SHORT COMMUNICATON

Relationship between use of sleep medication and accidental falls during hospitalization

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ABSTRACT

Falls are common in elderly patients, and prevention of fall is important for safety and for reduction of health care costs. Sleep medications are among many potential causes of fall. In this study, we examined relationship of sleep medication with fall from January 2017 to December 2017. 726 falls occurred in 442 patients, and the average age at the time of fall was 60.7 ± 23.8 years. Fall was most common in patients with neurological disease, followed by gastroenterological, ophthalmological, respiratory, and orthopedic conditions. Sleep medication was used in 223 falls (31%). Fall occurred at all times of day, but with a different distribution in patients with and without use of sleep medication. Thus, the rate of falls from 22:00 to 6:00 was significantly higher in patients using sleep medication (62% vs. 18%, p<0.01). There was also a significantly higher rate of multiple falls in patient using sleep medication (p<0.01). Zolpidem (25%, n=63), a non-benzodiazepine, was the most frequently used sleep medication, followed by brotizolam (16%, n=41) and etizolam (13%, n=32), which are both benzodiazepines. Multiple falls from 22:00 to 6:00 occurred significantly more frequently in patients using ≥2 types of sleep medications compared to one (53% vs. 17%, p<0.01). Taking multiple sleeping pills makes it easier to fall, and even drugs with a short half-life, which are considered to be safe, can cause falls at night in elderly patients. The results of this study show that careful selection of sleep medications is required to prevent fall in elderly patients.

Keywords: sleep medication, fall, elderly patients, hospitalization, risk management

INTRODUCTION

Falls are common adverse events in elderly patients, and fall can cause fracture that leads to a decrease in activities of daily living (ADL).[1-3] Therefore, prevention of fall is important for medical safety and for reduction of costs for nursing care.[4,5] Identification of causes of falls and initiation of appropriate intervention for these factors are important to prevent future falls. These causes are classified into external factors such as the presence or absence of steps and handrails, and type of footwear; and internal factors such as age-related deterioration of muscle

strength, visual acuity and hearing, and drug resistance.

The number of medications taken and use of sleep medication are also associated with falls.[6,7] The rate of use of sleep medications is high in elderly people due to an increase in sleep disorders with aging.[8] These include sleep onset disorder, mid-wake awakening, early awakening, and deep sleep disorder; thus, sleep medications are used for a wide variety of indications. It is clear that fall occurs due to complex involvement of many factors. Sleep medication for outpatients is important, but data from inpatients with a constant environment may be more useful for defining the relationship between fall and sleep medication. Thus, the purpose of the study was to examine the relationship of sleep medication with accidental fall in inpatients using data from fall incident reports.

MATERIALS AND METHODS

A total of 726 fall cases among admitted patients at our hospital from January 2017 to December 2017 were included in the analysis. The 726 falls (455 males, 271 females) occurred in 442 patients, and the average age at the time of a fall was 60.7 ± 23.8 years. The incidents of fall were examined retrospectively using a database in the hospital event reporting system. At our hospital, a clinical error or event is submitted as an incident or event report, regardless of whether it results in harm to a patient. A web-based reporting system is used to maintain anonymity and produce a blame-free system. This approach facilitates easy access for reporting, a shorter data entry time, better legibility of reports, and immediate information sharing among hospital staff. All reports are submitted to the patient safety management office for analysis, and these reports are used to develop measures for future improvements.

A fall was defined as an involuntary change of posture whereby a patient ended up lying on the floor. All patients with a fall were subsequently followed up until discharge. Demographic data (incidence of fall, sex, and age), time of occurrence, location of occurrence, and type of sleep medications were obtained from the database. The protocol of the study was approved by the Ethics Committee of Nagoya University Graduate School of Medicine.

For assessment of fall risk, we used a fall risk score that was originally developed by our fall working group. This score was evaluated routinely on admission, in each week of hospitalization, at the time of a fall, and as the medical condition changed. The risk was determined using a fall assessment score sheet comprising 33 items, including age, history of fall, ADL, and cognition (Table 1). The sum of the scores for these items served as the risk score. Patients were classified as grade 1 (low risk), grade 2 (moderate risk), and grade 3 (high risk) based on scores of 0–5, 6–15, and ≥16 and including at least one of all the major items, respectively.

Table 1   Risk assessment score sheet [a]

Assessment	Yes	No
Past history		
History of fall	1	0
History of syncope	1	0
History of convulsions	1	0
Impairment		
Visual impairment	1	0

Hearing impairment	1	0
Vertigo	1	0
Mobility		
Wheelchair	1	0
Cane	1	0
Walker	1	0
Need assistance	1	0
Cognition		
Disturbance of consciousness	1	0
Restlessness	1	0
Memory disturbance	1	0
Decreased judgment	1	0
Dysuria		
Incontinence	1	0
Frequent urination	1	0
Need helper	1	0
Go to bathroom often at night	1	0
Difficult to reach the toilet	1	0
Drug use		
Sleeping pills	1	0
Psychotropic drugs	1	0
Morphine	1	0
Painkiller	1	0
Antiparkinson drug	1	0
Antihypertensive medication	1	0
Anticancer agents	1	0
Laxatives	1	0
Dysfunction		
Muscle weakness	1	0
Paralysis, numbness	1	0
Dizziness	1	0
Bone malformation	1	0
Rigidity	1	0
Brachybasia	1	0

[a] Patients were classified into three groups: Grade 1 (low risk), Grade 2 (moderate risk), and Grade 3 (high risk) based on total scores of 0–5, 6–15, and ≥16 and including at least one item in each category, respectively.

Differences between two groups were analyzed by Mann-Whitney U test or Student t-test. All analyses were conducted using SPSS ver.25 for Window (IBM Inc., Chicago, IL), with p<0.05 considered to be significant.

RESULTS

The demographics of the patients with the 726 falls are shown in Table 2. Fall was most common in patients with neurological disease as the main primary disease, followed by gastroenterological, ophthalmological, respiratory, and orthopedic conditions. The fall risk scores placed 12%, 45%, and 43% of the patients in grades 1, 2 and 3, respectively; the location of most falls was in the hospital room (66%); and 51%, 38%, and 11% of patients had 1, 2 and ≥3 falls, respectively.

**Table 2** Demographics and characteristics of cases of fall

Variable	Cases
Demographic	
Falls (n)	726
Age (years)	60.7±23.8
Sex (male/ female)	455/271
Over 80 years of age	19% (138)
Over 60 years of age	68% (493)
Primary disease	
Neurological	27% (196)
Gastroenterological	19% (138)
Ophthalmology	12% (87)
Respiratory	8% (58)
Orthopedics	6% (44)
Cardiac	5% (37)
Pediatrics	5% (35)
Otolaryngology	5% (34)
Genecology	4% (29)
Others	9% (68)
Fall risk score	
Grade 1	12% (87)
Grade 2	45% (327)
Grade 3	43% (312)
Location	
Hospital room	66% (479)
Corridor	13% (94)
Restroom	8% (58)

Bathroom	4% (29)
Rehabilitation ward	2% (15)
Others	7% (51)
Number of falls (per patient)	
Once	51% (225)
Twice	38% (170)
Three or more times	11% (47)
Falls with sleep medication	31% (223)

Sleep medication was used in 223 falls (31%) (Table 2). The distribution of patients by age category is shown in Figure 1. Most falls involved patients in their 70s, followed by patients in their 80s and 60s (Figure 1). Fall occurred at all times, but with a different distribution in patients with and without use of sleep medication (Figure 2). The 228 falls from 22:00 to 6:00 included 139 falls with sleep medication (61%) (Figure 3A), and the rate of falls from 22:00 to 6:00 was significantly higher in patient using sleep medication (62% vs. 18%, p<0.01) (Figure 3B).
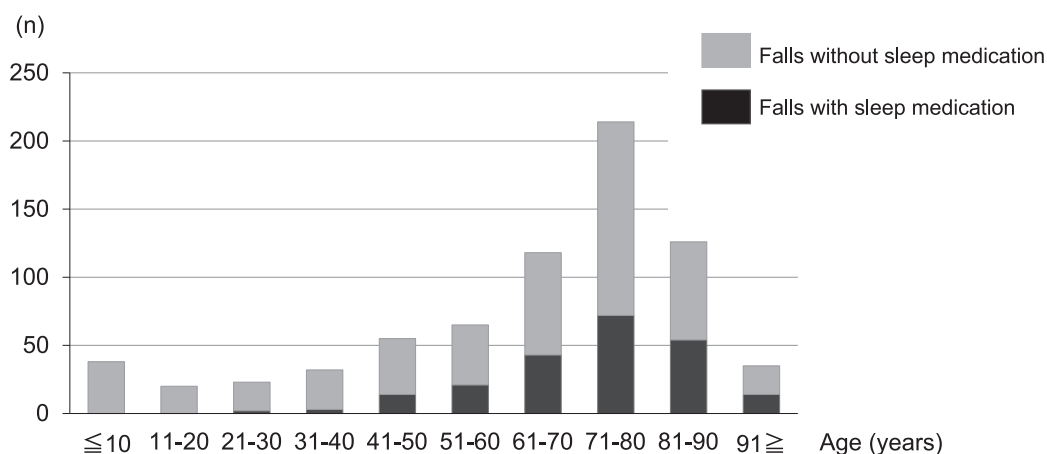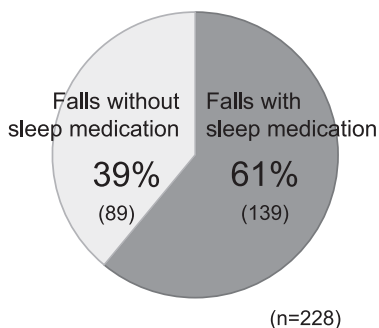

Fig. 1 Distribution of falls

Distribution of falls by age category.
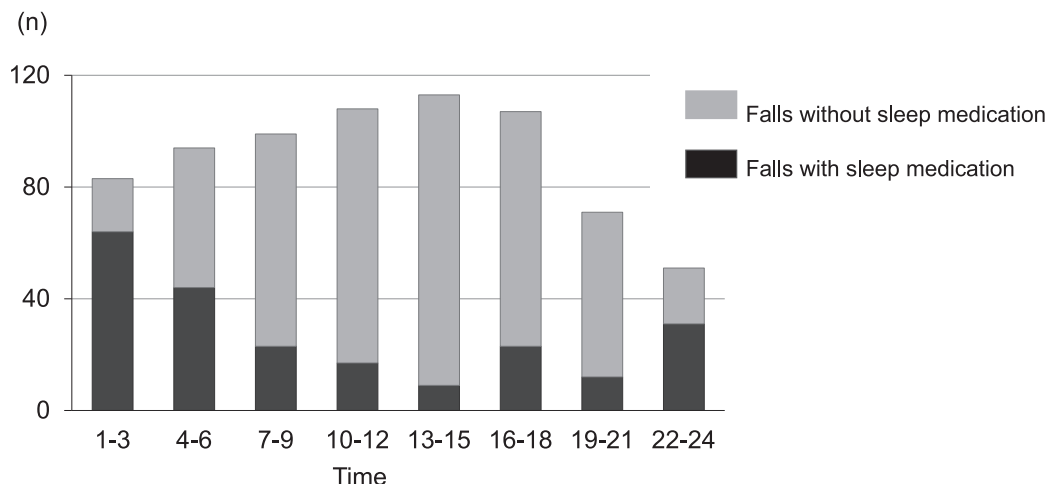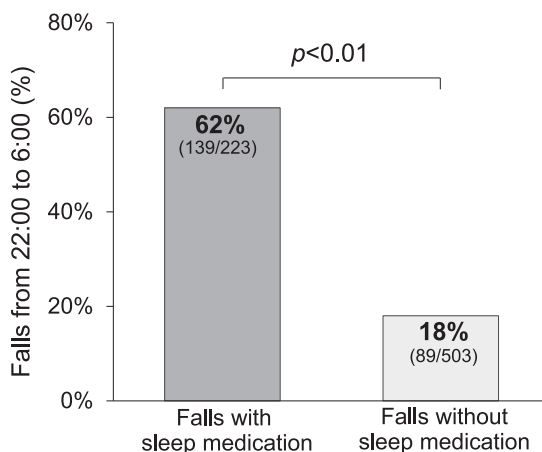
Fig. 2 Trends of falls
Distribution of falls by time, including in patients with and without sleep medication.

Fig. 3 Details of falls
Relationship between "fall from 22:00 to 6:00" and "sleep medication".
Fig. 3A: Rate of falls from 22:00 to 6:00 in patients with sleep medication.
Fig. 3B: Percentage of falls from 22:00 to 6:00 in patients with and without sleep medication (62% vs. 18%, p<0.01).

Use of sleep medication was significantly more frequent in patients over 60 and over 80 years old (p<0.01) (Table 3). There was a significantly higher rate of multiple falls in patients using sleep medication (p<0.01) (Table 4). The details of the sleep medication are shown in Table 5. Zolpidem (25%, n=63) was the most frequently used sleep medication, followed by brotizolam (16%, n=41) and etizolam (13%, n=32), including use of multiple medications. Multiple falls from 22:00 to 6:00 occurred significantly more frequently in patients using ≥2 types of sleep medications compared to those using one sleep medication (53% vs. 17%, p<0.01) (Figure 4).

Table 3 Comparison of falls with and without use of sleep medication

Variable	Falls with sleep medication (n=223)	Falls without sleep medication (n=503)	*P* value
Demographic			
Age (years)	64.1±22.4	59.2±23.7	<0.05
Female	36% (80)	38% (191)	n.s.
Over 80 years of age	30% (68)	18% (93)	<0.01
Over 60 years of age	82% (183)	62% (310)	<0.01
Fall risk score			
Grade I	11% (26)	12% (61)	n.s.
Grade II	46% (103)	45% (224)	n.s.
Grade III	42% (94)	43% (218)	n.s.
Location			
Hospital room	63% (141)	67% (338)	n.s.
Corridor	16% (35)	12% (59)	n.s.
Restroom	9% (19)	8% (39)	n.s.
Bathroom	4% (9)	4% (20)	n.s.
Rehabilitation ward	2% (5)	2% (10)	n.s.
Others	6% (14)	7% (37)	n.s.

Table 4 Comparison of number of falls with and without use of sleep medication

Variable	Patients with sleep medication (n=127)	Patients without sleep medication (n=315)	*P* value
Number of falls (per patient)			
Once	37% (47)	57% (178)	<0.01
Twice	39% (50)	38% (120)	n.s.
Three or more times	24% (30)	5% (17)	<0.01

Table 5 Details of use of sleep medications in patients with falls

Classification	Drug name	n
Very short half-life	Zolpidem (Myslee®)	25% (63)
	Zopiclone (Amoban®)	8% (21)
	Eszopiclone (Lunesta®)	8% (19)
Short half-life	Brotizolam (Lendormin®) [b]	16% (41)
	Etizolam (Depas®) [b]	13% (32)
	Rilmazafone (Rhythmy®) [b]	3% (7)

Intermediate half-life	Flunitrazepam (Silece®) [b]	4% (9)
	Nitrazepam (Benzarin®) [b]	2% (4)
Long half-life	Quazepam (Doral®) [b]	2% (6)
Others	Ramelteon (Rozerem®)	12% (29)
	Suvorexant (Belsomra®)	8% (19)
Total		250 [a]

[a] Overlap in some cases

[b] Benzodiazepine
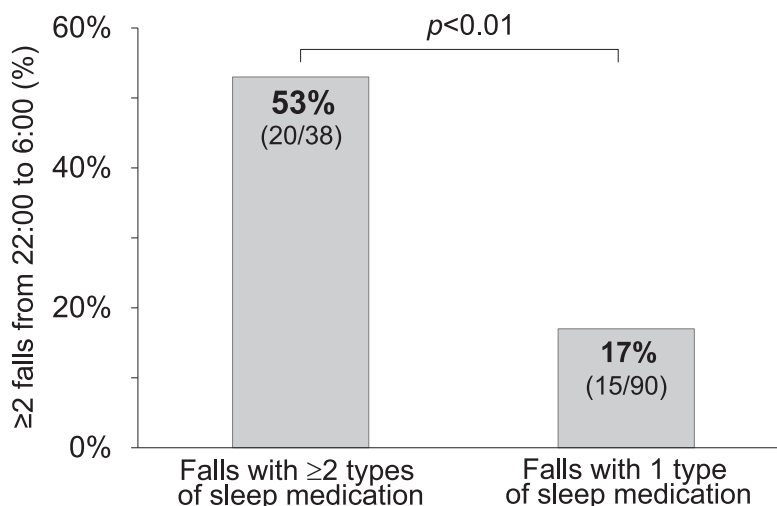
Fig. 4 Details of falls from 22:00 to 6:00 with sleep medication

Percentage of ≥2 falls from 22:00 to 6:00 in patients with ≥2 and only 1 type of sleep medication (53% vs. 17%, p<0.01).

DISCUSSION

Falls are a common health problem in elderly people, and in the adult population the incidence of fall increases with aging. We have previously shown a fall rate of 1.85% (3,925 / 212,617) for inpatients in all wards in our hospital from April 2012 to March 2017.[2] At admission to our hospital, nurses assess the potential for fall with patients and their families using a risk assessment score sheet, and a history of fall has a significant relationship with this fall risk score.[1,3,4] In our series, 49% of the patients had multiple falls; thus, in assessment of a patient who has previously fallen, it is important to examine the evaluation method from the perspective of preventing recurrence.

The most common sleep medication used in this study was zolpidem, which is in the non-benzodiazepine class, followed by brotizolam and etizolam, which are benzodiazepines. In previous reports, benzodiazepines have been found to increase the risk of falls and fractures,[7,9] and non-benzodiazepines are recommended for insomnia in elderly patients in the "Guidelines for proper use of sleep medication".[10] However, several previous studies have also found a fall

risk with non-benzodiazepines.[11,12] The results of the current study show that taking multiple sleep medications increases the risk of fall, and especially, the number of falls late at night and in the early morning increased significantly in patients who used multiple sleep medications. Thus, such patients should be especially careful about falls, and a combination of drugs should be used carefully. Also, as most sleep medications are metabolized in the liver, the effects of these drugs may be stronger in elderly patients due to their reduced metabolic function. For example, the half-life of zopiclone is 3.7 h, but this may be extended to as long as 16 h in elderly patients.[13] The risk of fall may be increased by this extended half-life, and this should be considered in selection of sleep medication, particularly in elderly patients with impaired physiological function. Therefore, it is important to be aware that even short-half-life sleep medications such as zolpidem and zopiclone can cause falls at night, especially in elderly people. Even sleep medications previously thought to be unlikely to be related to fall may not always be safe for elderly people, and it is necessary to warn patients taking these drugs of the possibility of falls.

There are some limitations in this study. First, the sample size is small. Second, non-fall patients were not examined, and the fall risk rate of each drug could not be determined with certainty. For example, although zolpidem was taken most often by patients with falls, it has a very short half-life and a minor muscle relaxant action. Thus, it was not possible to conclude whether zolpidem alone was significantly associated with falls. Third, drugs other than sleep medication were not examined, and factors such as environment maintenance, which is another cause of falls, and use of slippers as footwear, were not fully examined. Furthermore, it was not possible to examine the percentage of people on prescribed sleep medication with fall or the behavior of those with fall at night. However, our investigation of the relationship of sleep medication with accidental fall indicated that use of sleep medications was associated with fall late at night and in the early morning, and that multiple medications also had a significant relationship with multiple falls in the same period. Therefore, sleep medications appear to have a large impact on fall. Taking multiple sleeping pills makes fall more likely, and even drugs with a short half-life, which are considered to be safe, can cause falls at night in elderly people. Although the study focused on the hospital environment, sleep medications are also prescribed for many patients in outpatient settings. In this context, we believe that our results are not limited to hospitalization, but may also apply to patients at home. The findings indicate the importance of selection of sleep medication to prevent fall in all patients. It is also necessary to warn elderly patients of the possibility of falls, especially with use of sleep medications.

DISCLOSURE STATEMENT

REFERENCES

1   Kobayashi K, Imagama S, Ando K, et al. Incidence and characteristics of accidental falls in hospitalization. *Nagoya J Med Sci*. 2017;79(3):291–298. doi:10.18999/nagjms.79.3.291.
2   Kobayashi K, Ando K, Inagaki Y, et al. Measures and effects on prevention of fall: the role of a fall working group at a university hospital. *Nagoya J Med Sci*. 2017;79(4):497–504. doi:10.18999/nagjms.79.4.497.
3   Kobayashi K, Imagama S, Ando K, et al. Analysis of falls that caused serious events in hospitalized patients. *Geriatr Gerontol Int*. 2017;17(12):2403–2406. doi:10.1111/ggi.13085.
4   Kobayashi K, Ando K, Inagaki Y, et al. Characteristics of falls in orthopedic patients during hospitalization. *Nagoya J Med Sci*. 2018;80(3):341–349. doi:10.18999/nagjms.80.3.341.

5   Kobayashi K, Ando K, Suzuki Y, et al. Characteristics of outpatient falls that occurred in hospital. *Nagoya J Med Sci*. 2018;80(3):417–422.

6   Chen TY, Lee S, Buxton OM. A greater extent of insomnia symptoms and physician- recommended sleep medication use predict fall risk in community-dwelling older adults. *Sleep*. 2017;40(11). doi:10.1093/sleep/zsx142.

7   Kojima T, Akishita M, Nakamura T, et al. Polypharmacy as a risk for fall occurrence in geriatric outpatients. *Geriatr Gerontol Int*. 2012;12(3):425–430. doi:10.1111/j.1447-0594.2011.00783.x.

8   Kayukawa Y, Kogawa S, Tadano F, et al. Sleep problems in the aged in relation to senility. P*sychiatry Clin Neurosci*. 1998;52(2):190–192. doi:10.1111/j.1440-1819.1998.tb01024.x.

9   American Geriatrics Society, British Geriatrics Society, and American Academy of Orthopaedic Surgeons Panel on Falls Prevention. Guideline for the prevention of falls in older persons. *J Am Geriatr Soc*. 2001;49(5):664–672.

10   Japanese Society of Sleep Research. Practice guidelines for proper use and rest of sleeping medications. 2014. https://jssr.jp/files/guideline/suiminyaku-guideline.pdf. Accessed November 26, 2020.

11   Drake CL, Durrence H, Cheng, P, et al. Arousability and fall risk during forced awakenings from nocturnal sleep among healthy males following administration of zolpidem 10 mg and doxepin 6 mg: a randomized, placebo-controlled, four-way crossover trial. *Sleep*. 2017;40(7). doi:10.1093/sleep/zsx086.

12   Tom SE, Wickwire EM, Park Y, Albrecht JS. Nonbenzodiazepine sedative hypnotics and risk of fall-related injury. *Sleep*. 2016;39(5):1009–1014. doi:10.5665/sleep.5742.

13   Gaillot J, Le Roux Y, Houghton GW, Dreyfus JF. Critical factors for pharmacokinetics of zopiclone in the elderly and in patients with liver and renal insufficiency. *Sleep*. 1987;10 Suppl 1:7–21.