입원 노인환자의 의약품 사용과 낙상위험도 연구

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Medication use as a Risk Factor for Falls in Hospitalized Elderly Patients in Korea

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낙상은 노인의 건강을 위협하는 가장 심각한 문제 중의 하나이며, 조기사망, 신체손상, 운동장애, 심리학적 기능장애를 유발하는 원인이기도 하다. 본 연구의 목적은 국내 노인전문 요양병원 입원 환자들의 의약품 사용이 낙상에 미치는 영향을 평가하는데 있다. 후향적으로 원내 의무기록 정보를 이용하여 환자-대조군 연구를 수행하였고, 2008년 1월부터 2010년 12월까지 3년 기간에 입원한 65세 이상을 대상으로 하였다. 입원기간 중 낙상을 경험한 34명의 노인환자들을 환자군으로 선택하였으며 낙상을 경험하지 않은 68명의 노인환자들을 무작위 추출하여 1:2의 환자군:대조군 비율로 연구 대상 환자들을 선정하였다. 환자군이 복용한 의약품을 대조군이 복용한 의약품과 비교하였으며 각 계열별 의약품과 낙상위험도 관계를 평가하였다. 두 그룹간의 인구통계학적 특성은 유사하였고 연령, 성별, 복용 의약품 수, 고혈압 유무, 혈중 크레아티닌 수치, 혈중 나트륨 수치, 혈압 또는 심박수에 유의한 차이는 없었다. 항히스타민제와 본 연구에서 유일하게 기타 수면보조제로 분류된 졸피뎀이 유의하게 낙상위험도를 증가시켰다.

□ Key words - geriatrics, falls, medication use, risk factor

INTRODUCTION

Falls are a serious concern in hospitalized patients, and occur at a rate of at least 2.3 per 1000 patient-days.[1-5] Several studies showed that inpatient falls could cause increased length of stay, discharge to nursing facilities, physical injury, and hospitalization costs.[6-8] Falls and the related injuries are common, and lead to serious consequences especially in the elderly. Among hospitalized elderly patients, falls occur from 2% to 27% in acute care hospitals. Therefore, reducing risk factors for falls is important to prevent unwanted events.[9]

A number of risk factors for falls have been demonstrated, including gait and visual deficits, Parkinson's disease, arthritis, depression, or muscle weakness.[10-12] Medications that cause sedation, orthostatic hypotension, or psychomotor impairment are most frequently associated with falls. Nonsteroidal antiinflammatory drugs (NSAIDs), selective serotonin-reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), antipsychotic agents, benzodiazepines, anticonvulsants, and antihypertensives have been identified as risk factors for falls among elderly people.[13-18]

However, there are limited data regarding the effects of medication use on falls in the geriatric hospital setting in Korea. Although there are published studies conducted in other than Korea evaluating the effects of medication use as risk factors for falls, it may not be appropriate for health care professionals to apply the results to Korean patients directly. In Korea, medica-

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tions frequently used by patients can be different than those in other countries. Also risks of falls may vary with patient characteristics. The aim of this study was to evaluate the influence of medication use on falls among hospitalized elderly patients in the geriatric hospital in Korea.

METHODS

A retrospective case-control study in 102 elderly patients from January 2008 through December 2010 was performed in Y Geriatrics Hospital in Korea. Thirty-four elderly patients ($\geq$ 65 years old) who experienced falls were recorded on medical records between January 2008 and December 2010. These patients were selected as case patients for the study. For each fall, two patients who did not fall during hospitalization were selected as control patients (1:2). We excluded any patients who were admitted to the hospital for syncope or a reconstructive orthopedic procedure secondary to a fall-related injury from the study. Any patients who were unable to walk during hospitalization were also excluded.

All case patients and control patients' medical records were collected. Patients' demographics, vital signs, serum creatinine, serum electrolytes, number of medications, length of hospital stay, and current medical conditions were obtained for analysis. Medication use within 24 hours prior to each patient's fall was reviewed in case patients. For comparative purposes, medication use on day 110 of admission was assessed in control patients because the mean time to fall after admission was 110 days in case patients.

We compared the two groups in terms of general characteristics such as age, sex, number of medicines, length of stay in hospital, prevalence of hypertension, time to fall, serum creatinine concentration, sodium level, blood pressure, and heart rate. We then conducted a chi-squared test to determine whether there was an association between each class of medications and the risk of falls. Only those variables with p < 0.05 were retained for inclusion in a logistic regression analysis

with backward elimination. Medications for which p > 0.05 were excluded, as were those taken by <5 cases (or controls) because the chi-squared test could not be performed. Finally, multivariate comparisons were made by using backward stepwise logistic regression to identify medications that might be associated with falls. Estimates of the relative risk of falling are expressed as odds ratios (ORs) and 95% confidence intervals (CIs). All statistical analyses were performed with SPSS for windows, version 18.0 (SPSS Inc., Chicago, IL).

This study was carried out in accordance with the principles enunciated in the Declaration of Helsinki.

RESULTS

General characteristics are presented in Table 1. A total of 34 patients with documented falls met criteria for inclusion as case patients. Most of the patients were women (n = 78, 76.5%) and the mean age of these patients was 81 years. Age, sex, number of medications, prevalence of hypertension, serum creatinine, serum sodium, blood pressure, or heart rate was not significantly different between case patients and control patients. The mean time to a fall after admission among case patients was 110 days. Only length of stay in hospital was significantly different between case patients and control patients (p = 0.00). Case patients received more medications within the 24 hours preceding the fall than control patients did in the 24 hours preceding the comparison day of admission, but the difference did not statistically significant (mean±S.D., 3.26±1.54 and 2.72±1.48 medications, respectively; p < 0.088).

The chi-squared test of association between falls and the use of each medication class is shown in Table 2. It is noteworthy that use of anticholinesterases, calcium channel blockers, diuretics, NSAIDs, or propulsives was not significantly related to falls. There were insufficient numbers of case patients taking alpha antagonists, anticoagulants, antidiabetic agents, angiotensin II receptor blockers, beta antagonists, opioid analgesics, digoxin, antidepressants, or antipsychotics to enable

Table 1. Characteristics of case patients versus control patients

Characteristic		Case Patients ($n = 34$)	Control Patients ($n = 68$)	T-test[a]
Age (yr)	Mean±S.D.	81.18±6.63	80.88±6.33	0.22
Sex	No. (%)			
Male		8 (23.5)	16 (23.5)	0.00[d]
Female		26 (76.5)	52 (76.5)	
Length of stay (no. days)	Mean±S.D.	480.64±185.47	328.70±200.49	3.65*
Time to fall (no. days)	Mean±S.D.	109.59±132.35	NA[b]	
Serum creatinine conc. (mg/dL)	Mean±S.D.	1.22±0.41	1.22±0.51	-0.04
No. medications received within 24 hr preceding fall[c]	Mean±S.D.	3.26±1.54	2.72±1.48	1.72
Serum sodium conc. (mEq/L)	Mean±S.D.	134.44±6.96	134.26±5.48	1.42
Blood pressure (mmHg)	Mean±S.D.			
Systolic		129.12±17.30	127.21±16.92	0.53
Diastolic		80.00±12.80	80.15±12.28	-0.06
Heart rate	Mean±S.D.	71.47±9.18	73.04±9.42	-0.80
Prevalence of hypertension	No. (%)	25 (73.5)	50 (73.5)	0.00[d]

[a] Two-tailed.
[b] NA = not applicable.
[c] For control patients, determined on day 110 of admission.
[d] Chi-squared test.
*$p < 0.05$

Table 2. Results of chi-squared test of association between falls and use of each category of medications taken by case patients and control patients

Drug Category	No. of Case Patients ($n = 34$)	No. of Control Patients ($n = 68$)	Chi-squared test
Anticholinesterases	8	15	0.03
Anticonvulsants	14	12	6.61*
Antihistamines	8	5	5.33*
Benzodiazepines	10	5	8.79*
Calcium channel blockers	14	23	0.53
Diuretics	9	22	0.37
NSAIDs	12	33	1.61
Propulsives	14	25	0.19
Miscellaneous sleep aids	10	5	8.79*

*$p < 0.05$
NSAIDs = nonsteroidal antiinflammatory drugs.

chi-squared test to be performed.

Table 3 shows an intermediate step of logistic regression including significant and nonsignificant medications. Only antihistamines and miscellaneous sleep aids were associated with risk for falls at this point in logistic regression. Zolpidem was the only medication in the category of miscellaneous sleep aids in this study.

Anticonvulsants and benzodiazepines were eliminated without a significant change in likelihood. After all nonsignificant factors had been removed, the results of final regression model is shown in Table 4, with zolpidem increasing the risk of falls 7-fold (p = 0.001, OR =7.25, 95% CI = 2.17–24.26).

DISCUSSIONS

Inpatient falls in the elderly may further complicate patients' treatment plans and increase length of hospital stay. Identifying risk factors for falls in this patient population could improve fall-prevention strategies. This

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Table 3. Results of intermediate model of logistic regression analysis of association between falls and retained variables following chi-squared test

Drug Category	Odds Ratio	CI	P
Anticonvulsants	1.95	0.69 – 5.53	0.21
Antihistamines	4.31	1.18 – 15.79	0.03
Benzodiazepine	2.54	0.68 – 9.47	0.16
Miscellaneous sleep aids	4.71	1.29 – 17.20	0.02

CI = 95% confidence interval.

Table 4. Results of final model of logistic regression analysis showing medications associated with risk of falls

Drug Category	Odds Ratio	CI	P
Antihistamines	5.80	1.67 – 20.18	0.00
Miscellaneous sleep aids	7.25	2.17 – 24.26	0.00

CI = 95% confidence interval.

study assessed which medications were associated with an increased risk of falls among hospitalized elderly patients. There was no significant difference between case patients compared with control patients in terms of age, sex, number of medications, prevalence of hypertension, serum creatinine, serum sodium, blood pressure, or heart rate. Only length of stay in hospital was significantly different between case patients and control patients. This finding could have been caused by the fall itself because examinations and treatments related to the consequences of the fall could have delayed discharge.

Polypharmacy increases the likelihood of being exposed to medications that increase the risk of falls. The probability of using a medication that introduces risk increased proportionally from 25% with the use of only one medication to more than 60% when six or more medications were being taken.[19] Neutel and colleagues reported that the number of drugs taken was an important variable in the risk of falls.[20] However, the effect of polypharmacy on falls was not observed in this study since all patients were taking less than 5 medications and there was no significant difference in terms of number of medications taken between the case and control groups.

A study by Wang and colleagues demonstrated that

zolpidem exposed patients to nearly double the risk of hip fractures secondary to falls.[21] Use of zolpidem was also associated with the occurrence of falls in this study. Because the risk of falling with zolpidem is identified, the need for fall prevention might have been anticipated in patients receiving zolpidem, resulting in differences in nursing care or fall prevention efforts for these patients.

In Taiwan, a recent study showed significant increase in the risk of falls with antihistamines in hospitalized elderly patients, and the similar results was also shown in this study.[22]

Anticoagulants may also play a role in fall-related injury by increasing the risk of bleeding.[23] A significant fall risk in association with use of antidepressants has been reported in several studies.[15, 24-25] In this study, because the number of patients taking these two categories of medication was not enough to perform the chi-squared test, an association between those medications and falls was not observed.

Calcium channel antagonists have been identified as a risk factor for falls in other studies.[13, 26] However, no significant association was found between calcium channel antagonists and falls in this study.

Although several studies have shown an increase in risk of falls in association with use of benzodiazepines, we did not observe such a risk in this study.[27-29]

NSAIDs may potentially increase the risk of falls due to their adverse CNS effects such as confusion, dizziness or lightheadedness, drowsiness, and vision impairments in the elderly, and several studies have found an increased risk of falls among users of NSAIDs.[20, 30-31] However, these effects were not occurred in this study.

This study has several limitations. The presence of other known risk factors for falls, such as arthritis, dementia, acute delirium, previous hip fracture, impaired vision, environmental changes, stroke, and urinary urgency was not documented. Review of medication administration for control patients was performed on day 110 of admission because the mean time to fall after admission was 110 days. However, the time to fall had pretty broad ranges. Also, we may have

results different than those from other previous studies because of the following reasons. First, we didn't evaluate the effects of both individual medications and dosage on falls. Second, the number of patients included in this study was relatively small. Since it is a retrospective case-control study, further prospective studies should be conducted to confirm its findings before applying those to patients in clinical practice.

CONCLUSIONS

In hospitalized elderly patients, there was a significant association between the use of antihistamines or zolpidem and falls. When alternative medications are available, health care professionals should consider avoiding these drugs until further prospective studies are conducted to confirm or reject these risks.

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