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Article

Potentially inappropriate medication use in institutionalized older adults according to the Beers Criteria

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The need for specific care, coupled with new family arrangements, has contributed to the increasing institutionalization of elderly members. The purpose of this study was to evaluate drug use by institutionalized older adults according to Beers Criteria. This prospective, longitudinal study was conducted in the three non-profit long-stay geriatric care institutions of Campo Grande, in the Central-West region of Brazil. All subjects aged 60 years and above on November 2011 were included and followed until November 2012. Eighteen subjects were excluded and the final sample consisted of 133 individuals aged 60 to 113 years. Overall, 212 medications were used at geriatric care institution A, 532 at B, and 1329 at C. Thirty-four drugs were inappropriately prescribed 89 times at geriatric care institution A (41.98%), 49 prescribed 177 times at B (33.27%), and 91 prescribed 461 times at C (34.68%). Statistical differences in the inappropriate drug use were found between genders (p=0.007). The most commonly used potentially inappropriate medication were first-generation antihistamines (15.34%). There was a high frequency in the use of potentially inappropriate medications which can initiate marked side effects and may compromise the fragile health of institutionalized elderly. Thus, adopting the Beers Criteria in prescribing medication contributes to minimize adverse reactions and drug interactions.

Uniterms: Medicines/inappropriate use. Medicines/prescription. Polypharmacy. Elderly/inappropriate use of medicines. Beers Criteria.

A exigência de cuidados específicos, aliada aos novos arranjos familiares, tem contribuído para a crescente institucionalização dos idosos. O objetivo do presente trabalho foi avaliar o uso de medicamentos por idosos institucionalizados utilizando os Critérios de Beers. Este estudo longitudinal prospectivo foi realizado nas três instituições de longa permanência para idosos de Campo Grande, Centro-Oeste do Brasil. Todos os sujeitos com 60 anos ou mais foram incluídos em Novembro de 2011 e acompanhados até Novembro de 2012. Dezoito idosos foram excluídos, sendo a amostra final composta por 133 sujeitos com idade entre 60 e 113 anos. O total de medicamentos utilizados foi 212 na instituição A, 532 na B e 1329 na C. Foram identificados 34 medicamentos inapropriados, prescritos 89 vezes na instituição A (41.98%), 49 prescritos 177 vezes na B (67.29%) e 90 prescritos 460 vezes na C (34.61%). Este estudo demonstrou diferença estatística na utilização de medicamentos inapropriados entre os gêneros (p=0.007). Os anti-histamínicos de 1ª geração foram os medicamentos potencialmente inapropriados para idosos mais utilizados (15.34%). Houve elevada frequência no uso de MPI, os quais podem desencadear efeitos colaterais acentuados e comprometer mais a saúde fragilizada do idoso institucionalizado. Ainda, a adoção dos Critérios de Beers na prescrição contribui para minimizar as reações adversas e interações medicamentosas.

Unitermos: Medicamentos/uso inapropriado. Medicamentos/prescrição. Politerapia. Idoso/uso inapropriado de medicamentos. Critério de Beers.

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INTRODUCTION

Older adults have unique medication requirements as organ functions are reduced by age-related physiological changes. These changes affect the pharmacokinetics and pharmacodynamics of drugs, making it difficult to draw a clear-cut line between risks and benefits of their use in this population (Mangoni, Jackson, 2003; Baldoni *et al.,* 2010).

Drugs absorption may be impaired in elderly patients due to increasing gastric pH. This increase enhances the absorption of alkali drugs and reduces the absorption of acidic drugs. Aging also promotes reduced surface intestinal absorption and lower esophageal sphincter pressure and peristalsis (Baldoni *et al.,* 2010; Ferreira, 2010).

With increasing age, the amount of water in the body decreases, adipose mass increases and lean mass decreases. Thus distribution volume is less for water soluble drugs and greater for liposoluble drugs. Consequently, liposoluble drugs tend to accumulate in adipose tissue, increasing their plasma half-life and period of action, and the risk of adverse effects. Reduced distribution volume for water-soluble may increase their initial concentration in the central compartment, resulting in higher plasma concentrations (Baldoni *et al.,* 2010). Biotransformation can be affected by hepatic blood flow, which can be reduced by as much as half in the elderly. This results in reduced first pass metabolism and increased bioavailability of drugs (Mangoni, Jackson, 2003). There is a decrease in the activity of cytochrome P450 enzymes. Thus, some medications may continue to exert their effects for a longer than expected (Nobrega, Karnikowski, 2005). One example is diazepam, which has a half-life of 24 hours in younger patients and 90 hours in elderly patients (Mangoni, Jackson, 2003).

Renal function is an important parameter for the clearance of pharmaceutical agents, in the elderly; this function progressively declines with advancing age. Reduced renal blood flow, tubular clearance, and creatinine clearance and increase serum creatinine, result in two clinically significant effects - increased half-life and serum levels of drugs (Ferreira, 2010).

For drugs with a narrow therapeutic safety margin, such as digoxin, aminoglycosides and warfarin, serious side effects may occur in elderly patients if a dosage adjustment is not based on creatinine clearance value (Mangoni, Jackson, 2003; Baldoni *et al.,* 2010).

In relation to pharmacodynamics, modifications in the number of drugs, receptor affinity to drugs, and signal transduction, especially for agents that depress the central nervous system such as opioid analgesics, hypnotics and sedatives cause increased sensitivity to these triggered effects (Hutchison, O'Brien, 2007; Ferreira, 2010).

The need for specific care, coupled with new family arrangements, has contributed to increasing institutionalization of elderly family members. Institutionalized older adults differ from those who live with their families as they present specific characteristics such great frailty, impaired functionality, and physical, psychological and social dependence (Gorzoni, Pires, 2006). Comorbidities and chronic degenerative diseases make the elderly prone to using concomitant medications, increasing the risk of adverse events occurrence (Rajska-Neumann *et al.,* 2011; Liu *et al.,* 2012).

The 2000 Population Census of Brazil produced by the Brazilian Institute of Geography and Statistics (Instituto Brasileiro de Geografia e Estatistica - IBGE) revealed less than 100,000 senior citizens living in collective households, this represents less than 1% of the elderly population. Approximately 10 years later, a survey conducted by the Institute for Applied Economic Research (Instituto de Pesquisa Econômica Aplicada - IPEA) identified 3548 long-stay geriatric care institutions in Brazil, where 83,870 seniors citizens were living, 0.5% of the elderly population (IPEA, 2011).

The need for caution in prescribing drugs to older adults has led to the development of a number of tools to assist this practice. One of these resources is the Beers Criteria of potentially inappropriate medications (PIM) use in older adults, developed by Beers *et al.* (1991). These criteria were established to reduce the risks of iatrogenesis and adverse reactions. In 1997, the criteria were updated by Beers to include degrees of frailty. In 2003, Fick *et al.* reviewed the original guidelines and published the latest update in the following decade (Fick *et al.,* 2012). Potentially inappropriate medications (PIM) are medications or classes of medications that should be avoided in elderly patients of 60 or more years. Medications are placed in this category when they have no evidence-based indication, do not present cost-effectiveness, or there are safer alternatives (Varallo, Capucho, Planeta, 2011; Beers *et al.*, 1991).

In this context, several different instruments can be employed; these include the French list (Laroche, Charmes, Merle, 2007), the Medication Appropriateness Index (Hanlon *et al.*, 1992), the STOPP/START criteria (Gallagher *et al.*, 2008), the PRISCUS list (Holt, Schmield, Petra, 2010), the Korean list (Kim, Heo, Lee, 2010), IPET (Naugler *et al.*, 2000) and Beers Criteria (Beers *et al.*, 1991; Beers, 1997; Fick *et al.*, 2003; Fick *et al.,* 2012). The Beers Criteria is the most commonly used by researchers worldwide (Gorzoni, Fabbri, Pires, 2008; Ribeiro *et al.*, 2005).

Many of the studies on medication use in the

elderly focus on inpatients, outpatients or those living in the community (Flores, Mengue, 2005; Winit-Watjana, Sakulrat, Kespichayawattana, 2008; Lin *et al.,* 2011; Rajska-Neumann *et al.,* 2011; Varallo *et al.*, 2011; Liu *et al.,* 2012; Pinto, Ferre, Pinheiro, 2012), while research on drug use by elderly institutionalized adults is still scarce (Correr *et al.,*2007; Aguiar *et al.,* 2008; O'Mahony *et al.,* 2010; Fochat *et al.,* 2012).

The purpose of this study was to identify and quantify drug use in elderly institutionalized adults using the Beers Criteria (2012).

METHODS

Study design and setting

This prospective, longitudinal study was conducted in the three non-profit long-stay geriatric care institutions (herein designated A, B, and C) of Campo Grande in the Central-West region of Brazil. Non-profit long-stay geriatric care institutions are residential nursing homes for individuals of 60 years and over who have some degree of difficulty in performing daily activities and for those whose families lack the financial, physical, or emotional resources to provide them with the necessary care (ANVISA, 2005).

Study population

Subjects aged 60 years and over (Brasil, 2003) living at one of the non-profit long-stay geriatric care institutions of Campo Grande, Brazil, in November 2011 were included in the study and followed until November 2012.

Those institutionalized after November 2011 were excluded, as were those who died or were discharged from the institutions during the study period.

Data collection

Data was collected weekly from the subjects' medical records; the variables investigated were gender, age, number of prescribed drugs and identification of their active principles, and PIM occurrence according to the Beers Criteria (Fick *et al*., 2012), (*a*) potentially inappropriate medications for use in older adults independent of diagnoses or conditions, (*b*) potentially inappropriate medications for use in older adults considering diagnoses and conditions, and (*c*) medications that, although potentially inappropriate to older adults, can be used with caution.

Quantification of the total number of used drugs and evaluation of their unsuitability took into account the number of times the same drug was prescribed, so as to identify repeated exposure to PIM.

Data treatment and interpretation

Data were expressed as absolute and relative frequencies, means and standard deviations. Statistical analyses were performed using Epi Info software, version 3.5.1, 2008 (CDC, 2009) and BioEstat, version 5.0 (Ayres *et al.,* 2007). Associations between variables were compared using Pearson's Chi-squared test and prevalence ratio with 95% confidence interval (CI).

Ethical issues

The study was approved by the Federal University of Mato Grosso do Sul Research Ethics Committee (protocol number 2212/2011).

Healthcare professionals responsible for the subjects proposed their treatment and the study evaluations did not interfere with this process.

RESULTS

Table I shows the profile of the study population. During data collection, 18 subjects were excluded (16 died and two left the institutional setting). The final sample thus consisted of 133 individuals aged 60 to 113 years. Mean ages (by institution) were 77.94±7.94 years (A), 76.17±11.10 (B), and 78.49±10.15 (C).

Overall, 212 medications (with 91 active principles) were used at A, 532 (with 134) at B, and 1329 (with 265 active principles) at C. Mean numbers of active principles per individual were 12.47 ± 5:51 (A), 17.73 ± 8.9 (B), and 15.45 ± 9.63 (C).

Thirty-four drugs were inappropriately prescribed 89 times at A (41.98%), 49 prescribed used 177 times at B (33.27%), and 91 prescribed 461 times at C (34.68%). In all, roughly 35% of the drugs prescribed were classified as PIM and statistical differences were found between genders for inappropriate use of drugs (Pearson's Chi-squared test, $P = 0.007$) (Table II).

All subjects living at geriatric care institutions were treated with PIM, except one (1.33%) older adult from institution C, who did not use any medicine.

Table III lists the PIM used at the geriatric care institutions; the most commonly used were first-generation antihistamines (54/15.34%), non-steroidal anti-inflammatories (49/13.92%), and antipsychotics (49/13.92 %).

TABLE I – Characteristics of the study population

Variable	Long-stay geriatric care institution							
	A		B		C		Total	
	M n (%)	F n (%)	M n (%)	F n (%)	M n (%)	F n (%)	M n (%)	F n (%)
Initial number of subjects	11 (55.00)	9 (45.00)	21 (58.33)	15 (41.67)	52 (54.73)	43 (45.27)	84 (55.63)	67 (44.37)
Deaths	1 (5.00)	1 (5.00)	3 (8.33)	2 (5.55)	2 (2.10)	7 (7.36)	6 (3.97)	10 (6.62)
Discharge from institutional setting	0 (0.00)	1 (5.00)	1 (2.78)	0 (0.00)	0 (0.00)	0 (0.00)	1 (0.66)	1 (0.66)
Number of subjects in the sample	10 (58.82)	7 (41.18)	17 (56.67)	13 (43.33)	50 (58.14)	36 (41.86)	77 (57.89)	56 (42.10)
Age range (years)								
60-69	2 (11.76)	0 (0.00)	5 (16.67)	3 (10.00)	15 (17.44)	4 (4.65)	22 (16.54)	7 (5.26)
70-79	6 (35.29)	2 (11.76)	7 (23.33)	6 (20.00)	13 (15.12)	13 (15.12)	26 (19.55)	21 (15.79)
80-89	2 (11.76)	4 (23.53)	2 (6.67)	3 (10.00)	19 (22.09)	11 (12.79)	23 (17.29)	18 (13.53)
90-99	0 (0.00)	1 (5.88)	2 (6.67)	0 (0.00)	2 (2.32)	7 (8.14)	4 (3.01)	8 (6.01)
Over 100	0 (0.00)	0 (0.00)	1 (3.33)	1 (3.33)	1 (1.16)	1 (1.16)	2 (1.50)	2 (1.50)
Number of drugs prescribed per subject	115	97	263	269	714	615	1092	981

M: Male; F: Female

TABLE II – Potentially inappropriate medication for the elderly

Variables	Medication use				Total		*P*	RR (95% CI)
	Inappropriate		Appropriate					
	N	%	n	%	N	%		
Institution								
A	89	41.98	123	58.02	212	10.23	0.07	1
B	177	33.27	355	66.73	532	25.66		1.45 (1.25-1.69)
C	461	34.69	868	65.31	1329	64.11		1.36 (1.20-1.55)
Total	727	35.07	1346	64.93	2073	100.00	-	-
Gender								
Male	415	37.76	684	62.24	1099	53.01	0.007	1
Female	312	32.03	662	63.86	974	46.99		1.29 (1.16-1.42)
Total	727	35.07	1346	64.93	2073	100.00		

RR: Relative Risk; CI: Confidence Interval.

Those with less than 10% use were barbiturates at A (1/2.38%) and C (7/3.13%); levothyroxine at A (2/4.76%) and C (5/2.23%); oral mineral oil at institution B (1/1.16%) and C (6/2.67%); antiarrhythmics at institutions B (1/0.45%) and C (5/1.79%); spironolactone at B (2/2.32%) and C (4/1.78%); the antithrombotic ticlopidine (1/0.45%), central alpha-adrenergic agonists (5/1.79%), non-benzodiazepine hypnotics (1/0.45%), and Ergot mesylates (3/1.34%) at institution C; at all facilities, metoclopramide (1/2.38%, 1/1.16%, 7/3.12%, respectively at A, B and C) and muscle relaxants at A (1/2.38%), B (3/3.48%) and C (5/1.79%).

Table IV presents data on PIM use in older adults considering diagnoses or conditions. Potential interactions were also observed for PIM use on fewer than 10 occasions: cyclo-oxygenase 2 inhibitors at A (1/1.30%), B (2/1.49%) and C (6/1.80%) and diltiazem at C (1/0.30%), a calcium channel blocker, which is

TABLE III – Classification of potentially inappropriate medication for the elderly

Pharmacological class/drugs	Long-stay geriatric care institutions							
	A (n = 87)		B (n = 177)		C (n = 461)		Total (n = 725)	
	M	F	M	F	M	F	M	F
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
First-generation antihistamines	4 (9.52)	6 (14.28)	3 (3.49)	4 (4.65)	24 (10.71)	13 (5.80)	31 (8.81)	23 (6.53)
Antispasmodics	0 (0.00)	2 (4.76)	0 (0.00)	4 (4.65)	6 (2.68)	5 (2.23)	6 (1.70)	11 (3.12)
Anti-infective agents	1 (2.38)	1 (2.38)	0 (0.00)	3 (3.49)	3 (1.34)	2 (0.89)	4 (1.14)	6 (1.70)
Alpha-blockers	0 (0.00)	0 (0.00)	9 (10.46)	0 (0.00)	9 (4.02)	0 (0.00)	18 (5.11)	0 (0.00)
Digoxin (>0.125 mg/day)	0 (0.00)	0 (0.00)	2 (2.32)	0 (0.00)	6 (2.68)	3 (1.34)	8 (2.27)	3 (0.85)
Immediate-release nifedipine	0 (0.00)	0 (0.00)	5 (5.81)	1 (1.16)	3 (1.34)	1 (0.45)	8 (2.27)	2 (0.57)
Tertiary tricyclic antidepressants	5 (11.90)	3 (7.14)	7 (8.14)	5 (5.81)	1 (0.45)	5 (2.23)	13 (3.69)	13 (3.69)
Antipsychotics	1 (2.38)	1 (2.38)	4 (4.65)	4 (4.65)	21 (9.37)	18 (8.03)	26 (7.39)	23 (6.53)
Benzodiazepines	0 (0.00)	4 (9.52)	6 (6.98)	4 (4.65)	9 (4.02)	7 (3.12)	15 (4.26)	15 (4.26)
Insulin	0 (0.00)	0 (0.00)	3 (3.49)	0 (0.00)	8 (3.57)	6 (2.68)	11 (3.12)	6 (1.70)
Oral non-selective COX-inhibiting NSAIDs	1 (2.38)	8 (19.05)	6 (6.98)	8 (9.30)	18 (8.03)	8 (3.57)	25 (7.10)	24 (6.82)

Note: First-generation antihistamines: dexchlorpheniramine, cyproheptadine, promethazine, hydroxyzine, chlorpheniramine. Antispasmodics: hyoscine, scopolamine. Anti-infective agents: nitrofurantoin. Alpha-blockers: doxazosin. Tertiarytricyclic antidepressants, alone or in combination: amitriptyline, clomipramine, imipramine. Antipsychotics: haloperidol, olanzapine, risperidone, thioridazine. Short- and intermediate-acting benzodiazepines: alprazolam, lorazepam. Long-acting benzodiazepines: clonazepam, diazepam. Oral non-selective COX-inhibiting NSAIDs: ketoprofen, diclofenac, ibuprofen, meloxicam. M: Male; F: Female

potentially inappropriate for older adults with heart failure and chronic constipation.

Interactions involving pioglitazone with heart failure were seen at A (1/1/30%) and antipsychotic olanzapine and thioridazine at C (4/1.20%) with syncope, convulsion, delirium, dementia, falls/fractures, chronic constipation, benign prostatic hyperplasia, and Parkinson's disease. Muscle relaxants carisoprodol and cyclobenzaprine used at A (1/1.30%), B (3/2.24%) and C (5/1.50%) and oxybutynin, used for urinary incontinence at C (2/0.60%) should be used by older adults with delirium, dementia, chronic constipation, benign prostatic hyperplasia, or by those who suffered falls or fractures. Interactions involving hypnotics and sedatives with delirium were seen at A (1/1.30%) and C (7/2.10%); non-benzodiazepine hypnotics (zopiclone) and older adults with history of falls or fractures seen at C (1/0.30%), and with caffeine seen at A (1/1.30%) and B (1/0.75%) should also be avoided.

Figure 1 shows the results for PIM that can be used with caution. Antiplatelet agents (75/37.88%), antidepressants (56/28.28%), and antipsychotics (49/24.74%) predominated.

Antipsychotics: haloperidol, olanzapine, risperidone, thioridazine. Serotonin-noradrenaline reuptake–inhibiting antidepressants: duloxetine, venlafaxine. Selective serotonin reuptake–inhibiting antidepressants: citalopram, escitalopram, fluoxetine, paroxetine, sertraline. Vasodilators: dihydroergocristinemesylate, co-dergocrin, isosorbide, sildenafil, pentoxifylline, propatylnitrate.

DISCUSSION

Our results reveal the existence of risks related to medication use by institutionalized older adults in the three non-profit long-stay geriatric care institutions investigated. By providing a broad overview of PIM use by institutionalized older adults, this investigation encourages the development of mechanisms to evaluate risk-minimizing processes, so as to increase the likelihood of positive therapeutic outcomes for the geriatric population.

All used drugs were considered independent of formulation type or administration route, since the Beers Criteria (Fick *et al.,* 2012) does not discriminate between these parameters. The male predominance in the surveyed institutions contrasts with the greater life expectancy pattern seen in women in Brazil (IBGE, 2011) and in other studies on institutionalized older adults (Aguiar *et al.,* 2008; Fochat *et al.,* 2012). However Correr *et al.* (2007) found elderly males in the majority thus corroborating our finding. Our study also revealed greater use of PIM by males, but interpretation of this finding should take into account that drugs such as doxazosin (an alpha-blockers)

TABLE IV – Potentially inappropriate medication for the elderly by reason of drug–disease or drug–syndrome interactions capable of worsening the disease or syndrome

Pharmacological classification X drug–disease / drug–syndrome interaction	Long-stay geriatric care institution							
	A (n = 77)		B (n = 134)		C (n = 333)		Total (n = 540)	
	M	F	M	F	M	F	M	F
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
NSAID X heart failure; gastric/duodenal ulcer; chronic renal disease	1 (1.30)	8 (10.40)	6 (4.48)	10 (7.46)	18 (5.40)	9 (2.70)	25 (4.63)	27 (5.00)
Corticosteroid X delirium	6 (7.79)	4 (5.19)	10 (7.46)	13 (9.70)	44 (13.21)	32 (9.61)	60 (11.11)	49 (9.07)
Cilostazol X heart failure	2 (2.60)	1 (1.30)	5 (3.73)	3 (2.24)	11 (3.30)	6 (1.80)	18 (3.33)	10 (1.85)
Peripheral alpha blocker X syncope; urinary incontinence	0 (0.00)	0 (0.00)	9 (6.72)	0 (0.00)	9 (2.70)	0 (0.00)	18 (3.33)	0 (0.00)
Tricyclic antidepressants X syncope; chronic constipation; fractures; delirium; dementia; benign prostatic hyperplasia	5 (6.49)	3 (3.90)	7 (5.22)	5 (3.73)	2 (0.60)	6 (1.80)	14 (2.59)	14 (2.59)
Selective serotonin reuptake inhibitor X fractures	8 (10.39)	4 (5.19)	9 (6.72)	2 (1.49)	15 (4.50)	21 (6.31)	32 (5.92)	27 (5.00)
Haloperidol; risperidone X dementia and cognitive impairment; fractures; Parkinson's disease	1 (1.30)	1 (1.30)	4 (2.98)	4 (2.98)	19 (5.70)	16 (4.80)	24 (4.44)	21 (3.89)
Antihistamine (alone or in a combination of drugs) X delirium; dementia; fractures; chronic constipation; benign prostatic hyperplasia	4 (5.19)	6 (7.79)	3 (2.24)	4 (2.98)	28 (8.41)	14 (4.20)	35 (6.48)	24 (3.89)
Antispasmodic X delirium; dementia; fractures; chronic constipation; benign prostatic hyperplasia	0 (0.00)	1 (1.30)	0 (0.00)	4 (2.98)	6 (1.80)	5 (1.50)	6 (1.11)	10 (1.85)
Benzodiazepine X delirium; dementia; fractures	0 (0.00)	4 (5.19)	6 (4.48)	4 (2.98)	9 (2.70)	7 (2.10)	15 (2.78)	15 (2.78)
H2-receptor antagonist X delirium; dementia	7 (9.09)	1 (1.30)	10 (7.46)	5 (3.73)	9 (2.70)	7 (2.10)	26 (4.81)	13 (2.41)
Antiemetic X Parkinson's disease	3 (3.90)	2 (2.60)	3 (2.24)	2 (1.49)	9 (2.70)	5 (1.50)	15 (2.78)	9 (1.67)

NSAIDs: ketoprofen, ketorolac, diclofenac, ibuprofen, meloxicam. Corticosteroids: beclomethasone, betamethasone, budesonide, desonide, dexamethasone, fludrocortisone, fludroxycortide, hydrocortisone, prednisone, prednisolone, triamcinolone. Peripheral alpha-blockers: doxazosin. Tertiary tricyclic antidepressants: amitriptyline, clomipramine, imipramine, nortriptyline. Selective serotonin reuptake inhibitors: citalopram, escitalopram, fluoxetine, sertraline, paroxetine. Antihistamines: dexchlorpheniramine, cyproheptadine, promethazine, hydroxyzine, chlorpheniramine, dimenhydrinate, loratadine, meclizine. Antispasmodics: scopolamine and hyoscine. Benzodiazepines: alprazolam, lorazepam, flunitrazepam, bromazepam, nitrazepam, clonazepam, diazepam. H2-receptor antagonists: ranitidine. Antiemetics: metoclopramide, promethazine. M: Male; F: Female

- for benign prostatic hyperplasia - are restricted to male patients.

PIM use in our study was higher than seen by other investigators in Brazil. This may be because the study was longitudinal and used the updated Beers Criteria, which includes a larger number of PIM. Correr *et al.* (2007) and Aguiar *et al.* (2008) found 13.5% and 28.7% rates of PIM use, respectively. In Ireland, O'Mahony *et al.* (2010) described PIM prescription at 60% in long-stay geriatric care institutions.

Only one subject did not use PIM. This is a worrying finding, given the often compromised pharmacokinetic and pharmacodynamic profile of elderly individuals, which can compound the adverse effects of PIM. On the other hand, potentially inappropriate medication can be used in situations where the benefits outweigh the risks.

Lin *et al.* (2011), applying the Beers Criteria during an investigation of a rural community in Taiwan found that one third of elderly subjects had been prescribed at least one PIM (Fick *et al.,* 2003). On the same island, Liu

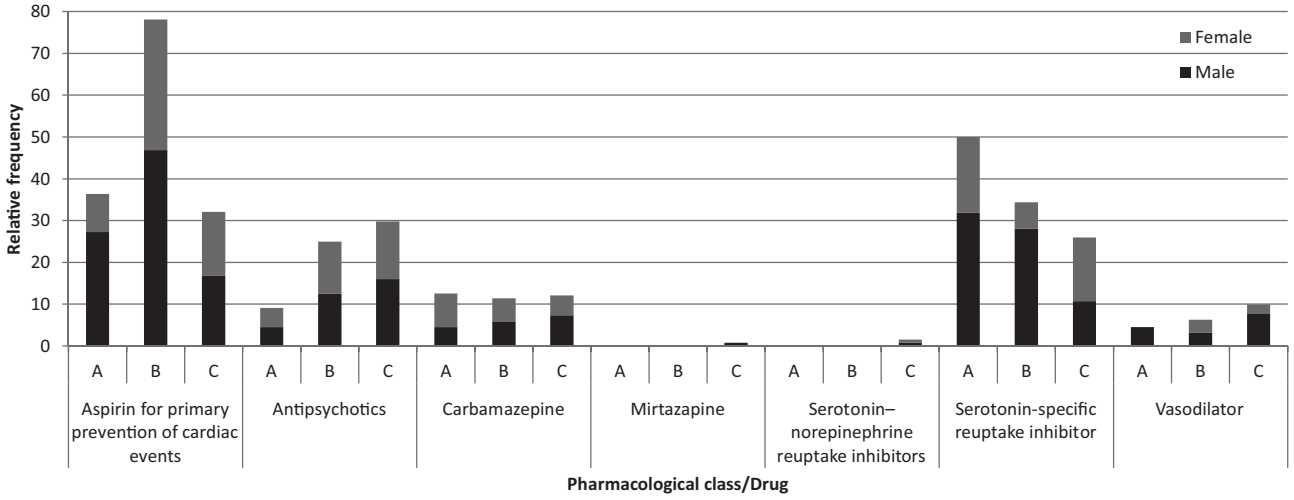

FIGURE 1 – Classification of potentially inappropriate medication to be used with caution in older adults.

et al. (2012) found that 36.2% of elderly patients had been prescribed at least one PIM when using STOPP (Screening Tool of Older Persons' Potentially Inappropriate Prescriptions) criteria, a resource developed in Ireland for PIM evaluation (Gallagher *et al.,* 2008).

The high number of prescriptions for first-generation anti-histamines, tricyclic antidepressants, and antipsychotics found at the geriatric care institutions investigated raises concerns. Caution is required in prescribing these agents, irrespective of patient clinical condition, as these drugs have a pronounced anticholinergic effect, progressively reduced clearance with advancing age, and increased tolerance when used as hypnotics. They can also increase the risks of confusion, dry mouth, constipation, blurred vision, urinary retention, and tachycardia (DiPiro *et al.,* 2011).

Drugs with pronounced anticholinergic effects are also categorized as PIM for older adults due to drug–disease or drug-syndrome interactions stemming from increased tissue responsiveness and central cholinergic hypofunction and dysfunction in old age and dementia (Bartus, 2000). Kim, Heo, Lee (2010) confirmed these effects while compiling a list of potentially inappropriate medications for elderly Koreans, with the aid of the Delphi method (Ablah *et al.,* 2013).

First- and second-generation antipsychotics increase the risks of stroke and cardiac QT-interval prolongation by altering the electrical properties of cardiac cells and causing hypotension (Risch, Groom, Janowsky, 1982). They can also trigger symptoms of Parkinson's by antagonizing dopamine receptors (Holt, Schmiedl, Petra, 2010). In this category, olanzapine and thioridazine should not be prescribed to patients with seizures, as these drugs reduce the neuronal excitability threshold (Muench, Hamer, 2010), they are PIM that can be prescribed with caution, owing to their potential to trigger or exacerbate the syndrome of inappropriate antidiuretic hormone secretion and hyponatremia, requiring that sodium levels be monitored when initiating the drug regime or changing doses. Monitoring is also necessary with the use of carbamazepine, mirtazapine, serotonin-noradrenaline reuptake–inhibiting antidepressants, and selective serotonin reuptake inhibitors (Fick *et al.,* 2012).

Metoclopramide, an antiemetic and prokinetic drug with antidopaminergic action, can cause extrapyramidal side effects, including tardive dyskinesia and Parkinsonian symptoms, which contraindicate its use unless indicated for gastroparesis (Kim, Heo, Lee*,* 2010).

Non-steroidal anti-inflammatory drugs (NSAID) were also prescribed, despite their enhanced side effects in elderly patients, which include gastrointestinal bleeding, ulcer induction, kidney failure, high blood pressure, and cardiovascular changes. Because NSAID promote fluid retention and exacerbate heart failure by decreasing prostaglandin production, they must not be prescribed to patients with heart failure (Sostres, Gargallo, Lanas, 2009).

Steroidal anti-inflammatories and H2-receptor antagonists are potentially inappropriate due to drug–disease interaction (Fick *et al.,* 2012). Steroidal anti-inflammatories suppress the hypothalamic-pituitary-adrenal axis and H2-receptor antagonists act on the central nervous system (Kenna *et al.,* 2011).

Among drugs for blood pressure control, alpha-blockers can increase the risks of syncope related to bradycardia and orthostatic hypotension. Methyldopa, a central-acting alpha agonist antihypertensive that decreases sympathetic discharge, is inappropriate given its potential to exacerbate depression (Kim, Heo, Lee*,*

2010). Immediate-release nifedipine, a calcium-channel blocker, induces hypotension and vasodilatation, lowers systemic vascular resistance, and compromises O_2 demand by myocardial cells (Kowey *et al.,* 2000; Kim, Heo, Lee, 2010). Direct vasodilators can exacerbate syncope episodes in patients with a history of this condition, and should therefore be used with caution (Kim, Heo, Lee, 2010; Fick *et al.,* 2012).

Among antiarrhythmics categorized as PIM, amiodarone is associated with toxicity, thyroid disorders, and cardiac QT prolongation and should therefore be avoided as first-line treatment for atrial fibrillation. Diltiazem can exacerbate heart failure by promoting urinary retention (Kowey *et al.,* 2000; Gallagher *et al.,* 2008).

The use of digoxin at doses higher than 0.125 mg/day for heart failure is not associated with additional benefits and may increase the risk of toxicity, as renal clearance is slower in the elderly and this drug has a low therapeutic index (Winit-Watjana, Sakulrat, Kespichayawattana, 2008; Mangoni, Jackson, 2003; Baldoni *et al.,* 2010; Pinto, Ferre, Pinheiro, 2012).

Restrictions are also placed on hypnotics and sedatives, particularly barbiturates, given the high rates of physical dependence, tolerance to sleep benefits, and risk of toxicity even at low doses (Holt, Schmiedl, Petra, 2010; Fick *et al.,* 2012).

Older adults develop increased sensitivity to benzodiazepines, owing to slower metabolism and biotransformation difficulties, which elevate the risks of cognitive impairment, delirium, falls, fractures, and accidents (Baldoni *et al.,* 2010). The Beers Criteria (Fick *et al*., 2012) categorize benzodiazepines as short-, intermediate-, and long-acting, and lists the following active principles: alprazolam, estazolam, lorazepam, oxazepam, temazepam, triazolam, clorazepate, chlordiazepoxide, chlordiazepoxide-amitriptyline, clonazepam, diazepam, flurazepam, and quazepam.

In Brazil, flunitrazepam, nitrazepam, and bromazepam are prescribed and were included in this investigation. These drugs were not considered by the Beers Criteria because there is no record of them at the Food and Drug Administration (FDA, 2013).

The non-benzodiazepine hypnotic eszopiclone, indicated for treatment of insomnia, is categorized as a PIM by the Beers Criteria, regardless of patient clinical condition. Zopiclone, a chiral drug used in racemic form and exhibiting pharmacological activity related to the eszopiclone enantiomer (Zuo *et al.,* 2013), is also classified as a PIM and should be avoided for chronic use because of its agonistic properties toward benzodiazepine receptors and side effects similar to these (Holt, Schmiedl, Petra, 2010).

No evidence of effectiveness has been found for Ergot mesylates, prescribed for headaches, memory impairment, cerebrovascular disease, and peripheral vascular disorders (Holt, Schmiedl, Petra, 2010).

Mineral oil by oral route should be avoided, since it reduces the cough reflex and increases the risk of aspiration and lipid pneumonia (Albuquerque Filho, 2006).

Pioglitazone (an antidiabetic agent) and cilostazol (a vasodilator) are considered potentially inappropriate medication for the elderly by reason of drug–disease or drug–syndrome interactions capable of worsening the disease or syndrome in patients with heart failure by exacerbating this condition while promoting urinary retention (Fick *et al.,* 2012).

PIM to be prescribed with caution include aspirin, used for primary prevention of cardiac events—despite a lack of evidence of benefits over risks in individuals aged 80 years and older, requires monitoring to prevent hemorrhagic events (Gallagher *et al.,* 2008).

We concluded that there was a high frequency of potentially inappropriate medication use which can initiate marked side effects such as hypotension, constipation, extrapyramidal effects, sedation, weakness, renal failure, sleep disorders and can compromise the fragile health of institutionalized elderly individuals. Therefore adopting the Beers Criteria in prescribing could contribute to minimize adverse reactions and drug interactions.

Awareness is required by all healthcare professionals with regard to changes experienced in old age. Drug prescription should address changes in pharmacokinetics and pharmacodynamics taking place during the aging process, so as not to compromise the health status of elderly individuals by inappropriate prescription. To improve care therapy in the elderly, safer alternatives should be sought within the same therapeutic class, there should be greater disclosure of lists like this between prescribers; and PIM lists or evaluation tools should be developed, which are appropriate to Brazil.

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