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Hypnotics Use and Falls in Hospital Inpatients Stratified by Age

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Abstract

Background: Little is known about the association between hypnotics use and falls among inpatients in young and middle-aged populations. We aimed to determine whether the use of hypnotics elevated the fall risk in adult inpatients aged 20 and above.

Methods: Patients admitted to the Kanto Rosai Hospital, Kanagawa, Japan, between April 1, 2013 and January 31, 2014 were followed up until discharge. We estimated the incidence rate ratio (IRR) and 95% confidence intervals (CI) of falls for the use of hypnotic drugs with a Poisson regression model, adjusted for sex, age, activities of daily living, and comorbidities.

Results: For the 6,949 inpatients whose medical records were examined, the incidence of falls was significantly higher in hypnotics' users than in non-users. The IRR was 1.52 (95% CI, 1.10-2.11). When stratified by age, the risk of hypnotics use in the patients aged 65 and above was statistically elevated (IRR, 1.48; 95% CI, 1.02-2.13); the risk in the patients aged 25-64 was elevated but not significant (IRR, 1.33; 95% CI, 0.63-2.81).

Conclusion: Usage of hypnotics elevated fall risk in the older inpatients, though this association was not significant in the young and middle-aged inpatients. Further studies are needed.

Keywords: Activities of Daily Living (ADL), falls, hypnotics, inpatients, older, young

1. Introduction

Preventing falls is a global concern in hospital settings (Cameron et al., 2012; World Health Organization, 2007). Falls can hamper patients' health and increase medical costs (Fields et al., 2015; Scuffham, Chaplin, & Legood, 2003).

In the older patient population, multiple risk factors are known to be associated with falls, one factor being the use of hypnotics (Huang et al., 2012; Park, Satoh, Miki, Urushihara, & Sawada, 2015). Another factor is a functional disability in activities of daily living (ADL), including mobility limitations and urinary incontinence (Chiarelli, Mackenzie, & Osmotherly, 2009; Hayakawa et al., 2014; Nakagawa et al., 2010).

Recently, fall risk has become a focus among younger patients, including young and middle-aged patients (Talbot, Musiol, Witham, & Metter, 2005). Two studies in Canada and the United States suggested that the use of hypnotics was also a pertinent risk factor for falls among patients of all ages (Cashin & Yang, 2011; Kolla, Lovely, Mansukhani, & Morgenthaler, 2013). However, earlier studies that investigated fall risks are few, and research on fall risks among younger patients is inconclusive (Talbot et al., 2005; Cashin & Yang, 2011; Kolla et al., 2013). We therefore examined the risk in younger patients, including the young and middle-aged, along with an older population.

We aimed to determine: (1) whether hypnotics use or functional disability in ADL increased fall risk among hospital inpatients aged 20 and above, using a retrospective design, and (2) whether the risks were significant when stratified by age.

2. Methods

We retrospectively created a de-identified dataset of patients in the Kanto Rosai Hospital, Kanagawa, Japan. The study period extended from April 1, 2013 to March 31, 2014. The patients in the study were admitted to the hospital between April 1, 2013 and January 31, 2014. We followed them from admission to discharge. Patients who remained in the hospital after March 31, 2014 were regarded as end-of-study censoring cases. The dataset contained clinical information, fall incidence, and hypnotics use. The Institutional Review Board of Kanto Rosai Hospital, Kanagawa, Japan approved the protocol of this study (Protocol Number 2014-12).

2.1 Inpatient Databases

Kanto Rosai Hospital was originally established as a medical institution for workers and laborers in the Tokyo-Yokohama industrial zone, but currently provides health services to the general public as well. The hospital maintains the following inpatient databases.

First, a clinical summary database that contains: 1) individual identification code, 2) sex, 3) age, 4) admission date, and 5) discharge date. Second, a database of the medical health claims system, called the Diagnosis Procedure Combination (Yasunaga, Hashimoto, Horiguchi, Miyata, & Matsuda, 2012), that contains information on a) comorbidities per International Classification of Diseases 10th Revision (ICD-10), and b) evaluation of ADL at admission by nurses (such as eating, dressing, walking, transferring to a wheelchair, and urinary continence). The latter is classified into three categories (independent, needed partial help, and needed full help). Third, a database of the clinical incidence report system, which contains information on fall incidence. Fourth, a database of electronic medical records, which contains information on drugs prescribed (drug name, prescription date, and date of medication discontinuation). After merging these databases, we created a dataset for analysis.

2.2 Inclusion and Exclusion Criteria

Inclusion criteria were patients aged 20 and above at admission, who were admitted to the hospital between April 1, 2013 and January 31, 2014. We excluded patients with missing data items. For patients who were admitted multiple times during this period, only data from the first admission period were used.

2.3 Main Outcome and Observation Period

The main outcome we studied was the incidence of falls. The definition of fall was “any type of fall, including a fall from the bed, a fall from a wheelchair, or a fall while walking”. We recorded falls as a dichotomous variable (yes/no).

We followed each patient from admission to discharge. The observation period was determined per right-censoring on the date of a fall incident or on March 31, 2014.

2.4 Definitions of Hypnotics Use and Functional Disability in ADL

Hypnotics use was defined as prescribing a patient with a hypnotic drug during the observation period. In accordance with the guidelines of the Japanese Society of Sleep Research, we defined all following hypnotics as a hypnotic drug in this study: Benzodiazepines (triazolam, etizolam, brotizolam, rilmazafone, lormetazepam, nimetazepam, flunitrazepam, estazolam, nitrazepam, quazepam, flurazepam, haloxazolam), non-benzodiazepines (zolpidem, zopiclone, eszopiclone), and melatonin receptor agonists (ramelteon) (Japanese Society of Sleep Research, 2013).

We assessed the mobility limitations of ADL (walking, transferring to a wheelchair) and urinary incontinence as functional disabilities. We then divided the patients into two groups: those who needed help in their ADL (partial or full help), and those who did not need any help in their ADL (independent) (Hayakawa et al., 2014).

2.5 Other Covariates

Age at admission was a continuous variable. The Charlson Comorbidity Index as per ICD-10 was used for controlling the baseline comorbidity (Quan et al., 2005). We divided the patients into those whose index score was 0, 1, or ≥2. In addition, we created two dummy variables for the specific fall risks of cerebrovascular disease (stroke) and diabetes (Jørgensen, Engstad, & Jacobsen, 2002; Lu et al., 2015). Insomnia was found to increase falls in previous studies (Avidan et al., 2005); however, we could not include a variable of insomnia in the final model because we found a strong collinearity between insomnia and the use of hypnotics in our dataset (correlation coefficient=0.87).

2.6 Statistical Analysis

Differences between the groups were assessed by *t*-test for continuous values, and by chi-squared test for percentages. We estimated the incidence rate ratios (IRRs) and 95% confidence intervals (CIs) for the use of hypnotics with the Poisson regression model, adjusted for sex, age, ADL, and comorbidity. We also estimated the IRRs and 95% CIs with additional adjustment for cerebrovascular disease and diabetes. We selected the Poisson regression because the likelihood test for over-dispersion was borderline insignificant (p=0.06).

For the sub-analysis stratified by age, we estimated the IRRs and 95% CIs for older inpatients (aged 65 and above) and for young and middle-aged inpatients (aged 20-64) based on previous studies (Talbot et al., 2005; Lu et al., 2015). In addition, we estimated the IRRs and 95% CIs for middle-aged inpatients (aged 41-64) to have a better picture of age group; we could not estimate those for the young patients (aged 20-40) because of the low incidence of falls. In the sub-analysis, we chose a binary variable of comorbidity (0 or ≥1) because no outcome was observed in the young and middle-aged patients whose comorbidity index score was 1.

All p-values were two-sided, and $p<0.05$ was considered statistically significant. Data were analyzed using STATA/MP13.1 (StataCorp LP, College Station, TX, USA).

3. Results

We initially included 7,370 patients aged 20 and above. We then excluded 421 patients (118 hypnotics' users; 303 non-hypnotics users) whose data were incomplete. As a result, we observed 6,949 inpatients during the study period. Observations of 21 patients (0.3%) were censored as end-of-study censoring cases. Hypnotics users constituted 21% of cases, and the mean age (SD) was 59 (19.9) years. The total number of falls was 147, and the total observation period was 91,513 person-days (the sum of total time in days contributed by all subjects). The baseline characteristics between hypnotics' users and non-users were different in each age group (Table 1).

Table 1. Characteristics of hypnotics' users and non-users among 6,949 inpatients aged 20 and over

Characteristics	Non-Users	Users	*p*-value [1]
Overall (age≥20)	n=5,469	n=1,480	
Female, n (%)	2,756 (50)	787 (53)	0.06
Age, mean (SD), in years	58 (20.0)	62 (19.0)	<0.001
Fall, n (%)	75 (1.4)	72 (4.9)	<0.001
Needed help in transferring to wheelchairs, n (%)	815 (15)	398 (27)	<0.001
Needed help walking, n (%)	736 (13)	381 (26)	<0.001
Needed help with urinary continence, n (%)	519 (9.5)	250 (17)	<0.001
Charlson Comorbidity Index, n (%)			
0	3,398 (62)	728 (49)	<0.001
1	829 (15)	224 (16)	
≥2	1,242 (23)	508 (34)	
Cerebrovascular disease	279 (5.1)	79 (5.3)	0.72
Diabetes	761 (14)	249 (17)	0.005
Observation period, mean (SD), in days	11 (14.9)	22 (24.4)	<0.001
Older (age≥65)	n=2,490	n=795	
Female, n (%)	1,135 (46)	436 (55)	<0.001
Age, mean (SD), in years	76 (7.3)	77 (7.2)	0.06
Fall, n (%)	59 (2.4)	58 (7.3)	<0.001
Needed help in transferring to wheelchairs, n (%)	608 (24)	307 (39)	<0.001
Needed help walking, n (%)	564 (23)	295 (37)	<0.001
Needed help with urinary continence, n (%)	430 (17)	203 (26)	<0.001
Charlson Comorbidity Index, ≥1, n (%)	1,413 (57)	554 (68)	<0.001
Cerebrovascular disease	197 (7.9)	70 (8.8)	0.42
Diabetes	514 (21)	181 (23)	0.20
Observation period, mean (SD), in days	13 (18.0)	27 (27.2)	<0.001

Young and middle-aged (age 20-64)	n=2,979	n=685	
Female, n (%)	1,621 (54)	351 (51)	0.13
Age, mean (SD), in years	42 (12.8)	45 (12.6)	<0.001
Fall, n (%)	16 (0.5)	14 (2.0)	<0.001
Needed help in transferring to wheelchairs, n (%)	222 (7.4)	96 (14)	<0.001
Needed help walking, n (%)	207 (7.0)	91 (13)	<0.001
Needed help with urinary continence, n (%)	89 (3.0)	47 (6.9)	<0.001
Charlson Comorbidity Index, ≥1, n (%)	658 (22)	208 (30)	<0.001
Cerebrovascular disease	82 (2.8)	9 (1.3)	0.03
Diabetes	247 (8.3)	68 (9.9)	0.17
Observation period, mean (SD), in days	9 (11.4)	16 (18.9)	<0.001
Middle-aged (age 41-64)	n=1,433	n=431	
Female, n (%)	573 (40)	221 (51)	<0.001
Age, mean (SD), in years	54 (7.3)	53 (7.5)	0.008
Fall, n (%)	14 (1.0)	13 (3.0)	0.002
Needed help in transferring to wheelchairs, n (%)	150 (10)	73 (17)	<0.001
Needed help walking, n (%)	131 (9.1)	69 (16)	<0.001
Needed help with urinary continence, n (%)	72 (5.0)	39 (9.1)	0.002
Charlson Comorbidity Index, ≥1, n (%)	569 (40)	175 (41)	0.74
Cerebrovascular disease	72 (5.0)	8 (1.9)	0.004
Diabetes	225 (16)	58 (13)	0.26
Observation period, mean (SD), in days	10 (14.5)	18 (22.3)	<0.001

Percentages may not total 100 because of rounding.

[1] *p*-value: *t*-test or chi-squared test.

Overall, the absolute incidence rate of falls per 1,000 person-days was 2.22 (72 falls/32,435 person-days) in hypnotics users and 1.27 (75 falls/59,078 person-days) in non-users. The IRR of hypnotics use was statistically elevated at 1.52 (95% CI, 1.10-2.11) (Table 2). Additional adjustment for cerebrovascular disease and diabetes showed the same trend (Table 2). The IRRs for age, disability in transferring to wheelchairs, and comorbidity were also elevated (Table 2). The IRR for diabetes showed an elevated tendency but was not significant (Table 2).

Table 2. Incidence rate ratios for falls adjusted with Poisson regression among 6,949 inpatients aged 20 and over

Characteristics	IRR (95% CI)	*p*-value	IRR (95% CI) [1]	*p*-value
Female (vs. male)	0.89 (0.64-1.23)	0.48	0.90 (0.64-1.25)	0.51
Age (continuous)	1.02 (1.01-1.04)	<0.001	1.02 (1.01-1.04)	<0.001
Use of hypnotics (vs. no)	1.52 (1.10-2.11)	0.01	1.51 (1.09-2.10)	0.01
Needed help in transferring to wheelchairs (vs. no)	2.14 (1.20-3.83)	0.01	2.23 (1.24-4.01)	0.007
Needed help walking (vs. no)	0.58 (0.28-1.19)	0.13	0.59 (0.31-1.13)	0.11
Needed help with urinary continence (vs. no)	0.71 (0.39-1.27)	0.24	0.70 (0.41-1.17)	0.17
Charlson Comorbidity Index (vs. 0)				
1	1.12 (0.64-1.98)	0.69	1.01 (0.58-1.78)	0.97
≥2	2.33 (1.49-3.63)	<0.001	1.94 (1.23-3.06)	0.004
Cerebrovascular disease (vs. no)	-	-	1.10 (0.66-1.84)	0.71
Diabetes (vs. no)	-	-	1.37 (0.94-2.00)	0.10

Abbreviation: IRR, incidence rate ratio; CI, confidence interval.

[1] Additional adjustment for cerebrovascular disease and diabetes concomitantly.

Table 3. Incidence rate ratios for falls adjusted with Poisson regression by age

Characteristics	IRR (95% CI)	*p*-value	IRR (95% CI) [1]	*p*-value
Older (age≥65)				
Female (vs. male)	0.96 (0.66-1.33)	0.81	0.96 (0.66-1.39)	0.82
Age (continuous)	1.01 (0.98-1.03)	0.63	1.01 (0.98-1.03)	0.59
Use of hypnotics (vs. no)	1.48 (1.02-2.13)	0.04	1.48 (1.02-2.13)	0.04
Needed help in transferring to wheelchairs (vs. no)	1.67 (0.87-3.21)	0.12	1.73 (0.90-3.34)	0.10
Needed help walking (vs. no)	0.61 (0.30-1.25)	0.18	0.59 (0.29-1.22)	0.16
Needed help with urinary continence (vs. no)	0.72 (0.40-1.29)	0.27	0.69 (0.38-1.25)	0.23
Charlson Comorbidity Index ≥1 (vs. 0)	2.18 (1.33-3.58)	0.002	1.92 (1.13-3.26)	0.02
Cerebrovascular disease (vs. no)	-	-	1.19 (0.69-2.05)	0.53
Diabetes (vs. no)	-	-	1.32 (0.88-1.98)	0.19
Young and middle-aged (aged 20-64)				
Female (vs. male)	0.68 (0.31-1.49)	0.33	0.68 (0.31-1.50)	0.56
Age (continuous)	1.05 (1.01-1.09)	0.01	1.05 (1.01-1.09)	0.01
Use of hypnotics (vs. no)	1.33 (0.63-2.81)	0.45	1.32 (0.62-2.81)	0.47
Needed help in transferring to wheelchairs (vs. no)	6.63 (1.97-22.3)	0.002	6.95 (2.03-23.7)	0.002
Needed help walking (vs. no)	0.42 (0.11-1.69)	0.22	0.40 (0.10-1.63)	0.20
Needed help with urinary continence (vs. no)	1.36 (0.44-4.24)	0.60	1.44 (0.46-4.53)	0.53
Charlson Comorbidity Index ≥1 (vs. 0)	0.77 (0.35-1.71)	0.52	0.67 (0.26-1.75)	0.41
Cerebrovascular disease (vs. no)	-	-	0.78 (0.16-3.75)	0.76
Diabetes (vs. no)	-	-	1.54 (0.55-4.33)	0.42
Middle-aged (aged 41-64)				
Female (vs. male)	0.78 (0.34-1.78)	0.56	0.78 (0.34-1.78)	0.56
Age (continuous)	1.02 (0.97-1.08)	0.49	1.02 (0.96-1.07)	0.58
Use of hypnotics (vs. no)	1.30 (0.60-2.82)	0.51	1.26 (0.58-2.76)	0.56
Needed help in transferring to wheelchairs (vs. no)	7.81 (2.25-27.0)	0.001	8.33 (2.35-29.5)	0.001
Needed help walking (vs. no)	0.35 (0.08-1.51)	0.16	0.34 (0.08-1.48)	0.15
Needed help with urinary continence (vs. no)	1.32 (0.39-4.44)	0.65	1.50 (0.44-5.05)	0.52
Charlson Comorbidity Index ≥1 (vs. 0)	0.74 (0.33-1.66)	0.47	0.66 (0.25-1.76)	0.41
Cerebrovascular disease (vs. no)	-	-	0.38 (0.05-3.08)	0.36
Diabetes (vs. no)	-	-	1.69 (0.58-4.94)	0.34

Abbreviation: IRR, incidence rate ratio; CI, confidence interval.

[1] Additional adjustment for cerebrovascular disease and diabetes concomitantly.

In the sub-analysis stratified by age, the absolute incidence rates of falls per 1,000 person-days in hypnotics users and in non-users were as follows: 2.70 (58 falls/21,498 person-days) versus 1.82 (59 falls/32,410 person-days) in the older patients; and 1.28 (14 falls/10,937 person-days) versus 0.60 (16 falls/26,668 person-days) in the young and middle-aged patients. The IRR of hypnotics use in the older patients was statistically elevated (IRR, 1.48; 95% CI, 1.02-2.13); the IRR in the young and middle-aged patients showed an elevated tendency that was not statistically significant (IRR, 1.33; 95% CI, 0.63-2.81) (Table 3). Additional adjustment for cerebrovascular disease and diabetes showed the same trend (Table 3). The IRR for comorbidity was elevated in the older patients, and the IRR for disability in transferring to wheelchairs was elevated in the young and middle-aged patients (Table 3). The IRR for diabetes showed an elevated tendency, but was not significant in either the older patients or the young and middle-aged patients (Table 3). The IRRs restricted to the middle-aged patients were almost identical to those of the young and middle-aged patients (Table 3).

4. Discussion

We found that the use of hypnotics elevated the overall risk of falls among inpatients; the incidence rate of falls in hypnotics' users was 1.5 times as high as that in non-users. When limited to patients aged 20–64, the association between the use of hypnotics and the risk of fall was not significant, but a significant association was found between mobility limitations in ADL and the risk of fall.

To our knowledge, our study is the first to compare the risk of fall between older and non-older inpatients. We also found that mobility limitations were an independent risk factor for falls among non-older inpatients. Our finding that the use of hypnotics increased falls among all inpatients concurred with those of two previous studies in Canada and the United States (Cashin & Yang, 2011; Kolla et al., 2013). The percentage of hypnotics' users in our cohort was similar to the mean reported in the Japanese general population (Kim, Uchiyama, Okawa, Liu, & Ogihara, 2000).

A recent systematic review suggested that the use of hypnotics was associated with falls in older patients, concurring with our findings (Park et al., 2015). Among the young and middle-aged inpatients in our study, the use of hypnotics tended to elevate the fall risk but was not a strong risk factor. This may be partially explained by the differences in drug metabolism by age. In general, metabolic processes are less efficient in older adults. Falls as adverse effects of the medication may be fewer in the young and middle-aged. In addition to the adverse effects of hypnotics (such as orthostatic hypotension, sedation, and sleep disturbance), fall risk increases (Park et al., 2015). Daytime sleepiness that increases fall risk in older adults may only affect the young and middle-aged to a lesser extent; our study patients had fewer comorbidities than patients in previous studies (Brassington, King, & Bliwise, 2000; Kolla et al., 2013). The weak statistical power owing to the small number of falls among the young and middle-aged inpatients in our study may also explain the statistical insignificance.

In a previous hospital-based study of older inpatients, one of the main risk factors for fall was an overall functional disability in ADL (Hayakawa et al., 2014). In our study, mobility limitations in ADL were also a significant risk factor in the young and middle-aged inpatients. A study among young and middle-aged restaurant workers suggested that engagement in a leisure-time physical activity (LTPA) may help to decrease occupational slips and falls (Caban-Martinez et al., 2014). That study, however, did not find a statistical significance between LTPA and fall prevention; in addition, spilled liquids and food are commonly found on restaurant floors. This external cause of slips and falls may invalidate a comparison with hospital patients. Nonetheless, activities to sustain or raise ADL functionality, such as physical exercise and rehabilitation, may play a key role in preventing falls in hospital settings.

In previous population-based studies, stroke and diabetes were also important risk factors for falls (Jørgensen et al., 2002; Lu et al., 2015). First, in a population-based study from Norway, the relative risk of stroke for fall was 2.3 (Jørgensen et al., 2002). Impaired dynamic balance caused by stroke has been associated with falls among post-stroke patients (Cho & Lee, 2013). In our study, the fall risk following a stroke was not significant; but if we multiplied the risk of cerebrovascular disease (IRR=1.1) by the risk of mobility limitations (IRR, 2.2), the fall risk of stroke patients became almost identical to that found by Jørgensen et al. (2002). Second, in a population-based study in Taiwan, the hazard ratios for fall with and without hypoglycemia were 1.63 and 1.13, respectively, and the fall risk of diabetics was higher in younger patients than in older patients (Lu et al., 2015). In addition, severe hypoglycemia had more influence on fall risk in the younger patients than in the older patients (Lu et al., 2015). These findings concurred with ours, that the IRR of diabetes was 1.37 and that the risk of fall in diabetics was higher in young and middle-aged patients than in older patients (IRR, 1.54 versus 1.32). However, our estimated fall risks of stroke and diabetes patients were not significant, and the fall risk associated with hypoglycemia in diabetic inpatients remains unclear in the current study; these risks should be examined further in hospital settings.

Our study has some limitations. First, this single-center study with a small fall incidence could not provide sufficient statistical power to calculate the risk of hypnotics use among young and middle-aged patients. We could not stratify the cohort into more than two groups because of the low incidence of falls. In addition, the study had a retrospective design, and subject to information bias. However, the information on hypnotics use was obtained from medical records, and the information on ADL was obtained at admission, which should minimize recall bias. Second, the excluded or censored observations in the study could raise the risk of skewing. However, the percentage of hypnotics' users in the excluded group was similar to the percentage in study subjects. The number of censored observations was low. Thus, this limitation could be negligible. Third, we could not evaluate the dose- and type-dependent effects of the hypnotics because we could not obtain this information. In addition, we could not evaluate other factors, such as potentially fall-related medications (including hypoglycemic or mental disorder medications) or insomnia. However, the use of hypnotics itself (in any dose or drug class) has been shown as the most relevant risk factor for fall in multiple pharmaceutical risks, regardless of insomnia (Cashin & Yang, 2011; Kolla et al., 2013; Park et al., 2015); thus, this limitation may not influence our results. Nevertheless, future work should include a design that would mitigate these limitations, while further evaluating a reduction in hypnotics use, such as substituting a non-pharmacological protocol (Agostini, Zhang, & Inouye, 2007), to prevent falls.

In summary, the use of sleep drugs elevated fall risk among inpatients regardless of age, though this association was not significant in the sub-analysis of the young and middle-aged inpatients. Further studies are needed for this population.

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Competing Interests Statement

The authors declare that there is no conflict of interests regarding the publication of this paper.

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