Sedative hypnotics use as the risk factor for fall incidents on geriatric patients

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ABSTRACT

Fall incident is one of geriatric syndromes that cause an increasing public health burden worldwide. The risk factors for falls incidents on geriatric patients have been identified included medication use. Benzodiazepine is a sedative hypnotic that found to be associated with an increase fall incidents. The aim of the study was to evaluate the influence of sedative hypnotics on the risk of fall incidents on geriatric patients. This was an observational study using cohort design involving 188 eligible geriatric patients comprising 94 patients who take sedative hypnotics and 94 patients who not. All pasients then underwent a test for functional mobility and fall risk using timed "up & go" test (TUG). The subjects who take ≤ 20 seconds to complete the TUG was considered to have low risk for fall incidents, whereas those who take > 20 seconds was considered to have high risk for fall incidents. The results showed that the use of sedative hypnotics, sex, and number of drugs taken were associated with fall incidents on geriatric patients. Geriatric patients who use sedative hypnotics were 2.41 times higher at risk of fall incidents than those who not use sedative hypnotics (95%CI;1.12-5.17; p = 0.023). Geriatric patients who take alprazolam were 2.78 times higher at risk of fall incidents compared to those who not take (95% CI: 1.49-5.19; p = 0.028). Furthermore, female geriatric patients were 3.29 times higher at risk of fall incidents compared to male geriatic patients (95%CI: 1.58-6.88; p = 0.001) and the use of ≥ 4 kinds of drugs were 2.76 times higher at risk of fall incidents compared to the use of < 4 kinds of drugs (95%CI:1.21-6.29; p = 0.015). In conclusion, sedative hypnotics is found to be a risk factor for fall incidents on geriatric patients.

ABSTRAK

Roboh adalah salah satu sindrom usia lanjut yang menyebabkan kenaikan beban kesehatan masyarakat di seluruh dunia. Faktor risiko roboh pada usia lanjut telah diidentifikasi termasuk penggunaan obat. Benzodiazepin termasuk golongan sedatif hipnotik yang terbukti berkaitan dengan kenaikan kejadian roboh. Tujuan penelitian ini adalah mengkaji pengaruh sedatif hipnotik terhadap risiko roboh pada pasien usia lanjut. Penelitian ini adalah penelitian observasional menggunakan rancangan kohort yang melibatkan 188 pasien usia lanjut yang memenuhi persyaratan. Pasien terdiri dari 94 orang yang menggunakan sedatif hipnotik dan 94 orang yang tidak menggunakan sedatif hipnotik. Semua subjek selanjutnya menjalani uji mobilitas fungsional atau risiko jatuh menggunakan tes *"up & go"* (TUG). Subjek yang memerlukan waktu ≤ 20 detik untuk menyelesaikan TUG diperkirakan mempunyai risiko roboh rendah, sedangkan subjek yang memerlukan waktu > 20 detik diperkirakan mempunyai risiko roboh tinggi. Hasil penelitian menunjukkan penggunaan sedatif hipnotik, jenis kelamin, jumlah macam obat yang digunakan berhubungan dengan kejadian roboh pada usia lanjut. Pasien usia lanjut yang menggunakan sedatif hipnotik mempunyai risiko jatuh 2,41 kali lebih tinggi dibandingkan dengan yang tidak menggunakan (95%CI:1,12-5,17; p = 0,023). Pasien usia lanjut yang menggunakan alprazolam berisiko jatuh 2,78 lebih tinggi dibandingkan dengan yang tidak menggunakan (95% CI: 1,49-5,19; p = 0,028). Selain itu pasien wanita berisiko jatuh 3,29 kali lebih tinggi dibandingkan laki-laki (95%CI: 1,58-6,88; p = 0,001), penggunaan ≥ 4 macam obat berisiko jatuh 2,76 kali lebih tinggi dibandingkan penggunaan < 4 macam obat (95%CI:1,21-6,29;

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p = 0,015). Dapat disimpulkan, sedatif hipnotik ditemukan sebagai faktor risiko roboh pada pasien usia lanjut.

Keywords: fall incidents - geriatric patients - sedative hypnotic drugs – risk faktor – timed up and go test

INTRODUCTION

Aging is natural part of life that represents the process of becoming older or the accumulation of changes in person over time.[1,2] In humans, aging refers to a multidimensional process of physical, psychological, and social changes. The geriatric population in the world, person ≥ 65 years, increases gradually in last decades due to rising life expectancy and/or declining birth rates.[3] In Indonesia in 1971, the geriatric population numbered 5.3 million (4.48%). It increased to be 8.0 million (5.45%) by 1980, 11.3 million (6.29%) by 1990, 14.4 million (7.18%) by 2000 and 24.0 million (9.77%) by 2010. Yogyakarta is a province with the largest geriatric population (13.04%) in Indonesia.[4]

The fast growth of elderly population worldwide potentially increases the *health burden of* the *population.* Fall incident is one of geriatric syndromes that cause an increasing public health burden worldwide.[5] Fall incidents in elderly people are approximately 35% in persons 65 years of age or older each year. Moreover two third of such cases the falls are recurrent during 6 months.[6] Falls incidents increases exponentially with age i.e. 30% in persons 65 years of age and over increases to 50% in persons 80 years of age and over.[7] Falls incidents account for approximately 10% of visits to the emergency department and 6% of urgent hospitalizations among elderly populations.[8] Fall incidents are associated with increased morbidity, disability, social isolation, and a lower quality of life.[9] Moreover, the falls incidents and its complications are the fifth caused of death in developing countries.[10]

The risk factors for falls have been reported included age, sex, predisposing medical conditions such as Parkinson's disease, stroke, incontinence, vision problems and medication use.[10-12] Medications related to an increased risk of fall incidents have been identified included sedative hypnotic, antihypertensive, diuretics, antiparkinson, antipsychotic, antidepressant, antihyperglycemic, non steroid antiinflammatory drugs (NSAID), and alcohol.[12,13] Benzodiazepines is a sedative hypnotic that found to be associated with an increase fall incidents. The benzodiazepines contribute up to 40% fall incidents in elderly patients, however a large number of these patients still being prescribed benzodiazepines.[13-15] This study was conducted to evaluate the influence of sedative hypnotic on the risk of fall incidents in elderly patients in the Geriatrics Polyclinic, Department of Internal Medicine, Dr. Sardjito General Hospital, Yogyakarta.

MATERIALS AND METHODS

Subjects

This was an observational study using cohort design involving the geriatric patients who attended in Geriatrics Polyclinic, Department of Internal Medicine, Faculty of Medicine/Dr. Sardjito General Hospital, Yogyakarta and met the inclusion and exclusion criteria. The study was conducted from July 2011 to March 2012. The inclusion criteria were geriatric patients 65 years of age or older, using sedative hypnotics, having clear and complete medical records data, willing to

participate in the study by signed an informed consent. The exclusion criteria are patients with difficulties to walk, using walking aids, and blind.

Procedure

Geriatric patients who attended in the Geriatric Polyclinic were selected. An explanation concerning the background, objectives and benefits of the study was given. Subjects who fulfilled the inclusion and exclusion criteria or their families were given an informed consent to be signed. Subjects were also given a questionnaire to be filled. The questionnaire consisted age, history of illnesses, sedative hypnotics and other drugs used. The use of sedative hypnotics was also gathered from medical records of the patients. Subjects were then divided into two groups. The first group was geriatric patients who use sedative hypnotics and the second group was geriatric patients who not use.

All subjects then underwent a test for functional mobility and fall risk using timed "up & go" test (TUG) as recommended by the American Geriatrics Society and the British Geriatric Society to predict the fall incidents.[16,17] A standard chair with armrests was used for all test. Subject was asked to stand up, using the armrests as necessary, walk past a line 3 meters a way, turn around and comeback and sit down in the chair. Subjects were timed from the point where their buttocks rose from the chair to when their buttocks touched the chair when returning to sitting. Sebject was asked to walk not run as quickly, but as safely as possible. The subjects who take d"20 seconds to complete the TUG was considered to have low risk for falling, whereas those who take >20 seconds was considered to have high risk for falling.

Statistical analysis

Data were presented in terms of *frequencies or percentages and analyzed using* a *computer software program.* Univariate analysis was employed to analyze the charactersitics of subjects. Bivariate analysis using Pearson Chi-square test or Fisher's Exact test was conducted to evaluate the relationship between the sedative hypnotics use and other comorbid factors as risk factors fall incidents. Multivariate analysis using logistic regression analysis was conducted to evaluate the comorbid factors which influence relationship between the sedative hypnotics use and fall incidents.

RESULTS

One hundred and eighty eight eligible subjects consisting of 94 subjects with- and 94 subjects without sedative hypnotic drugs selected from July 2011 to March 2012 were involved in this study. The characteristics of subjects are presented in TABLE 1. No significantly different on the characteristics of subjects was observed, except the amount of drugs use. Subjects who use < 4 drugs on group of the subjects with sedative hypnotic (70 subjects or 67.3%) were significantly higher than on group of subjects without sedative hypnotic (34 subjects or 32.7%). Conversely, subjects who use ≥ 4 drugs on group of the subjects with sedative hypnotic (24 subjects or 28.6%) were significantly lower than on group of subjects without sedative hypnotic (60 subjects or 71.4%) (p=0.000).

TABLE 1. Baseline characteristics of subjects (n or %)

Characteristic	With sedative hypnotic drug (n = 94)	Without sedative hypnotic drug (n = 94)	p	Total (n = 188)
Sex				
• Female	49 (46.7)	56 (53.3)	0.304	105 (55.9)
• Male	45 (54.2)	38 (45.8)		83 (44.1)
Age (years)				
• ≥ 75	32 (50.8)	31 (49.2)	0.877	63 (33.5)
• 65-74	62 (49.6)	63 (50.4)		125 (66.5)
History of fall incedents				
• Yes	20 (62.5)	12 (37.5)	0.121	32 (17.0)
• No	74 (47.4)	82 (52.6)		156 (83.0)
Drug amount				
• < 4 drugs	70 (67.3)	34 (32.7)	0.000	104 (55.3)
• ≥ 4 drugs	24 (28.6)	60 (71.4)		84 (44.7)
Antihypertensive use				
• Yes	87 (50.3)	86 (49.7)	0.788	173 (92.0)
• No	7 (46.7)	8 (53.3)		15 (8.0)
Antidiabetic use				
• Yes	14 (51.9)	13 (48.1)	0.85	27 (14.4)
• No	80 (49.7)	81 (50.3)		161 (85.6)
AINS use				
• Yes	45 (47.9)	49 (52.1)	0.560	94 (50)
• No	49 (52.1)	45 (47.9)		94 (50)
Comorbidity				
• = 4	25 (86.2)	4 (13.8)	0.000	29 (15.4)
• 1-3	69 (43.4)	90 (56.6)		159 (84.6)
Osteoarthritis				
• Yes	52 (50.5)	51 (49.5)	0.883	103 (54.8)
• No	42 (49.4)	43 (50.6)		85 (45.2)
Hypertension				
• Yes	87 (50.3)	86 (49.7)	0.788	173 (92.0)
• No	7 (46.7)	8 (53.3)		15 (8.0)
Diabetes mellitus				
• Yes	14 (51.9)	13 (48.1)	0.835	27 (14.4)
• No	80 (49.7)	81 (50.1)		161 (85.6)
Vertigo				
• Yes	6 (60.0)	4 (40.0)	0.747	10 (5.3)
• No	88 (49.4)	90 (50.6)		178 (94.7)

Bivariate analysis using Pearson Chi-square test or Fisher's Exact test was conducted to evaluate the relationship between the sedative hypnotics use, comorbid factors and fall incidents. The results are presented in TABLE 2. Sedative hypnotic drug use, female patients, aged ≥ 75 years, history of fall incidents, use ≥ 4 kind of drugs, comorbidity and osteoarthritis were found to be risk factors of fall incidents (p<0.05). Whereas, antihypertensive use, antidiabetic use, AINS use, hypertension, diabetes mellitus and vertigo were not found to be risk factors (p>0.05).

TABLE 2. Bivariate analysis of risk factors of fall incidents in geriatric patients

Risk factors	TUG ≥ 20 second (n = 66)	TUG <20 second (n = 122)	p	Relative Risk (RR)	95% CI
Sedative hypnotic					
• Yes	22 (23.4)	72 (76.6)	0.001[a]	ref	1.30-3.05
• No	44 (46.8)	50 (53.2)		2.00	
Sex					
• Male	20 (24.1)	63 (75.9)	0.005[a]	ref	1.17-2.82
• Female	46 (43.8)	59 (56.2)		1.81	
Age (years)					
• ≥ 75	37 (29.6)	88 (70.4)	0.026[a]	ref	1.06-2.27
• 65-74	29 (46.0)	34 (54.0)		1.55	
History of fall incedents					
• Yes	48 (26.7)	108 (69.2)	0.006[a]	ref	1.24-2.68
• No	18 (35.8)	14 (43.8)		1.82	
Number of drugs taken					
• < 4 drugs	16 (19.0)	68 (81.0)	0.000[a]	ref	1.55-4.09
• ≥ 4 drugs	50 (48.1)	54 (51.9)		2.52	
Antihypertensive use					
• Yes	4 (26.7)	11 (73.3)	0.581[b]	ref	0.56-3.18
• No	62 (35.8)	111 (64.2)		1.34	
Antidiabetic use					
• Yes	61 (37.9)	100 (62.1)	0.051[a]	ref	0.21-1.10
• No	5 (18.5)	22 (81.5)		0.48	
AINS use					
• Yes	31 (33.0)	34 (67.0)	0.541[a]	ref	0.76-1.66
• No	35 (37.2)	59 (62.8)		1.12	
Comorbidity					
• ≥ 4	51 (32.1)	108 (67.9)	0.041[a]	ref	1.06-2.45
• 1-3	15 (51.7)	14 (48.3)		1.61	
Osteoarthritis					
• Yes	23 (27.1)	62 (72.9)		ref	1.01-2.34
• No	43 (41.7)	60 (58.3)	0.036[a]	1.54	
Hypertension					
• Yes	4 (25.0)	12 (75.0)	0.427[b]	ref	0.60-3.44
• No	62 (36.0)	110 (64.0)		1.44	
Diabetes mellitus					
• Yes	61 (37.4)	102 (62.6)	0.089[a]	ref	0.23-1.20
• No	5 (20.0)	20 (80.0)		0.53	
Vertigo					
• Yes	61 (34.3)	117 (65.7)	0.311[a]	ref	0.76-2.80
• No	5 (50.0)	5 (50.0)		1.45	

Note: [a] Pearson Chi -Sque analysis; [b] Fisher's Exact test analysis

Further multivariate analysis using logistic regression showed that the use of sedative hypnotics, sex, and number of drugs taken were associated with fall incidents on geriatric patients, whereas age, history of fall incidents, comorbidity and osteoarthritis were not (TABLE 3). Geriatric patients who use sedative hypnotics were 2.41 times higher at risk of fall incidents than those who not use sedative hypnotics (95%CI;1.12-5.17; p=0.023).

Furthermore, female geriatric patients were 3.29 times higher at risk of fall incidents compared to male geriatic patients (95%CI: 1.58-6.88; p=0.001) and the use of ≥ 4 kinds of drugs were 2.76 times higher at risk of fall incidents compared to the use of <4 kinds of drugs (95%CI:1.21-6.29; p=0.015).

TABLE 3. Multivariate analysis of risk factors of fall incidents in geriatric patients

Risk factors	RR unadjusted	95% CI	p	RR adjusted	95% CI
Sedative hypnotic					
• No	ref	1.30-3.05	0.023	ref	1.12-5.17
• Yes	2.00			2.41	
Sex					
• Male	ref	1.17-2.82	0.001	ref	1.58-6.88
• Female	1.81			3.29	
Age (years)					
• 65-74	ref	1.06-2.27	0.079	ref	0.92-4.22
• ≥ 75	1.55			1.97	
History of fall incidents					
• No	ref	1.24-2.68	0.061	ref	0.95-5.72
• Yes	1.82			2.35	
Number of drugs taken					
• < 4 drugs	ref	1.55-4.09	0.015	ref	1.21-6.29
• ≥ 4 drugs	2.52			2.76	
Comorbidity					
• ≥ 4	ref	1.06-2.45	0.704	ref 0.82	0.31-2.20
• 1-3	1.61				
Osteoarthritis					
• Yes	ref	1.01-2.34	0.448	ref	0.63-2.84
• No	1.54			1.33	

Note. ref : reference, RR adjusted used logistic regression to evaluate risk factors with p-*value* <0.05 on bivariate analysis i.e. sedative hypnotics use, sex, age, history of fall incidents and number of drugs use, comorbidity and osteoarthritis

Bivariate analysis using Pearson Chi-square test was conducted to evaluate the relationship between kinds of sedative hypnotics use and risk of fall incidents. The results are presented in TABLE 4. The use of alprazolam significantly increased the risk of fall incidetns in geriatric patients, whereas the use od diazepam did not. Further multivariate analysis using logistic regression showed geriatric patients taking alprazolam were 2.78 times higher at risk of fall incidents compared to those who not take (95% CI: 1.49-5.19; p=0.028) (TABLE 5).

TABLE 4.   Bivariate analysis of the use of kinds of sedative hypnotics as the risk of fall incidents on geriatric patients

Risk factors	TUG ≥ 20 second N= 66 (%)	TUG < 20 second N= 122 (%)	RR (95%CI)	RR (95%CI)
Sedative hypnotics use				
• No	22 (23.4)	72 (76.6)	Ref	-
• Yes				
• Diazepam	1 (50.0)	1 (50.0)	1.43 (0.35- 5.80)	Ref
• Alprazolam	43 (46.7)	49 (53.3)	1.95 (1.28- 2.96)	1.07 (0.26 - 4.35)

TABLE 5.   Multivariate analysis of the use of alprazolam as the risk of fall incidents on geriatric patients

Characteristic	RR unadjusted	95% CI	p	RR adjusted	95% CI
Alprazolam					
• No	ref	1.28-2.96	0.028	ref	1.49-5.19
• Yes	1.95			2.78	

Note = ref : *reference*; RR *adjusted* used logistic regression to evaluate risk factors with p-*value* <0.05 on bivariate analysis i.e. alprazolam.

Bivariate analysis using *Fisher's Exact test* was conducted to evaluate the relationship between duration of the sedative hypnotics use and risk of fall incidents. The results are presented in TABLE 6. Durion of the sedative hypnotics use was not associated with fall incidents in geriatric patients.

TABLE 6. Bivariate analysis of duration of the sedative hypnotics use drug as the risk of fall incidents

Characteristic	TUG ≥ 20 second N= 28	TUG < 20 second N= 72	p-value	Relative Risk (RR)	95% CI
Period					
• < 1 months	1 (25.0)	3 (75.0)	0.620[a]	Ref	0.34-10.57
• ≥ 1 months	43 (47.8)	47 (52.2)		1.91	

Note :[a]*Fisher's Exact Test*

DISCUSSION

Our study showed that the use of sedative hypnotics were found to be a risk factor for fall incidents. Geriatric patients who use sedative hypnotic were 2.42 times higher at risk of fall incidents than those who not use sedative hypnotic. The studies concerning the use of sedative hypnotics as a risk factor for fall incidents in geriatric patients have been reported by some authors with paralel results. Woolcott *et al.*[11] reported that the use of sedative hypnotics were associated with fall incidents in geriatric patients. The risk of fall incidents in geriatric patients who use sedative hypnotics was 2.41 timer higher than in those who not use sedative hypnotics (95% CI: 1.35-1.62). Moreover, the increase in risk of fall incidents in geriatric patients who use sedative hypnotics was also reported by Sorock and Shimkin[15] (RR:1.53; 95% CI : 0.93- 2.52) and by Krauss *et al.*[16] (RR: 4.3; 95% CI: 1.6-11.5).

Benzodiazepines are sedative hypnotics that commonly used to treat sleeping disorders and anxiety problems in geriatric patients. The prevalence of benzodiazepines use is approximately 10-12%.[17] Several studies have been conducted to evaluate the association between benzodiazepines and falls incidents in geriatric patients. Most studies showed a significant association between the use of benzodiazepines and falls or fractures incidents.[18-20] The higher risk of fall incidents may due to decreased rate of metabolism of the benzodiazepines and due to greater susceptibility to central nervous system depression on geriatric patients.[21,22] These cause accumulation of the benzodiazepines in the body and may lead to excessive sedation with impaired psychomotor performance, ataxia, dysarthria, motor incoordination, diplopia, muscle weakness, vertigo, poor memory and concentration and mental confusion.[22]

Female geriatric patients were 3.29 times higher at risk of fall incidents than male patients in this study indicating that female sex as a risk factor for fall incidents. This result was similar with previous studies that showed a significant association between female sex and fall incidents in elderly. Bartlett *et al.*[20] reported that risk factors for falls were associated with statistically significant increases in the risk of receiving a new benzodiazepine prescription including being female (OR:1,20; 95%CI: 1.18-1.22). Buatois *et al.*[23] reportet that female sex as an independent determinant factor for recurrent falls (OR:1.62; 95%CI: 0.99-2.65). Elderly women much lose bone mass leading to markedly decreased bone mineral density and osteoporosis. Elderly women with low bone mineral densisty and osteoporosis are higher risk of fall.[20,23,24]

Furthermore, the study showed taking ≥ 4 kinds of drugs were 2.76 times higher at risk of fall incidents compared to taking <4 kinds of drugs (95%CI:1.21-6.29; p:0.015). Buatois *et al.*[23] reportet taking ≥ 4 drugs per day as an independent determinant factor for recurrent falls (OR:1.66; 95%CI: 1.06-2.60). Morover, Kuptniratsaikul *et al.*[25] reported that taking e"4 drugs 0.52 time higher increased fall incidents compared to taking <4 drugs. Polypharmacy has been universally accepted as an independent factor associated with the risk of fall related injuries.[26] Polypharmacy is often associated with pointless or inappropriate prescriptions that increase the likelihood of patients, particularly the elderly, manifesting sedation, confusion, balance disorders and complications caused by pharmacological interactions.[27]

CONCLUSION

In conclusion, the use of sedative hypnotics are a risk factor for fall incidents on geriatric pateints. Geriatric patients who take sedative

hypnotics are 2.41 times higher at risk of fall incidents than those who not take.

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