RESEARCH

COMPARATIVE EVALUATION OF POTENTIAL INAPPROPRIATE DRUG USE IN ELDERLY OUTPATIENTS USING THE BEERS 2019 AND TIME CRITERIA

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2022.259
2022; 25(1): 22-31

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Received: Nov 14, 2021
Accepted: Jan 26, 2022

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Abstract

Introduction: The potentially inappropriate medication list was established to reduce potentially inappropriate medications (PIMs), potential prescribing omissions (PPOs) and polypharmacy in elderly individuals. This study analyzed the drug use of geriatric patients in Turkey using the American 2019 Beers criteria and the Turkish Inappropriate Medication Use in the Elderly (TIME) criteria.

Materials and Methods: This cross-sectional descriptive survey study was conducted using 385 randomized patients aged over 65 years who were treated at the Kütahya Health Sciences University's Evliya Çelebi Training and Research Hospital Internal Medicine outpatient clinic. The patients included in the study were evaluated for PIMs according to the TIME and Beers criteria.

Results: While 73.2% of the 385 patients included in the study were in the 65–74 age range, 26.8% were aged ≥75 years; 67.8% were female and 32.2% were male. The prevalence of PIMs determined by the TIME based criteria was 33%, which was almost 3-fold than detected using the Beers criteria (Beers: 10.9%, TIME-to-STOP: 33%). The mean number of PIMs according to the TIME-to-STOP criteria was significantly higher than that according to the Beers criteria (p=0.01). The rate of cases with PIMs according to the TIME based criteria was significantly higher than that according to the Beers criteria (p<0.05). A significant association was found between polypharmacy and PIMs for both the TIME-based and Beers criteria (p<0.05).

Conclusion: The TIME-based criteria were more successful in evaluating PIMs among the elderly in Turkey. In addition, PIMs was significantly higher in polypharmacy patients.

Keyword: Geriatrics; Potentially Inappropriate Medication List; Inappropriate Prescribing; Polypharmacy.

INTRODUCTION

The number of elderly people is increasing worldwide, with 841 million people over 60 years old in 2013, and is expected to reach more than 2 billion by 2050 (1). As society ages, the health problems and social expectations of the elderly come to the forefront (2). The frequency of chronic diseases and drug use increases with age (3). Excessive drug use is an independent risk factor for drug-side effects and PIMs (4).

Polypharmacy can be defined as the concomitant use of five or more drugs, the use of at least one nonessential drug, or the use of more drugs than is clinically necessary. The frequency of polypharmacy among the elderly has been reported to be 23–39% (3, 5). Although the prevalence and disadvantages of PIMs, PPOs, and polypharmacy among the elderly have been known for many years, these problems persist. Drug side effects are 2–3 times more common among the elderly than in young people (6). In one study, it was determined that 6.5% of hospital admissions were due to drug-related complications; 80% of these were due to drug side effects (7).

The Beers and STOPP/START (Screening Tool of Older Person's Prescriptions/Screening Tool to Alert to Right Treatment) criteria were developed to prevent PIMs. The Beers criteria, which were last updated in 2019, are among the most preferred criteria for examining patient-related results and PIMs (8).

Turkish inappropriate medication use in the elderly (TIME) has been established (9). The TIME criteria were created based on the original STOPP and START criteria, taking into account the prescribing habits and the drug use attitude in our country and the ease of use in the clinic. The criteria have two types: criteria for preventing drugs that are not suitable for use in the elderly and misused in clinical practice (TIME-to-STOP) and criteria for drugs that are useful in the elderly but are not frequently used in clinical practice (TIME-to-START) (9).

In order to determine the amount of PIMs in patients aged 65 years and over in Turkey, this study examined the drugs that geriatric patients were using at the time of admission to the Internal Diseases outpatient clinic and evaluated them according to the recommendations of the American Geriatrics Society Beers 2019 and the TIME criteria created by the Academic Geriatrics Society of Turkey. Our study aimed to determine the prevalence of PIMs according to the TIME criteria and compare it to the results from the Beers 2019 criteria.

METHODS

Study design and data collection

This descriptive cross-sectional prospective survey study randomized 385 patients aged 65 years and over who were treated at the Kütahya Health Sciences University's Evliya Çelebi Training and Research Hospital Internal Medicine outpatient clinic for routine control between February 25, 2020 and December 31, 2020. The sample size was calculated as 385 with a significance level of 0.05 (95% confidence) for an infinite population of 50% prevalence. A simple random sampling method was used to select the study subjects. Out of the 2752 patients that visited the Internal medicine outpatient clinic during the dates of the study, 385 were randomized (patients assessed for eligibility n: 2752, Not meeting inclusion criteria n: 2110, randomly assigned n: 385). Only the first visit examinations of the patients between the dates of the study were evaluated, and the follow-up examinations were not taken into consideration. Of the first seven patients whose age was over 65 years, volunteers who met the study criteria and wanted to participate in the study were included in the study. Selection was carried out separately for the morning group and the afternoon group.

Inclusion and exclusion criteria

Individuals over 65 years of age were included in this study. Patients under 65 years of age and patients who were uncooperative with the doctor during the examination were excluded from the study.

Permits and approvals

Prior to the study, approval was obtained from the Kütahya Health Sciences University Non-Interventional Clinical Research Ethics Committee (2020/04-15). The volunteers included in the study were verbally informed about the study and their signatures were obtained using an Informed Voluntary Consent Form.

Clinical and laboratory findings

The patients were questioned through a face-to-face survey conducted in the polyclinic conditions to collect their general characteristics, which included age, sex, marital status, socioeconomic income level, education level, occupation, chronic habits, chronic diseases, and medications they used. Body mass index was calculated by measuring height and weight. The suitability of the drugs was evaluated using the 2019 Beers criteria and the TIME criteria. PIMs were determined separately for the TIME and the Beers criteria. We calculated the number of patients (%) in the total study population with PIMs and the total number of PIMs cases. Patients were considered to use drugs inappropriately if at least one PIM according to the relevant criteria.

Statistical analysis

The IBM SPSS Statistics 22 (IBM SPSS, Turkey) program was used to perform statistical analysis. The compatibility of the parameters with the normal distribution was evaluated using the Kolmogorov–Smirnov test, and it was determined that the parameters did not show a normal distribution. The Mann–Whitney U test and Wilcoxon sign test were used for comparison of quantitative data and for descriptive statistical methods (mean, standard deviation, frequency). The chi-square test, Fisher's exact test, and continuity (Yates) correction were used to compare qualitative data. The agreement between TIME-to-STOP and Beers was evaluated using the Kappa test. Significance was evaluated at a level of $p< 0.05$.

RESULTS

Of the 385 geriatric patients included in our study, 67.8% were female, 32.2% were male, 73.2% were between the ages of 65–74, and 26.8% were aged > 75 years. Other sociodemographic data of the patients are presented in Table 1. The chronic habits of our patients are shown in Table 2.

The distribution of chronic diseases among the patients was: 1.6% had none, 16.6% had one, 35.8% had two, 29.9% had three, 11.4% had four, 3.9% had five, 0.5% had six, and 0.3% had seven chronic diseases. The chronic disease distribution of the patients is shown in Table 3. The most common chronic diseases were hypertension, diabetes mellitus, and dyslipidemia.

Geriatric patients who met at least one relevant criterion were considered to have PIMs or PPOs. PIMs were detected in 127 (33%), and 42 (10.9%) patients according to the TIME-to-STOP and 2019 Beers criteria, respectively. PPOs was detected in 379 (98.4%) patients according to the TIME-to-START .

For PIMs and PPOs, there were no significant differences between the sexes ($p>0.05$). According to the TIME-to-START criteria, there was no significant difference between the number of diseases among cases with PPOs and cases without PPOs. According to the Beers criteria, there was no significant difference between the number of diseases in patients with or without PİMs ($p>0.05$). However, according to the TIME-to-STOP criteria, the number of diseases in patients with PIMs was significantly higher than that in patients without PIMs ($p<0.05$). The relationship between the number of chronic diseases and PIMs/PPOs is shown in Table 4.

The rate of cases with PIMs according to the TIME-to-STOP criteria was significantly higher than that according to the Beers criteria ($p<0.05$). The kappa value was 0.398 for the consistency in the detection of PIM between the TIME-to-STOP and Beers criteria (insignificant consistency: 0.0–0.20,

Table 1. Distribution of sociodemographic characteristics of the patients

		n	%
Age group	65–74 years	282	73.2
	≥75 years	103	26.8
Sex	Female	261	67.8
	Male	124	32.2
Marital status	Married	244	63.4
	Single	1	0.3
	Widowed	137	35.6
	Divorced	3	0.8
Income	Income less than expenses	74	19.2
	Income equals expense	281	73.0
	Income more than expenses	30	7.8
Education	Illiterate	108	28.1
	Less than 8 years of education	242	62.9
	More than 8 years of education	25	6.5
	College	10	2.5
Profession	Retired	175	45.5
	Housewife	205	53.2
	Worker	3	0.8
	Officer	0	0
	Owns business	1	0.3
	Unemployed	0	0
	Other	1	0.3

Data are expressed as n, %.

Table 2. Distribution of patient habits

		n	%
Tobacco	Smoker	56	14.5
	Non-smoker	307	79.7
	Quit smoking	22	5.7
Alcohol	Drinks	10	2.6
	Non-drinking	375	97.4
Exercise	Regular	53	13.8
	None	184	47.8
	Irregular	148	38.4

Data are expressed as n, %.

Table 3. Distribution table of chronic diseases

Chronic Diseases	n	%
Hypertension	275	71.4
Diabetes mellitus	246	63.9
Dyslipidemia	123	31.9
Heart diseases (coronary artery disease, arrhythmias, valve diseases, etc.)	74	19.2
Lung diseases (asthma, chronic obstructive pulmonary disease, etc.)	49	12.7
Thyroid diseases (hypothyroidism, hyperthyroidism, etc.)	39	10.1
Neurological and cerebrovascular diseases (Parkinson's, Alzheimer's, stroke, vertigo, etc.)	27	7.0
Osteoporosis	13	3.4
Kidney diseases (chronic renal failure, etc.)	13	3.4
Rheumatologic diseases (gout, rheumatoid arthritis, etc.)	12	3.1
Cancers (lung, bladder, breast, etc.)	11	2.9
Psychiatric diseases (psychoses, depression, etc.)	9	2.3
Other (cirrhosis, glaucoma, etc.)	15	3.9

Data are expressed as n, %.

Table 4. The relationship between the number of chronic diseases and PIMs/PPOs

			Number of chronic diseases	
		Mean	***Median***	***P* value**
PPO according to TIME-to START criteria	***Undetected (n=6)***	2.167 (1.4720)	2.5	0.703
	Detected (n=379)	2.485 (1.1159)	2.0	
PIM according to TIME-to STOP criteria	***Undetected (n=258)***	2.326 (1.0071)	2.0	**0.002***
	Detected(n=127)	2.795 (1,2683)	3.0	
PIM according to Beers 2019 criteria	***Undetected (n=340)***	2.446 (1.1012)	2.0	0.190
	Detected (n=45)	2.762 (1.2457)	2.5	

Mean (standard deviation.) and median. Data compared by Mann-Whitney U test. *p<0.05, statistically significant.
PIMs potentially inappropriate medications, PPOs potential prescribing omissions

low: 0.21–0.40, moderate: 0.41–0.60, good: 0.61–0.80, perfect fit: 0.81–1.00). According to these results, low consistency between the two tests was observed. There were 42 cases in which PIMs were detected by both the Beers and TIME-to-STOP criteria. There were no cases in which only the Beers criteria detected PIMs. There were 85 cases in which only the TIME-to-STOP criteria detected PIMs. There were 258 cases of PIMs that were not detected by either the Beers or TIME-to-STOP criteria. The mean number of patients with PIMs according to the TIME-to-STOP criteria was significantly higher than that identified by the Beers criteria (p=0.01).

The average number of drugs used by the patients included in the study was 5.127 (range: 1–14). PPOs were observed at a rate of 98.8% in cases without polypharmacy and 98.1% in cases with polypharmacy, with no significant difference between them, according to the TIME-to-START criteria. There was a significant correlation between the presence of polypharmacy and PIMs according to both the TIME-to-STOP and Beers criteria. The rates of PIMs according to the TIME-to-STOP and Beers criteria were, respectively, 40.8% and 16.9% in patients with polypharmacy, which were significantly higher ($p<0.05$ for each) than the respective 23% and 3.5% in patients without polypharmacy. The relationship between polypharmacy and PIMs/PPOs is shown in Table 5.

DISCUSSION

As patients age, the rate of chronic diseases and drug use increases. This leads to an increase in the frequency of PIMs/PPOs and polypharmacy. In addition to the decrease in the quality of life due to aging itself, the PIMs/PPOs and the complications related to polypharmacy increase fragility and further decrease the quality of life.

In this study, we compared the drugs used by geriatric patients who applied to the Internal Medicine outpatient clinic using the 2019 Beers criteria

Table 5. The relationship between polypharmacy and PIMs/PPOs

	TOTAL PATIENTS (n=385, %100)	Patients with polypharmacy (n=213, 55,3%)	Patients not with polypharmacy (n=172, 44,7%)
PPO according to TIME-to START criteria	379 (98.4%)	209 (54.3%)	170 (44.1%)
		p=0.696	
PIM according to TIME-to STOP criteria	127 (33%)	87 (22.6%)	40 (10.4%)
		p<0.001*	
PIM according to Beers 2019 criteria	45 (10.9%)	36 (9.3%)	6 (1.6%)
		p<0.001*	

Data are expressed as n (%) and compared by Chi Square test. *p<0.05, statistically significant.

PIMs potentially inappropriate medications, PPOs potential prescribing omissions

and the TIME criteria. Among the patients, 73.2% were "young old" between the ages of 65–74, while 26.8% of them were aged ≥75 years. There is limited literature on the comparison between national and international criteria for PIMs/PPOs, especially among the elderly. Therefore, we believe that our study is an important data source.

Most studies on PIMs utilize the Beers criteria that have been criticized for not being suitable enough for the prescribing practices in Europe and our country due to its origin being in the USA (10). Our study is the first geriatric study in Turkey that investigates the prevalence of PIMs evaluated by the TIME criteria and compares it with the results of the Beers 2019 criteria. In our study, the prevalence of PIMs determined by the TIME-to-STOP criteria was 33%, while that detected using the 2019 Beers criteria was only 10.9%. This suggests that the TIME-to-STOP criteria are more sensitive for detecting PIMs in the elderly in Turkey.

We also examined the prevalence of PPOs in the same clinical study using TIME-to-START criteria. According to the TIME-to-START criteria, PPOs were found in 98.4% of the cases. The Beers criteria contains a list of PIMs, but they do not account for PPOs. Considering the high rates found in our study, it is apparent that PPOs are at least as important as PIMs.

In a study conducted in Spain, at least one case of PIMS was detected in 71% and 68.5% of patients according to the 2015 Beers criteria and STOPP criteria respectively (11). In the same study, at least one case of PPO was detected in 58% of patients according to the START criteria (11). In another study, patients hospitalized in six large teaching hospitals in six different European countries, PIMs were found in 35% to 77% and PPOs was found in 51% to 73% of the patients according to the STOPP criteria and START criteria, respectively (12). Since these studies included patients requiring hospitalization, the prevalence of PIMs was found to be higher than that in our study. Since only patients who applied to the outpatient clinic were included in our study, slightly lower rates were found compared to those in the global literature.

Our study found that the rate of PPOs was higher than the rate of PIMs. Just as avoiding PIMs is important for preventing side effects, administering a drug that is needed is also very important for preventing the deterioration of the clinical condition. In some studies, it was shown that inadequate prescription of beta-blockers causes exacerbation of congestive heart failure and consequently has a great effect on hospitalizations (13,14).

Although the definition of polypharmacy has not been made precisely, it is defined as the simultaneous use of at least five drugs in many studies (5,15). In our study, the use of five or more drugs was accepted as polypharmacy and was detected in 213 (55.3%) of 385 patients. This is similar to a study conducted with outpatients in which total polypharmacy (≥5 drugs) was 62.3%, and excessive polypharmacy (≥10 drugs) was 9.7% (16). In a study investigating polypharmacy and prescription quality in the elderly using the Beers criteria (2003), it was observed that PIMs increased as the number of drugs used by patients increased (17). In a study in which PIMs in the elderly with comorbidities was evaluated using the Beers and STOPP criteria, it was observed that PIMs increased with the use of multiple drugs, according to both criteria (18). In our study, PIMs were significantly higher in the TIME and Beers criteria in patients with polypharmacy. This suggests that it is important to evaluate PIMs in the elderly who use multiple drugs and have multiple chronic diseases.

Among the distribution of the number of chronic diseases in our study, cases with two (35.8%) and three (29.9%) chronic diseases predominated. This is consistent with a geriatrics study conducted in Turkey, in which 23.7% of patients had two chronic diseases and 22.9% had with three chronic diseases (19). In our study, the number of chronic diseases in patients with PIMs, according to TIME-to-STOP criteria, was significantly higher than in patients

without PIMs. Given that the potential for PIMs increases with polypharmacy, it also increases as the number of chronic diseases increases.

When the distribution of chronic diseases is compared with studies conducted in our country, there are both similarities and differences. It is understood that these differences are due to the fact that the studies were conducted in different outpatient clinics, and there were differences in grouping the diseases. For example, the rates in our study compared with studies conducted in Çanakkale and Gaziantep were, respectively, hypertension (71.4%, 65%, 57%), thyroid diseases (10.1%, 7.8%), dyslipidemia (31.9%, 42%, 39%), diabetes mellitus (63.9%, 31%, 37%), and heart diseases (19.2%, 47%, 40%) (20,21). The distribution of chronic diseases in our study was consistent with other studies conducted in our country. For example, the distribution of hypertension in patients over the age of 65 years was found to be 71.4% in our study and 75.1% in the Turkish Hypertension Prevalence Study, which included 4992 people (22,23). In addition, our study showed a similar rate of dyslipidemia as the ELDER-TÜRK study (31.9% and 35%, respectively), in which 5694 people participated (22,24), and it had a similar rate of diabetes mellitus as the CAREFUL study that had 530 participants (63.9% and 59.4%, respectively) (22,25). These similarities suggest that the distribution of chronic diseases in our study is consistent with that of national studies, and that the data obtained in our study yielded reliable results.

The TIME and Beers criteria were created to facilitate clinical evaluation, but they are not sufficient on their own for guidance of appropriate drug selection. For this reason, it would be beneficial to make a multi-dimensional evaluation that considers the principles for reducing polypharmacy along with including more criteria that can be used in clinical evaluation of PIMs and PPOs in daily practice. We believe that this would be especially advantageous in Turkey for reducing the prevalence of PIMs and PPOs and their associated negative consequences. By developing practices to prevent PIMs and PPOs, great contributions can be made for protecting the health and preserving the quality of life among elderly patients. Consequently, this will relieve some of the burden on the health system and economy.

Among the worldwide literature, there are few studies that compare the national and international scales in PIMs among elderly patients. To the best of our knowledge, our study is the first to determine the prevalence of PIMs with the TIME criteria and compare it with the results of the Beers 2019 criteria. Therefore, we believe that the results of our study are an important data source both nationally and internationally.

Conflict of Interest: The authors declare no conflict of interest.

The data used in this article has been derived from the data in "Comparative evaluation of potential inappropriate drug use with Beers 2019 and TIME criteria in patients aged 65 and over admitted to internal medicine outpatient clinic" medical specialization thesis.

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