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- Birol ÇIBIK[1]
- Erkan Melih ŞAHİN[2]
- Mehmet Göktuğ KILINÇARSLAN[2]

CORRESPONDANCE

Mehmet Göktuğ KILINÇARSLAN
Çanakkale Onsekiz Mart University
Faculty of Medicine, Department
of Family Medicine
Çanakkale, Turkey

Phone: 2862636471
e-mail: goktugmk@gmail.com

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[1] Tokat State Hospital, Family Medicine Clinic
Tokat, Turkey
[2] Çanakkale Onsekiz Mart University
Faculty of Medicine, Department
of Family Medicine
Çanakkale, Turkey

RESEARCH

A POPULATION-BASED STUDY: THE APPROPRIATENESS OF DRUG USE IN THE ELDERLY ACCORDING TO BEERS CRITERIA

Abstract

Introduction: The elderly population has the highest rates of drug use and is more sensitive to drug effects. Inappropriate drug use can cause unwanted effects in such a population. We aimed to evaluate inappropriate drug use in the elderly population according to Beers criteria.

Materials and Method: This cross-sectional, descriptive study used a simple systematic method to select individuals aged >65 years residing in Kepez district of Canakkale. All medicines used by participants were identified and evaluated according to Beers criteria.

Results: The mean age of the participants was 74.1±6.5 (65–91) years. In our study, 95.7% of the participants had at least one chronic illness and 84.5% had at least three chronic illnesses. The mean total number of drugs used was 5.0±3.2 (0–15). According to Beers criteria, inappropriate drug use was detected in 35 (30%) instances. Non-steroidal anti-inflammatory drugs were the most frequent inappropriately used drugs in the study population [n=13 (11.2%)].

Conclusion: In this study, the rates of inappropriate drug use (35; 30%) were lower than those previously reported. Our findings underline the importance of adhering to guidelines for rational drug use in prescribing medications to elderly.

Keywords: Potentially inappropriate medication list; Drug interactions; Drug-related side effects and adverse reactions; Chronic disease; Inappropriate prescribing; Turkey

ARAŞTIRMA

TOPLUM TABANLI BİR ÇALIŞMA: YAŞLILARDA İLAÇ KULLANIMININ BEERS KRİTERLERİNE UYGUNLUK DURUMU

Öz

Giriş: Yaşlı popülasyon en yüksek ilaç kullanım oranına sahip olup ilaç etkilerine daha duyarlıdırlar. Uygunsuz ilaç kullanımı bu hastalarda istenmeyen etkilerin ortaya çıkmasına neden olabilmektedir. Bu çalışmada Beers kriterlerine göre yaşlılarda uygunsuz ilaç kullanımının değerlendirilmesi amaçlanmaktadır.

Gereç Yöntem: Kesitsel, tanımlayıcı desendeki araştırmamızda Çanakkale Kepez beldesinde ikamet eden 65 yaş ve üzeri bireylerden basit sistematik yöntemle örneklem seçildi. Çalışmaya alınan yaşlıların aktif kullandıkları tüm ilaçlar belirlenip Beers kriterleri açısından değerlendirildi.

Bulgular: Katılımcıların yaş ortalaması 74.1±6.5 65-91 idi. Çalışmamızda yaşlıların %95.7'sinde en az bir kronik hastalık, %84.5'inde ise en az üç kronik hastalık varlığı saptanmıştır. Yaşlıların kullandıkları toplam ilaç sayısı ortalama 5.0±3.2 0–15 idi. Beers kriterlerine göre toplam 35 (%30) durumda uygunsuz ilaç kullanımı saptandı. Çalışmamızda en sık uygunsuz kullanılan ilaç olarak 13 (%11.2) bireyde non-steroidal antienflamatuar ilaçlar saptandı.

Sonuç: Literatürdeki diğer araştırmalara göre daha az oranda olsa da çalışmamızda yaşlı hastalarda (35; %30) uygunsuz ilaç kullanımı olduğu saptanmıştır. Yaşlı hastalara ilaç reçete edilirken akılcı ilaç kullanım kurallarına uymanın önemi ortaya çıkmıştır.

Anahtar sözcükler: Potansiyel uygun olmayan ilaç listesi; İlaç etkileşimi; İlaç yan etkisi; Kronik hastalık; Uygunsuz reçeteleme; Türkiye

INTRODUCTION

Elderly individuals are more prone to experience drug adverse effects and drug–drug interaction because of physiological changes associated with ageing, which are liable to affect drug metabolism (1). The population that consumed the most drugs was aged ≥65 years, and 17%-19% consumed at least 10 drugs per week (2).

The use of drugs in elderly people is often inappropriate partly because of the complexities of prescribing as well as other patient, provider, and health-system factors so inappropriate prescribing in elderly people has therefore become an important public-health issue worldwide. Even while there are too many terms to describe prescribing quality (such as good, poor, optimal), the term of appropriate drug use can be used to express the quality level needed to be reached in practice (3).

Various criteria have been developed to guide appropriate drug use in elderly individuals and they can be grouped in 1. implicit criteria (judgement based) such as the Medication Appropriateness Index-MAI and 2. explicit criteria (criterion-based) such as Beers and STOPP/START criterias (4).

Explicit criteria are composed by literature review and expert consensus. Using explicit criteria is easier than using implicit criteria in practice because of explicit criteria are just focus on drugs and/or drug-disease relation without any need to clinical judgement (such as patient preferences, all medicines of patient) (5).

O'Mahony and Gallagher (6), offer six principles for selecting optimal explicit criteria: (i) organization based on physiological systems and rapid applicability in daily practice; (ii) inclusion of the more common errors of commission and omission in prescribing for older adults; (iii) generalizability to the global community of physicians and pharmacists; (iv) ease of interface with computer records of co-morbidities of patients and lists of drugs; (v) ability to reduce the prevalence of potentially inappropriate medications in older adults in different settings; and (vi) ability to reduce the incidence and negative impact of adverse drug reactions but there is no explicit criteria can fulfil all principles (4). Because of there is not any ideal criteria for screening inappropriate drug use, any of them can be selected according to situations such as for research or daily clinical routine (5).

The use of certain medications in elderly individuals should be avoided according to the Beers criteria developed by the American Geriatrics Society to prevent inappropriate drug use among elderly and updated in 2015 (Tables 2-4). In these criteria, all drugs with a high potential to cause adverse effects in elderly individuals are listed; adverse effects of each drug group are specified and recommendations for use are provided. Depending on the changes in kidney function and drug interactions in elderly individuals, special restrictions may be required with respect to dosage, dose interval and treatment duration. Beers criteria were found to be a highly useful guide for reducing inappropriate drug use, minimising drug-related adverse effects and reducing treatment costs (7). Inappropriate drug use rate according to Beers criteria change from %10.3 to %66.7 in literature (8,9).

Beers criteria has also some limitations but it is still widely used (10). Also Beers criteria is most cited explicit criteria in literature (4). STOPP/START has three implicit prescribing rules unlike Beers criteria, that means using STOPP/START criteria to screen inappropriate drug use need clinical judgement (11).

In this study we aimed to assess the appropriateness of drug use in the elderly population in the Kepez district of Canakkale on the basis of Beers criteria.

MATERIALS AND METHOD

Sampling methodology

This cross-sectional, descriptive study included 1161 individuals aged ≥65 years residing in Kepez district of Canakkale. The sample size is calculated 124 people for estimated prevalence for inappropriate drug use rate of 0.10 with the precision value of 0,05 (8). A simple systematic method was used to select the study sample. The list of elderly individuals was obtained from the Kepez Municipality and sorted according to age and sex. One from every 10 in a row like 1.-11.-21. were invited to participate in the study. The selected individuals were contacted via telephone calls or by personal visits to their residence addresses. In case the selected individuals were not reachable or did not meet the selection criteria, the next individual in the list was contacted till the set total number of targeted participants was achieved.

Inclusion and exclusion criteria

Individuals aged ≥65 years were eligible for the study. Exclusion criteria included presence of illness or disability that would prevent compliance with the study method (such as the presence of a psychiatric disorder that would disrupt reality assessment or a medical condition that would impair the ability to respond to questions).

Application

A total of 37 elderly persons could not be reached because of death, change in address or owing to errors in the recorded data. Two participants with dementia and hearing loss were excluded, whereas 36 (%31) participants were excluded because they did not agree to participate in the study. Data collection was completed after reaching 10% (116) of the target group.

Participants were invited to the Family Medicine clinic at the Canakkale Onsekiz Mart University Hospital for interview and 30 participants were interviewed at their home after they expressed their inability to visit the clinic. Written informed consent of the participants was obtained before administering the questionnaires. The data were anonymously recorded.

Permits and approvals

Before initiating the study, approval was obtained from the Clinical Research Ethics Committee at the Canakkale Onsekiz Mart University. Elderly individuals invited to participate in the study were provided verbal data regarding the study, and written consent was obtained.

Statistical analysis

Data were analysed using the descriptive features in IBM SPSS v20 software. Non-parametric analysis (Mann Whitney U test for two independent samples, Kendall's tau-b correlation) were used when appropriate.

RESULTS

Sociodemographic characteristics

Of the 116 elderly individuals, 56 (48.3%) were males and 60 (51.7%) were females. The mean age of the participants was 74.1±6.5 (65–91) years; there was no significant difference between the mean age of males (73.7±6.2 years) and those of females (74.4±6.8 years) (p=0,680). Furthermore, 77 (66.4%) participants were married and 39 (33.6%) were widowed. Seventy-five (64.7%) participants were primary school graduates. For male participants, the mean weight was 78.5±14.6 (range, 50–135) kg, mean height was 171.2±7.1 (155–195) cm and mean body mass index (BMI) was 26.7±5.6 kg/$m^{2.}$ For of female participants, the mean weight was 70.9±13.0 (44–110) kg, mean height was 155.7±7.0 (143–171) cm and mean BMI was 29.3±5.6 kg/m2.

Chronic diseases

In our study, 95.7% of the participants had at least one chronic illness and 84.5% had at least three chronic illnesses. Five (4.3%) participants stated that they did not have any chronic disease. The mean number of chronic diseases in the study population was 5.7±2.9 (0–12). The chronic diseases and their prevalence in our study population are given in Table 1.

Drug use, adverse effects and drug–drug interactions

Eleven (9.5%) participants were not using any medication. The mean total number of drugs used by the participants was 5.0±3.2 (0–15); the average daily dose of medication was 5.7±4.1 (0–26). In our study, the most frequently used medicines according to the anatomic therapeutic chemical classification were cardiovascular system drugs (69.8%), digestive system and metabolism drugs (62.1%), nervous system drugs (47.4%), blood and blood-forming drugs (44.8%), musculoskeletal drugs (37.1%), sensory organ drugs (13.8%) and respiratory system drugs (12.1%).

Sixty-four (55.2%) participants used five or more drugs per day. A positive correlation was observed between the number of medications used and age (tau-b=0.140; p=0.036). The total number of drugs used by female participants (5.6±2.9) was significantly higher than that used by male participants (4.3±3.4) (U=1208.0; p=0.009). There was no significant difference between female (6.0±3.4) and male (5.4±4.8) participants (U=1441.0; p=0.185) with respect to the number of daily medication doses. The incidence of chronic illness among the participants was positively correlated with the number of medications used (tau-b=0.546; p<0.001) and daily doses of medication (tau-b=0.470; p<0.001).

There was a positive correlation between the number of drugs used by the participants and the incidence of adverse effects (tau-b=0.288; p<0.001). The number of medicines used and the number of medicines taken daily were significantly higher in participants with adverse effects (7.0±3.1 and 8.2±3.5, respectively) than in those who did not have experience any adverse effects (4.4±3.0 and 4.9±4.0, respectively) (U=651.0; p<0.001 and U=580.0; p<0.001, respectively).

According to Beers criteria updated in 2015 by the American Geriatrics Society, Twenty-four (20.7%) participants were on long-term NSAID therapy. Eleven (9.5%) participants who use NSAIDs were using PPI, whereas 13 (11.2%) participants were inappropriately using NSAIDs. Forty-five (38.8%) participants were using proton-pump inhibitors (PPIs). Except for high-risk individuals such as those on long-term non-steroidal anti-inflammatory drug (NSAID) therapy, the use of PPI for more than 8 weeks is inappropriate in elderly individuals. We were unable to assess the appropriateness of use of PPIs owing to inadequate data regarding the duration of use of PPI (Table 2).

Inappropriate drug use that could cause aggravation of disease in elderly individuals owing to drug–disease interactions was also evaluated according to Beers criteria. Inappropriate NSAID use was detected in two (1.7%) of eight participants with chronic heart failure. In two (1.7%) of eight participants with dementia, inappropriate drug use, which could lead to disease aggravation, was detected. Participants with syncope, delirium and history of falls could not be evaluated because of inadequate data (Table 3).

Drug groups that are not suitable for use in combination in elderly individuals owing to drug–drug interactions were evaluated according to Beers criteria. In three (2.6%) participants, combined use of three CNS-active drugs



was detected, and in one (0.9%) participant, combined use of five CNS-active drugs was found (Table 4). Overall, we determined 35 (30%) instances of inappropriate drug use according to Beers criteria. The numbers and percentages of participants who met the 2015 Beers criteria are given in Tables 2-4.

Table 1. Prevalence of chronic diseases in the study population.

Diseases	n	%
None	5	4.3
Hypertension	76	65.5
Diseases of the sensory organs (cataract, glaucoma, visual defects, xerophthalmia, hearing loss, etc.)	69	59.5
Diseases of the gastrointestinal system (peptic ulcer, gastritis, reflux, constipation, irritable bowel disease, etc.)	65	56.0
Gonarthrosis	57	49.1
Cardiovascular diseases (coronary artery disease, arrhythmia, valve diseases, orthostatic hypotension, peripheral vascular diseases, etc.)	55	47.4
Hyperlipidaemia	49	42.2
Osteoporosis	40	34.5
Rheumatic diseases (joint rheumatism/aching joints, gout, etc.)	38	32.8
Diabetes mellitus	36	31.0
Neurological/cerebrovascular diseases (Alzheimer's disease, Parkinson's disease, ischaemic or haemorrhagic stroke, migraine, etc.)	36	31.0
Anaemia (Iron deficiency anaemia, chronic disease anaemia, etc.)	35	30.2
Benign prostatic hyperplasia	24	20.7
Psychological diseases (depression, anxiety, sleep disturbance, psychotic disorders, etc.)	21	18.1
Lung diseases (chronic obstructive pulmonary disease, asthma, etc.)	19	16.4
Cancer (lung, colon, stomach, breast, prostate, lymphoma, leukaemia)	13	11.2
Thyroid/parathyroid diseases	9	7.8
Urinary system diseases (urinary incontinence, urinary infection, chronic kidney disease, etc.)	9	7.8
Skin diseases/allergic disorders	6	5.2

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Table 2. Potentially inappropriate medication use in elderly individuals.

Organ system, therapeutic category and drugs	Rationale	Recommendation	Number of individuals (percentage)
Anticholinergics			
First-generation antihistamines *Brompheniramine, Carbinoxamine, Chlorpheniramine, Clemastine, Cyproheptadine, Dexbrompheniramine, Dexchlorpheniramine, Dimenhydrinate, Doxylamine, Diphenhydramine (oral), Hydroxyzine, Meclizine Promethazine, Triprolidine*	Highly anti-cholinergic; clearance reduced with advanced age, and tolerance develops when used as a hypnotic; risk for confusion, dry mouth, constipation and other anti-cholinergic effects or toxicity Use of diphenhydramine in situations such as acute treatment of severe allergic reaction may be appropriate	Avoid	-
Anti-parkinsonian agents *Benztropine (oral), Trihexyphenidyl*	Not recommended for preventing extrapyramidal symptoms in combination with anti-psychotics; more-effective agents available for treating Parkinson's disease	Avoid	-
Anti-spasmodics Atropine (excludes ophthalmic), Belladonna alkaloids, Clidinium-Chlordiazepoxide, Dicyclomine, Hyoscyamine, Propantheline, Scopolamine	Highly anti-cholinergic, uncertain effectiveness	Avoid	3 (2.6%)
Anti-thrombotics			
Dipyridamole, oral short-acting (not applicable to extended-release drug combination with aspirin)	May cause orthostatic hypotension; more-effective alternatives available; intravenous form acceptable for use in cardiac stress testing	Avoid	2 (1.7%)
Ticlopidine	Safer, effective alternatives available	Avoid	-
Anti-infective			
Nitrofurantoin	Potential for pulmonary toxicity, hepatotoxicity and peripheral neuropathy, particularly with long-term use; safer alternatives available	Avoid in individuals with creatinine clearance of <30 mL/min or for long-term suppression of bacteria	1 (0.9%)
Cardiovascular			
Peripheral alpha-1 blockers *Doxazosin* *Prazosin* *Terazosin*	High risk for orthostatic hypotension; not recommended as a routine treatment for hypertension; alternative agents have superior risk–benefit profile	Avoid use as an anti-hypertensive	-
Central alpha blockers *Clonidine* *Guanabenz* *Guanfacine* *Methyldopa* *Reserpine (>0.1 mg/d)*	High risk for adverse CNS effects; may cause bradycardia and orthostatic hypotension; not recommended as routine treatment for hypertension	Avoid clonidine as first-line anti-hypertensive. Avoid others as listed	-
Disopyramide	Disopyramide is a potent negative inotrope and therefore may induce heart failure in elderly individuals; strongly anti-cholinergic; other anti-arrhythmic drugs preferred	Avoid	-

Organ system, therapeutic category and drugs	Rationale	Recommendation	Number of individuals (percentage)
Dronedarone	Worse outcomes have been reported in individuals with permanent atrial fibrillation or severe or recently decompensated heart failure who are taking dronedarone	Avoid in individuals with permanent atrial fibrillation or severe or recently decompensated heart failure	-
Digoxin	Use in atrial fibrillation: should not be used as a first-line agent in atrial fibrillation because more-effective alternatives exist and it may be associated with increased mortality	Avoid as first-line therapy for atrial fibrillation	-
	Use in heart failure: questionable effects on risk for hospitalisation and may be associated with increased mortality in elderly individuals with heart failure; in heart failure, higher dosages not associated with additional benefit and may increase risk for toxicity	Avoid as first-line therapy for heart failure	-
	Decreased renal clearance of digoxin may lead to increased risk for toxic effects; further dose reduction may be necessary in individuals with stage 4 or 5 chronic kidney disease	If used for atrial fibrillation or heart failure, avoid dosages of >0.125 mg/d	-
Nifedipine, immediate release	Potential for hypotension; risk for precipitating myocardial ischaemia	Avoid	-
Amiodarone	Amiodarone is effective for maintaining sinus rhythm but has greater toxicities than other anti-arrhythmics used in atrial fibrillation; it may be a reasonable first-line therapy for individuals with concomitant heart failure or substantial left ventricular hypertrophy if rhythm control is preferred over rate control	Avoid amiodarone as first-line therapy for atrial fibrillation unless the individual has heart failure or substantial left ventricular hypertrophy	1 (0.9%)
Central nervous system			
Anti-depressants, alone or in combination *Amitriptyline Amoxapine Clomipramine Desipramine Doxepin >6 mg/d Imipramine Nortriptyline* Paroxetine *Protriptyline Trimipramine*	Highly anti-cholinergic, sedating and cause orthostatic hypotension; safety profile of low-dose doxepin (≤6 mg/d) comparable with that of placebo	Avoid	1 (0.9%)
Anti-psychotics First- (conventional) and second- (atypical) generation	Increased risk for cerebrovascular accident (stroke) and greater rate of cognitive decline and mortality in persons with dementia. Avoid anti-psychotics for behavioural problems of dementia or delirium unless non-pharmacological options (e.g. behavioural interventions) have failed or are not possible and the elderly individual is threatening substantial harm to self or others	Avoid, except for schizophrenia, bipolar disorder, or short-term use as anti-emetic during chemotherapy	3 (2.6%)
Barbiturates (Amobarbital and Butabarbital) *Butalbital Mephobarbital Pentobarbital Phenobarbital Secobarbital*	High rate of physical dependence, tolerance to sleep benefits, greater risk for overdose at low dosages	Avoid	-
Benzodiazepines *Short- and intermediate- acting* *Alprazolam Estazolam Oxazepam Temazepam Triazolam* *Long-acting* *Clorazepate Clonazepam Quazepam Diazepam Flurazepam Chlordiazepoxide (alone or in combination with amitriptyline or clidinium)*	Elderly individuals have an increased sensitivity to benzodiazepines and decreased metabolism of long-acting agents; in general, all benzodiazepines increase risk for cognitive impairment, delirium, falls, fractures and motor vehicle crashes in elderly individuals May be appropriate for seizure disorders, rapid eye movement sleep disorders, benzodiazepine withdrawal, ethanol withdrawal, severe generalised anxiety disorder and periprocedural anaesthesia	Avoid	-

Organ system, therapeutic category and drugs	Rationale	Recommendation	Number of individuals (percentage)
Meprobamate	High rate of physical dependence; very sedating	Avoid	-
Nonbenzodiazepine, benzodiazepine receptor agonist hypnotics Eszopiclone *Zolpidem* *Zaleplon*	Benzodiazepine receptor agonists have adverse events similar to those of benzodiazepines in elderly individuals (e.g. delirium, falls, fractures); increased emergency department visits and hospitalisations; motor vehicle crashes; minimal improvement in sleep latency and duration	Avoid	-
Ergoloid mesylates (dehydrogenated ergot alkaloids) Isoxsuprine	Lack of efficacy	Avoid	-
Endocrine			
Androgens *Methyltestosterone*	Potential for cardiac problems; contraindicated in men with prostate cancer	Avoid unless indicated for confirmed hypogonadism with clinical symptoms	-
Desiccated thyroid	Concerns about cardiac effects; safer alternatives available	Avoid	-
Oestrogens with or without progestins	Evidence of carcinogenic potential (breast and endometrium); lack of cardioprotective effect and cognitive protection in elderly women Evidence indicates that vaginal oestrogens for treating vaginal dryness are safe and effective; women with a history of breast cancer who do not respond to non-hormonal therapies are advised to discuss the risk and benefits of low-dose vaginal oestrogen (dosages of oestradiol <25 lg twice weekly) with their healthcare provider	Avoid oral and topical patch Vaginal cream or tablets: acceptable to use low-dose intravaginal oestrogen for managing dyspareunia, lower urinary tract infections and other vaginal symptoms	-
Growth hormone	Impact on body composition is small and associated with oedema, arthralgia, carpal tunnel syndrome, gynaecomastia, impaired fasting glucose	Avoid, except as hormone replacement after pituitary gland removal	-
Insulin, sliding scale	Higher risk of hypoglycaemia without improvement in hyperglycaemia management regardless of the care setting; refers to sole use of short- or rapid-acting insulins to manage or avoid hyperglycaemia in absence of basal or long-acting insulin; does not apply to titration of basal insulin or use of additional short- or rapid-acting insulin in conjunction with scheduled insulin (i.e. correction insulin)	Avoid	-
Megestrol	Minimal effect on weight; increases risk for thrombotic events and possibly death in elderly individuals	Avoid	-
Sulfonylureas, long-duration *Chlorpropamide* *Glyburide*	Chlorpropamide: prolonged half-life in elderly individuals; can cause prolonged hypoglycaemia; causes syndrome of inappropriate antidiuretic hormone secretion	Avoid	-
	Glyburide: higher risk for severe prolonged hypoglycaemia in elderly individuals		-
Gastrointestinal			
Metoclopramide	Can cause extrapyramidal effects, including tardive dyskinesia; risk may be greater in frail elderly individuals	Avoid, unless for gastroparesis	-
Mineral oil, given orally	Potential for aspiration and adverse effects; safer alternatives available	Avoid	-

Organ system, therapeutic category and drugs	Rationale	Recommendation	Number of individuals (percentage)
Proton-pump inhibitors	Risk of *Clostridium difficile* infection and bone loss and fractures	Avoid scheduled use for >8 weeks unless for high-risk individuals (e.g. oral corticosteroids or chronic NSAID use), erosive esophagitis, Barrett's esophagitis, pathological hypersecretory condition or demonstrated need for maintenance treatment (e.g. owing to failure of drug discontinuation trial or H_2 blockers)	-
Pain medications			
Meperidine	Not effective oral analgesic in dosages commonly used; may have higher risk for neurotoxicity, including delirium, than other opioids; safer alternatives available	Avoid, particularly in individuals with chronic kidney disease	-
Non-cyclooxygenase-selective NSAIDs, oral: *Aspirin (>325 mg/d) Diclofenac Diflunisal Etodolac Fenoprofen Ibuprofen Ketoprofen Meclofenamate Mefenamic acid Meloxicam Nabumetone Naproxen Oxaprozin Piroxicam Sulindac Tolmetin*	Increased risk for gastrointestinal bleeding or peptic ulcer disease in high-risk groups, including those aged >75 years or taking oral or parenteral corticosteroids, anticoagulants or antiplatelet agents; use of proton-pump inhibitor or misoprostol reduces but does not eliminate risk. Upper gastrointestinal ulcers, gross bleeding or perforation caused by NSAIDs occur in approximately 1% of individuals treated for 3–6 months and in approximately 2%–4% of individuals treated for 1 year; these trends continue with longer duration of use	Avoid chronic use, unless other alternatives are not effective and individual can take gastroprotective agent (proton-pump inhibitor or misoprostol)	13 (11.2%)
Indomethacin *Ketorolac, includes parenteral*	Indomethacin is more likely than other NSAIDs to have adverse CNS effects. Of all NSAIDs, indomethacin has the most adverse effects. Increased risk for gastrointestinal bleeding, peptic ulcer disease and acute kidney injury in elderly individuals	Avoid	-
Pentazocine	Opioid analgesic that causes CNS adverse effects, including confusion and hallucinations, more commonly than other opioid analgesic drugs; is also a mixed agonist and antagonist; safer alternatives available	Avoid	0
Skeletal muscle relaxants *Carisoprodol Chlorzoxazone Cyclobenzaprine Metaxalone Methocarbamol Orphenadrine*	Most muscle relaxants poorly tolerated by elderly individuals because some have anti-cholinergic adverse effects, sedation, increased risk for fractures; effectiveness at dosages tolerated by elderly individuals is questionable	Avoid	2(1.7%)
Genitourinary			
Desmopressin	High risk for hyponatraemia; safer alternative treatments	Avoid for treating nocturia or nocturnal polyuria	-

Ø: was not evaluated

Table 3. Potentially inappropriate medication use in elderly individuals owing to drug–disease or drug–syndrome interactions that may exacerbate the disease or syndrome.

Disease or syndrome	Drug(s)	Rationale	Recommendation	Number and percentage of individuals
Cardiovascular				
Heart failure	NSAIDs and COX-2 inhibitors; non-dihydropyridine CCBs (diltiazem, verapamil)—avoid only for heart failure with reduced ejection fraction Thiazolidinediones (pioglitazone, rosiglitazone) Cilostazol Dronedarone (severe or recently decompensated heart failure)	Potential to promote fluid retention and exacerbate heart failure	Avoid	2 (1.7%)
Syncope	AChEIs Peripheral alpha-1 blockers-*Doxazosin Prazosin Terazosin*-Tertiary TCAs Chlorpromazine Thioridazine Olanzapine	Increases risk for orthostatic hypotension or bradycardia	Avoid	-
		Central nervous system		
Chronic seizures or epilepsy	Bupropion Chlorpromazine Clozapine Maprotiline Olanzapine Thioridazine Thiothixene Tramadol	Lowers seizure threshold; may be acceptable in individuals with well-controlled seizures in whom alternative agents have not been effective	Avoid	-
Delirium	Anticholinergics Anti-psychotics Benzodiazepines Chlorpromazine Corticosteroids H2-receptor antagonists: -*Cimetidine Famotidine Nizatidine Ranitidine*-Meperidine Sedative hypnotics	Avoid in elderly individuals with or at a high risk for delirium because of the potential of inducing or worsening delirium. Avoid anti-psychotics for behavioural problems of dementia or delirium unless non-pharmacological options (e.g. behavioural interventions) have failed or are not possible and the elderly individual is threatening substantial harm to self or others Anti-psychotics are associated with a greater risk for cerebrovascular accident (stroke) and mortality in persons with dementia	Avoid	-
Dementia or cognitive impairment	Anticholinergics Benzodiazepines H2-receptor antagonists Nonbenzodiazepine, benzodiazepine receptor agonist hypnotics -*Eszopiclone Zolpidem Zaleplon*- Anti-psychotics, chronic and as-needed use	Avoid because of adverse CNS effects Avoid anti-psychotics for behavioural problems of dementia or delirium unless non-pharmacological options (e.g. behavioural interventions) have failed or are not possible and the elderly individual is threatening substantial harm to self or others. Anti-psychotics are associated with a greater risk for cerebrovascular accident (stroke) and mortality in individuals with dementia	Avoid	2 (1.7%)

Disease or syndrome	Drug(s)	Rationale	Recommendation	Number and percentage of individuals
History of falls or fractures	Anti-convulsants Anti-psychotics Benzodiazepines Nonbenzodiazepine, benzodiazepine receptor agonist hypnotics: -Eszopiclone Zaleplon Zolpidem- TCAs SSRIs Opioids	May cause ataxia, impaired psychomotor function, syncope, additional falls; shorter-acting benzodiazepines are not safer than long-acting ones If one of the drugs must be used, consider reducing use of other CNS-active medications that increase the risk for falls and fractures (i.e. anti-convulsants, opioidreceptor agonists, anti-psychotics, anti-depressants, benzodiazepinereceptor agonists, other sedatives and hypnotics) and implement other strategies to reduce fall risk	Avoid unless safer alternatives are not available; avoid anti-convulsants except for seizure and mood disorders Opioids: avoid, excludes pain management owing to recent fractures or joint replacement	-
Insomnia	Oral decongestants: -Pseudoephedrine Phenylephrine- Stimulants:- Amphetamine Armodafinil Methylphenidate Modafinil -Theobromines:- Theophylline Caffeine-	CNS stimulant effects	Avoid	1 (0.9%)
Parkinson's disease	All anti-psychotics (except aripiprazole, quetiapine, clozapine) Anti-emetics:- Metoclopramide Prochlorperazine Promethazine-	Dopamine-receptor antagonists with a potential to worsen parkinsonian symptoms Quetiapine, aripiprazole, clozapine appear less likely to precipitate worsening of Parkinson disease	Avoid	-
		Gastrointestinal		
History of gastric or duodenal ulcers	Aspirin (>325 mg/d) Non-COX-2 selective NSAIDs	May exacerbate existing ulcers or cause new or additional ulcers	Avoid unless other alternatives are not effective and individual can take gastroprotective agent (i.e. proton-pump inhibitor or misoprostol)	-
Kidney and urinary tract				
Chronic kidney disease stages IV or less (creatinine clearance of <30 mL/min)	NSAIDs (non-COX and COX-selective, oral and parenteral)	May increase risk for acute kidney injury and further decline of renal function	Avoid	-
Urinary incontinence (all types) in females	Oestrogen oral and transdermal (excludes intravaginal oestrogen) Peripheral alpha-1 blockers:-*Doxazosin Prazosin Terazosin*-	Aggravation of incontinence	Avoid in females	-
Lower urinary tract symptoms, benign prostatic hyperplasia	Strongly anti-cholinergic drugs, except anti-muscarinics for urinary incontinence	May decrease urinary flow and cause urinary retention	Avoid in males	-
Ø: was not evaluated				

Table 4. Potentially clinically important non-anti-infective drug–drug interactions that should be avoided in elderly individual.

Object drug and class	Interacting drug and class	Risk rationale	Recommendation	Number and percentage of individuals
ACEIs	Amiloride or triamterene	Increased risk of hyperkalaemia	Avoid routine use; reserve for individuals with demonstrated hypokalaemia while taking an ACEI	-
Anti-cholinergic	Anti-cholinergic	Increased risk for cognitive decline	Avoid, minimise the number of anti-cholinergic drugs	-
Anti-depressants (i.e. TCAs and SSRIs)	≥2 other CNS-active drugs	Increased risk for falls	Avoid total of ≥3 CNS-active drugs; minimise the number of CNS-active drugs	4 (3.4%)
Anti-psychotics	≥2 other CNS-active drugs	Increased risk for falls	Avoid total of ≥3 CNS-active drugs; minimise the number of CNS-active drugs	
Benzodiazepines and Non-benzodiazepine, benzodiazepine receptor agonist hypnotics	≥2 other CNS-active drugs	Increased risk for falls	Avoid total of ≥3 CNS-active drugs; minimise the number of CNS-active drugs	
Opioid receptor agonist analgesics	≥2 other CNS-active drugs	Increased risk for falls	Avoid total of ≥3 CNS-active drugs; minimise the number of CNS-active drugs	
Lithium	ACEIs Loop diuretics	Increased risk for lithium toxicity	Avoid, monitor lithium concentrations	-
Corticosteroids, oral or parenteral	NSAIDs	Increased risk for peptic ulcer disease or gastrointestinal bleeding	Avoid; if not possible, provide gastrointestinal protection	-
Peripheral alpha-1 blockers	Loop diuretics	Increased risk for urinary incontinence in elderly females	Avoid in elderly women, unless conditions warrant both drugs	-
Theophylline	Cimetidine	Increased risk for theophylline toxicity	Avoid	-
Warfarin	Amiodarone NSAIDs	Increased risk for bleeding	Avoid when possible; closely monitor international normalised ratio	-



DISCUSSION

Ageing is associated with an increase in the incidence of many diseases, particularly chronic diseases (12). In a study conducted in the United States, 86%–92% of individuals aged ≥65 years were found to have at least one chronic illness; whereas 30.7%–41.3% of individuals had at least three concomitant chronic illnesses (13). In our study, 95.7% of participants had at least one chronic disease, whereas 84.5% of participants had at least three chronic diseases. While the proportion of individuals with one chronic disease was comparable between the two studies, the rate of comorbidity in our study was much higher than that reported in the study conducted in the United States. Greater disease burden naturally leads to an increased drug use. The proportion of elderly individuals in the United States is 13%, and they account for 34% of the population that uses written prescriptions. It was found that 95% of elderly individuals use drugs at least once a week, and 12% use drugs ≥10 times per week (14). In the present study, 55.2% of participants used five or more medications per day, while a corresponding rate of 66.9% was recently reported in India (15).

Potentially inappropriate medication use

In our study, inappropriate drug use was found in 22.4% of the participants according to Beers criteria [NSAID (11.2%), antispasmodic drug (2.6%), muscle relaxant (1.7%) and dipiridamol (1.7%)]. Nitrofurantoin and amiodarone were each used by 0.9% of participants; these were considered inappropriate drugs for use in the elderly population. The use of PPI could not be assessed owing to lack of data regarding the duration of use.

Potentially drug–disease or drug–syndrome interactions

In our study, drug use in five (4.3%) participants were found to be inappropriate according to Beers criteria because of the potential for drug–disease interaction. Inappropriate drug use was detected in two (1.7%) of eight participants with chronic heart failure; all were attributable to inappropriate NSAID use. Doctors need to be careful while prescribing a combination of drugs to prevent unwanted situations; for example, non-dihydropyridine-derived calcium channel blockers are found in many anti-hypertensive medications and their use is not appropriate in individuals with chronic heart failure. Two (1.7%) of eight participants with dementia were categorised as those with inappropriate drug use (inappropriate use of anti-psychotic and H_2 receptor blocker, respectively). H_2 receptor antagonists are generally believed to be safe drugs; however, according to Beers criteria, these should be avoided in individuals with dementia. Although found at a very low rate in our study, in a previous study (15), H_2 receptor antagonists were found to be the most prescribed inappropriate drugs according to Beers criteria. In our study, one (0.9%) of the four participants with insomnia was categorised as an inappropriate drug user (inappropriate use of psychostimulant drug). Although we did not detect inappropriate use of oral decongestants in our study, doctors should avoid prescribing oral decongestants to individuals with complaints of insomnia because oral decongestants are found in many over-the-counter medications. Although these are included in Beers criteria, studies regarding syncope, delirium and falling history could not be assessed owing to inadequacy of data (Table 3).

Potentially drug–drug interactions

In our study, four (3.4%) participants had inappropriate drug use owing to potential drug–drug interactions according to Beers criteria. Three (2.6%) participants used a combination of three drugs that affected the central nervous system and one (0.9%) participant used a combination of five drugs (Table 4).

General considerations

In our study we found inappropriate drug use in 30% instances. These data are obtained from population based study and important for Turkey the country that have limited data about inappropriate drug usage. Studies conducted

overseas have yielded inconsistent results (16). A study in Switzerland found inappropriate drug use in 10.3% of elderly individuals (8). In another study 66.7% of elderly individuals used inappropriate drugs (9).

In general, earlier studies in the literature were conducted in individuals who were admitted to emergency services or hospitals with complaints of drug adverse effects. This may explain the lower rates of inappropriate drug use found in our study (35; 30%). Nevertheless, a community-based study in Spain found a higher prevalence (44.8%) of inappropriate drug use than that found in our study (17). Differences can be due to limitation of Beers criteria that it is not applicable outside the US (18).

According to our study results, the rate of inappropriate drug use among elderly individuals is at an unacceptable level. Therefore, adapting to the guidelines of rational drug use in elderly individuals for clinical practice is more important. NSAIDs were found to account for a large proportion of inappropriate drug use in our study. NSAIDs tend to be perceived as non-harmful by the population and are widely used as over-the-counter drugs (19). In addition to adapting to guidelines of rational drug use while prescribing drugs, population-based education interventions should be performed to reduce inappropriate drug use. The physician should follow the guidelines for rational drug use while prescribing drugs and should review the medicines used by elderly individuals during each follow-up visit.

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