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RESEARCH

DETERMINATION OF POLYPHARMACY AND INAPPROPRIATE DRUG USE IN PATIENTS AGED OVER 65 YEARS WHO PRESENTED TO THE EMERGENCY DEPARTMENT

ABSTRACT

Introduction: No study in the literature has reported the rate of inappropriate drug use among older patients admitted to emergency department in Turkey. This study aimed to evaluate polypharmacy and inappropriate drug use by elderly patients admitted to the emergency department.

Materials and Method: Patients aged ≥ 65 years were prospectively assessed for appropriateness of drugs they use between March and May 2016 according to both the 2012 Beers Criteria and STOPP Version 2 Criteria. Inappropriate drug use was separately assessed according to these criteria, and both patient and drug counts were calculated to assess inappropriate drug use in the study population. Age, gender, date of admission to the emergency department, blood pressure, pulse rate, respiratory rate, body temperature, oxygen saturation, state of consciousness, additional diseases, number of drugs used, names of drugs used, clinical outcome were recorded.

Results: Among 835 study participants, 406 (48.6%) were females and 429 (51.4%) were males. Mean age was 74.2 ± 6.6 years. The rate of polypharmacy and excessive polypharmacy was the highest in patients diagnosed with hypertension (35.0% and 16.0%, respectively) and lowest in patients diagnosed with chronic renal failure (2.0% and 2.0%, respectively). In total, 835 patients were using 5 637 drugs. Inappropriate drug use was present in 431 (51.6%) patients according to the STOPP Version 2 Criteria and in 441 (52.8%) according to the 2012 Beers Criteria.

Conclusion: Emphasis on inappropriate drug use will help physicians in the emergency department and other healthcare professionals reduce side effects and complications of medications and reduce emergency admissions to hospital.

Keywords: Inappropriate drug use; Potentially inappropriate medication list; Aged

ARAŞTIRMA

ACİL SERVİSE BAŞVURAN 65 YAŞ ÜZERİ HASTALARDA POLİFARMASİ VE UYGUNSUZ İLAÇ KULLANIMININ BELİRLENMESİ

Öz

Giriş: Türkiye’de acil servise başvuran yaşlı hastalarda literatürde herhangi bir uygunsuz ilaç kullanımı oranı bildirilmemiştir. Bu çalışma, acil servise başvuran yaşlı hastaların çoklu ilaç kullanımını ve uygun olmayan ilaç kullanımını değerlendirmeyi amaçlamıştır.

Gereç ve Yöntem: 65 yaşın üstündeki hastalar, 2012 Beers Kriterleri ve Yaşlı Kişilerin Potansiyel Olarak Uygun Olmayan Reçetelerinin Tarama Aracı Sürüm 2 Kriterlerine göre Mart ve Mayıs 2016 arasında kullandıkları ilaçların uygunluğu açısından prospektif olarak değerlendirildi. Uygun olmayan ilaç kullanımı, bu kriterlere göre ayrı ayrı değerlendirildi ve hem hasta hem de ilaç sayıları, çalışma popülasyonunda ki uygunsuz ilaç kullanımını değerlendirmek için hesaplandı. Yaş, cinsiyet, acil servise geliş tarihi, kan basıncı, nabız, solunum sayısı, vücut sıcaklığı, oksijen saturasyonu, bilinç durumu, ek hastalıklar, kullandığı ilaçlar ve isimleri ve klinik sonuçları kaydedildi.

Bulgular: 835 katılımcının 406’sı (% 49) kadın, 429’u (% 51) erkekti. Yaş ortalaması 74.18 ± 6.58 yılı Polifarmasi ve aşırı polifarmasi oranı, hipertansiyon tanısı alan hastalarda (sırasıyla% 35 ve % 16) en yüksek, kronik böbrek yetmezliği tanısı alan hastalarda en düşüktü (sırasıyla% 2 ve% 2). Toplamda 835 hasta 5.637 ilaç kullanıyordu. Yaşlı Kişilerin Potansiyel Olarak Uygun Olmayan Reçetelerinin Tarama Aracı Versiyon 2 Kriterlerine göre 431 (% 51.6) hastada uygunsuz ilaç kullanımı ve 2012 Beers kriterine göre 442 kişide (% 52.9) uygunsuz ilaç kullanımı mevcuttu.

Sonuç: Uygunsuz ilaç kullanımına önem verilmesi, acil servisteki hekimlerin ve diğer sağlık çalışanlarının ilaçların yan etkilerini ve komplikasyonlarını azaltmasına ve hastaneye acilen kabulü azaltmasına yardımcı olacaktır.

Anahtar sözcükler: Uygunsuz ilaç kullanımı; Potansiyel uygunsuz reçete; Yaşlılık

INTRODUCTION

In recent years, the awareness of potential risks of inappropriate drug use has increased along with polypharmacy (multiple drug use) in the older population (age, >65 years). Polypharmacy is a risk factor that is likely to cause undesirable consequences, such as hospitalization and falls, as older people are more vulnerable to drug–drug interaction, side effects, and dosing errors (1).

Although defined and classified in different ways in different resources, polypharmacy generally refers to the use of 5–10 drugs by a patient. Use of >10 drugs is defined as excessive polypharmacy (2). In older individuals, polypharmacy is quite common given that they are diagnosed with multiple diseases. In this group, polypharmacy makes treatment more complicated and increases length of hospitalization and costs (3). Approximately 30.0% of hospitalization results from problems related to drug use (4). Furthermore, older patients are more susceptible to side effects of drugs and thus cannot use every drug. Studies mostly refer to the 2012 Beers Criteria for Potentially Inappropriate Medication Use in Older Adults to evaluate the appropriateness of medication (5). Prescribing appropriate medications to older patients reduces side effects (6). The aim of this study is to determine the rate of inappropriate drug use in older patients who were admitted to our emergency department and to make recommendations to reduce inappropriate drug use.

MATERIALS AND METHOD

After approval was obtained from the local Ethics Committee, this study was conducted in the Emergency Department of Eskisehir Osmangazi University Hospital between March and May 2016 based upon a prospective and observational research design. Patients aged ≥ 65 years were included in the study. The exclusion criteria for participation in the study were age of <65 years and

not providing informed consent for participation. The following information was noted on the observation form for each patient: age, gender, date of admission to the emergency department, blood pressure, pulse rate, respiratory rate, body temperature, oxygen saturation, state of consciousness, additional diseases, number of drugs used, names of drugs used, clinical outcome after the provision of medical care (discharge, hospitalization (in the intensive care unit or related medical department), refusal of treatment, transfer to another healthcare center, death, and leaving the hospital against medical advice).

Drugs Used and Appropriateness According to the 2012 Beers and STOPP Version 2 Criteria

For the purpose of this study, statistical analyses were performed based on the following parameters:

- The appropriateness of drugs according to the 2012 Beers and STOPP Version 2 Criteria
- The number of inappropriate drugs
- Falls caused by inappropriate drugs, according to the 2012 Beers Criteria
- The organ system affected by inappropriate drugs, according to the STOPP Version 2 Criteria

Statistical Method

IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp. was used to perform statistical analyses. Categorical variables were presented as numbers (n) and percentages (%). Continuous data are given as a mean \pm standard deviation.

RESULTS

The study was conducted with 835 patients: 406 (48.6%) females and 429 (51.4%) males. The participants' mean age was 74.2 ± 6.5 years. The distribution of comorbidities in the participants is presented in Figure 1. The relationship between



comorbidities and number of drugs is provided in Table 1. Overall, 835 patients were using a total of 5,637 drugs. The average number of drugs used was 6.8 ± 3.2 . The distribution of patients by the number of drugs used is presented in Table 2.

According to the STOPP Version 2 Criteria, the number of inappropriate drugs used was 688 in total and the number of patients using inappropriate drugs was 431 (51.6%). The number of inappropriate drugs used was one drug in 241 (28.9%) patients, two in 137 (16.4%), three in 41 (4.9%), four in 10 (1.2%), and five in two (0.2%) (Table 3). According to the 2012 Beers Criteria, the number of inappropriate drugs used by participants was 843 and the number of patients using inappropriate drugs was 442 (52.9%). The number of inappropriate drugs was one drug in 205 (24.6%) patients, two in 133 (15.9%), three in 58

(6.9%), four in 33 (4.0%), five in 12 (1.4%), and six in one (0.1%) (Table 3).

Profiles of Inappropriate Drugs

According to the 2012 Beers Criteria, the most commonly used inappropriate drugs are SSRIs (122 patients, 14.6%), strong anticholinergics (97, 11.6%), NSAIDs (86, 10.3%), and aspirin (58, 6.9%). According to the STOPP Version 2 Criteria, the most common violations were related to the category of duplication (165 patients, 19.8%), cardiovascular system (107, 12.8%), use of antiplatelet drugs (103, 12.3%), and central nervous system (87, 10.4%). According to the STOPP Version 2 Criteria, the most frequently duplicated drugs were NSAIDs (66 patients, 40.0%), steroids for respiratory disorders (23, 14.0%), proton-pump inhibitors (18, 11.0%), thiazide diuretics (18, 11.0%), ASA (13, 8.0%), and paracetamol (13, 8.0%).

Table 3. Univariate and multivariate analyses for predictors of frequent premature ventricular contraction

Comorbidities		Number of drugs				Total
		0	1-5	6-9	>9	
DM	No	14 (2.0%)	255 (31.0%)	262 (31.0%)	79 (9.0%)	610 (73.0%)
	Yes	1 (0.1%)	46 (6.0%)	107 (13.0%)	71 (9.0%)	225 (27.0%)
HT	No	14 (2.0%)	149 (18.0%)	78 (9.0%)	13 (2.0%)	254 (39.0%)
	Yes	1 (0.1%)	152 (18.0%)	291 (35.0%)	137 (16.0%)	581 (70.0%)
COPD	No	15 (2.0%)	276 (33.0%)	276 (33.0%)	91 (11.0%)	658 (79.0%)
	Yes	0 (0.1%)	25 (3.0%)	93 (11.0%)	59 (7.0%)	177 (21.0%)
CRF	No	15 (2.0%)	289 (35.0%)	350 (42.0%)	133 (16.0%)	787 (94.0%)
	Yes	0 (0.1%)	12 (1.0%)	19 (2.0%)	17 (2.0%)	48 (6.0%)
CHF	No	15 (2.0%)	294 (35.0%)	325 (39.0%)	98 (12.0%)	732 (88.0%)
	Yes	0 (0.1%)	7 (1.0%)	44 (5.0%)	52 (6.0%)	103 (12.0%)
CAD	No	15 (2.0%)	251 (30.0%)	183 (22.0%)	37 (4.0%)	486 (58.0%)
	Yes	0 (0.1%)	50 (6.0%)	186 (22.0%)	113 (14.0%)	349 (42.0%)
Others	No	15 (2.0%)	70 (8.0%)	37 (4.0%)	11 (1.0%)	133 (16.0%)
	Yes	0 (0.1%)	231 (28.0%)	332 (40.0%)	139 (17.0%)	702 (84.0%)

DM, diabetes Mellitus; HT, hypertension; COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure; CHF, congestive heart failure; CAD, coronary artery disease

The use of anticholinergics in patients admitted to the emergency department after a fall was investigated, and seven of 35 patients were found to be inappropriately using anticholinergics according to the 2012 Beers Criteria and five were inappropriately using anticholinergics according to the STOPP Version 2 Criteria.

Table 2. Distribution of the number of drugs among patient.

Number	Number of patients	Percentage (%)
0	15	1.8
1-5	301	36.0
6-9	369	44.2
>9	150	18.0
Total	835	100.0

DISCUSSION

The participants' mean age was 74.2 ± 6.6 years. Given that life expectancy is 79.4 years in females and 73.7 years in males according to 2015 data, the older population provides an important source of information in Turkey.

The population census of Turkey in 2015 showed that the number of people aged ≥ 65 years was 6 495 239 (8.2% of the total population). There is limited information in the literature particularly with regard to the elderly. Because of the aging of the population in Turkey and lack of sufficient information in the literature, this study potentially provides a significant source of information for the treatment of older individuals.

This study has focused on inappropriate drug use in the elderly based on the STOPP Version 2 Criteria and 2012 Beers Criteria. Given that the number of similar studies is limited in the literature, the present study may play a guiding role in research.

Increase in the aging population has affected the entire healthcare system, particularly the

Table 3. Univariate and multivariate analyses for predictors of frequent premature ventricular contraction.

Number of Inappropriate drug use	2012 Beers Criteria		STOPP Version 2 Criteria	
	Number of patients	%	Number of patients	%
0	393	47.1	404	48.4
1	205	24.6	241	28.9
2	133	15.9	137	16.4
3	58	6.9	41	4.9
4	33	4.0	10	1.2
5	12	1.4	2	0.2
6	1	0.1	0	0.0
Total	835	100.0	835	100.0



emergency medicine services. In 2002, 58.0% of the population aged ≥ 75 years presented to emergency departments at least once in the United States. This rate corresponds to 39.0% of the total population (7).

This information suggests that the workload in emergency departments everywhere is expected to increase with the increase in the older population. The present study yields important data about polypharmacy and inappropriate drug use in elderly patients admitted to the emergency department.

In terms of comorbidities, Ünsal et al. reported in 2003 that patients aged ≥ 65 years presented most commonly to the emergency department because of hypertension (HT) and cardiovascular diseases (8). In the present study, the comorbidities were, in descending order of frequency, HT (69.5%), coronary artery disease (CAD) (41.8%), diabetes mellitus (DM) (26.9%), chronic obstructive pulmonary disease (COPD) (21.2%), and congestive heart failure (CHF) (12.3%). In this study, diseases such as HT, CAD, DM, COPD, and CHF were more frequently encountered probably because the data were collected from the emergency department.

The increase in the number of chronic diseases is considered to be one of the most important risk factors for polypharmacy. In the present study, we found that 44.2% of the patients were using six or more drugs and 18.0% of the patients were using 10 or more drugs. In this study, the average number of drugs was 6.6 ± 3.2 . Kaufman et al. conducted a study in the United States in 2002, wherein they reported polypharmacy in 57.0% of females and 44.0% of males aged ≥ 65 years. In the same study, they found that 12.0% of females and males were using 10 or more drugs (9).

In this study, the prevalence of inappropriate drug use was 51.6% according to the STOPP Version 2 Criteria and 52.9% according to the 2012 Beers Criteria. The worldwide prevalence of inappropriate drug use was reported to be 13.0%–35.0% according to the STOPP Version 2 and 2012 Beers Criteria (10). In a 2012 study by Blanco-Reina

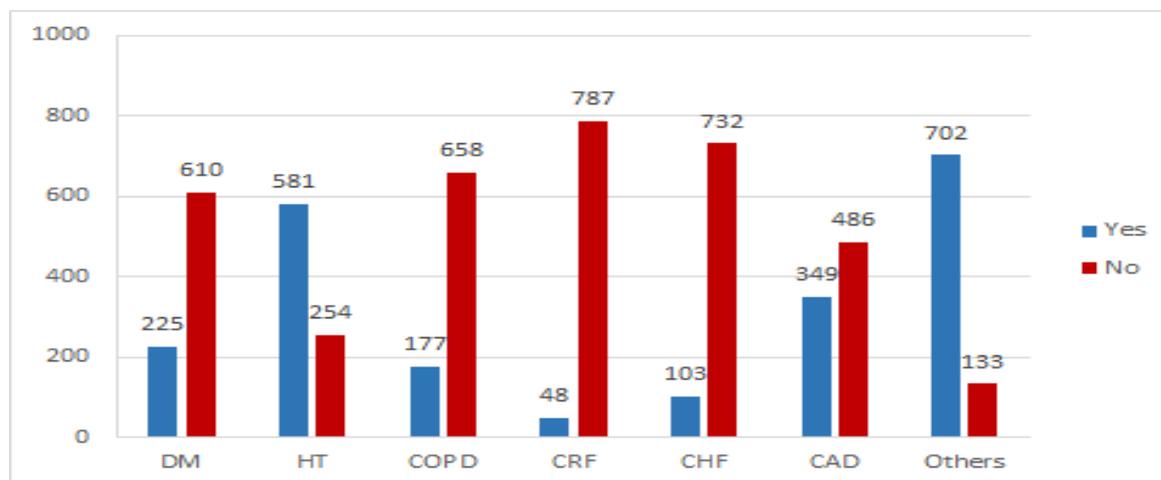
et al., the prevalence of inappropriate drug use was 24.3% according to 2003 Beers, 35.4% according to STOPP Version 1, and 44.0% according to 2012 Beers Criteria in 407 elderly patients admitted to primary healthcare centers (11). In a 2014 study by Jhaveri et al., the rate of inappropriate drug use was quite high according to the 2012 Beers Criteria (87.3%) in 676 elderly patients (average age, 72.7 years) who were hospitalized in tertiary healthcare centers (12). Davidoff et al. investigated the prevalence of inappropriate drug use in the United States in 2015 in 18 475 elderly patients and reported that the rate was 40.8% between 2006 and 2010 according to the 2012 Beers Criteria. In the United States, the most common inappropriately used drug was NSAID (10.9%) according to the 2012 Beers Criteria (13).

In a study by Lam et al. in 2015 with elderly patients treated and hospitalized in a tertiary healthcare center, it was reported that the rate of inappropriate drug use was 31.6% and 38.6% according to the STOPP Version 1 and 2012 Beers Criteria, respectively (14).

This study showed that NSAIDs are one of the most common inappropriately used drug classes. The use of NSAIDs is associated with increased gastrointestinal and cardiovascular risks, particularly in older patients. NSAIDs are also more likely to cause problems in renal function in older patients. Furthermore, a recent study found that NSAIDs constitute an independent risk factor for community-acquired hyperkalemia (15).

It is known that the inappropriate use of NSAIDs may cause gastric irritation, chronic blood loss, anemia, sodium retention, and kidney failure, particularly in patients aged >65 years. Drug-induced nephrotoxicity is likely to reduce the effectiveness of antihypertensive drugs. The use of NSAIDs is associated with a two-fold increased risk of chronic kidney disease, especially in patients aged >65 years. Furthermore, inappropriate use of NSAIDs is reported in patients with kidney failure (16, 17, 18).

Figure 1. Comorbidities of the patients.



DM, diabetes Mellitus; HT, hypertension; COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure; CHF, congestive heart failure; CAD, coronary artery disease.

In the present study, 35 patients presented to the emergency department after a fall. According to the STOPP Version 2 Criteria, 20.0% of these patients were taking drugs with apparent anticholinergic activity. It is known that inappropriate drug use increases the risk of falls in older patients. This is mostly associated with anticholinergic medications, as well as long-term use of benzodiazepines and psychotropic medications. Primary healthcare providers must pay special attention when prescribing medications with anticholinergic effects (e.g., tricyclic antidepressants and antihistamines) to elderly patients (19, 20).

An emphasis on inappropriate drug use will help physicians in the emergency department and other healthcare professionals reduce side effects and complications of medications and potentially reduce emergency admissions to hospitals. Thus, healthcare providers should pay more attention to inappropriate drug use, drug-drug interactions, and possible side effects of drugs, particularly in patients aged >65 years. It should also be emphasized that the 2012 Beers

and STOPP Version 2 Criteria are developed not to replace physicians' decisions but to guide them to appropriately prescribe medications.

This study has some limitations. This study was conducted in the emergency department. Therefore, no detailed information about patients, such as glomerular filtration rate or systolic ejection fraction, was available. Because there was no information regarding where patients lived, no comparison was made between patients living in their home and those living in geriatric care centers. This study was conducted in only one healthcare center.

In conclusion, inappropriate drug use is a major healthcare problem across the world. The 2012 Beers and STOPP Version 2 Criteria used in this study are not intended to replace clinical assessment but rather to facilitate and support clinical processes. Therefore, these criteria cannot be the only sources of information that guide medication choice. The aim of these criteria is to protect patients from the side effects of drugs and improve the quality of treatment while prescribing a minimum number of drugs. Based on the



findings of the present study, the 2012 Beers and STOPP Version 2 Criteria are recommended as a resource for prescribing drugs for elderly patients with the added benefit of improving the quality of healthcare services. The present study and previous worldwide studies suggest that these criteria are effective methods for determining inappropriate drug use.

To the best of our knowledge, the present study is the first investigation on the use of the

STOPP Version 2 and 2012 Beers Criteria to analyze polypharmacy and inappropriate drug use among elderly patients admitted to an emergency department and is considered to play a guiding role to healthcare services for the elderly in Turkey and around the world.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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