Midazolam Sedation for Upper Gastrointestinal Endoscopy in Older Persons: A Randomized, Double-Blind, Placebo-Controlled Study

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OBJECTIVES: To investigate the benefits and risks of using midazolam for sedation during upper gastrointestinal endoscopic procedures in older persons.

DESIGN: Randomized, double-blind, placebo-controlled study.

SETTING: A 304-bed geriatric university hospital.

PATIENTS: Sixty-five geriatric inpatients (mean age 84 ± 7) undergoing gastroscopy.

INTERVENTION: Sedation with either midazolam (30 μg/kg IV) or saline (placebo). All patients received supplemental oxygen during the procedure (2 L/minute).

MEASUREMENTS AND RESULTS: Patients' recall of their tolerance to the exam (categorical scale) and pain score were significantly in favor of midazolam at 2 and 24 hours. Multivariate analysis at 2 hours showed that midazolam increased the probability of good tolerance (odds ratio (OR) = 19.3; 95% confidence interval (CI) 2.2–170.4, $P = .008$). Circumstantial amnesia occurred at 24 hours in 84% (midazolam) versus 27% (placebo) ($P < .001$). With midazolam, mean sedation time was 83 ± 13 minutes and mean arterial pressure (MAP) was about 10 mm Hg lower without clinically significant hypotension. Hypoxemia ($SaO_2 < 92\%$) was more frequent in the midazolam group after endoscopy (44% vs. 18%, $P = .033$), but no major desaturation was observed. Cognitive function (Mini-Mental State Exam, MMSE) was similar before and 2 and 24 hours after the exam in both groups. Acute confusion was observed in two patients (1 midazolam, 1 placebo). In multivariate analysis, midazolam was associated with a higher risk of hypoxemia after endoscopy (OR = 3.5; 95% CI 1.1–10.8, $P = .029$) but not of confusion.

CONCLUSIONS: Under adequate surveillance, the benefits in terms of tolerance to the procedure of low-dose midazolam for upper gastrointestinal endoscopic sedation outweigh the risks in older people. **J Am Geriatr Soc 48:1398–1403, 2000.**

Key words: midazolam; sedation; gastroscopy; aged persons

Medical conditions requiring diagnostic endoscopy such as anemia, dyspeptic symptoms, acute upper gastrointestinal hemorrhage, or suspicion of malignancy are particularly frequent in older persons.[1–3] Whereas in the past older patients were often not investigated, nowadays endoscopy is increasingly carried out in such patients, because upper gastrointestinal endoscopy is generally considered a safe procedure in older people.[4] Indeed, Quine et al.[5] found that about 30% of all patients undergoing upper gastrointestinal endoscopy in the United Kingdom were over 70 years of age.

Endoscopic procedures are frequently performed under conscious sedation in adults, as shown by nationwide surveys.[6–8] Midazolam, alone or in combination, has become the standard sedative in past years, mostly because of its rapid onset and amnestic effect, which improves the patients' final perception of the procedure and further acceptance of repeated endoscopies.[9] However, although the benefit of using low-dose midazolam for upper gastrointestinal endoscopy has been demonstrated recently in a well-designed trial in younger adults,[9] many patients tolerate the procedure as well without sedation.[10,11]

Besides a beneficial effect on tolerance, midazolam may induce cardiopulmonary adverse events that should be considered as well, particularly in older persons. Conscious sedation has been associated with occurrence of hypoxemia during endoscopy,[12–16] increasing the risk of cardiopulmonary complications such as arrhythmias or myocardial ischemia.[14,17] Other risk factors such as concomitant use of narcotics,[4,7] obstructive effect of the endoscope,[14] emergency procedures[18] or impaired cardiopulmonary function[17,18] have been recognized as well, so that a causal relationship remains unclear. Nonetheless, it is well established that older patients, particularly those with underlying cardiac or pul-

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monary diseases, are at a higher risk of such adverse events.[14,17] Moreover, use of midazolam may precipitate cerebrovascular accidents or myocardial infarction[5] because of its dose-dependent hypotensive effect.[19]

To our knowledge, although about one-third of the patients undergoing endoscopy are over 70 years of age, there are no well-designed studies evaluating the risk/benefit ratio of using midazolam sedation for upper gastrointestinal endoscopy in this population. Most of the studies that included older patients used variable[11,16,17] or higher doses of midazolam,[10,17,20] or were either not placebo-controlled[16,17,20,21] or not randomized.[16,17,21] Therefore, we performed a randomized, double-blind, placebo-controlled trial in hospitalized older patients to investigate the effect of low-dose midazolam (30 μg/kg) on patients' tolerance, endoscopic performance, and occurrence of adverse events during and after upper gastrointestinal endoscopy.

METHODS

Study Design

We evaluated 94 consecutive geriatric inpatients requiring upper gastrointestinal endoscopy. The included patients provided written informed consent. The study protocol had been approved by the ethics committee of the University Hospitals of Geneva.

With the hospital pharmacy's assistance, patients were randomized in a double-blind manner to receive either midazolam (30 μg/kg IV; Roche/Pharma AG, Basel, Switzerland) or placebo (saline 0.9% IV). Randomization was blocked using random tables of 10 numbers[22] to ensure balance within each group. Lidocaine spray 10% (10 pushes = 100 mg; Astra Pharmaceutica AG, Dietikon Sweden) was used as premedication for local anesthesia of the pharynx. When the procedure was not well tolerated (more than two attempts to introduce the endoscope and/or defense reactions), an open dose of midazolam was given in a nonblinded fashion (variable dose). As generally recommended, an intravenous catheter was placed and all patients received oxygen via a nasal catheter (2 L/minute) to prevent hypoxemia during endoscopy.[23,24] All procedures were performed by an experienced endoscopist in a standardized environment using a flexible videoscope (Pentax, GmbH, Hamburg, Germany).

Study Population

We evaluated 94 consecutive inpatients. Exclusion criteria were (a) unwillingness to participate in the study, (b) MMSE score <20,[25] or (c) myasthenia gravis. Ten patients refused to participate and 16 were excluded because of a MMSE lower than 20. Three additional patients were excluded because of severe vomiting after lidocaine spray (1 patient) and because of severe esophageal stenosis precluding passage of the endoscope (2 patients). Sixty-five patients were finally included in the study (12 men and 53 women; median age, 85 years; range, 63 to 98).

We did not consider outpatients for two reasons, the first one is that outpatients are generally younger and healthier and therefore at lower risk of complications, and the second one is that the close 1-week follow-up performed in this study with inpatients would have been difficult to perform with outpatients.

Patients' Assessments of the Procedure

Tolerance, pain, and breathing difficulties were evaluated 2 and 24 hours after the endoscopy. Patients' recall of their tolerance was assessed by two questions: (1) "How did you tolerate the procedure?" (scored with a categorical scale: very well = 5, well = 4, moderately well = 3, badly = 2, very badly = 1) and (2) "Would you accept to repeat the examination under the same conditions?" (yes/no). To estimate the difference in the rate of poor tolerance between the two groups (absolute risk reduction, ARR)[26] and the number of patients that would need to be treated to prevent one poorly tolerated exam (number needed to treat, NNT = 1/ARR),[26] we arbitrarily defined answers to question 1 "very well" and "well" as good tolerance and the other answers as poor tolerance (binary scale). This binary scale was also used to perform a multivariate analysis. Pain and breathing difficulties were assessed by the patients on a categorical scale (not at all painful (respectively difficult) = 5, a little = 4, moderately = 3, very = 2, extremely = 1).

Endoscopists' Assessments of the Procedure

Quality of the procedure in terms of ease of the procedure and patients' collaboration was assessed immediately after the endoscopy by the endoscopist on a visual analog scale (VAS, 0–10; 0 = no problem, 10 = impossible).[9,27] In the event an open-label dose of midazolam was given, a second assessment of the ease of the procedure was performed by the endoscopist.

Cardiopulmonary and Neuropsychological Parameters

Heart rate, blood pressure, and arterial oxygen saturation (SaO_2) were monitored using an automated noninvasive blood pressure device (auto-inflation digital sphygmomanometer, Nidec Copal Electronics Corp., Tokyo, Japan) and pulse oximetry (BCI International Cat. No. 3301, Waukesha, WI). Monitoring was performed at standardized intervals: T1: baseline value; T2: 1 minute after premedication (lidocaine); T3: 1 minute after conscious sedation (midazolam or placebo); T4: introduction of endoscope; T5: during endoscopy (various time); T6: 2 minutes after the end of endoscopy; then, every half-hour for 1 to 4 hours after the beginning of endoscopy. A systolic blood pressure (sysBP) less than 100 mm Hg or a mean arterial pressure (MAP = 1/3 · [sysBP + (2× diasBP)]) less than 60 mm Hg were considered as hypotension, when the decrease was more than 20% of the baseline value. We defined tachycardia as a pulse rate over 100 beats/minute (variation >20% of baseline value). Hypoxemia was defined as a decrease of SaO_2 below 92% during more than 30 seconds.

The degree of sedation was assessed using the Observer's Assessment of Alertness/Sedation Scale (OAA/S) (1 = alert, 2 = lethargic, 3 = aroused by voice, 4 = aroused by shaking, 5 = deep sleep).[28] The time required for recovery was defined as the time between the administration of the medication and the time when the degree of sedation returned to a level of 1. A recovery time of more than 3 hours was defined as prolonged sedation.

Amnesia and cognitive function were evaluated 2 and 24 hours after the endoscopy. Circumstantial amnesia was determined using the following test (adapted from Ref. 29): three objects (key, pen, and scissors) were presented to the patient 2 minutes after midazolam/placebo injection. Recall

after 2 and 24 hours of none of the objects was defined as amnesia. Cognitive function was evaluated with the MMSE. A decrease of 3 points or more was defined as confusion.[30]

All other adverse drug reactions observed the day of the endoscopy were recorded. The patients' medical charts were consulted a week after the endoscopy and all adverse events having occurred during this period were noted.

Statistical Analysis

We estimated in an apriori power analysis (power 0.8, $\alpha < 0.05$) that the sample size necessary to detect a significant improvement in tolerance with midazolam was less than 40 subjects per group. The baseline characteristics of both groups were compared by one-way analysis of variance (ANOVA). Categorical variables were analyzed with the two-tailed Fisher's exact test. We used ANOVA or Kruskall Wallis test (when dealing with non-Gaussian distribution or a statistically significant Bartlett test) to compare continuous variables. Analysis of sedation scores and mean arterial pressure measurements were compared by ANOVA with a repeated measure design. Paired data were analyzed using the Wilcoxon matched-pairs signed rank test. Multivariate analysis was performed using stepwise forward and backward logistic regressions. Results are presented as mean ± standard error of the mean (SEM). A P-value of less than .05 was considered statistically significant.

RESULTS

Study Population

Demographic data and baseline cardiopulmonary parameters were similar in both study groups (Table 1). Presence of cardiopulmonary diseases and intake of comedications that might impact on sedation and cardiopulmonary status were not different in both treatment groups (Table 1). About 56% of the patients in the midazolam group were undergoing their first endoscopic examination compared with 55% in the placebo group ($P = 1.0$).

Patients' Assessments of the Procedure

About 94% of the patients in the midazolam group versus 67% in the placebo group assessed their tolerance to the exam as very good or good 2 hours after the procedure. The use of midazolam resulted in a marked improvement of the mean tolerance score at 2 and 24 hours (at 2 hours: 4.8 ± 0.1 vs. 3.9 ± 0.2, $P < .001$; at 24 hours: 4.8 ± 0.1 vs. 4.0 ± 0.2, $P < .001$), as shown in Figure 1. At 24 hours, poor tolerance was present in none of the patients having received midazolam compared with 24% in the placebo group (ARR = 24%). Expressed as the NNT, we determined that four patients had to be treated with midazolam to prevent one poorly tolerated exam. Multiple regression analysis showed that midazolam and previous endoscopic experience were associated with better tolerance at 2 hours ($OR_{midazolam}$ = 19.3, 95% CI 2.2–170.4, $P = .008$; $OR_{experience}$ = 7.0, 95% CI 1.3–39.2, $P = .026$). Age, gender, cognitive function, or amnesia had no significant influence on patients' tolerance. More patients would have agreed to repeat the procedure with midazolam than with placebo, however the difference did not reach statistical significance (93% vs. 82%, P = .261). Pain score was significantly better at 2 and 24 hours with midazolam as shown in Figure 1 (at 2 hours: 4.9 ± 0.1 vs. 4.1 ± 0.2, $P = .013$; at 24 hours: 4.9 ± 0.05 vs. 4.0 ± 0.2, $P = .006$). Breathing was not worsened by midazolam, 88% of the patients with midazolam and 76% of the patients with placebo reporting no difficulty at all at 2 hours ($P = .339$)(at 24 hours: 81% vs 73%, $P = .558$).

Table 1. Population Demographic Data and Baseline Cardiopulmonary Parameters

	Midazolam (n = 32)	Placebo (n = 33)
Sex (M/F)	5/27	7/26
Age (yr)	85 ± 1	83 ± 1
BMI (kg/m²)	24 ± 1	24 ± 1
MMSE score	25 ± 0.4	25 ± 0.5
Smoking (yes/no)	4/28	4/29
Alcohol (yes/no)	19/13	16/17
Medical history		
Heart failure	12 (38%)	18 (55%)
Angina pectoris	13 (41%)	15 (45%)
Recent myocardial infarct (< than 6 months)	2 (6%)	0
Anemia (Hb ≤ 10 g/dL)	1 (3%)	4 (12%)
COPD	2 (6%)	5 (15%)
Bronchopneumonia	6 (19%)	4 (12%)
Number of comedications	7 ± 0.5	7 ± 0.4
Antidepressants	4 (13%)	6 (18%)
Neuroleptics	4 (13%)	3 (9%)
Benzodiazepines	16 (50%)	16 (48%)
Opioids	5 (16%)	2 (6%)
SaO_2 (%)	94 ± 0.5	95 ± 0.3
MAP (mm Hg)	98 ± 2	101 ± 3

Results are presented as mean ± SEM. None of the differences are statistically significant ($P > .05$).

BMI, body mass index; MMSE, Mini-Mental State Exam; COPD, chronic obstructive pulmonary disease; SaO_2, oxygen saturation at room air; MAP, mean arterial pressure.

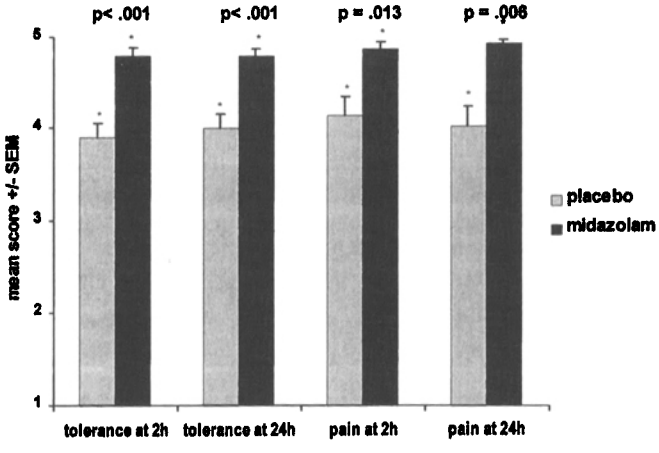

Figure 1. Tolerance and painscores at 2 and 24 hours, derived from patients' assessments (5-step categorical scale: Very well respectively not at all = 5 points; very badly respectively extremely = 1 point).

Endoscopists' Assessments of the Procedure

To test how effective the double-blinding was, the endoscopist was asked to guess after each procedure, which medication had been administrated. His evaluation was wrong in

9 cases (14%), false negative and false positive values being 16% and 12%, respectively.

Endoscopists' assessment of the ease of the procedure and the patients' collaboration was not different between the two groups (VAS-score$_{procedure}$: 0.7 ± 0.2 with midazolam vs. 1.8 ± 0.4 with placebo, P = .183; VAS-score$_{collaboration}$: 0.6 ± 0.2 vs. 1.6 ± 0.3, P = .533). No significant difference was observed in the duration of the procedure (6.5 ± .4 minutes with midazolam vs. 7.8 ± 0.7 minutes with placebo, P = .369). Only one incomplete procedure was observed in the placebo group. Three agitated patients in the placebo group received an open dose of midazolam. Supplemental midazolam did not improved significantly the ease of the procedure as assessed by the endoscopist before and after (VAS-score before 7.9 ± 1.0 vs. after 2.1 ± 0.9, P = .103)

Cardiopulmonary and Neuropsychological Parameters

Recorded adverse events are summarized in Table 2.

MAP adjusted for age and sex was globally similar in both groups (P = .401), as shown in Figure 2. A trend—although not significant—was observed between T4 and T6 (adjusted for basal MAP), showing a lower blood pressure of about 10 mm Hg with midazolam (P = .489). Transient hypotension was quite frequent (6% with midazolam, 3% with placebo, P = .613). However, no clinically significant hypotension necessitating treatment occurred. Tachycardia was observed in about 20% of the patients under midazolam and in more than 30% under placebo (P = .260).

Occurrence of hypoxemia (SaO_2 < 92%) was significantly more frequent after endoscopy with midazolam (44% vs. 18%, P = .033). The asymptomatic episodes of desaturation were managed with administration of oxygen (2 L/min). No clinically significant major desaturation was observed. In logistic regression analysis, midazolam was the only significant risk factor for hypoxemia following upper gastrointestinal endoscopy ($OR_{midazolam}$ = 3.5, 95% CI 1.1–10.8, P = .029).

Sedation score (OAA/S) adjusted for age and sex was significantly different between both groups (P < .001), as shown in Figure 3. Recovery time increased with midazolam (83.3 ± 13 minutes vs. 32.2 ± 14, P = .010). Prolonged sedation was more frequent with midazolam, but the difference was not statistically significant (19% vs. 9%, P = .303).

Table 2. Summary of Recorded Adverse Events and Statistical Comparison Between Both Groups. For Definitions of Adverse Events, See "Methods"

Adverse Events	Midazolam (n = 32)	Placebo (n = 33)	P Value
Transient hypotension	2 (6%)	1 (3%)	.613
Tachycardia	6 (19%)	11 (33%)	.260
Hypoxemia postendoscopy	14 (44%)	6 (18%)	.033
Prolonged sedation	6 (19%)	3 (9%)	.303
Amnesia			
at 2 hours	26 (81%)	6 (18%)	<.001
at 24 hours	27 (84%)	9 (27%)	<.001
Confusion			
at 2 hours	7 (22%)	4 (12%)	.339
at 24 hours	5 (16%)	4 (12%)	.470

Circumstantial amnesia occurred frequently with midazolam compared with placebo (at 2 hours: 81% vs. 18%, P < .001; at 24 hours: 84% vs. 27%, P < .001). Four patients having received midazolam had no recall of the endoscopic procedure at 24 hours (P = .053). In logistic regression analysis, midazolam was the only significant factor associated with occurrence of amnesia at 24 hours ($OR_{midazolam}$ = 14.4, 95% CI 4.2–49.0, P < .001).

Occurrence of impaired cognitive function was not associated with the use of midazolam, MMSE being similar in both groups at 2 and 24 hours. Mild confusion occurred frequently in both groups (22% with midazolam vs. 12% with placebo, P = .339). An acute confusional state characterized by disorientation, memory loss, and hyperactivity was observed in two patients after gastroscopy. One belonged to the midazolam group, the other one to the placebo group. However, this patient had received an open dose of midazolam during the procedure. No treatment was necessary. Both patients were still confused at 24 hours. The only independent risk factor associated with confusion in multivariate analysis was a basal MMSE <21 (OR = 6.4, 95% CI 1.1–37.3, P = .040).

Fever (14%) and confusion (14%) were the most frequently observed adverse events during the day following endoscopy. Cardiac events such as acute heart failure or angina pectoris necessitating drug treatment were observed in five patients with a cardiac co-morbidity (three patients with midazolam, 2 with placebo, P = .672) during the week following endoscopy. No cerebrovascular accidents occurred.

DISCUSSION

We investigated the benefit and safety of using low-dose midazolam for upper gastrointestinal endoscopy in older people. We found that giving midazolam to older adults undergoing gastroscopy significantly improved their tolerance to the exam and decreased the pain they incurred. These results confirm the beneficial effect of low-dose midazolam on patients' tolerance to gastroscopy, as observed previously in adults.[9,10] However, we could not demonstrate a significant beneficial effect in terms of ease or duration of the procedure, maybe because of the small number of patients included in our study.

Midazolam and previous endoscopic experience were the covariates associated with good tolerance in our multivariate analysis. Although we expected that the beneficial effect of midazolam would be due mainly to its amnestic effect, we did not find a significant effect of amnesia on tolerance. This suggests that other factors such as anxiolysis may be important. Indeed, low-anxiety as well as increasing age have been associated with better patients' tolerance to upper gastrointestinal endoscopy.[9] The unexpectedly high rate of good tolerance observed in our placebo group may have been due to the information given during the enrollment phase and the special care provided during the study, which may have alleviated most of the patients' fears before endoscopy.

Because of the age, the polymedication, and the polymorbidity of our patients, we expected a high incidence of cardiopulmonary adverse events with midazolam. Indeed, a transient decrease in the MAP of about 10 mm Hg was observed after midazolam administration. This is consistent with its direct dose-related decrease in systemic vascular resistance, occurring mostly in hypertensive patients and

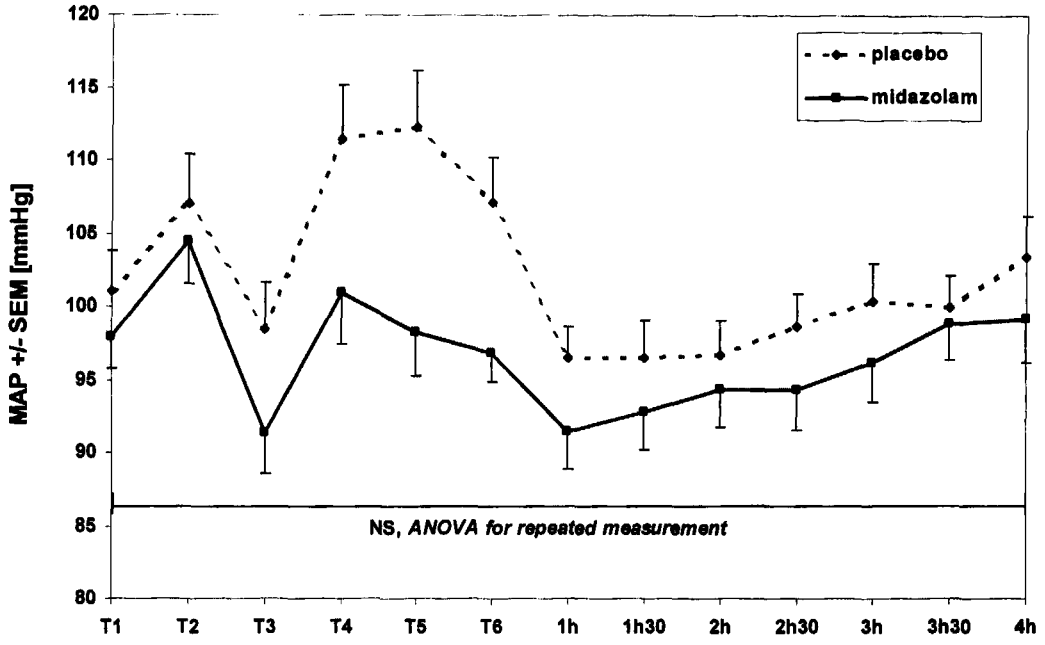

Figure 2. Evolution of mean arterial pressure in both groups measured at the following times: T1 = baseline value; T2 = 1 minute after premedication; T3 = 1 minute after conscious sedation (midazolam or placebo); T4 = introduction of endoscope; T5 = during endoscopy; T6 = 2 min after endoscopy; then 1 to 4 hours after conscious sedation.

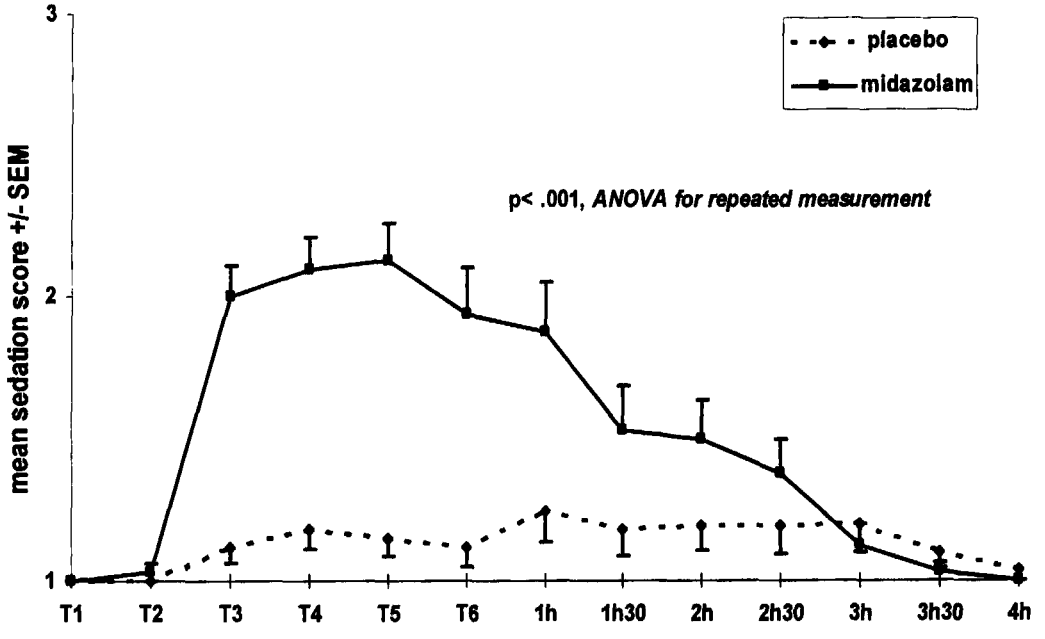

Figure 3. Evolution of sedation score in both groups measured at the following times: T1 = baseline value; T2 = 1 minute after premedication; T3 = 1 minute after conscious sedation (midazolam or placebo); T4 = introduction of endoscope; T5 = during endoscopy; T6 = 2 min after endoscopy; then 1 to 4 hours after conscious sedation.

those emotionally stressed.[19] However, no clinically significant hypotension occurred at the low dose we used. Moreover, no cases of cerebral or myocardial infarction were recorded during the 1-week follow-up. We could not detect any difference in the rate of cardiac disorders such as angina pectoris or acute heart failure, which occurred with equal frequency in both groups in a few patients with cardiac comorbidities. Low-dose midazolam can therefore be considered as safe in older persons in terms of cardiovascular effects during upper gastrointestinal endoscopy.

Regarding pulmonary function, no major desaturation occurred during endoscopy under continuous oxygen. This is in agreement with earlier studies showing that supplemental oxygen can prevent or at least decrease occurrence of hypoxemia during the procedure.[13,31] However, we observed a significant trend for hypoxemia to occur more frequently with midazolam in the postendoscopic period when oxygen was removed. Therefore, adequate surveillance and supplemental oxygen should be provided after gastroscopy in older patients who received midazolam.

Neuropsychological adverse events are of particular concern in older people. We observed a higher rate of midazolam-induced amnesia (>80%) at a given dose compared with younger Swiss patients (33%, mean age 47).[9] This may be explained by the increased sensitivity of older patients to the central nervous effects of midazolam.[32,33] Nonetheless, midazolam seemed not to alter cognitive function, although conclusions cannot be drawn from MMSE data alone. In this context, we observed two cases of acute confusion after endoscopy. Only one of these patients was in the midazolam group, but the other one received an open-label dose of midazolam during the procedure. Midazolam was not associated with an increased risk of confusion in multivariate analysis, a basal MMSE <21 being the only significant risk factor. However, many predisposing factors such as increasing age or brain disease, and many precipitating factors such as use of benzodiazepines or opioids, hypoxemia, infection, or cardiac disease are associated with occurrence of postoperative delirium in older people.[34,35] One of our patients had a basal MMSE of 20, and another suffered from bronchopneumonia and high fever, which could partly explain the occurrence of delirium. Nevertheless, we cannot exclude that midazolam may have contributed to or precipitated the delirium observed in these two patients.

In conclusion, this randomized, double-blind, placebo-controlled study showed that low-dose midazolam (30 μg/kg) increased patients' tolerance and reduced pain sensation during upper gastrointestinal endoscopy in older patients. Adequate postendoscopic observation of the patients is recommended, particularly regarding oxygen saturation and confusion in patients with a low basal MMSE. We found that under adequate surveillance, the benefits in terms of tolerance to the procedure of using low-dose midazolam for upper gastrointestinal endoscopic sedation outweigh the risks in the older patient.

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REFERENCES

1. Ania BJ, Suman VJ, Fairbanks VF et al. Incidence of anemia in older people: An epidemiologic study in a well defined population. J Am Geriatr Soc 1997; 45:825–831.
2. Ouatu-Lascar R, Triadafilopoulos G. Oesophageal mucosal diseases in the elderly. Drugs Aging 1998;12:261–276.
3. Nankhonya JM, Datta-Chaudhuri ML, Bhan GL. Acute upper gastrointestinal hemorrhage in older people: A prospective study in two neighboring districts. J Am Geriatr Soc 1997;45:752–754.
4. Arrowsmith JB, Gerstman BB, Fleisher DE, Benjamin SB. Results from the American Society for Gastrointestinal Endoscopy/U.S. Food and Drug Administration collaborative study on complication rates and drug use during gastrointestinal endoscopy. Gastrointest Endosc 1991;37:421–427.
5. Quine MA, Bell GD, McCloy RF et al. Prospective audit of upper gastrointestinal endoscopy in two regions of England: Safety, staffing, and sedation methods. Gut 1995;36:462–467.
6. Keefe EB, O'Connor KW. 1989 ASGE survey of endoscopic sedation and monitoring practices. Gastrointest Endosc 1990;36:S13–S18.
7. Daneshmend TK, Bell GD, Logan RFA. Sedation for upper gastrointestinal endoscopy: Results of a nationwide survey. Gut 1991;32:12–15.
8. Froehlich F, Gonvers JJ, Fried M. Conscious sedation, clinically relevant complications and monitoring of endoscopy: Results of a nationwide survey in Switzerland. Endoscopy 1994;26:231–234.
9. Froehlich F, Schwizer W, Thorens J et al. Conscious sedation for gastroscopy: patient tolerance and cardiorespiratory parameters. Gastroenterology 1995;108:697–704.
10. Fisher NC, Bailey S, Gibson JA. A prospective, randomized controlled trial of sedation vs. no sedation in outpatient diagnostic upper gastrointestinal endoscopy. Endoscopy 1998;30:21–24.
11. Solomon SA, Kajla VK, Banerjee AK. Can the elderly tolerate endoscopy without sedation? J R Coll Physicians Lond 1994;28:407–410.
12. Bell GD, Reeve PA, Moshiri M et al. Intravenous midazolam: A study of the degree of oxygen desaturation during upper gastrointestinal endoscopy. Br J Clin Pharmacol 1987;23:703–708.
13. Patterson KW, Noonan N, Keeling NW et al. Hypoxemia during outpatient gastrointestinal endoscopy: The effects of sedation and supplemental oxygen. J Clin Anesth 1995;7:136–140.
14. Liebermann DA, Wuerker CK, Katon RM. Cardiopulmonary risk of esophagogastroduodenoscopy. Gastroenterology 1985;88:468–472.
15. Barkin JS, Krieger B, Blinder M et al. Oxygen desaturation and changes in breathing pattern in patients undergoing colonoscopy and gastroscopy. Gastrointest Endosc 1989;35:526–530.
16. O'Connor KW, Jones S. Oxygen desaturation is common and clinically underappreciated during elective endoscopic procedures. Gastrointest Endosc 1990;36:S2–S4.
17. Thompson AM, Park KGM, Kerr F, Munro A. Safety of fibreoptic endoscopy: analysis of cardiorespiratory events. Br J Surg 1992;79:1046–1049.
18. Alcain G, Guillen P, Escolar A et al. Predictive factors of oxygen desaturation during upper gastrointestinal endoscopy in nonsedated patients. Gastrointest Endosc 1998;48:143–147.
19. Dundee JW, Halliday NJ, Harper KW, Brogden RN. Midazolam. A review of its pharmacological properties and therapeutic use. Drugs 1984;28:519–543.
20. Bell GD, Morden A, Coady T et al. A comparison of diazepam and midazolam as endoscopy premedication assessing changes in ventilation and oxygen saturation. Br J Clin Pharmacol 1988;26:595–600.
21. Marbet UA, Koller R, Herzer H. Ist die Prämedikation bei der gastroskopie gefährlich? Schweiz Med Wschr 1992;122:979–982.
22. Fisher RA, Yates F. Statistical Tables for Biological, Agricultural and Medical Research, 4th Ed. London: Oliver and Boyd, 1953.
23. Bell GD, McCloy RF, Charlton JE et al. Recommendations for standards of sedation and patient monitoring during gastrointestinal endoscopy. Gut 1991;32:823–827.
24. American Society of Anesthesiologists. Practice guidelines for sedation and analgesia by non-anesthesiologists. Anesthesiology 1996;84:459–471.
25. Folstein MF, Folstein SE, McHugh PR. "Mini-Mental State" a practical method for grading the cognitive state of patients for the clinician. J Psychiat Res 1975;12:189–198.
26. Sackett DL, Deeks JJ, Altman DG. Down with odds ratios! [EBM note]. Evidence-Based Med 1996;1:164–166.
27. Revill SI, Robinson JO, Rosen M, Hogg MIJ. The reliability of a linear analogue for evaluating pain. Anesthesia 1976;31:1191–1198.
28. Chernik DA, Gillings D, Laine H et al. Validity and reliability of the Observer's Assessment of Alertness/Sedation Scale: Study with intravenous midazolam. J Clin Psychopharmacol 1990;10:244–251.
29. American Psychiatric Association. Amnestic syndrome. In: Diagnostic and Statistical Manual of Mental Disorders (DSM IIIR), 3rd Ed., revised. Washington, DC: American Psychiatric Association, 1987, pp 108–109.
30. Jitapunkul S, Pillay I, Ebrahim S. Delirium in newly admitted elderly patients: A prospective study. Q J Med 1992;83:307–314.
31. Bell GD, Bown S, Morden A et al. Prevention of hypoxemia during upper-gastrointestinal endoscopy by means of oxygen via nasal cannulae. Lancet 1987;1:1022–1024.
32. Scholer SG, Shafer DF, Potter JF. The effect of age on the relative potency of midazolam and diazepam for sedation in upper gastrointestinal endoscopy. J Clin Gastroenterol 1990;12:145–147.
33. Greenblatt DJ, Harmatz JS, Shader RI. Clinical Pharmacokinetics of anxiolytics and hypnotics in the elderly: Therapeutic considerations (Part II). Clin Pharmacokinet 1991;21:262–273.
34. Parikh SS, Chung F. Postoperative delirium in the elderly. Anesth Analg 1995;80:1223–1232.
35. O'Keefe ST, Chonchubhair A. Postoperative delirium in the elderly. Br J Anaesth 1994;73:673–687.