Potentially inappropriate medication use among Brazilian elderly in a medication management program

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ABSTRACT

A descriptive, cross-sectional study of data from 15 elderly users of the Medication Therapy Management (MTM) service, delivered as a university extension project at a primary health unit in the city of Minas Gerais, Brazil was carried out. The objective of the study was to assess the use of potentially inappropriate medication (PIM) according to the Beers criteria (2015 version) and its relationship with drug-related problems (DRPs) identified both theoretically and by the students during the process of service provision. The MTM service adopted the methodology recommended in the theoretical framework of *Pharmaceutical Care Practice*. In addition, the knowledge on PIMs held by the Pharmacy students involved in the service was assessed by applying a semi-structured questionnaire. The majority of the patient population was in use of at least one PIM (60%), with a total of 10 PIMs prescribed to 9 patients. Each PIM corresponded to a single DRP (n=10). However, the Pharmacy students providing the service identified only three DRPs. All of the students interviewed reported knowing the PIM concept. However, the majority of students were unable to identify the PIMs in the pharmacotherapy of their patients. These results highlight the importance of the Beers criteria for identifying DRPs and the need for greater focus on these criteria during Pharmacy training.
Keywords: Beers Criteria. Medication Therapy Management. Potentially Inappropriate Medication. Inappropriate prescribing. Pharmaceutical care. Aged/ Older adults.

INTRODUCTION

Brazil is undergoing a rapid demographic transition (IBGE, 2013), a trend leading to increased demand for healthcare since the elderly population have more chronic health problems and account for a significant proportion of healthcare resources (Nascimento *et al*., 2014; Ribas & Oliveira, 2014). In addition, older adults often make chronic use of several medications concomitantly (polypharmacy) (Cuentro *et al*., 2014). The use of numerous medications is particularly concerning, given that aging is associated with physiological changes that can substantially alter the pharmacokinetics and pharmacodynamics of many drugs (Santos *et al*., 2015).

Some drugs are listed as Potentially Inappropriate Medications (PIMs) for their association with harmful health outcomes, presenting more risks than benefits when used by older adults (AGS, 2015). Moreover, elderly are often exposed to other types of inappropriate prescriptions containing drugs at overly high or low doses, with drug-drug interactions and therapeutic redundancy, which tend to have a greater clinical impact on elderly populations due to their physiopathologic peculiarities (Oliveira *et al*., 2011). All of these factors contribute to making the elderly age group especially susceptible to pharmacotherapy-related problems (Fick *et al*., 2008; Praxedes *et al*., 2011; Oliveira, 2011; Ribas & Oliveira, 2014).

In this context, managing the pharmacotherapy of the elderly constitutes an important tool for improving the quality of geriatric healthcare (Ribas & Oliveira, 2014), posing a challenge for all health professions, particularly Pharmacists (Fochat *et al*., 2012). In this respect, Medication Therapy Management (TMT) services can have a positive impact on health systems by improving the outcomes of medication therapy of patients through the prevention, identification and resolution of Drug-Related Problems (DRPs), grounded in the philosophical, methodological and management principles recommended by the practice of pharmaceutical care (Oliveira, 2011; Cipolle *et al*., 2012).

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Against this background, the objective of the present study was to assess the profile of PIM use and the presence of DRPs in the pharmacotherapy of elderly users of an MTM service provided at a primary health unit located in the metropolitan region of Belo Horizonte (Minas Gerais state) and to assess the knowledge on Beers criteria held by Pharmacy graduate students involved in the delivery of this service.

MATERIALS AND METHODS

A descriptive, cross-sectional study was carried out drawing on the data produced by the university extension project "Medication Therapy Management in Primary Health Care". A total of 15 elderly patients (≥ 60 years) attended under the project were included in the study. Data collection was performed from July to October 2015 based on documentation produced by MTM sessions provided by the project team, using a collection instrument developed by Grossi (2012).

Medication Therapy Management Service

With the aim of enhancing the MTM services delivered to the population, the Center for Studies in Pharmaceutical Care (CEAF) of the Pharmacy School of the Federal University of Minas Gerais (UFMG), in partnership with the Health Secretariat of a city in the metropolitan region, ran an extension project entitled "Medication Therapy Management in Primary Health Care". The project was initially implemented within a primary healthcare unit between August and December 2014.

Under this project, seven Pharmacy graduate students from the UFMG, supervised by three post-graduate pharmacy students affiliated to the CEAF, provided the MTM service to patients referred by the Family Health Teams of the health clinic. Besides weekly field activities, the students involved read theoretical subjects, tailored to develop the competencies needed to practice within an MTM service in primary care.

Identification of Potentially Inappropriate Medications

Among the medications in use by the older adults, the PIMs were identified according to the Beers 2015 criteria by applying the two main categories proposed by the American Geriatrics Society in the latest version of the criteria:1) PIM; and 2) PIM in the presence of a given health problem. Medications were also identified that, according to the Beers criteria, should be used with caution in the elderly (AGS, 2015). The PIM identified were also classified using the *Anatomical Therapeutic Chemical classification system* (ATC) (WHO, 2013.)

Identification of Drug-Related Problems

For each PIM identified, Drug-Related Problems (DRPs) were categorized by the study research team under "theoretical DRPs". The DRPs identified by the MTM team during patient follow-up were denominated "actual DRPs". All information available in the documentation produced

during the follow-up of each elderly patient at the MTM service was considered and the rational decision-making in the pharmacotherapy process (*Pharmacotherapy Workup*) proposed by Cipolle *et al.* (1998; 2012) and Oliveira (2011) was employed, resulting in the identification of the following DRP categories (Chart 1).

Chart 1. Categories of Drug-Therapy Related Problems according to Cipolle, Strand & Morley (2004 and 2012) and Oliveira (2011).

Drug-related problem	Description of drug-related problem
Unnecessary drug therapy	Patient has no medical indication justifying the use of the drug
Needs additional drug therapy	The patient requires more drug therapy to treat or prevent a health problem.
Ineffective drug	The medication is ineffective for producing the desired effect.
Dosage too low	The medication is not strong enough to produce the desired effect.
Adverse drug reaction	The medication is causing an adverse reaction in the patient.
Dosage too high	The medication dose is too strong causing detrimental effects.
Non-compliance	The patient is unable or unwilling to use the medication as recommended.

Assessment of Knowledge on PIMs held by Pharmacy Students

This stage involved the five students responsible for following the 15 elderly patients included in the study. The knowledge on PIMs held by these students was assessed by applying a semi-structured questionnaire.

Ethical aspects

The present study was approved by the Research Ethics Committee of the UFMG under protocol CAAE - 25780314.4.0000.0149. All participants, patients and pharmacy students included in the study signed a free and informed consent form.

RESULTS

Of the elderly patients included in this study, 13.3% (n=2) were aged 60-65 years, 33.3% (n=5) 66-74 years and 53.3% (n=8) ≥ 75 years. An average of 6.5 drugs per patient was found and most patients were in use of five drugs or more.

Profile of Potentially Inappropriate Medicine Use

The prevalence of use of at least one PIM in the sample studied was 60.0% (n=9), with a total of 43 different medications in use. Of all medications used, eight (18.6%) were classified as PIMs. With regard to classification according to the Beers criteria (AGS, 2015), of the total eight PIMs identified, seven (87.5%) were category 1 (PIM), and one (12.5%) was category 2 (PIM in the presence of a given health problem).The data is given in Table 1.

Table 1 – PIMs in use by the population studied (AGS, 2015).

PIMs identified	ATC Classification	Beers Category	Absolute frequency of use (n)
Cyclobenzaprine	M03 – muscle relaxants	1	1
Citalopram	N06 – psychoanaleptics	2	1
Clonazepam	N03 – antileptics	1	1
Digoxin	C01 – cardiac therapeutic	1	1
Phenobarbital	N03 – antileptics	1	1
Nortriptyline	N06 – psychoanaleptics	1	2
Omeprazole	A02 – medications for acid-related disorders	1	2
Promethazine	R06 – systemic use anti-histamine	1	1

Legends (Category according to Beers 2015):
1-PIM

2-PIM in the presence of a given health problem.

Chart 2 – Theoretical DRPs identified

Patient	PIM in use	Specificity of case	Rationale for being considered PIM by Beers (AGS, 2015)	Description of DRP and its cause (Cipolle, Strand & Morley, 2012)
A	Citalopram 20mg, MID	History of falls and femoral fracture	Increases risk of falls	Adverse Drug Reaction, medication unsafe for patient
	Omeprazole 20 mg, MID	Use for over 8 weeks	Risk of infection by Clostridium difficile, bone loss and fractures	Adverse Drug Reaction, medication unsafe for patient
D	Cyclobenzaprine 5 mg, MID	-	Anti-cholinergic effects, sedation, fracture risk, efficacy at doses tolerated by elderly is questionable	Unnecessary drug, no present medical indication.
E	Clonazepam 2 mg, BID	-	Increases risk of cognitive impairment, delirium, falls, fractures and road vehicle accidents.	Unnecessary drug, non-pharmacological therapy indicated.
F	Nortriptyline 25 mg, MID	-	Highly anti-cholinergic, can promote sedation and orthostatic hypotension;	Adverse Drug Reaction, medication unsafe for patient
G	Digoxin 0.25mg, MID	Dose >0.125mg/day	High doses increase risk of toxicity and promote no additional benefit	High dose, wrong dose.
H	Omeprazole 20 mg, MID	Use for over 8 weeks	Risk of infection by Clostridium difficile, bone loss and fractures	Adverse Drug Reaction, medication unsafe for patient
J	Nortriptyline 25 mg, MID	-	Highly anti-cholinergic, can promote sedation and orthostatic hypotension;	Adverse Drug Reaction, medication unsafe for patient
L	Phenobarbital 100mg, MID	-	Physical dependence, tolerance to benefits of sleep and risk of overdose at low doses	Adverse Drug Reaction, medication unsafe for patient
M	Promethazine 25 mg, MID	-	Tolerance risk when used as hypnotic, anti-cholinergic effects (confusion, dry mouth, wind, among others) and toxicity.	Adverse Drug Reaction, medication unsafe for patient

Half of the PIMs identified belonged to the "Nervous System" anatomical group where 66.7% of these drugs were associated with developing adverse anticholinergic effects (nortriptyline, cyclobenzaprine or promethazine, clonazepam and digoxin) (Gage *et al*., 2014; Gray *et al*., 2015; AGS, 2015).

Application of the Beers category for medications to be used with caution by elderly (AGS, 2015) revealed a further five medications (haloperidol, furosemide, spironolactone, hydrochlorothiazide and fluoxetine) besides the citalopram and nortriptyline, previously classified as PIMs by the other Beers categories used in the study (Table 2).

Drug-related problems

A total of ten theoretical DRPs (one for each PIM used by the elderly) and three actual DRPs were identified. None of the cases matched for proposed classification of theoretical and actual DRPs. The predominant category identified among the theoretical DRPs was safety, adverse drug reaction (n=8; 80%) as shown in Chart 2.

Knowledge on PIMs

All five students reported having encountered the PMI concept at some point, through reading scientific articles, while taking part in the extension project in question, when studying the matter at university, or during presentation of post-graduate studies. All students stated that they deemed it important to assess the use of these medications during MTM sessions.

The majority (80%) of the students reported that did not feel able to identify PIMs during clinical practice, citing

Table 2 – Medications to be used with caution by elderly present in the pharmacotherapy of the population studied (AGS, 2015).

PIMs identified	ATC Classification	Absolute frequency of use (n)
Citalopram	N06 – psychoanaleptics	1
Spironolactone	C03 – diuretics	2
Fluoxetine	N06 – psychoanaleptics	1
Furosemide	C03 – diuretics	7
Haloperidol	N05 – psycholeptics	1
Hydrochlorothiazide	C03 – diuretics	1
Nortriptyline	N06 – psychoanaleptics	2

the following reasons: the superficial manner in which the subject was taught during university training, lack of knowledge about the literature used to identify these drugs, and lack of clarity surrounding the PIM concept.

DISCUSSION

The average number of medications used per elderly patient in the present study (6.5 medications) was similar to that detected by Baldoni *et al*. (2014) (6.9 medications) among elderly users of a Basic Health Unit (UBS) in Ribeirão Preto-São Paulo state. However, the figure found in the present study proved higher than that detected by Blanco-Reina *et al*. (2014) (4.5 medications) in older adults from Lanzarote/Espírito Santo state and by Manso *et al*.(2015) (3.5 medications) among non-institutionalized elderly users of a private healthcare plan from São Paulo/São Paulo state. This disparity in average number of medications used might be attributed to the fact that many of the elderly patients included in the present study were referred to the MTM service by Family Health Teams because they were deemed complex patients in terms of pharmacotherapy.

Profile of Potentially Inappropriate Medicine Use
The prevalence of PIM use by the population studied (60.0%) was similar to the rate found by Baldoni *et al*.(59.2%) in Ribeirão Preto-São Paulo state. By contrast, the figure found in the present study was higher than that found by Huffenbaecher *et al*. (2012) in Araraquara-São Paulo state (26%), Blanco-Reina *et al*. (2014) in Lanzarote/Espírito Santo state (44%) and by Steinman *et al*. (2014) in California/USA (26%). However, the limited comparability of the cited studies with the present investigation should be noted, whereby the former all applied the 2012 version of the Beers criteria for prevalence analyses. Even after excluding cases of inappropriate use of omeprazole (the only drug recently added to the 2015 Beers criteria), the prevalence of PIM use in the present study remains high (53.3%).

Despite limitations concerning sample size, this result shows that PIM use is a reality among the elderly population studied, indicating the need for greater care in geriatric prescribing and confirming that, even in the presence of extensive evidence alerting to the dangers of PIM use, these drugs continue to be prescribed to older adults (AGS, 2012).

According to the ATC classification, 50% of the PIMs identified in this study belonged to the "Nervous System" anatomical group, similar to the rate found by Huffenbaecher *et al*. (2012) in Araraquara-São Paulo state (47.6%) and by Blanco-Reina *et al*. (2014) in Lanzarote/Espírito Santo state (59.3%). Most of these medications are controlled under Decree no.344/1998 issued by ANVISA (National Health Surveillance Agency, Brazil), i.e. they can be dispensed by medical prescription only. These points to the need for greater control of geriatric prescribing in the population studied.

Notably, the majority of the PIMs identified (66.7%) are associated with the development of anticholinergic effects in the literature. Recent studies have shown that besides causing problems such as tachycardia and intestinal constipation, medications exhibiting this property can increase the incidence of dementia among older adults when used chronically (Gage *et al*., 2014; Gray *et al*., 2015; AGS, 2015).

Another drug identified by some studies as a cause of adverse cognitive effects and increased mortality among older adults is phenobarbital, one of the PIMS identified in the present study (Ding *et al*, 2006). This barbiturate with low therapeutic index is a less safe alternative therapeutic drug than more recently developed anticonvulsants, especially in the absence of refractory conditions and/or status epilepticus (AGS, 2015; Minicucci *et al*.2006). This issue is highly relevant in view of the rising incidence of epilepsy in older adults worldwide (Pugh *et al*., 2004; Acharya & Acharya, 2014).

The antidepressants identified as PIMs in this study were classified as Selective Serotonin Reuptake Inhibitors (SSRI) (citalopram) and Tricyclic Antidepressants (TAD) (nortriptyline).Beyond the age of 70 years, the frequency of depression doubles every 5 years, with the condition present in one out of four individuals aged 85 years, justifying the use of these drugs by the older population (Felice *et al*.,2015).

The SSRI class is the first line of treatment for elderly, since these drugs are considered by many studies as safer than TAD in such patients given the adverse anticholinergic effects caused by the latter group of drugs. However, a number of different adverse effects have been reported in elderly patients in use of SSRI therapy, such as hyponatremia and upper gastrointestinal bleeding, as well as an increase in the incidence of falls and fractures, justifying the inclusion of this group in the list of medications to be used with caution in the Beers criteria (Taylor, 2014; Felice *et al*., 2015; AGS, 2015).

The identification of medications that should be used with caution by older adults in the present study is noteworthy. These medications can affect the secretion of the antidiuretic hormone and cause hyponatremia, where their use in older individuals should be monitored (AGS, 2015).

Drug-Related Problems

The discordance between "theoretical" and "actual" DRPs indicates the need for more comprehensive study of the peculiarities of geriatric pharmacotherapy during pharmacy training, including the subject of Beers criteria and their application in clinical practice for identifying and resolving DRPs. Following identification of the theoretical DRPs and confirmation in the clinical practice setting, the disparities were reported to the individuals running the MTM service, leading to the rectifying of treatment care plans of the patients involved in the study.

Knowledge on PIMs allows safety-related DRPs to be identified and avoided. In this context, Beers criteria is a useful tool for informing the MTM team about the risks involved in the use of PIMs by patients. In clinical practice, examining the actual use of medication allows indication and effectiveness problems to identified by following the logical rationale of decision-making in pharmacotherapy. This occurred in the cases of patients D and E that had indication-related DRPs (Chart 2). This impacts professional conduct since, beyond merely recommending switching the PIM for a safer available drug, it should promote its withdrawal and introduction of non-pharmacological treatment whenever possible.

Although highly useful in clinical practice, the Beers criteria should not replace the judgement of health professionals or serve as hard-and-fast rules for prescribing in geriatrics. Ultimately, healthcare calls for an individualized view of the patient (Resnick & Pacala, 2012). Indeed, incorporation of these medications into the pharmacotherapy of older adults is often necessary owing to patients´ individual needs. Notwithstanding, monitoring the safety parameters of PIM use is often complex and inadvisable. One example is the limitation and complexity of monitoring the impact of benzodiazepine use, a drug associated with increased risk of developing cognitive impairments, delirium, falls and fractures (AGS, 2015), with evidence showing this group of drugs can induce or aggravate episodes of confusion and increase the incidence of dementia and Alzheimer disease (Gage *et al*., 2014; Butlletí Groc, 2015; AGS, 2015).

Knowledge on PIMs

The discordance between "actual" and "theoretical" DRPs is congruent with the response given by 80% of the students that they do not feel able to identify PIMs during clinical practice. Thus, "knowing what a PIM is" was not enough to identify these medications in patients´ pharmacotherapy.

Pharmacists play a key role in enhancing geriatric pharmacotherapy, and are also able to provide training to other health professionals on PIMs and on appropriate geriatric prescribing. However, the prescribing of PIMs to elderly patients is often attributed not only to a lack of training of the prescribers but also to shortcomings in pharmacist training (Wahab, 2015).

It is therefore paramount that universities provide opportunities for students to hone the skills needed for clinical practice, ensuring training coordinated within the social setting. There is a need to go beyond a content-based model as, despite addressing this knowledge in theoretical classes, actual practice and execution are vital for true acquisition of knowledge (Walker *et al*., 2010; Almeida *et al*, 2014).

Walker *et al*.(2010) showed that the activities carried out at a university teaching hospital were important for Pharmacy students to gain experience and build self-confidence in clinical practice while also provided valuable patient care services. Schorr *et al*. (2014) demonstrated the positive impact of Pharmacy scholars on the safety of medications in a hospital settings, where over a 10-month period, the students detected a total of 4,085 DRPs in 6,551 patients. The students performed interventions for virtually all DRPs detected and resolved the majority of cases (74%).

Given the scenario in which the proportion of Brazilian elderly is set to rise in the coming years (Ribas & Oliveira, 2014) and that the use of PIMs is a reality in the elderly population globally (AGS, 2012; AGS, 2015), the importance of proper teaching-learning processes that promote the use of the latest Beers criteria as a guide in the care of geriatric patients by health professionals, particularly during medical prescribing and the TMT service is evident. Lastly, application of the Beers criteria can allow DRPs to be identified and avoided.

This study was derived from a University extension activity and has the limitation of a small sample size. Strengths of this study include its use of the PW documentation method, enabling global documentation of various aspects related to pharmacotherapy, and its pioneering application of the Beers 2015 criteria to address a subject hitherto seldom reported for the Brazilian milieu, namely, the importance of avoiding the use of inappropriate medications for the elderly.

RESUMO

Uso de medicamentos potencialmente inapropriado em idosos brasileiros em um programa de gerenciamento de medicamentos

Este estudo transversal descritivo foi realizado com dados de 15 idosos acompanhados em um Serviço de Gerenciamento da Terapia Medicamentosa ofertado como projeto de extensão universitária em uma unidade de atenção primária à saúde em um município de Minas Gerais, Brasil. Teve como objetivo avaliar a utilização

de medicamentos potencialmente inadequados (MPI) de acordo com os critérios de Beers (versão 2015) e sua relação com problemas relacionados ao uso de medicamentos (PRM) identificados teoricamente bem como aqueles identificados pelos estudantes durante o processo de provisão do serviço. O serviço seguiu a metodologia preconizada no arcabouço teórico de *Pharmaceutical Care Practice*. Além disso, por meio de um questionário semiestruturados, foi avaliado o conhecimento dos estudantes de Farmácia envolvidos no serviço acerca de MPI. A maioria da população utilizava pelo menos um MPI (60%), sendo que foram identificados 10 MPI que estavam prescritos para 9 idosos. Cada MPI correspondeu a um PRM teórico (n=10). No entanto, os estudantes de Farmácia oferecendo o serviço identificaram apenas três PRM. Todos os estudantes entrevistados relataram conhecer o conceito de MPI. Porém, a maioria não os identificou na farmacoterapia de seus pacientes. Estes resultados demonstram a importância dos critérios de Beers para identificação de PRM e a necessidade de melhorias na sua abordagem durante a graduação em Farmácia.

Palavras-chave: Critérios de Beers. Gerenciamento da Terapia Medicamentosa. Medicamentos potencialmente inadequados. Prescrição inadequada. Atenção Farmacêutica. Idosos.

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