CORRESPONDENCE

DIAZEPAM AND MIDAZOLAM FOR SEDATION DURING BRONCHOSCOPY

Sir,—It is regretted that the interesting paper by Korttila and Tarkkanen (1985) does not state which preparation of diazepam they used. The early relative potency studies of midazolam and diazepam were undertaken with the organic solvent preparation, Valium. A review (Dundee et al., 1984) of these puts the relative potency of the two drugs at about 1.5:2.1:1. However, if Korttila and Tarkkanen used the emulsion preparation (Diazemuls) this would be expected to be about 20% less potent than Valium and patients would have been given relatively less diazepam (Fee et al., 1984).

While the authors found no difference in duration of action of small doses, with larger doses (midazolam 0.3 mg kg\(^{-1}\) and diazepam 0.5 mg kg\(^{-1}\)) there is a very obvious difference in recovery time between the two benzodiazepines.

Changes in relative bioavailability, depending on the solvent, have been demonstrated for both midazolam and propofol (Cummings et al., 1984). It is thus important that authors should state which preparation of diazepam they used.

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REFERENCES


Consequently, we did not give relatively less diazepam, as might have been the case with the same dose of Diazemuls.

The half-life at elimination phase \((T^e_1)\), which is dependent on both volume of distribution \((V^m)\) and clearance \((C_l)\) of the drug:

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T^e_1 = \frac{V^m \times 0.693}{C_l}
\]

is important during continuous treatment with the drug (Duvaldestin, 1981). It has been suggested that a benzodiazepine derivative is “short acting” if its elimination half-life is less than, for example, 10 h and if it does not have a tendency to cumulate during continuous therapy in normal clinical doses.

With acute administration, for example i.v. sedation, recovery is associated with liquid solubility and distribution of the drug instead of elimination half-life (Duvaldestin, 1981). The half-life at distribution phase mirrors the movement of the drug from blood (and brain) to peripheral tissues and is related to the duration of action and recovery after acute drug administration.

The half-lives for the initial distribution phase have been reported to be similar for diazepam \((0.30 \pm 0.11 \text{ h})\) (Ghoneim et al., 1981) and midazolam \((0.31 \pm 0.08 \text{ h})\) (Greenblatt et al., 1984) which predicts that recovery after acute administration of both agents would also be similar. Jack and colleagues (1983) used a receptor binding model in rat brain to shed light on the onset and duration of action of diazepam, midazolam and lorazepam. Their studies indicate that both diazepam and midazolam occupied the receptors rapidly and disappeared from receptors faster than lorazepam, parallelling the relative onset and duration of the sedative and amnesic properties of these drugs in man.

Recently, Skelly and co-workers (1984) compared diazepam \(26 \pm 7 \text{ mg (mean \pm SD)}\) and midazolam \(13 \pm 3 \text{ mg (mean \pm SD)}\) as sedatives in 40 patients undergoing minor oral surgery. Recovery was thoroughly studied by six psychomotor tests repeated over 5 h. More amnesia was reported in the midazolam group and there was no significant evidence of the midazolam group recovering more quickly. The authors point out that significant impairment of delayed memory recall persisted in both groups throughout the investigation period.

Similarly to diazepam, in ambulatory practice each patient receiving i.v. midazolam sedation must have an escort when discharged from hospital and patients should refrain from driving or operating machinery for at least 12–24 h.

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