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RESEARCH ARTICLE

Potentially inappropriate drug prescribing in elderly hospitalized patients: an analysis and comparison of explicit criteria

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Abstract *Background* The management of therapy in elderly is a critical aspect of primary care. The physiopathological complexity of the elderly involves the prescription of multiple drugs, exposing them to a higher risk of adverse reactions. *Objective* Aim of this study was to assess the medication use and (potential) inappropriate medications and prescribing omissions in the elderly before and during hospitalization, according to the main tools in literature described, and their relation to the number of comorbidities. *Setting* The study was carried out by the Clinical Pharmacists at ISMETT, an Italian Research Institute. *Methods* The prescriptions of elderly, admitted in ISMETT between January and December 2012, were analyzed. The information about clinical profile of elderly and prescriptions was obtained from the electronic medical records. 2012 Beers criteria, Screening Tool of Older Person's Prescriptions/Screening Tool to Alert doctors to Right Treatment criteria, and Improving Prescribing in the Elderly criteria were used to evaluate the appropriateness of prescriptions. The correlation between the number of comorbidities and the different tools was analyzed with the Spearman correlation coefficient. The frequency analysis was done with the Pearson Chi square test. *Main outcome measure* Percentage of potentially inappropriate medications and prescribing omissions before/during hospitalization in elderly. *Results* 1027 elderly were admitted between January and December 2012. At admission and during hospitalization, according to Beers criteria 24 and 49 % of elderly had at least one potentially inappropriate medication, respectively; according to the Screening Tool of Older Person's Prescriptions criteria 21 and 27 %, respectively; according to the Improving Prescribing in the Elderly criteria 28 and 25 %, respectively; and then, according to Screening Tool to Alert doctors to Right Treatment criteria 28 and 33 % had at least one potentially prescribing omission, respectively. A significant correlation between comorbidities number and potentially inappropriate medications was found. *Conclusion* The number of potentially inappropriate medications globally increased during hospitalization. Statistical analysis showed that the comorbidity affects the level of inappropriate prescriptions. Specific tools can guide clinicians toward a more rational use of medicines and minimize probable complications related to multi-treatments.

Keywords Aging · Drug utilisation · Drug–drug interactions · Elderly · Hospital · Italy · Medicine use · Polypharmacy · Prescribing appropriateness index · Safety · Utilisation evaluation

Impact of findings on practice

- Applying explicit criteria can improve the number of appropriate medications and decrease the number of inappropriate choices.
- Explicit criteria ensure drug- and diagnosis-specific aspects of quality of drug therapy in elderly patients.
- There is significant positive correlation between the number of comorbidities and potentially inappropriate medications.

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Introduction

The management of drug therapy in elderly patients is a critical and relevant aspect of primary care. The elderly have many chronic disorders and, consequently, use more medications than individuals of other age groups. The ageing process is characterized by structural and functional changes affecting all organ systems and results in reduced homeostatic capacity. Changes in body composition, hepatic and renal function are responsible for an increase in the volume of distribution of lipid soluble drugs, reduced clearance of lipid soluble and water soluble drugs, respectively. All these changes lead to a prolongation of plasma elimination half-life. Significant pharmacodynamic changes also occur which, in general, tend to increase sensitivity to drugs [1–3].

According to the 2013 Observatory on the use of Medicines (OsMed) report, elderly over the age of 65 show a per capita cost for medicines reimbursed by the National Health Service (NHS) of up to three times the national average [4]. For every elderly person over the age of 65, the NHS has pharmaceutical costs almost six times higher than average costs for patients under 65 [4]. This is because only 50 % of those under the age of 65 require pharmaceuticals, while over 90 % of those over the age of 74 require them. Almost all people over the age of 74 take at least one drug. Those over the age of 65 account for more than 60 % of total costs (with the exception of drugs administered in hospital settings), and more than 65 % of the total Defined Daily Dose (DDD). In terms of consumption, people over 65 take an average of 2.7 units of drugs daily, which becomes 3.7 at the age of 74 [4].

In the last two decades, evidence has emerged of an increased prevalence of medication prescriptions considered potentially inappropriate in elderly patients from 2.2 to 35.6 % in Italy, depending on the population studied [5].

In a study by Fialova et al. [6], the prevalence of inappropriate medications was assessed in a sample of 2707 octogenarians who received home care services in 11 European countries, including Italy. It was observed that overall about 20 % of patients received at least one inappropriate drug prescription, with large differences among the countries, and with Italy second (26.5 %) for prevalence of inappropriate prescriptions. In July 2013, the Geriatric Working Group of the Italian Drug Agency (AIFA) conducted a survey on appropriateness of prescriptions in elderly Italian patients [7]. The data showed that half of the elderly population took 5–9 medications per day, and that 11 % of the elderly population took more than 10 medications per day. In total, about 7.5 million of Italian elderly took 5 or more medications per day. The assumption of a large number of drugs does not facilitate adherence to therapy. The AIFA study showed that about 50 % of patients with hypertension or with osteoporosis had low adherence to therapy, and the percentages were even higher for anti-diabetic and antidepressant medications. Low adherence to therapy therefore implies that patients cannot derive any benefit from the drugs they take (e.g., control of blood pressure, blood glucose control, prevention of fractures) [7].

Specific criteria have been developed to support the physicians choosing safer therapy in elderly. The most used criteria include: the Beers criteria [8], the *Screening Tool of Older Person's Prescriptions/Screening Tool to Alert doctors to Right Treatment* (STOPP/START) [9, 10], and the *Improving Prescribing in the Elderly Tool* (IPET) [11]. These are known as explicit criteria because focused on the drug or on the disease. Then explicit measures rely on fixed criteria that apply uniformly to all patients and can therefore be computerized and easily determined for large patient samples.

Aim of the study

Aim of this study was to assess the medication use, (potential) inappropriate medications (PIMs) and prescribing omissions (PPOs) in the elderly, before and during hospitalization, and their relation to the number of comorbidities.

Ethics approval

The ISMETT ethics committee approved this study (No. 0004858).

Method

Study population and data collection

This retrospective observational study was carried out by the Clinical Pharmacy Service at ISMETT (Istituto Mediterraneo per i Trapianti e Terapie ad alta specializzazione), a Research Institute in Palermo, Italy. Three tools were applied in the elderly admitted to ISMETT. All patients aged ≥65 years, admitted to ISMETT between January and December 2012, were enrolled. In the study, the information needed to evaluate the clinical profile of patients and appropriateness of prescriptions was obtained from the electronical clinical record "Sunrise Clinical Manager®—Eclipsys" and collected in an excel database. Four sets of explicit indicators were used to assess the

appropriateness of drug therapies, three of them (the 2012 Beers criteria, the STOPP criteria and the IPET criteria) point out the PIMs, while the START criteria underline the PPOs. For each patient, demographic (age and gender), date of admission and discharge, clinical history (diagnoses and co-morbidities), and drug therapy and dosage on admission and during the hospital stay by generic name and the Anatomical Therapeutic Chemical (ATC) classification system were recorded. For each criteria specific information were focused, in particular: for Beers criteria, dosage of digoxin, spironolactone and aspirin, indication of antiarrhythmic agents, benzodiazepines, alpha-1 agonists and alpha-1 blockers, and creatinine values in the case of nitrofurantoin and spironolactone prescription were recorded. For START criteria, dosage of digoxin and aspirin, comorbidity in case of digoxin, thiazide diuretics, β-blockers, calcium channel blockers, aspirin, tricyclic antidepressants, phenothiazines, selective serotonin reuptake inhibitors (SSRI), metoclopramide, anticholinergic antispasmodics, ipratropium in nebuliser solution, nonsteroidal anti-inflammatory drugs (NSAIDs) and antimuscarinic prescription, use of urinary catheter in case of alpha-blockers prescription, hyponatremia values in case of SSRI prescription were recorded. For START criteria, systolic blood pressure values in case of antihypertensives prescription were recorded. Then for IPET criteria, comorbidity in case of thiazide diuretics, tricyclic antidepressants and NSAIDs prescription were recorded.

Two specific excel databases were created for each set of the above criteria, one related to treatment recorded on admission, and one related to therapies prescribed during hospitalization. The information necessary for the application of appropriateness criteria were entered into each of these databases. Finally, a comparison was made between PIMs and PPOs recorded on admission and those carried out at the hospital. All single dosage prescriptions and all prescriptions for no longer than three-day therapy were excluded from the study because they were considered not clinically significant.

Statistical analysis

All values are expressed as mean ± SD. The correlation between the number of comorbidities and the different sets of indicators (the 2012 Beers criteria, the STOPP criteria and the IPET criteria) was analyzed with the Spearman correlation coefficient. The frequency analysis was done with the Pearson Chi square test. P values of <0.05 were considered statistically significant. The PPOs observed in the medications used at home and in hospital were expressed in percentage.

Results

A population of 1027 patients ≥65 years was included in the study. The mean patient age was 73.35 ± 5.6. Specifically, it was found that 89 % (917/1027) of the patients were between the ages of 65 and 80, and 97 % (892/917) of them suffered from 2 to 6 co-morbidities. Statistical analysis showed that the mean of co-morbidities per patient was 2.96 ± 1.286.

At admission, a medication reconciliation process was carried out on 90.5 % (929/1027) of patients. Information on medications used at home was not present in the electronic clinical record for the remaining 9.5 % (98/1027) of the patients. It was found that 95.5 % (887/929) of the medical reconciliation patients had taken a total of 4428 drugs. The remaining 4.5 % (42/929) had not undergone medications used at home. Analysis of the database related to the hospital prescriptions showed that a total of 12,740 drugs were prescribed to the 1027 admitted patients. Patients characteristics and diseases registered ad admission are showed in Tables 1 and 2.

At admission, medications used at home was reported in the electronic clinical record for 887 of the patients: 24 % (211/887) had at least one PIM according to the Beers criteria, 21 % (188/887) according to the STOPP criteria, and 28 % (249/887) according to the IPET criteria. The average of PIMs according to Beers, STOPP, and IPET criteria was 0.24 ± 0.501, 0.21 ± 0.476, and 0.29 ± 0.559, respectively. During hospitalization, 49 % (507/1027) of patients had at least one PIM according to the Beers criteria, 27 % (277/1027) according to the STOPP criteria, and 25 % (261/1027) according to the IPET criteria (Table 3).

The mean number of PIMs according to Beers, STOPP, and IPET criteria was 0.68 ± 0.818, 0.33 ± 0.618 and 0.57 ± 9.180, respectively.

At admission, using the START criteria, one or more appropriate medications were omitted in 28 % (246/887) of patients. This percentage reached 33 % (338/1027) when we also considered the medications used in hospital (Table 3).

The most prescribed drug/therapeutic classes of Beers, STOPP, IPET and START lists found in the medications used at home and in hospital, and the prescriptive trend in the two settings, are shown in the following tables (Tables 4, 5, 6, 7).

Analysis by age of the three groups with respect to the number of drugs consumed (≤5, 6–10, >10) did not produce statistically significant results ($P = 0.614$, Pearson Chi square). The statistical analysis carried out by applying the Spearman correlation coefficient (r) showed that there was a strong and significant correlation between the

Table 1 Patient characteristics

Variable	Category	No. of patients	% of patients
Gender	Men	641	62
	Women	386	38
Age (years)	65–70	377	37
	71–80	540	52
	81–90	103	10
	>90	7	1
Length of stay	0–7	589	57
	8–14	279	27
	15–21	87	8
	22–30	36	3.5
	>90	36	3.5
No. of co-morbidities	1	135	13
	2	274	27
	3	266	26
	4	226	22
	5	98	9.5
	6	26	2.5
No. of drugs at admission	0–5	528	60
	6–10	323	36
	>10	36	4
No. of drugs during hospitalization	0–5	49	15
	6–10	255	25
	>10	723	70

number of comorbidities and PIMs according to the adopted criteria (Table 8).

Discussion

Analysis of therapies recorded on admission showed that more than one half of elderly patients hospitalized at our institute between January 2012 and December 2012 regularly took up to five drugs per day. The number of medications taken by the elderly has increased during hospitalization, often in relation to the increased number of diseases diagnosed during the hospital stay or the need to correct a previously followed treatment schedule.

Comparing the results of Beers, STOPP, START, and IPET criteria, an increase in inappropriate prescriptions was observed during the hospital stay. Specifically, the percentage of patients with at least one PIM increased from 24 to 49 % according to the Beers criteria, and from 21 to 27 % according to the STOPP criteria. At the same time the percentage of patients with at least one PPOs increased from 28 to 33 % according to START criteria. The PIMs decreased only according to the IPET criteria, from 28 to 25 %.

Table 2 Diseases registered at admission

Diseases	No. of patients	% of patients
Hypertension	558	54
Suspected liver, intestine or lung lesion	397	39
Congestive heart failure	301	29
Diabetes mellitus	300	29
Heart disease	229	22
Liver disease	161	16
Previous cancer metastases	109	11
Chronic atrial fibrillation	101	10
Chronic Obstructive Pulmonary Diseases (COPD)	87	8.5
Chronic renal failure	82	8
Gastric disease	53	5
Depression	41	4
Osteoporosis	36	3.5
Cerebrovascular disease	32	3
Parkinson's disease	8	1

The general increase in PIMs is attributable to increased prescriptions of medications sometimes completely absent in medications used at home. For example, metoclopramide, ketorolac and indomethacin, considered potentially inappropriate according to the Beers criteria, were prescribed exclusively in the hospital. According to the STOPP criteria, an increased trend in the benzodiazepine prescription was observed. Drugs in the same therapeutic class, NSAIDs in patients with hypertension, and cardioselective β-blockers in patients with COPD, were prescribed more, contrary to the indications of the STOPP criteria. It is important to note that improper use of benzodiazepines may cause a reduction in vigilance and balance disorders. Also, before considering the association between drugs of the same class, it is always necessary to optimize the therapy with a single drug; and finally, it is useful to emphasize that the use of NSAIDs in hypertensive patients may increase the risk of worsening hypertension. Further data that should not be underestimated are those related to the prescription of β-blockers in patients with COPD. Although the European Society of Cardiology guidelines recommend the use of the entire class of β-blockers in chronic heart failure, the pharmacological properties of the individual agents are widely different, especially with regard to cardio-selectivity. For example, the β_1-selectivity of bisoprolol favors its use in patients with underlying respiratory problems [12]. The analysis of data relating to the STOPP criteria showed a high rate of β-blocker prescriptions in patients with diabetes mellitus, though it should be noted that there was a reduction in the

Table 3 Number of patients with PIMs and PPOs according to the adopted criteria

	Medications used at home		Medications used in hospital	
	% of patients	No. of patients	% of patients	No. of patients
Beers criteria	24	211	49	507
STOPP criteria	21	188	27	277
IPET criteria	28	249	25	261
START criteria	28	246	33	338

Table 4 Drug/therapeutic classes of beers criteria list found in the medications used at home and in hospital

	Medications used at home (%)	Medications used in hospital (%)	Δ (%)
Calcium channel blockers	21	5	−16
Benzodiazepines short or intermediate action	18.5	14	−4.5
Amiodarone	16	26	+10
Doxazosin	15	9	−6
Ticlopidine	14	6	−8
Propafenone/Sotalol	8.5	3.5	−5
Clonidine	6	2	−4
Benzodiazepines long action	4	0	−4
Tertiary tricyclic antidepressants	3	0	−3
Metoclopramide	0	38	+38
Ketorolac	0	14.4	+14.4
Indomethacin	0	12	+12

Δ = Difference between medications used in hospital and at home

Table 5 Drug/therapeutic classes of STOPP criteria list found in the medications used at home and in hospital

	Medications used at home (%)	Medications used in hospital (%)	Δ (%)
Diabetes mellitus (DM) and β-blockers	66	58	−8
Benzodiazepines	26	31	+5
Drugs of the same class	3	13	+10
NSAIDs and hypertension	0	6	+6
Heart failure of NYHA class III and diltiazem	0	4	+4
COPD and cardioselective β-blockers	0	3	+3

Δ = Difference between medications used in hospital and at home

trend during the hospital stay. β-blockers can cover hypoglycemia symptoms in these patients.

The data observed using the START criteria confirmed the results obtained applying the other tools. Indeed, during hospitalization, we observed an increase although slight of the PPOs.

Nevertheless, positive results as an increase in warfarin prescriptions in presence of chronic atrial fibrillation, statin therapy in patients with documented history of vascular disease, ACE inhibitors in chronic heart failure, PPI in presence of chronic severe gastro-esophageal acid reflux, inhaled β_2-agonists and corticosteroids for asthma, were also observed during hospitalization.

Though an overall reduction in inappropriate prescriptions was observed according to the IPET criteria, an increase in the prescriptive trend of β-blockers in patients with COPD, and NSAIDs in patients with moderate to severe hypertension, was observed. In addition, the prescription of β-blockers in patients with congestive heart failure increased. In contrast, a reduction in Ca-channel blockers (except amlodipine and felodipine) prescriptions in patients with congestive heart failure was registered during hospitalization. This class of drugs can lead to fluid retention and worsening of heart failure.

These results, also supported by statistical analysis, confirm that co-morbidity significantly affects the

Table 6 Drug/therapeutic classes of IPET criteria list found in the medications used at home and in hospital

	Medications used at home (%)	Medications used in hospital (%)	Δ (%)
β-blockers and congestive heart failure	75.5	85	+9.5
Calcium channel blockers (except amlodipine/felodipine) and congestive heart failure	28	4	−24
COPD and β-blockers	9	14	+5
Tricyclic antidepressants with active metabolites	3	2	−1
NSAIDs and hypertension	0	7	+7

Δ = Difference between medications used in hospital and at home

Table 7 Drug/therapeutic classes of START criteria list found in the medications used at home and in hospital

	Medications used at home (%)	Medications used in hospital (%)	Δ (%)
Warfarin in the presence of chronic atrial fibrillation	56	53.5	−2.5
Aspirin in the presence of chronic atrial fibrillation, where warfarin contra-indicated	0	38.5	+38.5
Statin therapy in patients with documented history of vascular disease	14	5	−9
Angiotensin coverting enzyme (ACE) inhibitors in chronic heart failure	68	60.5	−7.5
Regular inhaled β_2-agonists for mild to moderate asthma or COPD	80.5	38	−42.50
Inhaled steroid in moderate-severe asthma or COPD	64	0	−64
Antidepressant in the presence of clear-cut depression	26	23	−3
PPI in the presence of chronic severe gastro-esophageal acid reflux or peptic stricture requiring dilatation	66	47	−19
Metformin with type 2 diabetes ± metabolic syndrome	72	82	+10
ACE inhibitors in diabetes with nephropaty	23	77	+54
Aspirin or clopidogrel therapy in diabetes mellitus with hypertension	52	60	+8
Statin therapy in diabetes mellitus with hypercolesterolemia	53	67	+14

Δ = Difference between PPOs recorded in the medications used in hospital and at home

Table 8 Correlation between the number of comorbidities and PIMs according to the adopted criteria

	Admission		Hospitalization	
	r	*P*	r	*P*
Beers criteria	0.148	<0.0005*	0.113	<0.0005*
STOPP criteria	0.256	<0.0005*	0.355	<0.0005*
IPET criteria	0.301	<0.0005*	0.24	<0.0005*

* *P* values of <0.05 were considered statistically significant

inappropriateness of prescriptions. This result is not encouraging, particularly when considering that older patients suffer from more diseases, and invariably require multi-pharmacological treatment [6, 13, 14]. Using tools that can guide clinicians toward a more rational use of medicines, it is possible to minimize the probable complications related to multi-treatments.

These tools with the practitioners' expertise can better manage the most critical conditions based on the general framework of the patients and the diseases for which they were admitted.

However, many studies generally support that clinical pharmacist can play an important role in reducing unnecessary medication and in intercepting and acting on possible prescribing errors and/or recognizing drug-related problems. Processes for identifying medications for reduction included systematic pharmacist-initiated medication reviews and educational interventions targeting physicians and nursing staff.

It was demonstrated that, when these approaches were combined in a context of a multidisciplinary team, better effects on patients' health outcome were shown. Integration of skills and valuable information obtained from different healthcare professionals is fundamental to address medical complexity of the elderly [15–17].

Conclusion

The findings of this study indicate a considerable amount of PIMs being used, which should be avoided and replaced with other medications with less potential for adverse effects. The overall assessment of the elderly patient is essential in choosing the best-tailored therapy. Aging can lead to an increasing frequency of polypharmacy. The latter is often associated with a high incidence of severe adverse reactions, which can lead to increased hospitalization, and mortality, with a consequent increase in health system costs. It is imperative, therefore, to identify and implement programs that appropriately balance the possible risks and benefits of treatment. This study gave rise training sessions for clinicians and all health workers to raise awareness and implement the application of explicit criteria as tools for reducing inappropriate prescriptions and its consequences.

Also, for each patient, the clinical pharmacists have started to systematically ensure the medication reconciliation process at the transition of care in order to support clinicians in choosing the most appropriate and safer therapies in frail elderly patients.

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