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Intravenous midazolam for upper gastrointestinal endoscopy: A study of 800 consecutive cases relating dose to age and sex of patient

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In many endoscopy units midazolam is replacing diazepam as the intravenous sedative of first choice. Midazolam is approximately twice as potent as diazepam. Although generally considered a safe drug, there have been a number of recent reports, particularly in the elderly, of the drug causing hypotension, respiratory depression and even death. There have been at least ten studies comparing diazepam with midazolam for upper gastrointestinal endoscopy but many have involved relatively small numbers and none have adequately addressed the question of dosage in the elderly. We have carefully recorded the dose of intravenous midazolam used to produce adequate sedation prior to upper gastrointestinal endoscopy in 800 consecutive patients. The dose of midazolam decreased markedly with age in both male and female patients. There was a highly significant correlation in both sexes between age and the dose of midazolam (rho -0.787, $P < 0.001$ for males and rho -0.768, $P < 0.001$ for females). There was only a small difference in dose in men and women, an average of 1 mg; and no difference in dose over the age of 70 years. In patients over 70 years of age the dose of midazolam necessary for endoscopy is often so small that overdosage is all too easy.

Keywords midazolam relationship dose age

Introduction

There have been at least 10 studies comparing midazolam and diazepam as intravenous sedatives for upper gastro-intestinal endoscopy (Al-Khudhairi *et al.*, 1982; Bardhan *et al.*, 1984; Berggeren *et al.*, 1983; Brophy *et al.*, 1982; Cole *et al.*, 1983; Green *et al.*, 1984; Kawar *et al.*, 1984; Magni *et al.*, 1983; Whitwam *et al.*, 1983). None of these studies give adequate recommendations regarding dosage in the elderly. We found this surprising since (a) the half-life of midazolam is prolonged in elderly patients (Smith *et al.*, 1984) and (b) there have been reports to the C.S.M. of intravenous midazolam causing respiratory depression, hypotension and occasionally even death, particularly in elderly patients (C.S.M. Current Problems 14th February 1985). We therefore carefully recorded the dose of midazolam required to achieve adequate sedation prior to upper gastrointestinal endoscopy in 800 consecutive patients. This paper reports our results.

Methods

Eight hundred consecutive patients referred to GDB for upper gastro-intestinal endoscopy were included in the study. A lignocaine throat spray was given to anaesthetize the back of the throat. In most patients, approximately 2.5 mg

midazolam was administered intravenously over 30 s, while elderly patients received only 1 mg of the drug. The patient was actively engaged in conversation and adequate sedation was judged to have occurred when the patient became dysarthric and drowsy, but was still able to co-operate. If, after 1–2 min, adequate sedation had not been achieved, further increments of midazolam were given until the appropriate level of consciousness was reached. The age, sex and total dose of midazolam given to each patient was recorded.

Statistics

Analysis of variance has been used to compare means and the significance of differences between two means has been assessed using Student's *t*-test with the standard errors derived from the within group variance. The correlation between age and dose of midazolam has been examined using Spearmans rank correlation test.

Results

Eight hundred consecutive patients undergoing endoscopy were entered into the study but six patients were later excluded. Of the remaining 794 cases, there were 415 male and 379 female patients. The mean age of the whole group was 57.5 years and the mean dose of intravenous midazolam was 6.9 mg. The mean dose of midazolam required in the male patients was slightly greater than the female (7.4 mg *vs* 6.4 mg) but this was not significant.

There was a strong relationship in both males and females between the dose of midazolam used and the subject's age (rho -0.787, $P < 0.001$ for males and rho -0.768, $P < 0.001$ for females). This data is shown in Figure 1 and Table 1.

Only 7.2% (16/221) of the patients over 70 years of age required more than 5 mg midazolam.

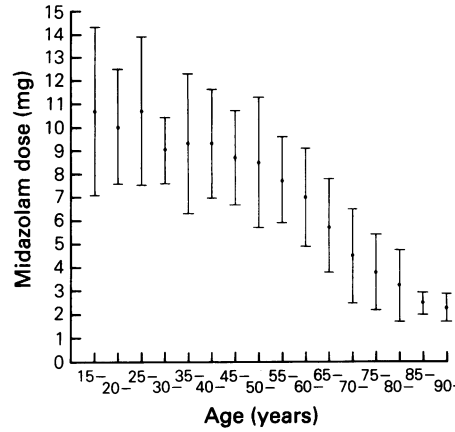

Figure 1 Relationship between age of patient and the mean dose (± 1 s.d.) of intravenous midazolam required to produce adequate sedation prior to upper gastro-intestinal endoscopy.

In contrast, most (478/573 = 83%) of patients less than 70 years of age required more than 5 mg midazolam.

Discussion

We confirm earlier smaller studies that midazolam is an effective intravenous sedative for upper gastro-intestinal endoscopy. In view of the strong relationship between age and dose of midazolam (see Figure 1) we recommend extreme caution when endoscoping elderly patients; many of whom may require only 0.25–0.5 of a single 10 mg ampoule to produce adequate sedation.

We hesitate to make precise recommendations regarding dosage in elderly patients since, of course, the measured end point (namely sedation adequate to permit endoscopy) is so subjective. Nevertheless, we now never draw up more than 5 mg of the drug into a single syringe when a patient over the age of 70 years is submitted to endoscopy.

Table 1 Mean dose of midazolam by age and sex

Age (years)	*Number of males*	*Dose (mg)*	*s.d.*	*Number of females*	*Dose (mg)*	*s.d.*
15–24	17	10.4	2.5	17	10.0	3.3
23–34	37	10.3	3.1	27	9.2	1.4
35–44	56	9.8	2.8	48	8.8	2.5
45–54	72	8.9	2.5	46	8.2	2.3
55–64	88	7.5	1.8	62	7.1	2.3
65–74	84	5.4	2.1	106	4.9	2.3
75–84	56	3.7	1.6	54	3.6	1.6
85+	5	2.3	0.3	19	2.4	0.5
	415	7.4	3.2	379	6.4	3.1

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