

POTENTIAL INAPPROPRIATE MEDICATION USE IN COMMUNITY – DWELLING ELDERLY PATIENTS. A QUALITATIVE STUDY

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Abstract

The elderly are frequently exposed to drug related problems. Inappropriate prescribing of unsafe medication or underuse of clinically indicated therapies can be identified using validated explicit criteria.

The objective of this study was to identify the characteristics of medication use among the community- dwelling elderly patients, by comparison with the Beers criteria, the STOPP and START instruments and with similar published research.

Reimbursed prescriptions that were delivered to elderly patients through one Romanian community pharmacy were analysed. Demographic characteristics, local availability of medications included in the applied criteria and patterns of medication use were identified.

Non-steroidal anti-inflammatory drugs, *Ginkgo biloba* standardised extract, zopiclone and zolpidem were the most frequent medications potentially associated with safety concerns. Potential underuse of prophylactic cardiovascular medications was frequent.

Several particularities concerning medication use among the Romanian community- dwelling elderly suggest the need for interventions designed to prevent inappropriate medication use.

Rezumat

Vârstnicii sunt frecvent expuși problemelor legate de terapia medicamentoasă. Prescrierea inadecvată a unor medicamente cu probleme de siguranță sau sub-utilizarea unor terapii pentru care există dovezi de eficacitate, poate fi identificată prin utilizarea unor criterii explicite de analiză, validate în diverse medii de îngrijire a vârstnicului.

Obiectivul lucrării a fost identificarea caracteristicilor utilizării medicamentelor în rândul vârstnicilor tratați în ambulator, prin comparație cu criteriile Beers, START și STOPP și prin raportare la studii similare.

Au fost analizate prescripțiile decontate de sistemul național de asigurări de sănătate și eliberate prin intermediul unei farmacie comunitare din mediu urban. Au fost descrise caracteristicile demografice, disponibilitatea locală a medicamentelor incluse în criteriile de analiză aplicate și particularitățile locale de prescriere la vârstnici.

Antiinflamatoarele nesteroidiene, extractul standardizat de *Ginkgo biloba*, zopiclona și zolpidemul au fost medicamentele cel mai frecvent asociate cu probleme potențiale de siguranță. A fost observată sub-utilizarea terapiilor cardiovasculare profilactice.

Particularitățile utilizării medicamentelor în rândul vârstnicilor români tratați în ambulator sugerează necesitatea unor intervenții de prevenire a utilizării inadecvate a medicamentelor.

Keywords: community- dwelling elderly, inappropriate medication use, community pharmacy.

Introduction

The elderly population represents a subgroup of patients prone to experience drug related problems (DRP), whether hospitalised, living in the nursing home or in the community. The main identified reasons explaining geriatric DRP, include complex age-related changes in pharmacokinetics and pharmacodynamics, simultaneous use of multiple prescription and over the counter drugs, involvement of several prescribers, presence of diverse underlying co-morbidities and also reduced patient adherence [1-3].

The use of potentially unsafe medications, adverse effects and drug interactions are among the most common DRP subtypes, that are commonly raised during the prescribing and monitoring stages of the medication use process [4,5]. 27.6% of DRP identified among the community-dwelling patients, have been evaluated as preventable [6]. Several studies identified positive associations between inappropriate prescribing (defined as situations where potential risk outweighs the potential benefit) to the elderly and various outcomes, such as risk of hospitalizations, emergency department visits, ambulatory services visits, deaths, increased health expenditures, lower health-related quality of life. Such associations were often demonstrated by the use of instruments, either explicit (criterion-based) or implicit (judgment-based), created to identify potential misprescribing (drugs to avoid) or underprescribing (underuse of clinically indicated, evidence based therapies) [7-13].

An example of explicit criteria is given by the Beers Criteria, which consist of 2 lists of medications considered inappropriate in the elderly, independent of or considering diagnosis. Originally developed in the USA in 1991 and later updated in 1997 and in 2003, they are still the most widely used criteria investigating inappropriate prescribing as they were meant to be used for analysis in primary care, secondary care or in the nursing homes. Comparing the rates of inappropriate prescribing identified with the Beers Criteria among other countries than the USA is difficult because of the different availability and pattern of use of the drugs included [8,14] and therefore, several country-specific versions were adapted [15-17].

The Irish STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions) and START (Screening Tool to Alert doctors to

the Right Treatment) criteria, suggested a more organized approach, with explicit rules for either avoiding certain medications presented according to physiological system (STOPP) or for initiating medications if certain medical conditions are present (START). Using this dual approach, detecting misprescribing and underprescribing, the STOPP and START criteria are currently being tested and validated in different environments of care [8,18].

Romanian data about the quality of medication use among the elderly population is lacking and therefore, the objective of this pilot study was to identify the main characteristics of medication use among the community- dwelling elderly patients, accessing the same urban community pharmacy, by comparison with the Beers, STOPP and START criteria and with similar published research.

Materials and Methods

Data source and study population

The analyzed database included prescriptions reimbursed by the national health insurance system, issued to patients ≥ 65 years old and delivered from one community pharmacy in Cluj-Napoca (Romania) during a five months period (September 2009- January 2010). One prescription form could contain one or more medications, and one patient could have several different prescriptions reimbursed each month. Over-the-counter medication and herbal supplements were excluded from the analysis as they were neither reimbursed nor registered for each patient. The medications prescribed could be intended for acute, chronic or as needed treatments, covering a single dose treatment to 90 days duration of therapy. The current legislation requires mentioning the diagnoses related to the medications prescribed on the prescription form, and one patient can choose freely the pharmacy delivering his medication.

Measures

The main study outcome was the identification of the most frequently used medications, which according to the Beers, STOPP and START criteria, or the therapeutic information available, could be considered as inappropriately prescribed to the study population.

Analysis

Patients' demographic data was analysed descriptively. The potentially inappropriate medications were selected from the mentioned criteria by taking into consideration the local availability (according to the Product Index of the National Agency for Medicines and Medical Devices, available online http://www.anm.ro/anm/anm_list.asp, last accessed

January 13th, 2011) and the patterns of drug use among the studied population, related to the safety and efficacy of use of the recommended treatments. The number of prescriptions containing potentially inappropriate medications was identified.

Results and Discussion

Demographic characteristics

During the five months period, 1,717 reimbursed prescriptions were delivered from the community pharmacy included in the study, with almost half being issued to the elderly. Some prescriptions represented repeated treatments to the pharmacy regular patients. The average age was 75 (65 to 100 years old) and the average number of prescribed medications delivered per patient was 4.10 (1 to 12) (table I).

Table I.
Demographic characteristics of the studied patients.

Characteristic	Value
Delivered prescriptions, n	1,717
Prescriptions delivered to the elderly, n (%)	857 (49.91)
Average age, n (range)	75.66 (65-100)
Comorbidities, (%)	
hypertension	22.22
ischaemic heart disease	15.55
hyperlipidaemia	10.74
peripheral or cerebral, circulatory diseases	9.63
osteoarthritis, rheumatoid arthritis, osteoporosis	9.26
benign prostatic hyperplasia	4.44
diabetes mellitus	3.7
heart failure	3.3
atrial fibrillation	3.3
other	17.86

Local availability of the medications enlisted in the applied criteria

Among the 84 medications or therapeutic classes included in the Beers Criteria independent of diagnoses or conditions, only 36 (42.85%) were found to be registered for use. The therapeutic classes mentioned in the STOPP criteria were found to be very similar to those locally available, with the exception of chlorthalidone, flurazepam, cyclizine, diphenoxylate, and chlorpropamide. The information available in the studied database excluded over-the-counter medications possibly used by the patients and as a consequence, several STOPP and START statements could not be applicable: criteria concerning use of aspirin as an antiplatelet agent or its interactions, criteria referring to dipyridamole, loperamide, to the majority of laxative products (except some lactulose specialities) or to the majority of calcium and vitamin D supplements. The application of 13 statements from the START criteria and of 19 statements from the STOPP criteria required

information concerning the clinical state or history of the patient, which was not available in the studied database, so these criteria could not be evaluated in our analysis.

Patterns of medication use among the elderly

Evaluating misprescribing, the gathered data showed frequent chronic use of non-steroidal anti-inflammatory drugs (NSAIDs), with or without gastroprotection, in the presence of cardiovascular pathology (table II). Monthly prescribed doses covered a duration ranging from 10 to 30 days of treatment, and the most frequent molecules were diclofenac, ketoprofen, ibuprofen, piroxicam, nimesulid, meloxicam, lornoxicam. Several criteria mentioned in the STOPP list pertained to the haemorrhagic risk induced by various associations with warfarin, aspirin or NSAIDs. Locally available vitamin K antagonist was acenocoumarol, with structural and pharmacological properties similar to those of warfarin. 8 prescriptions presented various associations of acenocoumarol, clopidogrel, pentoxifylline, diclofenac or meloxicam, which could increase bleeding risk, irrespective of the potential use of aspirin as an antiplatelet agent. Alternatives to NSAIDs, like opiate medications, although registered for the treatment of moderate to severe pain irrespective of origin, were restricted to the management of cancer pain. Tramadol was rarely preferred as an analgesic alternative to the NSAIDs (6 prescriptions intended for the elderly, from a total of 14 prescriptions reimbursed during the 5 months analysed), for an osteoarthritis diagnosis.

Concerning the medications related to the gastrointestinal system, the STOPP criteria item referring to the extended use of the proton pump inhibitor over 8 week duration was difficult to ascertain as not all patients were regular customers of the pharmacy. 22 prescriptions contained a potential use of proton pump inhibitors without an indication, as they were to be used daily for one month period, in the absence of a clear diagnosis or associated with NSAIDs prescribed for shorter periods of time.

As a local characteristic, *Ginkgo biloba* standardized extract was frequently prescribed for various neurologic or vascular indications (91% of all *Ginkgo biloba* specialities delivered during the 5 months interval from the pharmacy, 186/204 prescriptions) and its presence added to the potential bleeding risk (table II).

The STOPP criteria limit the use of benzodiazepines, as they increase fall risk among the elderly, without differentiating among their subclasses. Considering several structural and pharmacological similarities, zolpidem and zopiclone were the most frequently prescribed benzodiazepines, usually for a 30 days treatment (table II).

Table II.

Most frequent subtypes of drug-related problems among the 148 prescriptions with potential safety-related problems (representing 17.27% of the total 857 prescriptions delivered to the elderly).

Medication or therapeutic class with the indication mentioned on the prescription	Frequency of the potential DRP	Potential concern in the elderly population
NSAIDs regularly prescribed in osteoarthritis in the presence of cardiovascular disease	32 prescriptions (21.62%)	Increased risk for peptic ulceration or haemorrhage, cardiovascular thrombotic events, renal impairment, central nervous system adverse effects, frailty, falls or cognitive impairment associated with prolonged NSAIDs treatments. Possible reduced effectiveness of the coprescribed hypertension or heart failure therapies. Increased risk for gastrointestinal side effects with prolonged or repeated treatments without gastric protection.
Ginkgo biloba standardized extract prescribed regularly in vascular disease or cognitive deficits, in association with acenocoumarol, antiplatelet agents or non-steroidal anti-inflammatory drugs	24 prescriptions (16.21%)	Increased haemorrhagic side effects, anaemia and frailty when associated with antiplatelet agents, anticoagulants, NSAIDs.
zolpidem and zopiclone prescribed regularly for sleep disturbances	23 prescriptions (15.54%)	Increased risk for cognitive impairment and falls.
various associations with ACEI, ARB, spironolactone in heart failure or hypertension	19 prescriptions (12.83%)	Increased risk for hyperkalemia and frailty in the presence of renal impairment or in the absence of a thiazide or loop diuretic
0.25 mg digoxin daily or 0.25mg daily/ 5 days per week in heart failure	18 prescriptions (12.16%)	Increased risk of toxicity in the presence of renal impairment, favouring malnutrition, cognitive impairment and frailty.
metformin for type 2 diabetes	17 prescriptions (11.48%)	Increased risk for lactic acidosis in the presence of renal impairment, severe cardiovascular disease, dehydration. Possible anorectic properties and vitamin B12 deficiency favouring malnutrition and frailty.
amiodarone for ischaemic heart disease without mentioned atrial fibrillation	15 prescriptions (10.13%)	Increased risk of cardiac, non-cardiac toxicity and frailty. It is not considered a first-line therapy in atrial fibrillation. Romanian approved label states its possible use in the management of ischemic heart disease.

DRP - drug related problems, NSAIDs -Non-Steroidal Anti-Inflammatory Drugs, ACEI - Angiotensin Converting Enzyme Inhibitor, ARB - Angiotensin II Receptor Blocker

Strong anticholinergic medications like the tricyclic antidepressants or first generation histamine H1 antagonists were rarely used among this population, although they are intensively mentioned both in Beers and STOPP criteria. Selective serotonin re-uptake inhibitors and atypical molecules were the antidepressants of choice among these patients (73% representing 19 prescriptions issued to the elderly from a total of 26 delivered during the study period). Neuroleptics (haloperidol, risperidone, olanzapine, quetiapine) were seldom prescribed to the community-dwelling population analysed. Theophylline was recommended for chronic

obstructive pulmonary disease (66.66% of all theophylline prescriptions, that is 16 prescriptions from a total of 24 reimbursed prescriptions), either as monotherapy or associated with inhaled bronchodilators or corticosteroids, in daily doses less than 400 mg of an extended release form.

Digoxin was used for heart failure patients, in a locally adapted manner, mostly as a 5 day per week treatment, with 0.250 mg daily doses (table II). The Beers criteria recommend daily doses of 0.125 mg, while the STOPP criteria limit the daily dose, irrespective of diagnosis, to a maximum of 0.125mg per day, in the presence of impaired renal function. The identified pattern of use suggested increased average daily doses for digoxin (table II).

Concerning the underuse, the most frequently identified items from the START criteria, were those related to the cardiovascular system (table III). The analysis allowed for the identification of an increased off label use of trimetazidine, not mentioned among the START criteria, but attributable to the local pattern of medication use, as its use as monotherapy in stable angina or for arterial hypertension, suggested a possible underuse of established first-line therapies (table III).

Table III.

Most frequent subtypes of drug-related problems among the 121 prescriptions with potential efficacy-related problems or underuse of evidence based therapies (representing 14.12% of the total 857 prescriptions delivered to the elderly).

Medication or therapeutic class underused considering the indication mentioned on the prescription	Frequency of the potential DRP
beta-blockers or statins – in ischaemic heart disease	50 prescriptions (41.32%)
analgesics – in arthritic pain	38 prescriptions (31.40%)
trimetazidine as monotherapy in ischemic heart disease or hypertension	15 prescriptions (12.39%)
ACEI in heart failure	10 prescriptions (8.26%)
acenocoumarol or antiplatelet agents in atrial fibrillation	8 prescriptions (6.61%)

Interpretation

The limited overlap in medications availability (approximately 42%) indicates that the Beers criteria in their original form, could underestimate the prevalence of misprescribing, if one such future study would be intended. On the other hand, the European STOPP-START tools, share almost the same degree of medication availability and allowed for a more realistic approach, although the limited clinical information available on the analysed prescriptions, did not allow for their comprehensive application.

The Beers criteria were applied in several settings outside the USA, considering the local drug availability or with several adjustments judged necessary by the research teams involved. The published results present some similarities to ours, as the most commonly reported inappropriate medications were the benzodiazepines, several drugs with anticholinergic properties (mostly amitriptyline), doxazosin, amiodarone, NSAIDs, dipyridamole and ticlopidine, digoxin (>0.125 mg/day), ferrous sulphate (>325 mg/day), dextropropoxyphene, various associations increasing haemorrhagic risk; some authors reported the misuse or overuse of vasodilators, like pentoxifylline, *Ginkgo biloba* extracts or ergot alkaloids, in the context of reduced efficacy [16,17,19-29].

Fewer published studies evaluated the potentially inappropriate use of STOPP medications among the ambulatory elderly, but some statements revealed the same misprescribed medications as the Beers criteria, although with fewer resemblances to our study: aspirin, NSAIDs, benzodiazepines, proton pump inhibitors, furosemide, nonselective β -blockers, tricyclic antidepressants, antipsychotic drugs [19, 24,30].

Although the purpose of our investigation was not to identify factors associated with potentially inappropriate use among the ambulatory elderly, several studies conducted in diverse community-based settings, showed a frequent link between increasing number of medications, multiple comorbidities, advancing age, female sex or poor economic status [16,17,19,21,23,24,31,32].

Concerning the most frequent medications misused, both the Beers and STOPP criteria limit the use of NSAIDs, taking into consideration the fact that advanced age is a risk factor for cardiovascular, renal and haemorrhagic side-effects secondary to NSAIDs use [33,34]. In this population, they were frequently prescribed to control for pain associated with osteoarthritis. The use of over-the-counter analgesic medications, including acetaminophen, could not be analysed in the available database, so we cannot evaluate the degree of pain control in this situation. Further studies should clarify the distance between under- and misprescribing, as it would be interesting to know, how patients controlled their pain for the remaining period of time, in the case of the 10 days prescriptions, and furthermore, how many consecutive months in a row, the full dose treatments were prescribed. Relief of osteoarthritic pain in the elderly is difficult to attain and requires an individualised approach, as limited relief increases the risk for cognitive impairment, frailty and reduced quality of life [35,36]. Our study also revealed that NSAIDs are intensively recommended as an analgesic option, with a limited prescribing of tramadol,

codeine, their combinations with acetaminophen or other opioid, which of course, could also cause important side-effects in the elderly population, if inappropriately used.

Second, the standardised *Ginkgo biloba* extract is recommended by the national approved guidelines for the management of mild or moderate stages of dementia, as a second or third line therapy. At the time of the data collection, it was reimbursed by our health system for various forms of cerebral insufficiency or peripheral arterial disease and this study confirms its frequent use among the elderly. We also noticed a far less frequent use of specific therapies proposed for the treatment of dementia (data not shown), partly explainable through the relatively younger age of the population studied; we can conclude that the extract was the preferred treatment for mild forms of cognitive deficits among the elderly. Its effectiveness and safety are still a subject of debate [37,38], which allowed several attempts to limit its use, as one recently published French example [17,39]. In the context of unknown administration of antiplatelet agents and of an increased use of non-steroidal anti-inflammatory agents, the potential haemorrhagic risk of the Ginkgo extract could become significant for this population. On the other hand, in the case of patients at risk for polypharmacy, it would be perhaps necessary to reevaluate the treatments' benefit.

Furthermore, sedative medications like benzodiazepines and anticholinergics, were associated with an increased risk of falls in the elderly [40]. Several studies indicated that age over 80 years, long and short half-life benzodiazepines, higher doses, are factors linked with the risk of falls and fractures and it is therefore important to monitor and limit their use [41].

On the other hand, the application of the Beers and STOPP criteria revealed the limited use of medications with strong anticholinergic properties, by comparison with the number of criteria formulated to capture their misuse. Nevertheless, among our elderly population it would be important to consider the cumulative anticholinergic effects, presented by medications frequently used among this population, as their simultaneous use could increase the risk for central and peripheral side-effects among the elderly [42,43].

Various explicit or implicit strategies designed to evaluate dimension and type of underuse among the ambulatory elderly, indicated that cardiovascular and especially antithrombotic therapies intended as secondary prevention strategy, pain medications, antidepressants or calcium supplementation in osteoporosis represent the most frequently omitted medications [19,30,44,45]. These findings were in part confirmed in our

analysis, as some statements from the START tool, relating especially to the management of cardiovascular therapies could be considered as potential problems among the studied population. Possible reasons for underuse include, as mentioned elsewhere, the lack of evidence-based data ascertaining benefit among the elderly and especially among the oldest subgroup of patients, fear of reduced patient adherence with increasing number of recommended medications, especially in the cognitively impaired ones, fear of increasing polypharmacy, the costs and risks associated with it. On the other hand, the decision to omit certain clinically indicated medications, has to consider, on a case-by-case basis, the existing impairments in daily functioning or the diminishing cognitive capacities, the advancing age and especially the number and severity of co-morbidities. Several studies indicated the benefit of prophylactic therapies even among the elderly population, with a careful consideration of the benefit to risk ratio and in the context of a life expectancy justifying the risk of polypharmacy. It would be necessary to investigate the reasons for the underprescribing observed in our study that could improve geriatric pharmaceutical care. On the other hand, one approach suggested for improving the safety and efficacy associated with the elderly therapeutic regimens is to adequately train and actively involve the community pharmacists caring for this population [46-48].

Our retrospective study has several limits. Firstly it is based on the manual analysis of a written database and potential errors in the recording of the recommended treatment could not be controlled for. It is difficult to generalize our findings as a single clinical pharmacist evaluated the therapies delivered through one community pharmacy. The results could represent an underestimation of the actual inappropriate use, as information related to the administration of over the counter medications, reimbursed prescriptions delivered through different pharmacies or medications prescribed without reimbursement was not available. The patient's adherence could not be assessed. We could not correctly evaluate the context which influenced the physician's attitude, as details related to the cognitive ability, laboratory tests or the degree of disability of the patients under study were not available.

Conclusions

This qualitative study tried to identify some of the local patterns of medication prescribing among the community-dwelling elders and to assess their level of appropriateness. The medications recommended for the treatment of cardiovascular diseases were the most frequently encountered,

but also associated with the greatest potential risk of inappropriate use. Potential concerns are related to the necessity of an increased monitoring of the elderly patient who regularly uses cardiovascular medications, benzodiazepines or NSAIDs. To increase safety of the prescribed therapies, unclear indications should be avoided while safer alternatives should be considered. This study is among the first published, trying to describe the medication use among the Romanian elderly population and to compare it with other studies conducted in similar settings.

Further research is necessary to identify solutions for better medication use in the elderly, including the involvement of the community pharmacists caring for this population. Cumulating information from the pharmacy database with the patients clinical records and laboratory results, would allow for a comprehensive analysis of medication use among the elderly. They could also serve to create and to validate locally adapted criteria to help prevent the inappropriate medication use among Romanian elderly, the associated costs and adverse outcomes.

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