Inadequate knowledge of prescription drugs and their predictors in very old patients and their caregivers

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Abstract

Objective: Identify predictors of inadequate knowledge about the medication prescribed to very old outpatients and their caregivers. *Method:* The knowledge on the medication prescribed for 80 patients aged 80 years and over was assessed using a validated questionnaire to interview patients or their caregivers (when patients had communication difficulties, dementia, or any need for care to help them take the medication). Two hierarchical logistic regression models assessed the association between inadequate knowledge of the medication and sociodemographic and drug variables. *Results*: Thirty-nine (48.8%) respondents were caregivers. Inadequate knowledge was found in 81.5% (404/496) of medication prescribed. Route of Administration, Dose, Frequency, and Duration of Treatment were the aspects of greatest knowledge, whereas Adverse Effects, Precautions, Interactions, and Contraindications were the least known ones. In the first model, inadequate knowledge was associated to the level of education from complete elementary school to incomplete high school (Odds Ratio (OR): 0.12; p=0.018), from high school to incomplete higher education (OR: 0.12; p<0.001), complete higher education (OR: 0.13; p<0.001), agents acting on the renin-angiotensin system (RAS) (OR: 0.30; p=0.001), diuretics (OR: 0.31; p=0.013) and antithrombotic (OR: 12.59; p=0.027). In the second model, the predictors were caregivers (OR: 0.17; p<0.001), agents working in the RAS (OR: 0.33; p=0.002), diuretics (OR: 0.35; p=0.024) and antithrombotic (OR: 12.57;

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p=0.026). *Conclusion*: Most of the medication prescribed for very old people is not very well known. Also, advice on drug information should be more intensive to patients than to their caregivers, with a focus on safety information and targeted at antithrombotics.

INTRODUCTION

The stratum of very old people (i.e., 80 years and over)[1] has grown and will grow dramatically in Brazil[2] where 94.3% of very old people use at least one medication in the long term, and 19.5% use at least five[3].

There is evidence that the older the individual, the less they know about medications[4-6]. As an example, polymedicated Dutch patients in primary care aged 80 and over were 53% more likely to incorrectly remember the prescription for at least one medication prescribed compared to their younger peers (60-69 years)[6]. Also, knowledge about medication among old people is insufficient[4,6-9], which can lead to non-adherence to medication[7,10] and negative clinical implications such as inadequate anticoagulation control[5] and visits to the emergency service[11]. A cross-sectional study carried out with 348 patients aged 75 years illustrates this relation: while only 21% of them knew about the consequences of omitting a medication or dose prescribed, those who knew them were 1.8 times more likely to follow the pharmacotherapy prescribed, and 2.3 times more likely to follow the daily dose prescribed[7]. Also, patients well informed about the possible side effects of the medications being used can seek care to manage them before they become intractable and engage in preventive health behaviors[12].

Although knowledge of medication is important for their appropriate use, there is still no consensus on how to measure it, especially regarding the aspects investigated, and the method for classifying responses and calculating scores. For example, depending on the method, individuals are asked to name a range from one (e.g., indication[13]) to 11[14] aspects of knowledge on medication. Also, few studies have evaluated its predictors or exclusive knowledge of the medication used by old people. Age, gender, education, income, family arrangement, cognitive functionality, and the number of medications used are some of the independent predictors that have already been identified among old people[6,12,13].

To date, Brazilian studies investigating the knowledge on medication have applied questionnaires with no validity nor reliability evaluated. Also, they did not demonstrate the predictive factors for this outcome, which are necessary for the clinical practice for the early identification of patients at greater risk for insufficient knowledge, as well as for the adequate design of educational interventions capable of contributing in this context. Therefore, the present study aimed to assess the knowledge of the medication prescribed and to identify their predictors in very old outpatients and their caregivers.

METHOD

This cross-sectional study was carried out at the geriatric outpatient clinic of Hospital Universitário da Universidade de São Paulo in São Paulo (SP), Brazil, which provides geriatric care to individuals aged 80 years and over with at least one of the following conditions: dementia, Parkinson's disease, use of five or more medications, two or more falls in the previous year, functional decline, and use of walking aid. The patients treated at this outpatient clinic from March/2013 to February/2014 (N=251) were considered eligible. The geriatrician referred patients to a pharmaceutical appointment after their initial appointment, and the researcher responsible for the study (pharmacist) invited the patient to participate. Those who wanted to be interviewed and who took at least one medication were included. However, the caregivers were interviewed instead of the patients when they had communication difficulties (i.e., aphonia, dysarthria, or aphasia), dementia, or needed the care to help them use the medication. In this case, we made sure that the caregiver was responsible for managing the patient's medication. There were no exclusion criteria.

The decision not to interview the patient was made along with the geriatrician responsible for following them at the outpatient clinic and upon the medical diagnosis of aphasia and/or dementia, and/or the caregiver's report of being their current responsible for assisting the patient in taking the medication.

Information about the medication prescribed was collected from each patient's medical record based on the most recent prescription. The medications were identified according to the second level of the *Anatomical Therapeutic Chemical* (ATC)[15] code. The complexity of a patient's pharmacotherapy was measured by the Medication Regimen Complexity Index (MRCI) cross-culturally adapted to Brazilian Portuguese[16]. This tool is divided into sections A (dosage forms), B (dose frequency), and C (additional instructions such as the specific time of taking). Each section is scored based on the analysis of the patient's prescription, and the index is the sum of the scores of each section[16].

The sociodemographic data and that on the knowledge on medication were collected in a face-to-face interview with the patient or their caregiver conducted by the researcher responsible for the study (pharmacist). The monthly income was expressed in minimum wages (MW) of 678 Brazilian reais in 2013, and 724 Brazilian reais in 2014.

A Spanish questionnaire with 11 questions was used, and cross-culturally adapted to Brazilian Portuguese[17] to know about each of the medications listed in the most recent geriatrician prescription. Each question assesses one of the following aspects of interest regarding the use of medications: indication, dose, frequency, duration of treatment, Route of Administration, precautions, Adverse Effects, contraindications, effectiveness, interactions, and conservation[18]. The participants' answers were classified as correct (2 points), incomplete (1 point), unknown (0), or incorrect (-1 point)[14] according to their degree of agreement with the database *UpToDate* [19]. Two pharmacist clinicians rated the responses independently. If necessary, a third one was consulted. In the end, the knowledge on medication was numerically represented by the weighted average of the grades and grouped into four categories: none (0), insufficient (0.60 to 1.26), sufficient (1.27 to 1.60), and excellent (1.61 to 2.00)[14]. The questions have one of four possible weights: 1.20 (questions 2 to 5), 1.10 (questions 1 and 9), 0.85 (questions 6, 7, 8 and 10), or 0.60 (question 11)[14].

To facilitate the interpretation of the results, knowledge on medication was recategorized into a dichotomous variable: inadequate knowledge on medication (categories 'none' and 'insufficient' combined), and adequate (categories 'sufficient' and 'excellent' combined). Income, number of medications prescribed, and MRCI were categorized into tertiles.

Categorical and numerical variables were described as absolute and relative counts and medians with interquartile ranges, respectively. Bivariate and multivariate hierarchical logistic regression models were calculated to predict inadequate knowledge of medication (reference category: adequate knowledge of medication) from the knowledge information collected for all medications prescribed. The fixed effects were the following variables: age of the respondent, monthly income, education (without education to incomplete elementary school, complete elementary school to incomplete high school, complete high school to incomplete higher education, complete higher education), type of respondent (patient, caregiver), number of medications (<5, 5-6, ≥7), MRCI (<12.0, 12.0-18.9, ≥19.0), duration of medication use (first time, not the first time), prescription by generic name (no, yes), and the following ATCC (non-user, user): C09, B01, N06, A10, and C03. Only the five most prevalent second-level ATCCs were considered. The only random effect was to the intercept.

All variables with significance in the bivariate analysis entered the multivariate model in a single block. Pairs of variables were checked for associations using the chi-square and Kruskal-Wallis tests before carrying out the multivariate analyzes to avoid collinearity. Of the two variables, only that significantly associated with greater clinical and conceptual relevance was included in the multivariate analysis. A p-value <0.050 (two-tailed) was considered statistically significant.

The study was carried out following the ethical standards established in Resolution No. 466/2012 and Resolution No. 510/2016 of the Brazilian National Health Council. The research ethics committees of Hospital Universitário da Universidade de São Paulo (USP) (597.277-0) and Faculdade de Ciências Farmacêuticas da USP (346,199) approved the study. All participants signed a consent form.

RESULTS

Eighty individuals were included in the study, which represented 31.9% of the universe of eligible patients. Thirty-nine (48.8%) respondents were caregivers. The median age was 84.0 years for the group of patients, and 56.0 for the group of caregivers. According to gender, 31 (75.6%) of patients were females compared to 36 (92.3%) of caregivers. Regarding education, 25 (61.0%) of patients did not have incomplete primary education, in contrast to the five (12.8%) caregivers. In general, the number of medications prescribed was high, with 60 (75.0%) of patients using at least five medications (Table 1).

There were 496 medications prescribed identified by 39 different second-level ATCC. Most medications were already in use for some time (87.5%), and were prescribed by their generic name (74.2%). The five most prescribed ATCCs represented agents acting on the renin-angiotensin system (RAS) (C09; 10.9%), antithrombotic (B01; 9.1%), psychoanalytic (N06; 7.7%), antidiabetic (A10; 7.5%), and diuretics (C03; 6.3%) (Table 2).

The general knowledge was low, as adequate knowledge was observed only for 18.5% of the medications prescribed. Responses on the Route of Administration, Dose, Frequency, and Duration of Treatment were classified as correct in more than 80% of medications each. On the other hand, Adverse Effects, Precautions, Interactions, and Contraindications were correctly reported in less than 5% of medications each, being the least known information about medications (Table 2).

Table 1. Characteristics of patients (n=41) and caregivers (n=39) included in the study. São Paulo (SP), 2013-2014.

Variable	Total (N=80)	Patient (n=41)	Caregiver (n=39)
	Median (IQR)	Median (IQR)	Median (IQR)
Age	76.0 (56.3-84.0)	84.0 (83.0-87.0)	56.0 (49.0-60.0)
	Median (IQR)	Median (IQR)	Median (IQR)
Income (in MW)	2.5 (1.1-5.9)	2.2 (1.0-4.8)	2.9 (1.5-5.9)
Gender	N (%)	n (%)	n (%)
Male	13 (16.3)	10 (24.4)	3 (7.7)
Female	67 (83.8)	31 (75.6)	36 (92.3)
Education	N (%)	n (%)	n (%)
Incomplete elementary school	30 (37.5)	25 (61.0)	5 (12.8)
Elementary to incomplete high school	7 (8.8)	2 (4.9)	5 (12.8)
High school to incomplete higher education	23 (28.8)	5 (12.2)	18 (46.2)
Higher education	20 (25.0)	9 (22.0)	11 (28.2)
Medications prescribed	N (%)	n (%)	n (%)
<5	20 (25.0)	11 (26.8)	9 (23.1)
5-6	26 (32.5)	15 (36.6)	11 (28.2)
≥7	34 (42.5)	15 (36.6)	19 (48.7)
Medication Regimen Complexity Index	N (%)	n (%)	n (%)
<12.0	23 (28.8)	12 (29.3)	11 (28.2)
12.0-18.9	30 (37.5)	17 (41.5)	13 (33.3)
≥19.0	27 (33.8)	12 (29.3)	15 (38.5)

IQR: interquartile range; MW: minimum wage.

Table 2. Characteristics and knowledge of the medications prescribed according to the type of respondent. São Paulo (SP), 2013-2014.

Variable	Total (N=496) N (%)	Patient (n=261) n (%)	Caregiver (n=235) n (%)
Duration of medication use			
First time	62 (12.5)	23 (8.8)	39 (16.6)
Not the first time	434 (87.5)	238 (91.2)	196 (83.4)
Prescription by generic name			
No	128 (25.8)	71 (27.2)	57 (24.3)
Yes	368 (74.2)	190 (72.8)	178 (75.7)
ATCC C09 (agents acting at RAS)			
Non-user	442 (89.1)	233 (89.3)	209 (88.9)
User	54 (10.9)	28 (10.7)	26 (11.1)
ATCC B01 (antithrombotic)			
Non-user	451 (90.9)	237 (90.8)	214 (91.1)
User	45 (9.1)	24 (9.2)	21 (8.9)
ATCC N06 (psychoanalytic)			
Non user	458 (92.3)	252 (96.6)	206 (87.7)
User	38 (7.7)	9 (3.4)	29 (12.3)
ATCC A10 (antidiabetics)			
Non user	459 (92.5)	238 (91.2)	221 (94.0)
User	37 (7.5)	23 (8.8)	14 (6.0)
ATCC C03 (diuretics)			
Non-user	465 (93.8)	244 (93.5)	221 (94.0)
User	31 (6.3)	17 (6.5)	14 (6.0)
Knowledge of medications			
None	284 (57.3)	178 (68.2)	106 (45.1)
Insufficient	120 (24.2)	63 (24.1)	57 (24.3)
Sufficient	89 (17.9)	20 (7.7)	69 (29.4)
Excellent	3 (0.6)	0	3 (1.3)
Questions about the knowledge of medications classified as correct			
Route of Administration	424 (85.5)	211 (80.8)	213 (90.6)
Dose	417 (84.1)	200 (76.6)	217 (92.3)
Frequency	415 (83.7)	200 (76.6)	215 (91.5)
Duration of Treatment	402 (81.0)	191 (73.2)	211 (89.8)
Indication	242 (48.8)	102 (39.1)	140 (59.6)
Effectiveness	191 (38.5)	72 (27.6)	119 (50.6)
Storage	56 (11.3)	1 (0.4)	55 (23.4)
Adverse Effects	23 (4.6)	3 (1.1)	20 (8.5)
Precautions	10 (2.0)	2 (0.8)	8 (3.4)
Interactions	5 (1.0)	1 (0.4)	4 (1.7)
Contraindications	3 (0.6)	1 (0.4)	2 (0.9)

RAS: renin-angiotensin system.

The regression models were made considering all the medications prescribed (N=496). Significant associations were observed in the bivariate models only for age, education, type of respondent, ATCC C09, ATCC B01, and ATCC C03. As age was associated with education (p<0.001) and the type of respondent (p<0.001), it was not included in the multivariate regression analyzes. Also, as education was associated with the type of respondent (p<0.001), two multivariate models were calculated - one including the aforementioned ATCCs and education as independent variables, and the other including the same ATCCs and the type of respondent (Table 3).

Table 3 shows the two multivariate models predicting inadequate knowledge of medications at the medication level. In both models, the odds ratio (OR) of having inadequate knowledge on medications decreased significantly for elementary to incomplete high school, high school to incomplete higher education, complete higher education, caregivers, RAS agents, and diuretics. On the other hand, the OR of having inadequate knowledge of medications increased significantly for antithrombotics in both models.

Table 3. Bi and multivariate hierarchical logistic regression models predicting inadequate knowledge of medication (N=496). São Paulo (SP), 2013-2014.

Predictor	Inadequate knowledge of medications					
	OR * (95% CI)	p	OR** (95% CI)	p	OR*** (95% CI)	p
Gender						
Female	1					
Male	0.79 (0.24-2.59)	0.702				
Age of the respondent	1.05 (1.03-1.08)	<0.001				
Monthly income	1.00 (0.94-1.07)	0.972				
Education						
Incomplete elementary school	1		1			
Elementary to incomplete high school	0.16 (0.03-0.86)	0.033	0.12 (0.02-0.69)	0.018		
High school to incomplete higher education	0.14 (0.05-0.40)	<0.001	0.12 (0.04-0.35)	<0.001		
Higher education	0.16 (0.05-0.46)	0.001	0.13 (0.04-0.39)	<0.001		
Respondent						
Patient	1				1	
Caregiver	0.18 (0.08-0.42)	<0.001			0.17 (0.07-0.40)	<0.001
Number of medications						
<5	1					
5-6	1.82 (0.61-5.41)	0.279				
≥7	1.87 (0.66-5.28)	0.235				
Medication Regimen Complexity Index						
<12,0	1					
12,0-18,9	1.30 (0.46-3.66)	0.619				
≥19,0	1.52 (0.54-4.32)	0.431				
Duration of medication use						
First time	1					
Not the first time	0.71 (0.33-1.52)	0.374				

to be continued

Continuation of Table 3

Predictor	Inadequate knowledge of medications					
	OR * (95% CI)	*p*	OR** (95% CI)	*p*	OR*** (95% CI)	*p*
Prescription by generic name						
No	1					
Yes	0.74 (0.43-1.27)	0.275				
ATCC C09 (agents acting at RAS)						
Non-user	1		1		1	
User	0.33 (0.19-0.59)	<0.001	0.30 (0.15-0.61)	0.001	0.33 (0.17-0.66)	0.002
ATCC B01 (antithrombotic)						
Non-user	1		1		1	
User	15.00 (1.71-131.24)	0.015	12.59 (1.34-118.00)	0.027	12.57 (1.35-117.04)	0.026
ATCC C03 (diuretics)						
Non-user	1		1		1	
User	0.39 (0.18-0.88)	0.024	0.31 (0.12-0.78)	0.013	0.35 (0.14-0.87)	0.024
ATCC N06 (psychoanalytic)						
Non-user	1					
User	1.20 (0.63-2.29)	0.574				
ATCC A10 (antidiabetics)						
Non-user	1					
User	0.52 (0.23-1.17)	0.111				

CI: confidence interval; OR: odds ratio; RAS: renin-angiotensin system; *Not adjusted; **Adjusted: multivariate model including *education* and *codes C09, B01, and C03*; ***Adjusted: multivariate model including *respondent* and *codes C09, B01, and C03*.

DISCUSSION

The Brazilian Portuguese questionnaire applied in the present study was used in Spain[14,20] and Portugal[21] to assess the knowledge of patients over 18 years who attend community pharmacies to obtain one or more medications dispensed. *None* was the most prevalent category identified in 65.7%[14], 68.2%[20], and 82.5%[21] of patients, which matches our results. This shows the general deficiency in the knowledge of pharmacological treatment found in many other studies carried out with adults and/or old people, community residents, or outpatients from different countries and using different methods[4-9,22-24].

We found that information on the use and action of medications was the most widely known aspect of pharmacotherapy, whereas information on medication safety was the least known. These findings are consistent with the results of studies carried out in other countries, both with individuals over 18 years[14,21,24] and old individuals[5,7-9,12]. A probable explanation would be that health professionals tend to discuss with patients more about the use than the possible problems associated with medication (e.g., side effects) because they consider only the former as their professional responsibility[25]. As an example, in a sample of 412 old patients from two public outpatient clinics in Hong Kong, 72.2% were instructed about administration, 73.0% were not informed about the side effects of the medication prescribed during the appointment, prescription, or discharge[12].

It is believed that the group of caregivers had greater knowledge on medications, not only because they were younger and more educated, but also because of their experience in dealing with the difficulties in administering the medicines. They must know enough about the prescription to adapt the times of medication intake to the care routine and manage dose adjustments[26]. Besides, they feel responsible for monitoring side and toxic effects since

their patients may no longer be able to recognize and report them[26].

Education was negatively associated with inadequate knowledge of medication. This association was found in other old populations[8,12]. Although intuitive, this association is complex, and there may be stronger predictors of knowledge on medication than formal education. For example, two studies carried out with old patients living in the community did not show education as a significant and independent predictor of their knowledge on medication[6,13].

It is believed that the chances of having inadequate knowledge were lower for the agents acting in the RAS and for diuretics because patients generally seek and know the main information about them. A qualitative study carried out with hypertensive patients showed that although they did not know the name of the antihypertensive medication they used, they were aware it helped control blood pressure. Also, they often sought to learn more about antihypertensive medications through the mainstream media and the education of health professionals[23].

Antithrombotics were positively associated with inadequate knowledge, showing that our sample had less knowledge about these medications. Likewise, among 122 patients seen at an anticoagulation clinic in Hong Kong, half did not remember the effect of warfarin on the body, and about 70% were unaware of the possible complications resulting from the overdose of this medication[5]. The lack of safety information about antithrombotic agents can lead to serious consequences. For example, users of apixaban with little knowledge of possible drug interactions affecting the risk of bleeding were 85% more likely to regularly use over-the-counter medications with potentially serious interactions with apixaban (e.g., acetylsalicylic acid and St. John's wort - hypericum perforatum) compared to those with more knowledge[22].

Considering that old people may be exposed to clinical complications of pharmacotherapy due to their inadequate knowledge of medication, a joint effort including the multi-professional health team, government agents, and the pharmaceutical industry is necessary to create patient-centered educational programs. A study of 150 patients with chronic conditions showed that knowledge of medication was positively associated with patient satisfaction in having their doubts cleared by physicians[10]. In this sense, health professionals should regularly discuss with patients aspects of concern about the use of medicines (i.e., the process of use, the therapeutic objective, safety, and storage), and meet their needs by providing sufficient verbal and written information to ensure the proper use of medication.

One of the strengths of the present study was the use of a validated and reliable questionnaire. Still, it was the first time this tool was used to assess the knowledge of medication used exclusively by old people. The inclusion of caregivers was another positive point because as the old people living in the community get older, their need for a caregiver increases. Assessing the knowledge of caregivers rather than the patients is a reasonable comparison to the real world, as they may be responsible for administering medication to patients. Also, the literature about the knowledge on medication of caregivers of old people is scarce. Most studies are carried out with pediatric patients, and they assess the knowledge of the patient's clinical condition. Finally, the use of a hierarchical regression model enabled the characteristics of all medications prescribed to be evaluated as independent variables.

Some limitations of the present study must be mentioned. First, the sampling procedure excluded patients unwilling to participate (e.g., patients with gait disorders and caregivers late for work), which could have added some selection bias. Secondly, the inclusion of medications used for the first time may have underestimated the knowledge. Thirdly, no common predictors of inadequate knowledge on medication such as the number of medications were found, probably due to our limited sample size. Fourth, as caregivers were more educated than patients, it is questionable whether inadequate knowledge was associated with education or the caregiver's own condition. Nevertheless, the heterogeneity of the sample comprised of both patients and caregivers may have been a confounding factor, although one of the multivariate models included the respondent as an independent variable. Fifth, only one researcher

was responsible for applying the questionnaire, which did not have a previous calibration study and allowed for information bias. However, this is the same researcher responsible for the cross-cultural adaptation of the questionnaire to Brazilian Portuguese[17], thus they deeply knew its method of application and score. Sixth, despite the absence of a previous sample size calculation, the authors used a convenience sample representing 31.9% of eligible individuals. Future studies should be carried out with larger and more homogeneous samples to evaluate the strategies to improve knowledge of medication with controlled studies.

CONCLUSION

The vast majority of drugs prescribed for very old outpatients were little known. Adverse Effects, Precautions, Interactions, and Contraindications were aspects of less knowledge of medication. Education, the type of respondent, medications acting in the RAS, and diuretics were negatively associated with inadequate knowledge on medication; antithrombotic agents were positively associated with it.

Geriatricians, gerontologists, and other professionals who care for very old people should unquestionably advise them about the information on medications, especially those who take antithrombotic agents (e.g., warfarin, enoxaparin, platelet aggregation inhibitors, factor Xa inhibitors) and who do not depend on caregivers to help them take their medication. Also, education should focus on improving patient and caregiver knowledge on safety aspects of medication use such as side effects, precautions and warnings, interactions, and contraindications. Clinical care services should be organized to provide reliable written and verbal information on medication to patients.

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