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Research Article

The effect of the pharmacist's intervention on potentially inappropriate medication prescription in older adults in a Vietnamese hospital

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ABSTRACT

A high number of elderly patients are exposed to the risk of potentially inappropriate medications (PIMs). The Beers criteria, most recently in 2015, are the most widely cited criteria used to assess PIM prescribing for older patients. The purpose of this study was to evaluate the role of pharmacist's intervention in improvement of appropriate prescription for geriatric inpatients according to the 2015 Beers Criteria. The pharmacist's intervention method included training lectures on the Beers 2015 criteria in two hours for the medical doctors (MDs) of each study department; face-to-face visits with the MDs, and the notebook with the Beers 2015 provided to the MDs for reference. The study was designed as a before-and-after trial using medical records of patients aged 65 years or older, admitted to the one of three following study departments: endocrinology, cardiology, and neurology departments of Dong Nai General Hospital from 1st September 2015 to 30th June 2016. Data were analyzed using Statistical Package for Social Sciences (SPSS) Program, version 22.0. Binary logistic regression analysis was used to evaluate the factors associated with the prescription of PIMs.

The pharmacist's intervention had an impact on decreasing the PIM exposure (OR=0.337, CI 95% 0.207-0.551, $p<0.001$). There was a significant decrease ($p<0.05$) in the rate of PIMs with diazepam, amitriptyline, metoclopramide after pharmacist's intervention. The pharmacist team was able to make a statistically significant difference in the number of elderly patients being prescribed PIMs.

1. INTRODUCTION

Prescribing for older people, defined as those 65 years or older of age, is complex because of changes in body composition and multiple pathologies. Finding the balance between aggressively treating diseases and avoiding medication-related harm is an objective often set by healthcare professionals[1]. Potentially inappropriate medications (PIMs) are associated with adverse drug reactions and high economic outcomes. PIM is defined as medication that causes risk to the patient that exceeds the benefit[2]. For over 20 years, PIMs

prescriptions in adults 65 and older has been researched in more than 500 studies in long-term care settings, outpatient settings, and inpatient settings. The results indicated an association between certain medications and poor patient outcomes such as delirium, falls, and gastrointestinal bleeding[3]. Several criteria have been designed for identification of PIMs. Beers criteria was the first set of explicit criteria for inappropriate drug use in elderly developed in 1991 by Beers MH. at the University of California[4]. Since their development, the Beers criteria have become the most widely used and recognized explicit criteria for the detection of PIMs in older adults. The criteria was updated and expanded to include all geriatric care settings in 1997 and again in 2003[5,6]. In 2012, the panel was charged with updating the Beers list and rating the quality of evidence that supported the panel's recommendations. To accomplish the result, the panel systematically reviewed the literature, entertained public comment, and graded the published evidence during an open period, according to the Institute of Medicine standards. This approach ensured transparency and rigor. A modified Delphi method was used to achieve consensus on the panel's recommendations[3]. In 2015, the American Geriatrics Society (AGS) released updated Beers Criteria for PIM use in older adults[7]. The AGS review panel incorporated a number of meaningful changes to the Beers Criteria. The changes in the 2015 update are not as extensive as those of the previous update, but in addition to updating existing criteria, two major components have been added: 1) drugs for which dose adjustment is required based on kidney function and 2) drug–drug interactions. Neither of these new additions was intended to be comprehensive, because such lists would be too extensive. The goal of the 2015 AGS Beers Criteria continues to be improving the care of older adults by reducing their exposure to PIMs[7]. In Vietnam, 2015 AGS Beers criteria have been recently applied in clinical practice in some hospitals, such as Dong Nai General Hospital.

The aims of this study were to examine the prevalence of PIM prescriptions based on the updated 2015 Beers criteria in patients aged 65 years or older and to determine if pharmacist's intervention improved the prescription of PIMs for geriatric inpatients.

2. METHODS

2.1. Study Design and Setting

The study was designed as a before-and-after trial of pharmacist's intervention on the appropriateness of prescribing for the elderly based on 2015 Beers criteria. All prescribing medical doctors (MDs) worked at one of three following study departments, endocrinology, cardiology, and neurology departments of Dong Nai General Hospital. This study was conducted using medical records of patients aged 65 years or older, using at least one medication, admitted to the one of the study departments from 1st September 2015 to 30th December 2015 (pre-intervention phase, phase 1) and from 1st March 2016 to 30th June 2016 (after intervention phase, phase 2). For both phases of data collection, prescribing practices were recorded and analyzed from medical records. In the pre-intervention phase, the intervention to the MDs was not conducted. Between the two phases, pharmacists gave a training lecture on the Beers 2015 criteria in two hours for the MDs of each study department; the training was also conducted as face-to-face visits with the MDs. Moreover, the notebook with the Beers 2015 criteria was also provided to the MDs for reference. The appropriateness of the prescriptions of each phase was judged according to the Beers 2015 criteria.

2.2. Sample size

A required sample size for each group was calculated using the following formula to compare the rate of patients prescribed at least one PIM before and after intervention:

$$n = \frac{(z_{\frac{\alpha}{2}}\sqrt{2\bar{p}\,(1-\bar{p})} + z_{\beta}\sqrt{p_1(1-p_1) + p_2(1-p_2)})^2}{\Delta^2}$$

With $\bar{p} = \frac{p_1+p_2}{2}$ and $\Delta = p_1 - p_2$

p_1, p_2 are rates of patients with PIM before intervention and after intervention, respectively. $z_{\alpha/2} = 1.96$, $\alpha = 0.05$, reliability 95%; $z_{\beta} = 0.842$, $\beta = 0.2$, power = 0.8.

According to the study of Luu NTD (2012), p_1 was 46.2%[8]. In this study we desired to reduce the prevalence of patients using at least one PIM to 30%. Therefore, the minimum sample size for each group was 208. In this study, we selected 211 patients before intervention and 208 patients after intervention.

2.3. PIM criteria

Courses of therapy were assessed and classified as either appropriate or inappropriate. The Beers 2015 criteria ware used as the source to identify PIMs[7]. Beers PIMs were further classified into four categories: 1) PIMs used in older adults, 2) PIMs to be avoided in older adults due to Drug–Disease or Drug–Syndrome Interactions that may exacerbate the disease or syndrome, 3) Potentially clinically important non-anti-infective drug–drug interactions that should be avoided in older adults, 4) Non-anti-infective medications that should be avoided or have their dosage reduced with varying levels of kidney function in older adults**.** In this study, all medications given on a day were considered as one prescription. A prescription was considered to be inappropriate if it contained one or more drugs included in 2015 AGS Beers criteria. Exposure to PIMs was considered if an individual was dispensed at least one medication, identified with the Beers criteria for any duration and at any given time as inappropriate.

2.4. Statistical analysis

Data were analyzed using Statistical Package for Social Sciences (SPSS) Program, version 22.0. Patient's data were presented as mean ± S.D. or percentage. Binary logistic regression analysis was used to evaluate the influence of factors, includes age of the MDs, the degree of the MDs, intervention of pharmacist on the PIM prescription. The level of statistical significance was specified at $p < 0.05$.

Table 1. Characteristics of the study population before intervention and after intervention

Characteristics	Before intervention (n= 211)	After intervention (n=208)	p value*
Age of patient, years old			
65-69 (n (%))	27 (12.8)	39 (18.8)	0.185
70-74 (n (%))	52 (24.6)	39 (18.8)	
75-79 (n (%))	48 (22.7)	55 (26.4)	
80-84 (n (%))	54 (25.6)	39 (18.8)	
85-90 (n (%))	20 (9.5)	23 (11.1)	
≥90 (n (%))	10 (4.7)	13 (6.2)	
Sex of patient			
Male n (%)	69 (32.7)	63 (30.3)	0.595
Female n (%)	142 (67.3)	145 (69.7)	
Illness of patient			
Hypertension n (%)	108 (51.2)	107 (51.4)	0.958
Diabetes mellitus n (%)	48 (22.7)	66 (31.7)	**0.039**
Chronic kidney disease n (%)	22 (10.4)	26 (12.5)	0.505
Ischemic heart disease n (%)	20 (9.5)	37 (17.8)	**0.013**
Peptic ulcer n (%)	16 (7.6)	18 (8.7)	0.688
Atrial fibrillation n (%)	13 (6.2)	14 (6.7)	0.812
Insomnia n (%)	13 (6.2)	2 (1)	**0.004**
COPD[a] n (%)	8 (3.8)	6 (2.9)	0.606
Heart failure n (%)	7 (3.3)	15 (7.2)	0.074
Vestibular disorders n (%)	11 (5.2)	30 (14.4)	**0.002**
Age of Medical Doctor , years old			
< 30	133 (63)	129 (62)	0.966
30-40	62 (29.4)	62 (29.8)	
> 40	16 (7.6)	17 (8.2)	
The degree of the Medical Doctor			
MD[b]	104 (49.3)	120 (57.7)	0.123
Studying-MD special I	22 (10.4)	25 (12)	
MD special I	60 (28.4)	46 (22.1)	
MD-residency	7 (3.3)	9 (4.3)	
MD-master	18 (8.5)	8 (3.8)	

[a]COPD :chronic obstructive pulmonary disease , [b]MD: Medical Doctor, *: Chi-square test

Table 2: Inappropriately prescribed drugs according to the 2015 Beers criteria before and after intervention

PIM	Before intervention (n=211)		After intervention (n=208)		p value*
	Number of patients	%	Number of patients	%	
Diazepam	44	20.9	21	10.1	**0.002**
Amitriptyline	15	7.1	4	1.9	**0.011**
Methyldopa	8	3.8	5	2.4	0.413
Metoclopramide	8	3.8	1	0.5	**0.019**
NSAID[a]	8	3.8	5	2.4	0.413
Digoxin	1	0.5	2	1	0.554
Spironolactone	3	1.4	0	0	0.084

[a]NSAID: non-steroidal anti-inflammatory drugs ,[b]GFR: *glomerular filtration rate*, *: Chi-square test

2.5. Ethical consideration

The protocol of this study was approved by the Institutional Ethics Committee of Dong Nai General Hospital, Dong Nai Province, Viet Nam.

3. RESULTS

A total of 211 and 208 medical records were included before and after intervention, respectively. The baseline characteristics of the study population before and after intervention are shown in Table 1. Before intervention, 67.3% (54/211) of subjects were women. The individuals in the 80-84 years age group had the highest prevalence – 25.6%. There were no statistically significant differences before and after intervention in the characteristics of patients, such as gender, age, illnesses such as hypertension, chronic kidney disease, peptic ulcer disease, atrial fibrillation, COPD, heart failure. The proportion of patients with diabetes mellitus, ischemic heart disease and vestibular disorders in phase 2 was statistically significantly higher than that of phase 1. In contrast, the prevalence of patients with insomnia in phase 2 was statistically significantly lower than that of phase 1. There were no statistically significant differences between the two phases in the characteristics of MDs, includes age and degree of the MDs.

In the both two phases of study, 70.5% of patients took five to nine medications. The prevalence of patients had ten or more medications was 17.1%.

The prevalence of PIMs in patients before and after intervention were 34.1% and 23.1%, respectively. The most prevalent PIMs before intervention were diazepam (20.9%) and amitriptyline (7.1%) followed by methyldopa (3.8%), metoclopramide (3.8%) and non-steroidal anti-inflammatory drugs (NSAID) (3.8%). There was a significant decrease in the rate of PIMs after intervention with following drugs - diazepam (10.1% vs 20.9%, p=0.002), amitriptyline (1.9% vs 7.1%, p=0.011), meto-clopramide (0.5% vs 3.8%, p=0.019) (Table 2).

Table 3: Factors associated with prescription of PIM according to the 2015 Beers Criteria*

Factors	Odds ratio	p value	95% C.I
Intervention			
Yes	0.337	**<0.001**	0.207-0.551
No			
Age of Medical Doctor, years old			
< 30	4.414	**<0.001**	2.188-8.902
30-40	6.653	**0.001**	2.193-20.184
> 40			
The degree of the Medical Doctor			
MD[a]	1.060	0.881	0.492-2.286
Studying-MD special I	0.445	0.050	0.198-1.001
MD special I	0.452	0.242	0.119-1.712
MD-residency	0.921	0.873	0.335-2.534
MD-master			

* - Binary logisctic regression, [a]MD: Medical Doctor

The results of the binary logistic regression analysis to identify the factors associated with prescription of PIMs were presented in Table 3. The pharmacist's intervention had an impact on decreasing the PIMs exposure (odds ratio (OR)=0.337, confidential interval (CI) 95% 0.207-0.551, p<0.001)**.** MDs aged under 30 and the 30-40 years old prescribed higher rate of PIMs compared with the MDs more than 40 years age group (OR =4.414, CI 95% 2.188-8.902, p<0.001) and (OR=6.653, CI 95% 2.193-20.184, p=0.001), respectively.

4. DISCUSSION

Potentially inappropriate medications have been examined in many studies using Beers criteria[3]. It is important to update information about the prevalence of PIMs exposure based on the published Beers criteria. To our knowledge, this was the first study in Viet Nam to estimate prevalence of PIMs using the 2015 Beers criteria. The results from this research were compared to other research studies that used the 2012 Beers criteria. The results of the phase 1 of our study showed that PIM prescription was common for hospitalized older adults, PIM prescriptions were found in 34.1% of patients. The highest number of PIMs was four, almost of these individuals were dispensed one or two PIMs during the study period. The most common PIMs dispensed to the study population were diazepam and amitriptyline followed by methyldopa and NSAID. These results of our study were consistent with another study carried out by Brown JD et al. which showed that 34.1% of patients aged 65 years and older were exposed to one or more PIMs identified using the updated Beers 2012 criteria[9]. Higher prevalence of PIM prescribing was found in a study conducted in Korea, wherein 80.6% of the subjects were treated with at least one PIM, in Davidoff et al. study, wherein 42.6% patients exposed to PIMs, and in Blanco-Reina E et al. study wherein 44% subjects prescribed at least one drug based on 2012 Beers criteria[10-12]. The difference in prevalence of PIMs in various studies may be due to the differences in patient characteristics, prescribing patterns, locally recommended guidelines, availability of medications listed in Beers criteria.

Many studies define "polypharmacy" as a medication count of five or more medications[13]. An alternative definition for "polypharmacy" is the use of more medications than needed[13]. In our study, the prevalence of patients had ten or more medications were not too high (17.1%), this may be due to doctor concerns about drug interactions and side effects when using multiple drugs. But the prevalence of patients took five to nine medications was high (70.5%). A research carried out by Hajjar ER et al. (2005) in 384 patients found that 41.5% of elderly patients used five to eight medications, 37.2% of them used nine medications or more[14]. A South Korean study by You SN et al. showed that the prevalence of elderly patients using "polypharmacy" was relatively high, similar to our study, among 523,811 of subjects, 52.7% were on at least 5-8 medications, 12.5% were on 9 or more[10]. According to many studies, the use of "polypharmacy" is common in the elderly, with nearly 50% of patients taking unnecessary drugs. In particular, unnecessary drug use is also responsible for multiple drugs use in older patients[13]. On the other hand, it should be noted that, the elderly are associated with many different diseases. Current medical practice guidelines often require multiple medications to treat each chronic disease. Therefore, an elderly patient with at least two disease states, such as heart failure and chronic obstructive pulmonary disease, will usually use more than five medications[15].

In our study, the most common PIMs dispensed were diazepam, a long-acting benzodiazepine. The fact that benzodiazepines were one of the most commonly prescribed PIM classes was similar to the results of other studies. A research conducted in Viet Nam by Nguyen NDT. (2014) also showed that the prevalence of long-term use of benzodiazepine (diazepam) was highest (44%)[16]. Other international research showed similar results, in a research carried out by Pradhan et al. (2015) which identified benzodiazepin (diazepam, alprazolam) as the most common PIM prescribed to the older population (30%)[17]. Results from our study and others indicated that benzodiazepines were still widely used in Vietnam and other countries, although the use of benzodiazepines has been mentioned in the previous literature as it relates to undesired effects on the elderly[19]. According to the Beers 2015 criteria, the benzodiazepine (immediate, short-acting, and long-acting class) is strongly recommended to be avoided with a high level of evidence. Because older adults have increased sensitivity to benzodiazepines and decreased metabolism of long-acting agents. All

benzodiazepines increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle crashes in older adults. High prevalence of benzodiazepines use may be due to the efficacy of this class of drugs in the treatment of common symptoms in the elderly such as anxiety, restlessness, and insomnia. Most of the diazepam used in our study was indicated in the case of insomnia in the elderly, prolonged sleeplessness or insomnia due to other illnesses (musculoskeletal pain, bacterial pain, surgery, headache, vestibular disorders)[7].

A high proportion of patients was dispensed amitriptyline, an antidepressants. Amitriptyline is a tricyclic antidepressant which is considered inappropriate for the elderly due to its strong anticholinergic properties[7]. A significant use of medicines with anti-cholinergic properties and antipsychotics was of concern as prior research has shown that anticholinergic use among older people is associated with an increased risk of morbidity, mortality and cognitive decline. Amitriptyline is often indicated for sedation, anxiety relief and neuropathic pain in patients with diabetes mellitus. Other studies have also showed that amitriptyline was included in the high prevalence PIMs group[18].

In general, the use of PIM in the elderly increases the risk and undesired effects in the elderly. In case of compulsory use, careful monitoring is needed to prevent and detect possible adverse drug reactions (ADRs)[7]. Our study also showed that the rate of PIM with diazepam, amitriptyline, and metoclopramide after intervention was significantly lower than that in the pre-intervention phase ($p < 0.05$). Thus, pharmacist's intervention had a positive effect in reducing the frequency of use of most PIMs in elderly patients.

The pharmacists' intervention had an impact on decreasing the PIMs exposure in our study (OR=0.337, CI 95% 0.207-0.551, $p<0.001$). Although various kinds of educational interventions have been reported in previous reseacrches, the results were consistent[20-23]. According to Llic D et al., in 2015, the median number of inappropriately prescribed drugs according to the Beers criteria before education program for MDs was significantly higher than that after education program ($p < 0.001$)[21]. Wessell AM et al. conducted an intervention study in 2008 based on the Beers 1997 criteria. The team conducted intervention on 99 medical units over 4 years, the participants were provided with an information sheet about PIMs and were periodically tested for knowledge. The results showed that prevalence of patients prescribed PIMs was significantly decreased ($p < 0.001$) after intervention[23]. An another study carried out Melissa LP et al. (2010) using Beers 2003 criteria showed similar result. In that study, physicians were alerted using the prescription computer whenever a PIMs prescription occurred. After intervention, the average number of PIM prescriptions decreased from 11.56 ± 0.36 / day to 9.94 ± 0.12 / day ($p < 0.001$)[22]. Another study conducted by Brown BK and colleagues evaluated the role of pharmacists in PIM prescribing according to Beers 1997 criteria showed that before intervention 10.1% of patients prescribed PIMs, after intervention the prevalence was reduced to 2.02% ($p=0.02$), pharmacist's intervention reduced mean number of patients prescribed PIMs[24]. In general, intervention studies based on the Beers criteria all showed similar results to our study. The prevalence of patients given PIMs after pharmacists' intervention was significantly reduced compared to pre-intervention by pharmacists.

In our study, MDs aged under 30 and the 30-40 years prescribed PIMs with higher rate compared with the MDs more than 40 years age group. This could be explained that the older MDs have more experience in prescribing medications than the younger ones. In Vietnam, medical students graduate after they finish a six years academic program while in developed countries, their medical students must take a longer period of time to get the same degree. For instance, in United States, the time of medical program includes 4 years for basic science, 4 years for medicine studying and at least 2 years for practical courses. As the result, the young MDs in Vietnam have less experience as well as more medication errors in prescription than the older ones.

The limitations of this study must be acknowledged. It was conducted in a single center. The study should be replicated in different care settings to determine whether the results are generalizable to other patient groups. These limitations can be avoided by replicating the study in multiple centers.

5. CONCLUSION

This study was the first study in Viet Nam to evaluate the use of PIMs in the aged using the revised Beers criteria of 2015. This study

confirmed that PIM prescription was common among elderly patients. The pharmacist's intervention had an impact on decreasing the PIMs exposure. The use of Beers 2015 criteria to screen medication used in elderly patient leads to improve the prescribing appropriateness.

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Conflict of interest

None to declare

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Ethical approval

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