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Research Article

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Prevalence and predictors of potential drug-food interactions among the elderly using prescription drugs

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A**BSTRACT**

Drug-food interactions (DFI) occur when there is concomitant administration of a drug and a food that leads to an alteration in the kinetics or dynamics of the drug or nutrient, or the impairment of the nutritional status as a result of the administration of a drug. The elderly are at greatest risk of experiencing DFI, as they are more prone to chronic use of medications and polypharmacy. The objective this research is to determine the prevalence of potential drug-food interactions in the elderly using prescription drug. A cross-sectional study was conducted with 342 elderly serviced by a public primary care service. Potential drug-food interactions (PDFI) were identified through the MICROMEDEX ® Interaction database program. The prevalence of DFI was 58.5%, in a total of 278 potential interactions identified. Potential drug-food interactions most frequently occurred in patients who maintained a habit of eating and taking medication at the same time. Multivariate analysis revealed the increased chances of DFI with increasing amount of drugs in use by the elderly. Being diabetic and have poor knowledge about the use of drug therapy were also factors that increased the chance of occurrence of PDMI. The occurrence of DFI is more frequent than potential drug interactions. The drugs involved in most DFI are commonly used in the pharmacotherapy of diabetes and hypertension, and the factors that are associated with the occurrence of PDFI were the number of medications taken and the level of knowledge of the elderly about their pharmacotherapy.

Keywords: Elderly, Drug Food Interaction, Family Medicine.

INTRODUCTION

Drug-food interactions are a significant problem in clinical practice. Food can change the effect of drugs by interfering with the pharmacokinetic processes, such as absorption and elimination[1]. However, despite the extensive information found in the medical literature about the clinical relevance of these interactions, there is little information on the occurrence of these interactions in the population [2].

Drug-nutrient interaction occur when there is concomitant administration of a drug and a nutrient or food that leads to alteration in the kinetics or dynamics of the drug or nutrient, or the impairment of nutritional status as a result of the administration of a drug [2,3].

Studies on the epidemiology of drug-food interactions in order to direct standardized management approaches for preventing these interactions are scarce [1]. Some published studies have investigated the possible occurrence of drug-food interactions in institutionalized [4] and hospitalized [5] patients. However, there isn't reference information about the occurrence of these interactions in patients of primary health care services who live in the community.

Although drug-food interactions can occur in any patient, the elderly are at greatest risk of experiencing this [2,3], because they are more prone to chronic use of drugs and polypharmacy[6].

Since the interactions between drugs and food can result in decreased bioavailability of the drug, which predisposes to treatment failure, or a higher bioavailability, which increases the risk of adverse events and may even precipitate toxicity, its prevention and management are paramount in clinical nutrition and the success of the treatment.

The literature [2,3,7,8] demonstrates how the constituents of food can influence the bioavailability of drugs and vice versa. However, we are faced with the lack of practical information aimed at healthcare staff and especially to users of continuous medication, patients with chronic degenerative diseases, the elderly and those with poor nutritional status.

Therefore, the aim of this study was to determine the prevalence of potential drug-food interactions in the elderly using prescription drugs and to identify associated key factors.

EXPERIMENTAL SECTION

A cross-sectional epidemiological study was conducted, using household surveys. The sample consisted of 342 elderly accompanied by a primary care service, and recruited through random systematic allocation. Inclusion criteria were: age 60 years or more, be able to respond to the survey instrument, undergoing prescribed drug treatment and be accompanied by public service primary health care.

The variables investigated were: demographics (age and sex), socioeconomics (marital status, education and income), medication use, level of knowledge about the use of medicines, food consumption, access to health services (visits and hospitalizations) and aspects related to reported health (perceived health, chronic diseases, smoking and physical activity).

Food consumption was measured by the Food Consumption and Frequency Questionnaire (FCFQ) [9], and the other variables were measured by means of a form developed specifically for this study, and previously validated in a pilot study.

Information about the use of drugs corresponded to: name of medicines, vitamins and mineral supplements prescribed and non-prescribed medications in use at the time of the interview, its indication, and dose and respective schedule of administration. The active principles present in each pharmaceutical specialty were listed and classified according to the Anatomical-Therapeutical-Chemical Classification System (ATC) [10].

The level of knowledge about medication was performed using the criteria established by E Bonstra [11]. The knowledge was evaluated for each drug in use through questions regarding the drug name, indication, dose and frequency of administration. For each drug a score corresponding to the number of correct responses was established, assigning 1 point for each correct answer and 0 for each incorrect answer. The overall level of knowledge for each individual was calculated using the average score for all drugs in use. Thereafter, the score of knowledge of medication was categorized as satisfactory, for those who scored above 2.4 points which corresponded to 60% of the total points.

Potential drug-food interactions were defined as the temporal association between administration of a drug and administration of food [2]. The possible drug-food interactions have been identified through the DRUGDEX (2010)[12] base. This system provides information for the mechanism of action of each potential interaction, the latency period documented in the literature (excellent, good, bad or unknown) and severity, classified as:

(a) *Contraindicated*. Is contraindicated for concomitant use.
(b) *Principal/important.* The interaction can be life-threatening and/or require medical intervention to minimize or prevent serious adverse effects.
(c) *Moderate.* The interaction may result in exacerbation of the patient's clinical condition and/or require a change in therapy.
(d) *Minor.* The interaction would have moderate clinical effect. Manifestations may include an increase in frequency or severity of side effects, but usually do not require a major change in therapy.
(e) *Unknown.* Unknown.

This study did not evaluate the result of possible interactions, but did evaluate the risk of the patient using prescription drugs that could interact with food.

The data were entered with double entries and verified with "validate", a module of the Epi-Info Program, version 6.04 (WHO/CDC, Atlanta, GE, USA) to identify inconsistent events, and analyzed with the help of the software - Statistical Package for Social Sciences (SPSS) for Windows, version 12.0 (SPSS Inc, Chicago, IL, USA).

Statistical analysis consisted of: (a) descriptive analysis, (b) the Kolmogorov-Sminorv test to check the normal range of the continuous variables (c) the Pearson chi-square test and Kruskal-Wallis H test to test for pairing groups (d) binary logistic regression. All variables with p <0.25 in the bivariate analysis were included in the initial multivariate analysis, and then the variables with the highest p-value were removed one by one until only variables with statistical significance remained. The significance level for all statistical tests was set at 5%.

This research observed the rules of National Health Council of Brazil, and follows the principles of the Declaration of Helsinki, being assessed and approved by the Ethics Committee for the Federal University of Pernambuco following process nº 0388.0.172.000-08 and protocol nº 396/08.

RESULTS

Of the 342 elderly surveyed, 78.4% were female, the mean age was 70.6 years (SD = 7.6) and the most frequent age group of 26.6% were those from 60 to 64 years, configuring a population of young elderly. 94.7% of the respondents reported having at least one chronic disease, among the most prevalent diseases listed were hypertension (83.6%), followed by arthritis/rheumatism/arthrosis (37.4%), diabetes (23.4%), heart disease (11.1%), embolism/stroke (9.9%), chronic obstructive lung disease (6.7%) and neoplasm (3.5%).

All participants used the primary care service of the Brazilian Public Health System, the mean number of visits over the previous 12 months was 5.26 (SD = 3.7) and 6.7% had been hospitalized in the previous four months.

The average number of prescription medications in use was 2.78 (SD = 1.6), 951 drugs were reported, corresponding to 739 distinct drugs. The most widely used class of therapeutics was cardiovascular drugs (Table I). The use of drugs considered unsafe[13] for the elderly occurred in 21.6% of cases, 15.5% reported feeling adverse drug reactions and the level of knowledge in use of drug therapy was considered unsatisfactory in 46.8% of cases.

Table I. Use of drugs by therapeutic and pharmacological class, Brazil (n=342)

Classes and Subgroups	N	%
Cardiovascular Drugs	**408**	**42.9**
Diuretics	124	13
Drugs active on the renin-angiotensin system	107	11.2
Blockers of the alci's channels	37	3.9
B-blockers	19	2
Cardiac therapy	14	1.5
Hypolipidemics	4	0.4
Other	3	
Drugs for the Central Nervous system	**192**	**20,2**
Analgesics	80	8.4
Antiepileptic	4	0.4
Antiparkinsonian	6	0.6
Psychoanaleptics	20	2.1
Psycholeptics	26	2.7
Other	6	0.6
Drugs for Food and Metabolism Treatment	**165**	**17.3**
Antidiabetics	65	6.8
Antacids, antiulcers and antiflatulents	14	1.47
Mineral Supplements	18	1.9
Vitamins	5	0.5
Other	3	0.3
Other	**186**	**19.6**

Hydrochlorothiazide 25mg (14.4%), Captopril 25mg (10.8%), aspirin 100mg (9.2%), Metformin 850mg (3.7%) and simvastatin 40mg (2.9%) were the most widely used drugs.

58.5% of the elderly had at least one potential drug-food interactions, in a total of 278 potential interactions that were identified, with an average of 0.8 (SD = 0.97) interactions per individual.

The bivariate analysis revealed that the potential drug-food interactions had a higher prevalence with increasing number of medications used, poor knowledge of drug therapy and among patients with hypertension and diabetes (Table II).

Table II. Characteristics of the elderly according to exposure to potential drug-food interactions in elderly using essential prescription drugs

Characteristics	Exposed	Non Exposed	P
Age N(%)			
60-64	53 (58.2%)	38 (41.6%)	0.483*
65-69	54 (66.7%)	27 (33.3%)	
70-74	43 (60.6%)	28 (39.4%)	
75-79	27 (57.4%)	20 (42.6%)	
80-84	16 (44.4%)	20 (55.6%)	
85 and above	7 (73.8%)	9 (56.3%)	
Sex N(%)			
Masculine	46 (62.2%)	28 (37.8%)	0.684*
Feminine	154 (57.5%)	114 (42.6%)	
Marital Status N(%)			
With partner (a)	72 (60.2%)	47 (39.8%)	0.836*
Without partner (a)	128 (54.7%)	95 (42.6%)	
Education N(%)			
Illiterate	73(58.4%)	52 (41.6%)	0.776*
1 to 4 year of schooling	45 (57.7%)	33 (42.3%)	
5 or more years of schooling	82 (59.0%)	142 (41.5%)	
Income N(%)			
Less than R$560.00	137 (55.5%)	110 (44.5%)	0.261*
Between R$ 560.00 and 1120.00	46 (70.8%)	19 (29.2%)	
More than R$ 1120.00	17 (56.7%)	142 (41.5%)	
Drugs in use N(%)			
1-2	68 (41.0%)	98 (59.0%)	0.000*
3-4	95 (72.0%)	37 (28.0%)	
≥5	37 (84.1%)	7 (15.9%)	
Knowledge of drug therapy N(%)			
Satisfactory	89 (47.3%)	96 (52.7%)	0.000*
Unsatisfactory	114 (71.3%)	56 (28.7%)	
Hypertension N(%)			
No	13 (36.1%)	23 (63.9%)	0.000*
Yes	179 (62.6%)	107 (37.4%)	
Diabetes N(%)			
No	138 (55.3%)	121 (46.7%)	0.003*
Yes	60 (75.0%)	20 (25.0%)	
Neoplasia N(%)			
No	137 (41.5%)	193 (58.5%)	0.982*
Yes	5 (41.7%)	7(58.3%)	
COPD N(%)			
No	132 (41.4%)	187 (58.6%)	0.942*
Yes	10(43.5%)	13 (56.5%)	
Cardíac Disease N(%)			
No	131 (43.1%)	173 (56.9%)	0.400*
Yes	11(28.9%)	27 (71.1%)	
Stroke N(%)			
No	129 (41.9%)	179 (58.1%)	0.877*
Yes	13 (38.2%)	21 (61.8%)	
Arthritis/arthrosis/rheumatism N(%)			
No	82 (38.3%)	132 (61.7%)	0.204*
yes	60 (46.9%)	68 (53.1%)	
Average yearly Visits (DP)	5.6 (DP=3.7)	4.7 (3.5)	0.241**

(*) Chi-square
(**)Kruskal-Walis H Test

Table III. Classification of potential drug-food interactions observed in the elderly using essential prescription drugs, according to clinical significance and existence of documentation

Classification	Potential drug-food interactions n (%)
Severity	
Contra-indicated	-
Important	-
Moderate	126 (45.4%)
Minor	152 (54.6%)
unknown	-
Documentation	
Excellent	6 (2.1%)
Good	232 (83.1%)
Reasonable	40 (14.3%)
Unknown	1 (0.5%)

The classification of potential drug-food interactions according to their severity and existence of corroborative documentation of interactions can be seen in Table III.

PDFI frequently occurred in patients who maintained the habit of eating and taking medication at the same time. This event occurred more frequently among those using prescribed drugs such as captopril (36.3%), propranolol (17.9%), metformin (15.1%), alendronate (6.5%) and furosemide (2.1%).

Multivariate analysis revealed the increased chances of occurrence of PDFI with increasing amount of drugs in use by the elderly. Being diabetic and having poor knowledge about the use of drug therapy were also factors that increased the chance of occurrence of PDFI (Table IV).

Table IV. Multiple logistic regression of the prevalence of potential drug-food interactions in the elderly using prescription drugs

Variable	Odds ratio	IC (95%)	P
Diabetes			
No	-	-	-
Yes	1.944	1.055-3.582	0.033
Drugs in use			
1-2	-	-	-
3-4	1.560	0.621-3.920	0.000
≥5	5.517	2.256-13.491	0.000
Knowledge of drug therapy			
Satisfactory	-	-	-
Unsatisfactory	2.585	1.590-4.205	0.000

DISCUSSION

The prevalence of PDFI was found to be higher than the prevalence of potential drug interactions observed in studies with the elderly [14,15,16,17]. This may indicate a higher incidence of drug-food interactions in ordinary clinical practice pointing to the need for greater attention on the part of healthcare professionals and patients, to identify and correct management of these interactions.

Despite the greater frequency, PDFI tend to be less severe. It is known that the presence of food tends to alter the rate and/or extent of absorption of the drug, and this delay is important only if it is necessary to achieve a rapid effect and a peak of high concentration, however, for most chronic therapies, the rate of absorption is less important since the plasma level concentration is sustained [18,19].

The factors that contribute the most to the occurrence of PDFI were the number of medications in use, the level of knowledge about drug therapy and patients with diabetes. This finding reinforces the role of the health service as a cause of PDFI, and makes clear its importance in preventing and controlling these interactions.

The literature indicates [20] that among elderly, factors such as changes in physiology and nutritional status, associations with aging, low therapeutic adherence and polypharmacy, may lead to increased susceptibility to adverse drug events, including the interactions between drugs and food. Thus, the goals of pharmacotherapy for the elderly, in addition to the aspects of prevention and cure, are related to maintenance of functional independence, prevention of incapacities, and iatrogenic diseases and disabilities, in order to improve health-related quality of life [21].

To achieve satisfactory results in pharmacotherapy safely, especially among the elderly, has been a challenge. Studies have shown that poor levels of knowledge of patients about their drug therapy is related to lower therapeutic adherence [22,23] and failure in the administration of medicines [24,25], hindering the success of pharmacotherapy and thus endangering patients. In this study, the opportunity to present PDFI among elderly with poor knowledge of pharmacotherapy was higher than among those with adequate knowledge, reinforcing once again the important role of health services in the prevention of PDFI. Byeth [26] and colleagues demonstrated that patient education about warfarin, including drug-food interactions, was effective in preventing hemorrhaging complications in the elderly. The strategies used for education included education on the use of techniques to teach elderly to take an active role in their own care and to communicate timely information about their health, which is necessary for the monitoring of drug therapy, and for healthcare professionals the use of a book formatted specifically for the elderly containing information about treatment and the associated risks.

Another strategy to help promote the rational use of drugs and consequently to increase the success of pharmacotherapy reducing the risks, is the medication adequacy ratio developed by Hanlon [27,28] and colleagues.

This index is an instrument with demonstrated reliability and validity that can be used by physicians in routine assessment of drug therapy, including drug-food interactions.

The evaluation of PDFI revealed that one of the most common reasons that lead to the occurrence of interactions is the habit of taking drugs with meals. This habit is often stimulated by health care professionals who instruct the elderly in this practice as a form of increasing adherence to pharmacotherapy. Meals usually stimulate gastric and intestinal secretion [29]. The increase in secretions theoretically improves the dissolution of drugs in solid form. Drugs or foods that significantly impair gastrointestinal motility can precipitate toxicity as a result of more complete absorption. Yet, the increase in gastrointestinal motility can result in risk or therapeutic failure. Stomach distention by food, stimulates splanchnic flow, increasing pre-systemic metabolism. The clinical description of more common PDFI can be seen in Table V.

Table V. Description of potential drug-food interactions frequently observed in the elderly using essential prescription drugs

Medication	Frequency 278(100%)	Description of Mechanical Interaction	Conduct to be Adopted
Captopril	101 (36.3%)	The concurrent use of captopril with food decreases the absorption of captopril by 10% by 54%. Chronic treatment does not alter the pharmacokinetics in a consistent way with the exception of a slight prolongation of the terminal half-life of captopril.[30]	It is suggested that captopril be administered one hour before or two hours after meals[31,32,33,34].
Metformin in monotherapy	42 (15.1%)	Food significantly reduces the extent of the absorption rate of metaformin [35,36].	Administer metformin on an empty stomach to avoid a reduction in oral bioavailability.
Alendronate	18 (6.5%)	Administration with food reduces bioavailability by approximately 40% [37].	It is recommended that alendronate is administered two hours before a meal.
Furosemide	6 (2.1%)	Administration with meals results in a decrease of 30% in the bioavailability of furosemide [38,39,40,41].	Administer furosemide on an empty stomach to avoid a reduction in oral bioavailability of the drug and to maintain a more consistent diuretic effect.
Digoxin	3 (1.1%)	Meals rich in fiber (beans, cassava flour consumed at lunch and bran consumed at breakfast) reduces absorption [42].	In the administration of digoxin orally avoid concomitant intake of foods rich in fiber [43,44].
Warfarin	2 (0.7%)	Foods rich in vitamin K (beans, cassava, green vegetables) antagonize the anticoagulant effect thus reducing its effect[45,46,47,48]. The use of capsules of garlic supplements can increase the risk of hemorrhages, as garlic has anti-platelet effects [49,50].	Avoid garlic supplements and eating foods rich with excess vitamin K.

The clinical conditions that more often led to the occurrence of PDFI were hypertension and diabetes. The interactions between drugs and food in elderly diabetics not only vary depending on the drug used, but also with dietary patterns. The consequences of these interactions include: hyperglycemia, hyperglycemic state, neuropathies, and risk of cerebral stroke [51.] Thus, due to the high prevalence of hypertension and diabetes among the elderly, the morbidity associated with it, the greater susceptibility of elderly to the adverse effects associated with medication and more frequent PDFI associated with these diseases, it is necessary to develop and adopt the use of specific guidance protocols, and prevention and monitoring of PDFI for patients faced with diabetes and hypertension.

CONCLUSION

The occurrence of PDFI is more frequent than potential drug interactions, occurring in more than half of the elderly using essential prescription drugs and served by a public primary care service.

The drugs involved for the most part in PDFI are commonly used in the pharmacotherapy of diabetes and hypertension, such that DFI may lead to treatment failure, increase adverse reactions and toxic effects, and that the risk of treatment failure and the decrease in safety among the elderly is increased. Thus, the inclusion of information and behaviors related to drug-food interactions for treatment protocols specific to these diseases should be a priority.

The factors that were associated with the occurrence of PDFI were the number of medications taken and level of knowledge of the elderly about their pharmacotherapy. These results highlight the need for patients and health care professionals to educate themselves routinely, through educational programs aimed at increasing awareness and knowledge about issues related to drug-food interactions.

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