



Pattern of Use and Prevalence of Potentially Inappropriate Medications among Elderly Patients in a Malaysia Suburban Hospital

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Abstract

Introduction: Potentially inappropriate medications (PIMs) use among the elderly people is an important public health concern. **Objectives:** To investigate the prevalence of PIMs prescribed for the elderly patients and the factors associated with it. **Methods:** A cross-sectional study was conducted in a Malaysia suburban hospital involving community dwellers aged ≥ 60 years old who were admitted into the internal medicine discipline from 1 June to 31 December 2015. PIMs was screened with American Geriatrics Society 2015 updated Beers criteria. **Results:** There were 61.9% of the study subjects prescribed with at least one PIMs. The top three PIMs to avoid were proton-pump inhibitor (13.8%), prazosin (9.2%), and glibenclamide (8.7%). The most common PIMs to be used with caution in older adults was diuretic, specifically, loop diuretic 14.7%, thiazides 13.8%, and potassium-sparing diuretic 6.4%. Polymorbidity and polypharmacy were significantly associated with PIMs use, with $p=0.033$ and $p<0.001$ respectively. Study subjects with polypharmacy had an increase odds of 3 times (adjusted odds ratio=3.062, 95% CI 1.619:5.793) in having PIMs prescribed for them compared to those without polypharmacy. **Conclusion:** The prevalence of PIMs detected in this Malaysia suburban hospital was high. Polypharmacy was the only factor showed to be significantly associated with PIMs use.

Keywords: *Beers criteria, potentially inappropriate medications, elderly, geriatrics*

Introduction

Longer life expectancy is leading towards growing elderly population globally (Wan, Goodkind & Kowal, 2016). The global life expectancy at birth is expected to increase from 68.6 years in 2015 to 76.2 years in 2050, with older population representing 16.7% of total world population by then (Wan *et al.*, 2016). Yet, aging is identified as the main risk factor for major health problems, including cancer, cardiovascular disease and

neurodegeneration (Niccoli & Partridge, 2012), with high prevalence of chronic illnesses closely related to the number of medications consumed by the elderly (Charlesworth, Smit, Lee, Alramadhan, & Odden, 2015). An earlier study in the US reported that over 90% of the older population have been using at least one medication, with 12% older adults consumed at least 10 medications at any given time, and 23% took at least 5 prescription drugs

(Kaufman, Kelly, Rosenberg, Anderson, & Mitchell, 2002).

Due to the age-related physiological changes affecting different organ systems, elderly is more susceptible to adverse drug effects (Luisi, Owens, & Hume, 1999; Mangoni & Jackson, 2003). They are also more likely to have polypharmacy (Jyrkkä, Enlund, Korhonen, Sulkava, & Hartikainen, 2009; Montiel-Luque *et al.*, 2017) and potentially inappropriate medications (PIMs) use, which may be associated with more hospitalizations (Lau, Kasper, Potter, Lyles, & Bennett, 2005; Reich, Rosemann, Rapold, Blozik, & Senn, 2014), higher health care costs (Bradley *et al.*, 2012; Cahir *et al.*, 2010; Jano & Aparasu, 2007; Stockl *et al.*, 2010) and other health-related issues i.e. falls (Stockl, Le, Zhang, & Harada, 2010), cognitive decline (Stockl *et al.*, 2010), drug-related problems (Fick, Mion, Beers, & Waller, 2008), mortality (Jyrkkä *et al.*, 2009; Lau *et al.*, 2005), and quality of life (Jyrkkä *et al.*, 2009; Montiel-Luque *et al.*, 2017).

PIMs use among the elderly people is an important public health concern due to its high prevalence and complications (Morin, Laroche, Texier, & Johnell, 2016; Storms, Marquet, Aertgeerts, & Claes, 2017; Thomas, 2016). There are many tools available to screen for the presence of PIMs in the elderly patients of different settings. To the best of authors knowledge, there is no recent PIMs study conducted among Malaysia community-dwelling elderly admitted into the hospital using the latest American Geriatrics Society 2015 updated Beers Criteria.

In view of this, the current study aimed to estimate the pattern of use and prevalence of PIMs among the elderly patients presented upon admission to a Malaysia suburban hospital and to investigate the factors associated with PIMs use.

Materials and Methods

Study design and ethics

This retrospective, cross-sectional study was conducted in a suburban hospital in Malaysia, Port Dickson Hospital, over a period of four

months i.e. 1 May 2017 to 31 August 2017. The study was registered with Malaysia National Medical Research Registry (NMRR-16-2689-31499) and approval from Medical Research and Ethics Committee (KKM/NIHSEC/P17-612) was obtained prior to the start of the research.

Study subject

Community dwellers aged ≥ 60 years old who were admitted into the internal medicine discipline of Port Dickson Hospital from 1 June 2015 to 31 December 2015 met the inclusion criteria. Those without prescribed medications were excluded. Medication histories of the study subjects were recorded into the medication history assessment (CP1) forms by two clinical pharmacists. The CP1 forms with illegible handwriting, incomplete medication information e.g. incomplete name or dosage of the medications, and incomplete information on medical conditions were excluded. If a study subject had more than one duplicated prescription during the study period, only the first prescription would be used in the analysis to avoid data duplication. Two hundreds and eighteen study subjects were required for this study after accounting for five hundreds elderly patients' admission rate in year 2015, and setting the margin of error at 5%, confidence interval at 95%, and response distribution at 50%.

Study instrument

American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults (Fick *et al.*, 2015) was the main instrument used in the current study. There are five categories i.e. PIMs use in older adults according to organ system, therapeutic category, drugs; PIMs use in older adults due to drug-disease or drug-syndrome interactions that may exacerbate the disease or syndrome; PIMs to be used with caution in older adults; potentially clinically important non-anti-infective drug-drug interactions that should be avoided in older adults; non-anti-infective medications that should be avoided or have their dosage reduced with varying levels of kidney function in older adults. On the other hand, CP1 form was used to record medication history of study subjects. Relevant patients' information such

as underlying co-morbidities was retrieved from electronic health record when necessary. A standardized data collection form consisted of two components was designed for the purpose of this study. Part A recorded demographic and clinical variables i.e. age, sex, race, and co-morbidities, while part B included medications currently used by the study subjects and the presence of PIMs.

Data analysis

For the purpose of this study, the demographic and clinical variables were categorized as follow: age 60-69 or ≥ 70 years old, male or female, Malay or non-Malay, 1-3 co-morbidities or ≥ 4 co-morbidities (polymorbidity), and 1-4 medications or ≥ 5 medications (polypharmacy). For co-morbidity, cardiovascular diseases encompassed hypertension, coronary artery disease, atrial fibrillation, heart failure, sick sinus syndrome, and supraventricular tachyarrhythmia; bronchial asthma, chronic obstructive pulmonary disease, and chronic lung disease were grouped as respiratory disorder; epilepsy, Alzheimer's disease, Parkinson's disease, and myasthenia gravis were categorized as central nervous diseases; major depression disorder, schizophrenia, and alcohol dependency were grouped as psychiatric disorders. Type 2 diabetes mellitus, dyslipidemia, and chronic kidney disease were analysed individually for the association with PIMs.

Statistical analysis was performed by using IBM® SPSS Statistics version 23.0. Univariate analysis was performed to evaluate the association between demographic or clinical variables and the presence of PIMs by using Pearson's chi-square test or Fisher's exact test. Subsequently, all variables were included in the multiple logistic regression analysis. A confidence interval of 95% was utilized and results were considered statistically significant when two-tailed p-value was < 0.05 .

Result:

Socio-demographic and clinical variables

Out of 218 study subjects, 110 (50.5%) and 108 (49.5%) were male and female,

respectively. There were 109 (50%) study subjects aged ≥ 70 years old. Majority of them were Malay (n=89, 40.8%), followed by Chinese (n=71, 32.6%), and Indian (58, 26.6%). Approximately one third (n=60, 27.5%) of the study subjects had polymorbidity, while 75.7% (n=165) had polypharmacy. The distribution and percentage of the co-morbidities were as follow: type 2 diabetes mellitus, n=147 (67.4%); dyslipidemia, n=32 (14.7%); chronic kidney disease, n=45 (20.6%); hypertension, n=177 (81.2%); coronary artery disease, n=53 (24.3%); atrial fibrillation, n=11 (5.0%); heart failure, n=10 (4.6%); sick sinus syndrome, n=2 (0.9%); supraventricular tachyarrhythmia, n=1 (0.5%); chronic obstructive pulmonary disease, n=22 (10.1%); bronchial asthma, n=21 (9.6%); chronic lung disease, n=3 (1.4%); epilepsy, n=4 (1.8%); Alzheimer's disease, n=1 (0.5%); Parkinson's disease, n=4 (1.8%); myasthenia gravis, n=3 (1.4%); major depressive disorder, n=5 (2.3%); alcohol dependence, n=1 (0.5%).

Prevalence of potentially inappropriate medications

In total, there were 195 cases of PIMs detected out of 1436 medications taken by the study subjects. Most of them (n=135, 61.9%) had at least one PIMs prescribed for them. Proton pump inhibitors were the most common PIMs according to organ system, therapeutic category, and drugs. On the other hand, diuretics were the most frequent PIMs to be used with caution in older adults. Three types of drug did not have their dosages adjusted according to the kidney function for five study subjects. There was no prescribed drug fell into the category of PIMs use in older adults due to drug-disease or drug-syndrome interactions that may exacerbate the disease or syndrome and potentially clinically important non-anti-infective drug-drug interactions that should be avoided in older adults. There was 8 out of 135 (5.9%) study subjects hospitalized due to the use of PIMs (data not shown). Table I describes the number of study subjects prescribed with PIMs of different categories.

Factors associated with potentially inappropriate medications

Polymorbidity and polypharmacy were significantly associated with PIMs use, with $p=0.033$ and $p<0.001$ respectively. Results from multiple logistic regression showed that

study subjects with polypharmacy had an increase odds of 3 times (adjusted odds ratio=3.062, 95% CI 1.619:5.793) in having PIMs prescribed for them compared to those without polypharmacy. The association between socio-demographic/ clinical variables and the usage of PIMs was showed in Table II.

Table I: Number of Study Subjects Prescribed with Potentially Inappropriate Medications

PIMs according to organ system, therapeutic category, drugs	n (%)
Antiparkinsonian agents	
Benzhexol	3 (1.4)
Antithrombotic	
Dipyridamole	1 (0.5)
Ticlopidine	8 (3.7)
Cardiovascular	
Peripheral alpha-1 blockers (Prazosin)	20 (9.2)
Digoxin	5 (2.3)
Central nervous system	
Antidepressants (Amitriptyline)	1 (0.5)
Antipsychotics (Haloperidol)	2 (0.9)
Benzodiazepines (Lorazepam)	2 (0.9)
Endocrine	
Metformin/ Glibenclamide	17 (7.8)
Glibenclamide	2 (0.9)
Gastrointestinal	
Proton pump inhibitor ^a	30(13.8)
PIMs to be used with caution in older adults	
Aspirin for primary prevention of cardiac events	2 (0.9)
Vasodilator ^b	21 (9.6)
Diuretics	
Loop diuretic	32 (14.7)
Thiazide ^c	30 (13.8)
Spirolactone	14 (6.4)
Non-infective medications that should be avoided or have their dosage reduced with varying levels of kidney function in older adults	
Gabapentin	3 (1.4)
Ranitidine	1 (0.5)
Colchicine	1 (0.5)

^a esomeprazole, n=3; omeprazole, n=26; pantoprazole, n=1 ; ^b isosorbide dinitrate; ^c chlorthalidone, n=1; hydrochlorothiazide, n=29; PIMs=potentially inappropriate medications.

Table II: Association of Socio-Demographic and Clinical Variables with Potentially Inappropriate Medications Use in Study Subjects

Variables	PIM		p-value ^a
	Yes	No	
Age, n (%)			
<70	67 (61.5)	42 (38.5)	0.889
≥70	68 (62.4)	41 (37.6)	
Sex, n (%)			
Male	67 (60.9)	43 (39.1)	0.755
Female	68 (63)	40 (37)	
Race, n (%)			
Malay	57 (64.0)	32 (36.0)	0.593
Non-Malay	78 (60.5)	51 (39.5)	
Polymorbidity, n (%)			
Yes	44 (73.3)	16 (26.7)	0.033
No	91 (57.6)	67 (42.4)	
Co-morbidities			
Type 2 diabetes mellitus, n (%)			
Yes	91 (61.9)	56 (38.1)	0.992
No	44 (62.0)	27 (38.0)	
Dyslipidemia, n (%)			
Yes	21 (65.6)	11 (34.4)	0.641
No	114 (61.3)	72 (38.7)	
Chronic kidney disease, n (%)			
Yes	31 (68.9)	14 (31.1)	0.280
No	104 (60.1)	69 (39.9)	
Cardiovascular disease, n (%)			
Yes	114 (62.6)	68 (37.4)	0.627
No	21 (58.3)	15 (41.7)	
Respiratory disorder, n (%)			
Yes	25 (54.3)	21 (45.7)	0.233
No	110 (64.0)	62 (36.0)	
Central nervous system disease, n (%)			
Yes	12 (63.2)	7 (36.8)	0.908
No	123 (61.8)	76 (38.2)	
Psychiatric disease, n (%)			
Yes	3 (50.0)	3 (50.0)	0.676 ^b
No	132 (62.3)	80 (37.7)	
Polypharmacy, n (%)			
Yes	113 (68.5)	52 (31.5)	<0.001
No	22 (41.5)	31 (58.5)	

^a p<0.05 is considered as statistically significant; ^b Fisher's exact test; SD=standard deviation

Discussion:

The current study was conducted to investigate the prevalence and patterns of PIMs used in a suburban hospital in Malaysia. Factors associated with PIMs use were also explored in this study.

Collectively, proton-pump inhibitor (PPI) with unclear indication and prolonged duration of treatment (>8 weeks) was the leading PIMs to avoid in this study population. Similar result was seen in a European national study (2010), where PPI was reported as the major contributor of PIMs among elderly patients ≥70 years of age (Cahir *et al.*, 2010). A worrying trend was seen in the United States National

Health & Nutrition Examination Survey, which reported remarkable increase of PPI usage from 0.09% (95% CI 0.01:0.59) to 18.08% (95% CI 15.79:20.61) between 1988 and 2010 (Charlesworth *et al.*, 2015). Nonetheless, different prescribing patterns could be observed from other regions of the world. A population-based cross-sectional study conducted in southern Brazil showed that benzodiazepines were predominantly prescribed for elderly patients of the same age group (Lutz, Miranda, & Bertoldi, 2017). Multiple adverse health outcomes could be associated with unnecessary use of PPI in the elderly i.e. bone loss, fractures, *Clostridium difficile* infection, community-acquired

pneumonia, kidney disease, and dementia (Maes, Fixen, & Linnebur, 2017). These results were in-line with the effort by American Geriatric Society to include PPI as one of the PIMs to avoid in the elderly population (Fick *et al.*, 2015). In view of high PPI usage, multidisciplinary teams should actively engage in reviewing and deciding the appropriate indication and duration of PPI in elderly patients on a scheduled basis. In addition, elderly with prolonged PPI treatment should be monitored regularly for potential adverse health outcomes as aforementioned.

Prazosin, a peripheral alpha-1 blocker was commonly prescribed as an antihypertensive for the elderly in this study. Most of the study subjects prescribed with the drug were already prescribed with two or more antihypertensive agents, especially among those with chronic kidney disease. Limited choice of antihypertensive without contraindication or not requiring dose adjustment according to the kidney function might explain the use of prazosin among elderly patients with established kidney impairment. Given the fact that peripheral alpha-1 blocker may incur high risk of orthostatic hypotension, the drug is not safe for the elderly (Fick *et al.*, 2015). Therefore, alternative agents with superior risk-benefit profile should be considered before choosing peripheral alpha-1 blockers for the management of hypertension.

Surprisingly, oral hypoglycaemic agents containing glibenclamide (as single agent or in combination with metformin) were commonly prescribed for the management of type 2 diabetes mellitus among the study subjects. The drug is associated with higher risk of prolonged hypoglycaemia in the elderly population. In a study conducted by Greco *et al.* (2010), the researchers found that 76 hypoglycaemic episodes occurred among ninety-nine patients who were 80 years or older taking glibenclamide in eight year period (Greco, Pisciotta, Gambina, & Maggio, 2010). This is alarming especially if patients received their treatment from general practitioner without proper follow-up or routine monitoring. World Health Organization (2013) has recently replaced glibenclamide for gliclazide in the diabetes section of the list of essential medicines for people aged over 60 years due

to gliclazide's similar efficacy but lesser hypoglycaemia risk compared to glibenclamide (World Health Organization, 2013). A recent systematic review and analysis also reported hypoglycaemia risk was significantly lower for gliclazide compared to other sulphonylureas (Chan & Colagiuri, 2015). This makes gliclazide a safer alternative for the elderly if a sulphonylureas oral hypoglycaemic agent is required for their diabetes management.

Diuretics championed for the PIMs to be used with caution among the present study subjects. However, it is noteworthy that loop diuretic and potassium-sparing diuretic were mainly prescribed for the management of heart failure in the study population. Although this group of drugs may cause undesirable electrolyte imbalances or syndrome of inappropriate antidiuretic hormone secretion (Fick *et al.*, 2015), its use is necessary in heart failure cases. Loop diuretic was indicated for symptomatic control, while spironolactone was prescribed for its function as mineralocorticoid/aldosterone receptor antagonist in heart failure, as recommended in the international guidelines (Ponikowski *et al.*, 2016; Yancy *et al.*, 2013). On the other hand, thiazide was mainly used for the control of hypertension among the elderly, in-line with the treatment guideline (Whelton *et al.*, 2017). Scheduled renal profile monitoring and periodic dose adjustment are necessary to avoid diuretics' potential adverse effects. Elderly and their caregivers should also be educated regarding the adverse drug reactions from the use of diuretics and circumstances to seek for medical advice.

Isosorbide dinitrate is a vasodilator to be used with caution in the elderly because it may exacerbate episodes of syncope in individuals with history of syncope (Fick *et al.*, 2015). It aggravates arterial hypotension and orthostatic dysregulation, especially during acute and initial treatment with the drug (Häußinger & Bachmann, 1983). Therefore, it is recommended that the drug should be used with caution if it is deemed necessary. It is, however, beneficial for certain target population e.g. patients of African descent (Taylor *et al.*, 2004). Although this drug was common among the current study population, its use was limited to relieving angina

symptom among the elderly patients with coronary artery disease.

Studies had showed that PIMs use were associated with more hospital admission and/or emergency visits (Klarin, Wimo, & Fastbom, 2005; Perri *et al.*, 2005; Schmader *et al.*, 1997). A recent meta-analysis reported nonsteroidal anti-inflammatory drugs as one of the inappropriate medication classes more frequently related to hospital admissions (Oscanoa, Lizaraso, & Carvajal, 2017). The relationship between hospital admission and PIMs use was not explored in the current study and it can be investigated in the future. There are mixing reports on PIMs leading to more cases of adverse drug reactions. Laroche *et al.* (2007) and Onda *et al.* (2015) did not find inappropriate medications to be the major cause of adverse drug reactions in the elderly (Laroche, Charmes, Nouaille, Picard, & Merle, 2007; Onda *et al.*, 2015). In contrary, Chang *et al.* (2005) reported PIMs use caused higher rate of adverse drug reactions (Chang *et al.*, 2005). Knowing that elderly is prone to adverse drug effects because of their changes in physiological functions (Luisi *et al.*, 1999; Mangoni & Jackson, 2003), health care professionals have to be more wary when prescribing, dispensing and administering medications for this group of population. Due to the implicit or explicit nature of the screening tools available currently, these tools could be used in complementary to each other in order to detect PIMs earlier and suggest proper alternatives accordingly.

Studies had reported varying factors associated with PIMs use due to differences in target population or regions, socio-demographic background, screening tools employed and outcomes of interest considered. Yet, polypharmacy or high number of prescribed medications is revealed as the only consistent driving factor for PIMs use in both institutionalized or long-term care residents and community-dwellers (Morin *et al.*, 2016; Storms *et al.*, 2017; Endres, Kaufmann-Kolle, Knopf, & Thuermann, 2017). Same result was observed in this study. Home visit or home medication review is, therefore, an important cornerstone in reducing PIMs

among elderly resides in these settings. By reviewing their medications and health conditions periodically by health care professionals, existing and potential health problems relating to excessive or unnecessary medications used can be uncovered. This will possibly translate into lesser adverse drug effects/ events, morbidity, mortality, health-related costs, and perhaps better quality of life arise from fewer polypharmacy and PIMs use. In this context, pharmacists could contribute to reducing the incidence of PIMs, consequences of adverse drug events, and morbidity by providing home visit services to the elderly (Cheen *et al.*, 2016; Onda *et al.*, 2015).

Study limitations

The results described in the current study might not be representative of other regions of the country and should not be generalizable to other health care settings or elderly population with specific health conditions. The information regarding PIMs was also relied on medications brought by patients/ caregivers upon hospital admission. Therefore, there might be some missing data if the medications were left at home. Moreover, the analysis undertaken in the current study did not control for some important confounding factors such as disease severity, duration of illnesses, specific mental illnesses (e.g. dementia), activities of daily living, and other clinically important parameters. Another limitation is the fact that not all PIMs is being captured in the latest Beers criteria. Therefore, the prevalence of PIMs use among the elderly patients may be underreported.

Conclusion

The prevalence of PIMs detected in Port Dickson Hospital was high, as approximately 62% of the study population had at least one PIMs prescribed for them. From all variables studied, only polypharmacy was showed to be significantly associated with PIMs use. Although other health outcomes were not explored in this study, the current results can serve as a baseline data for quality improvement in the future. In addition, coming researches can be designed to look into the parameters mentioned and explore their association with PIMs use.

Conflicts of Interest

None.

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Authors' Contributions

Study concept and design were performed by Lau, B. T. and Shuhaila, A. Data collection and writing of the manuscript were implemented primarily by Muhammad-Azmin, K. A. and Lau, B. T. Ng, S. Y. was mainly responsible for data analysis and interpretation. All authors had complete access to the study data.

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