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RECOVERY OF INTENTIONAL DYNAMIC BALANCE FUNCTION AFTER INTRAVENOUS SEDATION WITH MIDAZOLAM IN YOUNG AND ELDERLY SUBJECTS

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Short title:

Intentional dynamic balance after sedation

Summary

Background and objective: Computerized dynamic posturography using an intentional postural sway task can be used to assess body-leaning ability and postural control ability to prevent falls. Falls are the leading cause of morbidity and mortality for the elderly. The purpose of the present study was to evaluate the recovery of intentional dynamic balance function after intravenous sedation with midazolam in elderly subjects in comparison with that in young subjects.

Methods: Midazolam was administered in small, divided doses over 4 to 5 minutes until the Wilson sedation score reached 3 in 20 young and 18 elderly male volunteers. A dynamic limits of stability test, in which subjects leaned their body intentionally as indicated by a cursor moving on a computer screen, was performed before (baseline) and 50, 70, 90, 110, and 130 minutes after administration of midazolam.

Results: The changes from baseline values of path sway and movement time 50 minutes after the administration of midazolam in elderly subjects (106.8±101.0 %, 4.6±3.0 seconds; mean±SD) were significantly greater than those (32.9±87.2%, 1.9±2.8 seconds) in young subjects (p=0.024, p=0.008), respectively.

Conclusions: The elderly show slower recovery of the intentional dynamic balance function than do young adults after intravenous sedation with midazolam.

Key words: CONSCIOUS SEDATION, MIDAZOLAM, AGED, RECOVERY OF FUNCTION, MUSCULOSKELETAL EQUILIBRIUM, intentional dynamic balance.

To assess street fitness for discharge after general anaesthesia or intravenous sedation, computerized dynamic posturography (CDP) involving movement of the center of gravity may be more rational and accurate than conventional computerized static-posturography (CSP) [1-5]. CDP is classified according to the types of postural control as CDP using perturbation stimuli [1-4] and CDP using an intentional postural-sway task [5-8]. The latter can be used to assess the recovery of daily voluntary actions such as holding objects by leaning the body and extending the arm without changes in the contact plane, and postural-control ability when the possibility of falls is predicted. In fact, this type of CDP was reported to be useful for predicting falls in the elderly [9]. However, only one study has evaluated the recovery of dynamic balance after intravenous sedation by CDP with intentional sway of the center of gravity as a task [5]. Furthermore, no such study has been performed in elderly subjects whose balance and psychomotor function, which are related to risk-avoidance ability, are decreased.

The purpose of the present study was to evaluate the recovery of intentional dynamic balance function after intravenous sedation with midazolam in elderly subjects in comparison with that in young subjects.

Subjects and Methods

After obtaining informed consent and the approval of the ethics committee of our institution, we enrolled 20 adult male volunteers younger than 30 years and 18 elderly male volunteers older than 60 years in this study. Long-term benzodiazepine users and those who suffered from liver, renal, or neuromuscular disorders were excluded from the study. Midazolam was administered in small divided-doses over four to five minutes until the Wilson sedation-score reached 3 (the eyes are closed, but the subjects respond to being called once or twice) [10]. After the designated depth of sedation was achieved, no additional sedatives were administered.

As a CDP with intentional postural-sway task, the dynamic limits of stability (dynamic LOS) test was performed before (baseline) and 50, 70, 90, 110, and 130 minutes after administration of midazolam with the Balance Master System (Neurocom International Inc., Clackamas, OR, USA). In this test, the subjects shifted their center of gravity by leaning their body to target frames indicated by a cursor moving on a computer screen, maintained the position for several seconds, and returned to the center frame, following the cursor. This action was repeated in five directions (forward, right oblique forward, right, left, and left oblique forward). The following two variables were measured: path sway (the percentage of the movement route to the shortest route) and movement time (the time required for the movement from the center of gravity to the indicated site). Values for each variable were expressed as the total in the five directions. As simple static balance tests, the single-leg test with eyes open and Romberg’s test were performed. The duration of standing was measured to a maximum value of 30 seconds. The percentage of subjects showing recovery was also calculated at each time point in CDP and simple dynamic balance tests. Recovery was defined as when the difference between the baseline and the value at each time point was 10% or smaller in CDP and when the duration of standing recovered to baseline value in simple tests.

This study was designed to have 80% power for detecting a difference of 70% (this value is equivalent to 10% of the baseline value of young subjects in a preliminary study) in path sway between the mean for elderly subjects and the mean for younger subjects. Intragroup differences were analyzed with repeated measures ANOVA, and subsequent multiple comparisons were performed with Dunnett’s test. Intergroup differences in the change from baseline values were analyzed with the unpaired t-test. Differences with a p value less than 0.05 were considered significant. Values are expressed as the mean ± standard deviation.

Results

Subjects' characteristics are summarized in Table 1. The sedative dose for the elderly group was 60.9% of that in the young group.

Changes in values of the dynamic LOS test are shown in Table 2. Baseline values of path sway and movement time in the elderly group were significantly greater than those in the young group. The changes from baseline values of path sway and movement time 50 minutes after the administration of midazolam in the elderly group (106.8±101.0 % and 4.6±3.0 minutes) were significantly greater than those (32.9±87.2% and 1.9±2.8 minutes) in the young group, respectively.

The baseline values of simple tests in the young and elderly groups were 30±0 and 30±0 seconds respectively, in Romberg's test and 30±0 and 22.8±9.3 seconds in the single-leg test. Changes in the percentage of subjects showing recovery in each test are shown in Table 3. The recovery percentage in the single-leg-test, but not in Romberg's test, was similar to those of the path sway test and movement time in the elderly group.

Discussion

In regard to baseline values of CDP with intentional postural sway, a significant decrease in balance function was seen in the elderly group compared with the young group. This result is consistent with results without sedation reported previously [8, 11]. Because the aged-related decrease in balance function is caused by decreases in the functions of sensory organs, transmission/integration areas, and motor organs [12], it is logical that balance function in the elderly is markedly decreased during center of gravity movement, for which balance function is important.

In regard to the results of CDP with intentional postural sway after intravenous sedation, the recovery in the young group after midazolam administration was relatively early. Fujiwara [13] has reported that voluntary postural control and postural control against predictable periodical perturbation stimuli are primarily associated with cerebral cortical control. Custon *et al*. [14] have reported that inhibition of balance function for unexpected perturbations after oral diazepam administration in elderly volunteers is due to inhibition of an automatic oligosynaptic spinal reflex via supraspinal modulation without conscious control. Therefore, unlike reflexive postural control via the brainstem against unexpected perturbations, voluntary postural control closely associated with the cerebral cortex may begin to recover relatively early during the recovery period with the disappearance of sedative effects in young adults. On the other hand, recovery of intentional postural sway function was slower in the elderly subjects than in young subjects, although the sedative dose in the elderly subjects was 60% of that in the young subjects, and even when values were adjusted to compensate for differences in baseline values. Reasons for this age-related difference is unknown. However, it may derive from age-related inhibitory effects of benzodiazepines on sensory organ and postural adjustment/integration in the cerebral cortex [12] and to age-related muscle relaxation effects of benzodiazepines via benzodiazepine 2 receptors on GABAA receptors in the spinal cord [15].

In Romberg's test of the present study, all subjects in both the young and elderly groups could stand with eyes closed for 30 seconds 50 minutes after midazolam administration. Therefore, the effects of this load may be too slight for bilateral leg standing. The single–leg test with the eyes open has been reported to be useful for assessing postural control ability and predicting falls in the elderly [8,16]. Also in the present study, the percentage of subjects showing recovery on the single-leg test was similar to that on the dynamic LOS test. Considering that CDP would appear to be too complex in the routine clinical setting, the single-leg test might be a useful clinical test for the elderly.

In summary, elderly subjects showed greater decreases in intentional dynamic balance function than did young adult subjects both before and after intravenous sedation with midazolam. Therefore, the intentional body sway test may be a useful dynamic balance test for detailed assessment of recovery from intravenous sedation with midazolam in the elderly, but may not be suitable in young adults.

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Table 1. Subjects' characteristics

	Elderly group (n=18)	Young group (n=20)
Age (years)	68.2±3.4 * (range, 61-72)	23.1±2.0 (range, 20-27)
Height (cm)	166.7±4.8	171.1±6.2
Weight (kg)	65.6±8.2	64.7±8.2
Body mass index (kg m-2)	23.7±3.1	23.1±2.0
Dose of midazolam (mg kg-1)	0.042±0.009 *	0.068±0.006

Values are means ±SD

*p＜0.001(vs Young group)

Table 2 Changes in values of dynamic LOS test after administration of midazolam in young and elderly groups (mean ± SD)

Test	Measure (unit)	Group	Baseline	50 min after	70 min after	90 min after	110 min after	130 min after
Dynamic LOS test	Path sway (%)	Young	720.3±59.0	761.1±82.6	721.0±56.1	713.3±58.6	708.6±49.5	710.5±55.4
		Elderly	858.9±82.5##	965.7±115.1** $	885.7±123.1	887.2±108.1	891.3±103.2	880.6±97.6
	Movement time (sec)	Young	12.4±1.8	14.3±2.7	13.3±1.9	12.8±1.6	12.4±1.5	12.6±1.7
		Elderly	19.6±4.1##	24.2±3.6* $$	20.5±5.0	20.6±5.0	19.3±4.8	19.5±5.0

*$p < 0.05$; **$p < 0.01$(vs baseline), ##$p < 0.01$(vs Young group with measured value), \$$p < 0.05$; \$\$$p < 0.01$(vs Young group with the change from baseline value)

Abbreviations: LOS, limits of stability

Young group; n=20, Elderly group; n=18

Table 3 Changes in the percentage of subjects showing recovery to all subjects in young and elderly groups

Test	Measure	Group	Baseline	50 min after	70 min after	90 min after	110 min after	130 min after
Dynamic LOS test	path sway	Young	100	60	95	100	100	100
		Elderly	100	39	61	89	89	100
	movement time	Young	100	45	70	80	80	80
		Eldery	100	22	67	83	94	100
Simple static test								
SLT(eyes open)	Time	Young	100	80	100	100	100	100
		Elderly	100	53	65	88	100	100
Romberg's test	Time	Young	100	100	100	100	100	100
		Elderly	100	100	100	100	100	100

Abbreviations: LOS, limits of stability; SLT, single-leg-test

Young group; n=20, Elderly group; n=18