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Study on the rational use of medications in the elderly

Estudo sobre a utilização racional de medicamentos em idosos

Estudio acerca del uso racional de medicamentos en ancianos

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This study aimed to analyze Potential Drug Interactions and Potentially Inappropriate Drugs for Elderly users of primary care pharmacies. Descriptive study with cross-sectional design with a sample of 384 elderly/caregivers, distributed among all six pharmacies in the city of Uberaba, MG, Brazil, in 2015. All prescriptions were analyzed and the drugs classified according to Anatomical Therapeutic Chemical Classification; and, in the MICROMEDEX® database and by the Beers-Fick Criterion (2015). 580 prescriptions were analyzed and 570 interactions were verified, with 47.4% of participants subject to at least one interaction; 54.7% used inappropriate drugs. The drugs most involved in the interactions were: omeprazole (19.5%), AAS (14.2%) and losartan (13.2%). There was a need to adopt managerial and educational measures that aim at more safety and therapeutic efficacy for the elderly.
Descriptors: Drug utilization; Drug interactions; Aged.

Este estudo teve como objetivo analisar as Interações Medicamentosas Potenciais e os Medicamentos Potencialmente Inapropriados para Idosos usuários das farmácias da atenção primária. Estudo descritivo com desenho transversal com amostra de 384 idosos/cuidadores, distribuídos entre todas as seis farmácias da cidade de Uberaba, MG no ano de 2015. Todas as prescrições apresentadas foram analisadas e os medicamentos classificados segundo a Anatomical Therapeutic Chemical Classification; e, na base de dados MICROMEDEX® e pelo Critério de Beers-Fick (2015). Foram analisadas 580 prescrições e verificadas 570 Interações, estando 47,4% dos participantes sujeitos a pelo menos uma interação; 54,7% utilizavam medicamentos inapropriados. Os medicamentos mais envolvidos nas interações foram: omeprazol (19,5%), AAS (14,2%) e losartana (13,2%). Verificou-se a necessidade de adoção de medidas gerenciais e educativas que visem mais segurança e eficácia terapêutica para os idosos.
Descritores: Uso de medicamentos; Interações medicamentosas; Idoso.

El objetivo de este estudio fue analizar las Interacciones Medicamentosas Potenciales y los Medicamentos Potencialmente Inapropiados para Ancianos de las farmacias de atención primaria. Estudio descriptivo con un diseño transversal con una muestra de 384 ancianos/cuidadores, distribuidos entre las seis farmacias de la ciudad de Uberaba, MG, Brasil, en 2015. Se analizaron todas las recetas presentadas y se clasificaron los medicamentos de acuerdo con la Anatomical Therapeutic Chemical Classification; y en la base de datos MICROMEDEX® y el Criterio de Beers-Fick (2015). Se analizaron 580 recetas y se verificaron 570 interacciones, con el 47,4% de los participantes sujetos a por lo menos una interacción; el 54,7% utilizaba medicamentos inapropiados. Los medicamentos más involucrados en las interacciones fueron el omeprazol (19,5%), el AAS (14,2%) y el losartán (13,2%). Se verificó que es necesario adoptar medidas de gestión y educación que objetivan lograr una mayor seguridad y eficacia terapéutica para los ancianos.
Descriptores: Utilización de medicamentos; Interacciones farmacológicas; Anciano.

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INTRODUCTION

More and more public health policies in Brazil are aimed at the elderly, recognizing the important age restructuring of the country, where, currently, 13% of its population corresponds to people over 60 years[1], and this index should reach 29.3% in 2050[2].

One of the great challenges for the aging population is the scarcity and/or restriction of resources for an increasing demand. The elderly consume more health services, hospitalizations are more frequent and the bed occupancy time is longer when compared to other age groups. This fact is due to the pattern of diseases of the elderly, which are chronic and multiple, and require constant monitoring, permanent care, periodic exams and continued use of medications[3], which reinforces the particularities of this age group.

In the elderly, pharmacotherapy requires a lot of attention, such as: adverse reactions to medications (ARM), problems with adherence to treatments, polypharmacy, use of potentially inappropriate medications for the elderly (PIM) and medication interactions (MI)[4]. The use of PIM and MI are characterized as special types of pharmacological responses, in which the effects of one or more drugs are altered by the simultaneous or previous administration of others, or by concurrent administration with food[5].

ARMs are another challenge of pharmacological treatment, being defined as a drug response that is harmful, unintentional, and that occurs in doses normally used in humans for the prophylaxis, diagnosis and treatment of diseases, or for the modification of a function physiological[6].

From this perspective, PIMs were investigated for scientific evidence about those to be avoided, due to insecurity, or the incidence of ARM and the lack of evidence on effectiveness, leading to the elaboration of an important list known as the Beers-Fick Criterion, which classifies drugs among those that should be avoided, dependent or independent of the disease and still at high and low risk[7].

In this sense, the present study aims to analyze Potential Medication Interactions and Potentially Inappropriate Medications for Elderly users of primary care pharmacies.

METHOD

This study was carried out in Uberaba, a city located in the Triângulo Mineiro region of the State of Minas Gerais, with an estimated population of 322,126 inhabitants in the year of the survey (IBGE[8], 2015), with the last update of 333,783 inhabitants (IBGE[9], 2019), being divided into three Health Districts (HD): HD I; HD II; and HD III.

The descriptive research with cross-sectional design was developed between March and July of 2015, in which all six basic pharmacies managed by the municipality were part of the study.

The bases for calculating the sample size[10] were based on the definition of the tolerable sample error (ε), α error (level of significance) and prevalence (P).

Considering the absence of studies in similar municipalities, the value for P was considered unknown, having been maximized and determined as 0.5. Based on the interval between the theoretical P values for the municipality (0.126) and the maximized P value (0.5) for elderly users of basic pharmacies, arbitrating in relation to ε, this value was assigned the value 0.05; for judging this value fully acceptable. The α value considered was 0.05 (1.96 - tabulated value of the standardized normal distribution for the 95% confidence interval). Below is the equation for determining the sample size:

$$n = \frac{Z^2\, \alpha/_2\, P(1\text{-}P)}{\varepsilon^2} \longrightarrow n = \frac{1.96^2 \,.\, 0.5\,(1 - 0.5)}{0.05^2} \quad n = 384.16 \longrightarrow \cong 384$$

In view of the value presented by the sample calculation, 384 individuals were included in the study. And, to be included in the study, the individual must be 60 years old or older, or

their representatives must be 18 years old or older and be characterized as caregivers, that is, responsible for managing the patient's pharmacotherapy.

Considering the number of visits to public pharmacies in the municipality, there was a proportional sharing of respondents between basic pharmacies, based on the number of monthly visits by each of them and the sample calculation, with a view to maintaining the proportionality of patients attended by pharmacies.

The participants were approached while waiting in line at the basic pharmacies and, after consenting to participate before signing the Free and Informed Consent Form (ICF), they were interviewed after the medication was dispensed. All medical prescriptions carried by them were photographed for further analysis, which was carried out individually, with a focus on investigating PMI and the prescribed PIM.

The PMI observed among the prescription drugs were checked and classified according to their severity and the quality of the scientific evidence[11]. Self-reported drugs were not included in this analysis. The verification of the prescribed PIM was carried out based on the Beers-Fick Criterion (2015)[12].

The collected data were transcribed in an electronic spreadsheet (EXCEL® 2007), followed by conference and descriptive analysis, obtaining simple frequency. The presentation of the drugs followed the Brazilian Common Denomination (BCD) and were classified by the Anatomical Therapeutical Chemical Classification System (ATC), for the description of the drugs and the most prescribed therapeutic classes[13].

In the present study, the Poisson Regression Model was used in the statistical analysis, with a significance level of 5% assumed, which is characterized by the analysis of data collected in the form of proportions or counting reasons, that is, it takes into account the total number of people with a certain disease (or condition)[14]. This regression model specifically made it possible to analyze the relationship between the number of PIM and the number of IMP.

This research was submitted and approved (approval number 1.999.382) by the Ethics Committee in Research with Human Beings through Plataforma Brasil, based on CAAE: 26520014.5.0000.5403, and meets the standards of Resolution 466/2012 of the National Council of health.

RESULTS

580 prescriptions were collected, with a total of 1289 prescription drugs, and of the total prescriptions, more than half (51.9%) had at least one active ingredient involved in an PIM, and the average of interactions per prescription was 1.9, and of the total PIM, six can be considered potentially dangerous (Table 1).

Table 1. Potentially dangerous drug interactions for the elderly, Uberaba-MG, 2015 (n = 384).

Medication A	*Medication B*	*Effect*	*Frequency (n)*
Loratadine	Ipratropium	May increase the anticholinergic effect of Loratadine	1
Dipyrone	Nimesulide	May increase the adverse effects/toxicity of cyclooxygenase-2 (COX-2) inhibitors	2
Ondansetron	Domperidone	May increase the risk of cardiotoxicity (QT prolongation)	1
Amiodarone	Fluoxetine	May increase the risk of cardiotoxicity (QT prolongation)	2
Total			6

Omeprazole was the main representative for the risk of PMI, corresponding to 19.5% of them, followed by AAS, with 14.2%, and losartan, with 13.2%. (Table 2).

Table 2. Drugs prescribed and considered inappropriate for the elderly, regardless of diagnosis or clinical condition, according to Beers' Criteria, Uberaba-MG 2015 (n = 1289).

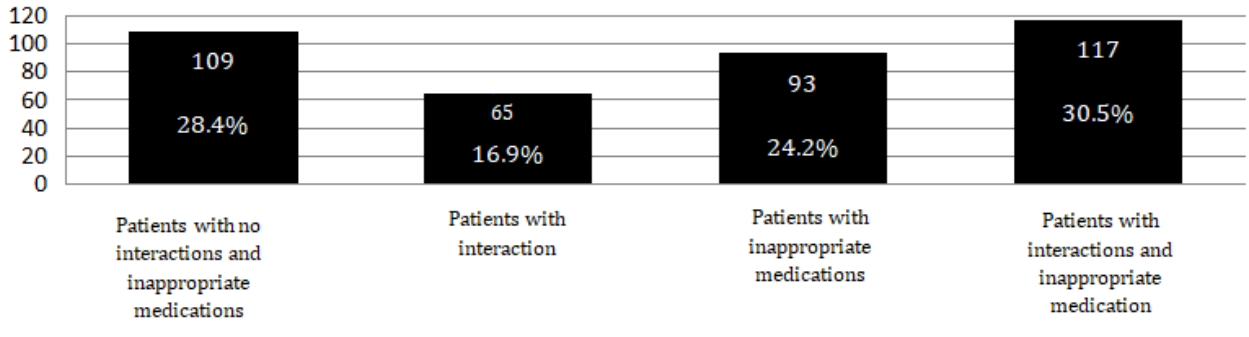
Inappropriate Medication	n	Frequency (%)
Benzodiazepines		
Diazepam 10mg	14	1.1 %
Antidepressives		
Amitriptyline 25mg	17	1.3 %
Fluoxetine 20mg	17	1.3 %
Antihistamine		
Dexchlorpheniramine	13	1.0 %
Cardiovascular		
Amiodarone 200mg	25	1.9 %
Methyldopa250mg	6	0.46 %
Nifedipine20mg	19	1.47 %
Doxazosina	1	0.08 %
Non-steroidal anti-inflammatory drugs (NSAIDs)		
Naproxen	1	0.08%
Proton pump inhibitors		
Omeprazole	129	10.0 %
Esomeprazole	1	0.08 %
Pantoprazole	2	0.16 %
Antimicrobial		
Nitrofurantoin	2	0.16 %
Mineral		
Ferrous sulphate	6	0.46 %
Myorelaxants		
Carisoprodol	4	0.32 %
Cyclobenzaprine	6	0.46 %
Oxybutynin	1	0.08 %
TOTAL	263	20.4 %

The drugs involved in PMI were analyzed for suitability for the elderly, according to the Beers Criteria 2015, and of the 17 inappropriate drugs found, 10 (58.8%) were included in the Municipal List of Essential Medicines (MLEM).

The use of at least one PIM was found in 54.7% (n = 210) of the elderly, of whom 55.7% were concomitantly subject to at least one potential drug interaction (Figure 1).

The existence of an association between the mean PIM and PMI per patient was analyzed using the Poison Regression Model, as these variables originate from discrete data. The results showed evidence of an association between these two variables, pointing out that for each inappropriate drug included in the drug treatment, the likelihood of interactions increases by 55.6%.

Figure 1. Patients using PIM and exposed to PMI, Uberaba-MG 2015, (n = 384).



DISCUSSION

Both the frequency of PMI and PIM are factors with a close relationship with iatrogenic conditions, being characterized as iatrogenic reactions resulting from the intervention of the doctor and/or other professionals of the health team responsible for direct care of patients, whether certain or wrong, justified or not, but resulting in harmful consequences for the patient's health; additionally, it is observed that hospitalized elderly are the biggest victims of iatrogenesis[15].

A study points out[16] that there is an association between the use of PIM with polypharmacy, polypathology and arterial hypertension and inferred that the clinical consequences of the use of PIM are important due to the greater risk of adverse events and negative impact on the functionality of the elderly. The greater number of drugs in use, specifically, is also directly related to the greater number of associated diseases, as evidenced in another study[17].

The association between the use of PIM and variables such as reduced socioeconomic status, visits to health services and use of prescription drugs may reflect the ignorance of the medical professional in relation to the prescription of drugs not recommended for the elderly; it can also result from the prescription of drugs that are more available in public services, to facilitate access for this population, but considered inadequate, such as amitriptyline, methyldopa and clopropamide[18].

In this sense, there is the possibility of replacing, for example, these last three drugs mentioned by others such as: nortriptyline, amlodipine and gliclazide, respectively, all being offered by MLEM, and the last one also offered by the Program *Aqui Tem Farmácia Popular*, being thus, all offered free of charge[19].

The PMI, in turn, presents itself in a very diversified way, which may be adequate or inadequate, simple or complex, in which the understanding of the causes is also complex, since they depend, in addition to the numerous theoretical possibilities of interference between drugs, factors related to the individual (age, genetic makeup, pathophysiological status, type of food) and medication administration (dose, route, interval and sequence of administration) that influence the treatment response[20].

The most common causes of drug interaction in individuals who live in multiple drug therapy are the ease in purchasing non-prescription drugs and the lack of information[21].

In the present study, the average of interactions per medical prescription was higher than that observed in a similar study (0.80)[22]. Corroborating the findings of the present investigation, another study pointed out that AAS was among the main drugs with potential for drug interaction[23].

In clinical application, PIMs can worsen the clinical condition of the elderly, intervene in quality of life and increase the risk of potentially serious and fatal events[12]; regarding PMI, investigation[24] estimated that 1 in 30 admissions of elderly patients in sectors of hospital urgency is related to adverse events related to the use of medications, and about half of these are suspected to have been caused by drug interactions.

The use of technologies in monitoring PMI and ARM recognition, such as computer-based screening, can help professionals to recognize potential and clinically significant interactions and adverse events. The software must have high sensitivity and specificity and high positive and negative predictive values. Likewise, the advantage of using computerized databases to assess the prescription of medications is evident[25].

A national study[22] pointed out some measures capable of promoting greater safety in drug therapies for the elderly in Brazil: the presence of geriatricians in government institutional programs, the clarification of the family (health education), caregivers and the elderly themselves about the potential consequences of non-judicious use of medications in old age; training of professionals in the prescription and indication of medication for the elderly; implementation of a pharmacovigilance system with special attention to the use of medicines

by older people; and making a package of medications suitable for the geriatric population available on the public network.

CONCLUSION

The results found in this study show a high percentage of elderly people exposed to PIM and PMI, thus showing similarity with several studies in other regions of Brazil. The present study shows that the average PIM per prescription is high, accompanied by the percentage of elderly people exposed, concomitantly, to these interactions and to the PIM, these indicators being observed in about 50% of the participants.

This work has limitations typically observed in cross-sectional studies, such as the impossibility of establishing a temporal relationship between events and, with this, the difficulty of defining causality. As an example, it is possible to mention the impossibility of affirming that the level of education of the participants is inversely proportional to the number of PMI and PIM.

In turn, this study has as its strong point, the methodological aspect of including individuals unable to personally withdraw their medications, as well as individuals with limited mobility, institutionalized and bedridden, through their representatives. It is also important to highlight the importance of the sample calculation performed, which allows inferring the robustness of the results obtained.

The data generated by the present study point to the need for management and preventive care measures that enable actions such as: replacing the PIMs with safer and more effective therapeutic options, in addition to dose adjustments generating longer intervals for administering medications, minimizing the incidence of administrations. concomitant and PMI; implementation of computerized alerts.

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CONTRIBUTIONS
Rodrigo Rodrigues Silva and **Leonardo Régis Leira Pereira** contributed to the conception, design, analysis and interpretation of data, writing and review. **Marília Silveira de Almeida Campos** participated in the design and analysis of data. **Álvaro da Silva Santos** worked on writing and reviewing.

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