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Recovery of postural stability following conscious sedation with midazolam in the elderly

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Abstract
Purpose. To investigate the differences in recovery of postural stability, after obtaining similar intravenous sedation levels with midazolam, in elderly and younger patients undergoing dental surgery.
Methods. We studied 15 elderly patients (>65 years) and 15 younger patients (<55 years) after intravenous sedation. Midazolam was carefully titrated over 4–5min until slow response to verbal commands, ptosis of the eyelid, or slight slurring of speech was obtained. Parameters were postural balance tests and an addition test, as a psychomotor function test.
Results. The dose of midazolam in the elderly group (0.045 ± 0.012 mg·kg^{-1}) was 62% of that in the younger group (0.074 ± 0.026 mg·kg^{-1}). In evaluation of the percentile rank of a balance test with a visual feedback system, which contained a dynamic balance element, recovery at 60min in the elderly group was significantly slower than that in the younger group. However, the recovery times for the balance test and the addition test, at which the significantly changed values were restored to the baseline values, were 120min and 90min, respectively, in both groups.
Conclusion. In the recovery from sedation, elderly patients had more difficulty in acquiring postural adjustment during movement than in maintaining a standing posture. If the dose is carefully administered, however, even elderly patients might be able to return home 2h after midazolam administration, as could the younger patients.

Key words Aged · Conscious sedation · Midazolam · Recovery · Postural stability

Introduction

The pharmacodynamics and pharmacokinetics of benzodiazepine in the elderly have been reported to differ from those in younger individuals [1–6]. Accordingly, excessive sedation and delayed recovery from conscious sedation can occur in the elderly. Because of the deterioration of visual, vestibular, and proprioceptive functions, and decreases in nerve conduction velocity and muscle strength, one would expect to find age-related differences in postural stability [7–10]. Therefore, careful evaluation of recovery is important in elderly outpatients. However, there have been very few reports on this subject. The purpose of the present study was to investigate the differences in recovery of postural stability after obtaining similar intravenous sedation levels with midazolam in elderly and younger patients.

Patients and methods

After obtaining Hokkaido University Graduate School of Dental Medicine Review Board approval and informed consent, 15 elderly patients (aged over 65 years; group A) and 15 younger patients (aged under 55 years; group B) were enrolled in the study. They underwent oral surgery or dental treatment with or without local anesthesia after intravenous administration of midazolam. Long-term benzodiazepine users and those who suffered from liver, renal, or neuromuscular disorders were excluded from the study. Midazolam was carefully titrated over 4–5min until slow response to verbal commands, ptosis of the eyelid, or slight slurring of speech was obtained. No incremental dose was given after the adequate sedation level described above was achieved. Parameters for the evaluation of recovery were postural balance tests (baseline, 60, 90, 120, and 150min after midazolam administration) and an addition test (baseline, 60, 90, and 120min after midazolam administration). The balance tests were designed to provide measurement of a standing body sway area (Fig. 1) using the Balance Master System (NeuroCom International, Clackamas, OR, USA). The device con-

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sists of a forceplate that rests on force transducers connected to a personal computer, and its display monitor is positioned at eye level. The tests require the subject to look straight ahead while standing as still as possible, initially with eyes open, then with eyes closed, and finally focusing on the monitor using visual feedback to maintain the position of a cursor (representing the subject's center of gravity [COG]) within a centrally positioned target box. For each test, data were recorded for 20s, and the "sway area" was calculated and expressed as a percentage of the subject's theoretical limits of stability (LOS) [10,11]. We also examined the percentile rank. This can be calculated automatically and compared with a clinically normal population for the three parameters described above, using this machine (5% or less representing a clinically abnormal score). In the addition test, double figures selected from a table of random numbers were added over a period of 1 min. The mean number of correct answers in two trials was recorded. The value measured at each time was compared with the preoperative baseline value and compared within the two groups. When there were already significant differences in the baseline values between the groups, a comparison of the values at each time was not calculated. The recovery time was defined as the time at which the value after midazolam administration was restored to the baseline.

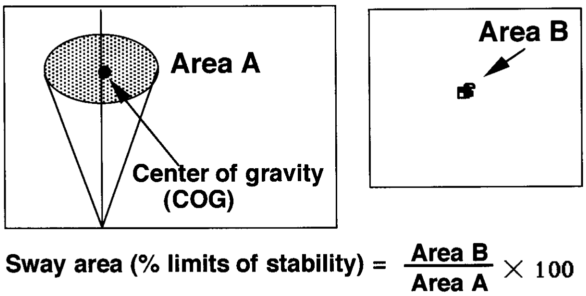

Fig. 1. The principle of measurement of the sway area in the balance test, using the Balance Master System (NeuroCom International). Area A (*dotted area*) represents the area over which the center of gravity (*COG*) can safely move without changing the base of support; that is, the theoretical limits of stability (LOS). *Area B* represents the actual area of the swaying of the COG

Statistical analyses were performed as follows. Intragroup differences were compared by the Friedman test followed by the multiple comparison (Contrast) test. For comparisons of continuous variables between the two groups, the Mann-Whitney *U*-test was used. The ratio of recovered patients was compared between the two groups by Fisher's exact probability test. Calculations were made with statistics programs (StatView and Super ANOVA; Abacus Concepts, Berkeley, CA, USA). A P value of less than 0.05 was considered statistically significant. All data values are presented as means ± SD.

Results

Patients' characteristics are summarized in Table 1. Eleven patients in group A underwent oral surgery and 4 underwent dental treatment. Twelve patients in group B received oral surgery and 3 received dental treatment. By evaluating the three parameters for the aimed sedation level described above, it was confirmed that there were no significant differences in the sedation level 5 min after the administration of midazolam. As shown in Table 1, the mean dose of midazolam administered was 2.60 ± 0.45 mg (0.045 ± 0.012 $mg \cdot kg^{-1}$) in group A. This was significantly less ($P < 0.001$) than that in group B (4.20 ± 1.18 mg, 0.074 ± 0.026 $mg \cdot kg^{-1}$). The dosage for group A was 62% of that in group B.

The times to recovery in the balance tests occurred within 120 min after midazolam administration in both groups (Fig. 2). Similarly, the rate of patients whose percentile rank of sway area recovered to normal limits 120 min after midazolam administration was more than

Table 1. Patients' characteristics

	Elderly group (group A; n = 15)	Younger group (group B; n = 15)	P value
Age (years)	72.1 ± 4.9 (range, 66–82)	34.7 ± 12.7 (range, 18–54)	$P < 0.001$
Male-to-female ratio	9:6	8:7	
Height (cm)	156.9 ± 10.6	162.0 ± 8.5	$P = 0.33$
Weight (kg)	58.8 ± 10.1	58.4 ± 10.6	$P = 0.8$
Body mass index ($kg \cdot m^{-2}$)	23.7 ± 2.7	22.2 ± 3.9	$P = 0.23$
Dose of midazolam (mg)	2.6 ± 0.45	4.2 ± 1.18	$P < 0.001$
Operation time (min)	29.7 ± 17.2	38.7 ± 19.3	$P = 0.35$

Values are means ± SD or n

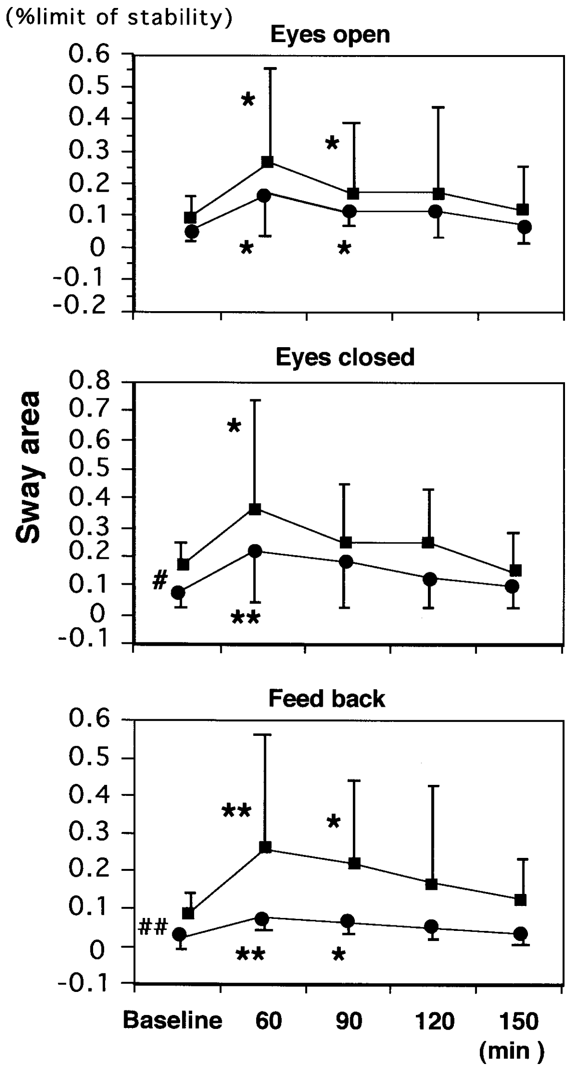

Fig. 2. Changes in the sway area in the balance test after midazolam administration. *Closed squares* are for group A, and *closed circles* for group B. $^{*}P < 0.05$; $^{**}P < 0.01$ (*vs* control), and $^{\#}P < 0.05$; $^{\#\#}P < 0.01$ (between the groups). Values are means ± SD. Although eyes-open and visual feedback values showed significant increases 60 and 90min after the midazolam injection in both groups, they were restored to the baseline values by 120min after the injection. Although the eyes-closed value showed a significant increase 60min after the injection in both groups, it was restored to the baseline value by 90min after the injection

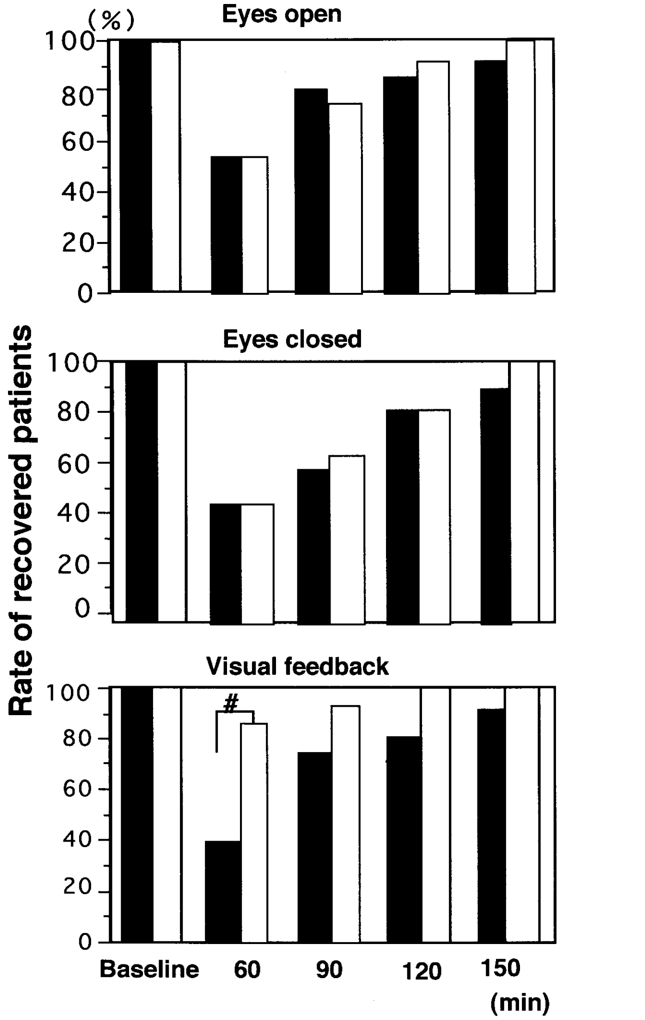

Fig. 3. Changes in patients' recovery in the sway area after midazolam administration. *Black columns* are for group A, and *white columns* for group B. $^{\#}P < 0.05$ (between the groups). The *vertical axis* represents the rate of patients whose percentile rank of the sway area recovered to within normal limits. The rate of recovery in the patients 60min after the injection of midazolam in the feedback test in group A was 40% (6 of 15 patients), which was significantly less than that (87%; 13 of 15 patients) in group B

80% for every parameter in both groups (Fig. 3). However, in group A, the rate of recovery of the visual feedback test 60min after the injection was 40% (6 of 15 patients), which was significantly less than that (87%; 13 of 15 patients) in group B (Fig. 3). The recovery for the addition test occurred 90min after midazolam administration in both groups (Fig. 4).

Accordingly, the recovery times for the balance test and the addition test were 120min and 90min, respectively, in both groups.

Discussion

Increases in postural sway have been demonstrated in elderly subjects, because of the physiological changes that are known to occur with aging (e.g., the deterioration of visual, vestibular, and proprioceptive functions, and decreases in nerve conduction velocity and muscle strength) [7–10]. Accordingly, the ability to maintain postural stability is an important factor in the assessment of recovery and "street fitness" after sedation [12]. It was reported that elderly volunteers were more sensitive to 10mg of oral diazepam than young adult volunteers [13]. However, there have been very few reports

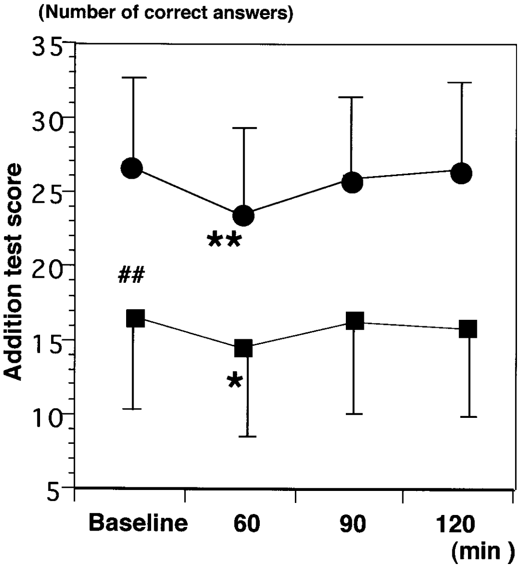

Fig. 4. The addition test score after midazolam administration. *Closed squares* are for group A, and *closed circles* for group B. $^{*}P < 0.05$; $^{**}P < 0.01$ (*vs* control), and $^{\#\#}P < 0.01$ (between the groups). Values are means ± SD. Although the addition test score showed a significant decrease 60 min after the midazolam injection in both groups, it was restored to the baseline value by 90 min after the injection

on the recovery of postural stability after conscious sedation in the elderly. In this study, the time to recovery of postural stability from the intravenous sedation with midazolam was 120 min in both the elderly group and the younger group.

One of the simplest and most widely used posturographic balance tests (static posturography) involves the measurement of spontaneous postural sway during quiet standing [14]. However, static measurement situations do not accurately describe the dynamic balancing situations encountered in real life [15]. Therefore, dynamic balance tests are thought to be more rational to detect balance disturbances and have been used extensively in clinical practice [7,10,15]. Maki et al. [16] reported that aging-related decreases in stability were more pronounced in the induced-sway test than in the spontaneous sway test. Although the parameters used in the present study were static measures, the visual feedback test contains a dynamic element. Therefore, some elderly patients swayed markedly when they tried to adjust their center of gravity, and the rate of recovery 60 min after midazolam administration was significantly lower in the elderly group than in the younger group. These results are in accordance with those of Maki et al. [16] described above. These results suggest that the elderly should not be judged as suitable for discharge even when the value of Romberg's test, which is often used as a simple clinical static balance test [12], returns to the control value. Falling on the way home, due to transient postural perturbation, is one of the most important concerns to avoid for elderly patients, because it often causes fractures of the proximal femur and a decrease in the quality of life. We hope that an easily measurable and safe postural-equilibrium evaluation system, which can sensitively reflect the ability to dynamically adjust posture, will be developed and used to evaluate the influence of conscious sedation on equilibrium in the elderly.

Various psychomotor tests have been used to assess recovery following intravenous sedation. Examples include the calculation test [17,18], choice reaction time, critical flicker-fusion threshold, the digit symbol substitution test, and the card-sorting test [19,20]. However, no gold standard has been established. In the present study, we used an addition test, a kind of calculation test, as an index of psychomotor function. The recovery time in the elderly group seemed to be 90 min after the injection, which was similar to that in the younger group. Bertz et al. [20] reported that recovery, measured by the digit symbol substitution test, in the elderly was significantly delayed in comparison with that in young adults after an intravenous infusion of alprazolam. We assume that this difference results from the differences in methods of administration, i.e., their report evaluated patients with the same dosage, whereas we evaluated recovery from a similar sedation level. The sedation level that we aimed for is roughly equivalent to a level 2 on the Ramsay sedation scale, or a level 4 on the observer's assessment of alertness/sedation score (OAA/S Score).

It is well appreciated that aging increases the sensitivity to the sedative effects of midazolam and prolongs the duration of its action [1–6]. The increasing pharmacodynamic sensitivity due to aging has been explained by EEG data [1], the dose for disappearance of reaction to verbal commands [2], and psychometric tests [3]. For pharmacokinetic factors, the elimination half-life was significantly prolonged and total clearance was significantly reduced [4,5], whereas no significant differences were seen in the distribution phase half-life and volume of distribution between younger and elderly patients [2,6]. In the present study, similar sedation levels were obtained in the elderly with 62% of the midazolam dosage needed for younger patients, probably because of pharmacodynamic effects. Because the midazolam dose administered was initially lower in the elderly, the pharmacokinetic effect may have been offset, resulting in the lack of a significant difference in the recovery time (within 2 h) between the groups.

In summary, our findings suggest that, during recovery from conscious sedation, elderly patients have more difficulty in acquiring postural adjustment during movement than in maintaining a standing posture. If the careful titration of midazolam is done, all patients might be able to return home within 2h after intravenous sedation, even those in the elderly group.

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