Potential drug interactions in the pharmacotherapy of elderly people in an educational program in the capital of Brazil

Interações medicamentosas potenciais na farmacoterapia de idosos de um programa educativo na capital do Brasil

Posibles interacciones medicamentosas en la farmacoterapia de adultos mayores en un programa educativo en la capital de Brasil

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RESUMO

Objetivo: Analisar as interações medicamentosas potenciais (IMP) na farmacoterapia dos idosos de um programa educativo do Distrito Federal no Brasil. **Método:** Estudo transversal realizado na Universidade do Envelhecer, um programa de extensão da Universidade de Brasília, com 150 idosos cuja com coleta de dados ocorreu no período de dezembro de 2022 a abril de 2023 por meio de ligações telefônicas. As IMP foram categorizadas em leve, moderada, grave e desconhecida. **Resultados:** O número de medicamentos, por idoso, variou de 1 a 13, com média de 3,1 e mediana igual a 2. A prevalência estimada de IMP foi de 42,6%. Dentre os participantes com IMP, verificou-se que 13 (20,3%) possuía pelo menos uma IMP grave, ao passo que 55 (85,9%) possuía pelo menos uma IMP moderada e 17 (26,5%) pelo menos uma IMP leve. Os medicamentos mais envolvidos em IMP grave ou moderada foram indapamida, metformina, hidroclorotiazida e anlodipino. **Conclusão:** A prevalência de IMP entre os idosos na comunidade do Distrito Federal é concordante a outros estudos brasileiros. Enfatiza-se a importância de ater-se à farmacoterapia geriátrica e identificação de IMP pelos profissionais de saúde a fim de possibilitar o uso apropriado de medicamentos por idosos.

Descritores: Saúde do Idoso; Uso de Medicamentosos; Interações Medicamentosas; Prática Farmacêutica Baseada em Evidências; Assistência Integral à Saúde.

ABSTRACT

Objective: To analyze potential drug interactions (PDIs) in the pharmacotherapy of elderly individuals enrolled in an educational program in the Federal District in Brazil. **Method:** Cross-sectional study carried out at the University of Aging, an extension program of the University of Brasília, with 150 elderly individuals. Data collection took place from December 2022 to April 2023 through telephone calls. PDIs were categorized as mild, moderate, severe, and unknown. **Results:** The number of medications per elderly individual ranged from 1 to 13, with a mean of 3.1 and a median of 2. The estimated prevalence of PDIs was 42.6%. Among the participants with PDIs, 13 (20.3%) had at least one severe PDI, while 55 (85.9%) had at least one moderate PDI, and 17 (26.5%) had at least one mild PDI. The drugs most frequently involved in severe or moderate PDI were indapamide, metformin, hydrochlorothiazide and amlodipine. **Conclusion:** The prevalence of PDI among elderly individuals in the community of the Federal District is consistent with other Brazilian studies. The importance of following geriatric pharmacotherapy and identifying PDI by health professionals is emphasized in order to enable appropriate use of medications by elderly individuals.

Descriptors: Health of the Elderly; Drug Utilization; Drug Interactions; Evidence-Based Pharmacy Practice; Comprehensive Health Care.

RESUMEN

Objetivo: Analizar posibles interacciones medicamentosas (PIM) en la farmacoterapia de adultos mayores en un programa educativo en el Distrito Federal de Brasil. **Método:** Estudio transversal realizado en la Universidad del Envejecimiento, programa de extensión de la Universidad de Brasilia, con 150 adultos mayores cuya recolección de datos se realizó entre diciembre de 2022 y abril de 2023 a través de llamadas telefónicas. Las PIM se clasificaron en leves, moderadas, graves y desconocidas. **Resultados:** El número de medicamentos por adultos mayores osciló entre 1 y 13, con promedio de 3,1 y mediana de 2. La prevalencia estimada de PIM fue de 42,6%. Entre los participantes con PIM, se encontró que 13 (20,3%) tenían al menos un PDI grave, mientras que 55 (85,9%) tenían al menos un PIM moderado y 17 (26,5%) al menos un PIM leve. Los medicamentos más implicados en la PIM grave o moderada fueron indapamida, metformina, hidroclorotiazida y amlodipino. **Conclusión:** La prevalencia de PIM entre adultos mayores de la comunidad del Distrito Federal concuerda con otros estudios brasileños. Se destaca la importancia de apegarse a la farmacoterapia geriátrica y a la identificación de la PIM por parte de los profesionales de la salud, para posibilitar el uso adecuado de los medicamentos por parte de los adultos mayores.

Descriptores: Salud del Anciano; Utilización de Medicamentos; Interacciones Farmacológicas; Práctica Farmacéutica Basada en la Evidencia; Atención Integral de Salud.

ORIGINAL

Introduction

Population aging is mainly due to the increase in life expectancy and reduced fertility[1]. Changes in the age profile of the population are notorious worldwide, a fact that in Brazil is even more pronounced, with a rapid and growing number of elderly people[2]. The 2022 demographic census, conducted by the Brazilian Institute of Geography and Statistics, showed that the population of persons aged 60 years and over reached 32,113,490 (15.6%), an increase of 56% compared to 2010, when the number of elderly people was 20,590,597 (10.8%)[3]. This scenario resulted in a change in the pattern of diseases, which began to present chronic characteristics, thus requiring continuous treatment[4,5].

The increasing consumption of drugs considerably increases the risk of potential drug interactions (IMPs), mainly because of polypharmacy. The elderly are more susceptible to adverse events due to their changes in pharmacokinetics and pharmacodynamics. Although it is difficult to determine a causal relationship, it is possible to predict some problems related to pharmacotherapy[6].

Interactions correspond to a clinical event that occurs when the effects and/or toxicity of a drug are modified by another drug, food, beverage or some environmental chemical agent that interferes with the action and/or toxicity of another drug[7]. The consequences of this interaction may be potentiation of the therapeutic effect, reduction of efficacy, emergence of adverse events, or may not cause any significant change in the action of the drug. Therefore, the interaction between drugs may be beneficial, unfavorable, or may not be of clinical importance.[8]

Research has shown that the risk of adverse events is high for people who use two or more drugs. It was noted that, in the elderly, the chance of adverse drug events can increase by 13% when two drugs are administered concomitantly, while when five drugs are used it can reach 58%. In more complex cases in which seven or more medications are consumed, the risk can reach up to 82%[9].

In Brazil, about 23% of the population is responsible for consuming approximately 60% of the national production of medicines, and this pattern is more evident among the elderly[10]. The study "Health, well-being and aging" (SABE), carried out in the city of São Paulo, had the participation of 2,143 elderly people and 86.7% of the interviewees used medications, among which 86% were prescribed by health professionals and 10.1% were self-medicating[11]. Similar data were observed in cities in other Brazilian states, where the prevalence of elderly people who used a prescribed medication ranged from 69.1% to 85%. This shows the high prevalence of medication consumption in this age group[12-14].

DIs are relevant in cases of hospitalizations, accounting for about 3 to 26% of adverse events manifested by patients[15]. Inadequate prescription can lead to an increase in problems related to therapy, in addition to causing changes in the profile of morbidity, mortality, and unnecessary health expenditures[16]. Thus, it is necessary to investigate this theme, especially in elderly people living in the community, to support clinical practice with a focus on comprehensive care. In this context, the present study aims to analyze the

PMI in the pharmacotherapy of the elderly in an educational program in the Federal District (DF) in Brazil.

Method

This is a cross-sectional study carried out at the University of Aging (UniSER), of the University of Brasília (UnB) with data collection between December 2022 and April 2023. The inclusion criteria were: people aged 60 years or older, enrolled in the social political educator course in gerontology at UniSER-UnB and having a fixed or mobile telephone for direct access. Elderly people hospitalized at the time of the interview or up to 30 days before, as well as those who lived in long-term care institutions for the elderly, were excluded.

The sample size was calculated for 150 participants and obtained through simple randomization. The interviews were conducted via telephone calls by previously trained researchers using a structured instrument with sociodemographic, lifestyle, clinical and medication use questions. Research Electronic Data Capture (REDCap) hosted on https://sds.unb.br/redcap-sala-de-situacao was adopted, which is a secure web application to create and manage online searches and databases[17].

The drugs were classified according to the Anatomical Terapeutical Chemical Classification (ATC) adopted by the World Health Organization18. The list of drugs per participant was entered into Micromedex Drug Interactions®. In addition, other sources were consulted such as Drugs.com® and Medscape® in order to identify the IMPs. Next, there was categorization as: unknown IMP (no information available); mild IMP (small clinical importance, consider risk assessment and possibility of drug substitution); Moderate IMP (moderate clinical relevance, avoid these combinations only in exceptional cases) and severe IMP (significant clinical importance, this combination should be avoided as the risk outweighs the benefit). In this analysis, we sought to describe moderate and severe MPIs.

The data were processed with the aid of R version 4.3.2. Absolute and relative frequencies were presented. Means were calculated with their respective standard deviations (SD) and median of the medications used by the elderly. The study followed the ethical precepts in force for research with human beings and was approved by the Research Ethics Committee of the Faculty of Ceilândia, UnB, obtaining opinion number 5.534.997 and Certificate of Presentation for Ethical Appreciation number 59219622.3.0000.8093.

Results

In this study, 150 elderly people participated, 132 (88%) of whom used medications. The number of medications per elderly person ranged from 1 to 13, with a mean of 3.1 (SD=2.1) and a median of 2. The estimated prevalence of IMP was 42.6%. The characterization of the sample, as well as the prevalence of PMI by variable, is presented in Table 1.

Among the people with IMP, it was found that 13 (20.3%) had at least one severe IMP, while 55 (85.9%) had at least one moderate IMP and 17 (26.5%) had at least one mild IMP. 217 IMPs were observed. The 10 most frequent drugs involved in severe or moderate IMP are described in Table 2, and according to the ATC classification, 4 drugs were in the group of drugs that act

on the cardiovascular system (indapamide, hydrochlorothiazide, amlodipine and losartan) and 4 that act on the nervous system (dipyrone, clonazepam, fluoxetine and nortriptyline).

Table 1. Sample characteristics and prevalence of PMI according to sociodemographic and clinical variables. University of Aging, Brasília, Federal District, Brazil. (n=150)

Variáveis	Amostra n (%)	Prevalência de IMP (%)
Sex		
Female	131 (87,3)	43,5
Male	19 (12,7)	36,8
Age (years)		
60 to 69	121 (80,7)	38,8
70 to 79	26 (17,3)	57,7
80 to 89	3 (2,0)	66,7
Self-reported color/race		
Non-white	92 (61,3)	45,6
White	58 (38,7)	37,9
Education (years of study)		
0 to 4	3 (2,0)	0
5 to 8	8 (5,3)	75,0
≥ 9	139 (92,7)	41,7
Marital status		
Without a partner	123 (82,0)	62,2
With partner	27 (18,0)	48,1
Geographic region of residence in the Federal District		
Central/Center-South	66 (44,0)	42,4
South/Southwest	49 (32,7)	55,1
North	20 (13,3)	30,0
East	8 (5,3)	25,0
West	7 (4,7)	14,3
Health self-assessment		
Very good/good	35 (23,3)	31,4
Fair/poor/very poor	115 (76,7)	46,1
Alcohol abuse		
No	132 (88,0)	42,4
Yes	18 (12,0)	44,4
Cigarette use		
No	122 (81,3)	40,2
Yes	28 (18,7)	53,6
Private health insurance		
No	53 (35,3)	43,4
Yes	97 (64,7)	42,3
Multimorbidity		
No	46 (30,7)	10,9
Yes	102 (68,0)	56,9
Polypharmacy		
No	122 (81,3)	32,0
Sim	28 (18,7)	89,3
Systemic Arterial Hypertension		
In	72 (48,0)	23,6
Yes	77 (51,3)	59,7
Diabetes		
No	120 (80,0)	35,0
Yes	27 (18,0)	74,1
Dyslipidemia		
No	86 (57,3)	32,6
Yes	60 (40,0)	56,7
Hypertriglyceridemia		
No	105 (70,0)	38,0
Yes	34 (22,7)	52,9

Table 2. The most frequent drugs involved in severe or moderate PMIs. University of Aging, Brasília, Federal District, Brazil.

Medicines	ATC Rating	Frequency of severe or moderate IMP (n)
Indapamide	C03BA11	17
Metformin	A10BA02	14
Hydrochlorothiazide	C03AA03	14
Amlodipine	C08CA01	12
Acetylsalicylic acid	B01AC06	12
Losartan	C09CA01	11
Dipyrone	N02BB02	8
Clonazepam	N03AE01	6
Fluoxetine	N06AB03	6
Nortriptyline	N06AA10	6

Discussion

From the analysis of the medications used by the elderly at UniSER in the Federal District, it was possible to estimate the prevalence of PMI at 42.6%. The frequency according to the sociodemographic and clinical variables allows reflection for the planning of possible interventions to be conducted by the health teams to avoid problems related to pharmacotherapy.

It is possible to draw a comparison between this research and that conducted among the elderly in Primary Health Care (PHC) in Lagoa Santa, Minas Gerais. This was a cross-sectional study whose inclusion criteria were people aged 60 years or older, who were part of the drug therapy management service and used at least two medications. The estimated prevalence of IMP was 4.9% in the sample. There were certain variables that contributed to the occurrence of IMP, such as female gender, polypharmacy, and multimorbidity[19].

The Beers Criteria is a crucial tool in clinical practice, as it is possible to analyze the benefits and risks of medications in the elderly, enabling the best choice of drug therapy that can reduce adverse events in the geriatric population. Consequently, it is possible to list potentially inappropriate medications for the elderly[20]. By appropriating these criteria, inappropriate medications were found in the sample studied. Acetylsalicylic acid is contraindicated in the treatment of primary cardiovascular disease as the risk of bleeding is increased. It is suggested to avoid the use of nortriptyline due to its sedative effect and the induction of orthostatic hypotension. Clonazepam, on the other hand, contributes to the process of physical dependence, since the elderly have low tolerability to benzodiazepines and the metabolism of this drug is decreased. Adverse events of this drug include falls, delusions, fractures, and cognitive impairment[20]. Therefore, it is emphasized that PMIs become a concern among the elderly who use these drugs listed.

Dipyrone, indapamide, hydrochlorothiazide, and fluoxetine are also mentioned in the Beers criteria. The indication is to avoid the use of dipyrone for a long time due to the risk of bleeding and peptic ulcer and the association with a gastric protector is effective. Fluoxetine should be used with caution by this age group. Concomitant administration of more than three active agents in the central nervous system, such as antidepressants, antiepileptics, and antipsychotics, should be avoided due to the increased risk of falls and

fractures. Diuretics should be used with caution due to the syndrome of inappropriate antidiuretic hormone secretion which increases antidiuretic hormone secretion, causing water retention and hyponatremia[20].

Metformin is a biguanide considered the first choice for the treatment of type 2 diabetes mellitus. It is responsible for controlling hyperglycemia, but in isolation, it does not cause hypoglycemia. However, it was often responsible for severe or moderate IMPs in geriatric patients. The most common adverse effects are nausea, gastrointestinal upset, vitamin B12 deficiency, and lactic acidosis.[21,22]

The association of metformin with indapamide, hydrochlorothiazide, and gliclazide was commonly described in the pharmacotherapy of the elderly investigated. However, it is essential to stick to these associations, as metformin with other oral antidiabetic drugs increases the risk of hypoglycemia[22]. Diuretics increase glycemic levels, interfering with glucose control through the action of metformin, in addition, the risk of hypokalemia is increased.[23]

The use of diuretics was notorious in the sample studied. Hydrochlorothiazide and indapamide were the most frequent. Hydrochlorothiazide is a thiazide diuretic that acts on the distal tubule. It is considered the first choice for the treatment of stage 1 hypertension since it can contribute to the reduction of events such as stroke and acute myocardial infarction. Due to its lower calcium excretion, it is convenient to administer it in elderly people who are at risk of osteoporosis. The main harmful effects of this drug are erectile dysfunction, loss of potassium and magnesium, and hypochloremic alkalosis, resulting from decreased uric acid excretion[21].

Indapamide has the ability to reduce blood pressure, causing fewer metabolic changes compared to other related drugs[21]. The diuretics described obtained more IMP with the classes of non-steroidal anti-inflammatory drugs (NSAIDs) and antidiabetics, especially dipyrone and metformin. NSAIDs suppress the antihypertensive activity of thiazide and similar diuretics, thus ineffective blood pressure control[24]. The concomitant use of oral antidiabetic drugs and diuretics tends to hyperglycemia, making glycemic control difficult[25].

Amlodipine is a calcium channel blocker used for the treatment of systemic arterial hypertension and related diseases. When starting drug therapy, it is necessary to be prudent with elderly patients, as they are more susceptible to liver or cardiac dysfunctions. Consequently, a lower dose should be administered. The most common adverse events are pulmonary and peripheral edema, heart failure, headache, dizziness, rash, nausea, constipation, and abdominal pain[26].

The drug combinations, which resulted most in MPI with amlodipine, involved antidepressants and statins. One study identified that the association of amlodipine with antidepressants caused swelling of the lower limbs and headache[27]. The concomitant use of amlodipine and simvastatin has a daily limit of 20 mg, as there is a risk of plasma levels of simvastatin increasing, triggering myopathies, including rhabdomyolysis[28].

Among the limitations is the underestimation of the prevalence of PMIs, since the drugs used were self-reported. However, the participants were asked to be in possession of the prescriptions, boxes and package inserts of the medications during the interview. Nor was a clinical investigation carried out on the elderly who presented PMI to ascertain the real damage caused by the

simultaneous use of medications. On the other hand, it is noteworthy that this study carried out with a sample of elderly people living in the community allows a discussion on the subject in order to avoid problems related to pharmacotherapy.

Acknowledgment

Conclusion

The prevalence of MPI among the elderly in the community of the Federal District is in agreement with other Brazilian studies. Health teams should stick to the list of drugs involved in IMP in order to avoid damage. The importance of identification and monitoring of these PMI by health professionals is emphasized in order to promote safe and effective pharmacological therapy. The need for special attention to the elderly is emphasized, as they are more susceptible to adverse events and drug interactions due to the high number of diseases and medications, as well as the physiological changes inherent to aging.

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