ORIGINAL ARTICLE

POTENTIALLY INAPPROPRIATE ANTIDEPRESSANT USE IN OLDER PEOPLE COMPARED WITH THE ADULT POPULATION IN TÜRKIYE

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Abstract

Introduction: The prevalence of polypharmacy in older people contributes to potentially inappropriate prescribing, which is evaluated using various criteria. Depressive disorders are serious issues for older adults. In this study, the prescribing rates of potentially inappropriate antidepressants in older age groups in Türkiye were compared with younger age groups.

Materials and Method: All electronic prescriptions including those for antidepressants, in Türkiye, issued by family physicians in 2019 were obtained using the Prescription Information System. Data were analyzed using the Beers Criteria 2019 update.

Results: Of all prescriptions, 0.63% written for older people (65 years and over) were "Potentially Inappropriate Medication" classified antidepressant medications. A significantly lower percentage of "Potentially Inappropriate Medication" classified prescriptions, was observed for older people compared to the rate of total prescriptions (30.6% vs 32%). Paroxetine and amitriptyline had the highest prescription rates for older people. Older people received significantly more "Drugs to be Used With Caution" (35.6% vs. 32%). The top five most frequently prescribed "Drugs to be Used With Caution" for older people were escitalopram, sertraline, duloxetine, citalopram, and mirtazapine.

Conclusions: There was a lower rate of prescribing of "Potentially Inappropriate Medication" for older people (65 years and over) than for younger (between 18-65 years) people. This suggests that family physicians are aware of the potential inappropriateness of specific antidepressants and prescribe them less frequently. Additionally, increased prescribing of "Drugs to be Used With Caution" in elderly can be associated with the limited availability of completely safe drugs in this population.

Keywords: Antidepressive Agents; Geriatrics; Potentially Inappropriate Medication List; Prescriptions.

INTRODUCTION

While 9.7% of the worldwide population was aged 65 and older in 2022, according to United Nations data, it is expected to increase to 11.7% in 2030 and 16.4% in 2050 (1). According to the 2023 statistics of the Turkish Statistical Institute, this age group constitutes 10.2% of the total population in Türkiye and it is estimated to increase to 12.9% in 2030, 16.3% in 2040, 22.6% in 2060, and 25.6% in 2080 (2).

Depression and other psychiatric disorders are serious issues in older people. These disorders can also mimic dementia and other neurological disorders, or simply coexist with them. The incidence of depressive disorders was found to be 12.3% in a meta-analysis that examined older people in nine European nations, whereas the prevalence of a depressed mood ranged from 26% to 40%, in the same study (3).

Several criteria have been devised to improve the safety of medication use for "Potentially Inappropriate Medications" (PIMs) in older people. The Beers Criteria, first published by the American Geriatrics Society (AGS) in 1991 and subsequently revised, were one of the earliest and most widely used sets of criteria (4). The Beers Criteria is a list of prominent PIMs that physicians typically avoid prescribing to older people, in most circumstances, except for specific diseases or conditions.

The main aim of this study is to evaluate the differences in the use of drugs considered potentially inappropriate for the elderly across different age groups. Identifying the differences in the usage of these drugs, especially between the elderly and younger individuals, is important. This evaluation will provide guidance on whether there is sufficient awareness among primary care physicians regarding the use of these drugs in the elderly.

MATERIALS AND METHOD

Research Authorization and Data Collection

This study was conducted in collaboration with the Rational Drug Use Department of the Turkish Medicines and Medical Devices Agency. The study protocol was signed for data sharing with the Ministry of Health (MoH). Before commencing the study, permission was obtained from the Gazi University Clinical Research Ethics Committee. (07.12.2020, Decision no: 818). All prescriptions written electronically by family physicians to patients aged 15 years and older in Türkiye in 2019 and registered in the Prescription Information System (PIS) were accessible. An analysis of antidepressant drugs prescribed electronically by family physicians to patients aged 15 and older was performed on data obtained through the PIS, which is under the administration of the MoH. The evaluation of the "appropriateness" of prescriptions for antidepressant medication in the database was performed using the "Beers Criteria 2019 update" (4). The prescription data utilized in this research pertain to the year 2019; thus, the prescribed medications from that year were assessed based on the 2019 version of the Beers Criteria. Anatomical Therapeutic Chemical Classification (ATC) codes for PIMs were determined, and data were extracted from the prescription pool accordingly.

Study Groups

According to the Beers Criteria, PIMs in older people are grouped under five headings: "1" medications that are potentially inappropriate in most older adults, "2" those that should typically be avoided in older adults with certain conditions, "3" drugs to be used with caution, "4" drug-drug interactions, and "5" drug dose adjustment based on kidney function (4). In this study, only the drugs classified under headings "1" and "3" were analyzed because detailed clinical information for the other headings could not be obtained from the PIS. Accordingly, the study groups were evaluated under two headings: "Potentially Inappropriate Medication (PIM)" and "The Drugs To be Used With Caution (DUC)".

PIM Group: As this study focused only on

antidepressant medications, herafter PIM refers to "Potentially Inappropriate Antidepressant". PIMs include amitriptyline, amoxapine, clomipramine, desipramine, doxepine (> 6 mg/day), imipramine, nortriptyline, paroxetine, protriptyline, and trimipramine. The criteria for defining these drugs as potentially inappropriate were: highly anticholinergic, sedating, and cause orthostatic hypotension; safety profile of low-dose doxepin (≤6 mg/day) comparable to that of placebo. A high level of evidence suggests that these antidepressants should not be prescribed for older people (4). Among the medications listed in this category, only amitriptyline, clomipramine, imipramine, and paroxetine were licensed and available for prescription in Türkiye in 2019.

DUC Group: Antidepressant Drugs to be Used with Caution" (DUC) according to the Beers Criteria are: mirtazapine, Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs), Selective Serotonin Reuptake Inhibitors (SSRIs), and Tricyclic Antidepressants (TCAs). The purpose of establishing this group by the AGS was to identify drugs for which there is some cause for concern but for which the evidence and/or clinical context is still insufficient to merit inclusion in the PIM group. In this study, the medications evaluated in this category (licensed and prescribed in Türkiye) were: citalopram, escitalopram, duloxetine, fluoxetine, fluvoxamine, maprotiline, milnacipran, mirtazapine, sertraline, and venlafaxine. These drugs are reported as "to be used with caution". It should be noted that duloxetine, venlafaxine, and mirtazapine can only be prescribed by family physicians if a "drug report" has previously been issued by a specialist physician.

Evaluation of Prescriptions Containing PIMs

Evaluations were performed based on the ratio of PIM-containing prescriptions to the total number of prescriptions (for all indications) in the study cohort. However, a PIM may have been prescribed to a patient more than once in the year. Additionally, a single prescription may contain more than one PIM. In this scenario, each PIM was analyzed as a separate prescribing event. However, since this study aimed to determine the number of times an antidepressant PIM was prescribed, the PIS provided appropriate data.

In the study, the prescription rates of the PIMs were analyzed by four patient age groups: 15-24 years; 25-64 years; 65-79 years; and 80 years and older. Differences in the prescription rates of PIMs for older people between the older and younger age groups were determined.

Statistics

Descriptive statistics are expressed as frequencies and percentages for categorical variables. Analyses were performed using SPSS software (version 23.0; IBM software). Statistical significance was set at $p < 0.05$. Differences between groups were compared using the chi-square test with the Yates continuity correction method.

RESULTS

General prescribing characteristics

A total of 139,288,644 electronic prescriptions (for all indications) were issued by family physicians to the people aged 15 and older in Türkiye in 2019. Nine percent of these prescriptions were issued to people aged 15-24 years, 59% to people aged 25-64 years, 25% to people aged 65-79 years, and 7% to people aged 80 years and older. However, 20% of the population was aged 15-24 years, 68% was aged 25-64 years, 10% was aged 65-79 years and 2% was aged 80 years and over (Figure 1). The demographic population distribution of the relevant age groups was compared with the distribution of the overall prescription rates across age groups. Prescriptions for people under 65 years were lower

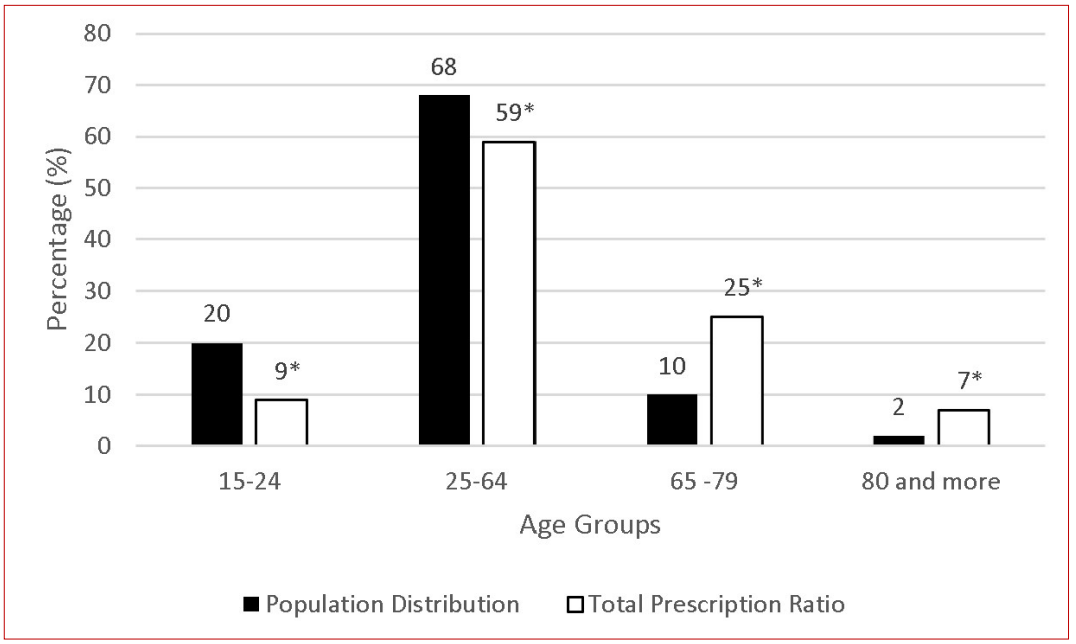

Figure 1. Distribution of total prescription ratios by age groups and comparison with population distribution. The black bars show the population distribution and the white bars show the total prescription ratios issued to individuals in the relevant age group (*p<0.05, different from the population distribution group, Chi-square).

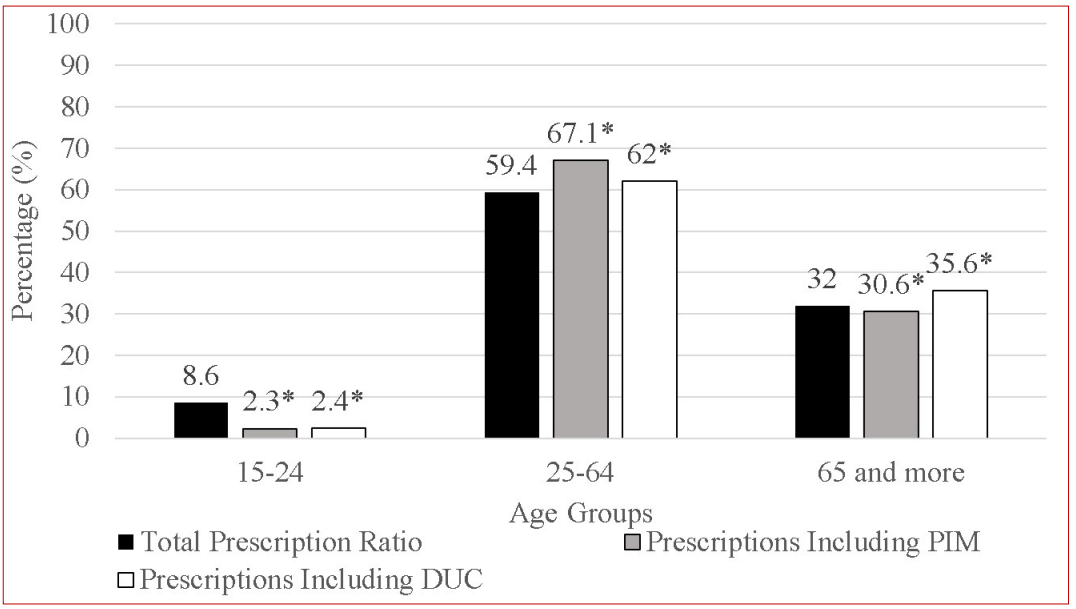

Figure 2. Comparison of the prescription rates of PIM and DUC containing prescriptions by age group with the ratio of total prescriptions by age group. The black bars show the percentage of total prescriptions issued, the gray bars show the percentage of prescriptions including a PIM, and the blank white bars show the percentage of prescriptions including a DUC in the respective age group (*p<0.05, different from total prescriptions, Chi-square). PIM: Potentially Inappropriate Medications, DUC: Drugs Used with Caution

Table 1. Comparison Of The Prescription Rates Of PIM And DUC Containing Prescriptions By Age Group With The Ratio Of Total Prescriptions By Age Group

	15-24	25-64	65 and more	Total	p-value
Total presccriptions ratio	11.921.951 (8.6%)	82.745.090 (59.4%)	44.621.603 (32%)	139.288.644	<0.05
Prescriptions Including PIM	20.788 (2.3%)*	615.427 (67.1%)*	281.128 (30.6%)*	917.343	<0.05
Prescriptions Including DUC	118.839 (2.4%)*	3.070.017 (62%)*	1.762.784 (35.6%)*	4.951.640	<0.05

** p<0.05; different from total prescriptions ratio, chi-square*

PIM: Potentially Inappropriate Medications, DUC: Drugs Used with Caution

and prescriptions for people 65 years and older were significantly higher than prescriptions for the overall cohort (p<0.05, different from the population distribution group, Chi-square).

PIMs

There were 281,128 PIM-containing prescription for people 65 and older. Of all prescriptions (44.621.603), 0.63% prescriptions written for older people were PIM-classified antidepressant medications. The prescription rates of these drugs, which are not recommended for use in older people, were 0.17% (20.788 out of 11.921.951 prescriptions) for those in the 15-24 years group and 0.75% for those in the 25-64 years group (615.427 out of 82.745.090 prescriptions). When the distribution of "PIM" group prescriptions and total prescriptions by age groups were compared, the 65 years and older group were presecribed a significantly lower percentage of PIMs (30.6% vs. 32%) (Figure 2, Table 1).

Table 2. Prescription Rates of PIM Group Drugs. (A) Number and Rates of Prescription of PIM Group Drugs for Older People, (B) Prescription Rates of PIM Group Drugs by Age Group

(A) Number and Rates of Prescription of PIM Group Drugs for Older People					
Drugs	Prescription number		Percentage (%)		
Paroxetine	178.831		63.6		
Amitriptyline	83.754		29.8		
Clomipramine	15.891		5.7		
Imipramine	4.200		1.5		
Total	281.128		100		
(B) Prescription Rates of PIM Group Drugs by Age Group					
Drugs	15-24 (%)	25-64 (%)	65 and older (%)	Total (%)	P
Total	8.6	59.4	32	100	
Paroxetine	2.0*	68.0*	30*	100	<0.05
Amitriptyline	1.8*	61.9*	36.3*	100	<0.05
Clomipramine	4.6*	76.8*	18.6*	100	<0.05
Imipramine	7.4*	56.9*	35.7*	100	<0.05

** p<0.05; different from total prescriptions ratio, chi-square*

PIM: Potentially Inappropriate Medications

Paroxetine (63.6%) and amitriptyline (29.8%) had the highest prescription rates among the four PIMs (amitriptyline, clomipramine, imipramine, and paroxetine) in the older age group (Table 2A). Amitriptyline (36.3%) and imipramine (35.7%) were more frequently prescribed for the 65 years and older group compared to the total prescription rate (32%). Amitriptyline (61.9%), clomipramine (76.8%), and paroxetine (68%) were prescribed significantly more frequently for the 25-64 years group compared to the overall prescription rate (59.4%). All drugs were prescribed less frequently in the 15–24 years group compared to the overall prescription rate (Table 2B).

Medications prescribed to the older age groups were internally re-evaluated. The prescription rates of amitriptyline (25.1%) and imipramine (25.2%) for the 80 years and older group were significantly higher than the total prescription rate (22.2%) for this group. In the 65-79 years group, the prescription rates of clomipramine (85.6%) and paroxetine (80.5%) were higher compared to the total prescription rate (77.8%) for this group (Figure 3).

DUC

For all prescriptions issued to people aged 65 years and older, DUCs accounted for 3.95%. The prescription rates of DUCs were compared with the overall prescription rates within each age group. Older patients received significantly more DUC prescriptions than the total prescription rate (35.6% vs. 32%). Additionally, it was higher in the 24-64 years group (62% vs. 59.4%); however, it was lower in the 15–24 year group (2.4% vs. 8.6%) (Figure 2, Table 1).

The top five most frequently prescribed DUCs for older people were: escitalopram (40.2%), sertraline (25.7%), duloxetine (11%), citalopram (7.5%), and mirtazapine (7.4%) (Table 3A). When the percentage distributions of prescriptions containing these drugs among age groups were compared with the percentages of all prescriptions for the relevant age groups, it was observed that the prescription rates of escitalopram (26.3%), sertraline (24.8%), citalopram (26.4%), and mirtazapine (33.6%) for those in the 80 years and older group were higher than the total prescription rate (22.2%).

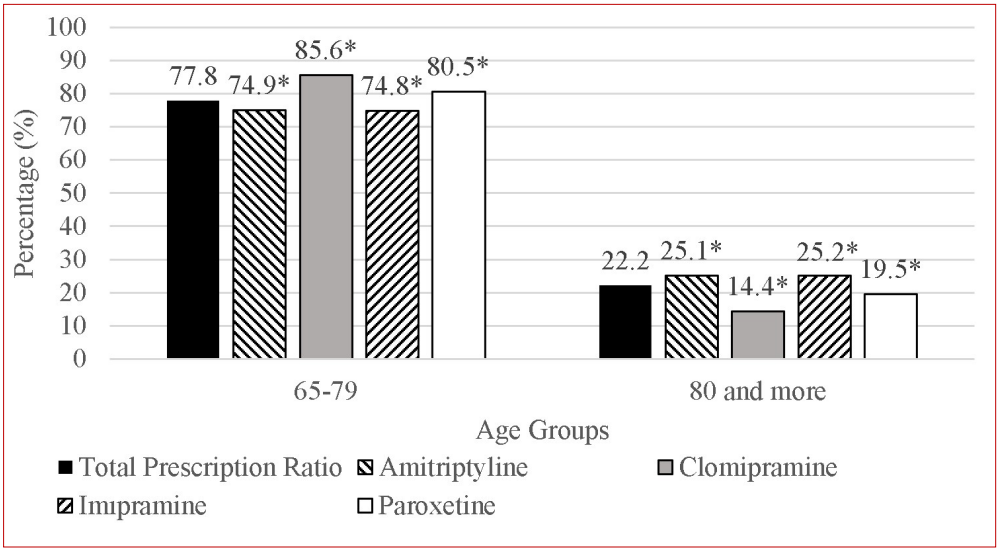

Figure 3. Distribution of prescriptions, including PIM in the older age group and comparison with the total prescription ratio. (*p<0.05; different from total prescription ratio, Chi-square) PIM: Potentially Inappropriate Medication

However, in the 65-79 years group, this pattern was reversed (p<0.05; chi-square). The prescription rates of DUCs based on each age group showed that the prescription rates of DUC for the 65 years and older group were higher for escitalopram (42.8%), maprotiline (42.2%), mirtazapine (46.5%), sertraline (37.8%), and citalopram (47.7%) than for the total prescription rate (32%). In contrast, in the 25-64 years group, they were lower than the total prescription rate. Moreover, in the 25-64 years group, the prescription rates for duloxetine (69.8%), fluoxetine (77.6%), fluvoxamine (73.3%), milnacipran (73.3%), and venlafaxine (77.6%) were higher than the total prescription rate (59.4%) (Table 3B).

Prescriptions containing DUCs were evaluated in older age groups. Prescriptions containing DUCs were prescribed to 75.8% of the 65-79 years group, and 24.2% of the 80 years and older group.

Table 3. Prescription Rates of Drugs to be Used With Caution. (A) Number and Rates of Prescription of Drugs to be Used With Caution fro Older People, (B) Prescription Rates of Drugs to be Used With Caution by Age Group

(A) Number and Rates of Prescription of Drugs to be Used With Caution for Older People					
Drugs	Prescription Number			Percentage	
Escitalopram	709.027			40.2	
Sertraline	453.383			25.7	
Duloxetine	201.651			11.4	
Citalopram	132.768			7.5	
Mirtazapine	130.929			7.4	
Venlafaxine	93.194			5.3	
Fluoxetine	81.695			4.6	
Fluvoxamine	5.936			0.3	
Maprotiline	3.446			0.2	
Milnacipran	3			0.001	
All Drugs	1.762.784			100	
(B) Prescription Rates of Drugs to be Used With Caution by Age Group					
	15-24 (%)	25-64 (%)	65 and (%)	Total	p
Total	8.6	59.4	32	100	<0.05
Essitalopram	1.4*	55.8*	42.8*	100	<0.05
Sertraline	3.6*	58.6*	37.8*	100	<0.05
Duloxetine	0.7*	69.8*	29.5*	100	<0.05
Sitalopram	1.0*	51.3*	47.7*	100	<0.05
Mirtazapine	2.4*	51.1*	46.5*	100	<0.05
Venlafaxine	1.8*	77.6*	20.6*	100	<0.05
Fluoxetine	6.3*	77.6*	16.1*	100	<0.05
Fluvoxamine	5.5*	73.3*	21.2*	100	<0.05
Maprotiline	1.6*	56.2*	42.2*	100	<0.05
Milnacipran	6.7*	73.3*	20.0*	100	<0.05

** p<0.05; different from total prescriptions ratio, chi-square*

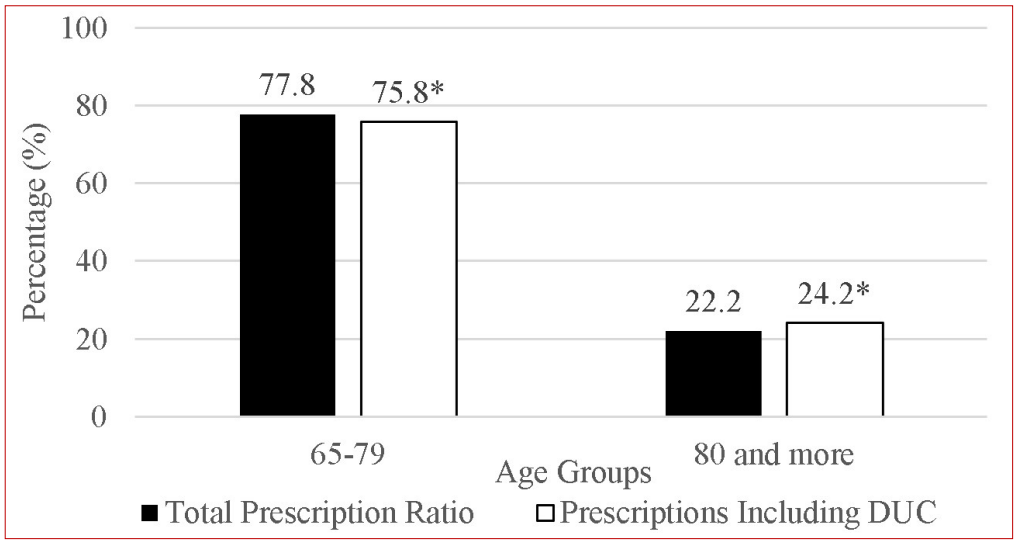

Figure 4. Distribution of prescriptions, including DUCs by age group and comparison with total prescription ratios. The black bars show the total prescription ratio, and the blank white bars show the percentage of prescriptions containing a DUC issued to individuals in the relevant age group (*p<0.05; different from the total prescription group, Chi-square). DUC: Drugs Used with Caution.

Compared with the total prescription rate, there was a lower percentage of prescriptions containing DUCs in the 65-79 years group (75.8% vs 77.8%) and a higher percentage in the 80 years and older group (24.2% vs 22.2%) (Figure 4).

DISCUSSION

The findings of this study show the prevalence of the use of PIMs among people aged 65 years and older. Furthermore, comparative data on the use of these drugs across various age groups have been presented. When interpreting these results, the following approach should be taken into account. The percentage-based data obtained in our results have been compared with the overall prescribing rates. The results demonstrated that the PIM prescription rate for older people was lower than the overall prescription rate. This suggests that family physicians are aware of the potential inappropriateness of specific antidepressants and prescribe them less frequently.

Tseregounis et al. demonstrated that prescription rates increased with patient age (5). According to the findings of our study, family doctors in Türkiye tended to write more prescriptions for patients aged 65 years and older relative to their percentage of the population. This finding is consistent with the literature and holds true even when people 80 years and older are considered separately.

A study highlighted that the prevalence of inappropriate medication prescriptions among general practitioners was initially 37.3%, which improved to 23.6% after training on the Beers criteria, demonstrating the potential for education to enhance compliance (6). Despite this improvement, the overall rates suggest that a substantial proportion of prescriptions remain inappropriate, indicating a need for ongoing education and adherence to the criteria.

In our study, the rate of PIMs prescriptions according to the Beers Criteria was 0.63%. In a 2008 study conducted in Brazil, PIMs prescription rates according to the Beers Criteria were 0.9% among

5,732 individuals aged 60 years and older (7). In another study conducted in France between 2008 and 2010 involving 2,350 individuals aged 70 years and older, the prescription rate for PIMs according to the Beers Criteria was 5%. (8). When these studies were evaluated together, the prescription rate for PIMs for older people ranged from 0.9% to 5%, which is higher than the 0.63% reported in the present study.This study presents, for the first time, on a national scale for the Turkish population, the prescription rates of PIMs by family physicians. In addition, a comparison of data within different age groups of the population was performed. The results demonstrated that the PIM prescription rate for older people was lower than the overall prescription rate. Furthermore, as age increases (particularly older than 80 years), the rate of PIM prescriptions continues to decrease. This suggests that family physicians are aware of the possibility of prescribing PIMs for older people. Moreover, considering the comparison with earlier studies, the lower rate is encouraging.

However, that amitriptyline, clomipramine, imipramine, and paroxetine, which fall under the PIM category, are still being prescribed to individuals aged 65 years and older is of concern. This could be due to the drugs being included in the depression treatment guidelines in Türkiye and worldwide, as well as the possibility that they are used rarely due to inadequate responses with safer alternatives, except for paroxetine, among other SSRIs (9).

In this study, the use of drugs classified as PIMs for those 65 years and older by the Beers Criteria was analyzed among people between the ages of 15 and 65 years. When compared to the percentage of total prescriptions, the use of these drugs was significantly lower in the 15–24 years group and significantly greater in the 25–64 years group. The lower prevalence of depression and the presence of special warnings for all antidepressant medications in this age group may be responsible for the reduced use of these drugs in the 15–24 years group (10, 11).

Paroxetine, is a PIM that is most frequently prescribed to older people (63.6%), followed by amitriptyline (29.8%). As a member of the SSRI class of antidepressants, paroxetine is used to treat depression. However, SSRIs are frequently used for conditions other than major depression, including Post-Traumatic Stress Disorder, Obsessive-Compulsive Disorder (OCD), generalized anxiety disorder, and social anxiety disorder (11). Furthermore, SSRIs are not only recommended as first-line drugs in national and international treatment guidelines but are also considered to have a safer adverse effect profile compared to other medications (12). This explains the continuation of paroxetine use for older people, despite its considerable anticholinergic effects.

In this study, prescriptions for drugs such as clomipramine and imipramine were prescribed to people aged 65 years and older at relatively low rates (5.7% and 1.5%, respectively). Apart from its off-label use for stress incontinence in the older age group, imipramine is not widely used in this demographic. It is mostly used to treat nocturnal enuresis in young people (10). Clomipramine, on the other hand, is primarily used in the treatment of OCD, and its prevalence in the 25-64 years group is higher than that in the older age group (13). Additionally, while the prevalence of OCD in older people is approximately 0.6%, the prevalence of major depressive disorders is high, ranging from 28.4% (14, 15). Therefore, it is not surprising that amitriptyline, which is FDA approved only for major depressive disorders, was the second most frequently used PIM after paroxetine in this study. Amitriptyline is known to be used off-label in diseases such as insomnia, migraine prevention and ADHD (16). However, family physicians may avoid using it in this way. In the United States, it has been shown that among the PIMs prescribed to those aged 65 years and older, paroxetine (68%) and amitriptyline (18%) are similar to the findings in this study (17).

The potential to trigger or worsen Syndrome of Inappropriate Antidiuretic Hormone (SIADH)

necessitates a careful assessment of the use of antidepressant medications in older people. If these medications are to be used, it has been advised that close monitoring of the serum sodium level be performed before initiating therapy or adjusting the dosage.

The prevalence of SSRI-induced hyponatremia in patients with a history of depression appears to be significant, particularly among older adults. A study reported that out of 21 patients treated with SSRIs, 9 developed hyponatremia within an average of 2.5 weeks, with a mean sodium level of 126 mEq/L, indicating a notable risk associated with these medications (18). Additionally, a retrospective cohort study found a significant decrease in serum sodium levels (mean change of -1.00 mmol/L) within 30 days of initiating SSRIs (19).

In this study, DUC-containing prescriptions constituted 3.95% of all prescriptions for older people. These drugs are prescribed more frequently to older people relative to the population size. However, in the 15-24 years group, they were prescribed less frequently relative to the population size. The drugs that were prescribed more frequently to older people include escitalopram, citalopram, maprotiline, and mirtazapine. The preference for escitalopram and citalopram may be due to their lower drug interactions (20). Nevertheless, the QT-prolonging deleterious effects of escitalopram have garnered significant attention, particularly in recent literature (21). In addition, maprotiline, a TCA, should be used with caution for older people due to its anticholinergic effects (22). Despite the possible adverse effects, there has been no decrease in the prescription rates of these medications for older people. However, from another perspective, it is also a reality that there is not a definitive "gold standard" antidepressant that can be safely used for older people. The choice of medication for older people should be evaluated specifically based on the patient and drug selection (23). Therefore, owing to the limited availability of alternative and safer drugs, physicians prescribing these medications at higher rates than expected based on their knowledge of the literature of these indications should not be negatively evaluated.

In this study, among the drugs that require cautious use for older people, the prescription rates of duloxetine, fluoxetine, fluvoxamine, milnacipran, and venlafaxine were lower than those in the 25-64 years group. Venlafaxine may not be the drug of choice for older people because of its potential to increase blood pressure and its adverse arrhythmic effects (24). Duloxetine does not have a significantly higher efficacy than SSRIs but carries a higher risk of severe hyponatremia (25). Fluoxetine and fluvoxamine are known among SSRIs because of their inhibitory effects on cytochrome P450 enzymes, which lead to more frequent drug interactions. Therefore, they may not be preferred for older people, where polypharmacy is a common issue (20). Although milnacipran is more tolerable than TCAs, it does not have a significant advantage over SSRIs in terms of efficacy (26). All of these drugs mentioned, evaluated under the "DUC" category for older people, are not considered inappropriate for the 25-64 years group. In line with this information, our data indicate that these drugs are prescribed more frequently for younger people. Furthermore, considering the indications, duloxetine is used not only for major depressive disorders but also for generalized anxiety disorder and treatment of fibromyalgia. These conditions are less frequently encountered with increasing age (27).

Fluoxetine is commonly used in the treatment of obsessive-compulsive disorders and its prevalence decreases with age. (28).

This study is the first nationwide study conducted in Türkiye that evaluated the prescription of PIMs for older people issued by family physicians. The study also compared the rate of medication use with that of younger people based on the Beers criteria. This study observed a remarkably low rate

of prescription of antidepressant PIMs for older people by family physicians. Furthermore, the use of these medications among older people was lower than that among younger people. This suggests that family physicians are aware of the potential inappropriateness of specific antidepressants for older people and prescribe them less frequently.

LIMITATIONS

As prescription data were obtained from the PIS, only the number of medication prescriptions could be accessed, and detailed clinical information was not available. This study exclusively evaluated prescriptions from primary care physicians, and access to prescriptions from healthcare institutions in secondary and tertiary care settings was not possible. Another significant limitation is that, in Turkiye, family physicians can prescribe duloxetine, milnacipran, mirtazapine, and venlafaxine only to patients with the approval of specialist physicians.

Therefore, the prescription of these medications by family physicians should only be considered as represcriptions because of the requirement for a specialist physician report.

Conflict of Interests: The authors declare no conflicts of interest.

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