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# Small bolus injections of intravenous midazolam for upper gastrointestinal endoscopy: a study of 788 consecutive cases

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1 A recent audit of upper gastrointestinal endoscopy carried out by the Royal College of Surgeons of England [1] has shown that the majority of endoscopists use a bolus injection rather than a slow intravenous titration of benzodiazepine for intravenous sedation. In this study we have confirmed the theoretical premise that a reduced dose of midazolam is required when given as a bolus. A mean dose of 4.65 mg midazolam intravenously has been found to be effective and safe in sedating patients under 70 years ($n$ = 552). The dose of midazolam needed is reduced in older patients: patients over 70 years ($n$ = 236) needed a mean dose of 1.89 mg.

2 Topical pharyngeal anaesthesia was not required with these doses of midazolam, and it was our impression that the examination was equally well tolerated with a similar degree of anterograde amnesia as in the previous study.

3 Our data, together with the results of the audit [1], would suggest many endoscopists are employing unnecessarily large and at times potentially dangerous doses of intravenous sedation in elderly patients and that the vast majority of upper gastrointestinal endoscopies can be performed successfully, without topical pharyngeal anaesthesia, using a bolus injection technique with a reduced dosage of sedative agent.

**Keywords** midazolam bolus *vs* titration dose age endoscopy

## Introduction

The majority of upper gastrointestinal endoscopies performed in both the United Kingdon [2] and the United States of America [3] are carried out under intravenous sedation. In the USA most procedures are carried out using a combination of an opioid analgesic, such as pethidine, together with a benzodiazepine [3], whereas in the UK endoscopists more commonly use a benzodiazepine as sole agent [2]. Midazolam is the benzodiazepine of choice in the USA [3], while diazepam and midazolam are used with similar frequency in the UK [1, 2].

Most complications and deaths resulting from upper gastrointestinal endoscopy are cardiopulmonary in nature [4, 5]. Many of these may be related to the use of intravenous sedation. Sedation may be administered either slowly, titrated against its effect over 2–3 min, or rapidly as a bolus.

It has been observed with anaesthetic induction agents that increasing the speed of injection increases potency [6], in association with increased drug concentration [7].

There are potential problems with both rapid bolus and slow titration injection methods. It has previously been demonstrated by ourselves [8] and others [9], that if a rapid bolus injection is given the dose of sedative required is smaller, but the degree of arterial oxygen desaturation at the time of the examination is much greater than when a slow titration method is chosen. Conversely, titrating the sedation would be expected to eliminate some of the perioperative respiratory depression, however it leaves the patient with a greater sedative load to eliminate, and the possibility of a prolonged postoperative recovery phase. This carries with it the attendant dangers of respiratory depression and obstruction leading to hypoxia, and a reduction in ability to protect the airway from regurgitated gastric contents.

The risk of aspiration is further compounded by the widespread use of topical pharyngeal anaesthesia for upper gastrointestinal endoscopy, by means of a 10% weight/volume lignocaine throat spray. The evidence that local anaesthetic throat sprays are beneficial

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is poor [10] and our group now only employ topical pharyngeal anaesthesia in patients being endoscoped without intravenous sedation.

We have previously described our results giving midazolam as a titrated dose over 2–3 min to 800 consecutive patients. Those pateints also received topical pharyngeal anaesthesia. We related the dose required for adequate sedation to the age and sex of the patient [11]. However, a large prospective study by the Audit Unit of the Royal College of Surgeons [1] has shown that the majority of endoscopists in the two regions audited (East Anglia and North West) appear to be using a more rapid injection technique (either a very rapid bolus or injecting over 20–30 s) and that the use of topical pharyngeal anaesthesia was widespread (77% of the audit cases sedated with midazolam).

Theoretically, the bolus dose of midazolam (used by those audited endoscopists [1] who employed a bolus injection to sedate their patients) ought to be considerably smaller than we had described using the careful titration technique [11]. We were also interested to see if the audited endoscopists who had additionally used either a lignocaine throat spray for topical pharyngeal anaesthesia or supplemental opioid analgesics, used a smaller dose of midazolam for sedation than those using it as a sole agent.

The purpose of the present study was to determine the effectiveness of a small bolus injection of intravenous midazolam in a large group of patients undergoing upper gastrointestinal endoscopy without topical pharyngeal anaesthesia. We decided to study 800 consecutive cases in order to relate this to our previous study of the use of titrated midazolam administration [11]. This paper reports our results and demonstrates the difference in dose of midazolam used by our group when compared with others currently as reported to the Upper Gastrointestinal Endoscopy Audit Project [1].

## Methods

Eight hundred consecutive patients referred to GDB for upper gastrointestinal endoscopy were included in the study. All patients were endoscoped by one operator (GDB) under direct vision using a Pentax FG34X or FG29X forward viewer. If patients were considered too sick to be given intravenous sedation or themselves requested that the examination be performed without intravenous sedation they were not sedated and excluded from further study. All patients were given supplemental oxygen at a rate of 2 l $min^{-1}$ either using nasal cannulae or a modified mouth guard [12], and monitored both clinically and with pulse oximetry. Additionally, all patients had an indwelling intravenous cannula inserted.

Patients under the age of 50 years were initially given 5 mg midazolam as a rapid intravenous bolus injection over 2–3 s. Patients between 50 and 70 years received 3–5 mg midazolam at the discretion of the endoscopist (GDB). No patient over 70 years was given more than 2 mg midazolam and patients over the age of 80 years were only given 1–1.5 mg midazolam.

Further incremental doses of midazolam were only given exceptionally; if the patient was judged to be inadequately sedated, if oesophageal intubation proved difficult or in the presence of a pre-existing factor such as known alcoholism or intercurrent therapy with high dose oral benzodiazepines. No patient received any opioid supplementation.

## Results

Only 12 of the 800 consecutive patients endoscoped during the study received no sedation. These were excluded from further consideration. Thus 788 patients remained to analyse. There were 437 male patients with a mean age of 58.2 years (s.e. mean 0.84; range 15–93). The 351 female patients had a mean age of 56.7 years (s.e. mean 0.93; range 15–93).

The mean dose of midazolam used was 3.8 mg (s.e. mean 0.05; range 0.75–10). There was no significant difference between male and female patients: mean doses were 4.0 mg (s.e. mean 0.07) and 3.7 mg (s.e. mean 0.08) respectively. All 788 patients were successfully endoscoped. The mean doses of midazolam by age and sex are given in Table 1. None of these 788 patients received any topical pharyngeal anaesthesia.

In all there were 236 patients aged 70 years or over and 552 aged under 70 years. The mean dose of midazolam in patients 70 years and over was 1.89 mg (s.e. mean 0.03), with only two patients receiving more than 2.5 mg and 50% receiving 2 mg. In those patients under 70 years the mean dose of midazolam was 4.65 mg (s.e. mean 0.03), with only seven patients receiving more

**Table 1** Mean dose of midazolam against age and sex. Bolus study

| | *Patient numbers* | | | *Dose (mg)* | | | *s.e. mean* |
|---|---|---|---|---|---|---|---|
| *Age (years)* | *Male* | *Female* | *All* | *Male* | *Female* | *All* | *All* |
| 15–24 | 17 | 10 | 27 | 5.1 | 5.3 | 5.2 | 0.12 |
| 25–34 | 32 | 28 | 60 | 5.0 | 5.2 | 5.1 | 0.07 |
| 35–44 | 77 | 36 | 113 | 5.0 | 4.9 | 5.0 | 0.05 |
| 45–54 | 58 | 51 | 109 | 5.0 | 4.9 | 5.0 | 0.04 |
| 55–64 | 79 | 63 | 142 | 4.5 | 4.4 | 4.5 | 0.08 |
| 65–74 | 99 | 66 | 165 | 3.2 | 3.1 | 3.2 | 0.08 |
| 75–84 | 62 | 84 | 146 | 1.8 | 1.8 | 1.8 | 0.03 |
| 85+ | 13 | 13 | 26 | 1.5 | 1.3 | 1.4 | 0.08 |
| All | 437 | 351 | 788 | 4.0 | 3.7 | 3.8 | 0.05 |

than 5 mg, 72% receiving 5 mg and 23% receiving 2.5 mg or less.

No patient in the study had any serious episode of hypoxia. Intravenous flumazenil was given in 11 (1.4%) cases. In all 11 cases this was after the completion of the endoscopy and in 9 of the 11 cases this was a precautionary measure rather than because of severe respiratory depression or overtly excessive sedation.

For the purposes of comparison the mean dose of midazolam by age and sex from our previous titration study [11] is given in Table 2. The mean doses of midazolam given as a bolus were significantly lower at all age groups than in the previous titration study ($P < 0.001$). Figure 1 compares the results of both studies graphically. The groups are reasonably well matched. Although not formally tested in the present study, it was our impression that the degree of anterograde amnesia following the smaller bolus doses of midazolam was similar to that experienced in the earlier titration study [11]. Likewise, although not formally tested it was also our impression that the ease of intubation and patient acceptability of the procedure was unaffected by the omission of topical pharyngeal anaesthesia.

## Discussion

In the present study we have confirmed an earlier pilot study [8] and demonstrated that it is possible to effectively and safely sedate patients undergoing upper gastrointestinal endoscopy using small bolus injections of midazolam with adequate monitoring and the use of supplemental oxygen. A bolus injection is much quicker than the titration method [8]. The dose of sedative required is also greatly reduced. The use of topical pharyngeal anaesthesia was unnecessary, confirming the finding of Chuah *et al.* [10]. A predisposition to aspiration of gastric contents may therefore be avoided.

Two of us (MAQ and GDB) have been involved in a prospective audit of upper gastrointestinal endoscopy carried out by the Audit Unit of the Royal College of Surgeons of England [1]. Over 14,000 upper gastrointestinal endoscopies were surveyed, of which 6,067 were performed using intravenous sedation with midazolam. The majority of these patients were sedated using a modified bolus injection technique (over 20–30 s) and not the careful titration technique described in our previous study [11]. Therefore, the dose of midazolam used for sedation by the audited endoscopists ought to equate more closely to the doses used in our present study than the higher doses recommended from our previous study [11] using slow titration. However, the mean doses of midazolam used by the audited endoscopists was greater in all age groups than in this study (overall mean 5.7 mg, s.e. mean 0.03, *vs* 3.8 mg, s.e. mean 0.05, a difference in the means of 1.9 mg, 95% confidence limits 1.73–2.09 mg). In patients over 75 years the mean midazolam dose is higher even than that found effective in our previous titration study [11], (see Figure 2, $P < 0.001$) in both instances. The difference in the means was 0.7 mg in patients aged between 75 and 85 years, 95% confidence limits 0.33–1.07 mg. In patients over 85 years the difference in the means was 1.29 mg, 95% confidence limits 0.60–1.99 mg). Doses were dangerously excessive in some individual cases among the 75 and over age group. Tables 3, 4, 5, and 6 and Figure 3 show the mean dose of midazolam by age reported from this audit, both in total and also further broken down to sub-groups (when it was used in isolation, in conjunction with pethidine or topical pharyngeal anaesthesia with lignocaine, respectively).

In the small sub-group of patients given midazolam in conjunction with pethidine the mean dose was higher than in those receiving midazolam as a sole agent (7.1 mg, s.e. mean 0.42 *vs* 5.9 mg, s.e. mean 0.09, a difference in the means of 1.2 mg, 95% confidence limits 0.39–2 mg). There was, however, a minimal reduction in midazolam dose given when topical anaesthesia was used (5.6 mg, s.e. mean 0.04, *vs* 5.9 mg, s.e. mean 0.09, $P = 0.008$, a difference in the means of 0.3 mg, 95% confidence limits 0.11–0.49 mg).

After its launch, early clinical work on midazolam was carried out assuming its potency to be twice that of diazepam (13–16]. Even in these studies there is some hint that this may not be a true reflection of potency, as the studies all mention greater amnesia and one [13] demonstrated greater respiratory side effects when diazepam and midazolam were given in a 2:1 ratio. The current data sheet recommendations for midazolam [17] give 0.07 mg $kg^{-1}$ as a guideline for the total use necessary for sedation, but they also stress that a smaller dose should be given initially and that 2 min should pass before any further increments are given. By

**Table 2** Mean dose of midazolam by age. Titration study [11]

| | *Patient numbers* | | | *Dose (mg)* | | | *s.e. mean* |
|---|---|---|---|---|---|---|---|
| *Age (years)* | *Male* | *Female* | *All* | *Male* | *Female* | *All* | *All* |
| 15–24 | 17 | 17 | 34 | 10.4 | 10.0 | 10.2 | 0.50 |
| 25–34 | 37 | 27 | 64 | 10.3 | 9.2 | 9.8 | 0.33 |
| 35–44 | 56 | 48 | 104 | 9.8 | 8.8 | 9.3 | 0.26 |
| 45–54 | 72 | 46 | 118 | 8.9 | 8.2 | 8.6 | 0.22 |
| 55–64 | 88 | 62 | 150 | 7.5 | 7.1 | 7.3 | 0.16 |
| 65–74 | 84 | 106 | 190 | 5.4 | 4.9 | 5.1 | 0.16 |
| 75–84 | 56 | 54 | 110 | 3.7 | 3.6 | 3.7 | 0.15 |
| 85+ | 5 | 19 | 24 | 2.3 | 2.4 | 2.4 | 0.10 |
| All | 415 | 379 | 794 | 7.4 | 6.4 | 6.9 | 0.11 |

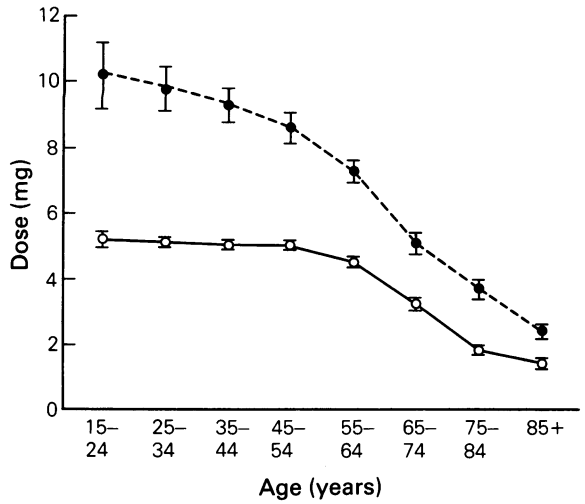


**Figure 1** Dose of midazolam *vs* age (mean ± 2 s.e. mean). ○ bolus, ● titrated.

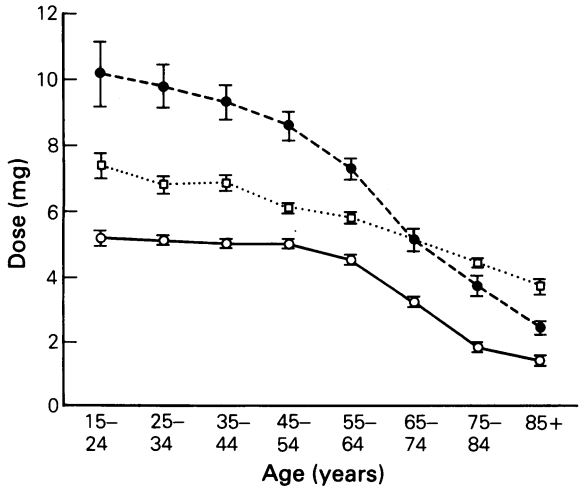


**Figure 2** Dose of midazolam *vs* age (mean ± 2 s.e. mean). ○ bolus, ● titrated, □ audit data (overall).

**Table 3** Mean dose of midazolam used against age. Audit figures from East Anglia and the North West (1991) [1]. (All patients who received midazolam)

| *Age (years)* | *Patient numbers* | *Dose (mg)* | *± s.e. mean* |
|---|---|---|---|
| 15–24 | 236 | 7.38 | 0.19 |
| 25–34 | 507 | 6.81 | 0.13 |
| 35–44 | 742 | 6.88 | 0.11 |
| 45–54 | 919 | 6.34 | 0.08 |
| 55–64 | 1135 | 5.80 | 0.07 |
| 65–74 | 1306 | 5.14 | 0.05 |
| 75–84 | 980 | 4.40 | 0.06 |
| 85+ | 245 | 3.69 | 0.11 |
| All | 6070 | 5.71 | 0.03 |

contrast, diazepam data sheets [18, 19] suggest that 0.2 mg $kg^{-1}$ as a sedation dose, which would reflect a potency ratio of 3:1. As further work including studies of the electroencephalographic effects of both drugs to give dose-response curves [20–24] has been carried out, the ratio of potency has been demonstrated to be nearer 5:1. For both drugs the recommendations are to reduce dosage in the elderly, in the case of midazolam to half

**Table 4** Mean dose of midazolam used against age. Audit figures from East Anglia and the North West (1991) [1]. (Midazolam as sole agent)

| *Age (years)* | *Patient numbers* | *Dose (mg)* | *± s.e. mean* |
|---|---|---|---|
| 15–24 | 30 | 7.4 | 0.62 |
| 25–34 | 65 | 7.5 | 0.34 |
| 35–44 | 87 | 7.4 | 0.31 |
| 45–54 | 157 | 7.1 | 0.20 |
| 55–64 | 181 | 6.1 | 0.19 |
| 65–74 | 221 | 5.3 | 0.16 |
| 75–84 | 166 | 4.0 | 0.18 |
| 85+ | 33 | 3.0 | 0.35 |
| All | 941 | 5.9 | 0.09 |

**Table 5** Mean dose of midazolam used against age. Audit figures from East Anglia and the North West (1991) [1]. (Midazolam used in combination with pethidine)

| *Age (years)* | *Patient numbers* | *Dose (mg)* | *± s.e. mean* |
|---|---|---|---|
| 15–24 | 1 | 15.0 | — |
| 25–34 | 6 | 8.5 | 0.90 |
| 35–44 | 4 | 8.8 | 1.25 |
| 45–54 | 1 | 10.0 | — |
| 55–64 | 3 | 8.0 | 2.02 |
| 65–74 | 16 | 6.8 | 0.70 |
| 75–84 | 11 | 5.8 | 0.75 |
| 85+ | 5 | 5.2 | 0.18 |
| All | 47 | 7.1 | 0.42 |

**Table 6** Mean dose of midazolam used against age. Audit figures from East Anglia and the North West (1991) [1]. (Midazolam used in conjunction with local anaesthetic spray)

| *Age (years)* | *Patient numbers* | *Dose (mg)* | *± s.e. mean* |
|---|---|---|---|
| 15–24 | 192 | 7.3 | 0.21 |
| 25–34 | 397 | 6.7 | 0.15 |
| 35–44 | 588 | 6.7 | 0.12 |
| 45–54 | 704 | 6.1 | 0.08 |
| 55–64 | 872 | 5.7 | 0.08 |
| 65–74 | 995 | 5.0 | 0.05 |
| 75–84 | 752 | 4.5 | 0.06 |
| 85+ | 195 | 3.8 | 0.12 |
| All | 4695 | 5.6 | 0.04 |

the normal adult dose or less. Therefore, the suggested initial dose of midazolam is not to exceed 1 mg [17].

We were particularly concerned to see that the trend was to use a similar or even higher dose of midazolam when also giving pethidine, although patient numbers are small in this group (mean 7.1 mg, $n = 47$, s.e. mean 0.42). By contrast in the USA, the mean dose of midazolam used found in a review of drug usage during gastrointestinal endoscopy was 3.4 mg (s.d. 2.6) [3]. Recent guidelines [25] strongly suggest that the endoscopist should give the opioid drug first, and then slowly give one quarter the dose of benzodiazepine which would have been used as the sole agent. This is based on work showing that with some opioids midazolam exhibits a synergistic sedative effect [26, 27], while with others the effect is at least additive [28]. In the report from an International Forum on 'Quality control in

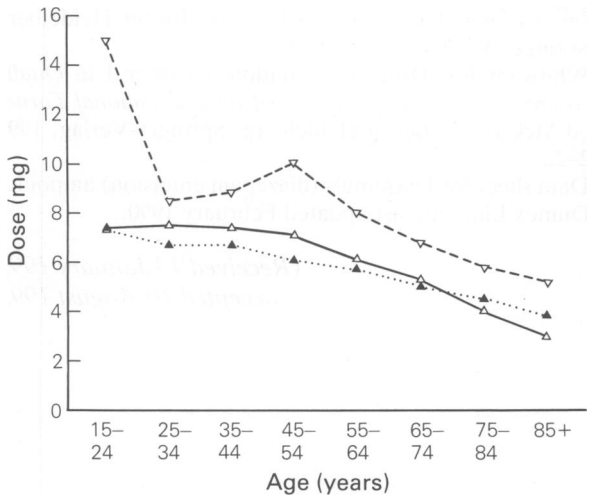


**Figure 3** Dose of midazolam *vs* age. Audit figures from East Anglia and the North West. △ sole agent, ▲ with topical anaesthetic, ▽ with pethidine.

endoscopy' [29, 30] the recommendations went further saying that only 25–30% of the opioid drugs usual dose should be given, followed by a 2–5 min pause (depending on the drug used) to allow it to produce its effect before administering the reduced dose of benzodiazepine. This point is also made in all relevant data sheets [17–19, 31].

From our present study and previous quoted work we feel that the dose of sedation used by many endoscopist is too high, particularly in the elderly and at risk patients. We belive that many complications may be prevented by using smaller doses of sedation in combination with supplemental oxygen and appropriate monitoring (at least pulse oximetry).

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## References

1 Quine MA, Bell GD, McCloy RF, Devlin HB, Hopkins A. A prospective audit of upper gastrointestinal endoscopy in two regions: safety staffing and sedation methods. *Br med J* (in press).
2 Daneshmend TK, Bell GD, Logan RFA. Sedation for upper gastrointestinal endoscopy: the results of a nationwide study. *Gut* 1991; **33**: 12–15.
3 Arrowsmith JB, Gerstman BB, Fleischer DE, Benjamin SB. Results from the American Society for Gastrointestinal Endoscopy—US Food and Drug Administration collaborative study on complication rates and drug use during gastrointestinal endoscopy. *Gastrointest Endosc* 1991; **37**: 421–427.
4 Habr-Gama A, Waye J. Complications and hazards of gastrointestinal endoscopy. *World J Surg* 1989; **13**: 1993–2201.
5 Hart R, Classen M. Complications of diagnostic gastrointestinal endoscopy. *Endoscopy* 1990; **22**: 229–233.
6 Aveling W, Bradshaw AD, Crankshaw DP. The effect of speed of injection on the potency of anaesthetic induction agents. *Anaesth Intensive Care* 1978; **6**: 116–119.
7 Crankshaw DP, Rosler A, Ware M. The short term distribution of thiopentone in the dog. *Anaesth Intensive Care* 1979; **7**: 148–151.
8 Bell GD, Antrobus JHL, Lee J, Coady T, Morden A. Bolus or slow titrated injection of midazolam prior to OGD? Relative effect on oxygen saturation and prophylactic value of supplemental oxygen. *Aliment Pharmac Ther* 1990; **4**: 393–401.
9 Swain DG, Ellis DJ, Bradbury H. Rapid intravenous low dose diazepam as sedation for upper gastrointestinal endoscopy. *Aliment Pharmac Ther* 1990; **4**: 43–48.
10 Chuah SY, Crowson CP, Dronfield MW. Topical anesthesia in upper gastrointestinal endoscopy. *Br med J* 1991; **303**: 695.
11 Bell GD, Spickett GP, Reeve P, Morden A, Logan RFA. Intravenous midazolam for upper gastrointestinal endoscopy: a study of 800 consecutive cases relating dose to age and sex of patient. *Br J clin Pharmac* 1987; **23**: 241–243.
12 Bell GD, Quine A, Antrobus JHL, *et al.* Upper gastrointestinal endoscopy: a prospective randomised study comparing the efficacy of continuous supplemental oxygen given either via the nasal or oral route. *Gastrointest Endosc* 1992; **38**: 319–325.
13 Aun C, Flynn PJ, Richards J, Major E. A comparison of midazolam and diazepam for intravenous sedation in dentistry. *Anaesthesia* 1984; **36**: 589–593.
14 Korttila K, Tarkkanen J. Comparison of diazepam and midazolam for sedation during local anaesthesia for bronchoscopy. *Br J Anaesth* 1985; **57**: 581–586.
15 McGimpsey JG, Kawar P, Gamble JAS, Browne ES, Dundee JW. Midazolam in dentistry. *Br dent J* 1983; **155**: 47–49.
16 Whitwam JG, Al-Khudairi D, McCloy RF. Comparison of midazolam and diazepam in doses of comparable potency during gastroscopy. *Br J Anaesth* 1983; **55**: 773–777.
17 Data sheet for Hypnovel (midazolam) ampoules, Roche last updated April 1992.
18 Data sheet for Diazepam injection BP, CP Pharmaceuticals Limited, last updated October 1991.
19 Data sheet for Valium (diazepam) ampoules, Roche, last updated September 1991.
20 Buhrer M, Maitre PO, Crevoisier C, Hung O, Stanski DR. Comparative pharmacodyanmics of midazolam and diazepam. *Anesthesiology* 1988; **69**: A642.
21 Galletly D, Forrest P, Purdie G. Comparison of recovery characteristics of diazepam and midazolam. *Br J Anaesth* 1988; **60**: 520–524.
22 Halim B, Schneider I, Claeys MA, Camu F. The use of midazolam and flumazenil in locoregional anaesthesia: an overview. *Acta anaesthesiol scand* Suppl. 1990; **34/92**: 42–46.
23 Nuotto EJ, Korttila KT, Lichtor JL, Ostman PL, Rupani G. Sedation and recovery of psychomotor function after intravenous administration of various doses of midazolam and diazepam. *Anesth Analg* 1992; **74**: 265–271.
24 Buhrer M, Maitre PO, Crevoisier C, Stanski DR. Electroencephalographic effects of benzodiazepines. II. Pharmacodynamic modeling of the electroencephalographic effects of midazolam and diazepam. *Clin Pharmac Ther* 1990; **48**: 555–567.
25 Bell GD, McCloy RF, Charlton JE, *et al.* Recommendations for the standards of sedation and patient monitoring during gastrointestinal endoscopy. *Gut* 1991; **32**: 823–827.
26 Ben-Shlomo I, Abd-El-Khan H, Ezry J, Zohar S,

Tverskoy M. Midazolam acts synergistically with fentanyl for induction of anaesthesia. *Br J Anaesth* 1990; **64**: 45–57.
27 Vinik HR, Bradley EL, Kissin I. Midazolam-alfentanil synergism for anaesthetic induction in patients. *Anesth Analg* 1989; **69**: 213–217.
28 Tverskoy M, Fleysham G, Ezry J, Bradley EL, Kissin I. Midazolam-morphine sedative interaction in patients. *Anesth Analg* 1989; **68**: 282–285.
29 Geller E. Report of workshop on drugs for sedation. Chapter 2 in *Quality control in endscopy. Report of an International Forum*, ed McCloy R. Berlin Heidelberg, Springer-Verlag, 1991; 22–29.
30 Whitwam JG. Drugs for sedation. Chapter 1 in *Quality control in endoscopy. Report of an International Forum.* ed McCloy R. Berlin Heidelberg. Springer-Verlag, 1991; 2–22.
31 Data sheet for Diazemuls (diazepam emulsion) ampoules, Dumex Limited, last updated February 1990.

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