



HOKKAIDO UNIVERSITY

Title	Study on the usefulness of precise and simple dynamic balance tests for the evaluation of recovery from intravenous sedation with midazolam and propofol.
Author(s)	Fujisawa, T.; Takuma, S.; Koseki, H. et al.
Citation	European Journal of Anaesthesiology, 24(5), 425-430 https://doi.org/10.1017/S0265021506001876
Issue Date	2007-05
Doc URL	https://hdl.handle.net/2115/25174
Rights	Copyright © 2007 Cambridge University Press. The paper has been accepted for publication and may appear in a revised form, subsequent to editorial input by Cambridge University Press, in the journal published by Cambridge University Press.
Type	journal article
File Information	EJA24-5.pdf



Address correspondence to:

Toshiaki Fujisawa

Department of Dental Anesthesiology, Graduate School of Dental Medicine,

Hokkaido University

kita-13 Nishi-7, Kita-ku, Sapporo 060-8586, Japan

Tel and FAX: +81-11-706-3738

E-mail address: fujitosi@den.hokudai.ac.jp

STUDY ON THE USEFULNESS OF PRECISE AND SIMPLE DYNAMIC
BALANCE TESTS FOR THE EVALUATION OF RECOVERY FROM
INTRAVENOUS SEDATION WITH MIDAZOLAM AND PROPOFOL

T. Fujisawa, S. Takuma, H. Koseki, K. Kimura, and K. Fukushima

Toshiaki Fujisawa, Shigeru Takuma, Hiroyo Koseki, Kunie Kimura, and Kazuaki
Fukushima

Department of Dental Anesthesiology, Graduate School of Dental Medicine, Hokkaido
University

Short title:

Simple dynamic balance test after sedation

Summary

Background and objective: Dynamic balance involving movement of the center of gravity is important for the evaluation of street fitness after sedation. The purpose of this study was to compare the recovery of dynamic balance after intravenous sedation with propofol and midazolam, and to investigate the usefulness of precise and simple dynamic balance tests to evaluate the recovery.

Methods: Fourteen young male volunteers underwent intravenous sedation with propofol and midazolam for an hour each at an interval of more than 1 week. Computerized dynamic posturography (CDP) using a multi-axial tilting platform, 10-m maximum-speed walking (MSW) test, and the timed “up & go” (TUG) test (subjects stand up from a chair, walk 5-m and back with maximum-speed, and sit down again) were performed before and after sedation. **The increase in each variable of the tests described above represents reduction of function.**

Results: The **score** of the CDP was significantly lower in propofol sedation than that in midazolam sedation till 40 min after the end of sedation ($p=0.006$). The **scores** of MSW test and TUG test were significantly lower in propofol sedation than that in midazolam sedation till 60 min after the end of sedation, respectively ($p=0.035$ and $p=0.042$). The TUG test and MSW test were well and significantly correlated with the CDP in midazolam sedation (TUG test vs. CDP; $r=0.66$, p less than 0.01, and MSW test vs. CDP; $r=0.53$, p less than 0.01).

Conclusions: The TUG test and MSW test are useful simple dynamic balance tests well correlated with precise CDP for the evaluation of the recovery of dynamic balance from midazolam sedation in younger adults.

Key words: CONSCIOUS SEDATION, PROPOFOL, MIDAZOLAM, RECOVERY OF FUNCTION, MUSCULOSKELETAL EQUILIBRIUM; dynamic balance, computerized dynamic posturography, simple test

Introduction

As intravenous sedation with midazolam or propofol is sometimes used with regional block in monitored anesthesia care for ambulatory surgery [1, 2], the evaluation of recovery of balance, particularly dynamic balance involving movement of the center of gravity, is important for safe discharge after sedation. Although many studies have compared the usefulness of propofol in sedation with that of midazolam [3, 4], our literature search did not reveal any studies of comparison of the recovery of dynamic balance after the injection of the two sedatives. Computerized dynamic posturography (CDP) with unpredictable perturbation stimuli is reported to be a sensitive and reliable method for the assessment of dynamic balance after sedation [5]. However, the application of CDP to daily clinical practice may be difficult due to economic considerations and the long test time. Therefore, if simple dynamic balance tests that are well correlated with precise CPD can be introduced, they may be useful in clinical practice.

The purpose of the present study was to compare the recovery of dynamic balance after intravenous sedation with propofol and midazolam, and to investigate the usefulness of precise and simple dynamic balance tests.

Subjects and Methods

After informed consent of the subjects and the approval of the ethics committee of our institution were obtained, 14 young male volunteers were enrolled in this study. They underwent intravenous sedation with propofol and midazolam for an hour each at an interval of more than 1 week. The sedation level aimed for was the Wilson's sedation score 3 (Table 1) [3]. For propofol sedation, target controlled infusion was started with the initial target blood concentration set at $2.2\mu\text{ g ml}^{-1}$ with a target controlled infusion (TCI) pump, **TCI pump TE-371 (Terumo Inc., Tokyo, Japan)**. **The TCI system used was the Diprefusor (AstraZeneca Pharmaceuticals, Macclesfield, UK) and the**

pharmacokinetic model used was Marsh's model [6]. Immediately after the target sedation level was achieved during induction, the target blood concentration was manually reset to the same value as the calculated effect-site concentration. Then the infusion rate was automatically regulated to make the calculated blood concentration follow the target blood concentration. For midazolam sedation, midazolam (a total of about 0.07 mg kg⁻¹) was administered in divided small doses over 4 to 5 min until optimal sedation was achieved, followed by the start of continuous infusion of two-thirds of the induction dose per hour. To maintain optimal sedation, the target blood concentration of propofol or the continuous infusion rate of midazolam was finely adjusted according to clinical signs and the bispectral index (BIS) with a BIS monitor A2000 (Aspect Medical Systems, Newton, MA, USA) during sedation for an hour. **When subjects continued opening their eyes or responded to verbal commands very slowly, the infusion conditions of propofol and midazolam were changed by 0.1 microgram ml⁻¹ and 0.1mg h⁻¹, respectively.**

Precise and simple dynamic balance tests, psychomotor function tests, and grip strength test were performed each time points described as Figure 1. A dynamic balance test using CDP with unpredictable random perturbation stimuli was performed by a Stability System (Biodex Medical Inc., Shirley, NY, USA) as described previously [5]. Briefly, The subject was instructed to maintain a standing position for 20 seconds on an unstable platform that tilted in all directions according to changes in body weight applied to the tip of the toes and the heels. The degree of platform tilt from the horizontal line in all directions during the test was expressed as the stability index.

As simple dynamic balance tests, the maximum-speed walking (MSW) test, in which the time required to walk 10 m at the maximum speed was measured [7], and the timed 'up & go' (TUG) test were performed. In the TUG test, the time required for the subject to stand up from a chair, walk forward for 5 m and return to the chair at maximum speed, and sit on the chair again was measured [8]. As simple psychomotor

function tests, the digit symbol substitution test (DSST) and the Trieger dot test (TDT) were performed. The DSST was performed for 90 seconds using the Japanese version of the manual for the Wechsler Adult Intelligence Scale-Revised. **The subjects draw the appropriate symbol under the digit following predetermined rules. The number of correct answers was scored.** In the TDT, a geometric figure was drawn by connecting a series of dots with a ball-point pen. **The number of dots left outside the line drawn was scored.** The grip strength of subject's dominant hand was measured with a Smedley Hand Dynamometer (Matsumiya, Tokyo, Japan). **The increase in each variable except DSST and the grip strength test represents reduction of function.**

This study was designed to have 80% power of detecting a difference of 0.24 degree (this **score** is equivalent to 15% of baseline **score** of young subjects in preliminary study) in stability index between the mean **score** in propofol sedation and the mean **score** in medazolam sedation. Data were processed as follows. In the precise and simple dynamic balance, psychomotor function, and muscle strength tests, intragroup differences were analyzed with Friedman's χ^2 r-test, and subsequent multiple comparisons were performed with the Wilcoxon signed-ranks test with Bonferroni correction. **Intergroup differences in the change from the baseline score were compared with the Wilcoxon signed-ranks test in the precise and simple dynamic balance, psychomotor function and muscle strength tests and BIS.** The relationship between CDP and the two simple dynamic balance tests was assessed with correlation coefficient. P values of less than 0.05 were considered significant. **Scores** are expressed as the mean \pm standard deviation.

Results

The mean age, height, body weight, and body mass index of the subjects were 23.9 ± 1.75 years (range, 22-28 years), 170.9 ± 5.7 cm (range, 164-184 cm), 62.5 ± 5.6 kg (range, 54-72 kg), and 21.4 ± 1.8 kg m⁻² (range, 19.0-24.9 kg m⁻²), respectively. The total

doses of propofol and midazolam used for 1 hour were 4.75 ± 0.91 mg kg⁻¹ and 0.11 ± 0.01 mg kg⁻¹, respectively. The BIS scores were maintained in the range from 73 to 83 during infusion of the sedatives (Fig. 2).

The scores of the dynamic balance test, MSW test and TUG test were significantly lower in propofol sedation than in midazolam sedation till 40, 60 and 60 min after the end of sedation, respectively (Table 2). The scores of DSST and grip strength test were significantly greater in propofol sedation than in midazolam sedation till 70 min and at least 30 min after the end of sedation, respectively (Tables 2 and 3). There was a well and significant positive correlation between the results of the simple dynamic balance tests and the CDP with midazolam sedation (TUG test vs. CDP; $r=0.66$, $p < 0.01$, and MSW test vs. CDP; $r=0.53$, $p < 0.01$), although a good correlation was not found with propofol sedation (TUG test vs. CDP; $r=0.3$, $p < 0.05$, and MSW test vs. CDP; not significant).

Discussion

The recovery of dynamic balance function assessed by CDP after the injection of midazolam for intravenous sedation has been reported [5, 9-11], but no studies on propofol sedation have been reported. We confirmed that propofol is more suitable than midazolam for intravenous sedation in the outpatient clinic with regard to street fitness using precise and simple dynamic balance tests in the present study.

Custon *et al.* [12] found that anterior tibialis activation, a medium-latency response, was delayed 1 hour after oral diazepam administration in elderly volunteers; thus, they speculated that diazepam delayed the brainstem-controlled oligosynaptic spinal reflex, resulting in inhibition of balance function. In the present study, intravenous infusion of midazolam may have inhibited dynamic balance function by a similar mechanism. The DSST showed that the recovery was significantly slower in the midazolam sedation than in propofol sedation until 70 minutes after the cessation of continuous infusion,

This result suggests that the difference in the recovery of dynamic balance between the two sedatives is partly associated with a delay in psychomotor function, such as the power of attention, the power of prediction, and strategy choice for the maintenance of balance function. In the present study, midazolam caused a significantly greater reduction in grip strength than did propofol during and until 30 min after the cessation of sedation. Midazolam is well known to act on the spinal pathway to reduce muscle strength and reflexes from a study on evoked motor extremity responses [13]. Propofol also has a dose-dependent effect on motor evoked potential [14, 15]. However, propofol is metabolized rapidly and the concentration used for sedation is low; thus, the reductive effect of propofol on motor function can be distinguished in the recovery period. Therefore, the differences in the recovery of dynamic balance function between the two sedatives may be associated with the difference in muscle relaxant effect in the two sedatives.

In this study, we tried to maintain the target sedation level on the basis of clinical signs and were able to maintain BIS values in the range between 73 and 83. In sedation with midazolam or propofol, BIS values of 75 to 89 indicate a sedation level at which the subject has no airway obstruction and responds to verbal stimuli [16, 17]. Therefore, we speculate that the desired conscious sedation level was maintained overall in the present study. The BIS values were lower in propofol sedation than in midazolam sedation in the last 20 minutes of the sedative infusion. However, this relation between propofol and midazolam was reversed 10 minutes after the cessation of infusion. These results indicated that recovery from propofol sedation was more rapid.

We previously reported that the intentional body sway test was useful for the evaluation of recovery from intravenous sedation in the elderly, but was not suitable for young adults [11]. CDP is classified according to the types of postural control as CDP using an intentional postural sway task [11, 18, 19] and CDP using perturbation stimuli

[5, 9, 10]. As falls may occur in any direction in daily life, multidirectional mechanical perturbation is a desirable stimulus condition for CDP [20]. Such a stimulus also prevents habituation. The CDP performed for young adults in the present study fulfills the conditions mentioned above, and is reported to be a reliable precise test for the evaluation of postural control ability against unpredictable perturbation stimuli [5]. On the other hand, a simple test that is well correlated with a precise CDP is necessary for wide clinical application [21]. The TUG test had results most strongly correlated with those of CDP with perturbation stimuli **in midazolam sedation** in the present study. The test originated from the “Get-up and Go” test developed by Mathias [22] as a simple balance function test, in which the risk of falls was qualitatively classified using a 5-point scale for the elderly. Podsiadlo et al. [23] measured the time required to complete the actions. Shumway-Cook [24] used MSW, and Shimada [8] used MSW and extended the distance from original 3 m to 5 m. The TUG test has many advantages in clinical use, such as proven differences between fall and non-fall groups, a proven correlation with balance function, good reproducibility, high sensitivity and specificity, applicability to the elderly, short measurement time, low cost, and no requirement for wide space [8, 22-27]. We used the TUG test with MSW as modified by Shimada [8]. Well correlation between balance and the MSW has also been demonstrated [7, 28, 29]. The TUG test used in the present study requires rapid acceleration and deceleration, a turn during high-speed walking, and rapid sitting down with a turn. We think the TUG test is more suitable than the MSW test for assessing entire motor function closely associated with balance function in the ambulatory setting with regard to the actions described above, its stronger correlation coefficient with a reliable CDP, and no requirement for large space.

The TUG test and MSW test both had well and significant positive correlations with CPD in midazolam sedation, but not with propofol sedation in the present study. The detailed reasons for this result remain unclear. However, as grip strength, that is, the

maximum power of hand and finger muscles, recovered within from 10 to 30 minutes after the cessation of propofol infusion, the ability to walk with maximum speed seemed to be already recovered at most time points at which dynamic balance tests were performed. Therefore, a small difference in values between before and after sedation may decrease the correlation coefficient between CDP and simple dynamic balance tests in propofol sedation. **CDP detected a difference of dynamic balance between midazolam and propofol for 40 minutes, whereas the MSW and TUG tests showed differences up to 60 minutes in the present study. This may have derived from the difference of recovery of muscle power between the two sedatives because the performance of the MSW and TUG tests may need more muscle power than CDP.**

In summary, precise and simple dynamic balance tests can detect the difference of recovery speed of dynamic balance after midazolam and propofol sedation. The TUG test and MSW test are both useful, simple dynamic balance tests well correlated with precise CDP for the evaluation of the recovery of dynamic balance from midazolam sedation in younger adults.

References

1. Avramov MN, Smith I, White PF. Interactions between midazolam and remifentanyl during monitored anesthesia care. *Anesthesiology* 1996 **85**: 1283-1289.
2. Janzen PR, Christys A, Vucevic M. Patient-controlled sedation using propofol in elderly patients in day-case cataract surgery. *Br J Anaesth* 1999 **82**: 635-636.
3. Wilson E, David A, Mackenzie N, Grant IS. Sedation during spinal anaesthesia: Comparison of propofol and midazolam. *Br J Anaesth* 1990; **64**:48-52.
4. Polster MR, Gray PA, O'sullivan G, Mccarthy RA, Park GR. Comparison of the sedative and amnesic effects of midazolam and propofol. *Br J Anaesth* 1993; **70**: 612-616.
5. Fujisawa T, Takuma S, Koseki H, Kimura K, Fukushima K. Assessment of the recovery of dynamic balance after intravenous sedation with midazolam. *J Anesth* 2005; **19**: 26-30.
- 6. Marsh B, White M, Morton N, Kenny GN. Pharmacokinetic model driven infusion of propofol in children. *Br J Anaesth*. 1991; 67: 41-48.**
7. Suzuki k, Imada G, Iwaya T, Handa T, Kurogo H. Determinants and predictors of the maximum walking speed during computer-assisted gait training in hemiparetic stroke patients. *Arch Phys Med Rehabil* 1999; **80**: 179-82.
8. Shimada H, Obuchi S, Kakurai S, Uchiyama Y. Relationship between balance function and falls among the frail elderly persons(in Japanese). *Sogo-riha* 2000; **28**: 961-6.
9. Gupta A, Ledin T, Larsen LE, Lennmarken C, Odkvist LM. Computerized dynamic posturography. A new method for the evaluation of postural stability following anaesthesia. *Br J Anaesth* 1991; **66**:667-672.
10. Makker R, Bailey P, Royston R, Kulinskaya E. Computerized dynamic posturography to assess recovery comparing general anaesthesia with sedation and local

anaesthesia for day case nasal surgery. *Anaesthesia* 2001; **56**: 1090-1115.

11. Fujisawa T, Takuma S, Koseki H, Kimura K, Fukushima K. Recovery of intentional dynamic balance function after intravenous sedation with midazolam in young and elderly subjects. *Eur J Anaesthesiol* 2006; **23**: 422-425.

12. Custon TM, Gray SL, Hughes MA, Carson SW, Hanlon JT. Effect of a single dose of diazepam on balance measures in old people. *J Am Geriatr Soc* 1997; **45**: 435-440.

13. Schonle PW, Isenberg C, Crozier TA, Dressler D, Machetanz J, Conrad B. Changes of transcranially evoked motor responses in man by midazolam, a short acting benzodiazepine. *Neurosci Lett* 1989; **101**: 321-324.

14. van Dongen ER, ter Beek HT, Aarts LP, et al. The effect of two low-dose propofol infusions on the relationship between six-pulse transcranial electrical stimulation and the evoked lower extremity muscle response. *Acta Anaesthesiol Scand* 2000; **44**: 799-803.

15. Nathan N, Tabaraud F, Lacroix F, et al. Influence of propofol concentrations on multipulse transcranial motor evoked potentials. *Br J Anaesth* 2003; **91**: 493-497.

16. Liu J, Singh H, White PF. Electroencephalogram Bispectral analysis predicts the depth of midazolam-induced sedation. *Anesthesiology* 1996; **84**: 64-69.

17. Singh H. Bispectral Index (BIS) monitoring during propofol-induced sedation and anaesthesia. *Eur J Anaesth* 1999; **16**: 31-36.

18. Persson F, Kristensen BB, Lund C, Kehlet H. Postural stability after inguinal herniorrhaphy under local infiltration anaesthesia. *Eur J Surg* 2001; **167**: 449-452.

19. Liston RAL, Brouwer BJ. Reliability and validity of measures obtained from stroke patients using the Balance Master. *Arch Phys Med Rehabil* 1996; **77**: 425-430.

20. Commissaris DA, Nieuwenhuijzen PH, Overeem S, de Vos A, Duysens JE, Bloem BR. Dynamic posturography using a new movable multidirectional platform driven by gravity. *J Neurosci Methods* 2002; **113**: 73-84

21. El-Kashlan HK, Shepard NT, Asher AM, Smith-Wheelock MS, Telian SA.

Evaluation of clinical measures of Equilibrium. *Laryngoscope* 1998;**108**: 311-319

22. Mathias S, Nayak USL, Isaacs B. Balance in the elderly patients: The “Get-up and Go” test. *Arch Phys Med Rehabil* 1986; **67**: 387-9.

23. Padsiadlo D, Richardson S. The timed “Up & Go”: A test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc* 1991; **39**: 142-8.

24. Shumway-Cook A, Brauer S, Woollacott M. Predicting the probability for falls in community-dwelling older adults using the Timed Up & Go test. *Phys Ther* 2000; **80**: 896-903.

25. Dite W, Temple VA. A clinical test of stepping and change of direction to identify multiple falling older adults. *Arch Phys Med Rehabil* 2002; **83**: 1566-71.

26. Chiu AY, Au-Yeung SS, Lo SK. A comparison of four functional tests in discriminating fallers from non-fallers in older people. *Disabil Rehabil* 2003; **25**: 445-50.

27. Lin MR, Hwang HF, Hu MH, Wu HD, Wang YN, Huang FC. Psychometric comparisons of the timed up and go, one-leg stand, functional reach, and Tinetti balance measures in community-dwelling older people. *J Am Geriatr Soc* 2004; **52**: 1343-8.

28. Dettmann MA, Linder MT, Sepic SB. Relationships among walking performance, postural stability, and functional assessments of the hemiplegic patient. *Amer J phys Med* 1987; **66**: 77-90.

29. Imms FJ, Edholm OG. Studies of gait and mobility in the elderly. *Age and Ageing* 1981; **10**: 147-56.

Figure legends

Figure 1 Protocol

Figure 2 Serial changes in BIS scores

Square: propofol group, rhombus: midazolam group, #: $p < 0.05$, ##: $p < 0.01$ (between the groups **with the change from the baseline score**), (mean \pm SD, n=14)

Table 1 Wilson's sedation scores

Score	Degree of sedation
1	Fully awake and orientated
2	Drowsy
3	Eyes closed but rousable to command
4	Eyes closed but rousable to mild physical stimulation (earlobe tug)
5	Eyes closed but unrousable to mild physical stimulation

Table 2 Comparison of propofol and midazolam in precise and simple dynamic balance tests and psychomotor function tests (mean ± SD) n=14

Tests	Measures (unit)	Drug	Baseline	20 min after	40 min after	60 min after	80 min after	100 min after
CDP								
Dynamic balance test	Stability Index(degree)	propofol	1.45±0.21	2.01±0.34** ##	1.40±0.27##	1.44±0.24	1.41±0.18	1.46±0.20
		midazolam	1.61±0.21	3.12±0.74**	2.11±0.50*	1.83±0.34	1.59±0.27	1.54±0.28
Simple dynamic balance test								
MSW test	time (sec)	propofol	4.17±0.42	4.59±0.62** ##	4.21±0.51##	4.16±0.42#	4.15±0.42	4.15±0.44
		midazolam	4.33±0.43	5.31±0.56**	4.81±0.39*	4.55±0.42	4.40±0.43	4.50±0.42
TUG test	time (sec)	propofol	7.44±0.64	8.41±1.05** ##	7.47±0.79##	7.27±0.72#	7.34±0.68	7.3±0.71
		midazolam	7.71±0.68	10.60±1.32**	8.71±0.83*	7.96±0.77	7.65±0.76	7.70±0.76
				30 min after	50 min after	70 min after	90 min after	110 min after
Psychomotor function test								
DSST	number	propofol	84.2±9.1	81.9±10.1##	85.8±9.5##	85.9±8.9#	84.5±9.2	85.1±9.6
		midazolam	82.4±11.6	69.1±11.7**	74.8±10.2**	80.0±11.1	80.8±12.0	81.1±10.9
TDT	number	propofol	2.00±1.65	3.39±1.84* ##	3.11±2.08	3.04±1.84	2.75±1.55	2.44±1.62
		midazolam	2.82±1.93	5.86±1.88**	3.61±1.06	3.64±2.18	3.41±1.77	3.01±1.51

*:p <0.05, **:p <0.01 (vs Baseline), #:p <0.05, ##:p <0.01 (vs midazolam group with the change from the baseline score)

Abbreviations: CDP, computerized dynamic posturography; MSW, maximum speed walking; TUG, timed 'up & go'; DSST, digit symbol substitution test; TDT, Trieger dot test

X min after means X minutes after end of infusion

Table 3 Comparison of propofol and midazolam in grip strength test (mean \pm SD) (n=14)

Test (unit)	Drug	Baseline	30 min after starting of IVS	Immediately after end of IVS	10 min after end of IVS	30 min after end of IVS
Grip strength (kg)	propofol	41.1 \pm 8.3	32.4 \pm 5.9** ##	32.4 \pm 4.5** #	37.8 \pm 5.4* ##	42.4 \pm 5.2 ##
	midazolam	42.8 \pm 7.2	24.2 \pm 8.4**	25.6 \pm 9.3**	30.1 \pm 7.0**	37.8 \pm 4.5*

*p <0.05; **p <0.01 (vs baseline), #p <0.05; ##p <0.01 (vs midazolam group with the change from the baseline score).

Abbreviations: IVS, intravenous sedation

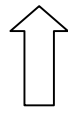
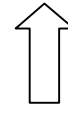
Starting infusion of propofol or midazolam

End of infusion of propofol or midazolam

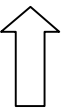
X min after end of infusion (min)

Baseline -60 -30 -15 0 10 20 30 40 50 60 70 80 90 100 110

Precise and simple dynamic balance tests



Psychomotor function tests



Grip strength test



BIS monitor



