Advance Access Publication Date: 9 February 2018



Article

Potentially inappropriate medication and hospitalization/emergency department visits among the elderly in Korea

HA-LIM JEON¹, JUHEE PARK¹, EUNA HAN², and DONG-SOOK KIM¹

¹Department of Research, Health Insurance Review & Assessment Service, Hyeoksin-ro 60, Wonju-si, Ganwon-do, Seoul 26465, South Korea, and 2College of Pharmacy, Yonsei Institute of Pharmaceutical Science, Yonsei University, 162-1 Songdo-Dong, Yeonsu-Gu Incheon, South Korea

Address reprint requests to: Dr. Dong-Sook Kim, Senior Researcher, Department of Research, Health Insurance Review & Assessment Service, Hyeoksin-ro 60, Wonju-si, Ganwon-do, Seoul 26465, South Korea. Tel: +82-33-739-0922; Fax: +82-33-739-5842; E-mail: sttone@hira.or.kr

Editorial Decision 27 November 2017; Accepted 11 January 2018

Abstract

Objective: To investigate the association between potentially inappropriate medicine (PIM) use, defined using the American Geriatric Society (AGS) 2012 Beers criteria, and the risk of hospitalization or emergency department (ED) visits in elderly patients, and to examine the most frequently used PIMs among patients with adverse outcomes.

Design/Setting: This was a retrospective study using National Health Insurance claims data from 2010 to 2012.

Intervention(s): Elderly patients who took PIMs are compared to those who were not taking PIMs. Study participants: Elderly patients (n = 79552) who visited medical institutions in Jeju Island during 2011.

Main outcome measure: Hospitalization and ED visits were evaluated according to whether the patients took PIMs during the study period. The most frequent medications used by the PIM group were also investigated.

Results: The likelihood of hospitalization was higher in older patients who took at least one PIM than in those who were not taking PIMs during the study period (odds ratio 2.25, 95% confidence interval 2.09-2.44). Patients taking PIMs were more likely to visit EDs (odds ratio 1.59, 95% confidence interval 1.50-1.67). Among patients who were hospitalized or visited EDs, 45.5% had taken at least one PIM on that day. The most commonly used PIMs included chlorpheniramine maleate, diazepam, metoclopramide HCI and diclofenac sodium.

Conclusion: Our findings indicate that PIM use can lead to negative health consequences, providing further evidence of the inappropriateness of these medications. Thus, pharmaceutical policies regarding PIM use may need to be implemented for elderly adults in Korea.

Key words: Beers criteria, elderly, potentially inappropriate medication, hospitalization, emergency department visit

Introduction

Elderly adults often take several medications simultaneously to treat various chronic diseases [1]. Moreover, as major biological functions decline throughout adult life, which can cause changes to pharmacokinetic characteristics such as absorption, distribution, metabolism and excretion, older people may be more vulnerable to adverse drug reactions (ADRs). Previous studies have reported that two-thirds of nursing home residents [2] and 35% of elderly outpatients [3] experience adverse drug effects. In addition, 15.7% of nursing home residents were hospitalized because of ADRs in one previous study [2], and 10% of outpatients with ADRs reportedly visited the emergency room [3]. These findings indicate that if drugs are administered to older patients without taking their pharmacological characteristics into account, ADRs and other serious health problems can occur [2–5].

A potentially inappropriate medication (PIM) is defined as a drug for which the potential risk of adverse events may outweigh the benefit. It is important to recognize PIMs, as this can help healthcare providers to prevent patients' drug-related problems [6]. The Beers Criteria are one of the most widely used explicit lists of PIMs for the elderly. Beers and colleagues developed these criteria through an evidence-based comprehensive literature review and expert panel consensus by using the Delphi method [7]. These criteria were originally created for nursing home residents in 1991 and were revised in 1997 and 2003 to expand them to all settings of geriatric care [7–9]. The Beers criteria are divided into two categories: PIMs and classes to avoid in older adults (independent of their diagnosis) and PIMs to avoid in older adults with certain diseases and syndromes (considering their diagnosis). With the emergence of new drugs and clinical evidence, the Beers Criteria were updated again by the American Geriatric Society (AGS) in 2012 [10]. In developing the 2012 AGS Beers Criteria, one additional category (medications to be used with caution in older adults) was added, and the AGS expert panel began grading the strength and quality of each PIM statement.

Many earlier studies have been conducted to investigate the risk of PIM use based on the Beers Criteria. For example, Jano et al.

performed a systematic literature review and found a significant association between the use of PIMs included in the 1997 Beers Criteria and hospitalizations in the majority of studies conducted using 1-2 years data of the community setting in the united states [11]. Two Taiwanese studies defining PIMs according to the 2003 Beers criteria reported higher rates of hospitalization and emergency room visits among patients who had taken PIMs than among those who had not [12, 13]. Furthermore, one study revealed that patients who had been prescribed Beers high-severity sedatives showed a 22% increased risk for falls or fractures compared to the control group [14]. A few studies defining PIMs using the 2012 AGS Beers criteria also exist [15-21]. For example, PIM exposure was related to greater hospitalization rates in older patients in Switzerland [15], and associated with 2-fold increased risks of adverse drug events, emergency department visits and hospitalization in the United States [16]. However, to the best of our knowledge, there is no previous study examining the health outcomes related to PIM use in Korea according to the 2012 AGS Beers criteria. Thus, the aims of this study were to (i) investigate the association between PIMs based on the 2012 AGS Beers criteria and the risk of hospitalization or emergency department (ED) visits, and to (ii) examine frequently used PIMs among patients with adverse outcomes.

Methods

Data source

Administrative medical claims data from the Health Insurance Review and Assessment Service (HIRA) were used for the analyses. In South Korea, all medical institutions submit claims, including the

<i>Jeju</i> Island in 2011			
No. of claims			
records			
6,428,670			
	Exclusion of patients with a cancer diagnosis in the year prior to the index date (2010)		Excluded (n = 149
No. of claim records		PIM users	Non-PIM users
6,392,279	Classification into 1-year periods from the index date	69,886	9,517
	•		Monitoring (2 years)
		Hospitalization and ED visits	
		PIM users	Non-PIM users
		42,124	2,977
		(12,997	(825
		hospitalizations,	hospitalizations
		27,127 ED	2,152 ED visits
	No. of claim records	Exclusion of patients with a cancer diagnosis in the year prior to the index date (2010) No. of claim records Classification into 1-year periods from	records 6,428,670 Exclusion of patients with a cancer diagnosis in the year prior to the index date (2010) No. of claim records 6,392,279 Classification into 1-year periods from the index date Hospitalization PIM users 42,124 (12,997 hospitalizations,

Figure 1 The cohort construction process.

52 Jeon et al.

treatment history, for all individuals covered by the National Health Insurance (NHI) to the HIRA, and the HIRA reviews these medical claims and assesses the quality of care. HIRA's medication claims records include the following information: disease, drug code, brand name, generic name, route of administration, amount in a single dose, daily dose, total number of days covered by the prescription or number of doses administered, and date when care was started.

The patient characteristics included in the analyses were as follows: age, sex, number of prescriptions filled during the study period and the prescription information, which covers the date and duration of the prescription, prescribed drugs' international non-proprietary names (INN), dosage, route of administration and prescriber's identification number. The therapeutic drug class was classified using the World Health Organization's Anatomical Therapeutic Chemical classification system [22]. The healthcare provider information included the location of the clinic or hospital, type of healthcare facility and provider specialty. The HIRA approved the data analysis protocol.

Study design and study population

This study was designed as a retrospective cohort study of the period from 1 January 2011 to 31 December 2012. The subjects consisted of elderly patients aged 65 years and older who visited medical institutions in Jeju Island, Korea's largest island, at least once between January and December 2011. The first visit to a medical institution in Jeju Island during the reference period was noted as the index date. As the full medical data were recorded, including the nationwide medical institutions that the patients had visited during the post-index period, the hospitalization and ED visits of each subject in the 24 months after the index date could be monitored. To reduce the confounding effects, patients with cancer as a prior diagnosis were excluded from the cohort (Fig. 1).

Exposure and outcome measures

The exposure was defined as prescribing PIMs to older patients. PIMs were identified from the drug file of the HIRA in accordance with the 'Medications to avoid regardless of disease' list, which is one of the three categories in the AGS 2012 Beers criteria [10]. The listed drugs in Korea were used for the analysis.

The outcome measures included hospitalization and ED visits, and these outcomes were investigated until the end of the monitoring period. The follow-up period for a subject continued until any of the following incidents occurred: (i) hospitalization or ED visit for any reason, (ii) death or (iii) completion of the 2-year study period.

The independent variable was PIM use, and the confounding variables were the patients' demographic parameters (including age at index date, sex and regional characteristics), comorbidities and medical history.

The patients were categorized according to age (65–74 years [reference group], 75–84 years and 85 years or older), type of medical institution they visited (tertiary hospital [reference group], general hospital, hospital, clinic and health center), type of health insurance (national health insurance [reference group], medical aid and veteran care), Charlson comorbidity index (0 points [reference group], 1 or more points), presence of a certain disease or condition (osteoarthritis, osteoporosis, history of fractures, cerebrovascular disease and chronic obstructive pulmonary disease), type of medical departments where they were treated (general practice [reference group], internal medicine, neurology, psychiatry, surgery, orthopedics, neurosurgery, anesthesiology and pain medicine, ophthalmology, otolaryngology, dermatology, family medicine and others).

Statistical analysis

Variables were compared between the groups using the chi-square test and Student t-test, as appropriate. We calculated the hospitalization and ED visit rates to compare the risks between patients who had been prescribed PIMs and patients without PIMs. In addition, logistic regression analysis was used to estimate the relationships between PIM use and the outcomes after adjusting for confounding factors. All statistical analyses were conducted using SAS version 9.1 (SAS Institute Inc., Cary, NC, USA), with a significance level of $\alpha \le 0.05$.

Additional analysis: recently used medications

Elderly patients who were hospitalized or visited EDs were categorized into the 'current PIM use group', defined as those who were currently taking at least one PIM on the event day; 'intermediate PIM use group', defined as those who had used a PIM between 1 and 60 days prior to the incident; and 'past PIM use group', defined as those who had used a PIM between 61 and 365 days prior to the incident. There was also a group of patients who had not used PIMs over a year before the incident. Based on these categories of PIM use status, we calculated the following ratios of PIM use for the current and intermediate groups, respectively:

The ratio of current or intermediate PIM use among patients who experienced an incident = (the number of patients who had taken PIMs in the current or intermediate group/the number of patients who had taken PIMs at least once during the 1-year preindex period and experienced hospitalization or ED visits) × 100.

Results

General characteristics

In 2011, a total of 79 552 elderly individuals visited medical institutions in Jeju Island. After excluding elderly patients with cancer, 69 886 patients with PIM use were included in this study.

Among patients who had used PIMs during the 1-year pre-index period, 12 997 (18.6%) were hospitalized and 27 127 (38.8%) had visited EDs. Compared to patients who did not use PIMs (hospitalization, 8.7%; ED visits, 22.6%), the proportions of hospitalization and ED visits for patients who used PIMs were higher.

PIM use was more common in female patients (62.4%), and the majority of patients using PIMs were aged between 65 and 74 years (63.0%). In patients with PIM use, 73.1% of patients had a Charlson comorbidity index of ≥ 1 points. Most patients visited clinics (81.4%). In terms of the medical department where the patients were treated, the internal medicine department was most frequently visited (44.4%). Similarly, in the group of patients without PIMs, most patients were women (53.3%) and aged 65–74 years (61.5%). However, among these patients, the proportion of patients with a Charlson comorbidity index of ≥ 1 points was relatively low, at 49.8%. In terms of the medical institution visited, most patients visited clinics (62.5%), followed by general hospitals (19.0%) (Table 1).

ED visits and hospitalization

Table 2 shows the risks of hospitalization and ED visits for each characteristic, obtained from the multivariate logistic regression analysis. The risk of ED visits was significantly higher for patients using PIMs compared to patients without PIM use (adjusted odds ratio [OR] 1.59, 95% confidence interval [CI] 1.50–1.67), as was the risk

Table 1 General characteristics of the study subjects with/without PIM use

Characteristics	No. patients with PIM use (%)	No. patients without PIM use (%)	Total
Total	69 886 (88.0)	9517 (12.0)	79 403
Outcome			
Hospitalization	12 997 (18.6)	825 (8.7)	13 882
ED visit	27 127 (38.8)	2152 (22.6)	31 279
Sex			
Male	26 291 (37.6)	4441 (46.7)	30732
Female	43 595 (62.4)	5076 (53.3)	48 671
Age group			
65–74 years	44 019 (63.0)	5851 (61.5)	49 870
75–84 years	20 738 (29.7)	2493 (26.2)	23 231
85 years and older	5129 (7.3)	1173 (12.3)	6302
Type of health insurance			
Health insurance	63 033 (90.2)	8665 (91.1)	71 698
Medical aid	6799 (9.7)	836 (8.8)	7635
Veteran care	54 (0.1)	16 (0.2)	70
Charlson comorbidity index			
0 points	18 835 (27.0)	4779 (50.2)	23 614
1 or more points	51 051 (73.1)	4738 (49.8)	55 789
Arthritis			
No	56 293 (80.6)	8826 (92.7)	65 119
Yes	13 593 (19.5)	691 (7.3)	14 284
Osteoporosis			
No	32 818 (47.0)	7564 (79.5)	40 382
Yes	37 068 (53.0)	1953 (20.5)	39 021
History of fractures			
No	58 253 (83.4)	8849 (93.0)	67 102
Yes	11 633 (16.7)	668 (7.0)	12 301
Type of medical institution			
Tertiary hospital	353 (0.5)	61 (0.6)	414
General hospital	8229 (11.8)	1811 (19.0)	10 040
Hospital	1296 (1.9)	217 (2.3)	1513
Clinic	56 852 (81.4)	5952 (62.5)	62 804
Dental hospital	654 (0.9)	436 (4.6)	1090
Health center	2502 (3.6)	1040 (10.9)	3542
Department			
General practice	4592 (6.6)	1315 (13.8)	5907
Internal medicine	31 038 (44.4)	4331 (45.5)	35 369
Neurology	1928 (2.8)	403 (4.2)	2331
Psychiatry	1744 (2.5)	89 (0.9)	1833
Surgery	1770 (2.5)	209 (2.2)	1979
Orthopedics	17 873 (25.6)	1037 (10.9)	18 910
Neurosurgery	775 (1.1)	116 (1.2)	891
Anesthesiology and pain medicine	556 (0.8)	72 (0.8)	628
Ophthalmology	2141 (3.1)	665 (7.0)	2806
Otolaryngology	1121 (1.6)	158 (1.7)	1279
Dermatology	1137 (1.6)	157 (1.7)	1294
Family medicine	2270 (3.3)	228 (2.4)	2498
Dental medicine	815 (1.2)	450 (4.7)	1265
Others	2126 (3.0)	287 (3.0)	2413

of hospitalization (adjusted OR 2.25, 95% CI 2.09–2.44). Fracture and arthrosis were the most common reasons for hospitalization, accounting for 34% of cases. Other reasons for hospitalization and ED visits included cataract, pneumonia, dementia, cerebral infarction, arthritis, fracture and angina.

Proportions of patients recently using PIMs

Among patients who were hospitalized or visited EDs, 45.5%, 36.0% and 11.5%, were in the current, intermediate and past PIM use groups.

Table 3 shows the PIMs most frequently used by the patients within the current and intermediate groups who had been hospitalized or visited EDs. Among the anticholinergic drugs, 8.2% and 7.1% of patients who had taken chlorpheniramine maleate at least once during the 1-year pre-index period and who had experienced hospitalization or ED visits were in the current and intermediate PIM use groups, respectively. For diazepam, a central nervous systemacting drug, 7.7% of patients having used diazepam and experiencing hospitalization or ED visits were in the current use group, and 8.8% were in the intermediate use group. In case of metoclopramide, a gastrointestinal drug, 22.0% of total metoclopramide users who

54 Jeon et al.

Table 2 Multivariate logistic regression analysis of factors influencing hospitalization and ED visits

Characteristics	ED visits		Hospitalization	
	OR (95% CI)	P-value	OR (95% CI)	P-value
PIM use	1.59 (1.50–1.67)	<0.0001	2.25 (2.09–2.44)	< 0.0001
Female sex	0.86 (0.83-0.89)	< 0.0001	1.01 (0.97-1.06)	0.5577
Age (reference: 65–74 years)				
75–84 years	1.06 (1.03-1.10)	0.0005	1.17 (1.12-1.22)	< 0.0001
≥85 years	0.96 (0.90-1.01)	0.1367	1.43 (1.33-1.53)	< 0.0001
Type of insurance (reference: health insurance)				
Medical aid	2.09 (1.98-2.19)	< 0.0001	0.75 (0.70-0.80)	< 0.0001
Veteran care	0.82 (0.49-1.37)	0.4547	0.74 (0.41-1.32)	0.3032
Charlson comorbidity index (reference: 0 points)			
1 point or higher	1.49 (1.43-1.54)	< 0.0001	1.52 (1.45-1.60)	< 0.0001
Arthritis	1.35 (1.30-1.41)	< 0.0001	0.96 (0.91-1.01)	0.1078
Cardio-cerebrovascular disease	1.23 (1.19-1.27)	< 0.0001	1.36 (1.31-1.42)	< 0.0001
Chronic obstructive pulmonary disease	1.21 (1.14-1.28)	< 0.0001	1.46 (1.37–1.56)	< 0.0001
Osteoporosis	1.61 (1.56-1.67)	< 0.0001	0.98 (0.94-1.02)	0.3793
History of fractures	1.34 (1.28-1.39)	< 0.0001	1.67 (1.59–1.75)	< 0.0001
Type of medical institution (reference: tertiary h	ospital)			
General hospital	0.79 (0.64–0.97)	0.0256	0.87 (0.70-1.08)	0.2075
Hospital	0.68 (0.54-0.86)	0.0013	1.32 (1.04–1.68)	0.0252
Clinic	0.91 (0.74-1.11)	0.3375	0.44 (0.35-0.54)	< 0.0001
Dental hospital	0.52 (0.39-0.71)	< 0.0001	0.36 (0.25-0.52)	< 0.0001
Health center	0.64 (0.51-0.81)	0.0002	0.46 (0.35-0.59)	< 0.0001
Treatment specialty (reference: general practice)				
Internal medicine	1.33 (1.21-1.45)	< 0.0001	0.92 (0.82-1.03)	0.1268
Neurology	1.10 (0.97-1.25)	0.1289	0.71 (0.61-0.82)	< 0.0001
Psychiatry	1.19 (1.04-1.35)	0.0112	1.08 (0.92-1.27)	0.3379
Surgery	1.50 (1.32-1.71)	< 0.0001	0.91 (0.77-1.08)	0.2909
Orthopedics	1.67 (1.52-1.83)	< 0.0001	1.05 (0.94-1.18)	0.4058
Neurosurgery	1.28 (1.08-1.51)	0.0038	1.36 (1.12-1.64)	0.0016
Anesthesiology and pain medicine	1.67 (1.39-2.01)	< 0.0001	0.86 (0.67-1.11)	0.2569
Ophthalmology	0.95 (0.84-1.07)	0.3777	2.13 (1.85-2.45)	< 0.0001
Otolaryngology	1.30 (1.12-1.51)	0.0005	0.95 (0.78-1.15)	0.5913
Dermatology	0.99 (0.85-1.16)	0.9325	0.88 (0.72-1.06)	0.1809
Family medicine	2.46 (2.18–2.77)	< 0.0001	0.67 (0.57-0.79)	< 0.0001
Dental medicine	0.89 (0.72-1.11)	0.3016	0.67 (0.50-0.90)	0.0069
Others	1.15 (1.01-1.29)	0.0309	1.12 (0.96-1.30)	0.1376

had been hospitalized or visited EDs during the study period were taking the drug currently, while patients with 'intermediate' use were 4.2%. With regard to pain relief drugs, including diclofenac sodium, 15.9% of patients hospitalized or visiting EDs were in the current PIM use group, while 5.9% were in the intermediate PIM use group.

Discussion

The results of the present study revealed statistically significant increased risks of hospitalization and ED visits for elderly patients using PIMs. In patients who had recently taken (1–60 days before the incident) or were currently taking PIMs at the time of their hospitalization or ED visits, the most frequently used medications included chlorpheniramine, diazepam, metoclopramide and diclofenac. Among these high frequency drugs, only diazepam accounted for a higher proportion among the 'intermediate' users (8.8%) than the 'current' users (7.7%). Diazepam is a long-acting drug that can induce adverse effects in the elderly due to their slowed metabolism [23]; thus, adverse effects may appear slightly later compared to other drugs. On the other hand, metoclopramide and diclofenac accounted for higher percentages of patients currently using medications in comparison to the intermediate group; this is thought to

result from these drugs being associated with higher risks of acute adverse effects.

As a compulsory social insurance, the NHI covers almost all South Korean residents. There is also no primary care physician system in Korea, and most providers are paid according to service fees. For these reasons, Korean residents have easy access to medical institutions and an ability to choose and switch care among various providers relatively easily. This leads to frequent patient–physician encounters, and the patients may hence be prescribed numerous drugs. Therefore, PIM-related outcomes are of special concern in Korea. Especially, due to the rapid increase in the elderly population, PIM-related outcome research needs to be performed across the Korean healthcare spectrum.

Our results are consistent with the conclusions drawn by Reich et al. [15] and Brown et al. [16]. Reich et al. examined the association between PIM use and hospitalizations in an elderly population using the 2012 Beers criteria and PRICUS criteria. They reported that the adjusted hazard ratio (HR) was 1.13 (95% CI 1.07–1.19) for 1 PIM and 1.63 (95% CI 1.40–1.90) for more than 3 PIMs, as compared to no PIM exposure [15]. Brown et al. showed that PIM use, as determined by the 2012 Beers criteria, associated with adverse drug events (HR 2.17, 95% CI 2.01–2.34), ED visits (HR

Table 3 Most frequent medications implicated in cases of hospitalization or ED visits

Medications	PIM users experiencing hospitalization or ED visits				
	Total	Current PIM use		Intermediate PIM use	
	No. patients	No. patients	(%)	No. patients	(%)
Total	45 101	20 499 (45.5)		16 223 (36.0)	
Anticholinergics					
Chlorpheniramine maleate	34 836	2841 (8.2)		2489 (7.1)	
Hydroxyzine HCl	16 109	550 (3.4)		865 (5.4)	
Cardiovascular					
Digoxin	1839	423 (23.0)		271 (14.7)	
Central nervous system					
Diazepam	26 471	2044 (7.7)		2316 (8.8)	
Zolpidem	7007	1063 (15.2)		587 (8.4)	
Alprazolam	9634	796 (8.3)		1005 (10.4)	
Amitriptyline HCl	7702	499 (6.5)		710 (9.2)	
Lorazepam	3575	837 (23.4)		207 (5.8)	
Quetiapine fumarate	2804	596 (21.3)		255 (9.1)	
Endocrine					
Human insulin	2908	1274 (43.8)		38 (1.3)	
Insulin lispro	1242	556 (44.8)		18 (1.5)	
Gastrointestinal					
Metoclopramide HCl	21 614	4760 (22.0)		907 (4.2)	
Pain relief					
Diclofenac sodium	28 187	4480 (15.9)		1659 (5.9)	
Meloxicam	12 730	950 (7.5)		1446 (11.4)	
Ibuprofen	11 089	535 (4.8)		780 (7.0)	
Piroxicam	9468	492 (5.2)		574 (6.1)	
Mefenamic acid	7863	690 (8.8)		617 (7.9)	
Pethidine HCl	7872	2537 (32.2)		80 (1.0)	
Orphenadrine citrate	6877	636 (9.3)		808 (11.8)	
Ketorolac tromethamine	4669	1419 (30.4)		44 (0.9)	
Methocarbamol	3756	515 (13.7)		212 (5.6)	

- (1) Current PIM use: Currently taking at least one PIM.
- (2) Intermediate PIM use: Used PIM(s) 1-60 days prior to the hospitalization or ED visit.

2.00, 95% CI 1.96–2.04) and hospitalization (HR 2.03, 95% CI 1.98–2.07) in an adjusted time-varying monthly lag model [16]. However, some studies based on the 2012 Beers criteria found no relationships between PIM exposure and adverse outcomes [17–21]. This might be because of differences in external factors (e.g. the characteristics of the study population, national healthcare system, study setting, etc.) or internal factors of the Beers criteria such as issues with its predictive validity [11, 17, 24].

Recently, in 2015, the AGS updated the Beers criteria [25]. When it comes to the list of 'Medications to avoid regardless of disease', compared to the 2012 criteria, proton pump inhibitors (PPIs), desmopressin and meclizine as an anticholinergic were added, and antiarrhythmic drugs (except amiodarone), trimethobenzamide, mesoridazine and chloral hydrate were removed. Kim *et al.* examined the trend of PPI prescriptions from 2005 to 2008 in Korea using NHI claims data, and reported that the amount of PPI claims increased by 56% over the period [26]. Given this rapid increase in PPI use, using the 2015 Beers criteria, there may be PIM users in the non-PIM user group of this study. This could result in the risk of hospitalization/ED visits related to PIM exposure being underestimated. As the other drugs included or excluded in the latest criteria were used by only a few patients in our study or not available in Korea, we

presume that the results would not be highly affected by omitting or adding these drugs.

Nevertheless, the present study has the following limitations. Due to the nature of claims data, only utilization of prescribed drugs was identified, and PIMs as over-the-counter drugs were excluded from the analysis. This might contribute to an underestimated risk of PIM-related outcomes. We could also not reveal the mechanisms and processes by which PIM use increases hospitalization and ED visits among elderly individuals. Moreover, the term 'elderly' confers considerable heterogeneity of health status; thus, it may not be appropriate to restrict PIM use by strict age criteria. Older adults have substantial inter-individual variability in health, disability, age-related changes, polymorbidity and associated polypharmacy, making any generalizations regarding medication recommendations difficult [27]. Additionally, there might be a difference in hospitalization and ED visits between several disease states. Although several disease states were adjusted to minimize confounding effects. we could not consider other important health conditions such as functional status. The health insurance claims data are transferred from medical institutions to the HIRA for expense compensation, so there may be issues regarding the disease name code accuracy (e.g. upcoding in order to legitimize the use of various treatments and

⁽³⁾ The ratio of current or intermediate PIM use among patients who experienced an incident = (the number of patients who had taken PIMs in the current or intermediate group/the number of patients who had taken PIMs at least once during the 1-year pre-index period and experienced hospitalization or ED visits) × 100. PIM, Potentially inappropriate medication.

56 Jeon et al.

drugs). The possibility of imprecise codes would be a concern in this study if the diseases of the patients had been taken into account.

Despite these limitations, we believe that our results have some important implications regarding the association between PIM use and hospitalization/ED visits. These findings may help implement evidence-based policies concerning careful PIM use among elderly patients in Korea.

Conflict of interest statement

None declared.

References

- Hajjar ER, Hanlon JT, Artz MB et al. Adverse drug reaction risk factors in older outpatients. Am J Geriatr Pharmacother 2003;1:82–9.
- Cooper JW. Adverse drug reaction-related hospitalizations of nursing facility patients: a 4-year study. South Med J 1999;92:485–90.
- Hanlon JT, Schmader KE, Koronkowski MJ et al. Adverse drug events in high risk older outpatients. J Am Geriatr Soc 1997;45:945–8.
- Turnheim K. When drug therapy gets old: pharmacokinetics and pharmacodynamics in the elderly. Exp Gerontol 2003;38:843–53.
- Gallagher P, Barry P, O'Mahony D. Inappropriate prescribing in the elderly. J Clin Pharm Ther 2007;32:113–21.
- Fick DM, Mion LC, Beers MH et al. Health outcomes associated with potentially inappropriate medication use in older adults. Res Nurs Health 2008;31:42–51.
- Beers MH, Ouslander JG, Rollingher I et al. Explicit criteria for determining inappropriate medication use in nursing home residents. UCLA Division of Geriatric Medicine. Arch Intern Med 1991;151:1825–32.
- Beers MH. Explicit criteria for determining potentially inappropriate medication use by the elderly. An update. Arch Intern Med 1997;157:1531–6.
- Fick DM, Cooper JW, Wade WE et al. Updating the Beers criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. Arch Intern Med 2003;163:2716–24.
- American Geriatrics Society Beers Criteria Update Expert P. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc 2012;60:616–31.
- Jano E, Aparasu RR. Healthcare outcomes associated with Beers' criteria: a systematic review. Ann Pharmacother 2007;41:438–47.
- Lin HY, Liao CC, Cheng SH et al. Association of potentially inappropriate medication use with adverse outcomes in ambulatory elderly patients with chronic diseases: experience in a Taiwanese medical setting. Drugs Aging 2008;25:49–59.
- Chen YC, Hwang SJ, Lai HY et al. Potentially inappropriate medication for emergency department visits by elderly patients in Taiwan. Pharmacoepidemiol Drug Saf 2009;18:53–61.

14. Stockl KM, Le L, Zhang S et al. Clinical and economic outcomes associated with potentially inappropriate prescribing in the elderly. Am J Manag Care 2010;16:e1–10.

- Reich O, Rosemann T, Rapold R et al. Potentially inappropriate medication use in older patients in Swiss managed care plans: prevalence, determinants and association with hospitalization. PloS One 2014;9:e105425.
- 16. Brown JD, Hutchison LC, Li C et al. Predictive validity of the Beers and screening tool of older persons' potentially inappropriate prescriptions (STOPP) criteria to detect adverse drug events, hospitalizations, and emergency department visits in the United States. J Am Geriatr Soc 2016;64: 22–30
- Cahir C, Moriarty F, Teljeur C et al. Potentially inappropriate prescribing and vulnerability and hospitalization in older community-dwelling patients. Ann Pharmacother 2014;48:1546–54.
- 18. Ishii S, Kojima T, Ezawa K et al. The association of change in medication regimen and use of inappropriate medication based on Beers criteria with adverse outcomes in Japanese long-term care facilities. Geriatr Gerontol Int 2017:17:591–97.
- Pasina L, Djade CD, Tettamanti M et al. Prevalence of potentially inappropriate medications and risk of adverse clinical outcome in a cohort of hospitalized elderly patients: results from the REPOSI Study. I Clin Pharm Ther 2014;39:511–5.
- Tosato M, Landi F, Martone AM et al. Potentially inappropriate drug use among hospitalised older adults: results from the CRIME study. Age Ageing 2014;43:767–73.
- 21. van der Stelt CA, Vermeulen Windsant-van den Tweel AM, Egberts AC et al. The Association between potentially inappropriate prescribing and medication-related hospital admissions in older patients: a nested case control study. Drug Saf 2016;39:79–87.
- WHO. Anatomical Therapeutic Chemical (ATC) Classification. Oslo: WHO Collaborating Centre for Drug Statistics Methodology, 2013.
- Greenblatt DJ, Harmatz JS, Shader RI. Clinical pharmacokinetics of anxiolytics and hypnotics in the elderly. Clin Pharmacokinet 1991;21: 165–77.
- 24. Bjerre LM, Ramsay T, Cahir C et al. Assessing potentially inappropriate prescribing (PIP) and predicting patient outcomes in Ontario's older population: a population-based cohort study applying subsets of the STOPP/START and Beers' criteria in large health administrative databases. BMJ Open 2015;5:e010146.
- 25. By the American Geriatrics Society Beers Criteria Update Expert Panel. American geriatrics society 2015 updated Beers criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc 2015;63: 2227–46.
- Kim KM, Cho YK, Bae SJ et al. Prevalence of gastroesophageal reflux disease in Korea and associated health-care utilization: a national population-based study. J Gastroenterol Hepatol 2012;27:741–5.
- Fialova D, Onder G. Medication errors in elderly people: contributing factors and future perspectives. Br J Clin Pharmacol 2009;67:641–5.