Potentially inappropriate medication prevalence and associated factors such as depression and dementia: An analysis of middle-aged and elderly Brazilians

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Abstract

Introduction: PIM use constitutes a public health problem. The objective of this study was to establish the prevalence potentially inappropriate medications (PIM) use and the associated factors, such as signs and symptoms of depression and cognitive deficit among middle-aged and elderly Brazilians.

Methods: A cross-sectional population study was performed with 2,350 people, aged between 55-103 years, registered in the primary health care. PIM was defined by updated 2019 Beers criteria. Studied variables were sociodemographic, lifestyle and health, and signs and symptoms of depression and cognitive deficit. Multinomial regression analysis was executed.

Results: The prevalence of PIM use was 65.4%. Former and current smokers, regular self-perception of health, polypharmacy, and individuals with signs and symptoms of depression and cognitive deficit were significantly associated with PIM use. Antiarrhythmics, antihistamines and antiadrenergic agents were the highest PIM class used for individuals with signs and symptoms of depression and cognitive deficit.

Conclusions: PIM is prevalent among middle-aged people, a population that was previously under-researched, as well as among elderly people. Cognitive impairment alone or together with depression symptoms were associated factor for a PIM use. Knowledge of the pharmacoepidemiology of PIM is an important for the promotion of the rational use of drugs in public health.

Keywords: Potentially inappropriate medication, Middle age, Elderly, Depression, Dementia, Public health.

INTRODUCTION

People worldwide are living longer. Between 2015 and 2050, the proportion of the world's population over 60 years will nearly double from 12% to 22%. (1) The elderly population is one of the most vulnerable in terms of health. One related factor to poor health in the elderly is socioeconomic disadvantage (SED) status. Education, place of residence, health beliefs and behaviour, occupation, income, access to health services and the environment in which people live contribute to low health status in the middle-aged and elderly. (2)

Aging has a great impact on social and health care policy planning, because there is a growing burden of underlying diseases. One difficulty in prescribing for multimorbid patients is the risk of Potentially Inappropriate Medication (PIM). PIM use, may occur whenever the benefits of using some medications are outweighed by the risks and/or whenever avoidance of drug use in specific settings is suggested by scientific evidence. (3) It is a common problem in older persons, ranging from a prevalence of 11.5% to 62.5% of the elderly population. It is associated with adverse effects, hospitalization, morbidity, mortality and high health services cost. (4)

One way to identify PIM prescribing is to use validated screening tools that incorporate explicit prescribing indicators, such as the Beers criteria that is the most widely used approach to assess the quality of drug prescribing among the elderly.(5) This tool provides a list of PIM or drug classes that should generally be avoided in the treatment of elderly.(6) There are other international criteria have been defined with the intent of preventing PIM for elderly.(7-10)

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Traditionally, the focus of PIM has been on older people (especially those ≥65 years) due to the high prevalence of medication use in this age group and the organic aging process. However, there is evidence that multimorbidity is also prevalent in middle-aged people. (11) As yet, there has been little consideration of PIM in this age group.(2)

Depression and cognitive disorders, including dementia, are common in aging. (12,13) Most research on PIM has focused on the elderly rather than depression and dementia specifically.(14,15) Barbiturates, phenytoin, and benzodiazepines are some examples of drug classes that cause deterioration of several basic human abilities: concentration, mental energy, mood and memory.(13)

The objectives were to determine the prevalence of PIM use and associated factors, among them signs and symptoms of depression and cognitive deficit in middle-aged and elderly Brazilians.

METHODOLOGY

Settings

This study involved a subset of patients of the PENCE (Program de Envelhecimento Cerebral) in Porto Alegre City, Brazil. The collection of data related to this study took place from January 2013 to December 2015 and enrolled individuals registered on the Family Health Strategy (FHS) of the Hospital São Lucas catchment area of Porto Alegre City.

The FHS is a proactive community public health care approach implemented by the Brazilian Ministry of Health. It is characterized by active and continued health promotion and monitoring at the community level. The FHS prioritizes locations with people living in SED and identifies and enrolls all local inhabitants based on their dwelling place (geographic-based registration) covered by each FHS team. For the constitution of PENCE, initially and continuously, the community health agents of the FHS teams were trained to use the research tools.

Study design and Population

A cross-sectional population-based survey study design was developed to evaluate the association between the presence of PIM and sociodemographic, lifestyle and health predictors, with a focus on the signs and symptoms of depression and cognitive deficit. The target population of the study was individuals of both sexes that were 55 years of age or older. Adults aged 55 to 59 years were classified as middle-aged, and those aged 60 years or more were called the elderly. For inclusion in the study, it was necessary that the patients used at least one medication continuously.

Outcome and variables studied

The primary determinant was the presence of PIM, which was initially identified using the 2015 Beers criteria.(16) In 2019 Beers criteria went through an update which implied an adjustment of the data presented for this new version.(6) To assess a complete pharmacological evaluation, community health workers revised all drugs regularly used together with participants (and with their representatives if necessary) as part of a wide multidimensional evaluation designed for the PENCE to optimize information since the first home-visit approach in the registration. If the individual were previously enrolled, a complementary home visit included data to improve or complement information of the medical records at the FHS. Subsequently, drugs were coded according to the Anatomical Therapeutic Chemical (ATC) classification system recommended by the World Health Organization. (17) The community health workers have previously received training in order to qualify and standardize the data collection.

In this study, 48 PIM items were identified irrespective of disease diagnoses or conditions. Dimenhydrinate, meclizine, meperidine and mineral oil were not used by any patient. Acetylsalicylic acid and insulin, which are inappropriate only for certain conditions, were not included in this study, because we did not have the information on the dosages and the form of release of these drugs. Drugs that are not available in the Brazil were not considered.

The following covariates from the PENCE study were examined as potential associated factors:

• Socioeconomic status (sex, age, education level, marital status/living with a partner, individual and family income; the last measured in relation to the minimum Brazilian wage of USD 280);

• Lifestyle information, including smoking habits (current, ex, or never) and alcohol use (dichotomous);

• Self-perceived health (examined as very good/good vs. regular vs. bad/very bad), number of comorbidities (according to number of chronic diseases by self-report of the patient);

• Number of drugs prescribed. As polypharmacy users were classified individuals who used five or more medications.

The presence of depressive symptoms was ascertained using the Geriatric Depression Scale abbreviate (GDS-15). Patients with a GDS

score ≥6 were considered depressed. (18) Cognitive function was obtained using the Vellore Screening Instrument for Dementia,(19) which is composed of 10 cognitive patient test items and 10 informant items. To consider presence of signs or symptoms of cognitive deficit, the questionnaire score for the patient needed to be ≤11 points or the questionnaire score for the informant needed to be ≥5 points. Was used the classification ''normal'' or ''impaired''.

Statistical analysis

Data were analyzed using Statistical Package for the Social Sciences (IBM SPSS® Inc. Chicago, Illinois, version 20). The variables were described in terms of frequency, mean and standard deviation. Associations between categorical variables were tested using Pearson's chi-square test. In specific cases, the chi-square test for linear tendency (ordinal variables with few categories) was used. To compare the means between the groups was used analysis of variance (one way ANOVA). In the comparison of dichotomous variables with a quantitative variable large sample size or normal distribution, we used the Student's t-test (considering the equality of variance tested by Levene test). To examine independent factors related to PIM and to improve control for confounding variables a multivariate analysis through multinomial logistic regression was performed. The model entry criterion for independent variables was P<0.20 in the univariate analyses. All variables with P<0.05 remained in the final model. The predetermined level of significance used was P<0.05. Confidence intervals of 95% were used for all calculations.

Ethical considerations

This study was approved by the Ethical Research Committee of the Pontifícia Universidade Católica do Rio Grande do Sul (number 826.858) and Porto Alegre Municipal Secretariat of Health (number 1.003.962), according to the Guidelines and Norms Regulating Research of Resolution 466/12 of the National Health Council of the Ministry of Health.

RESULTS

The 2,350 individuals included in the study were aged between 55 and 103 years (mean age, 67.3 ± 8.6 years), and comprised mostly females (70.5%). Many of these people had four to seven years of education (36.7%), were married or in a stable union (43.5%), and lived with a partner (49.9%). More than half received less than the minimum monthly wage (59.1%) and a little more than half of the households (57.2%) received one to three minimum wages.

The prevalence of PIM was 65.4%. Table 1 shows the association between PIM with sociodemographic variables. The presence of PIM was associated with increasing age (70 years or older) and more years of study (8 years or more). It is important to note that at all levels, PIM prevalence was high, even among middle-aged (63.0%) and illiterate (59.6%) individuals. We found an association between lifestyle and health data, and PIM (Table 2). Individuals who did not consume alcohol, who presented a poorer self-perception of health, who had more number of chronic diseases (especially two or more), and who used polypharmacy, and those with changes in instruments GDS-15, Vellore or both had a higher frequency of PIM use.

To identify associated factors with PIM prescription in prevalent users, multinomial logistic regression analysis was conducted (Table 3). When mutually adjusting for all variables presented in the table, associated factors with PIM prescribing were: being an ex-smoker (OR 1.06; 95% CI 1.00-1.12) or current smoker (OR 1.10; 95% CI 1.02-1.18), regular self-perception of health (OR 1.09; 95% CI 1.02-1.16), taking three or four drugs (OR 1.88; 95% CI 1.65-2.15) -especially those exposed to polypharmacy (OR 2.80; 95% CI 2.48-3.16) - and individuals with instruments Vellore-classified as impaired (OR 1.14; 95% CI 1.03-1.26) and both GDS-15 and Vellore-presented altered results (OR 1.12; 95% CI 1.04-1.21).

Among the drugs which were most frequently prescribed, the study found that the most common was omeprazole (25.5% total population; 39.2% PIM-users) followed by glibenclamide (8.9% total population; 13.6% PIM-users), amitriptyline (6.1% total population; 9.3% PIM-users), ibuprofen (5.5% total population; 8.5% PIM-users) and diazepam (4.3% total population; 6.7% PIM-users).

Table 4 presents the results of the multivariate analysis for the prevalence of PIM use. The results are classified according to their pharmacology class of individuals who exhibit signs and symptoms of depression (GDS-15) and/or cognitive deficit (Vellore). Individuals with symptoms of depression make more use of antiadrenergic agents, centrally acting (OR 3.63; 95% CI 1.35-9.78) and antihistamines for systemic use (OR 5.33; 95% CI 1.93-14.73). Antiarrhythmics (class I and III) (OR 11.14; 95% CI 2.58-48.09), anxiolytics (OR 2.83; 95% CI 1.65-4.86), antidepressants (OR 2.28; 95% CI 1.46-3.55) and antihistamines for systemic use (OR 3.56; 95% CI 1.04-12.21) were more prescribed for those with signs and symptoms of both depression and cognitive impairment. The blood glucose lowering drugs (excl. insulin) (OR 0.53; 95% CI 0.31-0.91) were prescribed less for this latter group. This analysis was adjusted by smoker, self-perception health and number of drugs variables.

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Table 1. Potentially Inappropriate Medication (PIM) according to the sociodemographic variables in the PENCE study (N = 2,350).

VARIABLES		POPULATION		PIM-USERS		PIM NUMBER			
		N (%)		%	P		M ± SD	P	
Gender									
	Male	693 (29.5)		66.1	0.672*		2.01 ± 0.95	0.656#	
	Female	1657 (70.5)		65.2			1.98 ± 1.06		
Age (years)									
	55 - 59	494 (21.3)		63.0	0.001$		1.94 ± 1.02	0.663&	
	60 - 69	986 (42.6)		62.5			2.00 ± 1.08		
	70 - 79	600 (25.9)		69.5			2.03 ± 1.02		
	≥80	235 (10.2)		72.3			1.96 ± 0.88		
Education (years)									
	0	257 (11.2)		59.6	0.005$		2.00 ± 1.08	0.500&	
	1 - 3	604 (26.3)		64.7			2.05 ± 1.04		
	4 - 7	842 (36.7)		66.4			1.95 ± 0.96		
	≥8	580 (25.3)		69.3			2.01 ± 1.10		
Marital status									
	Single	385 (16.9)		62.3	0.411*		1.91 ± 1.00	0.551&	
	Married/stable union	994 (43.5)		66.1			1.99 ± 1.01		
	Divorced	251 (11.0)		68.5			2.03 ± 1.18		
	Widowed	654 (28.6)		65.6			2.03 ± 1.01		
Living with partner									
	No	1073 (50.1)		65.5	0.966*		2.00 ± 1.04	0.855#	
	Yes	1067 (49.9)		65.6			1.99 ± 1.01		
Individual income (minimum wage)									
	0	195 (9.6)		62.1	0.477$		1.99 ± 1.02	0.851&	
	<1	1002 (49.5)		67.8			2.04 ± 1.04		
	≥1 - 2	612 (30.2)		67.3			1.99 ± 1.01		
	≥2	215 (10.6)		60.0			2.02 ± 1.03		
Family income (minimum wage)									
	<1	554 (29.4)		67.0	0.821$		1.99 ± 1.04	0.560&	
	≥1 - 3	1078 (57.2)		65.8			2.02 ± 1.03		
	≥3	252 (13.4)		66.7			2.10 ± 1.06		
TOTAL POPULATION		2350 (100)		65.4			1.99 ± 1.03		

*Pearson's chi-square test; $Chi-square test for linear tendency; #Student t test; &One way ANOVA. M: mean; SD: standard deviation; CI: confidence interval. Minimum wage USD 280,00.

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Table 2. Potentially Inappropriate Medication (PIM) according to the lifestyle and health variables in the PENCE study (N = 2,350).

VARI-ABLES		POPULA-TION		PIM-USERS		PIM NUM-BER			
		N (%)		%	P		M ± DP	P	
Smoker									
	No (never)	976 (43.2)		63.8	0.072*		1.98 ± 1.02	0.402&	
	Ex-smoker	852 (37.7)		68.7			2.03 ± 1.03		
	Yes	430 (19.0)		64.2			1.94 ± 1.04		
Alcohol use									
	No	1716 (78.1)		67.8	0.001*		1.99 ± 1.03	0.699#	
	Yes	482 (21.9)		59.8			1.97 ± 1.00		
Self-per-ceived health									
	Great/Good	913 (39.3)		55.0	<0.001$		1.80 ± 0.93	<0.001&	
	Regular	1179 (50.7)		70.9			2.04 ± 1.01		
	Poor/Very poor	234 (10.1)		78.6			2.29 ± 1.25		
Number of chronic diseases									
	0	257 (11.3)		53.7	<0.001$		1.57 ± 0.86	<0.001&	
	1	877 (38.4)		53.7			1.72 ± 0.93		
	2	623 (27.3)		71.4			2.07 ± 1.00		
	≥3	524 (23.0)		84.5			2.37 ± 1.08		
Number of drugs									
	1 - 2	623 (26.5)		31.3	<0.001$		1.22 ± 0.45	<0.001&	
	3 - 4	721 (30.7)		59.9			1.60 ± 0.70		
	≥5 (Poly-pharmacy)	1006 (42.8)		90.6			2.34 ± 1.09		
Depression and/or cognitive deficit									
	Normal	1305 (56.0)		60.1	<0.001*		1.91 ± 0.95	0.001&	
	Depression	548 (23.5)		70.4			2.13 ± 1.15		
	Cognitive deficit	180 (7.7)		72.2			1.86 ± 0.85		
	Depression and cogni-tive deficit	296 (12.7)		77.7			2.09 ± 1.12		
TOTAL POPULA-TION		2350 (100)		65.4			1.99 ± 1.03		

*Pearson's chi-square test; $Chi-square test for linear tendency; #Student t test; &One way ANOVA. M: mean; SD: standard deviation; CI: confidence interval.

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Table 3. Multivariate analysis of the associated factors with Potentially Inappropriate Medication (PIM) in the PENCE study (N = 2,350).

VARIABLES	PIM-USERS			
	OR	IC 95%	P	
Smoker				
	No (never)	1		
	Ex-smoker	1.06	(1.00 - 1.12)	0.044
	Yes	1.10	(1.02 - 1.18)	0.018
Self-perceived health				
	Great/Good	1		
	Regular	1.09	(1.02 - 1.16)	0.011
	Poor/Very poor	1.07	(0.980 - 1.17)	0.130
Number of drugs				
	1 - 2	1		
	3 - 4	1.88	(1.65 - 2.15)	<0.001
	≥5 (Polypharmacy)	2.80	(2.48 - 3.16)	<0.001
Depression and/or cognitive deficit				
	Normal	1		
	Depression	1.02	(0.96 - 1.09)	0.473
	Cognitive deficit	1.14	(1.03 - 1.26)	0.009
	Depression and cognitive deficit	1.12	(1.04 - 1.21)	0.002

Regression logistic multinomial. OR: odds ratio; CI: confidence interval.

Table 4. Prevalence of Potentially Inappropriate Medication (PIM), according to their pharmacology class, among individuals who exhibit signs and symptoms of depression and/or cognitive deficit.

ATC	VARIABLE	NORMAL		DEPRESSION	COGNITIVE DEFICIT		DEPRESSION AND COGNITIVE DEFICIT	
		n (%)	n (%)	OR (CI 95%)	n (%)	OR (CI 95%)	n (%)	OR (CI 95%)
A02B	Drugs for peptic ulcer and gastro-oesophageal reflux	305 (38.9)	168 (43.5)	1.09 (0.83 - 1.43)	44 (33.8)	0.75 (0.49 - 1.13)	87 (37.8)	0.92 (0.65 - 1.28)
A10B	Blood glucose lowering drugs, excl. Insulins	120 (15.3)	52 (25.0)	0.86 (0.59 - 1.26)	15 (11.5)	0.71 (0.39 - 1.30)	21 (9.1)	0.53 (0.31 - 0.91)***
C01A	Cardiac glycosides	19 (2.4)	18 (4.7)	1.74 (0.86 - 3.52)	5 (3.8)	1.87 (0.67 - 5.18)	7 (3.0)	1.29 (0.49 - 3.38)
C01B	Antiarrhythmics, class i and iii	3 (0.4)	4 (1.0)	3.59 (0.78 - 16.61)	1 (0.8)	2.10 (0.21 - 20.49)	6 (2.6)	11.14 (2.58 - 48.09)**

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C02A	Antiadren-ergic agents, centrally acting	7 (0.9)	11 (2.8)	3.63 (1.35 - 9.78)***	1 (0.8)	0.88 (0.11 - 7.27)	3 (1.3)	1.71 (0.42 - 7.01)
C02C	Antiadren-ergic agents, peripherally acting	17 (2.2)	4 (1.0)	0.50 (0.15 - 1.62)	4 (3.1)	1.49 (0.49 - 4.56)	3 (1.3)	0.59 (0.15 - 2.31)
M01A	Antiinflam-matory and antirheumat-ic, non-ste-roids	86 (11.0)	41 (10.6)	0.89 (0.58 - 1.37)	14 (10.8)	0.99 (0.54 - 1.82)	28 (12.2)	1.06 (0.64 - 1.75)
M03B	Muscle relax-ants, centrally acting agents	20 (2.6)	10 (2.6)	0.77 (0.32 - 1.84)	1 (0.8)	0.28 (0.04 - 2.16)	6 (2.6)	0.60 (0.20 - 1.78)
N03A	Antiepileptics	32 (4.1)	28 (7.3)	1.62 (0.93 - 2.83)	6 (4.6)	1.10 (0.45 - 2.70)	19 (8.3)	1.74 (0.91 - 3.33)
N05B	Anxiolytics	38 (4.8)	36 (9.3)	1.47 (0.88 - 2.46)	9 (6.9)	1.32 (0.60 - 2.92)	34 (14.8)	2.83 (1.65 - 4.86)*
N06A	Antidepres-sants	78 (9.9)	50 (13.0)	1.38 (0.92 - 2.06)	13 (10.0)	0.99 (0.53 - 1.85)	47 (20.4)	2.28 (1.46 - 3.55)*
R06A	Antihista-mines for systemic use	6 (0.8)	15 (3.9)	5.33 (1.93 - 14.73)**	1 (0.8)	1.00 (0.12 - 8.41)	6 (2.6)	3.56 (1.04 - 12.21)***

OR: odds ratio; CI: confidence interval. Regression logistic multinomial. As reference was used the patients who did not present any changes in the GDS-15 and Vellore instruments. The p-values were adjusted by the variables of: smoker, self-perceived health, and number of drugs.

DISCUSSIONS

Our study revealed a PIM very high prevalence rate in community-dwelling middle-age and elderly people, and the rate rose with increasing age. The overall prevalence of inappropriate prescription in elderly people showed wide variations: from 2.9% to 38.5%. (20) In national studies, the prevalence ranged from 20.6% to 48.0%.(24-27) Few studies have been conducted with middle-aged individuals to assess the PIM prevalence. Using the PROMPT criteria, developed specifically for this population, the prevalence of PIM use was 42.9% in the Republic of Ireland and 21.1% in Northern Ireland. (21) Several factors may contribute to this variation. Different countries use different sets of medications due to registration issues. There is, hence, no universal list of medications and criteria for assessing the overall medication use by patients.

If the higher prevalence of PIM observed is related to SED, this relationship could be driven by a number of factors. Lower socioeconomic status and health literacy can have an adverse effect on the quality of patient-doctor communication and the degree of patient involvement in shared decision making. These circumstances, in turn, may potentially impact on the quality of care and the risk of PIM.(22,23) Poorer health has been reported in SED areas,(24) especially in patients with multimorbidity(11,25) and exposed to polypharmacy,(26) with an increased prevalence of long-term conditions including depression, anxiety, pain and coronary heart disease.(27) However, most of these studies were carried out in high-income countries and deserve some careful examination since comparative groups' levels of health literacy and income are very different from those in low- and middle-income countries.

Associated factors for PIM use that remained in the multivariate analysis are, in part, similar to those regularly found in the literature. (21,28) In some studies, regular self-reported health and being an ex-smoker or current smoker were correlated with use of an increasing number of drugs taken,(29,30) and showed the direct relationship of these variables with the increased frequency of PIM use. The most important predicting factor the probability of PIM use was the polypharmacy; this strong association has also been evident among the middle-aged and older populations. (21,31) The most likely hypothesis is that each drug used had a certain probability of being inappropriate, thus proportionally increasing a subject's likelihood of undergoing an inappropriate therapy with each additional medication. Similarities in PIM use between middle-aged and older people may suggest that interventions aimed at improving inappropriate prescribing could include both age groups. Thus far, studies aimed at improving appropriate polypharmacy have been performed mostly in

older patients and have shown some evidence of a reduction in PIM. (32,33)

Cognitive impairment alone, or in conjunction with symptoms of depression, was an associated factor for a PIM prescription. Older people with dementia and/or depression symptoms are particularly vulnerable to use of a large number of drugs, their effects and adverse reactions.(14,34) Prior research in dementia patients has described that PIM may exacerbate cognitive impairment,(35,36) or relied on prescription medication data to calculate PIM rates in dementia patients,(37) or sought to demonstrate that PIM use increases the risk of developing dementia(38) Perhaps there is a bidirectional relationship between PIM and the risk for dementia. It is therefore important to identify and pay attention to PIM use, put the drug use into perspective and carry out a careful risk-benefit evaluation when considering prescribing to members of this group.

The five most common drugs of PIM used by patients in our sample were omeprazole, glibenclamide, amitriptyline, ibuprofen and diazepam. A recent systematic review and meta-analysis of published studies demonstrated an increased risk of dementia among users of proton pump inhibitors (e.g., omeprazole) and described the possible molecular basis of this association.(39) There is some biological plausibility to the hypothesis that proton pump inhibitors can cross the blood-brain barrier.(40) They may increase both production(41) and degradation(42) of amyloid, at least in animal models, and bind to tau(40) There is also evidence of reduced levels of B12 and other nutrients among proton pump inhibitors users that could possibly relate to an increased risk of dementia.(43) Prescriptions of high-risk medications expose patients to frequent and severe adverse drug events. Alternative low-risk medications should be prescribed when available. There is, therefore, a need to move towards interventions that can improve the quality of medication prescriptions in all age groups. (20)

The patterns of inappropriate prescriptions vary considerably within therapeutic classes. The most frequently reported PIM classes are psychotropic or cardiovascular drugs, since most PIM has been identified in these groups of drugs. (20,44) Individuals with cognitive impairment and depression symptoms were at increased use of antiarrhythmics. Amiodarone was the most widely used medication of this class and is associated with multiple toxicities such as thyroid disorders, QT prolongation and pulmonary disorders. (16) In the management of arrhythmias in the elderly, it is important to evaluate the risk and benefit of amiodarone and, when indicated, it is essential to monitor the process of its use to enable the prevention or early identification of adverse events.

There are previous evidence suggesting that patients with cognitive impairment and dementia make greater use of antidepressants with anticholinergic properties (e.g., amitriptyline) and anxiolytics (e.g., benzodiazepines). (45,46) Amitriptyline, the third most frequent active agent in our analysis, is often used to treat neuropathic pain. However, it is common to use this medication for psychiatric symptoms, such as a depressive mood or insomnia. The use of antidepressants may cause clinically relevant adverse effects due to their anticholinergic activity, and their ability to induce sedation and orthostatic hypotension, and to stimulate the central nervous system. (6) They should be used with caution, due to the damage they can cause in the psychomotor function, increasing the risk of falls and fractures.(47) Benzodiazepines also were often used in older adults for the treatment of insomnia, depression, or anxiety. But in older adults, they may increase sensitivity to benzodiazepines and decrease metabolism of long-acting agents; in general, all benzodiazepines increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle crashes in older adults. (6) In addition, they are used often to treat behavioral symptoms of dementia, despite the lack of evidence for their effectiveness.(48)

Individuals with only depressive symptoms or with associated cognitive impairment have a greater chance of using medications classified as antihistamines. This finding is particularly worrisome because antihistamines present strong anticholinergic properties and are known to increase the risk of cognitive impairment and falls in older adults. (16) Furthermore, the risk of antihistamine use as a sleep aid may be particularly high in this population given the high prevalence of sleep disturbance in persons with dementia and depression. (49) Unfortunately, despite these risks, the use of non-prescription PIMs is indiscriminate and may go undetected.

We acknowledge that our study has limitations. Our results apply to the population belonging to FHS, that is, focused on those in primary health care, and thus may not be representative of the entire Brazilian population. The PIM pattern in our study is completely influenced by the medications available in the Brazilian Unified Health System. This is due to the striking characteristic of the studied population being individuals with SED conditions. The Brazilian Unified Health System list of available drugs is designed for the general population and the specifics of the elderly have not been considered. In order to assess health conditions, we used as a surrogate the data we thought to be the most reliable: the number of medications used, number of chronic diseases, and self-perceived health status. The lack of data on dosage (acetylsalicylic acid) and the form of release (insulin) could underestimate the consumption of PIM, since these were excluded from the analysis. Thus, for evaluation of the PIM only the active principles of the drugs were considered, dose information, renal alterations and drug interactions were not evaluated. The limitations of a cross-sectional and descriptive study should be considered, such as the lack of quality control of the information provided and the lack of cross-checks between variables, and the impossibility of establishing the temporality of the associated factors. Adjustments concerning the lifestyle and health data factors within the multinomial logistic regression models lessened these differences.

CONCLUSIONS

This study has shown that PIM is prevalent in middle-aged people, a population previously under-researched, and elderly people. By targeting the aging population, the middle-aged individuals will be the focus for health provision in the future. The knowledge of the pharmacoepidemiology of PIM is important information for the promotion of the rational use of drugs in primary health care. Cognitive impairment alone, or together with depressive symptoms, was an associated factor for a PIM prescription. Antiarrhythmics (classes I and III), centrally acting antiadrenergics, antihistamines, anxiolytics and antidepressants were the most commonly PIM class used. The prevention and recognition of PIM represents an area of concern in the delivery of healthcare. Conducting medication reviews is a method often recommended to identify and solve PIM, to optimize drug treatment and to improve patient health outcomes. These results could help health professionals and panel experts to plan future Brazilian criteria.

Conflict of interest statement

The authors declare no conflict of interest regarding the present study. This work had no financial support. The present form of the manuscript has been approved by all of the authors, and all authors have significantly contributed to the content of the manuscript.

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