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Original Article

Medication Errors and Potentially Inappropriate Medication Use in Elderly Patients Admitted to the General Internal Medicine Outpatient Clinic of a University Hospital

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ABSTRACT

Background The frequency of chronic diseases, number of drugs used, and number of medication errors have increased in the elderly. In this study, we aimed to determine the prevalence of potentially inappropriate medication (PIM) use and medication errors in elderly patients admitted to a university hospital and to identify the influencing factors.

Material and Methods In this prospective cross-sectional study, the patients' characteristics, drug use patterns, and medication errors in the previous month were recorded in detail. Following this, PIM use was assessed according to the 2015 Beers Criteria.

Results A total of 721 elderlay patients (60.9% female and 39.1% male) were included in this study. The mean number of drugs used by the patients per day was 4.6±2.8 and the rate of polypharmacy was 49.4%. The rate of medication errors was 54.2%, that of PIM use was 30.1%, and that of adverse drug reactions was 22.5%; these rates were higher in patients with polypharmacy. The most common medication error, PIM use, and adverse drug reaction were the omission of a daily dose (36.5%), inappropriate use of proton pump inhibitors (10%), and gastrointestinal system-related symptoms (7.7%), respectively. Diabetes mellitus and depression were found to be independent factors associated with medication errors.

Conclusions In the present study, patient-related medication errors, PIM use, and adverse drug reactions were more frequently observed in elderly patients with polypharmacy. In addition, medication errors were more commonly observed in elderly with diabetes mellitus and depression.

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Introduction

In recent years, the elderly population has been increasing worldwide. Aging is associated with a decrease in organ functions and an increase in the frequency of chronic diseases and the number of drugs used. Changes in the pharmacokinetics and pharmacodynamics of drugs due to age-related physiological changes, an increased risk of adverse drug reactions (ADRs) and drug-drug interactions due to polypharmacy are the main factors that make the management of elderly patients difficult.[1,2]

Polypharmacy increases in the cost of treatment, need for hospitalization, rate of treatment nonadherence, and prevalence of medication errors.[2,3] Treatment nonadherence by the patient and the prescription of potentially inappropriate medications (PIMs) by the physician are the main medication errors observed in elderly patients. Omitting to take medication, taking the wrong dose of medication, taking medication at the wrong time than the recommended one, and taking the wrong medication are the main types of patient-related treatment nonadherence and medication errors.[4-6] PIM use in the elderly is also an important problem, and various criteria have been established to assess it in recent years, particularly the Beers Criteria and Screening Tool of Older Person's Prescriptions (STOPP) Criteria.[7,8] The present study included elderly patients admitted to the general internal medicine outpatient clinic of a university hospital. The aim of this study was to assess the patients' socio-demographic characteristics, concomitant chronic diseases, medication use features, frequency of polypharmacy and patient-related medication errors, and also rate of PIMs use according to the 2015 Beers Criteria and the influencing factors in order to contribute to the existing literature.

Material and Methods

This prospective cross-sectional study was conducted after obtaining approval from the local ethics committee. Patients aged ≥65 years who were admitted to the General Internal Medicine Outpatient Clinic of Bursa Uludag University Hospital in Turkey between July 1, 2012 and January 1, 2013 and provided informed consent were included in the study.

Patient information, such as age, gender, marital status, people they lived with, educational status, concomitant chronic diseases, drugs used, ADRs, and also patient-related medication errors in the previous month, were recorded on a questionnaire form via face-to-face interviews. The daily use of ≥5 drugs was accepted as polypharmacy, while that of ≥10 drugs was accepted as excessive polypharmacy in the present study.[9,10] The patients' PIM use was assessed according to the 2015 Beers Criteria.[7]

The main types of patient-related medication errors are as follows:

1. Dose omission error: Skipping or not taking the daily dose of at least one drug.
2. Wrong time error: Taking drugs outside the recommended time.
3. Wrong dose error: Taking drugs at a dose lower or higher than the daily recommended dose or duplicating the dose.
4. Wrong drug error: Taking drugs with an inappropriate indication or taking drugs prescribed to other family members by mistake.

PIMs are grouped as follows according to the 2015 Beers Criteria.[7]

1. Table 2-related PIMs: Taking drugs that should be avoided in the elderly.
2. Table 3-related PIMs: Taking drugs that should be avoided due to drug-disease or drug-syndrome interactions in the elderly.
3. Table 4-related PIMs: Inappropriately using drugs that should be used with caution in the elderly.
4. Table 5-related PIMs: Taking drugs that should be avoided due to clinically important drug-drug interactions in the elderly.
5. Table 6-related PIMs: Inappropriately using drugs that should be avoided or reduced in dosage due to renal impairment in the elderly.

Statistical Analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 21. Pearson's chi-square, Fisher's exact chi-square and Freeman Halton tests were used for comparing categorical variables. The Kruskal-Wallis test was used to compare more than two independent groups, and the Mann-Whitney U

test was used to compare two independent groups. Relationships between variables were analyzed using the Spearman correlation coefficient. Binary logistic regression analysis was performed to identify factors that independently affected medication errors. *p* values < 0.05 were considered statistically significant.

Results

A total of 721 patients admitted to the General Internal Medicine Outpatient Clinic for a period of 6 months were included in the present study. The sociodemographic characteristics of the patients are shown in Table 1.

Table 1. Demographic and anthropometric characteristics of the groups.

	Number (%)
Gender	
Female	439 (60.9)*
Male	282 (39.1)
Age group	
65-74 year-old	571 (79.2)*
≥75 year-old	150 (20.8)
Marital status	
Single	8 (1.1)
Married	472 (65.5)
Divorced	18 (2.5)
Widowed	223 (30.9)**
Household status	
Alone	111 (15.4)*
With spouse	471 (65.3)
With children	130 (18)**
With close relative	4 (0.6)
Nursing home	5 (0.7)
Educational status	
Illiterate	118 (16.4)**
Just literate	71 (9.8)
Primary school	314 (43.6)
Secondary school or above	218 (30.3)**

* p<0.01, ** p<0.001.

The number of female patients was higher in the present study. Moreover, most patients were aged 65-74. The mean age of the patients was: 70.9±5.1 years (females: 70.6±4.9 years, males: 71.5±5.3 years), and their median age was 70 years, (range: 65-89 years). The distribution of age groups was similar among female and male patients. The prevalence of losing their spouse, living alone, living with children and being illiterate was higher in female patients, while that of having secondary school and higher education levels was higher in male patients.

A total of 677 (93.9%) patients had at least one concomitant chronic disease. The mean number of concomitant chronic diseases in the patients was 2.5±1.4 (range: 0-7, median: 2), with the prevalence being significantly higher in females than males (2.7±1.3 vs 2.3±1.5, p<0.001). The most common chronic diseases were hypertension (n=473, 65.6%), diabetes mellitus (n=261, 36.2%), dyslipidemia (n=188, 26.1%), and coronary artery disease (n=136, 18.9%). Of the chronic diseases noted, the prevalence of hypertension, osteoporosis, goiter-hypo/hyperthyroidism (p<0.001), dyslipidemia, depression (p<0.01), and osteoarthrosis (p<0.05) was significantly higher in females, while that of coronary artery disease (p<0.001) was significantly higher in males. The patients' drug use characteristics are shown in Table 2, and their rates of polypharmacy, PIM use, and patient-related medication errors are shown in Table 3.

Cardiovascular system (CVS) drugs were the most commonly used drugs in both genders. The use of endocrine system drugs, psychiatric drugs (p<0.001), and analgesic-anti-inflammatory drugs (p<0.01) was higher in female patients. In terms of age groups, endocrine system drugs (p<0.05) were more commonly used in the "65-74 year-old" group, while CVS drugs (p<0.05) were more commonly used in the "≥75 year-old" group. In total, 162 patients (22.5%) experienced ADRs. ADRs were significantly higher in patients with polypharmacy (8.2% in patients taking 1-4 drugs per day vs 14.3% in patients taking ≥5 drugs per day, p<0.01), and there was no difference between genders and age groups. Moreover, 254 (35.2%) patients reported that they used non-prescription drugs, while 109 (15.1%) patients reported that they used alternative therapy. There was no difference between genders and age groups in this regard.

Table 2. Drug use characteristics of the patients.

	Number (%)
Most frequently used drug groups	
Cardiovascular system drugs	573 (79.5)
Endocrine system drugs	410 (56.9)
Gastrointestinal system drugs	192 (26.6)
Psychiatric drugs	108 (15)
Respiratory system drugs	97 (13.5)
Most frequently used drugs	
ASA	223 (30.9)
ACEI/ARB±hydrochlorothiazide	173 (24)
Beta blockers	170 (23.6)
Metformin	168 (23.3)
PPIs	152 (21.1)
Most frequently ADRs	
Gastrointestinal system intolerance	54 (7.5)
Allergic skin reaction	25 (3.5)
Hypoglycemia	25 (3.5)
Non-prescription drug use	
NSAIDs	128 (17.8)
Analgesics	96 (13.3)
Vitamins	28 (3.9)
Others	45 (6.2)
Alternative treatment use	
Herbal products	88 (12.2)
Massage-spa	11 (1.5)
Acupuncture	2 (0.3)
Others (fish oil, ozone etc.)	13 (1.8)

ASA: acetylsalisylic acid, ACEI: angiotensin converting enzyme inhibitor, ARB: angiotensin receptor bloker, PPIs: proton pump inhibitors, ADRs: advers drug reactions, NSAIDs: nonsteroidal antiinflammatory drugs.

The mean number of drugs used by the patients per day was 4.6±2.8 (range: 0-15, median: 4). Female patients used a significantly higher number of drugs than male patients (4.9±2.7 vs 4.1±3.0, p<0.001); however, there was no difference in the number of drug used between different age groups. A positive correlation was noted between the number of chronic diseases and the number of drugs used (r= -0.579, p<0.001). 35 (4.8%) patients were not taking any drug, while 686 (95.2%) patients were taking at least one drug. 356 (49.4%) patients had polypharmacy, with the rate of polypharmacy being higher in females than in males (56.2% vs 38.7%, p<0.01).

A total of 528 medication errors were noted in 391 (54.2%) patients (gender-wise distribution: 335 errors in 250 female patients and, 193 errors in 141 male patients; age-wise distribution: 411 errors in 314 patients in the 65-74 year-old group and 117 errors in 77 patients in the ≥75 year-old group); there was no difference between genders and age groups in this regard. The prevalence of medication errors was significantly higher in patients with polypharmacy (28.8% in patients taking 1-4 drugs per day versus 75.7% in patients taking ≥5 drugs per day, p<0.001). As the number of concomitant chronic diseases increased, the number of medication errors significantly increased (2.3±1.4 concomitant chronic diseases in patients without medication errors vs 3.0±1.4 in those with medication errors, p<0.001).

Retrospective binary logistic regression analysis was performed to assess the relationship between medication errors and age, gender, educational status, number of comorbid chronic diseases, most common concomitant chronic diseases, polypharmacy, non-prescription drug use, and alternative therapy use. The results revealed that polypharmacy (odds ratio [OR]: 1.12, 95% confidence interval [CI]: 1.05-1.19, p<0.001), diabetes mellitus (OR: 1.55, 95% CI: 1.1-2.1 p=0.009), and depression (OR: 2.6, 95% CI: 1.26-5.4, p=0.009) were independent factors associated with medication error.

In total, 264 instances of PIMs in 217 (30.1%) patients (gender-wise distribution: 168 instances in 136 female patients and, 96 instances in 81 male patients; age-wise distribution: 160 instances in 127 patients in the 65-74 year-old group, and 104 instances in 90 patients in the ≥75 year-old group). The rate of PIM use was significantly higher in patients with polypharmacy (17.6% in patients taking 1-4 drugs per day vs 47.5% in patients taking ≥5 drugs, p<0.001). As the number of concomitant chronic diseases increased, the rate of PIM use significantly increased. The number of chronic diseases in patients not using PIMs was

Table 3. Distribution of the number of drugs used, potentially inappropriate medications used, and patient-related medication errors by gender and geriatric age groups.

	Gender			Age group	
	Female	Male	Total	65-74 year-old	≥75 year-old
Number of drugs used					
1-4 drugs	178 (40.5)	152 (53.9)	330 (45.8)	255 (44.7)	75 (50)
5-9 drugs	222 (50.5)*	91 (32.3)	313 (43.4)	251 (44)	62 (41.3)
>10 drugs	25 (5.7)	18 (6.4)	43 (6)	32 (5.6)	11 (7.3)
Medication errors					
Dose omission error	165 (37.6)	98 (34.8)	263 (36.5) 206	206 (36.1)	57 (38)
Wrong time error	137 (31.2)	69 (24.5)	(28.6)	163 (28.5) 35	43 (28.7)
Wrong dose error	29 (6.6)	2 (7.8)	51 (7.1)	(6.2)	16 (10.6)
Wrong drug error	4 (0.9)	4 (1.4)	8 (1.1)	7 (1.2)	1 (0.6)
Total**	250 (56.9)	141 (50)	391 (54.2)	314 (55)	77 (51.3)
PIMs					
Table 2-related PIMs	121 (27.6)	70 (24.8)	191 (26.5)	122 (21.3)	69 (46.0)*
Table 3-related PIMs	12 (2.7)	7 (2.5)	19 (2.6)	12 (2.5)	5 (3.3)
Table 4-related PIMs	14 (3.2)	8 (2.8)	22 (3.1)	3 (0.5)	19 (12.7)*
Table 5-related PIMs	18 (4.1)	10 (3.5)	28 (3.9)	20 (3.5)	7 (5.3)
Table 6-related PIMs	3 (0.7)	1 (0.4)	4 (0.6)	3 (0.5)	1 (0.7)
Total***	136 (31)	81 (28.7)	217 (28.3)	127 (20.8)	90 (56.7)

*p<0.001, **Some patients have more than one medication error, ***Some patients have more than one potentially inappropriate medication use.

2.2±1.5, while that in patients using PIMs was 2.9±1.5 (p<0.001). The use of Table 2- and Table 4-related PIMs was higher in the ≥75 year-old group. No difference was found between gender and age groups with regard to the other categories of PIMs. The most common instances of Table 2-related PIM use were the inappropriate use of PPIs (n=72), potent anticholinergics (n=44), NSAIDs (n=24), antithrombotics (n=16), and digoxin (n=15), while those of Table 3-related PIM use was inappropriate drug use in patients with dementia (n=9) and heart failure (n=5). The most common Table 4-related PIM use was inappropriate use of acetyl salicylic acid (ASA) (n=22), while the most common Table 5-related PIM use was the combined use of antidepressants and ≥2 central nervous system-active drugs (n=19). With regard to Table 6-related PIMs, 4 patients used drugs without dose reduction in accordance with the degree of renal insufficiency.

Discussion

Polypharmacy is commonly observed in elderly. In community-based telephonic survey conducted in 1998 and 1999 in the USA,[10] the rates of polypharmacy and excessive polypharmacy were reported to be 57% and 12% in elderly females and, 44% and 12% in elderly males, respectively. Moreover, the rate of polypharmacy was reported to be 59.6% in a study conducted in patients living in a nursing home in Turkey,[11] 26.7% in a study conducted in 67 primary care practices in Germany,[12] 47.6% in a study on female patients in a geriatric outpatient clinic in Turkey,[13] and 45% in a study on patients aged ≥75 year-old who were admitted to the emergency services in England.[14] In the case of hospital-based studies, in a study on patients admitted to 5 hospitals in Norway,[15] the rate of polypharmacy on admission was reported to be 47%. In another study conducted

in 38 internal medicine wards in Italy,[16] the rate of polypharmacy was 51.9% on admission and 67% at discharge. Similarly, in the present study, the rates of polypharmacy and excessive polypharmacy were found to be 49.4% and 6%, respectively.

Chronic diseases are the most common cause of polypharmacy. In a study elderly females admitted to a geriatrics outpatient clinic in Turkey,[13] the most common chronic diseases were found to be hypertension (75.3%), depression (45.5%) and dementia (39.4%). Moreover, in a study on patients hospitalized in internal medicine clinics in Italy, the most frequent diagnoses were hypertension (57.8%), diabetes mellitus (24%) and coronary heart disease (23%).[16] In another study on patients hospitalized in Jordan, the most frequent diagnoses were hypertension (74.4%), diabetes (58.7%) and chronic kidney disease (34.2%).[17] Similarly, in the present study, the most common chronic diseases were found to be hypertension (65.6%) and diabetes (36.2%).

Medication errors may occur at various stages, such as prescribing the medication, supplying the medication, injecting the medication, and taking the medication home. PIMs associated with the prescription phase and medication errors made by patients at home were assessed in the present study.

The use of PIMs is common in the elderly. In a community-based study conducted at the homes of 423 elderly people in Brazil,[18] the rates of PIM use according to the 2012 Beers Criteria and STOPP Criteria version 2 were found to be 42.1% and 46.2%, respectively. The most common PIMs reported in that study were clonazepam-benzodiazepine, amiodarone-antiarrhythmic drugs, and glibenclamide/glyburide-sulfonylureas. In another study on patients who were admitted to a geriatrics outpatient clinic of a university hospital in Turkey[19] between 2010 and 2014, examination of the files of 667 randomly selected patients according to the 2012 Beers Criteria and STOPP Criteria version 2 revealed that the rates of PIM use were 33.3% and 39.1%, respectively. In that study, the 3 most common PIMs according to the 2012 Beers Criteria were antipsychotics, selective serotonin reuptake inhibitors (SSRIs) and nonsteroidal antiinflammatory drugs (NSAIDs). In another study on 835 patients who were admitted to an emergency department in Turkey,[20] the rates of PIM use according to the 2012 Beers Criteria and STOPP Criteria version 2 were found to be 52.9% and 51.6%, respectively. In that study, the most common PIMs according to the 2012 Beers Criteria were SSRIs, potent anticholinergics, NSAIDs, and ASA.

Moreover, in a study on 456 patients hospitalized in the department of geriatric care of a university hospital in China,[21] the rate of PIM use according to the 2012 Beers Criteria was found to be 44.7%, while that according to the 2015 Beers Criteria was found to be 53.5%. In that study, the most common PIMs according to the 2015 Beers Criteria were PPIs, benzodiazepines and benzodiazepine receptor agonists.

In a retrospective study examining the records of 95 elderly people in two assisted living facilities in the USA,[22] the rate of PIM use was found to be 60% according to the 2015 Beers Criteria. The most common PIM was central nervous system agents in that study. Moreover, in a study on 351 patients admitted to internal medicine and surgical wards in Jordan,[17] the rate of PIM use was 29.3% on admission and 47.2% during hospitalization according to the 2015 Beers Criteria. The most common PIMs before admission were PPIs (26.2%), alpha blockers (5.1%) and digoxin (4%) in that study. PPIs were also the most common PIMs during hospitalization (42.5%), followed by alpha blockers (4.8%) and metoclopramide (4.3%). In another study evaluating the data of 2231 patients using pharmacy records in Argentina,[23] 1623 patients (72.75%) were found to have received at least one PIM during the study period according to the 2015 Beers Criteria. In that study, the most common PIMs were anxiolytics (46.03%), PPIs (29.67%), and NSAIDs (22.37%).

Compared with the 2012 Beers Criteria, the most important changes in the 2015 Beers Criteria are the addition of 2 new tables on specific drug interactions and specific drugs requiring renal dose adjustment. In addition, PPIs and endocrine drugs have been added to the table of drug categories. PPIs have been added to the PIM list with instructions to ''avoid use for > 8 weeks except in high-risk patients (eg, patients taking oral corticosteroids or chronic NSAIDs) or those with erosive esophagitis, Barrett's esophagus, pathological hypersecretory condition, or therapeutic failure of H2 blockers''.[7,24] PPIs were

found to be the most frequently used PIM in the present study, according to 2015 Beers Criteria, similar to previous findings.

Patient-related medication errors are a relatively less researched issue. Instances of medication nonadherence in the form of dose omission error, dosage errors and wrong drug errors are frequently reported medication errors.[4] In a study conducted in the USA,[25] the rate of medication nonadherence in 147 elderly patients in a period of 2 weeks after discharge from the hospital was found to be 30.6%. In another study conducted by interviewing 382 elderly patients in Spain,[3] medication errors were noted in 75% of the patients. Moreover, 4% of the patients were found to have ≥ 4 medication errors. In the present study, 54.2% of the patients had medication errors, with the most common medication errors being dose omission (36.5%) and wrong time errors (28.6%); these errors were significantly higher in patients with polypharmacy ($p<0.01$).

The main limitation of the present study was that the data were obtained from a single center. However, we think that our data represent the patient profile of a tertiary university hospital in our country.[13] Another limitation was that the data of the drugs used by the patients were based on their own statements. However, to minimize this risk, the patients were asked to bring their drugs at the next visit, and were questioned in detail about their drug use patterns, medication errors and ADRs. In addition, the patients' files and the Social Security Institution prescription system were examined in order to obtain the most accurate information about the drugs used by the patients.

Conclusions

In conclusion, similar to previous findings, the present results revealed that the number of drugs used and the rates of polypharmacy increased with an increase in the number of chronic diseases. Consequently, the rates of medication errors, PIM use and ADRs also increased. Therefore, to reduce the potential risks in the elderly, a comprehensive geriatric assessment should be performed for all patients, drugs should be prescribed according to rational drug use recommendations and patients should be explained in detail about how to use their drugs. Following this, at each visit, patients should be carefully questioned how they use the drugs and about drug-induced adverse effects.

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Conflict of interest

The authors declared that there are no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Authors' Contribution

Study Conception: CD; Study Design: CD, EP; Supervision: CD, EP, DS; Fundings: EP, CD; Materials: EP; Data Collection and/ or Processing: EP, CD; Analysis and/or Interpretation: CD, EP, DS; Literature Review: EP, CD, DS; Writer: EP, CD, DS; Critical Review: CD, EP, DS; Statistics: DS.

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