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DO HEALTHCARE PROFESSIONALS EDUCATE PATIENTS ON DRUG-FOOD INTERACTIONS?

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ABSTRACT: *Introduction:* Food-drug can have a significant influence on the therapeutic success of the drug and on the adverse effect profiles of many drugs being administered. This study assessed the prevalence of potential drug-food interactions and orientation of health professionals on the proper use of medicines.
Methods: Cross-sectional study which included 517 patients aged 18 years or over between May-August 2012. The analysis of the information included estimates of central tendency, variability and proportions. Multivariable analysis was performed by the Statistical Learning Theory Exhaustive CHAID algorithm was used to define of cut-offs for the complexity of pharmacotherapy and prioritize patients more likely to take their medications incorrectly with regard to food.
Results: 1786 drugs were used by patients. Captopril and omeprazole were the most incorrectly used. Total of 66.0% of patients reported that they had not received any information on their pharmacotherapy and 95.2% stated that they had doubts or difficulties that could have been resolved by the pharmacist. An absence of additional information to those strictly necessary for compliance with the regimen of drugs prevailed (89.7%). The most common inaccuracy was taking a drug with food that should be taken on an empty stomach to improve absorption of the drug (57.7%).
Conclusion: Professionals, in general, do not seem to warn their patients to take their medications on a full or empty stomach, at least in writing medications. Health professional awareness of the drug administration process can reduce medication errors and may contribute to the optimization of pharmacotherapy.

KEYWORDS: Food-drug interactions, medication errors, complexity of pharmacotherapy, patient education, pharmacoepidemiology.

INTRODUCTION

Interactions between drugs and food occur when a food or nutrient changes the effectiveness of a drug, or when it interferes with the individual's nutritional status [1,2]. These interactions are gaining recognition in the healthcare system, given that the total bioavailability, pharmacokinetics, pharmacodynamics and therapeutic efficacy of drugs may be altered due to concomitant intake (or not) with food [3]. The mechanisms related to the effects of food on drug absorption include, among others decreased, increased or retarded absorption [4,5]. Considering the clinical effects, the reduction of bioavailability may occur, which predisposes to a therapeutic failure, or there may be an increase leading to risks of adverse effects and toxicity [6–8].

The drugs possess guidelines on food in order to maximize the effect or to reduce toxicity in the gastrointestinal tract [1,8]. Many patients are unaware of or do not understand these instructions and take their medicines incorrectly, which predisposes to a medication error [9]. The drug-food interactions comprise one of the medication errors, which fall within the administration time errors. These errors occur during the prescribing, dispensing, administration and monitoring of medication use process and its principal cause is an inadequate knowledge of clinical pharmacology [10–12]. In a study involving 2,874 opportunities for errors, 10 errors were due to time of administration and were related to drugs that interact with food or other drugs [11].

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As the number of medications, the dose and the duration of the therapeutic regimen increases, so does the regimen complexity, which culminates with an increased risk of interactions [2,9], however, most of them can be easily recognized [2,13]. The pharmacist could help to minimize medication errors associated with drug-food interactions as they hold the necessary knowledge and are accessible to the population in the health system. However, re-engineering of the professional practice with a focus on direct patient needs is required. This is because nowaday their major responsibility is give them "access" to drugs and does not contribute to the solution of post-access problems, such as drug-food interactions and their consequences[14].

There is a shortage of epidemiological studies involving drug-food interactions and their consequences, probably due to difficulties in obtaining adequate samples, lack of infrastructure for the study and especially lack of research interest due to the non-recognition of the problem and its clinical significance [15]. This study analyses the prevalence of drug-food interactions and their possible implications, as well as the existence of information in medical prescriptions for the prevention and clinical performance of the pharmacist for patients seen in primary healthcare.

METHODS

A cross-sectional study on patterns of drug use related to healthcare and drug-food interactions in a city, with approximately 200,000 inhabitants. It is an industrial and health reference for 55 municipalities in the Midwest region of the state of Minas Gerais, Brazil. It is part of a larger study that examined pharmacotherapy in primary health care. In the original study, the random sample was estimated considering the accuracy of 4.0%, statistical significance 5.0% and the outcome occurrence of non-adherence to therapy in 36.8% of the population totalling 427 individuals. For possible losses and stratifications, 20.0% was added resulting in a total of 517 people. For the patient selection, this sample was proportional to number of dispensations amount in one of five public pharmacies. The patients were selected by a random draw [16].

The inclusion criteria were inhabitants of the area covered by the municipality aged 18 years or over, with prescription at least one drug during the collection period. The exclusion criteria at the time of collection were the use of any medication whose prescription was not available or withdrawal of medication by a third party.

Data collection was conducted by trained Pharmacy scholars under the supervision of a Pharmacist between May and August 2012 in five primary health care pharmacies considering the pharmacy hours of operation and on weekdays at different times. It was requested to patient show their prescription (all of which were conducted by hand) followed by a questionnaire that was administered by an interviewer who subsequently instructed the patient on how to use the drugs [16]. For the analysis of the (in) correct use of medication related to the feed, we considered only oral medication that has been used for patients.

The dependent variable "patient with (in) appropriate drug use" was analysed by considering referential TRUVEN [17] in relation to time of feeding and administration of medications reported by the patient. This variable was stratified into "all in correct use", "a least one incorrectly use", and "all incorrectly use".

The independent variables used were: socio-demographic data (gender, age, educational level, marital status, people in the household); clinical conditions with self-reported medical diagnosis (number of diseases, cardiovascular diseases and endocrine metabolic diseases) according to International Classification of Diseases, version 10 (ICD-10) [18]; indicators of access/utilization of healthcare services (private health insurance, medical appointments, additional information on requirements, pharmaceutical appointments, drugs, access, information on the drug received at the pharmacy, and doubt or difficulty to be resolved by the pharmacist); characteristics of pharmacotherapy [Potential Clinical Impact of Drug-therapy Problems (PDTP), complexity of pharmacotherapy and adherence]; and existence of written technical recommendations in the medical prescription.

The complexity of pharmacotherapy was defined by the Medication Regimen Complexity Index (MRCI) [19] and validated in Brazil [20]. The MRCI is an instrument used to measure a treatment regimen complexity for an individual patient, and it is divided into 3 sections: A (dosage forms), B (dosing frequency), and C (additional information, such as take at specific times and relation to food) [16]. The complexity index is the sum of the points (scores) for the 3 sections [19].

Adherence was assessed by the question "How often can you follow the instructions for dosage of this medicine?". Self-reported adherence was stratified on the Likert scale (1 – every time, 2 – most times, 3 – sometimes, 4 – hardly any time, 5 – never). For the complete treatment regimen, it was considered as non-adherence if the patient did not adhere to at least one drug.

The analysis of the information included estimates of central tendency, variability and proportions. Multivariable analysis was performed by the Statistical Learning Theory Exhaustive CHAID (chi-squared automatic interaction detector) algorithm

with Pearson's chi-square test and and Bonferroni adjustments. This analysis was used to define of cut-offs for the complexity of pharmacotherapy and prioritize those patients who may be at higher risk of clinically relevant food-drug interactions in order to optimize of health care services. Analysis criteria included ranking of variables in the model: statistical significance of 5.0%, a total of 50 cases in the parent node and 30 cases in the child node, and up to three hierarchical levels, as well as cross-validation by 10 sub folds. For constructing the database and for analyses, the SPSS program was used.

This study was conducted in accordance with ethical standards, and it was approved by the Ethics Committee on Human Research of the Hospital São João de Deus under the number, 154/2011.

RESULTS

The majority of 517 patients were female (73.5%), with up to four years of study (62.8%) and living with a partner (54.9%). The median age was 58.8 years (P_{25}= 50.5; P_{75}= 66.3). Considering the profile of clinical conditions with medical diagnosis, the median was 2.0 diseases (P_{25}= 2.0; P_{75}= 3.0), however a total of 265 had up to three cardiovascular diseases and 371 patients had one or more endocrine metabolic diseases. In relation to access and use of healthcare services, 34.0% of patients had private health plans, had a median of 3.0 medications prescribed (P_{25}= 2.0; P_{75}= 5.0), most of them had all drugs by public health system (89.0%).

Whereas clinical follow-up, the patient had a median of 3.0 annual medical appointments (P_{25}= 2.0; P_{75}= 5.0) and a median of zero appointments by the pharmacist in a year. A total of 66.0% of patients reported that they had not received any information on their pharmacotherapy. Despite the low provision of medication therapy management services, 95.2% stated that they had doubts or difficulties that could have been resolved by the pharmacist regarding the use of medications. Considering safety indicators and effectiveness of pharmacotherapy, 53.0% of respondents had some PDTP. The complexity of pharmacotherapy was 8.5 (P_{25}= 5.0; P_{75}= 13.5) and self-reported adherence to pharmacotherapy was 74.5% (Table 1).

Patients with all medications in correct use, with at least one drug incorrectly used and all drugs incorrectly used were compared by bivariate analysis, and age, number of diseases, endocrine metabolic diseases, number of drugs, PDTP, complexity of pharmacotherapy and adherence ($p<0.01$) and gender ($p= 0.04$) were statistically significant.

Table 2 shows the profile of drug use in relation to food and the characteristics of pharmacotherapy. Of the 1,786 drugs used by patients, most were oral solid (95.1%). Simvastatin and hydrochlorothiazide were the drugs most appropriately taken by patients. In contrast, captopril and omeprazole were the most inadequately administered, both must be used on an empty stomach.

An absence of additional information to those strictly necessary for compliance with the regimen of drugs prevailed (89.7%). The most common technical recommendation of drug administration was to take with or without food (42.6%). Despite information provided by health professional is insufficient, only few drugs were in incorrect use regarding food (16.7%).

Table 1. Factors associated with correct use of drugs in relation to food. Minas Gerais - Brazil, 2012

Characteristics	All patients (n= 517)	Patients and their drugs			p value[a]
		Correct use (n=310)	At least one in incorrect use (n=196)	Incorrect use (n=11)	
Socio-demographic characteristics					
Gender Female % (n)	73.5 (380)	77.1 (239)	67.3 (132)	81.8 (9)	= 0.04*
Age P_{50} (P_{25}; P_{75})	58.8 (50.5; 66.3)	55.8 (47.8; 65.0)	61.9 (54.5; 67.9)	53.4 (44.3; 60.4)	<0.01*
Years of Schooling % (n)					>0.05
Non-literacy	7.5 (39)	7.7 (24)	7.1 (14)	9.1 (1)	
1 a 4	55.3 (286)	53.6 (166)	57.7 (113)	63.6 (7)	
5 a 11	33.1 (171)	34.5 (107)	31.1 (61)	27.3 (3)	
>11	4.1 (21)	4.2 (13)	4.1 (8)	-	
Lives with a partner % (n)	54.9 (284)	56.4 (175)	52.6 (103)	54.5 (6)	>0.05
Number of inhabitants per household P_{50} (P_{25}; P_{75})	3.0 (2.0; 4.0)	3.0 (2.0; 4.0)	3.0 (2.0; 4.0)	2.0 (2.0; 5.0)	>0.05
Clinical conditions					
Diseases P_{50} (P_{25}; P_{75})	2.0 (2.0; 3.0)	2.0 (1.0; 3.0)	3.0 (2.0; 4.0)	1.0 (1.0; 3.0)	<0.01*
Cardiovascular diseases % (n)	***(n= 265)***	***(n= 137)***	***(n=124)***	***(n=4)***	>0.05
1	94.3 (250)	94.9 (130)	93.6 (116)	100.0 (4)	
2	5.3 (14)	5.1 (7)	5.6 (7)	-	
3	0.4 (1)	-	0.8 (1)	-	
Endocrine/ metabolic diseases % (n)	***(n= 371)***	***(n= 202)***	***(n= 163)***	***(n= 6)***	<0.01*
1	55.8 (207)	61.9 (125)	46,6 (76)	100.0 (6)	
2	38.5 (143)	33.2 (67)	46,6 (76)	-	
3	5.7(21)	4,9 (10)	6.8 (11)	-	
Access and use of health care services					
Private Health care assistance % (n)	34.0 (176)	34.8 (108)	32.2 (65)	27.3 (3)	>0.05
Acquisition of drugs by public health					
All drugs	89.0 (460)	90.0 (279)	86.7 (170)	100.0 (11)	>0.05
At least one drug	10.6 (55)	9.4 (29)	13.3 (26)	0.0(0)	
None drug	0.4 (2)	0.6 (2)	0.0 (0)	0.0 (0)	
Drugs P_{50} (P_{25}; P_{75})	3.0 (2.0; 5.0)	2.0 (2.0; 4.0)	4.0 (3.0; 6.0)	1.0 (1.0; 2.0)	<0.01*
Medical appointments P_{50} (P_{25}; P_{75})	3.0 (2.0; 5.0)	3.0 (2.0; 5.0)	3.0 (2.0; 6.0)	2.0 (2.0-5.0)	>0.05
Pharmaceutical appointments P_{50} (P_{25}; P_{75})	0.0 (0.0; 0.0)	-	-	-	>0.05
Had doubt or difficulty to be resolved by the pharmacist % (n)	95.2 (492)	92.2 (286)	99.5 (195)	100.0 (11)	>0.05
Received any information about drug in the pharmacy % (n)					
No	66.0 (341)	66.8 (207)	63.3 (124)	90.9 (10)	>0.05
Most often	28.4 (147)	28.0 (87)	30.6 (60)	0.0 (0)	
Hardly ever	5.6 (29)	5.2 (16)	6.1 (12)	9.1 (1)	
Characteristics of pharmacotherapy					
PDTP[b] (yes)	53.0 (274)	41.6 (129)	71.9 (141)	36.4 (4)	<0.01*
Complexity of pharmacotherapy P_{50} (P_{25}; P_{75})	8.5 (5.0; 13.5)	7.0 (4.0; 11.0)	12.5 (8.0; 17.0)	4.5 (2.0;6.0)	<0.01*
Adherence % (n)	74.5 (385)	72.3 (224)	78.6 (154)	63.6 (7)	<0.01*

[a] *Pearson's chi-square with Bonferroni adjustment.*

[b] *Potential Clinical Impact of Drug-therapy Problems*

** = Statistically significant difference.*

Table 2. Characteristics of pharmacotherapy and its suitability in the presence of food. Minas Gerais. Brazil. 2012

Characteristics	All (n= 1786)	Drugs			
		Correct use (n= 1323)	Incorrect use (n= 298)	Treatment initiation (n= 100)	Another route of administration (n= 65)
Characteristics of pharmacotherapy % (n)					
Pharmaceutical form and route of administration (n= 1786)					
Solid oral: capsules and tablets	95.1 (1698)	99.0 (1310)	99.3 (296)	9.2 (92)	-
Other oral forms[a]	1.2 (22)	1.0 (13)	0.7 (2)	0.7 (7)	-
Injectable: vials and ampoule	1.5 (26)	-	-	0.1 (1)	38.4 (25)
Cream and ointment	0.4 (7)	-	-	-	10.8 (7)
Drops and nasal spray	0.7 (13)	-	-	-	20.0 (13)
Aerosol	0.4 (7)	-	-	-	10.8 (7)
Transdermal patch	0.7 (13)	-	-	-	20.0 (13)
More prescribed drugs	**% (n)**	**% (n; position)**	**% (n; position)**	**% (n; position)**	**% (n; position)**
Sinvastatin	9.9 (177)	12.7 (168; 2)	-	9.0 (9; 1)	-
Hydrochlorothiazide	9.7 (173)	12.8 (170; 1)	-	3.0 (3; 5)	-
Losartan	8.0 (143)	10.7 (141; 3)	-	2.0 (2; 6)	-
Omeprazole	5.3 (95)	3.4 (45; 8)	15.1 (45; 2)	5.0 (5; 3)	-
Captopril	5.3 (94)	1.5 (20; 14)	24.8 (74;1)	-	-
Metformin	5.3 (94)	6.0 (80; 5)	2.7 (8; 8)	6.0 (6; 2)	-
Levothyroxine	4.9 (87)	5.5 (73; 6)	4.7 (14; 4)	-	-
AAS	4.7 (84)	6.2 (82; 4)	0.7 (2; 14)	-	-
Propranolol	2.6 (47)	3.5 (46; 7)	-	1.0 (1; 7)	-
Atenolol	2.2 (40)	3.0 (40; 9)	-	-	-
Other	42.1 (752)	34.6 (458)	52.0 (155)	74.0 (74)	100.0 (65)

[a] *Gums, lozenges, solution, suspension, sublingual spray/tablet, gargles, mouthwash.*

Table 3. Characteristics of using drugs related to food. Minas Gerais. Brazil. 2012

Characteristics	All (n= 1786)	Drugs			
		Correct use (n= 1323)	Incorrect use (n= 298)	Treatment initiation (n= 100)	Another route (n= 65)
Profile of adequacy of use of drugs % (n)					
Additional information in prescriptions					
No	89.7 (1603)	89.0 (1177)	93.0 (277)	88.0 (88)	93.8 (61)
Yes	10.3 (183)	11.0 (146)	7.0 (21)	12.0 (12)	6.2 (4)
Relationship with food	61.2 (112)	60.9 (89)	66.7 (14)	75.0 (9)	0.0 (0)
Take on an empty stomach	21.9 (40)	23.3 (34)	23.8 (5)	8.3 (1)	0.0 (0)
Specific care with drug	15.3 (28)	13.7 (20)	9.5 (2)	16.7 (2)	100.0 (4)
Do not lie down after you take the drug	1.6 (3)	2.1 (3)	0.0 (0)	0.0 (0)	0.0 (0)
Technical recommendation of administration in relation to food					
Ingest your drug with food or without food	42.6 (760)	57.5 (760)	-	-	-
Ingest the drug with food	28.9 (516)	29.8 (395)	40.6 (121)	-	-
Ingest the drug without food	19.3 (345)	12.7 (168)	59.4 (177)	-	-
Start of treatment or other route	9.2 (165)	-	-	100.0(100)	100.0 (65)
Appropriateness of use of drugs in relation to food					
Correct	83.3 (1488)				
Incorrect (n= 298)	16.7 (298)				
Empty stomach to maximize effect and uses full stomach	57.7 (172)	-	57.7 (172)	-	-
Full stomach to reduce irritation and uses an empty stomach	30.9 (92)	-	30.9 (92)	-	-
Full stomach for absorption and uses an empty stomach	10.7 (32)	-	10.7 (32)	-	-
Incorrect gastric contents	0.7 (2)	-	0.7 (2)	-	-
Potential Clinical Significance (n= 298)					
Ineffectiveness of pharmacotherapy	67.4(201)		67.4(201)		
Insecurity of pharmacotherapy	32.6 (97)	-	32.6 (97)	-	-

The most common inaccuracy was to take a drug with food that should have been taken on an empty stomach to improve absorption of the drug (57.7%) (Table 3). The most common potential consequence of the incorrect use of drugs was risk of

ineffectiveness of pharmacotherapy (67.4%). The drugs used most incorrectly were captopril (24.8%) and omeprazole (15.1%). Hydrochlorothiazide was the drug that most correctly used (12.8%), followed by simvastatin(12.7%) and losartan (10.7%) (Table 2).

The hierarchization of independent variables for "Patient in (in) appropriate drug use" maintained in the final model the complexity of pharmacotherapy and health conditions number ($p<0.01$). The greater the complexity of pharmacotherapy, the lower was the proportion of drug used correctly. The analysis proposed cut-off points for the scores of MCRI, and for most strata, complexity was enough to explain the whole distinction of drug administration. Most patients with MCRI≤ 4.0 (87.5%) used all their medication correctly in relation to the mode of use, and this relation was demonstrated in third level was MCRI≤ 2.0 (93.8%). In contrast, the majority of patients (86.0%) with scores MCRI>18.0 used at least one drug incorrectly in relation to feeding. Health condition number was important for explain drug use in higher than 4.0 through 12.0 MCRI index in direct way (~20.0% reduction) (Figure1).

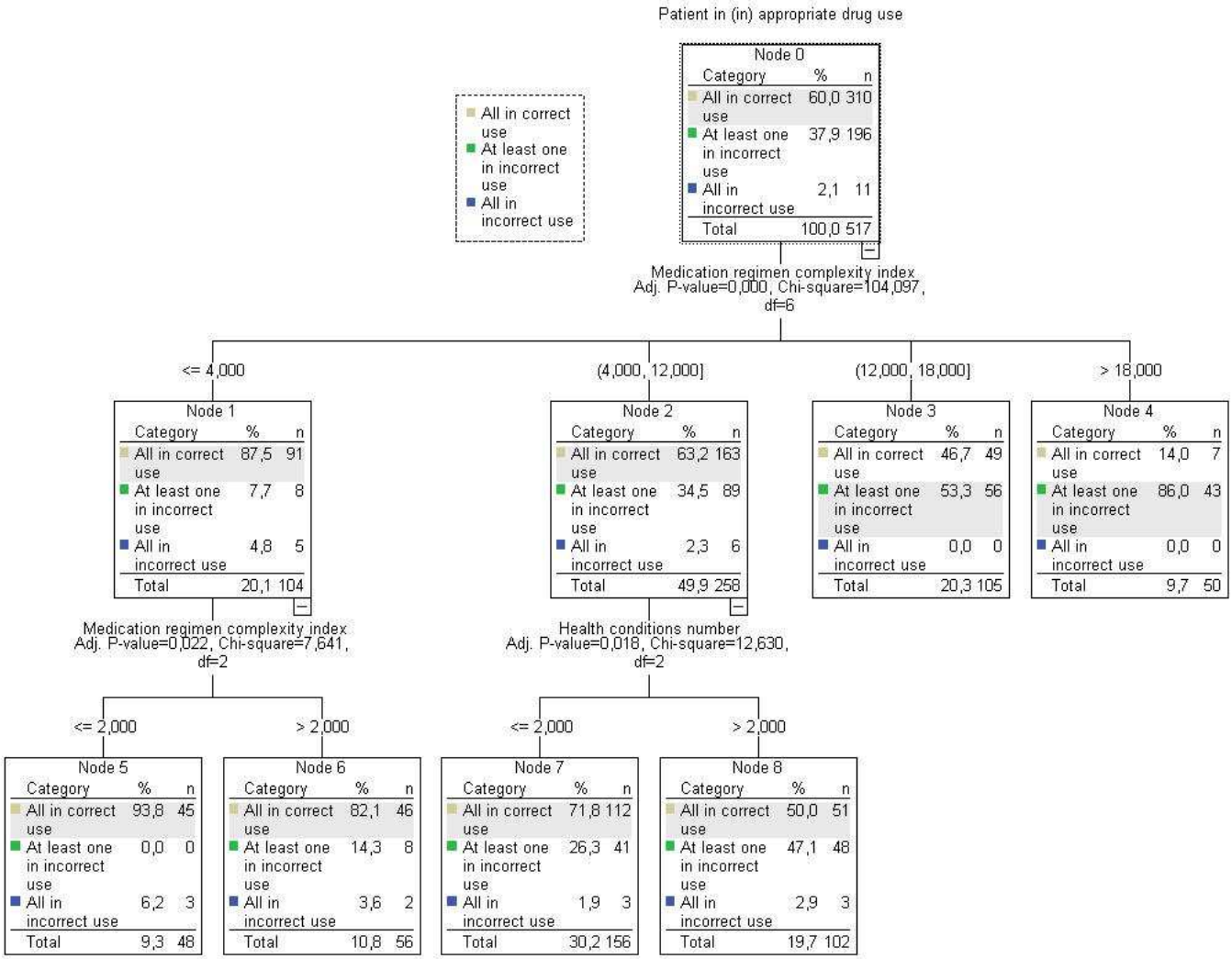

Figure 1. Multivariate analysis by the theory of statistical learning of the factors associated with the use (in) appropriate of drugs with regard to food

DISCUSSION

In this study, the prevailing patient was female, adult/elderly, with low education, living with a partner and had chronic diseases, especially cardiovascular and endocrine metabolic diseases. Pharmacotherapy showed a considerable proportion of inappropriate use of drugs that was strongly associated with the increase in complexity of pharmacotherapy, followed by health conditions number. In the bivariate analysis, age, number of medications, PDTP and adherence to pharmacotherapy were also statistically significant. As for healthcare, use of the public system to access services and drug predominated, yet an absence of explicit guidance on prescription and low access to clinical pharmacist services prevailed.

Once the patient's recruitment in pharmacies was performed on office hours, the high number of women is justified, since the working hours of healthcare centers, mainly with regard the primary care, do not meet the male demand. It happens due to the incompatibility male population availability embedded in the labor market. In turn, the elderly people who do not develop labor activities visit the healthcare centers more frequently [21]. The low schooling is comparable to other studies [22–25] as well as the marital status of the existence of spouse [22, 23]. This shows the likely external validity of the findings despite the limitations of cross-sectional studies, such as the impossibility of causal inference and the possibility of memory bias.

The median number of drugs used by respondents was similar to that found by other authors [26]. In other studies, it was higher, yet most studies occurred in different scenarios, such as hospitals [25, 27, 28]. Drugs that act on the cardiovascular system and digestive tract were the most prescribed which is consistent with the reported nosological profile of the prevalence of cardiovascular and endocrine metabolic diseases, as well as with the findings of other authors [23, 29-32]. Some authors, similar to this study, found hydrochlorothiazide as one of the most prescribed drugs [23, 28, 33].

In Brazil, there is the public funding policy and guarantee of universal access to healthcare technologies [34]. In this study, there was a great use of public services in a manner similar to other Brazilian studies [23, 24, 35, 36], notably in regard to access to drugs [23]. However, these findings are different those of other countries in which predominates access by private health insurance [28, 37]. The WHO's Global Action Plan for the Prevention and Control of Noncommunicable Diseases (NCDS) aims to ensure 80.0% availability of the affordable basic technologies and essential medicines required to treat major noncommunicable diseases in both public and private facilities [38].

Considering the access to health professionals, the number of medical appointments per year was possibly appropriate, given the prevalence of chronic conditions that can be followed up by biannual consultations for controlled patients [23]. That the professional should evaluate potential interactions of clinical importance [39] before prescribing is essential for preventing health problems. Despite this, it seems that advice to patient about drug-food interactions did not occur or was not written in the prescription. These findings are similar to other studies [1, 40]. Most spoken information provided during interactions with health professionals is forgotten and there is often little time available for this in consultations [41]. In addition to the frequent absence of instructions on the prescription, the study also found a lack of clarity or ambiguity that caused interpretation and medication errors [31]. In a study conducted in an elderly Brazilian population, only 37.21% of patients received instructions from their doctor [1].

Absence of written instructions for patients in prescription, maybe are consequence of verbal education. In an American study conducted in outpatient primary care clinics, 77.4% of the individuals reported that their doctor explained how to take the medication [40]. However, this type of education requires the patient capacity to process and retain information, which does not always coincide with their ability [42]. Generally, patients prefer a combination of oral instructions and written information [43], probably due, in part, to the fact that the patients might forget half of what they have been told within five minutes of a health consultation and remember only 20.0% of the information passed on to them. However, retention of information by patients can be improved by 50.0% if additional written information is provided, and consequently the use of written information also maximizes health professionals' time, helps reduce time spent on repetition of routine information and prevent errors [44].

Pharmacists as healthcare providers have an obligation to provide guidance to patients on the correct use of their medications [45]. However, clinical pharmacist service was almost inexistent despite it was necessary. Pharmacy technicians routinely dispense medications and the pharmacist may not be directly involved in counselling and specific patient concerns[40]. The pharmaceutical report a lack of time to fulfil one's professional obligations due to an increase in their workload[46].

In contrast to the findings of low provision of aid services to patients post-access to drugs, evidence shows that the pharmaceutical care improves medication use and health results [47]. In one study in intensive care units, drug interactions were reduced in 65.0% by the pharmacist [48].

After interventions by pharmacists to solve PDTP there were greater adherence to pharmacotherapy [49, 50] and patients report better knowledge about their disease and are satisfied with the pharmacist's work [51]. Some authors have shown that

pharmaceutical interventions can prevent about 60.0% of PDTP [52], and can reduce the number of drugs, thus promoting patient adherence and avoiding the adverse reactions, thus contributing to improving the quality of life and decreasing healthcare costs [27]. Highlighting the absence of this type of care in this study, it was identified that 50.0% of respondents had some PDTP. These results differ from those documented in the literature. In a study conducted in hospitals, a PDTP frequency of 15.7%was found, with the most common being drug interactions [52]. In an emergency service hospital, the prevalence was 31.6% PDTP [53]. In another study involving only the elderly with chronic diseases, the prevalence was 87.0% [54].

In multivariable analyses, a complexity of pharmacotherapy and the number of clinical conditions were significantly associated with use of medicines in relation to food. The association we found suggests that when it is impossible to instruct all patients about the correct use of their medications in relation to food, patients should be prioritized as the scores of complexity of pharmacotherapy, taking into account the cut-offs and the number of diseases. Some authors claim, identification of patients with a highly complex therapy can be used as an indicator to prioritize patients with multiple chronic health conditions number and problems in their pharmacological therapies [16].

Complex therapies can also cause a decrease in adherence [55-57]. In contrast, our study indicated an increase in adherence in this type of therapy. We affirm limitation in measure adherence, given the self-report adherence by patient, which can cause unreliable results associated with information and memory bias.

Medication errors related to incorrect drug administration maybe did drug's effectiveness be reduced or insecurity increased [6, 58]. The most common drug administration errors are those with food restrictions, it suggest correct use random [59]. Captopril was the drug in which we observed the most inappropriate use, associated with concomitant food similar to other studies [2, 60]. The consequence of these medication errors is to reduce the drug absorption by approximately 15.0% to 54.0% [1, 61-63]. Between 1999 and 2010, the prevalence of antihypertensive consumption increased from 47.8% to 60.5% [64], which highlights the importance of proper guidance on taking these drugs. The second-most incorrectly used drug was omeprazole. Its rate, but not the extent, of absorption is affected by food, causing a reduction in the maximum concentration of 63.0% and 24.0% of the area under the curve [65, 66].

The results of this study on the types of medication error of administration for food are difficult to compare with the literature, because most studies have also analysed inadequate doses, drugs taken by the wrong patient, at the wrong time, unauthorized drugs prescribed by the doctor and omission in this category [12, 14, 29, 67–69]. In a study conducted in a teaching hospital in France, a value of less than 2.3% for medication errors related to the concomitant intake with food was found [29].

Intervention to solve food-drug use problems can increase health results. In a study conducted in two Dutch hospitals, there was a reduction of administration errors after interventions to promote the correct administration of drugs in patients with enteral feeding tubes [70].

CONCLUSION

This study identified low prevalence of drug-food interaction despite few professional patient educations, suggesting correct use random or due to verbal instructions. Professionals, in general, do not seem to warn their patients to take their medications on a full or empty stomach, at least in writing. There are indications that health professionals that are aware of the drug administration process can reduce medication errors and can contribute to the optimization of pharmacotherapy.

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COMPETING INTERESTS

We declare no conflict of interest.

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