The Evaluation of the Prevalence of Improper Medication Use in Patients Age of 65 and over in Internal Diseases and Neurology Intensive Care Units in Terms of Stopp-Start Criteria

İç Hastalıkları ve Nöroloji Yoğun Bakım Ünitelerinde Yatan 65 Yaş ve Üstü Hastalarda Uygunsuz İlaç Kullanim Prevalansının Stopp-Start Kriterleri Açısından Değerlendirilmesi

Ayşegül Özdağ Erdil[1], Hakkı Zafer Güney[2]

[1] Gazi Üniversitesi Tıp Fakültesi Farmakoloji Anabilim Dalı, Ankara, Türkiye
[2] Gazi Üniversitesi Tıp Fakültesi Farmakoloji Anabilim Dalı, Ankara, Türkiye

ABSTRACT

Introduction: Physiological changes are seen in many systems in the body related to aging. Treatment modalities and drug prescribing processes need to be re-evaluated in the geriatric population.
To elaborate on polypharmacy, the number of drugs the individual should use must also be defined effectively.
Various criteria have been developed for prescribing and using drugs for elderly individuals. The most used of these criteria is called the Beers criteria. STOPP and START criteria are other criteria used.
Material and Method: Our study aimed to retrospectively evaluate the prevalence of inappropriate drug use in patients aged 65 and over who were hospitalized in the Internal Medicine and Neurology Intensive Care Units of Ankara Atatürk Training and Research Hospital in terms of STOPP-START criteria.
Results: Study group consists of 168 (58,3%) female and 120 (41,7%) male. A total of 727 diseases were diagnosed in 288 patients. 201 of these were "Cerebrovascular Diseases," 153 were "Hypertension." While the most common STOPP criterion main group and single criterion were antiplatelet anticoagulant agent group (35,7%), "Presence of a drug class causing duplication (Aiming optimum level with a single drug before adding a new agent) (23,2%)", respectively. At the same time, the most common START criterion main group and single criterion were cardiovascular system group (94,5%), and "Statin therapy in patients who are near the end of life or who are not older than 85 years of age, with a history of coronary, cerebral or peripheral vascular disease", respectively (70,2%).
Conclusion: It is seen that the study results are generally similar to the national literature. There are partisan differences between the study results and the international literature. It is anticipated that these differences can be attributed to the diagnostic criteria used, study group selection, and study design differences.

Keywords: START criteria, STOPP criteria, Polypharmacy, Geriatrics

ÖZET

Giriş: Yaşlanma ile ilişkin vücutta bulunan birçok sistemde fizyolojik değişiklikler görülmektedir. Bu değişikliklerin ışığında geriatrik popülasyonda hem tedavi modalitelerinin hem de ilaç reçetelendirme süreçlerinin yeniden değerlendirilmesi gerekmektedir.
Hasta tarafından birden fazla ilacın kullanılması olarak da bilinen polifarmasi tanımının detaylandırılabilmesi için, bireyin gerçekte kullanması gereken ilaç sayısının da efektif biçimde tanımlanması gerekmektedir. Yaşlı bireylere ilaç reçetelendirilmesi ve kullanımı konusunda çeşitli kriterler geliştirilmiştir. Bu kriterlerden en çok kullanılanı ise Beers kriterleri olarak adlandırılır. STOPP ve START kriterleri de kullanılan diğer kriterlerdir.
Yöntemler: Çalışmamızda, Ankara Atatürk Eğitim ve Araştırma Hastanesi İç Hastalıkları ve Nöroloji Yoğun Bakım Ünitelerinde yatan 65 yaş ve üstü hastalarda uygunsuz ilaç kullanım prevalansının STOPP-START kriterlerin açısından retrospektif olarak değerlendirilmesi amaçlanmıştır.
Bulgular: Çalışmaya alınan 288 hastanın 168'i kadın (%58,3), 120'si erkektir (%41,7). 288 hastada toplam 727 hastalık tanısı konulduğu saptanmıştır. Bu 727 tanının 201'i "Serebrovasküler Hastalıklar" iken, 153'ü "Hipertansiyon"dur. En sık saptanan STOPP kriter ana grubu antitrombosit antikoagülan ajan grubu (%35,7) iken, en sık saptanan tekil STOPP kriteri, "Duplikasyona sebep olan ilaç sınıfı varlığı (yeni bir ajan eklemeden önce tek ilaçla optimum düzey hedeflenmesi) (%23,2)"dir. En sık saptanan START kriter ana grubu kardiyovasküler sistem grubu(%94,5) iken, en sık saptanan tekil START kriteri, "Yaşamının sonuna yaklaşmış ya da 85 yaşından büyük olmayan, öyküsünde koroner, serebral ya da periferal vasküler hastalığı olan hastalarda statin tedavisi"dir (%70,2).
Sonuç: Çalışma sonuçlarının ulusal literatür ile genel anlamda benzerlik gösterdiği görülmektedir. Çalışma sonuçları ile uluslararası literatür arasında kısmi farklılıklar vardır. Bu farklılıkların, kullanılan tanı kriterleri, çalışma grubu seçimi, çalışma tasarım farklılıklarına atfedilebileceği öngörülmektedir.

Anahtar Sözcükler: START Kriteri, STOPP Kriteri, Polifarmasi, Geriatri

ORCID IDs: A.Ö.E.0009-0009-0491-5885,H.Z.G.0000-0003-3371-8150

INTRODUCTION

The time spent with time is known as "aging." The state of showing the effects of the increasing life year on individuals is called "old age"(1). According to the World Health Organization (WHO), individuals aged 65 and over are called "old," and individuals aged 85 and over are called "very old."

Physiological changes are seen in many systems in the body related to aging. In the light of these changes, both treatment modalities and drug prescribing processes need to be re-evaluated in the geriatric population.

Although it is possible to draw a general framework for the effects of aging on both the pharmacodynamic and pharmacokinetic systems, it should be considered that there may be different effects for each drug in public. In this context, it is possible to summarize the pharmacodynamic changes as follows:

Drug absorption: There are controversial results in the literature regarding the relationship between increasing age and absorption (2). Although there are publications in the literature that age does not affect absorption, these publications are relatively few. In the majority of publications in the literature, it is stated that the relationship between age increase and absorption varies according to the drug (2,3).

First-pass effect and bioavailability of the drug: Secondary to the decrease in liver mass in elderly patients, blood flow to these areas also decreases. Therefore, it can be said that the first-pass effect of drugs with exceptionally high clearance is reduced. However, an increase in bioavailability with age has been reported for drugs with a prolonged first-pass effect. In addition to this situation, it has been reported that the activation of angiotensin-converting enzyme (ACE) inhibitors, which are frequently used in the elderly population, decreases due to the change in the first pass effect (4).

Distribution of the drug in the body: It is known that the changes in total body water and lean body weight seen in the body with the increase in age have a severe effect on the distribution of drugs in the body. This situation manifests itself as less volume of distribution, especially in water-soluble drugs such as gentamicin, lithium, theophylline. This indicates that the loading doses of these agents, which have a smaller volume of distribution, in other words, higher serum concentrations, should be lower2.

Unlike hydrophilic drugs, the volume of distribution of lipophilic drugs increases with aging. The most important reason for this is the increase in the elimination half-life due to the decrease in renal clearance. This mechanism in lipophilic drugs such as lidocaine and thiopental is characterized by more prolonged than expected drug effects and an increase in the frequency of side effects in elderly individuals (2).

Connection with proteins: Acidic drugs (phenytoin, salicylate) are usually albuminous, and essential anesthetics (such as lidocaine) bind to alpha-1 acid glycoproteins. Although it is known that the concentration of alpha-1 acid glycoprotein is not significantly affected by increasing age, albumin, an indicator of liver synthesis capacity, is a protein whose concentration decreases in the presence of malnutrition and acute disease, which is common in the elderly.

Elimination: It is known that GFR, which is an essential parameter for drug elimination, decreases with age. The decrease in the filtration of drugs by the kidneys, in a way, brings about an increase in the toxic effects of the drug. Evaluation of harmful effects, especially in pills with a narrow therapeutic index, is an even more critical parameter.

Age-related GFR decreases affect the elimination of some drugs such as water-soluble antibiotics, diuretics, digoxin, water-soluble beta-blockers, lithium, and some NSAIDs (2). The clinical significance of decreased renal excretion varies depending on the drug's toxic effect. Hepatic extraction rate, also known as the separation capacity of the drug, and hepatic blood flow play an essential role in the hepatic elimination of drugs It is known that the elimination of drugs with a high hepatic extraction rate (such as propranolol) is limited by blood flow. Still, the elimination of drugs with a low extraction rate (such as diazepam warfarin) is not affected by hepatic blood flow changes(5).

It can be said that the generally accepted view in terms of pharmacokinetics in drug administration in elderly individuals is the principle of "start with a low dose, increase slowly" (5).

It is known that just as the pharmacokinetic properties of drugs are affected by increasing age, their pharmacodynamic properties are also affected by advancing age. These changes are generally summarized as drug concentration at the receptor site drug-receptor interaction (receptor number, affinity, secondary response, and cell response).

However, studies on the interactions of pharmacodynamic parameters with age are rare in the literature and have been conducted on specific drug groups (2).

To elaborate the definition of polypharmacy, also known as the patient's use of more than one drug, the number of medications that the individual should use must also be defined effectively. Although this number varies by definition, it is stated in the literature that this number varies between 5 and 10 (6). Although the literature has noted that the purpose of polypharmacy is related to the drugs prescribed in the literature, herbal medicines and over-the-counter medications should also be added to the polypharmacy calculation.

There are specific reasons why elderly individuals are prone to polypharmacy (7);
• Polypharmacy increases the possible drug-drug interaction and the frequency of inappropriate drug prescribing.
• Polypharmacy increases the "prescription drug cascade" seen in the elderly. A prescription drug cascade is a side effect of a prescribed drug being perceived as a symptom of an emerging medical condition and prescribing another medication.
• Polypharmacy significantly reduces drug compliance, especially in elderly individuals with impaired vision and hearing.

Various criteria have been developed for prescribing and using drugs for elderly individuals. The most used of these criteria is called the Beers criteria. The Beer criteria were created in 1991 to evaluate inappropriate drug use and the most cited consensus panel (8). It was first published in 2008 and revised in 2015. In comparison studies with the Beers (2003) criteria in the past, although the agreement was found in many areas, it is stated that STOPP criteria better show drug-drug interactions. In 2008, another criterion called START (Screening Tool to Alert Doctors to Right Treatment) was established to guide the use of drugs recommended for use in the elderly inappropriate indications and based on evidence and to provide a focus on when they can be used (9).

Our study aimed to evaluate the prevalence of inappropriate drug use in terms of STOPP-START criteria in patients aged 65 and over hospitalized in the Internal Medicine and Neurology Intensive Care Units of Ankara Atatürk Training and Research Hospital.

MATERIALS and METHODS

Study Design Our research was carried out with the approval of Gazi University Ethics Committee dated 21/12/2017 and numbered E.181706, in Ankara Atatürk Training and Research Hospital (research permit numbered 28295788-799) in patients aged 65 years and over, hospitalized in Internal Diseases and Neurology Intensive Care Units between 2010-2017 has been made. Our cross-sectional analytical study examined patients aged 65 years and older hospitalized in the Internal Medicine-Neurology intensive care unit of Ankara Atatürk Training and Research Hospital. Medicine and disease information can be accessed from the patients' files; drug profiles were evaluated retrospectively without any intervention.

STOPP/START criteria were chosen for use in this study to detect prescribing nonconformities and omissions.Patients aged 65 years and older, hospitalized in both intensive care units whose drug profiles and disease information was found wholly and entirely in the hospital automation system were included in the study.

Statistical Analysis: The SPSS 22.0 statistical package program analyzed the research data. The descriptive Findings section presents categorical variables as numbers and percentages as statistical analysis. Continuous variables are presented as mean±standard deviation for normally distributed data and median (min, max) for non-normally distributed data. The difference in frequency between the groups was compared using chi-square tests for categorical variables. Conformity of continuous variables to normal distribution was evaluated using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). Descriptive analyzes were assessed with an independent sample t-test between groups for parameters known to be normally distributed. In this study, the statistical significance level will be accepted as $p < 0.05$. p=0.000 levels were shown as $p < 0.001$ in the study.

RESULTS

Of the 288 patients included in the study, 168 (58.3%) were female, and 120 (41.7%) were male. The mean age of the study group was 79.84 ±6.71 years. The mean age of female individuals was statistically significantly higher than the average age of male individuals (81.11 vs. 78.08; p<0.001).

When the disease diagnoses of the study group were examined; A total of 727 diseases were diagnosed in 288 patients. While 201 (27.6%) of these 727 diagnoses were "Cerebrovascular Diseases," 153 were "Hypertension." Diseases in the study group are shown in Table 1.

Table 1. Diseases in Study Group

	Name of the Disease(s)	Study Group (n:727)	
		n	%
Diseases (Main Group)			
Cardiovascular System (n:531)	Cerebrovascular Disease	201	37,9
	Hypertension	153	28,8
	Chronic Atrial Fibrillation	57	10,2
	Kidney Disease	48	9,0
	Heart Disease with Normal Systolic Ventricular Function	24	4,5
	Supraventricular Tachycardia	15	2,8
	Class III and IV Heart Failure	12	2,3
	Bradycardia	9	1,7
	Coronary Stent	6	1,1
	Peripheral Arterial Diseases	6	1,1
	Deep Vein Thrombosis	3	0,6
	TOTAL	531	73,0
Central Nervous System (n: 36)	Dementia	30	83,3
	Parkinson	6	16,7
	TOTAL	*36*	*4,9*
Respiratory System (n:51)	COPD	36	70,6
	Asthma	9	17,6
	Hypoxemia	6	11,8
	TOTAL	*51*	*7,0*
Musculoskeletal System (n:3)	Gout	3	100,0
	TOTAL	*3*	*0,4*
Endocrine System (n:60)	Diabetes Mellitus, Type II	60	100,0
	TOTAL	*60*	*8,25*
Gastrointestinal System (n:6)	Peptic Ulcer	3	50,0
	Gastrointestinal Reflux	3	50,0
	TOTAL	*6*	*0,8*
Others (n:40)	Prostate-Related Diseases	21	53,8
	Malignity	18	46,2
	TOTAL	*40*	*5,5*

When the drugs used by the study group were examined; It was seen that 288 patients had a history of using 912 drugs in total (Mean number of drugs used: 3.16). 13.8% of 912 drugs used are PPIs. (n:123) The study group was divided into <5 and ≥5 drug use, according to the number of drugs they used.

While the number of patients using <5 drugs was 147, 141 patients used 5 or more drugs. There is no statistically significant difference between the number of drug use and gender (p: 0.24). The relationship between the number of drug use and gender is shown in Table 2.

Table 2. Relationship Between the Number of Drug Use and Gender

		Number of Drugs <5		Number of Drugs≥5		p[**]
		(n)	(%)[*]	(n)	(%)[*]	
Gender	Female(n:168)	90	53,6	78	46,4	0,31
	Male(n:120)	57	47,5	63	52,5	

* Percentage of Line, ** Chi-square test

While the mean age of individuals with <5 drugs used is 79.57, the mean age of individuals with ≥5 drugs is 80.13. There is no statistically significant difference between the two groups (p:0.48)

When the STOPP criteria applied to the study group were examined, it was observed that a total of 168 STOPP criteria were met in 288 patients. While the most common STOPP criterion main group was the antiplatelet anticoagulant agent group (35.7%), the most frequently detected single STOPP criterion was "The presence of a drug class causing duplication (targeting an optimum level with a single drug before adding a new agent" (23%, 2nd).

When the START criteria applied to the study group were examined, it was seen that a total of 111 START criteria were met in 288 patients. While the most common START criterion main group was the cardiovascular system group (94.5%), the most common single START criterion was "Statin therapy in patients who are close to the end of life or who are not older than 85 years of age, with a history of coronary, cerebral or peripheral vascular disease".(70.27%).

DISCUSSION

It is observed that the proportion of the elderly population in the total population has increased both in our country and around the world, with the developments in the field of geriatrics on a national and international scale. Considering this situation and the physiological processes brought about by old age, it would not be wrong to say that the number of drugs prescribed in this population will also increase. Along with drugs' pharmacodynamic and pharmacokinetic properties, the problems caused by multiple drugs should be examined in detail and integrated into geriatric patient care management. For this reason, various criteria have been developed to screen prescription non-compliance, such as the STOPP/START criteria.

Considering the distribution of chronic diseases in the study group, 727 diseases were diagnosed in 288 patients, and 73.0% of these 727 diagnoses are classified under the category of cardiovascular system diseases. The mean number of diagnoses was determined as 2.52. In the study of Kocadağ, this number was found as 3.54 (10)

Although the frequencies of comorbidities vary between studies and countries, cardiovascular diseases are generally the most common comorbidity group. In the survey conducted by Bozkurt, circulatory system diseases were seen in 41.24% of the cases(11). Although it is proportionally lower, Ertem et al. In the study he carried out, it was shown that one-third of the study group had circulatory system diseases (12). His research emphasized that the most common comorbidities were hypertension, ischemic heart diseases, diabetes, and dyslipidemia(13). Apart from disease-system grouping, in terms of single diseases, the most common comorbidities in our study were cerebrovascular disease (27.6%) and hypertension (21.04%).

The international literature, Pitkala et al. The most common comorbidities in 3219 cases followed in Finland were hypertension, coronary artery disease, memory-related diseases, cerebrovascular diseases, and diabetes mellitus (14). Steinman et al. In their study, it was stated that hypertension is the most common cause of comorbidity (15).

Although the causes of comorbidity are similar, the frequencies of comorbidity differ between studies. The main reason for this situation is the lack of standardization of diagnostic criteria. Although the lack of standardization in the hospitalization, follow-up, or diagnosis process of the cases does not make a fundamental difference in terms of the causes of morbidity, it can make a significant difference in terms of frequencies.

In our study, 288 patients had a total of 912 drug use histories. The average number of drugs used was found to be 3.16. The average number of drugs used in Kocadağ's study was found to be 4.51(10). The mean number of drugs used in Bozkurt's study was also found to be 6.54 (11), 6.1 (16) in Bay's study, 5.4 (17) in Terzi's study, and 4.5 in Dişçigil's study (18).

When evaluated on a drug basis, the use of proton pump inhibitors (PPI) is seen as the most frequently used drug in the study group. 123 PPI usage is seen in the study group. It was shown that 333 (36.5%) of 912 drugs in the study group consisted of drugs related to the cardiovascular system. In the study of Kocadağ, the dominance of using drugs associated with the cardiovascular system was emphasized (10).

Our study determined the cut-off value for the number of drug use as five. It is difficult to say whether this value can be used as an objective predictive value because it is impossible to obtain a complete medical and drug use history of all patients hospitalized in the intensive care unit.

As a result of the STOPP criteria applied to the study group, it was observed that 168 STOPP criteria were met in 288 patients. The most common criterion among the STOPP criteria is antiplatelet/anticoagulant agents. Among the STOPP criteria groups, the most common single standard is the "presence of drug class causing duplication" (23.2%). In the study conducted by Uçar, the most common STOPP criterion according to the 2008 STOPP criteria is any drug (33.1%) prescribed without an evidence-based clinical indication (19). The number of studies evaluating the STOPP and START criteria's in intensive care is limited in our country. In Kocadağ's study, Beers criteria were used, and the most inappropriate drug according to these criteria was determined as proton pump inhibitors (10). In Bozkurt's study, polypharmacy was evaluated according to the EU (7)-PIM list, and theophylline is the most inappropriate drug; respiratory system drugs were reported to be the most inappropriate drug group (11).

In a study conducted in Switzerland, the most common STOPP criterion was benzodiazepines and neuroleptics in people with recurrent falls (20). Ryan et al. 2008 STOPP criteria were used in their study.

Here, the most common STOPP criterion is; It has been reported to use full-dose PPI for longer than eight weeks for a patient with peptic ulcer diagnosis (21). The two main differences between this study and our study are that the criteria used are different (STOPP 2008 and 2014), and the study group consists of different samples (outpatient clinic patients and intensive care unit patients). In a study conducted in Spain, 2008 STOPP criteria were also applied, and the most common criterion was the use of benzodiazepines in patients with falls (22).

Borges et al. In their study, only cardiovascular and endocrinological parameters were evaluated, and statin therapy was determined as the most common START cause in patients who are near the end of life or who are not older than 85 years of age and who have a history of coronary, cerebral or peripheral vascular disease. Ryan et al. The most common START criterion was determined as the use of aspirin (23). San Jose et al. Calcium and Vitamin D supplementation are the most common START criteria in osteoporosis (21). Gallagher et al. In a multicenter study conducted by him (22), it was seen that at least one criterion according to the START criteria was met in 31% of the population (24). This is similar to our study. The most common single criterion was San Jose et al. and Lozano-Montoya et al. Like their studies, calcium and Vitamin D support osteoporosis patients (24,25). While it is seen that the START criteria related to cardiovascular diseases are generally met in our country, Kara et al. in his study, similar to international studies, the criterion of "calculating/vitamin D supplementation in a patient known to have osteoporosis" is the most common START criterion (13)

One of our study's essential advantages was carried out in Turkey's leading metropolitan city, Ankara. However, we also believe that this study, carried out with many patients in intensive care services, especially on a national basis, will significantly contribute to the literature. However, the study's retrospective nature brought about the failure of clinical pharmacists to have the expected effect in the decision-making process. In addition, the lack of standardization during both the diagnosis and the evaluation of the criteria is a common shortcoming of both this study and other studies conducted in this context.

In conclusion, it can be said that the results of our study are compatible with the literature and that clinical pharmacists should play an active role during the hospitalization and patient management of the geriatric population.

Conflict of interest
No conflict of interest was declared by the authors.

REFERENCES

1. Beğer T and Yavuzer H. Yaşlılık ve yaşlılık epidemiyolojisi. Klinik gelişim. 2012; 25: 1-3.

2. Wold RS, Lopez ST, Yau CL, et al. Increasing trends in elderly persons' use of nonvitamin, nonmineral dietary supplements and concurrent use of medications. Journal of American Dietetic Association. 2005; 105: 54-63

3. Saraf AA, Petersen AW, Simmons SF, et al. Medications associated with geriatric syndromes and their prevalence in older hospitalized adults discharged to skilled nursing facilities. Journal of Hospital Medicine. 2016; 11: 694-700.

4. Morris CA and Avorn J. Internet marketing of herbal products. Journal of American Medical Association. 2003; 290: 1505-9.

5. Alldred DP, Kennedy MC, Hughes C, Chen TF and Miller P. Interventions to optimise
prescribing for older people in care homes. Cochrane Database Systematic Review. 2016; 2: CD009095.

6. Rochon P. Drug Prescribing for Older Adults. In: Givens J, (ed.). UpToDate, 2021

7. Fried TR, O'Leary J, Towle V, Goldstein MK, Trentalange M and Martin DK. Health
outcomes associated with polypharmacy in community-dwelling older adults: a systematic review. Journal of American Geriatrics Society. 2014; 62: 2261-72.

8. McLeod PJ, Huang AR, Tamblyn RM and Gayton DC. Defining inappropriate practices in prescribing for elderly people: a national consensus panel. Canadian Medical Association Journal. 1997; 156: 385-91.

9. Barry PJ, Gallagher P, Ryan C and O'Mahony D. START (screening tool to alert doctors to the right treatment)--an evidence-based screening tool to detect prescribing omissions in elderly patients. Age Ageing. 2007; 36: 632-8.

10. Kocadağ B. Evde Sağlık Hizmetleri Birimine Kayıtlı 65 Yaş ve Üzeri Hastalarda Polifarmasi ve Uygunsuz İlaç Kullanımının Değerlendirilmesi. Aile Hekimliği. Muğla: Muğla Sıtkı Koçman Üniversitesi, 2016.

11. Bozkurt E. Adıyaman Eğitim ve Araştırma Hastanesinde 65 Yaş ve Üzeri Yatan Hastalarda Uygunsuz İlaç Kullanımının İncelenmesi ve Polifarmasi Varlığı. Tıbbi Farmakoloji. Adıyaman: Adıyaman Üniversitesi, 2018.

12. Ertem Ö, Kasım Ġ, Özkara A, Koç E, Kahveci R, Şencan İ. Hastanede Yatan Yaşlı Hastalarda Uygunsuz İlaç Kullanımı. Eurasian Journal of Family Medicine. 2015; 4: 117-25.

13. Kara O, Arik G, Kizilarslanoglu MC, et al. Potentially inappropriate prescribing according to the STOPP/START criteria for older adults. Aging Clinical and Experimental Research. 2016; 28: 761-8.

14. Pitkala KH, Strandberg TE and Tilvis RS. Inappropriate drug prescribing in home-dwelling, elderly patients: a population-based survey. Archives of Internal Medicine. 2002; 162: 1707- 12.

15. Steinman MA, Landefeld CS, Rosenthal GE, Berthenthal D, Sen S and Kaboli PJ. Polypharmacy and prescribing quality in older people. Journal of American Geriatrics Society. 2006; 54: 1516-23.

16. Bay İ. Yaşlılarda Uygunsuz İlaç Kullanımının 2012 Beers Kriterleri ve STOPP Versiyon 2 Kriterleri ile Değerlendirilmesi. İç Hastalıkları. İstanbul: İstanbul Üniversitesi, 2015

17. Terzi H. Yaşlıların Kullandıkları İlaçların Uygunluğunun Beers Kriterleri Açısından Değerlendirilmesi. Sağlık Bilimleri Enstitüsü. Ankara: Gazi Üniversitesi, 2014.

18. Dişçigil G, Tekinç N and Anadol Z. Toplum İçinde Yaşayan ve Bakımevinde Kalan Yaşlılarda Polifarması. Türk Geriatri Dergisi. 2006; 9: 117-21.

19. Uçar M. Koroner Yoğun Bakım ve İç Hastalıkları Yoğun Bakım Servisinde Yatan 65 Yaş ve Üzeri Hastalarda Uygunsuz İlaç Kullanım Prevalansının Tespit Edilmesi. İç Hastalıkları Anabilim Dalı. Isparta: Süleyman Demirel Üniversitesi, 2016.

20. Lang PO, Hasso Y, Drame M, et al. Potentially inappropriate prescribing including under-use amongst older patients with cognitive or psychiatric co-morbidities. Age and Ageing. 2010; 39: 373-81.

21. Ryan C, O'Mahony D, Kennedy J, Weedle P and Byrne S. Potentially inappropriate prescribing in an Irish elderly population in primary care. British Journal of Clinical Pharmacology. 2009; 68: 936-47

22. San-Jose A, Agusti A, Vidal X, et al. Inappropriate prescribing to the oldest old patients admitted to hospital: prevalence, most frequently used medicines, and associated factors. BMC Geriatrics. 2015; 15: 42.

23. Borges EP, Morgado M and Macedo AF. Prescribing omissions in elderly patients admitted to a stroke unit: descriptive study using START criteria. International Journal of Clinical Pharmacology. 2012; 34: 481-9.

24. Gallagher P, Lang PO, Cherubini A, et al. Prevalence of potentially inappropriate prescribing in an acutely ill population of older patients admitted to six European hospitals. European Journal of Clinical Pharmacology. 2011; 67: 1175-88.

25. Lozano-Montoya I, Velez-Diaz-Pallares M, Delgado-Silveira E, Montero-Errasquin B and Cruz Jentoft AJ. Potentially inappropriate prescribing detected by STOPP-START criteria: are they really inappropriate? Age of Ageing. 2015; 44: 861-6.