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Characteristics of inappropriate multiple medication use in older urological outpatients

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ABSTRACT

Objectives: To investigate polypharmacy and potentially inappropriate medications (PIMs) in elderly patients visiting the urology department for lower urinary tract symptoms (LUTS).
Methods: We retrospectively analyzed digital medical records of individuals over the age of 65 who visited the urology department for LUTS. This cross-sectional study was conducted in 10 hospitals located in South Korea, between September 2017 and December 2017. All prescribed medications were analyzed using electronic medical records. The updated 2015 Beers criteria were used to identify and assess the appropriateness of the prescribed drugs in elderly patients.
Results: We analyzed a total of 2143 patients aged over 65 years from 10 institutions. The mean age was 74.2 ± 6.26 years (65–97), 1634 (76.2%) were men. Patients took a mean of 6.48 ± 2.46 medications (range 0–18), and polypharmacy was found in 1762 patients (82.2%). The number of patients who received PIMs at least once was 1579 (73.7%). The average number of PIMs used per patient was 1.31 ± 1.25 (0–7). PIM use ratio was 18.9 ± 0.15% (0–67%). The number of chronic diseases, and concurrent medication and polypharmacy were predictive factors associated with PIM use.
Conclusion: Our multi-institutional results show that a substantial proportion of elderly patients took PIMs when visiting the urology department. Factors associated with PIMs were the number of chronic diseases and polypharmacy. Medication use in elderly patients, especially in urology, should be monitored carefully.

1. Introduction

The global population has been aging considerably since the mid-20th century. South Korea joined the list of aging societies (7%–14%) in 2000 and has one of the fastest aging populations (Suh et al., 2017). Although the population over 65 years of age currently accounts for approximately 13.2% of the total population in South Korea, it is estimated that elderly persons will comprise more than one-third of the total population by 2050 (Park, Park, Song, Sohn, & Kwon, 2017). As the population is aging, the prevalence of chronic diseases is increasing

Abbreviations: AGS, American Geriatrics Society; ATC, anatomical therapeutic chemical; BPH, benign prostate hyperplasia; LUTS, lower urinary tract symptoms; PIMs, potentially inappropriate medications; UI, urinary incontinence

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and polypharmacy is becoming a common problem in the clinical management of aged adults. However, the issue of multiple medications is more complex than simply adding up the number of medications being used. Potentially inappropriate medications (PIMs) have been defined as medications that have an unfavorable risk/benefit balance in many adults (Steinman et al., 2015). The use of PIMs in elderly people can result in an increased risk of adverse drug events, morbidity and mortality, as well as in the increased utilization of healthcare resources (Walsh, O'Riordan, Kearney, Timmons, & Byrne, 2016). Therefore, it is essential to optimize drug prescriptions in geriatric populations to avoid these clinical and economic implications (Grina & Briedis, 2017).

Lower urinary tract symptoms (LUTS) are common in older adults and the prevalence of LUTS increases with increasing age because the aging process is associated with many changes in the lower urinary tract (Cho, 2016; Jung, Kim, & Cho, 2015). Along with the increase in the elderly population, the number of patients visiting the department of urology due to benign prostate hyperplasia (BPH) or urinary incontinence (UI) is rising (Cho, 2016; Choi & Bae, 2016). In addition, chronic diseases are commonly diagnosed in geriatric populations, and they are associated with concomitant neurogenic bladder or other voiding difficulties (Lee et al., 2017). Elderly patients are often characterized by declining physiology and combined use of multiple drugs and they are at risk of adverse drug reactions due to drug interactions. Multiple drug use has been shown to be common among the elderly with LUTS. On the other hand, LUTS becomes a side effect of many medicines (Hashimoto et al., 2015). For example, old adults with UI are more likely to use antihistamines, angiotensin II receptor blockers, antipsychotics, antidepressants, anticonvulsants, or benzodiazepines (Afonso, Verhamme, Stricker, Sturkenboom, & Brusselle, 2011). Therefore, in the elderly population, polypharmacy seems to occur at the highest frequency in older patients receiving LUTS medications.

Several assessment tools have been developed to detect inappropriate prescribing in the elderly population (Abdulah et al., 2018). One of the most widely used tools with international acceptance are the American Geriatrics Society (AGS) Beers criteria. These consists of a list of inappropriate drugs that should be avoided by geriatric patients and were most recently updated in 2015 (By the American Geriatrics Society Beers Criteria Update Expert, P., 2015). Previous studies have reported high rates of polypharmacy in older adults because of the presence of multiple chronic diseases (Charlesworth, Smit, Lee, Alramadhan, & Odden, 2015; Onoue et al., 2018). In addition, there have been many studies about the prevalence of PIMs according to the AGS Beers criteria(Baldoni Ade et al., 2014; Sakr, Hallit, Haddad, & Khabbaz, 2018). Furthermore, studies indicating an association between polypharmacy and PIMs have also been reported (Paque et al., 2019). However, to the best of our knowledge, no study has systematically evaluated polypharmacy or PIMs in aged urology patients in a multi-institutional setting.

For these reasons, in this study, we aimed to investigate the current extent of polypharmacy and PIMs according to the 2015 AGS Beers criteria (By the American Geriatrics Society Beers Criteria Update Expert, P., 2015) in elderly patients visiting the department of urology for LUTS.

2. Methods

2.1. Study design and data acquisition

We retrospectively analyzed digital medical records of individuals over the age of 65 who visited the urology department for LUTS. This cross-sectional study was conducted in 10 hospitals located in the metropolitan area of South Korea, between September 2017 and December 2017. Three of the 10 participating hospitals were located in Seoul, three in the Gyeonggi Province, two in the Chungcheong Province, one in the Jeolla Province and one in the Gyeongsang Province (Fig. 1). The distribution of the participating hospitals was relatively even throughout the country.

Fig. 1. Geographic location of 10 Hospitals in South Korea.

We investigated baseline demographic data, physical characteristics, the types and number of chronic diseases, all prescribed medications the patients were taking, and experienced adverse drug reactions using electronic medical records. Injected drugs and topical ointments were excluded from the drug count. The dispensed drugs were classified according to the Anatomical Therapeutic Chemical (ATC) classification system, as recommended by the World Health Organization. Age was categorized into three groups: 65 to 74, 75 to 84, and over 85 years.

2.2. Polypharmacy and PIMs

Most studies have defined polypharmacy according to the number of medications taken by the patient. For this study, we defined polypharmacy as the concurrent use of five or more oral drugs (Haider, Johnell, Weitoft, Thorslund, & Fastbom, 2009; Linjakumpu et al., 2002). The total number of medications was calculated by summing the number of medications reported by each patient. The updated 2015 AGS Beers criteria were used to identify and assess the appropriateness of the prescribed drugs in elderly patients. PIMs were determined according to the 2015 Beers criteria. PIM use was defined as patients who received PIMs at least once and the prevalence of PIMs was calculated by dividing the number of patients with at least one PIM by the total number of patients. The PIM items per patient were determined by the average number of PIMs used per patient, and the PIM use ratio was calculated by dividing the total number of PIMs by the total number of medications per patient

2.3. Ethics approval

The Institutional Review Board of the Hallym University Kangnam Sacred Heart Hospital approved this study's protocol (2017-07-023-002).

2.4. Statistical analysis

Data are expressed as means and standard deviations. A *p*-value was calculated using the independent *t*-test, Pearson's chi-squared test, and one-way analysis of variance. Linear regression was performed to assess the relationship between the number of PIMs and medications. The influence of risk factors for PIM prescription was calculated using multivariate logistic regression and odds ratios (ORs) with 95% confidence intervals. All tests with p-value < 0.05 were considered as statistically significant. IBM SPSS Statistics version 23 software (IBM Corporation, Armonk, NY) was used to carry out all statistical analyses.

3. Results

3.1. Demographic characteristics

We analyzed a total of 2143 patients aged over 65 years from 10 institutions. The mean age was 74.2 ± 6.26 years (65–97), 1634 (76.2%) were men, 509 (23.8%) were women. The majority of the patients was 65 to 74 years of age; this group accounted for 53.5% of all patients. The demographic characteristics are shown in Table 1.

3.2. Comorbidities

The average number of comorbidities was 1.77 ± 1.18 and 85.3% of patients had more than one chronic disease. The most common chronic disease was hypertension (44.0%) and the second was musculoskeletal disease (33.6%). The prevalence of other chronic diseases is summarized in Table 1.

3.3. Number of concurrent medications and polypharmacy

Patients took a mean of 6.48 ± 2.46 concurrent medications (range 0–18), and polypharmacy was found in 1762 patients (82.2%).

3.4. PIM use, the number of PIMs used per patient, and PIM use ratio

The number of patients who received PIMs at least once according to the 2015 Beers criteria was 1579 (73.7%). Their characteristics were assessed by splitting the total study population into two groups (classified as PIMs and Non-PIMs). Patients receiving PIMs at least once had a high number of chronic diseases, a high number of medications, and polypharmacy (Table 1). The average number of PIMs used per patient was 1.31 ± 1.25 (0–7). Males and patients with polypharmacy had a higher number of PIM use per patient than females and those with non-polypharmacy. The PIM use ratio, defined as the ratio of total amount of PIMs to all medications per patient, was 18.9 ± 0.15% (0–67%). However, there were no significant differences in PIM use ratio according to sex, age or polypharmacy (Table 2).

Table 1
Demographic characteristics, comorbidities and medications in relation to PIM use.

Characteristics	Total n = 2143	PIMs n = 1579 (73.7%)	Non-PIMs n = 564 (26.3%)	P-value
Sex				0.561
Male	1634 (76.2%)	1209(74.0%)	425(26.0%)	
Female	509 (23.8%)	370(72.7%)	139(27.3%)	
Age	74.2 ± 6.26	74.2 ± 6.41	74.1 ± 5.82	0.791
65-74	1,147 (53.5%)	853 (54.0%)	294 (52.1%)	0.433
75-84	881 (41.1%)	636 (40.3%)	245 (43.4%)	
≥85	115 (5.4%)	90 (5.7%)	25 (4.4%)	
Chronic disease (number)	1.77 ± 1.18	1.99 ± 1.19	1.15 ± 0.93	< 0.001
0	315 (14.7%)	140 (8.9%)	175 (31.0%)	
1	638 (29.8%)	478 (30.3%)	160 (28.4%)	
2	555 (25.9%)	359 (22.7%)	196 (34.8%)	
3	542 (25.3%)	519 (32.9%)	23 (4.1%)	
≥4	93 (4.3%)	83 (5.3%)	10 (1.8%)	
Chronic disease (type)				
Hypertension	943 (44.0%)	691 (43.8%)	252 (44.7%)	0.706
Musculoskeletal	719 (33.6%)	527 (33.4%)	192 (34.0%)	0.773
Diabetes	522 (24.3%)	384 (24.3%)	138 (24.5%)	0.944
Hyperlipidemia	418 (19.5%)	314 (19.9%)	104 (18.4%)	0.457
Coronary heart	141 (6.6%)	107 (6.8%)	34 (6.0%)	0.538
Dementia	74 (3.5%)	59 (3.7%)	15 (2.7%)	0.229
Others	248 (11.6%)	181 (11.5%)	67 (11.9%)	0.791
Number of concurrent medications	6.48 ± 2.46	6.85 ± 2.27	5.44 ± 2.66	< 0.001
0	23 (1.0%)	1 (0.1%)	22 (3.9%)	
1-4	358 (16.7%)	127 (8.0%)	231 (41.0%)	
5-9	1,596 (74.5%)	1318 (83.5%)	278 (49.3%)	
10-14	149 (7.0%)	118 (7.5%)	31 (5.5%)	
≥15	17 (0.8%)	15 (0.9%)	2 (0.4%)	
Polypharmacy				< 0.001
< 5	381 (17.8%)	128(8.1%)	253(44.9%)	
≥5	1762 (82.2%)	1451(91.9%)	311(55.1%)	
Classification of Medications				
Genitourinary	2.26 ± 1.23	2.30 ± 1.22	2.24 ± 1.17	0.378
Cardiovascular	0.95 ± 0.76	0.95 ± 0.76	0.95 ± 0.76	0.883
Gastrointestinal	0.64 ± 0.76	0.64 ± 0.77	0.63 ± 0.75	0.615
Neuropsychiatric	0.44 ± 0.64	0.45 ± 0.65	0.43 ± 0.60	0.431
Endocrine	0.41 ± 0.68	0.41 ± 0.68	0.41 ± 0.68	0.823
Musculoskeletal	0.21 ± 0.50	0.20 ± 0.50	0.24 ± 0.51	0.108
Others	0.46 ± 0.71	0.47 ± 0.71	0.42 ± 0.69	0.127

Table 2
The number of PIMs used per patient (PIM items/patient) and the proportion of total amount of PIMs to all medications per patient (PIM use ratio).

Characteristics	PIM items/patient (mean ± SE)	P-value	PIM use ratio % (mean ± SE)	P-value
Overall	1.31 ± 1.25 (0-7)		18.9 ± 0.15 (0-67%)	
Sex Male	1.37 ± 1.28	< 0.001	19.1 ± 0.15	0.343
Female	1.13 ± 1.11		18.4 ± 0.15	
Age		0.504		0.482
65-74 (853)	1.35 ± 1.25		19.2 ± 0.15	
75-84 (636)	1.26 ± 1.23		18.4 ± 0.15	
85-94 (88)	1.29 ± 1.24		20.0 ± 0.14	
≥95 (2)	1.33 ± 2.31		16.7 ± 0.29	
Polypharmacy		< 0.001		0.305
< 5	0.27 ± 0.61		16.0 ± 0.13	
≥5	1.54 ± 1.23		17.2 ± 0.05	

3.5. Classification of medications

According to the ATC classification, medications for the genitourinary system, which were used by most patients (88.4%), were most commonly used, and the second were for the cardiovascular system, which were used by 68.5% of the studied group. The use of gastrointestinal medication was observed in 47.8% of the patients. Table 1 shows the mean number of medications according to drug subcategories and the comparison according to the presence or absence of PIM use. There was no significant difference between patients with and without PIM use when analyzed according to the type of prescribed medication.

3.6. Risk factors for PIM

Table 3 presents a summary of the results of the multivariate analysis using logistic regression to identify predictors of the PIM use according to personal characteristics. The number of chronic diseases and concurrent medication and polypharmacy were predictive factors associated with PIM use. However, there was no significant association between the sex, age and classification of medications and PIM use.

Table 3
Independent risk factors for PIM use associated with the personal characteristics and the medication type.

Characteristics	OR (95% CI)	P-value
Sex		
Female	1	
Male	1.07 (0.85, 1.34)	0.561
Age		
65-74	1	
75-84	0.90 (0.73, 1.09)	0.271
≥85	1.24 (0.78, 1.97)	0.361
Chronic disease (number)		
0	1	
1	3.73 (2.81, 4.97)	< 0.001
2	2.30 (1.73, 3.04)	< 0.001
3	28.21 (17.58, 45.27)	< 0.001
≥4	10.38 (5.19, 20.74)	< 0.001
Polypharmacy		
< 5	1	
≥5	9.22 (7.22, 11.79)	< 0.001
Classification of medications		
Genitourinary	1.04 (0.96, 1.12)	0.378
Cardiovascular	0.99 (0.87, 1.13)	0.883
Gastrointestinal	1.03 (0.91, 1.17)	0.615
Neuropsychiatric	1.06 (0.91, 1.24)	0.449
Endocrine	1.02 (0.88, 1.17)	0.822
Musculoskeletal	0.86 (0.71, 1.03)	0.105
Others	1.12 (0.97, 1.28)	0.127

4. Discussion

In the present study, we collected data from the urology departments of 10 hospitals to investigate polypharmacy and the appropriateness of prescription drugs and obtained a uniform sample across the country compared to the population distribution. To the best of our knowledge, this is the first study to examine the polypharmacy and PIMs of Korean old adults in the department of urology.

We found that the mean number of medications per visit was 6.5 and polypharmacy (≥5 medications) was relatively high (82.2%) among the study subjects. Multiple medication use has been shown to be prevalent among older adults with LUTS (Hashimoto et al., 2015). Several drugs can cause LUTS, thus starting the use of new medications for its treatment, and this repetition causes more and more drugs to be taken. Therefore, this high prevalence of polypharmacy can explain the frequent occurrence of adverse drug events associated with LUTS-causing drugs in patients with LUTS (Hashimoto et al., 2015).

Polypharmacy is the use of more than one medication concomitantly. It has been defined in different ways, but one of the most commonly used definitions is the concurrent use of five or more drugs (Haider et al., 2009). Depending on the definitions used and the study design, other studies have shown that the prevalence of polypharmacy among the elderly ranged approximately from 5% to 78% (Fulton & Allen, 2005; Haider et al., 2009). Furthermore, depending on their status as inpatient or outpatient, the prevalence of polypharmacy in older adults can be up to 37% in the outpatient setting and up to 92% in those who are hospitalized (Maggiore et al., 2014). Despite the high prevalence in the present study, our findings are in agreement with previous reports. We investigated the outpatient records of urology departments and found that older patients tend to take multiple medications for LUTS and other diseases.

Polypharmacy has been reported in several studies to be associated with PIMs (Baldoni Ade et al., 2014; Onoue et al., 2018; Sakr et al., 2018). The use of PIMs was measured based on the 2015 AGS Beers criteria. Dr. Mark Beers first created the Beers criteria in 1991, through a consensus panel of experts by using the Delphi method. The criteria were originally published in the Archives of Internal Medicine in 1991(Fick et al., 2003) and were updated in 1997, 2003, 2012 and 2015. (By the American Geriatrics Society Beers Criteria Update Expert, P., 2015) We have chosen to apply the 2015 AGS Beers criteria consensus group as this is the most recent update of the original Beers criteria. A higher prevalence of PIM use (73.3%) was found in our investigation. Depending on which tool is used, PIM use is estimated to be between 4.8% and 45.6% among the older adult population (Sakr et al., 2018). The higher percentage of PIM use we detected according to 2015 Beers criteria can be explained by the fact that this is a geriatric urology-based study. We included older adults who visited the urology department for LUTS; they had several comorbidities including genitourinary diseases.

Our findings show that males present more PIM items than females according to the 2015 Beers criteria, and this is different from other studies (Haider et al., 2009; Sakr et al., 2018; Sheikh-Taha & Dimassi, 2017). The reason is presumably that the majority of the participants were male (76.2%), and had BPH with LUTS. As expected, a higher number of PIMs per patient was associated with a higher number of medications. PIMs has been shown to be associated with polypharmacy. In a multivariate logistic regression test, we found that the number of chronic diseases, and concurrent medications and polypharmacy were associated with a higher risk for PIM use. The more chronic diseases in these patients, the more prescribed medications they use, which is an important factor for polypharmacy and is also associated with the increased risk of PIM use.

Despite these findings, our study is characterized by several limitations. This evaluation of polypharmacy and PIM use was a retrospective and cross-sectional analysis, which might not have sufficient power for a high level of evidence. In addition, only 10 urology

departments of hospitals in South Korea were involved and the patients there might not be representative of the entire Korean geriatric population. Despite these limitations, the present study provides useful evidence on polypharmacy and PIM use in urology departments in South Korea. To the knowledge of the authors, no prior studies have performed on a geriatric urology population, although they were on older populations in general. Despite the data not being based on insurance claims, the current nationwide analysis of polypharmacy using actual data from clinics may be invaluable in reducing the burden of polypharmacy in the field of urology.

5. Conclusions

Our multi-institutional results show that a substantial proportion of elderly patients took PIMs when visiting the urology department. Factors associated with PIMs use according to the 2015 Beers criteria were the number of chronic diseases and concurrent medications and polypharmacy. The use of medication in elderly patients, especially in the field of urology, should be monitored carefully because polypharmacy can increase the risk of PIMs, leading to adverse drug reactions. Further research using data of the Korean Health Insurance Review and Assessment (KHIRA) on outpatient prescription claims is planned to compare with the overall prevalence of PIM prescriptions.

Conflict of interest

None declared.

Author contributions

Cho ST: study concept and design, acquisition of data, statistical analysis, interpretation of data, drafting, critical review of manuscript and revision of manuscript. Kim JS, Noh J, Moon HS, Min SK, Bae SR, Bae JH, Seo YJ, Chang Y, Jeong CW, Kim HJ: acquisition of data, interpretation of data, Han JH: revision of manuscript, statistical analysis, review of manuscript. All authors approved the final version of the manuscript.

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