Inappropriate Medications Use Among Elderly Patients in Babylon Province

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ABSTRACT
Background: Inadequate or inappropriate medication treatment is a major risk factor for medication-related diseases. Determining the prevalence of potentially inappropriate prescription and drug-disease interactions in hospitalized patients is an important step to resolving these problems.
Methods: A sample of 500 geriatric patients hospitalized between June 2021 and December 2021 were included in the study. Medication prescribed before (usual medication), during, and at hospital discharge was considered.
Results: The prevalence of prescription of at least one inappropriate drug on hospital admission, during hospitalization, and at discharge was 9.8 %, 3.6%, and 2.4 % respectively. The drugs most frequently implicated in hospital admission were diazepam, digoxin, iron products, chlorpheniramine, and amitriptyline. The significant adverse drug-disease interaction on hospital admission, during hospitalization, and at discharge was 13.0%, 3.2%, and 3.4%, respectively. The variables number of drugs at admission and the number of diseases and the pain item of the COOP/WONCA score were statistically significant.
Conclusions: The study reveals the existence of potentially inappropriate drug prescriptions or potentially adverse drug-disease interaction in hospitalized patients in our environment. Polypharmacy, polypathology, and the presence of chronic pain were associated with potentially inappropriate prescriptions.
Keywords: Drugs, adverse effects; medication prescription.

INTRODUCTION

Drug-induced diseases in the elderly are gaining importance as the population of older adults has increased. The previous researches suggest that inadequate or inappropriate medication treatment is a major risk factor for these medication-related diseases. Inadequate medication is defined as when the risk outweighs the benefit. The risk-benefit ratio of some drugs is influenced by the changes in pharmacokinetics and pharmacodynamics related to the aging process. Prescribing an inappropriate drug to the elderly population exposes them to a risk of morbidity and mortality. Adverse drug reactions (ADRs) are the most serious consequences of inappropriate prescription. ADRs, when they are not recognized, can in turn lead to the prescription of additional medications to the detriment of the quality of life. Consequently, the aforementioned ADRs can result in superfluous hospitalizations and an increase in morbidity and mortality [1,2].

Recent meta-analysis studies estimated that 4.7% of all hospitalizations were due to ADRs. Studies limited to the elderly found frequencies as high as 17%. The most effective way to prevent ADRs in old-age patients is by reducing the number of inappropriate prescriptions [3].

In 1991 Beers et al. developed the Explicit Criteria for Inappropriate Medication in the elderly, which were later updated in 2019 using the expert consensus technique and evidence-based medicine concepts [4]. They include drugs that should be avoided in geriatric patients and other drugs whose dosage, frequency of administration or duration should not exceed certain limits. Several of these drugs were considered unsuitable because safer alternatives exist or because their side effects are extremely unsuitable for the elderly, in addition to that, some agents were considered inappropriate due to their questionable efficacy [4, 5].

The criteria for improper use are also referred to the use of drugs that exceed the maximum dose or that exceed the usual duration and that therefore causes a high frequency of adverse reactions and are of questionable necessity [6]. For example, iron products should not exceed the dose of 325 mg/day; if the doses are higher, they are not absorbed, but their adverse reactions increase [4]. On the other hand, if the user is unique or very infrequent, it is also considered inappropriate, since the desired effect is not achieved. Beers *et al* also identified the drugs that should be avoided in patients with a history of one of the 14 diseases, which they called a drug-disease interaction [6], in addition to the identification of four drug-drug interactions that must be avoided (e.g. warfarin, either with aspirin, NSAIDs, dipyridamole or ticlopidine) and three drugs with specific recommended doses in elderly: 1) Digoxin, at maximum dosage limit of 0.125 mg/day, except in patients with atrial fibrillation; 2) short half-life benzodiazepines with maximum total daily dose (oxazepam >60 mg, zolpidem >5 mg, lorazepam >3 mg, alprazolam >2 mg); and, 3) ferrous sulfate, at a maximum dose of 325 mg/day [7].

Stuck *et al.* [8] modified Beers' original list by applying it to patients cared for at home. This list is called

the Modified Beers Criteria and includes gastrointestinal antispasmodics, but excludes methyldopa and propranolol.

The objective of this study is to determine the prevalence of inappropriate prescription drugs in the elderly population, before, during, and at discharge from one of the hospitals in Babylon province in Iraq.

METHODS

Our study is a prospective, descriptive, cross-sectional, and observational study. The study was conducted on patients hospitalized at the Al-Imam Ali Hospital, in Babylon province, Iraq. A sample of 500 patients over 60 years of age hospitalized between June 2021 and December 2021 was obtained.

A special questionnaire was developed for our study, which included demographic data such as age, gender, marital status, race, and educational level. Other variables evaluated were the number of hospitalizations in the previous 12 months, the number of drugs at admission (regular medication or before hospitalization), during hospitalization, and at discharge (or death) of the patient. For the evaluation of mental status, the Lobo cognitive mini-examination [12] was used; for the evaluation of activities of daily living (ADL), the Katz index and the COOP/WONCA score were used to qualify the quality of life and functional health evaluation [13]. If the patient had a sensory disorder or a Lobo cognitive mini-examination score less than 17, the COOP/WONCA score was made by the caregiver and, in the absence of the caregiver, the rating was made by the interviewing physician.

The 2019 Beers criteria on inappropriate medication prescription were used [6]. The detection of potentially improper medication and potential adverse drug-disease interaction was followed by communication to the treating physician to suspend the study. The drug was detected as inappropriate; exceptionally, at discharge, they continued with the same drug, especially when said drug had a different indication than that stipulated in the Beers criteria [6].

Potentially inappropriately prescribed drugs were recorded as well as adverse drug-disease interactions. The drugs that the patient was taking before being hospitalized (usual medication), during hospitalization, and at the time of discharge were also noted; in each of the cases, it was correlated with whether the prescribed medication was potentially inappropriate or presented an adverse drug-disease interaction.

To establish the statistical differences of the variables concerning the group with and without inadequate prescription, the chi-square test was used for categorical variables and the Wilcoxon rank-sum test for continuous variables.

Ethical approval:
The study was approved by the Ethics Board of University of Babylon.

RESULTS

The total number of hospitalized patients studied was 500. A total of 592 patients were admitted, having included 500 in the study; 92 cases were excluded because they did not have medication information before hospitalization or the patient/caregiver did not remember them. In-hospital mortality of the patients studied was 5.2% (26 deaths). The mean age was 75.2 years (range: 60 to 87 years), 52% male, 58% married, and 50% with a primary education level **(Table 1).**

Table 1. Demographic characteristics of the studied population

Characteristics	Values
Age (years, mean±SD)	75.2±8.8
Sex	Male 52%
	Female 48%
Marital status	Married 58%
	Widower 31%
	Single 7%
	Divorced 4%
Degree of instruction	Illiterate 5%
	Primary 50%
	Secondary 30%
	Higher education 15%

The mean number of recorded illnesses was 4.1, the mean impairment in daily activities (feeding, continence, transferring, attending to the toilet, dressing, bathing) was 2.6, and 72% had at least one impairment in activities of daily living (ADL). The mean number of drugs on admission (usual medication before being hospitalized), during hospitalization, and at discharge were 3.2, 4.5, and 2.3, respectively (**Table 2**).

Table 2. Clinical characteristics of the population studied

Characteristics	Values
Number of drugs on admission (mean±SD)	3.2±2.1
Number of drugs during hospitalization (mean±SD)	4.5±2.1
Number of drugs at discharge (mean±SD)	2.3±1.5
Number of diseases (mean±SD)	4.1±1.1
Number of hospitalizations In the previous 12 months (mean±SD)	1.2±1.0
Number of deficiencies in activities of daily life (mean±SD)	2.6±2.3
Activities of daily living: Katz Index	A 28% (independent) B12% (independent for all except one) C14% (dependent on bathing and one other) D 9% (dependent for bathing, dressing, and one other) E 7% (dependent for bathing, dressing, toileting, and one other) F11% (dependent for bathing, dressing, toileting, transferring, and one other) G 19% (dependent for all)
Quality of life and functional evaluation health: COOP/WONCA score (mean±SD) Score depends on a five-point ordinal scale ranging from 1 (the best) to 5 (the worst)	Physical capacity 3.8±1.0 Feelings 3.3±0.9 Daily activities 3.7±1.0 Social activities 3.8±1.0 Change in social status 3.7±1.0 Health status 4.0±0.8 Pain 2.6±1.2 Social support 2.8±1.0 Quality of life 3.8±1.0

The prescription of at least one inappropriate medication was detected on hospital admission, hospitalization, and discharge in 9.8 %, 3.6%, and 2.4%, respectively **(Table 3)**.

The five most frequently inappropriately prescribed medications were diazepam, digoxin (doses greater than 0.125 milligram/day), iron (doses greater than 325 milligram/day), chlorpheniramine, and amitriptyline. During hospitalization, the most frequent drugs were diazepam and hyoscine butyl bromide, although the prevalence of inappropriate prescriptions was much lower.

Table 3. Frequency of potentially inadequate prescription medications

Drug	On admission	During discharge	Hospitalization
Diazepam	14	4	-
Digoxin	13	4	3
Iron	6	-	-
Chlorpheniramine	5	-	-
Amitriptyline	4	2	2
Methyldopa	3	-	-
Alprazolam	2	4	7
Hyoscine butyl bromide	2	4	-
Total (%)	49 (9.8)	18 (3.6)	12 (2.4)

Potentially adverse drug-disease interaction was observed at admission, during hospitalization, and at discharge in percentages of 13.0%, 3.2%, and 3.4%, respectively.

The five most frequent potentially adverse drug-disease interactions were peptic ulcer disease with non-steroidal anti-inflammatory drugs, chronic obstructive pulmonary disease with beta-blockers and sedatives, diabetes mellitus and beta-blockers (in patients with oral hypoglycemic drugs), and, finally, benign prostatic hypertrophy with amitriptyline and chlorpheniramine (**Table 4**).

Table 4. Frequency of significant adverse drug-disease interactions

Illness	On admission	During discharge	Hospitalization
Peptic ulcer disease			
Diclofenac	13	-	-
Ibuprofen	7	-	-
Aspirin	3	-	-
Piroxicam	1	-	-
Benign prostatic hypertrophy			
Chlorpheniramine	5	-	-
Amitriptyline	1	2	2
Diabetes Mellitus			
Propranolol	3	-	-
Atenolol	5	2	2
Chronic obstructive pulmonary disease			
Alprazolam	3	2	2
Atenolol	3	-	-
Diazepam	1	-	-
Propranolol	3	1	2
Constipation			
Morphine	3	3	4
Codeine	1	1	-
Hyoscine	2	-	-
Peripheral vascular disease			
Atenolol	3	3	4
Coagulation disorders limited those on anticoagulation			
Ibuprofen	1	-	-
Piroxicam	1	-	-
Diclofenac	2	-	-
Bronchial asthma			
Atenolol	1	1	-
Propranolol	3	1	1
Total (%)	65 (13.0%)	16 (3.2%)	17 (3.4%)

The prescription of potentially improper medication or potentially adverse drug-disease interaction on the hospital admission was related to the following variables: number of medications on admission, number of illnesses, and COOP/WONCA score to qualify the quality of life and evaluation of functional health.

The variables that were not found to be statistically significant were: age, sex, marital status, race, schooling, Katz index, number of hospitalizations 12 months before hospitalization when entering the study, and in-hospital mortality. The variable's medications number at admission and the illnesses number and the pain COOP/WONCA score were statistically significant (**Tables 5 and 6**). Collaterally, it was shown that the history of prescription of potentially improper medication or potentially adverse drug-disease interaction at admission had a very significant frequency of suffering an adverse drug reaction compared to the group without the described history; In addition, the first group indicated, the adverse drug reaction was the direct cause of hospitalization in 26.1% of the cases.

Table 5. Potentially inappropriate prescription medications or adverse drug-disease interaction: relationship with numbers of drugs and diseases

Variable	Patients WITH potentially inadequate prescription or interactions (n=115) (23%) (Mean and standard deviation)	Patients WITHOUT potentially inadequate prescription or interactions (n=385) (77%) (Mean and standard deviation)	P-value
Number of diseases	5.0±1.0	3.9±1.0	<0.001
Number of drugs upon admission	4.6±1.8	2.8±2.0	<0.001

Table 6. Potentially inappropriate prescription medications or adverse drug-disease interaction: functional status and quality of life according to COOP/WONCA

Items of score COOP/ WONCA	Patients WITH potentially inadequate prescription or interactions (n=115) (23%) (Mean and standard deviation)	Patients WITHOUT potentially inadequate prescription or interactions (n=385) (77%) (Mean and standard deviation)	P-value
Physical fitness	4.2±0.8	3.6±0.9	0.061
Feelings	3.6±0.8	3.3±0.9	0.123
Daily Activities	4.1±0.9	3.5±0.9	0.843
Social Activities	4.3±1.0	3.6±1.0	0.129
Changes in the health status	4.1±1.0	3.5±0.9	0.760
Health status	4.4±0.7	3.9±0.8	0.756
Pain	3.3±1.2	2.4±1.1	<0.001
Social Support	3.1±1.0	2.7±1.0	0.772
Quality of life	4.3±1.0	3.7±0.9	0.479

The last table below shows hospitalizations due to adverse drug reactions in patients with potentially inappropriate medications or potentially adverse drug-disease interactions.

Table 7. Hospitalizations due to adverse reactions to medication in patients with prescription potentially inappropriate medications or potentially adverse drug-disease interactions

Adverse drug reaction	Frequency n=115
NSAID-induced upper gastrointestinal bleeding	13
Glibenclamide-induced hypoglycemia (in patients with beta-blockers)	7
Digitalis poisoning	5
Diazepam-induced falls syndrome (with hip fracture)	3
AV block 3rd degree	1
Aspirin gastrointestinal bleeding dose >325 mg/day	1
Total (%)	30 (26.1)

DISCUSSION

The prevalence of prescription of potentially inappropriate medication in hospitalized patients at the time of hospitalization was 9.8%, with the prevalence found during hospitalization and at discharge being much lower. A direct association was found between the prescription of significant improper medication or potentially adverse drug-disease interaction with the medications number, the number of diseases and the rating of pain in the COOP/WONCA score to qualify the quality of life and functional evaluation of the Health.

On the other hand, the prescription of significant improper medication or potentially adverse drug-disease interaction detected at hospital admission was significantly related to hospitalization for adverse drug reaction, the latter being the direct cause of hospitalization in 26.1% of cases.

The prevalence of potentially inappropriate prescriptions of 9.8% at hospital admission is not very different from other studies. Chin *et al*. found a prevalence of 10.6% in patients older than 65 years at admission to emergency service [11]; during hospitalization and at patient discharge, the prevalence were 3.6% and 5.6%, respectively. In our study, they were 3.6% and 2.4% concerning the same conditions. There is another study by Onde *et al.* [12], whose objective was in-hospital prevalence only, finding that 14.6% of patients hospitalized in a group of Italian university hospitals had at least one inappropriately prescribed medication. Most studies on the prevalence of this problem are related to older adults from outpatient clinics, nurseries, and the homeless. Liu *et al*. conducted a meta-analytic study of the main studies published up to 2001. Of the 11 studies analyzed, the prevalence ranged from 40% in nurseries to 21.3% in elderly outpatients [15].

In the present study, the drugs most frequently inappropriately prescribed before hospitalization were diazepam, digoxin (doses greater than 0.125 milligram/day), iron (doses greater than 325 milligram/day), chlorpheniramine, and amitriptyline. In the studies by Chin *et al.* (10), were diphenhydramine, indomethacin, and meperidine; In the investigations of Onder *et al.* [14], the frequency of drugs was ticlopidine, digoxin, amitriptyline, chlordiazepoxide, and diazepam; finally, in the meta-analytical studies by Liu col., propoxyphene, amitriptyline, benzodiazepines, and dipyridamole are included [15].

The prevalence of potentially adverse drug-disease interaction at hospital admission, hospitalization, and discharge was 13.0%, 3.2%, and 3.4%, respectively. Comparatively, other studies report only 5%, 0.6%, and 1.2% in the three cases mentioned above, although this last study was in elderly patients in an Emergency service

[11]. In our study, the most frequent potentially adverse drug-disease interactions were peptic ulcer disease with NSAIDs, chronic obstructive pulmonary disease with beta-blockers and sedatives, diabetes mellitus and beta-blockers (in patients with oral hypoglycemic drugs), and, finally, benign prostatic hypertrophy with amitriptyline and chlorpheniramine. In the study by Chin *et al.,* coagulation disorders related to anticoagulation and chronic obstructive disease were the most frequent; both interact with beta-blockers, NSAIDs, aspirin, and sedative-hypnotics [11].

Golderber *et al.* [16] published that up to 21.5% had this medication-related problem. However, it should be noted that the population studied by these authors was made up of patients considered to be at high risk, taking more than 3 medications, and older than 50 years of age.

A history of multiple drugs and polypathology were the most consistent predictors of significant improper drug prescription or potentially adverse drug-disease interaction. Polypharmacy itself is a factor closely related to the high incidence of adverse drug reactions [17]. Another of the predictive factors of the problem under study was the pain item of the COOP/WONCA score. Chronic pain management, according to studies by Bernabei *et al*., is currently inadequate, especially in the elderly with neoplasms [18].

From the results obtained in the present study, it is possible to make some recommendations for the prevention of the prescription of significant improper medication and potential adverse drug-disease interaction, such as: encouraging the rational use of drugs in the elderly, disseminating Beers' explicit criteria on potentially inappropriate prescription and education on important aspects of drug administration in the elderly, especially topics on pain therapy in this age group.

There are some limitations in the present study. One of the main ones is that the findings cannot be generalized to other hospitals. The reality of the hospital differs significantly from that of other hospitals. Larger studies involving more than one hospital are necessary to know the true dimension of the problem of significant improper medication prescription and potential adverse drug-disease interaction in the elderly. On the other hand, research is needed that includes the follow-up of patients after discharge, to observe the influence on the quality of life, morbidity, and mortality resulting from the problem of our study.

CONCLUSIONS

The present study on the potentially inappropriate use of medications in older adults, detected the prescription of one or more inappropriate medications on hospital admission, at hospitalization, and finally at

discharge in 9.8 %, 3.6 %, and 2.4 %, respectively. The five most common potentially adverse drug-disease interactions were peptic ulcer disease with NSAIDs, chronic obstructive pulmonary disease with beta-blockers and sedatives, diabetes mellitus and beta-blockers (in patients with oral hypoglycemic drugs), and, finally, benign prostatic hypertrophy with amitriptyline and chlorpheniramine. Further studies on this topic are recommended, ideally at the national level, to find out the patterns; and, with these data, design intervention programs to avoid the inappropriate prescription of drugs in the elderly.

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