International Journal of Clinical Pharmacy (2019) 41:888–894
https://doi.org/10.1007/s11096-019-00842-2

RESEARCH ARTICLE

Potentially inappropriate medications in older kidney transplant recipients: a Brazilian prevalence study

Iwyson Henrique Fernandes da Costa[1,5] · Renan Morais e Silva[1] · Juliana de Oliveira Carlos[1] · Maria Cleonice Araújo Silva[1] · Maria Karine Cavalcante Pinheiro[1] · Bruna Cristina Cardoso Martins[2] · Paula Frassinetti Castelo Branco Camurça Fernandes[3] · Marjorie Moreira Guedes[4]

Received: 8 June 2018 / Accepted: 3 May 2019 / Published online: 15 May 2019

Abstract

Background Older kidney transplant recipients take a larger number of medications than younger patients, but there is currently no evidence that this affects health outcomes or that is it associated with potentia medicine-related problems. *Objective* To evaluate the prevalence and number of potentially inappropriate medications in older kidney transplant recipients and also the possible associated factors (sex, age, comorbidities, number of medications, etc.). *Setting* A renal post-transplant ambulatory outpatient clinic of a university hospital in Fortaleza, Brazil. *Method* PIMs were defined according to the Beers criteria, version 2015. Medications were classified following the Anatomical Therapeutic Chemical Classification System. Chi squared tests and analysis of variance were used for the analyses. *Main outcome measure* Prevalence of potentially inappropriate medications and medication groups with higher prevalence rates of PIMs, including associated factors. *Results* Among 143 kidney transplant recipients, 77.6% had at least one potentially inappropriate medication as part of their prescription regime. Medication groups that were most implicated in PIM are medicines that act on the alimentary tract and metabolism (55.9%), cardiovascular system (32.2%) and nervous system (21.7%). We detected a high prevalence (63.6%) of self-medication (use of OTC medicines without indication of a healthcare professional) among the population studied. There was a statistically significant association between the number of prescribed medications and the presence of potentially inappropriate medication in the prescription regime ($P < 0.01$). *Conclusion* Our data draw attention to the need of medicine therapy management by clinical pharmacists and clinicians in this group of patients and also assessing the real clinical impacts of these medications in the prescription regimes of elderly renal transplant patients.

Keywords Beers criteria · Brazil · Kidney transplant · Older adults · Polypharmacy · Potentially inappropriate medications

Impacts on practice

- Potentially inappropriate medications among elderly kidney transplant recipients are an important problem in Brazil that needs attention and further monitoring by clinical pharmacists.
- PIMs with a high prevalence in elderly kidney transplant patients are medicines that act on the alimentary tract and metabolism, cardiovascular system, and nervous system.
- The high number of prescribed potentially inappropriate medicines in elderly kidney transplant patients shows the need of medicine therapy management.

✉ Iwyson Henrique Fernandes da Costa
iwyson@gmail.com

1 Programa de Residência Integrada Multiprofissional em Assistência Hospitalar à saúde, Assistência em Transplantes da Universidade Federal do Ceará, Fortaleza, Brazil

2 Universidade Federal do Ceará, Fortaleza, Brazil

3 Serviço de Nefrologia e Transplante Renal do Hospital Universitário Walter Cantídio, Fortaleza, Brazil

4 Serviço de Farmácia Clínica do Hospital Universitário Walter Cantídio, Fortaleza, Brazil

5 Hospital Universitário Walter Cantídio, Rua Capitão Francisco Pedro 1290, Rodolfo Teófilo, Fortaleza, Ceará 60430-372, Brazil

Introduction

Like almost everywhere, the Brazilian population is also aging, and has an increasing number of older adults (aged 60 or older). A decade ago, there were 39 elderly for every 100 young people, while within 30 years there will be an estimated 153 elderly people for every 100 young people [1]. Older people frequently experience multimorbidities and, as a result, several different medicines are prescribed. The average daily intake of medicines is 3.2 and 1.8 among institutionalized and community-dwelling elderly, respectively [2]. This makes the population of older adults more vulnerable to potentially inappropriate medications (PIM), and increases the risk of adverse medicine events, medicine interactions, and, consequently, health care costs. Use of PIMs is therefore not advisable, and safer alternatives should be considered [3, 4].

Chronic kidney disease (CKD) is one of the comorbidities that is observed in older people. Kidney transplantation is currently the best available treatment when CKD reaches its end stages [5]. Besides providing a better quality of life, it also enables a higher survival than what is offered by other forms of renal replacement therapy [6]. In 2009, 10.8% of newly enlisted patients for transplant in Brazil were 60 years or older; this number increased ten times since 1999 [7]. In 2014, in some Brazilian transplantation centers, the number of older kidney transplant recipients increased to 21% [8].

Prevalence data on the use of PIMs among non-institutionalized elderly people in Brazil are limited. In recent studies, this prevalence ranged between 21.7 and 59.2% [9, 10]. A previous study in Japan has already presented the prevalence of inappropriate prescriptions in elderly hemodialysis patients [11]. So far, no study has assessed this prevalence in kidney transplant patients. In this regard, there is evidence from a study in the US, that older kidney transplant recipients take a larger number of medications than younger recipients, but there is not yet evidence of the implications of this observation on health outcomes and medicine-related problems [12].

In 2015, the American Geriatrics Society (AGS) updated the Beers criteria [13]; as in previous versions [14], the criteria present lists of PIMs to be avoided in older adults. This version now includes medicines that should be avoided or adjusted based on renal function and medicine–medicine interactions documented to be associated with harm in elderly patients [13]. PIMs listed in the Beers criteria may exacerbate the health condition and the prognosis of elderly people and negatively influence therapeutic outcomes [3].

The evidence of a relationship between age and number and type of medications prescribed in renal transplant patients is already available in the literature [11]. Nevertheless, the real prevalence of PIM use among older kidney transplant recipients is unknown and needs to be clarified, in order to guide healthcare providers when prescribing managing these patients and to understand which factors are associated with the prevalence of these PIMs.

Aim of the study

To assess the prevalence and number of PIMs in older renal transplant recipients and to explore possible associated factors such as age, sex, comorbidities, number of medications and self-medication practice.

Ethics approval

The research ethics committee of the university hospital of Fortaleza provided ethical approval (no. 2.174.931). Participants signed an informed consent form prior to beginning the study.

Method

Study design and setting

This was a cross-sectional prospective quantitative exploratory study. It was developed in a kidney post-transplant outpatient clinic in a university hospital from April 2017 to September 2017 in Fortaleza, Ceará, Brazil. Organ transplant programs have been growing in Brazil, and Ceará is one of the leading states [15]. In 2017, more than 200 kidney transplants have been done in the eight transplant centers in the state, a number above the national average [16].

The clinic has an extensive specialized service and belongs to the hospital, which is maintained by the federal government and offers quaternary health care of high complexity. It also offers clinical follow-up to pre- and post-kidney transplant patients by a multidisciplinary healthcare team. By 2017, more than 1500 post-kidney transplant patients were followed at our center, the second largest in absolute numbers of the state [16].

Sample

We used a convenience sample made up of post-kidney transplant patients who received pharmaceutical care services (therapeutic medicine monitoring, health education, pharmaceutical dispensing, medicine regimen review, pharmacotherapeutic follow-up, etc.) in the outpatient clinic and voluntarily agreed to participate in the study.

We included kidney transplant individuals aged 60 and older, who were enrolled in and participated in post-transplant ambulatory care. We considered the definition of older adults in the study, according to the National Policy of Healthcare for the Elderly in Brazil, which was published in 2006 [17]. We excluded patients who had limited information in their medical records or were transferred to another transplant center.

Data

Data were collected from direct structured interviews with individuals and recorded in pharmaceutical forms developed for this purpose. Medical records with laboratory examinations and healthcare team notes were also used as data sources. A trained clinical pharmacist conducted interviews during the individual's regular consultation with the pharmacist. All clinical pharmacists involved in the interviews were previously trained about the data collection forms and the inclusion criteria. A 2 weeks pilot with 30 patients was necessary for the last adjustments in the structured interviews. The data collection took place in the pharmacist's office, guaranteeing privacy and confidentiality of the information. The information collected included age; sex; time of transplant; type of donor; comorbidities; allergy history; use of medication, including self-medication (that is, use of OTC medicines without recommendation of a healthcare professional); herbal medicines; and dietary supplements.

Measurements

The Beers criteria, which were updated in 2015 [13], were used for PIM identification and assessment of safety in each individual's medicine prescriptions. Although Beers criteria were designed for use in adults aged 65 or older, we extrapolated this to the Brazilian population (aged 60 or older) as previously done by other studies [9, 10]. The anatomical main groups and therapeutic subgroups of medications were classified according to the Anatomical Therapeutic Chemical Classification System (ATC), defined by the World Health Organization (WHO) Collaborating Centre for Medicine Statistics Methodology. The ATC system classifies the active substances on the basis of five different levels, according to anatomical, pharmacological, chemical, and therapeutic properties. The prevalence of PIM was calculated by dividing the number of individuals with at least one PIM by the total number of individuals and expressed as percentage. The prevalence of PIM of each therapeutic group was calculated by dividing the number of individuals with at least one PIM of that therapeutic group by the total number of individuals.

Statistical analyses

Parametric data were presented as the percentage (categorical variables) and the mean ± standard deviation or median and percentile (continuous variables). To verify an association between PIM and the variables (age, sex, comorbidities, number of medication and self-medication practice), we used both parametric and non-parametric tests. The independence between the number of PIMs and epidemiological variables, as well as self-medication, was tested using a Chi squared test (X^2). We used the one-way analysis of variance (ANOVA) to verify an association between the number of medications and PIMs and, posteriorly, in paired comparisons (Tukey–Kramer test). All analyses were performed using Excel (Microsoft corp., Redmond, WA), and a P value less than 0.05 (two tailed) was used to indicate statistical significance.

Results

Population

During the study period, 150 individuals were identified, but seven met the exclusion criteria. Participants were aged 60 to 82 years (mean 66.5 ± 5.3 years), of whom 65.7% were male. We observed a mean of 8.9 ± 2.6 medications per patient, both prescribed or not (range 3–15) (Table 1).

Clinical profile and potentially inappropriate medications

There were a total of 1247 medications reported. The pharmacological groups more frequently used, according to the ATC classification, were the medicines that act on the cardiovascular system (28.5%), followed by medications for the alimentary tract and metabolism (23.4%), antineoplastic and immunomodulating agents (22.0%), systemic hormonal preparations (excluding sex hormones and insulins) (8.1%), and medications that affect blood and blood-forming organs (6.8%). Other pharmacological groups were used at a frequency of use less than 5.0%.

Among the 1247 medications, 183 (14.7%) were considered potentially inappropriate according to the 2015 Beers criteria. Table 2 presents the number and distribution of identified PIMs according to the ATC system and the prevalence of PIM in each therapeutic group, highlighting medicines that act on the alimentary tract and metabolism. The most frequent PIMs among our patients per therapeutic group were respectively: omeprazole (46.9%) along with other proton pump inhibitors (PPI) (4.9%); clonidine and doxazosin with 19.6% and 13.3% patients, respectively; and finally benzodiazepines with 18.9%.

Table 1 Kidney transplant patient characteristics (N = 143)

Characteristics	Value
Demographic	
Male [n (%)]	94 (65.7)
Age (years) [mean ± SD]	66.5 ± 5.3
Transplant	
Time of transplant (years), median (P25–P75)	6.5 (3.3–10.7)
Type of donor [n (%)]	
Deceased	122 (85.3)
Living related	18 (12.6)
Living unrelated	3 (2.1)
Kidney failure cause [n (%)]	
Hypertension	43 (30.1)
Diabetes mellitus	36 (25.2)
Polycystic kidney disease	23 (16.1)
Chronic glomerulonephritis	17 (11.9)
Undetermined	27 (18.9)
Clinical	
Number of comorbidities [mean ± SD]	2.5 ± 0.9
Number of comorbidities [n (%)]	
≤ 1	20 (14.0)
2	52 (36.4)
≥ 3	71 (49.6)
Hypertension [n (%)]	117 (81.8)
Dyslipidemia [n (%)]	95 (65.0)
Diabetes mellitus [n (%)]	80 (55.9)
Allergy history [n (%)]	
Yes	22 (15.4)
Self-medication [n (%)]	
Yes	91 (63.6)
Number of medications, mean ± SD	8.9 ± 2.6

n sample size, *P25* 25th percentile, *P75* 75th percentile, *SD* standard deviation

Table 3 presents the results of the association tests among the number of PIMs present in the prescriptions for older kidney transplant recipients with the following variables: sex, age, comorbidities, number of medications and self-medication behavior.

Discussion

Our results relied on a sample that was predominantly male; in contrast, others studies with older adults in Brazil [9, 10, 19–21] and worldwide [22, 23] that relied on a sample that was predominately female. The trend of a higher proportion of females was also observed in some studies [24, 25], even with elderly hemodialysis patients [11] and elderly renal transplant patients [12]. Regarding mean age, our findings were similar to studies in Southeastern Brazil [7, 26], but lower than other national studies [9, 19, 21]. That might be explained by the fact that there are only a small number of renal transplants in patients older than 70 years in our center, and graft survival may depend of several other variables.

Depend on the type of donor, the deceased donor was the most frequent, and this result agreed with another Brazilian study [7] and an American study that enrolled kidney transplant patients [12]. Hypertension was the main cause of CKD in our study, as was also observed in a study of hemodialysis patients in São Paulo [27]. Diabetes, on the other hand, was the main cause of renal transplant in three other studies [7, 11, 12]. Despite this, the number of patients with either hypertension or diabetes was almost equal in our study.

The number of comorbidities also agreed with other results in the literature [10, 11, 20], in which this number was greater than two chronic diseases per patient. Hypertension was the most prevalent comorbidity, followed by dyslipidemia, which was a finding that was also reported by Cassoni et al. [20], Andrade et al. [19], and Chisholm et al. [12]. This trend can be easily explained by the high prevalence of hypertensive people in the Brazilian population, which is approximately 30% [21, 28].

The present study exhibited high numbers regarding self-medication behavior. This number was higher than previous Brazilian results, which ranged from 5.6 to 35.7% [10, 20, 21]. What is particularly concerning about our data is that a previous study found that self-medication practice is associated with poor schooling and worse self-rated health [21], possibly being a risky behavior in this specific group of patients.

When compared to a sample of elderly renal transplant recipients in the United States [12], the mean number of medications per patient (12.4 ± 3.7) was higher compared to our study (8.9 ± 2.6); nevertheless, our results were higher than other Brazilian studies that included elderly people [9, 10, 20, 21]. This finding is mainly the result of patients having to take immunosuppressant therapies, such as calcineurin inhibitors, mycophenolic acid and sometimes also glucocorticoids (according to the protocol of our center), in addition to therapies for other comorbidities (for example, hypertension, diabetes, and dyslipidemia).

To date, we did not find any studies that have adopted the 2015 Beers criteria for PIM identification. Nonetheless, the prevalence of elderly people with at least one PIM was higher in our study compared to any other national study [9, 10, 19–21] that adopted the 2012 Beers criteria, except for Lima et al. [29], who reported 82.6% of elderly patients with at least one PIM in long-term care homes. The numerous factors for the variation in PIM frequency in Brazil, such as different kinds of sample (community dwelling, hospital, long term care home) in the studies, continental dimensions country, socio-economic

Table 2 Number and prevalence of potentially inappropriate medications in older adult according to Beers criteria (2015) and the ATC classification

Number of patients with PIMs [n (%)]			
0			32 (22.4)
1			60 (41.9)
≥ 2			51 (35.7)
Total			143 (100)
ATC[a] Classification	Number of medicines [n (%)]	PIM [n (%)]	Prevalence (%)
A: alimentary tract and metabolism medicines	292 (23.4)	86 (47)	55.9
Medicines for acid-related disorders	103 (8.2)	74 (40.4)	
Others	189 (15.2)	12 (6.6)	
C: cardiovascular system medicines	356 (28.5)	55 (30.0)	32.2
Antihypertensives	248 (19.9)	48 (26.2)	
Others	108 (8.6)	7 (3.8)	
N: nervous system medicines	60 (4.8)	35 (19.1)	21.7
Psycholeptics	23 (1.8)	23 (12.6)	
Others	37 (3.0)	12 (6.5)	
Others ATC[a] groups	539 (43.3)	7 (3.9)	4.9
Total	1247 (100)	183 (100)	

[a]*ATC* Anatomical Therapeutic Chemical Classification System [18], *PIM* potentially inappropriate medication, *n* sample size

Table 3 Association between demographic and clinical variables of older kidney transplant recipients and the number of PIMs (N = 143)

Variables	Number of PIMs			*p*
	0	1	≥2	
Age				0.25[a]
60–65 years	18	26	28	
66–70 years	10	22	10	
> 70 years	4	12	13	
Sex				0.86[a]
Male	22	38	34	
Female	10	22	17	
Comorbidities				0.63[a]
Diabetes mellitus	17	32	31	
Hypertension	23	47	47	
Others	2	5	1	
Number of medications (mean ± SD)	7.3 ± 2.5	8.7 ± 2.8	10.1 ± 1.9	< 0.01[b]
Self-medication				0.19[a]
Yes	22	33	36	
No	10	27	15	

PIM potentially inappropriate medication, *SD* standard deviation

[a]Based on Chi squared test (X^2)

[b]Based on one-way analysis of variance (ANOVA)

differences, have already been reported in the literature [21, 29]. However, no other studies that assessed PIMs among elderly transplant patients in Brazil have been found for comparison.

In Table 2, it is noticeable that the people in the group who were taking the higher number of PIMs were medicines of alimentary tract and metabolism, with a prevalence of almost 56%. This pattern was different in some other studies [10, 22, 23, 30]. For example, Cassoni et al. [20] in their study with community elderly in Sao Paulo and Kondo et al. [22] with older inpatients in France have found a higher prevalence in people who use medicines that act on the cardiovascular system. Even though, cardiovascular medicines were the most frequent pharmacological group among our patients and PIM prevalence in this group was higher than 30%.

We observed a large number of prescriptions for acid-related disorders, especially PPI. This marked difference may be explained by the fact that PPI were included in the most recent version of the Beers criteria [13] due to a more accentuated risk in elderly people of developing infection by *C. difficile*, osteopenia, and fractures. Because of this recent inclusion, it was not highlighted by other older studies. Nevertheless, inappropriate use of PPI has been demonstrated by other studies, not only in elderly populations, and is a relevant topic to be discussed in our clinical practice [30, 31]. The benefits of the therapy with PPI must be closely monitored and discontinued as soon as it is no longer needed [32].

After statistical analyses, we found no significant associations between PIM and the following variables: age (none of the age ranges), sex, and comorbidities. Similarly, Kondo et al. [11] did not find any associations between sex, age, and presence of PIM prescriptions in their study with elderly hemodialysis patients in Japan.

We found a significant association between the number of prescription medicines and the number of PIMs, which was also found by Lutz et al. [10], Cassoni et al. [20], Kondo et al. [11], Undela et al. [33], and Nisthala et al. [24]. In other words, the higher the number of prescription medicines, the greater the number of PIMs. This provides further evidence that polypharmacy puts our sample of elderly kidney transplant recipients at risk of having PIM in their prescriptions.

There was no association between the practice of self-medication and the presence of PIM in our study, diverging from some other studies [10, 21], which considered self-medicating behavior to be risky for elderly people because of PIM exposure. That could be explained by the fact that great part of our patients was herbal medicines users, which are not contemplated in the Beers criteria.

Due to the large amount of prescription medicines, older renal transplant patients are also at risk of PIMs. Brazil is the third country in with respect to the number of renal transplants, behind only the USA and China, emphasizing the importance of our sample. This demonstrates that constant care and review of pharmacotherapy of this group of patients by the nephrologist, clinical pharmacist and healthcare team is necessary.

Our study has some limitations because it is a relatively small sample size in a single center, even when considering that it is a specific group of patients. In addition, the Beers criteria have been developed with a focus only on medications marketed in the United States, and as previously said, designed for a population aged 65 or older, while we considered individuals aged 60 or older. This might have overestimated the prescription of PIM in our population and cannot be generalized to other countries.

Conclusion

The highest prevalence of PIMs in elderly kidney transplant patients were among medications that act on the alimentary tract, cardiovascular system and nervous system. The large number of medications per patient was as a risk factor for presence of PIM. For the first time, this study brings together data on elderly renal transplant recipients and PIMs. From this perspective, the fact that PIMs were present in the majority of prescription regimes of elderly kidney transplant patients highlights the necessity of careful management of therapies in this specific group of patients. Thus, this study and this specific group of renal transplant recipients presents important results. Future investigations with a larger number of individuals should focus on assessing the real clinical impacts of these PIMs in the prescription regimes of elderly renal transplant patients.

Acknowledgements The authors are truly grateful to all patients who participated in this study. They also would like to thank all members of the Kidney transplant healthcare team of the University Hospital in Fortaleza, Brazil.

Funding None

Conflicts of interest The authors declare that they have no conflict of interest.

References

1. Miranda GMD, Mendes ACG, Silva ALA. Population aging in Brazil: current and future social challenges and consequences. Rev Bras Geriatr Gerontol. 2016;19(3):507–19.
2. Marchini AMPS, Deco CP, Silva MRV, Lodi KB, Rocha RF, Marchini L. Use of medicines among a Brazilian elderly sample: a cross-sectional study. Int J Gerontol. 2011;5(2):94–7.
3. Deliens C, Deliens G, Filleul O, Pepersack T, Awada A, Piccart M, Praet JP, Lago LD. Drugs prescribed for patients hospitalized in a geriatric oncology unit: potentially inappropriate medications and impact of a clinical pharmacist. J Geriatr Oncol. 2016;7(6):463–70.
4. Nam Y, Han JS, Kim JY, Bae WK, Lee K. Prescription of potentially inappropriate medication in Korean older adults based on 2012 Beers criteria: a cross-sectional population based study. BMC Geriatr. 2016;16(118):1–9.
5. Ojo AO, Hanson JA, Meier-Krisesche H, Okechukwu CN, Wolfe RA, Leitchman AB, Agodoa LY, Kaplan B, Port FK. Survival in recipients of marginal cadaveric donor kidneys compared with other recipients and wait-listed transplant candidates. J Am Soc Nephrol. 2001;12(3):589–97.
6. Cornella C, Brustia M, Lazzarich E, Cofano F, Ceruso A, Barbé MC, Fenoglio R, Cella D, Stratta P. Quality of life in renal transplant patients over 60 years of age. Transpl Proc. 2008;40(6):1865–6.
7. Orlandi PF, Cristelli MP, Aldworth CAR, Freitas TV, Felipe CR, Silva Junior HT, Pestana JO. Long term outcomes of elderly kidney transplant recipients. J Bras Nefrol. 2009;37(2):212–20.
8. David-Neto E, Romano P, Triboni AHK, Ramos F, Agena F, Almeida Rezende Ebner P, Altona M, Galante NZ, Brambate Carvalhinho Lemos F. Longitudinal pharmacokinetics of Tacrolimus in elderly compared with younger recipients in the first 6 months after renal transplantation. Transplantation. 2017;101(6):1365–72.
9. Martins GA, Acurcio FA, Franceschini SCC, Priore SE, Ribeiro AQ. Use of potentially inappropriate medications in elderly in Viçosa, Minas Gerais State, Brazil: a population based survey. Cad Saúde Pública. 2015;31(11):2401–12.
10. Lutz BH, Miranda VIA, Bertoldi AD. Potentially inappropriate medications among older adults in Pelotas, Southern Brazil. Rev Saúde Pública. 2017;51(52):1–12.
11. Kondo N, Nakamura F, Yamazaki S, Yamamoto Y, Akizawa T, Akiba T, Saito A, Kurokawa K, Fukuhara S. Prescription of potentially inappropriate medications to elderly hemodialysis patients: prevalence and predictors. Nephrol Dial Transpl. 2015;30:498–505.
12. Chisholm MA, Melroy J, Johnson M, Mulloy LL, Spivey CA. Is age associated with the number or types of medications prescribed to renal transplant recipients? J Am Geriatr Soc. 2007;55(3):389–94.
13. American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American Geriatrics Society 2015 updated beers criteria

for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2015;63(11):2227–46.
14. Campanelli CM. American geriatrics society updated Beers criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2012;60:616–31.
15. Fernandes PFCBC, Siqueira RA, Girão ES, Siqueira RA, Mota MU, Marques LCBF, Andrade SCA, Barroso WM, Silva SL, Santos BGR, Oliveira CMC. Dengue in renal transplant recipients: clinical course and impact on renal function. World J Transpl. 2017;7(1):57–63.
16. Brazilian Association of Organ Transplantation. Brazilian register of transplants-registro brasileiro de transplantes (Brazil). 2017;13(4):1–104.
17. Ministry of Health (Brazil). Ordinance no. 2528, from October 19th 2006. Approves the National Policy of Healthcare for the Elderly in Brazil. Union Official Diary of the Federative Republic of Brazil, Oct 19th 2006, Section 1.
18. WHO Collaborating Centre for Drug Statistics Methodology, ATC classification index with DDDs, 2018. Oslo, Norway. 2017.
19. Andrade KVF, Silva Filho C, Junqueira LL. Prescription of potentially inappropriate medications for older adults: a cross-sectional study in psychiatric institution. J Bras Psiquiatr. 2016;65(2):149–54.
20. Cassoni TCJ, Corona LP, Romano-Lieber NS, Secoli SR, Duarte YAO, Lebrão ML. Use of potentially inappropriate medication by the elderly in São Paulo, Brazil: SABE Study. Cad Saúde Pública. 2014;30(8):1708–20.
21. Santos TRA, Lima DM, Nakatani AYK, Pereira LV, Leal GS, Amaral RG. Medicine use by the elderly in Goiania, Midwestern Brazil. Rev Saúde Púbica. 2013;47(1):94.
22. Pandraud-Riguet I, Bonnet-Zamponi D, Boucier E, Buyse M, Laribe-Caget S, Frémont P, Pautas E, Verny C, Hindlet P, Fernandez C. Monitoring of potentially inappropriate prescriptions in older inpatients: a French multicenter study. J Am Geriatr Soc. 2017;65(12):2713–9.
23. Cahir C, Moriarty F, Teljeur C, Fahey T, Bennett K. Potentially inappropriate prescribing and vulnerability and hospitalization in older community-dwelling patients. Ann Pharmacother. 2014;48(12):1546–54.
24. Nishtala PS, Bagge ML, Campbell AJ, Tordoff JM. Potentially inappropriate medicines in a cohort community-dwelling older people in New Zealand. Geriatr Gerontol Int. 2014;14:89–93.
25. Napolitano F, Izzo MT, Di Giuseppe G, Angelillo IF, the Collaborative Working Group, Collaborative Working Group CastaldoVincenzoHospital S. Giuseppe Moscati, Avellino De StefanoAndreo AHospital Santa Maria della Pietà, Nola, Naples Dell'AversanoRaffaeleHospital Pellegrini, Naples di MauroMaurizioHospital San Paolo, Naples IodiceVincenzoHospital of Marcianise, Caserta IovineCarmineHospital SS. Anna e Sebastiano, Caserta MatarazzoGiuseppeHospital San Giovanni Bosco, Naples otaGiacomoHospital S. Rocco, Sessa Aurunca, Caserta SciambraAntonioHospital Evangelico Villa Betania, Naples. Frequency of inappropriate medication prescription in Hospitalized elderly patients in Italy. PLoS ONE. 2013;8(12):e82359.
26. Blay SL, Laks J, Marinho V, Figueira I, Maia D, Coutinho ESF, Quintana IM, Mello MF, Bressan RA, Mari JJ, Andreoli SB. Prevalence and correlates of Elder abuse in São Paulo and Rio de Janeiro. J Am Geriatr Soc. 2017;65:2634–8.
27. Ribeiro RCHM, Oliveira GASA, Ribeiro DF, Bertolin DC, Cesarino CB, Lima LCEQ, Oliveira SM. Characterization and etiology of the chronic renal failure in a countryside nephrology unit of São Paulo State. Acta Paul Enferm. 2008;21:207–11.
28. Picon RV, Fuchs FD, Moreira LB, Riegel C, Fuchs SC. Trends in prevalence of hypertension in Brazil: a systematic review with meta-analysis. PLoS ONE. 2012;7(10):1–10.
29. Lima TJV, Garbin CAS, Garbin AJI, Sumida DH, Saliba O. Potentially inappropriate medications used by the elderly: prevalence and risk factors in Brazilian care homes. BMC Geriatr. 2013;13(52):1–7.
30. Bradley MC, Motterlini N, Padmanabhan S, Cahir C, Williams T, Fahey T, Hughes CM. Potentially inappropriate prescribing among older people in the United Kingdom. BMC Geriatr. 2014;14(72):1–9.
31. Molloy D, Molloy A, O'Loughlin C, Falconer M, Hennessy M. Inappropriate use of proton pump inhibitors. Ir J Med Sci. 2010;179(1):73–5.
32. Morschel CF, Mafra D, Eduardo JCC. The relationship between proton pump inhibitors and renal disease. Braz J Nephrol. 2018;40(3):301–6.
33. Undela K, Bansal D, D'Cruz S, Sachdev A, Tiwari P. Prevalence and determinants of use of potentially inappropriate medications in elderly inpatients: a prospective study in a tertiary healthcare setting. Geriatr Gerontol Int. 2014;14:251–8.