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Original Article

Evaluation of polypharmacy and its effects in geriatric age group patients applying to the internal diseases outpatient clinic

Sinem Gürcü[1], Melisa Şahin Tekin[2], Pınar Yıldız[3], Göknur Yorulmaz[4]

[1]Eskişehir City Hospital, Department of Pharmacy, Eskişehir, Turkey

[2]Eskişehir Osmangazi University, Faculty of Medicine, Department of Internal Medicine, Eskişehir, Turkey

[3]Eskişehir Osmangazi University, Faculty of Medicine, Department of Internal Medicine, Eskişehir, Turkey

[4]Eskişehir Osmangazi University, Faculty of Medicine, Department of Internal Medicine, Division of Endocrinology, Eskişehir, Turkey

ORCID IDs of the authors

SG: https://orcid.org/0000-0001-8534-7369

MŞT: https://orcid.org/0000-0002-4077-7258

PY: https://orcid.org/0000-0002-3625-9829

GY: https://orcid.org/0000-0001-8596-9344

Correspondence:

Author: Sinem Gürcü

Address: Eskişehir City Hospital, Department of Pharmacy, Eskişehir, 26100, Turkey

Phone: +90 530 294 86 58

e-mail: sinemgurcu@yahoo.com.tr

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Abstract

Objective: The world population is aging and the elderly population is trying to cope with chronic diseases and multiple drug use. Polypharmacy can be defined as the combined use of four or more drugs. Pharmacokinetic and pharmacodynamic changes of drugs and drug-drug interactions in old age may affect this age group much more. In the study, it was aimed to determine the levels of drug interactions in geriatric age group patient prescriptions.

Methods: In this study, drug-drug interactions were investigated in outpatients over the age of 65 who had 4 or more drugs prescribed. A total of 119 prescriptions were included in the study. The average number of drugs in prescriptions is 5.23 (min 4 max 12).

Results: No statistically significant difference was found between the mean age of men and women in the study. The group of drugs that interact most frequently is antidiabetic drugs. In second place are diuretics and nonsteroidal anti-inflammatory drugs (NSAIDs); angiotensin converting enzyme (ACE) inhibitor drugs are in the third place.

Conclusion: Prevention of polypharmacy and its related problems will benefit both the patient and the cost. By avoiding polypharmacy or at least by following guidelines when prescribing, geriatric patients' drug compliance will increase, all side effects and interactions that may be caused by inappropriate drug use will be kept to a minimum, and possible hospitalizations and health expenses will be reduced in this way.

Keywords: Drug-drug interaction, geriatrics, polypharmacy.

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INTRODUCTION

With economic development, a drop in the birth rate, and an increase in the use of modern medicine, the world's population is aging quickly. The population's aging is now recognized as a significant personal and social phenomenon. In the United States of America (USA), there are currently about 35 million people over the age of 65, and by 2030, this number is projected to rise to 70 million (1). According to the World Health Organization (WHO), in 2025, there will be about 2 million people who are 60 or older, and by 2050, 80% of those 2 million elderly people will still be living in developing nations (2). Numerous medications are used to treat chronic diseases, which become more prevalent as people age. It is challenging to control therapy for geriatric patients because to changes in medication metabolism caused by pharmacodynamic and pharmacokinetic factors, an increase in side effects, and drug interactions. In the literature, polypharmacy is defined in various ways. In accordance with the National Service Framework (NSF), polypharmacy is the use of four or more medications (3). Though it can be argued that polypharmacy may be advantageous to the patient when it is controlled so that drugs can interact favorably in some treatments, such as those for hypertension, it may also present potential issues due to side effects that are expected or unexpected, toxic effects, and drug interactions. Drug side effects can be more severe in the elderly due to changes in physiologic activities in aging systems, which can impact the pharmacokinetic and pharmacodynamic properties of medications. Saliva production declines, gastrointestinal motility slows with age, and body fat mass rises as muscular mass falls. Drug effects in the body change as a result of variations in renal and hepatic blood flow, two organs that are crucial to drug metabolism (4, 5). The elderly are a sensitive group for a variety of reasons, thus drug usage in this community shouldn't be compared to that in other adults. Prescriptions for elderly individuals were examined in this study. It was intended to increase awareness that common outpatient prescriptions could cause significant issues for patients by carefully examining drug interactions in prescriptions.

MATERIALS AND METHODS

In the study, the prescriptions of patients over the age of 65 who applied to the Internal Medicine Polyclinic for any reason between January 2021 and June 2021 were retrospectively analyzed. Patients' demographic data were collected from patient files retrospectively. The number of drugs in the prescription was determined as a minimum of 4, prescriptions with 3 or fewer drugs were not included in the study. The drug interactions were analyzed by using RxMediaPharma™, a software program available for only medical professionals by purchasing. Drug interactions are classified into three levels, "Low", "Moderate" and "Major", according to the clinical severity of the interaction. Low-level interactions, such as decreased elimination of vitamin B12; moderate interactions include additive interactions that are not serious when some drugs are used together, and major-level interactions include interactions that can be life-threatening. Power analysis was not performed in the study. Prescriptions suitable for the study design in the geriatric population were included in the study.

Statistical analysis:

Statistical Package for the Social Sciences (IBM SPSS) 21.0 program was used for statistical evaluation. A P-value lower than 0.05 was considered statistically significant. Data are given as numbers or %. The Chi-square test was used to compare categorical variables.

RESULTS

A total of 119 prescriptions were included in the study. 46.22% (n=55) of the prescriptions belonged to women and 53.78% (n=64) of them belonged to men. The average number of drugs in prescriptions was 5.23 (min 4 max 12). The average age of

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prescription holders was 69.44 years. The mean age of female patients was 69.56 (min 65 max 85); the mean age of male patients was 69.32 (min 66, max 82). There was no significant difference between the mean age of women and men (p=0.061).

A total of 4 major, 46 moderate, and 10 low-level interactions were detected in 119 prescriptions in the study, and no interaction was detected in 22 prescriptions. The interaction contents are indicated in Table 1.

Table 1. Drug interactions and classification

Interaction	**Number**
Major	
Quinolone x Antidiabetics	3
Antigut x Diltiazem	1
Moderate	
Antidiabetics x Beta-blockers	5
Antidiabetics x Angiotensin-Converting Enzyme (ACE) inhibitors	5
NSAID x Corticosteroid	5
Diuretics x Digitals	4
NSAID x ACE inhibitors	4
Diuretics x ACE inhibitors	4
Antidiabetics x Thiazide	4
Antiplatelets x Statins	4
PPI x Oral iron preparations	3
Antiplatelets x PPI	3
Antiplatelets x Pentoxifylline	3
Quinolones x Oral iron preparations	2
Low	
Metformin x B12	6
Iron x Zinc	4

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When all interactions are examined, the most frequently interacting group of drugs is antidiabetic drugs. In second place were diuretics and nonsteroidal anti-inflammatory drugs (NSAIDs); Angiotensin Converting Enzyme (ACE) inhibitors were in third place.

DISCUSSION

The purpose of drug therapy is to improve the management of diseases and thus to increase the patients' quality of life. Drug-related side effects or drug interactions are more common in older ages due to the increased frequency of chronic diseases, the increase in the number and types of drugs used, the use of prescription or non-prescription drugs, herbal treatments, dose repetition due to forgetfulness, and differences in the pharmacokinetic and pharmacodynamic properties of drugs. The problems associated with polypharmacy can be listed as drug side effects, drug-drug interactions, increased treatment expenditures, compliance issues to treatment' increased hospitalization and increased medication errors (6). In a study in Italy, it was reported that almost all patients aged 75 and overused at least one drug per day, and one-third of them used five or more drugs (7). In the meta-analysis Rollason et al. published, they reported that 20% of geriatric patients aged 70 and overuse five or more drugs (8). In studies about geriatric patients, the number of daily drug use was reported as 2-5 (9). In this study, we found the average number of drugs in prescriptions is 5.23, which is consistent with the literature. It is important because the increase in the number of drugs used is associated with the increase in drug interactions and drug side effects.

In our study, we found that quinolones and antidiabetics were used together in 3 different prescriptions. Quinolones have been associated with disorders in blood glucose homeostasis resulting from their effects on ATP-sensitive potassium channels of the pancreatic beta cell that regulate insulin secretion. For this reason, serious abnormalities in blood glucose levels may occur when these two drug groups are used together (10, 11). Diltiazem, an inhibitor of CYP450 3A4, when co-administered with colchicine can significantly increase serum concentrations of colchicine. One interaction was determined in our study. If colchicine is to be used together with CYP450 3A4 inhibitor drugs, it is recommended to reduce the dose of colchicine (12). Absorption of quinolones is significantly reduced due to chelation by cations such as iron salts. In our study, this interaction was observed in 2 prescriptions. However, the gap between the intake times of these two drugs (2-4 hours before or 4-6 hours after the quinolone intake) may not be clinically significant as it will minimize the interaction (13). Beta-blockers present pharmacodynamic interactions with antidiabetic drugs. Beta-blocker drugs may mask the symptoms of hypoglycemia such as tremors and sweating caused by antidiabetic drugs. It is known that cardioselective beta-blockers are safer than non-cardioselective agents in diabetic patients. However, the same risks associated with hypoglycemia apply to cardioselective beta-blockers. In our study, we detected this interaction in 5 prescriptions, and therefore, in clinical practice, patients should be warned about the symptoms of hypoglycemia if they use these drugs together (14, 15). Diuretics may predispose patients who are using digoxin to arrhythmias due to hypokalemia and hypomagnesemia. These two groups of drugs, which are included in 4 different patient prescriptions in our study, can be frequently prescribed by physicians. Therefore, when these drugs are used together, if patients experience symptoms of possible digoxin toxicity or electrolyte disturbances, such as weakness, drowsiness, muscle aches or cramps, nausea, anorexia, visual disturbances, or irregular heartbeat, they may be advised to consult a physician (16, 17). When nonsteroidal anti-inflammatory drugs are used together with ACE inhibitors, the risk of renal failure and a decrease in hypotensive effect are observed. In the study, interactions between NSAIDs and ACE inhibitors were observed in 4 prescriptions. When the past medical records of these four patients were analyzed, it was thought that they had taken NSAIDs for a short time. The use of NSAIDs for more than one week may pose a risk in terms of interaction, and it is recommended to monitor the patient's blood pressure (18). Because thiazide diuretics antagonize the hypoglycemic effect of antidiabetics, they

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increase blood sugar levels (19). By competitively blocking the binding of the Intrinsic Factor-Vitamin B12 complex to its receptor depending on calcium, metformin may result in decreased oral vitamin B12 absorption (20). ACE inhibitors can increase the effectiveness of oral antidiabetics (21). When diuretics and ACE inhibitors are used together, the hypotensive effect is increased additively. This interaction may be a convenient effect in clinical practice (22).

When clopidogrel and proton pump inhibitors (PPI) are used together, pantoprazole may decrease the serum concentrations of clopidogrel's active metabolites. The bioactivation of clopidogrel occurs by the enzyme CYP450 2C19.Since proton pump inhibitors have been shown to inhibit CYP450 2C19, an interaction is possible leading to decreased therapeutic efficacy and formation of the active metabolite of clopidogrel (23). Pentoxifylline prolongs the prothrombin time. Since clopidogrel inhibits platelet aggregation, the risk of bleeding increases when used simultaneously with pentoxifylline (24). Atorvastatin may inhibit the antiplatelet activity of clopidogrel by preventing its conversion to its active metabolite via CYP3A4 (25). The combined use of proton pump inhibitors (PPIs) and oral iron, which is seen in 3 prescriptions of our study group patients, is seen much more frequently in our geriatric patient prescriptions in our daily practice. Since PPIs reduce gastric acidity, gastrointestinal absorption of iron, which is dependent on an acidic environment, is impaired and iron absorption decreases (26). Concomitant use of corticosteroids and nonsteroidal anti-inflammatory drugs (NSAIDs) may increase the potential for serious gastrointestinal (GI) toxicity, including inflammation, bleeding, ulceration, and perforation. In this study, this interaction was observed in 5 different prescriptions (27). The interactions of oral iron and zinc preparations seen in four different prescriptions are potentially due to decreased absorption of each other (28).

In Steinman et al.'s study, it was observed that 128 of 196 patients (65%) had at least one inappropriate drug use, and the frequency of inappropriate drug use increased as the number of drugs used increased (9). According to the data of the Ministry of Health of the Republic of Turkey, 2 billion 19 million boxes of drugs were consumed in 2016 (29). In these data, analgesics are in the first place and antibiotics are in the second. According to Organization for Economic Co-operation and Development (OECD) data, Turkey ranks first place in the world with 42.2 per thousand antibiotic consumption (30). According to Masoodi et al.'s study in 2008, it was shown that adverse drug effects can be seen in 15% frequency with the use of two drugs; and raise to 58% with the use of five drugs (31). Adverse drug effects include drug side effects and drug interactions, and drug interactions are preventable adverse drug effects. For this reason, drug interactions should also be considered when prescribing.

There is a need for widespread use of algorithms such as BEERS and TIME TO STOP, TIME TO START that provide physicians with the opportunity to evaluate before prescribing drugs, to prevent problems associated with the irrational use of prescriptions and polypharmacy in the geriatric patient group (32-36).

In these criteria, drugs that are not suitable for use in the elderly patient group and potential interactions have been brought to the attention of physicians. Again, in line with the TIME criteria, physicians will have the chance to review drug contents and interactions before starting a new drug, and this will reduce drug side effects that elderly individuals frequently encounter in daily life. Polypharmacy, which is very common in the elderly, is an important medical condition that increases morbidity and mortality. It impairs quality of life and increases costs in both developed and developing countries. This situation makes it even more important to raise awareness of polypharmacy and take precautions, if possible. Because of this, before starting a new drug to elder people, a comprehensive geriatric evaluation should be made with an interdisciplinary approach, the indication should be made sure, the current functional capacity should be evaluated, and a new drug should be started by considering other drugs that are constantly used.

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Limitations:

Due to the retrospective design of the study, the inability to differentiate the drugs used by the patients and the duration of use is the limitation of our study. Larger data can be obtained with longer periods and larger samples.

CONCLUSION

The most important condition for the prevention of polypharmacy, and the problems that may develop due to it, is awareness. It is necessary to act with the knowledge that prescribing medication for an elderly patient is as important as making a diagnosis, and to be aware that we can provide benefits without harming the patient. By avoiding polypharmacy, or at least by prescribing follow guideline when prescribing, geriatric patients' quality of life will increase, all side effects and interactions that may result from inappropriate drug use will be kept to a minimum, and possible hospitalizations and health expenses will be reduced.

Conflicts of interest: The authors declare no conflict of interest.

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Ethical approval and consent to participate: All the methods in the study were approved by the Non-Interventional Clinical Research Ethical Committee of Eskişehir Osmangazi University (Date: 14/12/2021 #459). The study was carried out in accordance with the statement of Helsinki Declaration.

Authorship Contributions: Design of the study; SG, GK - Supervision; MŞT, PY, GK - Data collection &/or processing; SG, MŞT - Performed data analysis; SG - Literature search; SG - Written by; SG, PY, MŞT and GK - Critical review; PY, GK.

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