Potentially inappropriate medications prescribed to patients at the Reference Center in Health Care for Old People

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Abstract

Objective: To analyze the pharmacotherapeutic profile of the old people assisted at a Reference Center in Health Care for Old People regarding the use of potentially inappropriate medications (PIM) using three screening criteria and to determine factors associated with the prescription of PIM. Method: Cross-sectional study with data obtained by retrospective review of the medical records of the old people, attended between 2017 and 2018 by a geriatric doctor. To identify the PIM, the Beers Criteria, the Screening Tool of Older Persons' Potentially Inappropriate Prescriptions (STOPP) and the Brazilian Consensus on Potentially Inappropriate Medications for Old People were used. Characteristics related to the sociodemographic profile (age and sex), lifestyle (smoking and alcohol consumption), clinical (diseases) and pharmacotherapeutic (medications and Medication Regimen Complexity Index - MRCI) were evaluated. *Results:* 406 medical records were analyzed and 3,059 prescription medications were identified, of which 32.1% are PIM according to STOPP Criteria, 14.4% by the Brazilian Consensus and 11.7% by the Beers Criteria. In total, 81.1% of the old people had at least one PIM. Poisson regression demonstrated an association between the prescription of PIM with polypharmacy, a greater number of signs and symptoms and a higher MRCI value in at least one of the criteria. The strength of agreement between the PIM criteria was moderate. *Conclusions:* Most of the analyzed medical records had at least one prescribed PIM, and the STOPP Criteria identified a greater amount of PIM. Strategies must be implemented to improve the pharmacotherapy of old people with attention to those who have factors associated with PIM in their profile.

Keywords: Health of the Elderly. Potentially Inappropriate Medicaton List. Polypharmacy.

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INTRODUCTION

The aging process is generally associated with the appearance of multiple diseases and, consequently, with the greater need to implement pharmacological therapies[1-3]. Thus, the use of medication is one of the main therapeutic approaches for controlling diseases and improving the expectation and quality of life of old people[1-3]. In the United States, in 2015, about 90% of the old people over 65 years old used at least one medication[3]. In Brazil, in 2015, the prevalence of use of more than five medications by old people in primary care, characterizing polypharmacy, was 18.1%[4].

The use of multiple medications, associated with the natural physiological modifications of aging, leads to the need for a rational prescription of medications, given the propensity of medication-related problems (MRP)[1-3] and associated damages, such as mental confusion, falls and functional decline[5]. MRP in old people may be associated with the use of Potentially Inappropriate Medications (PIM), medications for which the risk of adverse events exceeds the benefits they can offer. A medication can also be considered inappropriate when used in excessive doses or for a prolonged period, in combination with other medications, when there is duplication of therapeutic classes, drug-disease interactions and underprescription[6-10].

The proportion of old people who use some PIM depends on the location studied and the tools used for analysis[11], but about 20% to 65% of the old people use at least one PIM[5]. The evaluation of the discharge prescription of old people from a public hospital in Minas Gerais, Brazil, showed that 58% included some PIM[12]. The use of PIM is associated with the occurrence of adverse drug reactions (ADRs), hospitalizations and increased health costs[11,13,14]. It is estimated that PIM are related to a 44% higher chance of ADR and 27% higher chance of hospitalization[11]. Associations between PIM and higher chance of death (OR 2.22) has been reported, especially with medications that can increase the risk of falls, such as benzodiazepines[15].

The need to monitor the use of PIM in the old people population led to the development of lists presenting implicit (based on clinical judgment) and explicit (based on the use of defined criteria) criteria for the classification of PIM[16]. The Beers Criteria[8] was the first list launched and, together with the Screening Tool of Older Persons' Potentially Inappropriate Prescriptions (STOPP)[17] are the most referenced tools[11]. In Brazil there is the Brazilian Consensus on Potentially Inappropriate Medication for Old People (BCPIM), developed based on the criteria of Beers and STOPP as a way to obtain a tool that reflected the reality of the country's prescriptions[18].

Estimates of the prevalence of PIM represent an important indicator of the quality of health care, regarding pharmacotherapy[6]. Knowing the PIM prescription pattern and investigating groups most affected by the use of these medications can help rationalize pharmacotherapy, improving old peoples' health outcomes. Thus, this study aimed to analyze the pharmacotherapeutic profile of the old people assisted at a Reference Center in Health Care for Old People (CRASPI) regarding the use of PIM using three screening criteria and to determine factors associated with the prescription of PIM.

METHOD

A cross-sectional study, which used a retrospective review of medical records of old people treated in secondary health care by geriatric physicians. The study was approved by the Research Ethics Committee, CAEE nº 77479917.1.0000.5083.

The study was carried out in a specialized secondary care clinic, CRASPI, located in a city of about 1.5 million inhabitants in the Midwest region of Brazil. Patients are seen at this unit via the Brazilian Unified Health System (SUS). The primary care physician makes the referral via regulation and, according to the clinical picture, the old people are selected by a regulating physician from the Municipal Health Department according to the availability of vacancies for care at CRASPI. The old people are accompanied by a geriatrician and are treated on average every three to six months as needed, depending on the adaptation to the new therapeutic regimes established, requested tests and identified health problems. The returns are scheduled by the physician himself at the end of each consultation.

The study sample was randomly selected among the 1045 old people attended at the health unit during 2017 and 2018. The parameters considered for calculating the sample size were a margin of error of 5%, frequency expectation of 50% for all observed characteristics and 99% confidence level. Thus, the defined sample size was 406 patients.

Numbers were randomly generated between 1 and 1,045 for patients registered in the unit's system. Subsequently, an online random-number generator was used to select the sample, with 406 different numbers being drawn. Randomized records that did not meet the inclusion criteria were excluded from the sample and a new drawing was carried out to replace it. Thus, the sample number (n=406) corresponds to the total of medical records analyzed in this study. Medical records were included in which there was a record of at least one medication prescribed by the geriatrician, presenting dosage data.

Data were collected by a clinical pharmacist from January to November 2018. Training sessions were performed as a pre-test before retrospective analysis of medical records to decrease variability. Due to the fact that in the medical records, in the item medications in use, the information "according to the previous prescription" or the expression "keep the others" appears, it was necessary to analyze the latest prescriptions to actually identify all the medications that were prescribed to the old person by the geriatrician. In this way, the last four consultations were analyzed to obtain sufficient information regarding the prescribed medications, diagnosed diseases and signs and symptoms.

The prescribed medications were categorized as appropriate or inappropriate, using three lists of explicit criteria for PIM assessment: Beers Criteria (2015 version)[6], STOPP Criteria (2015 version)[17] and BCPIM (2016 version)[18]. As a dependent variable, PIM was considered assessed by each of these criteria.

Regarding the Beers Criteria[6], the following lists were considered to classify medications as PIM: PIM to be avoided for old people; PIM for use in old people with certain clinical conditions/diseases; potential interactions that should be avoided and; PIMs that should be avoided or reduced in dose depending on kidney function.

In view of the STOPP[17] criteria, the items in section A (indication of the drug) were not considered: criteria A1 (any drug prescribed without clinical evidence based on evidence) and A2 (any drug prescribed beyond the recommended duration, in which the duration of treatment is well defined), due to the lack of necessary information for such analysis. Finally, regarding BCPIM, the lists were considered: medications that should be avoided regardless of clinical conditions and medications that should be avoided in certain clinical conditions/diseases[18].

The variables considered independent in the study were: sociodemographic profile (age and sex); profile of lifestyle habits (alcohol and tobacco consumption); clinical profile [length of follow-up at the service (in months), diagnosed diseases (types and quantity) and signs/symptoms (types and quantity)]; and the pharmacotherapeutic profile [prescription medications, number of medications and Medication Regimen Complexity Index (MRCI)].

The prescribed medications were identified by the active principle and classified up to the second level of the Anatomical Therapeutic Chemical (ATC) classification system[19]. The number of medications prescribed was assessed to determine the practice of polypharmacy (prescription of ≥5 medications)[20]. The MRCI was calculated, considering the actions necessary for the administration of the medication, such as pharmaceutical form, frequency of doses and additional information considered when using the medication. This index is divided into three sections (A/B/C), each item has a specific weight and the final MRCI value is obtained by adding the scores of each section[21,22]. The complexity of pharmacotherapy was classified according to the scores: MRCI ≤9 (low); MRCI >9 and ≤16.5 (average) and MRCI >16.5 (high)[23].

Descriptive statistics was used to summarize the distribution of patients' characteristics in general and considering those with and without PIM prescription for each of the criteria. Categorical variables were presented in relative and absolute frequencies. The normality of numerical data was assessed by the Kolmogorov-Smirnov test and medians followed by the interquartile range (IQR) were calculated for data with non-normal distribution. Inferential analysis used the chi-square and Fisher's exact tests,

with a significance level of 5%. Poisson regression with robust variance was used and variables with $p<0.20$ in the bivariate analysis were included in the multiple model. The measure of association between variables was Prevalence Ratio (PR), with a 95% Confidence Interval (CI). The Kappa coefficient (k) was used to assess the degree of agreement of the three instruments regarding the presence or absence of PIM among patients. As a parameter for classifying the degree of agreement, the following kappa values were adopted: <0 poor; 0.01-0.20 slight; 0.21-0.40 fair; 0.41-0.60 moderate; 0.61-0.80 substantial; and 0.81-1.0 almost perfect[24].

RESULTS

Among the 406 old people who had their medical records analyzed, 70.4% (n=286) were women, with a median age of 81 years (IQR=75-87). The old people had a median follow-up time in the service of 72 months (IQR=30-96) and as for lifestyle habits involving alcoholism and smoking, 1.5% (n=6) of the medical records had the information of alcohol consumption and 3.9% (n=16) of tobacco. The characteristics of the studied sample and the presence of PIM in the prescription are shown in Table 1.

Regarding clinical characteristics, a total of 2,655 diseases were identified in the medical records, with a median of six (IQR=5-8) diseases per patient. The most frequent diseases in the studied group were systemic arterial hypertension (n=328, 12.4%), depression (n=208, 7.8%), dyslipidemia (n=180, 6.8%), osteoporosis (n=177, 6.7%), diabetes mellitus (n=118, 4.4%) and arthrosis (n=115, 4.3%). In total, 1,441 signs/symptoms were reported in the medical records, representing a median of three (IQR=2-5) signs/symptoms per old person. The main signs/symptoms found were fall (n=133, 9.3%), insomnia (n=98, 6.8%), chronic constipation (n=86, 6.0%), lower limb edema (n=76, 5.3%), arthralgia (n=74, 5.1%) and dyspepsia (n=61.4.2%).

As for the pharmacotherapeutic profile, a total of 3,059 medications were prescribed. The old people used a median of seven (IQR=6-9) medications. The prevalence of polypharmacy was approximately 86.0% (n=349), and 78.8% (n=320) of patients with at least one PIM were categorized as patients taking five or more medications. The complexity of pharmacotherapy, calculated by the MRCI, had a median score of 19 (IQR=14-24.5) and 61.3% (n=249) of the old people had a ≥16.5 score (high complexity).

When considering the three criteria used together, of the 406 patients, 87.9% (n=357) had at least one prescribed PIM. When each criterion was analyzed separately, 84.4% (n=343) of the old people had at least one PIM according to the STOPP criteria; 66.8% (n=271) by BCPIM and 56.9% (n=231) by Beers' Criteria.

Regarding the 3,059 medications prescribed, it was found that 32.1% (n=983) were PIM according to the STOPP Criteria; 14.4% (n=441) by BCPIM and; 11.7% (n=357) by the Beers Criteria. For each old person, there was a median prescription of two PIMs according to the STOPP Criteria, and at least one PIM according to the Beers Criteria and the BCPIM.

The medications that act on the cardiovascular system were the most prescribed (28.9%, n=887). Of these, 27.0% (n=267) were considered as PIM by the STOPP Criteria; 8.6% (n=38) by BCPIM; and 1.2% (n=4) by the Beers Criteria. The medications that act on the nervous system were the second most prescribed class (26.7%, n=817), with 63.5% (n=226) being inappropriate according to the Beers Criteria; 52.7% (n=232) by BCPIM and; 36.4% (n=361) by the STOPP Criteria (Table 2).

Omeprazole, quetiapine and escitalopram were the most frequently prescribed PIMs according to the three criteria used. Omeprazole was considered inappropriate in 10.7% (n=105) of the prescriptions by the STOPP Criteria, in 23.8% (n=105) by the BCPIM and in 17.9% (n=64) by the Beers Criteria. The distribution of the main prescribed PIMs, according to each criterion, are described in Table 3.

Poisson regression demonstrated an association between a higher prevalence of PIM prescription with polypharmacy, a greater number of signs and symptoms and a higher MRCI value in at least two of the studied criteria (Table 4). As for the agreement between the criteria in the identification of individuals with PIM prescription, moderate agreement was observed when the three criteria were

evaluated together (k=0.567, 95% CI=0.511-0.623). The agreement between the Beers criteria and the BCPIM showed a higher kappa value (k=0.659, 95% CI=0.584-0.734) (Table 5).

Table 1. Sociodemographic, clinical and pharmacotherapeutic characteristics of the old people attended at the referral center regarding the prescription of inappropriate medications (n = 406). Goiânia, GO, 2018.

Variables	Total n (%)	Beers criteria n (%)	*p*	*STOPP* criteria n (%)	*p*	BCPIM n (%)	*p*	All criteria n (%)	*p*
Sex									
Male	120(29.6)	61(15.0)	0.110[b]	99(24.4)	0.495[b]	76(18.7)	0.344[b]	103(25.4)	0.401[b]
Female	286(70.4)	170(41.9)		244(60.1)		195(48.0)		254(62.6)	
Age (years)									
≤ 70	41(10.1)	22(5.4)	0.659[b]	35(8.6)	0.869[b]	28(6.9)	0.825[b]	36(8.9)	0.979[b]
> 70	365(89.9)	209(51.5)		308(75.9)		243(59.9)		321(79.1)	
Tobacco Consumption									
Yes	16(3.9)	8(2.0)	0.570[b]	15(3.7)	0.485[a]	10(2.5)	0.713[b]	15(3.7)	0.705[a]
No	390(96.1)	223(54.9)		328(80.8)		261(64.3)		232(57.1)	
Alcohol consumption									
Yes	6(1.5)	3(0.7)	1.000[a]	6(1.5)	0.596[a]	4(1.0)	1.000[a]	6(1.5)	1.000[a]
No	400(98.5)	288(70.9)		337(83.0)		267(65.8)		351(86.5)	
Number of signs/symptoms									
None	17(4.2)	5(1.2)	0.019[b]	9(2.2)	0.000[b]	6(1.5)	0.005[b]	11(2.7)	0.003[b]
≥ 1	389(95.8)	226(55.7)		334(82.3)		265 (65.3)		346(85.2)	
Number of diseases									
1 to 5	156(38.4)	78(19.2)	0.027[b]	125(30.8)	0.056[b]	87(21.4)	0.000[b]	128(31.5)	0.004[b]
6 to 15	250(61.6)	153(37.7)		218(53.7)		184(45.3)		229(56.4)	
Number of medicines									
1 to 4	57(14.0)	21(5.2)	0.001[b]	36(8.9)	0.000[b]	20(4.9)	0.000[b]	37(9.1)	0.000[b]
≥ 5 (polypharmacy)	349(86.0)	210(51.7)		307(75.6)		251(61.8)		320(78.8)	
Follow-up time (in months)									
≤ 12	20(4.9)	9(2.2)	0.271[b]	18(4.4)	0.752[a]	12(3.0)	0.511[b]	18(4.4)	1.000[a]
> 12	386(95.1)	222(54.7)		325(80.1)		259(63.8)		339(83.5)	
Pharmacotherapy Complexity Index									
≤ 16.5	164(40.4)	80(19.7)	0.007[b]	118(29.1)	0.000[b]	88(21.7)	0.000[b]	126(31.0)	0.000[b]
> 16.5	242(59.6)	151(37.2)		225(55.4)		183(45.1)		231(56.9)	

[a]Fisher's exact test; [b]Chi-square test; p<0,05; *STOPP: Screening Tool of Older Persons' Potentially Inappropriate Prescriptions;* BCPIM: Brazilian Consensus on Potentially Inappropriate Medication for old people.

Table 2. Distribution of prescribed and potentially inappropriate medications for old people classified by pharmacological group according to the ATC classification[a] (n=3.059). Goiânia, GO, 2018.

Anatomical group/Therapeutic group	Prescribed n(%)	STOPP criteria n(%)	BCPIM n(%)	Beers criteria n(%)
Cardiovascular system	887(28.9)	267(27.0)	38(8.6)	4(1.2)
Agents acting on the renin-angiotensin system - C09	255(8.3)	99(10.0)	-	-
Lipid-modifying agents - C10	237(7.7)	-	-	-

to be continued

Continuation of Table 2

Anatomical group/Therapeutic group	Prescribed n(%)	STOPP criteria n(%)	BCPIM n(%)	Beers criteria n(%)
Beta blocking agents - C07	114(3.7)	36(3.6)	3(0.7)	-
Diuretics - C03	110(3.6)	66(6.7)	1(0.2)	-
Calcium channel blockers - C08	82(2.7)	38(3.9)	-	-
Cardiac therapy - C01	42(1.4)	16(1.6)	27(6.1)	1(0.3)
Antihypertensives - C02	19(0.6)	11(1.1)	7(1.6)	3(0.9)
Vasodilators - C04	2(0.1)	1(0.1)	-	-
Nervous system	817(26.7)	361(36.4)	232(52.7)	226(63.5)
Psychoanaleptics - N06	442(14.5)	169(17.1)	87(19.9)	87(24.5)
Psycholeptics - N05	127(4.1)	126(12.7)	107(24.1)	114(31.9)
Antiepileptic - N03	95(3.1)	26(2.6)	25(5.7)	13(3.7)
Analgesics - N02	90(2.9)	14(1.4)	13(3.0)	12(3.4)
Antiparkinsonian medications - N04	38(1.25)	19(1.9)	-	-
Other nervous system drugs - N07	25(0.8)	7(0.7)	-	-
Alimentary tract and metabolism	656(21.4)	200(20.3)	130(29.5)	80(22.4)
Mineral Supplements - A12	266(8.7)	24(2.4)	-	-
Medicines used in diabetes - A10	172(5.6)	47(4.8)	1(0.2)	1(0.3)
Drugs for acid-related disorders - A02	137(4.5)	129(13.1)	129(29.3)	79(22.1)
Blood and hematopoietic organs	254(8.3)	93(9.4)	13(3.0)	34(9.5)
Antithrombotic medications - B01	209(6.8)	83(8.4)	13(3.0)	34(9.5)
Anti-anemic preparations - B03	45(1.5)	10(1.0)	-	-
Skeletal muscle system	243(7.9)	45(4.6)	8(1.8)	5(1.4)
Medicines for treating bone diseases - M05	144(4.7)	42(4.3)	-	-
Anti-inflammatory and anti-rheumatic products - M01	79(2.6)	-	8(1.8)	-
Muscle relaxants - M03	7(0.2)	3(0.3)	5(1.1)	5(1.4)
Systemic hormonal preparations. excluding sex hormones and insulins	93(3.1)	1(0.1)	2(0.5)	1(0.3)
Corticosteroids for systemic use - H02	4(0.1)	1(0.1)	2(0.5)	1(0.3)
Respiratory system	61(2.0)	8(0.8)	5(1.1)	5(1.4)
Medicines for obstructive airway diseases - R03	51(1.7)	3(0.3)	-	-
Antihistamines for systemic use - R06	6(0.2)	5(0.5)	5(1.1)	5(1.4)
Urinary genito system and sex hormones	21(0.7)	8(0.8)	7(1.5)	2(0.6)
Urological - G04	18(0.6)	8(0.8)	5(1.1)	1(0.3)
Urinary genito system and sex hormones	21(0.7)	8(0.8)	7(1.5)	2(0.6)
Sex hormones and system modulators - G03	2(0.1)	-	2(0.4)	1(0.3)
Anti-infectives for systemic use	1(0.03)	-	1(0.2)	-
Antimicrobials - J01	1(0.03)	-	1(0.2)	-
Others	500(15.8)	12(1.2)	7(1.6)	3(0.9)
Phytotherapics	8(0.3)	n/a	n/a	n/a
Total	3059(100)	983(100)	441(100)	357(100)

[a]Anatomic Therapeutic and Chemical Classification; - None available; n/a: Not applicable; *STOPP: Screening Tool of Older Persons' Potentially Inappropriate Prescriptions;* BCPIM: Brazilian Consensus on Potentially Inappropriate Mediciation for Old People.

Table 3. Distribution of most prescribed PIM according to the Beers, STOPP and BCPIM criteria (n=406). Goiânia, GO, 2018.

Medicines	*STOPP* criteria n (%)	BCPIM n (%)	Beers criteria n (%)
Acetylsalicylic acid	51(5.2)	7(1.6)	28(7.8)
Sodium alendronate	41(4.2)	*	*
Alprazolam	9(0.9)	9(2.0)	9(2.5)
Amiodarone	10(1.0)	25(5.7)	**
Amlodipine	32(3.3)	*	*
Citalopram	18(1.8)	30(6.8)	35(9.8)
Clonazepam	23(2.3)	22(5.0)	22(6.2)
Donepezila	37(3.8)	1(0.2)	1(0.3)
Escitalopram	28(2.8)	26(5.9)	30(8.4)
Esomeprazole	9(0.9)	9(2.1)	4(1.1)
Gliclazide	31(3.2)	*	*
Hydrochlorothiazide	50(5.1)	**	*
Losartana	63(6.4)	*	*
Omeprazole	105(10.7)	105(23.8)	64(17.9)
Pantoprazole	14(1.4)	14(3.2)	10(2.8)
Quetiapine	60(6.1)	47(10.7)	53(14.8)
Risperidone	11(1.1)	9(2.0)	9(2.5)
Sertraline	5(0.5)	6(1.4)	9(2.5)
Trazodone	33(3.4)	6(1.4)	1(0.3)
Zolpidem	13(1.3)	12(2.7)	13(3.6)
Others	452(46)	133(30.2)	75(21)
Total	**983(100)**	**441(100)**	**357(100)**

PIM: Potentially inappropriate medications; *STOPP: Screening Tool of Older Persons' Potentially Inappropriate Prescriptions);* BCPIM: Brazilian Consensus on Potentially Inappropriate Medication for Old People; *Medication not considered potentially inappropriate by the criterion; **No old person had the conditions specified for the medication to be classified as potentially inappropriate.

Table 4. Factors associated with the prescription of potentially inappropriate medications for old people according to Poisson regression with robust variance (n=406). Goiânia, GO, 2018.

Variables	Beers criteria		*STOPP* criteria		BCPIM	
	p	*PR* (95%CI)	*p*	*PR* (95%CI)	*p*	*PR* (95%CI)
Polypharmacy	0.031	1.53 (1.04-2.25)	-	-	0.004	1.76 (1.19-2.60)
Number of signs/ symptoms (≥1)	-	-	0.026	1.60 (1.05-2.43)	0.040	1.91 (1.03-3.56)
MRCI (>16.5)	-	-	0.011	1.17 (1.03-1.33)	0.038	1.21 (1.01-1.47)

CI: Confidence interval; PR: Prevalence Ratio; *STOPP: Screening Tool of Older Persons' Potentially Inappropriate Prescriptions;* BCPIM: Brazilian Consensus on Potentially Inappropriate Medication for Old People; MRCI: Medication Regimen Complexity Index; 95%CI: 95% confidence interval.

Table 5. Agreement between the Beers, STOPP and BCPIM Criteria in identifying potentially inappropriate medications for old people (n=406). Goiânia, GO, 2018.

Criteria	Kappa	95%CI	Agreement
Beers-Stopp	0.281	0.166-0.397	Fair
Beers-Consensus	0.659	0.584-0.734	Substantial
Stopp-Consensus	0.400	0.291-0.505	Fair
Beers-Stopp-Consensus	0.567	0.511-0.623	Moderate

CI: Confidence interval; *STOPP: Screening Tool of Older Persons' Potentially Inappropriate Prescriptions;* BCPIM: Brazilian Consensus on Potentially Inappropriate Medication for Old People; 95%CI: 95% confidence interval.

DISCUSSION

This study, based on the review of the medical records of patients attended at a center for the care of old people, showed that the prescription of PIM is frequent among patients. Approximately 88% of the old people had at least one prescribed PIM, when considering the analysis of the medications by the three criteria together. Separately, 84.4% of the old people had at least one PIM according to the STOPP criteria; 66.8% by BCPIM and 56.9% by Beers' Criteria.

The percentages of PIM use by the old people can vary according to the study location, characteristics of the population studied and the prescribers, and the criteria used[25]. In this sense, the generalization of our results based on other studies is difficult due to different ways of collecting data and applying the criteria (considering that it is not always that all items of the criteria are applied in a consensual way). A study carried out with old people attended at a basic health unit in Belo Horizonte, MG, Brazil, found a prevalence of PIM prescription for the old people of 53.7% by the Beers criteria and 55.9% by the BCPIM[25]. A survey conducted with old people from the community of Juiz de Fora, MG, Brazil, using the STOPP criteria identified that 46.2% of the old people used at least one PIM and 50.0% by the Beers criteria[26]. A study using Beers Criteria in Medicare beneficiaries identified that 24.2% of the old people used PIM[13]. In hospital discharge prescriptions, PIM was found in 59.1% of the old people by STOPP[15] and in 58.4% by BCPIM[12].

Although the results found in this study show a higher prevalence of PIM than in studies carried out in units that are not specialized in the health of old people, it must be considered that the fact that the medication is included in one of these lists does not prevent it from being included in the therapeutic regimen. Therefore, there is an indication that the risks/benefits are observed and that the patient is monitored. In the sample studied, about 95% of the old people had been followed by a geriatrician for more than a year[18]. So, one of the great challenges about these medications is the way they are prescribed, requiring greater attention in the assessment of risks and benefits when they cannot be avoided, so that, thus, the doctor can safely prescribe[27].

In this study, the greatest exposure to PIM was due to the prescription of omeprazole, quetiapine and escitalopram, medications belonging to the class of proton pump inhibitors (PPIs), atypical antipsychotics and antidepressants (selective inhibitors of serotonin reception-SSRI), respectively. This profile, in which PPI is the main cause of PIM exposure in old people, is similar to that in the literature[28]. The characterization of these medications as inappropriate is related to the fact that the prolonged use of PPI causes and potentiates osteoporosis, fractures, renal failure, risk of infection with *Clostridium difficile* and deficiency of vitamins and minerals[6,17,18].

According to the three criteria analyzed, PPIs are inappropriate when used for more than eight weeks. The STOPP and BCPIM Criteria are mandatory regarding the prolonged use of PPI for more than eight weeks. The Beers Criteria, on the other hand, consider its use appropriate for more than eight weeks only when the patient has peptic ulcer, Barrett's esophagus, esophagitis or is in chronic use of corticosteroids or non-steroidal anti-inflammatory

medications[6]. One of the main reasons attributed in the literature as a cause of prolonged use of PPI in old people is the non-withdrawal of the medication when the indication for which it was prescribed is no longer present, education of health professionals regarding the prolonged use of PPI in old people[29].

Quetiapine was the antipsychotic most commonly identified as PIM. The STOPP criteria and the Beers criteria consider, in general, all medications belonging to this class as PIM[6,17], whereas the BCPIM specifies which antipsychotics are inappropriate within the class[18]. According to the STOPP criteria, antipsychotics are inappropriate when prescribed for old people with dementia or Alzheimer's, cognitive impairment and/or to treat behavioral changes, as they increase the risk of stroke, which can also aggravate chronic constipation and, still, for presenting potential to cause gait ataxia, parkinsonism, hypotension and falls[17]. They are also inappropriate when prescribed as a hypnotic to treat insomnia, together with another antipsychotic or medication with anticholinergic properties, due to the potential risk of causing falls[17]. The Beers Criteria consider them inappropriate when they are prescribed for old people with behavioral changes due to dementia, cognitive impairment, Alzheimer's, delirium, falls/fractures, or because they are prescribed with two other medications that activate the central nervous system (CNS) as benzodiazepines, non-benzodiazepine hypnotics, tricyclic antidepressants, SSRIs and/or opioids[6].

According to the BCPIM, antipsychotics are inappropriate when prescribed to treat behavioral problems of dementia or insomnia, for old people with Alzheimer's, cognitive impairment, delirium, and for those with benign prostatic hyperplasia, falls/fractures and with Parkinson's disease, as it can aggravate these clinical conditions[18]. In the STOPP[17] and Beers criteria[6], unlike BCPIM, quetiapine is considered safe to be prescribed for old people with Parkinson's. This medication is considered appropriate when prescribed to treat schizophrenia or panic syndrome, only by the Beers Criteria[6].

In this study, among SSRIs, escitalopram was the most identified as PIM. The STOPP Criteria, Beers Criteria and BCPIM consider SSRIs to be inappropriate for old people only under certain clinical conditions[6,17,18]. According to the STOPP Criteria, SSRIs are inappropriate when prescribed together with an acetylcholinesterase inhibitor, as this interaction can promote a reduction in heart rate, it is also inappropriate for old people with chronic constipation or hyponatremia[17]. According to the Beers Criteria, they are inappropriate when prescribed to patients with reports of falls/fractures or who are using two other CNS-activating medications such as benzodiazepines, non-benzodiazepine hypnotics, tricyclic antidepressants, other SSRIs and/or opioids[6]. According to BCPIM, they are considered inappropriate when prescribed to patients who report falls/fractures or hyponatremia[18].

In the present study, by the Beers and BCPIM criteria, the prevalence of PIM was higher in individuals with polypharmacy and by the STOPP and BCPIM criteria, the prevalence was higher in individuals exposed to more complex therapies. Polypharmacy and the medication regimen complexity index (MRCI) are factors associated with PIMs found in other studies as well. Another factor associated with a higher prevalence of PIM in the STOPP and BCPIM criteria was the greater number of signs/symptoms, which may reflect more health problems that need to be treated[30,31].

Although there is still no gold standard categorization for the MRCI, according to the proposal by Pantuzza et al. the overall score for the complexity of pharmacotherapy among old people at the referral center is high[23]. This high complexity may be related to the large amount of prescription medications, to be used several times a day or in alternate doses. Other factors that can contribute to a higher MRCI score are polypharmacy and health problems profile, since old people with more health problems tend to have more complex pharmacotherapy[30,32]. The MRCI has satisfactory psychometric properties that allow measuring the complexity of therapy for old people[22]. This characterization can contribute to greater patient safety, helping to select those who need pharmacotherapeutic follow-up for possible treatment optimization, thus increasing the chances of reducing MRP and improving adherence[23,30,32,33].

The strength of agreement between the criteria for screening PIM was moderate, this can be explained by the fact that they present some differential points to define a medication as PIM. The agreement between BCPIM[18] and the Beers Criteria was substantial, this may be related to the fact that the BCPIM was developed based on the Beers Criteria[10] 2012, which had few changes for the 2015 version[6]. Among STOPP[17] and BCPIM[18] Criteria, the agreement was fair, this can be justified by the fact that BCPIM was based on the 2008 version of the STOPP Criteria and in this study the 2015 version was used, with the addition of 15 new criteria. The fair agreement presented between Beers Criteria and STOPP Criteria can be attributed to the fact that these two lists differ more in terms of the criteria for classifying a medication as PIM. In addition, this is one of the few studies using the four lists of the Beers Criteria, which provides greater sensitivity in the screening of PIMs and may have contributed to a higher frequency of these medications. Thus, the complementary use of these instruments is recommended in the decision-making process[18,34], however, in clinical practice, using three lists may be impractical due to the service flow. In this way, the ideal would be to use the most current one, which includes the standardized medications in place and whose professional is able to perform better the screening of the PIMs.

Regarding the strengths, this study collected data from patients seen in secondary care directly from the medical records, including old people with many concomitant diseases and using a large number of medications. In the characterization of the PIM, three different PIM evaluation criteria were used, with different characteristics, presenting the results identified for each one. Although there is no gold standard list to identify PIM, using the Beers Criteria (2015)[6], STOPP Criteria (2015)[17] and BCPIM[18] it was possible to obtain relevant information for the general characterization of inappropriate prescriptions in the old people studied.

Regarding the limitations of the study, the findings reflect the pattern of prescription of medicines in a health unit, so that trends may occur by the prescribers of the place. In addition, not all clinical patient data were available for collection, and information that would be useful in the classification of PIMs, such as results of creatinine clearance and glomerular filtration rate, and identification of advere drug events were not present. Another point to be considered is that the Beers Criteria, version 2015, was used for PIM analysis, and not the 2019 update[35]. The use of the previous version is justified by the fact that the prescriptions analyzed are from the years 2017 and 2018 and the data collection took place in 2018, before the update was released. The purpose of this new update was to determine whether new criteria should be added, removed or changed in the recommendations and interaction with diseases, thus, new studies can be carried out considering these recent changes[35].

CONCLUSIONS

The prescription of potentially inappropriate medications (PIM) was a common finding in the analysis of the medical records of a referral center in health for old people, and the three criteria used showed moderate agreement in the identification of PIM. At least one PIM was prescribed for approximately 90% of the old people, 86% were on therapeutic regimens with five or more medications, and about 60% had highly complex therapies prescribed. The factors associated with the prevalence of PIM were polypharmacy, a greater number of signs/symptoms and a higher Medication Regimen Complexity Index (MRCI).

Thus, strategies must be implemented to improve the pharmacotherapy of the old people with due attention to those who have these associated factors in their profile. This reinforces the importance of effective monitoring of the old people, in order to reduce the adverse events that such medications may cause, in addition to stimulating the deprescription in this population group. This action can be benefited with the participation of a clinical pharmacist trained in the review of medicines and specialized in gerontology. In addition, educational interventions aimed at prescribers can help ensure a more appropriate prescription process. Future studies can be carried out to investigate whether the description of PIM helps in reducing the signs and symptoms presented and in improving the quality of life. In

addition, an update on the Brazilian Consensus on Potentially Inappropriate Medication for Old People, based on the updated version of the Beers and STOPP Criteria is suggested, in order to obtain a more complete list to be implemented in the clinical routine, ensuring the safety of the older patient.

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