Sedative-Hypnotic Drug Use and Polypharmacy Patterns Associated With Risk of Falls and Fractures in Elderly by Osteoporosis Status : A Korean Nationwide Senior Cohort Study

EPH210

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BACKGROUND

The rapid aging of South Korea has led to a growing use of sedative-hypnotic drugs (SHDs) among the elderly, raising concerns about SHD polypharmacy and the increased risk of falls and fractures. Given the rising prevalence of osteoporosis in this population, further investigation is needed to understand its role in SHD-related risks.

OBJECTIVES

This research examined fall and fracture risks linked to sedative-hypnotic drug (SHD) use among elderly individuals with and without osteoporosis, using a representative Korean population cohort.

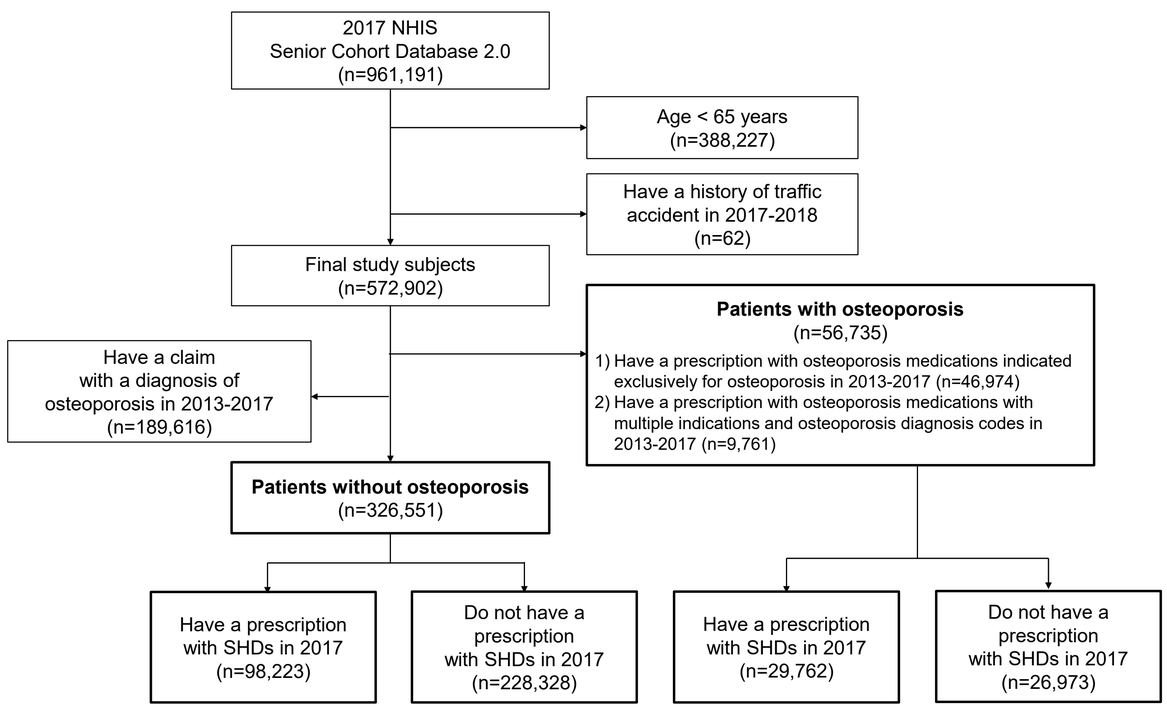
METHODS

We analyzed data from Korea's National Health Insurance Senior Cohort Database, identifying 572,902 individuals aged 65+ in 2017 (Figure 1). Using 2013-2017 claims data, we identified osteoporotic patients (n=56,735) as individuals receiving osteoporosis medications prescribed exclusively for osteoporosis, or those receiving multi-indication osteoporosis medications with osteoporosis diagnosis. Non-osteoporotic patients (n=326,551) had no osteoporosis-related claims during 2013-2017. SHD users were defined as those with at least one prescription for sedative-hypnotic drugs (SHDs) in 2017, categorized into benzodiazepines, non-benzodiazepines, antidepressants, and antipsychotics (Table 1). SHD users were followed for one year from their first prescription to identify subsequent falls or fractures; non-users were identified as having a fall or fracture if they had a relevant claim at any time in 2017. Bivariate analyses compared fall/fracture incidence by SHD use and by the number of concurrently prescribed SHD ingredients and categories, separately. Logistic regression was used to evaluate the association between SHD use and fall/fracture risk, adjusting for demographics, prior fractures, and comorbidities. Subgroup analyses examined fall, fracture, and combined risks, stratified by osteoporosis status.

Table 1. Sedative-hypnotic drugs included in this study

Drug class	ATC Codes[a]	Drug class	ATC Codes[a]
Benzodiazepine		**Non-benzodiazepine**	
Short acting		Zolpidem	N05CF02
Triazolam	N05CD05	**Antidepressants**	
Etizolam	N05BA19	Trazodone	N06AX05
Mexazolam	N05BA25	Amitriptyline	N06AA09, N06CA01
Intermediate acting		Nortriptyline	N06AA10
Clonazepam	N03AE01	Mirtazapine	N06AX11
Alprazolam	N05BA12	**Antipsychotics**	
Bromazepam	N05BA08	Quetiapine	N05AH04
Clotiazepam	N05BA21	Chlorpromazine	N05AA01
Lorazepam	N05BA06, N05BA56		
Long acting			
Flurazepam	N05CD01		
Flunitrazepam	N05CD03		
Clobazam	N05BA09		
Diazepam	N05BA01		

[a] In the Anatomical Therapeutic Chemical (ATC) classification system, the active substances are divided into different groups according to the organ or system on which they act and their therapeutic, pharmacological and chemical properties



NHIS National Health Insurance Service, *SHD* sedative-hypnotic drug

Figure 1. Flowchart of identifying study subjects

RESULT

Of the total 383,286 patients, 56,735 (14.8%) had osteoporosis, and 326,551(85.2%) did not (Table 2). Compared to those without osteoporosis, patients with osteoporosis were more likely to be female (90.06%), older (27.60% aged 75–79 years), have a history of prior fractures (46.79%), and have a higher Charlson Comorbidity Index (CCI ≥2, 53.53%).

Table 2. Baseline characteristics of study subjects

Characteristics	Total No. of patients (%)	With osteoporosis	Without osteoporosis	*p*-value[a]
Total No. of patients	383,286 (100)	56,735 (100)	326,551 (100)	-
Sex				
Male	208,505 (54.40)	5,640 (9.94)	202,865 (62.12)	< 0.0001
Female	174,781 (45.60)	51,095 (90.06)	123,686 (37.88)	
Age, years				
65-69	134,537 (35.10)	11,559 (20.37)	122,978 (37.66)	< 0.0001
70-74	93,627 (24.43)	12,780 (22.53)	80,847 (24.76)	
75-79	80,570 (21.02)	15,658 (27.60)	64,912 (19.88)	
80-84	50,123 (13.08)	11,349 (20.00)	38,774 (11.87)	
85+	24,429 (6.37)	5,389 (9.50)	19,040 (5.83)	
Type of NHS program enrolled				
NHI	361,148 (94.22)	50,263 (88.59)	310,885 (95.20)	< 0.0001
Medical aid	22,138 (5.78)	6,472 (11.41)	15,666 (4.80)	
Have prior fractures				
No	308,592 (80.51)	30,188 (53.21)	278,404 (85.26)	< 0.0001
Yes	74,694 (19.49)	26,547 (46.79)	48,147 (14.74)	
CCI				
0	167,185 (43.62)	16,605 (29.27)	150,580 (46.11)	< 0.0001
1	70,543 (18.40)	10,928 (19.26)	59,615 (18.26)	
2	64,613 (16.86)	10,225 (18.02)	54,388 (16.66)	
3	40,333 (10.52)	8,497 (14.98)	31,836 (9.75)	
4	17,781 (4.64)	4,185 (7.38)	13,596 (4.16)	
5+	22,831 (5.96)	6,295 (11.10)	16,536 (5.06)	

[a] Chi-square tests across the patients with osteoporosis and patients without osteoporosis

NHS National Health Security, *NHI* National Health Insurance, *CCI* Charlson Comorbidity Index

SHD users demonstrated elevated fall/fracture incidences than non-users in both groups: 25.29% vs. 20.56% (osteoporotic) and 5.71% vs. 3.43% (non-osteoporotic) (Table 3). Among osteoporotic patients, incidence increased from 24.06% with one ingredient, to 27.63% with two, and 31.57% with three or more. Among non-osteoporotic patients, rates were 5.43%, 6.58%, and 7.43%, respectively. A similar dose-response pattern was observed for the number of SHD categories. Adjusted odds ratios indicated an elevated risk with SHD use, compared to non-users: 1.287 (95% CI: 1.236–1.341) for osteoporotic and 1.543 (95% CI: 1.488–1.600) for non-osteoporotic patients (Table 4). Subgroup analysis demonstrated a greater fracture risk among non-osteoporotic patients, whereas osteoporotic patients had a higher fall risk (Figure 2).

Table 3. Incidence of falls or fractures among Korea elderly prescribed with sedative-hypnotic drugs

Characteristics	With osteoporosis			Without osteoporosis		
	With falls or fractures (%)	Without falls or fractures (%)	*p*-value[a]	With falls or fractures (%)	Without falls or fractures (%)	*p*-value[a]
Total no. of patients	13,072 (23.04)	43,663 (76.96)		13,451 (4.12)	313,100 (95.88)	
Have a prescription with SHDs						
No	5,546 (20.56)	21,427 (79.44)	< 0.0001	7,840 (3.43)	220,488 (96.57)	< 0.0001
Yes	7,526 (25.29)	22,236 (74.71)		5,611 (5.71)	92,612 (94.29)	
Number of concurrently prescribed SHD ingredients						
1	5,325 (24.06)	16,806 (75.94)	< 0.0001	4,260 (5.43)	74,198 (94.57)	< 0.0001
2	1,461 (27.63)	3,826 (72.37)		911 (6.58)	12,929 (93.42)	
3+	740 (31.57)	1,604 (68.43)		440 (7.43)	5,485 (92.57)	
Number of concurrently prescribed SHD categories[b]						
1	5,438 (24.09)	17,131 (75.91)	< 0.0001	4,325 (5.43)	75,277 (94.57)	< 0.0001
2	1,538 (28.15)	3,925 (71.85)		936 (6.61)	13,214 (93.39)	
3+	550 (31.79)	1,180 (68.21)		350 (7.83)	4,121 (92.17)	

[a] Chi-square tests across the SHD users and non-users

[b] SHD categories refer to benzodiazepines, non-benzodiazepines, antidepressants, and antipsychotics.

SHD sedative-hypnotic drugs

Table 4. Logistic regression analysis results of the association between sedative-hypnotic drug use and risk of falls or fractures in elderly with and without osteoporosis

Variables	With osteoporosis[a]		Without osteoporosis[b]	
	Adj OR	95% CI	Adj OR	95% CI
Have a prescription with sedative-hypnotic drugs				
No	ref.	-	ref.	-
Yes	1.287	1.236-1.341	1.543	1.488-1.600
Sex				
Male	ref.	-	ref.	-
Female	0.902	0.845-0.963	1.166	1.125-1.208
Age, years				
65-69	ref.	-	ref.	-
70-74	1.194	1.117-1.276	0.994	0.948-1.042
75-79	1.367	1.284-1.455	1.099	1.046-1.153
80-84	1.590	1.489-1.698	1.162	1.099-1.229
85+	1.704	1.576-1.843	1.302	1.215-1.395
Type of NHS program enrolled				
NHI	ref.	-	ref.	-
Medical aid	0.975	0.915-1.038	1.127	1.048-1.213
Have a past diagnosis of fracture				
No	ref.	-	ref.	-
Yes	2.591	2.486-2.701	3.315	3.195-3.440
CCI				
0	ref.	-	ref.	-
1-3	0.940	0.896-0.985	1.170	1.127-1.215
4+	0.995	0.937-1.057	1.267	1.195-1.344

[a] Analyzed among 56,735 individuals with osteoporosis

[b] Analyzed among 326,551 individuals without osteoporosis

adj OR adjusted odds ratio, *CI* confidence interval, *ref.* reference, *SHD* Sedative-hypnotic drugs, *NHS* National Health Security, *NHI* National Health Insurance, *CCI* Charlson Comorbidity Index

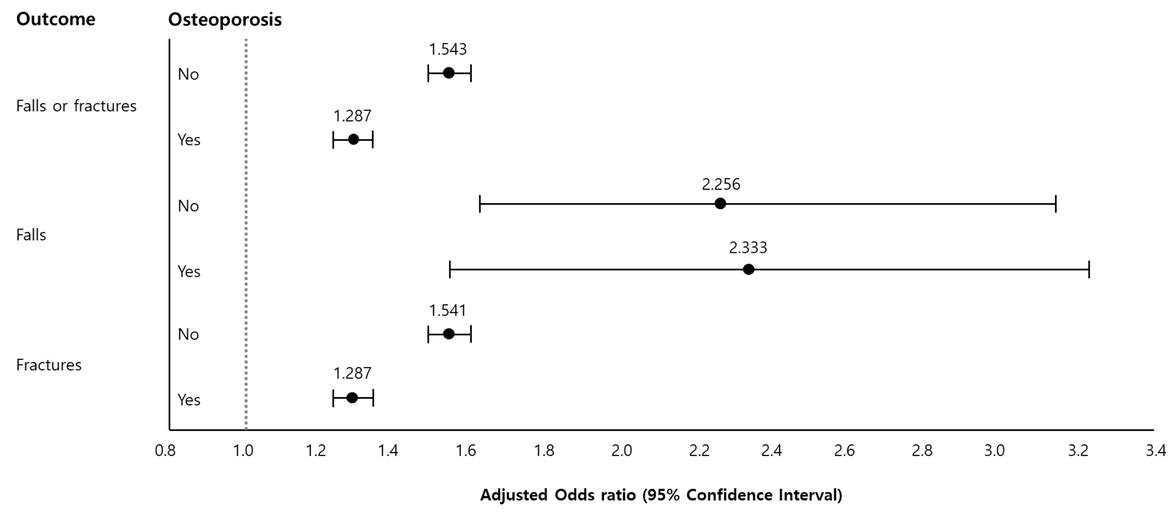


Figure 2. Subgroup analysis results for the logistic regression analysis of the association between the SHD use and risk of falls, fractures, and combined outcomes, stratified by osteoporosis status

CONCLUSION

SHD use was linked to increased fall and fracture risks regardless of osteoporosis status in elderly individuals, with incidence especially higher among those exposed to SHD polypharmacy. Higher fracture risk in non-osteoporotic patients potentially indicates insufficient preventive interventions, while increased fall risk in osteoporotic patients probably stems from underlying frailty. These results underscore the need for safer prescribing and initiatives to reduce SHD polypharmacy and related harm in older adults.

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