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Eskişehir Osmangazi University Health Application and Research Hospital Multiple Drugs Usage and Prevalent Using the Frequency of 65 Years and Patients Applied to Neurology Policlinic

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Abstract:
Objective: *Increased comorbid diseases, pharmacokinetics and pharmacodynamic changes in elderly causes drug side effects more common in the elderly. The aim of our study was to determine the prevalence of multiple drug use and inappropriate drug use in elderly patients.*
Materials and Methods: *The study included 474 volunteer patients aged 65 years and older who applied to Eskişehir Osmangazi University Health Application and Research Hospital Neurology Clinic. According to the Beers 2015 and STOPP version 2 criteria, the suitability of the drugs used by the patients, the criteria which are not appropriate according to the criteria of inappropriate drugs and how many criteria violations are evaluated.*
Results*: In elderly patients, the prevalence of polypharmacy was found to be 39.1% with the use of STOPP version 2 and the rate of inappropriate drug use with Beers 2015 was found to be 33.3%.*
Conclusion: *The use of inappropriate medication should be considered in elderly people who use a large number of drugs because of more than one chronic disease. In elderly patients, the treatment dose should be individualized, drug side effects and drug interactions should be taken into consideration and guidelines should be taken for correct indications.*

Keywords: *Elderly, Neurology, Polypharmacy*

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I. Introduction

Although there are different definitions of polypharmacy, it is generally defined as the use of 5-10 drugs. The use of more than 10 drugs is characterized as excessive polypharmacy (1). There are many causes of multiple drug use in the elderly. The most important reason is multiple disease (2). The administration of another drug to treat the side effect caused by the drug used is called prescription cascade and is an important cause of multiple drug use. When the patients apply to more than one physician, physicians prescribing unconscious drug cause polypharmacy with the use of more than one drug with the same active substance (3). The other important reasons of polypharmacy are physicians do not pay attention to drug effects and drug interactions, hospitalizations in the last six months, many drug expectations of patients, symptomatic treatment in elderly, tendency of doctors to start a new drug, sale of non-prescription medicine, depression, vision, hearing problems, cognitive dysfunction, carer insufficiency, patient satisfaction and low education level (4).

Elderly patients are more susceptible to drug side effects and need more hospitalization because of side effects. Polypharmacy; drug-drug interaction, drug incompatibility, hospitalization rate and mortality risk are also associated with an increase (5). In addition, with the use of multiple drugs, weight loss, functional and cognitive impairment, and the incidence of urinary incontinence increases (6). Polypharmacy results in increased drug side effects, inappropriate drug use, increased hospitalization, increased treatment costs and medication errors (7). Approximately 30% of hospitalizations are caused by problems with drugs (8). In addition, the use of 4 or more drugs is associated with an increased risk of falls and the risk of recurrent falls (9).

Progress in the health sector in Turkey and in the world and has prolonged the life expectancy of improving living standards. Therefore, the elderly population is increasing. Increased drug use with age,

pharmacodynamic and pharmacokinetic changes increase drug side effects. Improper prescribing may be defined as medical prescription incompatible with accepted medical standards'. In many studies, the suitability of drugs is evaluated according to Beers' criteria (10). When writing a prescription, writing medicines that comply with these criteria reduce the side effects and costs associated with the drugs. The aim of this study is; To determine the use of multiple drugs in patients over 65 years of age, the appropriateness of the drugs used according to the STOPP (Screening Tool of Older Person's Prescription) and Beers criteria, and to investigate the effect of inappropriate drug use on clinical outcome.

II. Material and Method

Our study is a prospective, observational study involving 474 patients. The patients' complaints to the polyclinic, additional diseases, the drugs and the number of drugs used, sociodemographic information of the patients and the fall conditions in the last year were recorded in the data form. According to the Beers 2015 and STOPP version 2 criteria, the suitability of the drugs used by the patients, the criteria which are not appropriate according to the criteria of inappropriate drugs and how many criteria violations are evaluated. The study was evaluated with Modified Morisky Scale. The answers of the questions were determined as yes and no. The second and fifth questions were answered with 0 points, yes and 1 points; The answer to the first, third, fourth and sixth questions was rated as 0 points and no answer was 1 point. The first, second and sixth questions indicate a low motivation level of 0 points or 1 point, and a high motivation level greater than 1 point. If it gets 0 points or 1 points from the third, fourth and fifth questions, it shows the higher level of knowledge if it gets higher than 1 point. (11).

In the statistical analysis of the data, the package programs of IBM SPSS Statistics 21.0 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) were used. Continuous data are given as mean ± standard deviation, median (Q1-Q3). Categorical data are given as percentage (%). Shapiro Wilk Test was used to determine the appropriateness of data to normal distribution. Spearman's correlation coefficients were calculated for variables that did not conform to normal distribution in evaluating the direction and magnitude of correlation between variables. Pearson's chi-square and Pearson chi-square analyzes were used in the analysis of the cross tables. Cohen Kappa Test was applied to determine the level of compliance, conformity and similarity of the violation criteria. A p value of <0.05 was considered as a criterion for statistical significance.

III. Results

The mean age of the patients was 71.19 ± 6.1 years. Of the 474 patients included in the study, 213 (44.9%) were female and 261 (55.1%) were male. When the marital status of the patients was examined, 6 (1.3%) were single, 333 (70.3%) were married, 23 (4.9%) were divorced, and 112 (23.6%) had lost their spouse. There were 127 (26.8%) non-readers, 258 (54.4%) primary school graduates, 54 (11.4%) high school graduates and 35 (7.4%) high school graduates. When the average monthly income status was evaluated, there were 220 (46.4%) patients with minimum wage limit and 254 (53.6%) patients with minimum wage level.

When the number of additional diseases was examined, it was observed that the patients with a minimum of 0 were at least 7 additional diseases (Median = 3.00 (2.00-4.00)). When the chronic diseases of the patients were examined, the most common diseases were HT (Hypertension) (62.7%), SVO (Cerebrovascular accident) (42.8%), DM (Diabetes Mellitus) (33.3%), CAD (Coronary Artery Disease) (23.8%), Parkinson's disease. (17.9%), Dementia (13.3%), Neuropathy (7.2%), Chronic Obstructive Pulmonary Disease (7.0%), Epilepsy (6.1%), HF (Heart Failure) (4.9%), CRF (Chronic Renal Failure) (%) 3.6), Gastrointestinal System diseases (1.5%), Migraine (0.2%), Multiple Sclerosis (0.2%) was found. 474 patients were taking 2573 medications in total. The average number of drugs they used was 5.42 ± 2.51; The median was 5.00 (4.00 - 7.00).

Table 1. Number of Drugs Used and Patient Distribution

Number of Drugs Used	Number of patients	Percent (%)
1 – 5	284	59.9
6 – 9	161	34.0
10 ≤	29	6.1
Total	474	100.0

There was no statistically significant relationship between the number of drugs used and the age of the patients ($r = 0.039$, $p = 0.397$). When the relationship between the chronic diseases of the study group and the number of drugs they used was examined, the most common polypharmacy among all chronic diseases was CRF (58.8%), neuropathy (52.9%), HF (52.2%) and the most frequent polypharmacy (10.6%) in patients with CAD. Among the neurological diseases, the most common polypharmacy was neuropathy with 52.9% and the most common polypharmacy was 6.3% with dementia. In our study, when the drugs used by the patients were

evaluated according to the Beers criteria, a total of 357 inappropriate uses were detected. The use of inappropriate drug was determined in 193 (40.7%) patients according to the Beers criteria. When the drugs used by the patients were evaluated according to the STOPP criteria, a total of 284 inappropriate use cases were determined. According to the STOPP criteria, 187 (39.5%) patients had inappropriate drug use (Table 2).

Table 2. Unsuitable Drug Use according to Beers and STOPP ver.2 Criteria

Number of Violated Violations	Beers Criteria		STOPP Ver. 2 Criteria	
	Number of patients	Percent (%)	Number of patients	Percent (%)
0	281	59.3	287	60.5
1	101	21.3	119	25.1
2	52	11.0	47	9.9
3	24	5.0	14	3.0
4	7	1.5	6	1.3
5	6	1.3	1	0.2
6	1	0.2	0	0.0
7	1	0.2	0	0.0
9	1	0.2	0	0.0
Total	474	100	474	100

Table 3 shows the distribution of inappropriate drug use according to Beers and STOPP criteria by sex, age and number of drugs.

Table 3. Distribution of Violation Criteria According to Gender, Age and Drug Number

		Use of inappropriate medicine by Beers	Use of inappropriate medicine by STOPP	According to Beers and STOPP
Gender	**Female**	91	79	52
	Male	102	108	71
Age group	**65-84**	189	184	121
	85≤	4	3	2
Medicine	**1-5**	84	82	50
	6-9	86	83	56
	10≤	23	22	17

The number of patients using inappropriate drugs according to at least one of the Beers and STOPP criteria is 257 (54.2%). In 63.7% of 193 patients who violated the Beers criteria, 65.7% of 187 patients with a violation of the STOPP criterion, STOPP criteria violation, also a Beers criterion violation. There was a moderate significant relationship between Beers and STOPP criteria (Kappa = 0.412; p <0.001). There was a statistically significant relationship between the number of additional diseases and the number of Beers and STOPP criteria violations. (Table 4).

Table 4. Additional Disease - Relationship Between Beers and STOPP Criteria Number of Infringements

	Beers Criterion Number of Violations	Stopp Criterion Number of Violations
Total Number of Additional Diseases	0.196; <0.001	0.185; <0.001

Spearman Correlation Test

Most frequently used drugs according to Beers criteria are COX (Cyclooxygenase) non-selective NSAID (Non-Steroidal Anti Inflammatory Drug) 30 (6.3%) people, peripheral alpha blocker 26 (5.5%) people, antipsychotic 18 (3.8%) people, antidepressants and metoclopramide was identified as 12 (2.5%) individuals (Table 5). According to the Beers criteria, the most frequently used drug group was cardiovascular system (8.2%) and central nervous system (8.0%) criteria (Table 5).

Table 5. Use of Potentially Unsuitable Drugs to Avoid in Elderly People

Organ, System, Drug Groups	Inappropriate Drug	Number of patients	Percent (%)
Anticholinergics	**No**	461	97.2
	Yes- Antihistamine	4	0.9
	Yes- antispasmatic	9	1.9
Antithrombotic	**No**	474	100.0
	Yes	0	0.0
Anti-infective	**No**	472	99.6
	Yes	2	0.4
Cardiovascular	**No**	435	91.8
	Yes- Peripheral alpha blocker	26	5.5

	Yes- Digoxin	11	2.3
	Yes- Amiodaron	2	0.4
Central Nervous System	**No**	436	92.0
	Yes- Antidepressants	12	2.5
	Yes- Antipsychotic	18	3.8
	Yes- Benzodiazepine	7	1.5
	Yes- Barbiturate	1	0.2
Endocrine	**No**	467	98.5
	Yes	7	1.5
Gastrointestinal	**No**	462	97.5
	Yes- Metoclopramide	12	2.5
Pain	**No**	443	93.4
	Yes- COX non-selective NSAIDs	30	6.3
	Yes- Skeletal muscle myorelaxant	1	0.3

The most common criteria violations by STOPP criteria are; Antiplatelet / anticoagulant drugs were detected in 65 (13.8%) patients, duplications were found in 58 (12.2%) patients, SSS drugs were in 39 (8.1%) patients and 29 (6.1%) patients in the elderly increased the risk of falling (Table 6).

Table 6. Breakdown of Criteria According to STOPP Criteria

Pharmaceutical Groups	Inappropriate Drug	Number of patients	Percent (%)
Duplication	**No**	416	87.8
	Yes	58	12.2
Cardiovascular System Drugs	**No**	459	96.8
	1 Criteria violation	15	3.2
Antiplatelet /Anticoagulant Drugs	**No**	409	86.2
	1 Criteria violation	48	10.2
	2 Criteria violation	17	3.6
Central Nervous System Drugs	**No**	435	91.9
	Yes-Tricyclic Antidepressants	3	0.6
	Yes-Delirium-Anticholinergic	11	2.3
	Yes-Acetylcholinesterase	15	3.2
	Yes-Dopamine Agonist	3	0.6
	Yes-Antihistamine	3	0.6
	Yes-Urinary Neuroleptic	1	0.2
	Yes-Parkinson's-Antipsychotic	1	0.2
	Yes-Psychosis-Neuroleptic	1	0.2
	Yes-Dementia-Neuroleptic	1	0.2
Gastrointestinal System Drugs	**No**	469	98.9
	Yes	5	1.1
Respiratory System Drugs	**No**	466	98.4
	Yes- Antimuscarinic	3	0.6
	Yes- Non-Selective Beta Blocker	3	0.6
	Yes- Benzodiazepine	2	0.4
Musculoskeletal Drugs	**No**	460	97.0
	Yes	14	3.0
Urogenital System Drugs	**No**	457	96.4
	Yes- Antimuscarinic	17	3.6
Endocrine System Drugs	**No**	466	98.3
	Yes- Sulfonylurea	6	1.3
	Yes- Thiazolidinediones	1	0.2
	Yes- Beta Blocker	1	0.2
Drugs That Increase the Risk of Falling in the Elderly	**No**	445	93.9
	Yes- Benzodiazepine	11	2.3
	Yes- Neuroleptic	18	3.8
Analgesic Drugs	**No**	473	99.8
	Yes	1	0.2
Antimuscarinic /Anticholinergic Drug Burden	**No**	464	97.9
	Yes	10	2.1

When the motivation and information status of the patients according to the modified Morisky treatment compliance scale, 108 (22.7%) patients had high motivation and 148 (31.2%) patients had high level of knowledge. When motivation status is examined, it is seen that marital status, education level and monthly average income have a significant effect on motivation level. When the Beers and STOPP criteria and the impact of their numbers on the motivation status were analyzed, it was observed that the number of STOPP criteria violations and their existence had a significant impact on motivation, and that the number of Beers criteria violations had a significant impact on motivation but the presence of criteria did not affect. When the factors affecting the levels of knowledge were examined, it was seen that the age group, marital status,

education level and monthly average income had a significant effect on the level of knowledge, and the number and presence of STOPP and Beers criteria violations did not significantly affect the knowledge level.

IV. Discussion and Conclusion

In the study of Qato et al. In the USA between the ages of 57-85, the use of multiple drugs was found to be 35-40% in individuals aged 75-85 years (12). In the study performed by Sacred et al., 1433 people aged 65 years and older; 84.7% of the participants stated that they used at least 1 drug that they used continuously (13). Istanbul University Faculty of Medicine, Geriatrics Department clinic registered 65 years and in studies in patients on inappropriate use of drugs that can be detected by STOPPER version 2 39.1%, and the inappropriate use of drugs detected by Beers in 2012 was 33.3% (14). In our study, when the drugs used by the patients were evaluated according to the Beers criteria, the use of inappropriate drugs in 193 (40.7%) patients and the inappropriate use of medication in 187 (39.5%) patients were determined according to STOPP criteria. The difference in the health system in the country, is variable accessibility to patients' health units, ease of patient access to prescription drugs, awareness about drugs, we believe the knowledge and socio-cultural differences as the reason for the variability between countries of improper drug use. Since we could not evaluate all the criteria due to the fact that data such as glomerular filtration rate and systolic ejection fraction could not be evaluated, we found that the rates we found are actually much higher.

Beers and STOPP criteria were evaluated in the studies. Brown J.D. et al. (2012) found a moderate agreement (kappa = 0.58) between the 2012 Beers Criteria and STOPP Criteria in the US study (15). Bahat et al. In 2017, Beers found moderate compliance (kappa = 0.44) when he evaluated the consistency between the 2012 and STOPP criteria (16). In our study, it was found that there was a moderate significant relationship between Beers and STOPP criteria (kappa = 0.412; p <0.001). Bahat G. et al. According to STOPP, most frequently used drugs were aspirin (14.8%), antipsychotics (13.9%), anticholinergics (13.0%), antipsychotics according to Beers criteria (29.4%), SSRI (Selective Serotonin Reuptake Inhibitors) (14.4%). It was found to be NSAID (9.3%) (14). In a study conducted on patients diagnosed with new Alzheimer's disease in Norway and a healthy control group, it was found that the number of drugs used by Alzheimer's patients was higher and they used more anticholinergic, sedative and antidepressant drugs (17).

In our study, the most frequently used drugs according to the Beers criteria were COX non-selective NSAID (6.3%), peripheral alpha-blocker (5.5%), antipsychotic (3.8%), antidepressants and metoclopramide (2.5%). According to the Beers criteria, the most frequently used drug group was cardiovascular system (8.2%) and central nervous system (8.0%). The most common criteria violations by STOPP criteria are; Antiplatelet / anticoagulant drugs (13.8%), duplication (12.2%), central nervous system drugs (8.1%), and drugs that increase the risk of falling in the elderly (6.1%). There are significant differences between countries and studies among the drugs used as inappropriate by STOPP or Beers criteria. The reason for this is probably due to the prevalence of disease in society, the differentiation of prescribing practice and the differences in drug content-forms available in the market.

An important consequence of the use of multiple drugs in the elderly is a fall. Examples of drugs that may cause falls include sedative / hypnotics, antiarrhythmic drugs, diuretics, antidepressants, antihypertensives, neuroleptics, antiparkinsonian agents, antidiabetics and anticonvulsants (18). In our study, the most common neuroleptic drugs were 3.8% and the benzodiazepines were 2.3%. The findings of our study suggest that inappropriate drug use should be considered especially in elderly people with multiple chronic diseases. In elderly patients, the treatment dose should be individualized, the side effects and drug interactions should be taken into consideration and the drug should be started according to the guidelines and the correct indications should be followed.

As a result, the aim of Beers and STOPP criteria is to increase the appropriateness of prescribing, increase the quality of the drug and to reduce inappropriate drug use. Current criteria are effective in determining inappropriate drug use in our country. We believe that it would be useful to increase the clinical use of our country to reduce the prevalence of inappropriate drug use and related negative consequences.

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