the gas-chromatographic method described by Arnold (1975). Drugs used during anaesthesia and the period after operation included halothane, thiopentone, pancuronium, trimethazine, ketamine, paracetamol and salicylic acid. The possibility that any or all of these drugs may have affected the determination of the diazepam concentration was assessed.

Statistical methods

Each serum concentration was standardized to a given dose of 1 mg kg⁻¹, whereafter serum concentrations at corresponding intervals were tested with the Wilcoxon rank sum test (Colton, 1974) at the 95% confidence level with the zero hypothesis that...
there was no difference between the two methods of administration.

RESULTS
The interference measurements did not suggest that the diazepam peaks included any of the other drugs given to the patients.

After the rectal solution the serum concentration of diazepam increased rapidly, whereas suppositories caused a slower increase, but to a higher serum concentration (fig. 1). The suggested sedative value of 150 ng ml\(^{-1}\) (Mattila et al., 1981) was exceeded in five of the seven children given the rectal solution at 5 min and in all of them at 10 min. Diazepam concentrations were not measured at 5 min after suppositories, but at 10 min only three of the seven children had serum concentrations greater than 150 ng ml\(^{-1}\) and at 40 min one was still below this value.

The rectal solution group had its peak median value of 619 ng ml\(^{-1}\) (range 315–945) at 30 min, whereas in the children receiving suppositories, the peak median value of 848 ng ml\(^{-1}\) (range 560–1141) was obtained at 2 h ± 15 min. At 10 and 20 min the diazepam concentration after rectal solution was significantly greater than after suppositories, the reverse being the case at 2 h ± 15 min. At all other intervals there were no statistically significant differences between the two methods of administration. The median values after suppositories were, however, higher at all intervals after 1.5 h.

![Fig. 1. Serum concentrations of diazepam (median and range) in two groups of children (n = 7), treated with diazepam 1 mg/kg body weight rectally, either as a solution (•) or as suppositories (△).](https://academic.oup.com/bja/article/57/6/578/272047)
anaesthetic or the early postoperative period, since many surgical procedures in children are rather short. A smaller dose given earlier will decrease this peak, but will make the degree of sedation less predictable. In our opinion the rapid increase and well maintained serum concentrations associated with the use of a rectal solution of diazepam is to be preferred. It also allows a wide variation in administration time and a smooth recovery after minor paediatric surgery.

REFERENCES


