Potentially inappropriate medications in elderly

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Summary

Objective: To compare PRISCUS with Beers-Fick in detecting potentially inappropriate medication (PIMs) in elderly at their first outpatient geriatric visit. **Methods:** Retrospective medical record analysis by PRISCUS and Beers-Fick adapted to Brazilian pharmacopoeia, comparing the finding of PIMs at the first outpatient geriatric visit by both criteria. **Results:** Cases had mean age of 77.4 ± 7.7 years (64 females and 36 males), and mean consumption of 3.9 ± 2.5 drugs. This study found statistical significance for the numbers of women using benzodiazepines and men using salicylates. The mean was 0.5 ± 0.7 PIMs/patient by Beers-Fick criteria and 0.7 ± 0.8 PIMs/patient by PRISCUS. Medications most often reported by Beers-Fick criteria were: benzodiazepines, methyldopa and ergot-derived drugs. Medications most often reported by PRISCUS criteria were: benzodiazepines, antihypertensive drugs, and tricyclic antidepressants. No statistical significance was found when the number of elderly patients with PIMs was compared between both criteria. Statistical significance was found (PRISCUS versus Beers-Fick) for the consumption of long acting benzodiazepines and laxatives. Both criteria do not include drugs such as vitamins, herbal medications, and eye drops, reported by a percentage of cases. **Conclusion:** Both criteria are useful to prevent PIMs in the elderly, with PRISCUS being more updated and comprehensive, but they are not complete for the Brazilian outpatient reality.

Keywords: Iatrogenic disease; prescription drugs; elderly care; medication reconciliation.

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Introduction

Significant percentages of elderly have several concomitant diseases, which leads to the concomitant use of three or more medications[1-4]. In parallel, changes in body composition and kidney and liver functions caused by natural human aging are observed[5]. Thus, pharmacokinetic and pharmacodynamic interference exists among various drugs, some of them prescribed regularly in clinical practice[5-6]. This medication consumption pattern, associated with age-linked diseases and changes, constantly triggers side effects and drug interactions with serious outcomes for patients in this age group[4-8].

Medication intake involves serial steps – prescription, communication, dispensation, administration, and clinical follow-up –, making it a complex and iatrogenic-prone act, particularly in the elderly. A significant portion of these adverse events can be prevented at the prescription stage[9]. Lists of potentially inappropriate medications (PIMs) – defined as drugs at risk of causing more side effects than benefits in the elderly – are useful aids in clinical practice regarding the preventive action. Several lists have been published over the last two decades[10-15]. Versions of Beers criteria[10,11] and later, Beers-Fick criteria[13] have become the most cited and used worldwide[9,16]. However, there is criticism of these criteria, particularly regarding their drug scope and adaptability to specific pharmacopoeias in each country[9,14-16]. In the search for reducing the criticized aspects of Beers-Fick criteria, Holt et al.[17] defined a PIM list for the elderly – termed PRISCUS – primarily to be used in Germany. The generated list – a total of 83 drugs in 18 drug classes – includes comments for clinical practice and therapeutic options.

Which list or criteria are used in PIM evaluations in Brazil? A survey performed in PubMed on April 23, 2011 with the following keywords: Beers Fick criteria Brazil OR Beers criteria Brazil OR potentially inappropriate medication elderly Brazil OR inappropriate prescription elderly Brazil retrieved six articles[6,18-22], all of them with a methodology based on Beers-Fick criteria[13]. A survey at SciELO, using the same keywords and on the same date, located seven articles[4,5,18-22]; five of which had been already retrieved by the former portal[18-22] and two more[4,5], the first of which[4] cites another report by Beers[23] and the second[5] comments on the first two versions of Beers criteria[10,11]. Thus, no PIM list or criteria for the elderly have been developed in Brazil. The studies published in Brazil follow a global trend, as they use literature based on articles produced by Beers et al.[10,11,13,23].

Considering the above description, the question asked is: would the PRISCUS[17] list adapted to Brazilian pharmacopoeia be more adequate than Beers-Fick[13] criteria to detect PIMs in elderly Brazilian patients?

Objectives

To compare the PRISCUS[17] list with Beers-Fick[13] criteria to detect PIMs in the elderly assessed at the first outpatient geriatric visit.

Methods

Review of elderly outpatients' medical records through the PRISCUS[17] list adapted to Brazilian pharmacopoeia (Box 1). The same number of cases and same methodology as in a study published in 2006[1] by the authors regarding the applicability of Beers-Fick criteria[17] also adapted to Brazilian pharmacopoeia (Box 2) at the first outpatient geriatric visit were used.

The patients were attended to by the authors in an outpatient facility belonging to the Irmandade da Santa Casa de Misericórdia de São Paulo between the years 2000 and 2004. Later on (2005), through analysis of the standard history taking used at the institute, the drugs in continuous use on the days preceding the first geriatric assessment between 2000 and 2004 were reviewed. Both Beers-Fick[13] criteria and the PRISCUS list[17] were used to define PIM quantitative and qualitative values. PIM standards for the elderly were sequentially compared between the two adapted criteria/lists[13,17] (Boxes 1 and 2). The expected result aims to determine the PIM prevalence in elderly at the onset of outpatient geriatric follow-up. The statistical analysis used a chi-squared test (Yates's and/or Fisher's exact test, both with an alpha of 5.0%), dividing the number of cases into females and males and into ages 74 and younger and 75 and older. The cases were further divided according to the main PIM classes used by both criteria[13,17] studied.

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Results

The cases consisted of 100 elderly people (64 females and 36 males) with a mean age of 77.4 ± 7.7 years and a mean consumption of 3.9 ± 2.5 drugs in continuous use/patient (Table 1). Statistical significance was reached for the number of women using benzodiazepines and men using salicylates.

By Beers-Fick[13] criteria, 0.5 ± 0.7 PIMs/patient and by the PRISCUS[17] list 0.7 ± 0.8 PIMs/patient were observed. The drugs in Beers-Fick[13] criteria most often reported by the elderly assessed were: benzodiazepines, methyldopa, ergot-derived drugs, amitriptyline, and amiodarone. The drugs in the PRISCUS[17] list most often reported by the same patients were: benzodiazepines, antihypertensives, tricyclic antidepressants, ergot-derived drugs, and laxatives. No statistical significance could be found upon comparing the global number of elderly patients using PIMs between both criteria[13,17]. However, statistical significance was found by the PRISCUS[17] list *versus* the Beers-Fick[13]

Box 1 – PRISCUS[17] list of potentially inappropriate medications for the elderly adapted to Brazilian pharmacopoeia

Anti-inflammatory drugs	**Antihistamine drugs**	**Extended-release BZDs**
Ketoprofen	Clemastine	Bromazepam
Etoricoxib	Chlorpheniramine	Clobazam
Phenylbutazone	Dimethindene	Chlorazepate
Indomethacin	Hydroxyzine	Chlordiazepoxide
Meloxicam	Triprolidine	Diazepam
Piroxicam	**Antiemetic drugs**	Flunitrazepam
Antihypertensive drugs	Dimenhydrinate	Flurazepam
Clonidine	**Ergotamine and ergot-derived drugs**	Nitrazepam
Doxazosin	Dihydroergocryptine	**Short-medium-acting BZDs**
Methyldopa	Ergotamine	Alprazolam
Nifedipine	**Typical neuroleptics**	Lorazepam > 2mg
Prazosin	Clozapine	**"Z-agents"**
Reserpin	Fluphenazine	Zolpidem > 5 mg
Terazosin	Haloperidol > 2 mg	Zopiclone > 3.75 mg
Antiplatelets	Levomepromazine	Other sedatives
Ticlopidine	Olanzapine > 10 mg	Diphenhydramine
Antiarrhythmic drugs	Thioridazine	**Antiepileptic drugs**
Digoxin	**Tricyclic antidepressants**	Phenobarbital
Quinidine	Amitriptyline	**Opiates**
Sotalol	Clomipramine	**Laxatives**
Antibiotics	Imipramine	**Miscellaneous**
Nitrofurantoin	Maprotoline	Pentoxifylline
Muscle relaxants	**Serotonin reuptake inhibitors**	Naftidrofuryl
Baclofen	Fluoxetine	Nicergoline
Antispasmodic drugs	**MAO inhibitors**	Piracetam
Oxybutynin	Tranylcypromine	
Tolterodine		

MAO, monoamine oxidase, BZDs, benzodiazepines.

Box 2 – Drugs not recommended in the elderly, regardless the diagnosis or clinical condition due to high side effects risk, with safer drugs marketed in Brazil being preferentially prescribed by Beers-Fick[13] criteria

Thioridazine	Amiodarone	Chlorpropamide
Barbiturates (except fenobarbital)	Digoxin > 0.125 mg/day (except in atrial arrhythmias)	Estrogen therapies (oral route)
Benzodiazepines	Disopyramide	Thyroid extract
Lorazepam > 3.0 mg/day	Methyldopa	Methyltestosterone
Alprazolam > 2.0 mg/day	Clonidine	Nitrofurantoin
Chlordiazepoxide	Nifedipine	Ferrous sulfate
Diazepam	Doxazosin	Cimetidine
Chlorazepate	Dipyridamole	Ketorolac
Flurazepam	Ticlopidine	Ergot and ciclandelata
Fluoxetine (daily)	**Non-steroidal anti-inflammatory drugs**	**Muscle relaxants and antispasmodic drugs**
Amitriptyline	Indomethacin	Carisoprodol
Antihistamine drugs	Naproxen	Chlorzoxazone
Chlorpheniramine	Piroxicam	Cyclobenzaprine
Hydroxyzine	**Laxatives**	Orphenadrine
Cyproheptadine	Bisacodyl	Oxybutynin
Tripelenamine	Cascara sacred	Hyoscyamine
Dexchlorpheniramine	Mineral oil	Propantheline
Promethazine	**Appetite supressants**	Belladona Alkaloids
Prometazina	**Amphetamines**	Meperidine

criteria for long acting benzodiazepine and laxative consumption. Both criteria do not include drugs such as vitamins, herbal medicines, and eye drops reported by a percentage of cases (Table 1).

Discussion

Periodical review of drugs used by the elderly must be an intrinsic part of clinical practice. Several concomitant and usually chronic diseases generate a potential for concomitant and significant medication consumption[1-4]. The association of medication use with pharmacokinetic and pharmacodynamic aging-linked changes creates conditions for a high risk of side effects and drug-drug interactions observed in the elderly[4-8].

Usually, there is a higher number of females and patients older than 70 among the elderly in need of a special care in drug prescription[4,6,20-22]. These data were also observed in the present cases and are warranted by the remarkable female longevity and the progressive multiplicity of chronic diseases in older age groups[24-27]. The mean medication use among the elderly reviewed in this study was another parallel outcome correlated with that reported in the literature[4,6,8,20,22]. Thus, lists and/or criteria of inappropriate medications for elderly are effective both in detecting use and in avoiding prescription.

The subsequent issue is: which criteria and/or lists would be more appropriate to the Brazilian reality, since no national tool that meets this clinical practice need could be found in the literature?

Potentially inappropriate medication guidelines for the elderly, such as Beers-Fick[13] criteria, are time-honored in the literature and used in several countries. They are practical and easily memorized, although they do not consider local realities as for the standard of medications delivered and prescribed to certain populations[9,12,14-16,18,19]. The PRISCUS list[17], primarily conceived for German pharmacopoeia, intends to be wider, as it contains drugs not mentioned by the Beers-Fick[13] criteria. In the current study, a slight numeric PIM difference favoring the list was observed,[17] possibly resulting from its higher discrimination of drug classes and drugs over the Beers-Fick criteria[13] (61 *versus* 52 drugs marketed in Brazil – Boxes 1 and 2).

Both PIM evaluation tools detected approximately 21 drugs in common, notably benzodiazepines, antihypertensive drugs, ergotamine and ergot-derived drugs, laxatives, antiarrhythmic drugs, anti-inflammatory drugs, and antidepressants. However, a number of details differentiate them, such as the larger number of drugs separately cited in the Beers-Fick[13] criteria and drug classes with no mention to PIMs linked to them in the PRISCUS list[17]. Differences are also noted between them, such as in lorazepam contraindicated dosage and no doses for alprazolam, fluoxetine, and digoxin[13,17]. Phenobarbital is further contraindicated in the PRISCUS[17] list, but there is an indication by the Beers-Fick criteria[13]. Thus, they are two useful tools for clinical practice, but attention to a few details is recommended when they are used.

Table 1 – Case characteristics obtained by reviewing 100 elderly outpatients' medical records and main medications or pharmacological groups used in these patients

Characteristics	Females			Males			Total	p
Mean age (years)	75.0 ± 7.1			78.4 ± 7.9			77.4 ± 7.7	NS
Number of patients	64			36			100	-
On medications	57			32			89	NS
Mean medication consumption	3.7 ± 2.5			4.3 ± 2.5			3.9 ± 2.5	NS
Drug(s)	**≤ 74**	**≥ 75**	**Total**	**≤ 74**	**≥ 75**	**Total**		
Benzodiazepines	3	18	21	2	2	4	25	0.03*
Vitamins	6	8	14	5	4	9	23	NS
Thiazide diuretics	3	12	15	1	7	8	23	NS
Antidepressants	3	8	11	3	7	10	21	NS
Beta-blockers	2	8	10	5	4	9	19	NS
Salicylates	-	5	5	4	8	12	17	0.002*
Statins	1	5	6	4	3	7	13	NS
Cinnarizine-flunarizine	3	5	8	1	3	4	12	NS
Gingko biloba	2	4	6	-	5	5	11	NS
Calcium	5	5	10	1	-	1	11	NS

*females vs. males on medication or not; NS, nonsignificant.

The presence of significant percentages of vitamin, cinnarizine-flunarizine, and Gingko-biloba users in the present sample is noteworthy, since both evaluation tools[13,17] did not analyze the potential inappropriateness of these drugs. This caution is warranted, since chronic use of antivertigo medication, such as cinnarizine and flunarizine, might trigger movement disorders[28]; the combination of Gingko-biloba and salicylates and/or non-steroidal anti-inflammatory drugs enhances the inhibition of platelet aggregation and raises bleeding risk[29]; and indiscriminate vitamin intake shows no evidence of benefits to users[30].

Conclusion

Both criteria are useful for detecting PIMs in the elderly, with PRISCUS list being more updated and comprehensive, but care should be taken – they are not complete for the Brazilian outpatient reality.

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