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Full Length Research Paper

A study of the prevalence of potentially inappropriate medications (PIMs) in Thai adults

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Potentially inappropriate medications (PIMs) are a common problem in older adults and are associated with negative outcomes. The objectives of this study were to evaluate the prevalence of and the factors associated with the use of PIMs by elderly patients in an outpatient setting of the tertiary care hospital. A retrospective medical record audit was randomly reviewed in 308 elderly patients in 2010. Beers criteria (2003) and the screening tool of older persons' potentially inappropriate prescriptions (STOPP) were used to identify PIMs. The results showed that the median number of medicines per patient was 5.6 (inter-quartile ranges 3.5 to 7). Prevalence of PIMs determined by Beers criteria and STOPP was 19.2 and 31.5%. The only factor that exhibited associations was the higher number of prescription medications based on STOPP criteria (odds ratio 1.2, 95% confidence interval 1.1 to 1.4), p<0.05. PIMs are highly prevalent among older adults in the tertiary care setting and are associated with greater number of medications based on STOPP. Beers criteria are a less sensitive tool than STOPP to detect PIMs for Thai older adults.

Key words: Beers criteria, screening tool of older persons' potentially inappropriate prescriptions (STOPP) criteria, Thai older adults, medication errors, inappropriate drug use.

INTRODUCTION

Older adults are likely to have co-morbidities that require multiple medications. Potentially inappropriate medications (PIMs) are defined as medications which take more risks than benefits, medications with clinically significant drug-drug or drug-disease interactions and the possible omission of potentially useful medications (Chen et al., 2012). PIMs are a common problem in older adults and are associated with negative outcomes including a significant risk of adverse drug events, increased healthcare costs, and hospitalization that increases morbidity and mortality up to 100,000 deaths per year in the US (Wehling, 2011). Polypharmacy, a practice that is the use of more medication than is clinically indicated or warranted, has an increasing trend in this population (Michocki, 2001). The US reported that persons at the age of 65 and above, in approximately 44 and 57% of men and women take 5 or more drugs, and 12% take 10 or more drugs. There is evidence that the number of concomitant medications of 5 or more is associated with different percentages of adverse outcomes such as frailty 6.5, disability 5.5, mortality 4.5, and falls 4.5 (Gnjidic et al., 2012). Although PIMs are prevalent in older adults, many can be preventable which consequently decreases poor outcomes (Page et al., 2010).

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Screening tools to detect PIMs have been formulated to help physicians and pharmacists including Beers criteria and screening tool of older persons' potentially inappropriate prescriptions (STOPP). Beers criteria were originated in 1991 and latest updated in 2012 (American Geriatrics Society, 2012). It was designed to identify PIMs of older adults in primary care, secondary care, and nursing homes. It detected inappropriate medication use in the US and European countries at about 21.3 to 28.8% and 9.8 to 38%. A recent systematic review reports that the prevalence of PIMs varies from 11.5 to 62.5% among community-dwelling elderly in which the majority of the studies were conducted in the US using Beers criteria (Guaraldo et al., 2011). The STOPP was developed in 2008 to decrease the limitations of the Beers criteria. It provides good inter-rater reliability with a kappa-coefficient of 0.75 and 0.68 (Fick et al., 2003; Gallagher et al., 2008; Ryan et al., 2009). The advantages of the STOPP consist of greater inter-rater reliability, inclusion of both American and European drugs, organization and structure based physiological systems, and a short time to complete (about 3 min) (Page et al., 2010). It has been found that STOPP is more sensitive than Beers criteria to detect PIMs in European countries (Miguel et al., 2010; O'Mahony et al., 2010). For Asian countries, the prevalence of PIMs based on Beers criteria in ambulatory care visits and emergency department visits of Taiwan were 19.1 and 19.3% (Chen et al., 2009; Lai et al., 2009). In the nursing home setting of Malaysia, the reported prevalence of PIMs was 32.7 and 23.7% based on Beers criteria and STOPP (Chen et al., 2012). These results indicated that STOPP is less sensitive than Beers criteria to detect PIMs. Factors associated with PIMs can be classified as patient, physician, and visit characteristics. These factors are varied in different studies. The factors associated with patient characteristics are female sex, low educational level, advanced age, black skin color, and longer stays in nursing home. For physician characteristics, significant factors associated with PIMs are male sex, older age, family medicine/general practice, and the factors related to visit characteristics are greater numbers of drug prescribed, primary care setting, and use of medications supplied by the government (in Brazil) (Chen et al., 2012, 2009; Guaraldo et al., 2011; Lai et al., 2009; Oliveira et al., 2012). Common medications associated with PIMs are short-acting nifedipine, methydopa, first-generation antihistamines, muscle relaxants/ antispasmodics, and long-acting benzodiazepines.

In Thailand, PIMs used among Thai elderly have not been studied widely. Using a Delphi technique with the three-round survey of 16 geriatric medicine experts to determine high-risk medication use found that about 80% of practices embraced the use of high-risk drugs with potential adverse reactions, drug-disease interactions, and drug-drug interactions. The most common groups of high-risk medications were for the central nervous, musculoskeletal and cardiovascular systems (Winit-Watjana et al., 2008). Application of Beers criteria and STOPP in this population has not been studied broadly. Therefore, the primary objective of the present study was to evaluate the prevalence of PIMs using Beers (2003) criteria and STOPP in the geriatric outpatient care of the internal medicine department. The secondary objective was to identify factors-associated with PIMs.

MATERIALS AND METHODS

Study participants

A retrospective medical record audit was carried out for all patients of the age of 65 years of age or older, who attended the Internal Medicine Outpatient Clinic of Srinagarind Hospital Medical School between January 2010 and December 2010 and who had at least consecutive three-month visits and took at least one daily medication. The exclusion criterion was being a terminally-ill patient defined as patient who is diagnosed with disease(s) that cannot be cured or adequately treated and that is reasonably expected to result in the death within a short period of time such as advance cancer and advance dementia. Because this patient was more likely to have higher rates of inappropriate medications, they were not being representative of independently living community-based elderly patients.

Instrument

The instruments used in this study were Beers criteria, STOPP, and Charlson Co-morbidity Index (CCI). The Beers criteria version 2003 was used to identify PIMs in this study. The Beers criteria are explicit and composed of two comprehensive lists of medications to be avoided in older people both independent of diagnosis and considering diagnosis. Many of the criteria, however, are controversial (Fick et al., 2003). STOPP consists of 65 clinically significant criteria based on physiological systems for potentially inappropriate prescribing in older people (Fick et al., 2003; Gallagher et al., 2008; Ryan et al., 2009). Each criterion is accompanied by a brief reason for the inappropriate prescribing. CCI was developed in 1987. It is a weighted index to predict 1-year patient mortality. It is correlated with disability, readmission, and length of stay outcomes using comorbidity data from hospital chart reviews. The final CCI score is the sum of 19 predefined comorbidities that were assigned weights of 1, 2, 3, or 6. These weights were based on the magnitude of the adjusted relative risks associated with each comorbidity in a Cox proportional hazards regression model and incorporate increasing age as an independent risk factor. This tool was used to quantify the chronic illness status of the older persons (Hall et al., 2004; Needham et al., 2005; Ryan et al., 2009).

Procedure

The patient demographic data including medical histories, current diagnoses and current medications were recorded by a physician. The CCI using an electronic application would be calculated and recorded for each patient. Beers criteria (2003) and STOPP were applied to their clinical datasheets. All recorded disease states and medical conditions were coded to facilitate data analysis. Disease codes were assigned so that each disease was given a unique number from 1 to 308 and was then grouped according to the principal physiological system affected.

Statistical analyses

Demographic data variables which included baseline characteristics including patient characteristics (e.g. CCI, number of prescribed medications) and physician characteristics (that is, age group, sex

and specialty) were divided into dichotomous or polytomous variables. All variables were summarized using descriptive statistic presentations in percentages, means and standard deviations. If the distribution of these data was not a normal distribution, then medians, and inter-quartile ranges were used instead. The prevalence of PIMs was defined as having as least one PIM based on explicit criteria. Multiple logistic regression analysis was used to determine the strength and direction of the association between PIMs and the possible predictors. The results are presented as odds ratios, and 95% confidence intervals (CIs). A test result with $p<0.05$ was considered statistically significant. All analyses were undertaken using STATA version10 (StataCorp, College Station, TX).

Sample size

Sample size calculations were based on the estimated prevalence of potentially inappropriate prescriptions using Beers criteria and STOPP from literature reviews (Fick et al., 2003; Lai et al., 2009; Ryan et al., 2009). The estimation of a population proportion with a specified absolute precision formula was used to calculate this (Chirawatkul, 2008). A sample size of at least 270 participants was sufficient to achieve this at the significance level of 0.05.

Ethics approval was provided by Ethics Committee of the Faculty of Medicine, Khon Kaen University as instituted by the Helsinki Declaration.

RESULTS

Demographics

Descriptive demographics of the 308 study subjects are shown in Table 1. Male and female numbers were equal. Median age was 72.8 years and median number of prescribed drugs was about 6. The educational level of study subject could be identified in 70% of subjects and the majority of them were lowly educated (≤ 6 years of education). Regarding comorbidity, the average CCI was 4.7±3.5. The top 5 common diagnoses were hypertension, diabetes, dyslipidemia, cerebrovascular diseases and musculoskeletal conditions. Focusing on physician characteristics, most were male sex, 40 years old or younger and staff specialists in internal medicine. The median numbers of medications prescribed per age category are as shown in Figure 1. There was no statistical significance of the numbers in each age group ($p>0.05$).

Potentially inappropriate medications (PIMs) determined by Beers criteria and STOPP

Prevalence of PIMs determined by Beers criteria and STOPP was 19.2 and 31.5%. There was a statistically significant difference between both criteria with prevalence rate ratios (PRR) of 6.6, 95% confidence intervals (CI) of 4.9 to 8.8, $p<0.05$. Majority of the subjects were prescribed with 1 PIM (10.1 and 16.7% for Beers criteria and STOPP, respectively). The median number of PIMs prescribed using Beers criteria was 1 (inter-quartile range (IQR); 1 to 2) and for STOPP was 2 (IQR: 1 to 3). The common medications associated with PIMs are shown in Table 2. According to Beers criteria, calcium channel blockers, anticholinergics and tricyclic antidepressants (50%) were the common medications associated with PIMS based on considering diagnosis whereas amitriptyline group, chlordiazepoxide-amitriptyline and perphenazine-amitriptyline (27.5%) were the most common medication prescribed independent of diagnosis. Followed by use of short-acting benzodiazepines over than recommended doses (25%). Regarding PIMs identified by STOPP, about one-fifth of all PIMs were medications that adversely affect falling patients (that is, benzodiazepines) and thus were the leading medications.

Predictors of potentially inappropriate medications

Multiple logistic analyses showed that only a higher number of prescription medications increased the risk of PIMS based on STOPP with an odds ratio (OR) of 1.2 (95% CI: 1.1 to 1.4), $p<0.05$ and subjects with hypertension showed a decrease in risk of PIMs identified by both Beers (OR: 0.2; 95%CI: 0.1 to 0.6) and STOPP (OR: 0.3, 95% CI: 0.1 to 0.6), $p<0.05$ after adjusted with the number of drugs, age of patient, patient's gender, patient's educational level, comorbidity of subjects, CCI, physician's age, physician's specialty and physician's gender.

DISCUSSION

This study confirms the high prevalence of PIMs among older adults (Guaraldo et al., 2011; Lai et al., 2009; Ryan et al., 2009). In this study, approximately 20 to 30% of older adult who attended internal medicine outpatient setting had at least 1 PIM. Comparing these results to prior studies, the figures varied from 16.3 to 62.5% (Guaraldo et al., 2011). This can be explained by the diversity in the severity of disease in the study subjects. The study included subjects with underlying medical illnesses who attended internal medicine outpatient clinic in a tertiary care setting, so the disease severity is likely to be higher than primary care setting, confirming the high mean CCI (4.7±3.5). STOPP was more sensitive than Beers criteria to identify PIMs in this study, supporting previous reports (Miguel et al., 2010; O'Mahony et al., 2010). This is however the reverse of the results of some studies e.g. study in nursing homes of Malaysia. This may also be explained by the differences in drug availability and prescribing practices (Chen et al., 2012).

Considering PIMs using Beers criteria and STOPP, anticholinergics in particular tricyclic antidepressants, benzodiazepines (long term use of long-acting group or short-acting group with higher than usual doses), NSAIDs and aspirin (ASA), and muscle relaxants and antispasmodics

Table 1. Patient demographics and physician characteristics.

Demographic	Total (N=308)
Male	157 (51%)
Age (years); median (IQR)	78 (68,77)
Age range	65-95
Educational level	
No data	54 (30.52%)
≤ 6 years of education	133 (43.18%)
7-12 years of education	44 (14.29%)
>12 years of education	37 (12.01%)
Median number of prescribing drugs (IQR)	5.6 (3.5,7)
Mean CCI (±SD)	4.7 (3.5)
Top 5 common diseases	
Hypertension	137 (44.5%)
Diabetes	85 (27.7%)
Dyslipidemia	56 (18.2%)
Cerebrovascular diseases	46 (14.9%)
Musculoskeletal conditions	43 (14%)
Physician characteristics	(N=306, unavailable=2)
Male physician	211 (69%)
Physician age group	
≤ 40 years	130 (42.5%)
41-50 years	78 (25.5%)
> 50 years or over	98 (32%)
Physician position	
Resident and fellow	114 (37.2%)
Staff	192 (62.8%)

IQR: Inter-quartile range, N: total number of subjects, CCI: Charlson Co-morbidity Index, SD: standard deviation.

showed the high proportion using both criteria. As compared to prior studies, the common medications related to PIMs were diverse according to study setting. Nevertheless, benzodiazepines and tricyclic antidepressants associated with PIMs in this report is similar to that of other reports (Buck et al., 2009; Chen et al., 2012; Lai et al., 2009). Other common prescriptions related to PIMs that were not identified in this study were short-acting nifedipine and fluoxetine (Buck et al., 2009; Oliveira et al., 2012). The possible explanation is the inclusion criteria of this study; shorting-acting nifedipine was usually prescribed in patients with particular conditions e.g. systemic scleroderma with Raynaud phenomenon which commonly occurs in a younger age group, but the study subjects in the older age group usually have atherosclerotic-related diseases such as hypertension, diabetes and dyslipidemia. Therefore, long-acting calcium channel blockers were the majority of prescriptions for hypertensive treatment. This study reviewed prescriptions only from the internal medicine outpatient setting, so fluoxetine which is usually prescribed by a psychologist cannot be identified as medication-related to PIMs. The high proportion of PIMs in this study may reflect a lack of understanding the prescribing medication principles in the elderly and public health policy that limits the use of elderly-friendly medications. Therefore, physicians do not have many choices for drug prescription. For example, amitriptyline is a common medication prescribed for neuralgia. Other safer drugs are spared in case of amitriptyline failure or having an adverse effect from this medication.

Regarding factors associated with PIMs, this study can identify only that a higher number of prescription medications predicts PIMs using STOPP which is similar to prior studies (Buck et al., 2009; Chen et al., 2012; Guaraldo et al., 2011; Lai et al., 2009; Oliveira et al.,

Table 2. Lists of common medications associated with inappropriate prescriptions.

Criterion	Top 5 common medication		%
Beers	**Considering diagnosis**		
	Constipation	Calcium channel blockers, anticholinergics and tricyclic antidepressants	50
	GU/DU	NSAIDs and aspirin	25
	Blood clotting disorders/receiving anticoagulant therapy	NSAIDs, aspirin, dipyridamole, ticlopidine and clopidogrel	25
	Cognitive impairment	Barbiturates, anticholinergics, antispasmodics, muscle relaxants and CNS stimulants	25
	Depression	Long-term benzodiazepine use, sympatholytic agents: methyldopa, reserpine and quanethidine	25
	Independent diagnosis		
	Amitriptyline, chlordiazepoxide-amitriptyline and perphenazine-amitriptyline		27.5
	Doses of short-acting benzodiazepines: doses >lorazepam 3 mg; oxazepam 60 mg; alprazolam 2 mg; temazepam 15 mg; triazolan 0.25 mg		25
	Anticholinergics and anthistamines: chlorpheniramine, diphenhydramine, hydroxyzine, cyproheptadine, promethazine, tripelennamine and dexchlorpheniramine		20
	Muscle relaxants and antispasmodics		17.5
	Indomethacin		2.5
	Short –acting dipyridamole		2.5
STOPP	Drugs that adversely affect fallers	Benzodiazepines	22.35
	Endocrine system	Glibenclamide or chlorpropamide with type 2 DM	8.24
	Central nervous system and psychotropic drugs	Long-term, long-acting benzodiazepine	8.24
	Cardiovascular system	ASA at dose > 150 mg/day	7.06
	Cardiovascular system	ASA with no history of CAD, CVD or PVD	7.06
	Gastrointestinal system	PPI for PUD at full therapeutic dosage for > 8 weeks	3.53

GU: Gastric ulcer, DU: duodenal ulcer, NSAIDs: nonsteroidal anti-inflammatory drugs, CNS: central nervous system, DM: diabetes mellitus, ASA: aspirin, CAD: cardiovascular disease, CVD: cerebrovascular disease, PVD: peripheral vascular disease, PPI: proton pump inhibitor, PUD: peptic ulcer disease.

2012). Beers criteria are likely less sensitive in this study because many medications documented in Beers criteria are not widely used or available in this setting, for example drugs such as propoxyphene and combination products, trimethobenzamide and reserpine. Other predictive factors associated with PIMs such as female sex, low educational level, advanced age, and physician characteristics could not be identified. Hypertension showed decreased odds ratios of PIMs in both Beers criteria and STOPP, similar to one report (Chen et al., 2012). The results cannot conclude that hypertension is a protective factor associated with PIMs. A possible reason is the hypertension guidelines are world-wide and recommend prescribed antihypertensive medications that are rather safe for the elderly. There were a number of hypertensive subjects in this study.

This study represents pattern of prescribing medication regarding geriatric pharmacotherapy in an outpatient setting of a tertiary care hospital.

Nonetheless, it is not necessary that the prescription of PIMs will cause adverse events in older adults. Because there have been controversies about applying Beers criteria and STOPP in different settings and that these criteria focus on explicit criteria, they may not be useful in specific medical conditions; individual assessment remains the key factor in the consideration of prescription (Chen et al., 2012; Fick et al., 2003). These criteria can be a good clinical tool to help physicians and pharmacists considering possible

medication-related adverse effects and for reduction of drug-related costs, overall healthcare costs, adverse drug event-related hospitalizations, and improving care in older adults (Chen et al., 2012; Fick et al., 2003). En-couraging physicians and pharmacists to use a screening tool for PIMs as one of geriatric assessments would be worthwhile. The STOPP criteria are likely more sensitive to the outpatient setting among Thai older adults. Further research to study about the benefits of STOPP and Beers criteria is required in the area of negative outcomes, e.g. hospitalization rates, emergency visit rates and healthcare costs and focusing on different settings, e.g. community, hospital and institutional care, among Thai older adults. Additionally, it is essential to develop a new medication reviewing tool that is suitable for Thai older adults. An effective approach can lead to improve the appropriateness of prescribing in the ambulatory care setting and decreases adverse outcomes related to PIMs.

There were several limitations in this study. Firstly, data were collected retrospectively; some information was unavailable in all subjects such as educational level and over-the-counter drugs, and some conditions such as constipation might not be documented in medical records even though the subjects had that condition. Therefore, the prevalence of PIMs might be underestimated. Se-condly, this study was conducted prior to updated Beers criteria in 2012 ("American Geriatrics Society Updated Beers Criteria for potentially Inappropriate Medication Use in Older Adults", 2012). Therefore, identification of PIMs in this study is based on Beers criteria version from 2003. Finally, this study reviewed medication prescribing in the internal medicine outpatient clinic only. Thus the actual proportion of PIMs might be higher if the patients took medication from other sources.

Conclusions

Potentially inappropriate medications are of a high prevalence in a geriatric ambulatory setting of a tertiary care hospital. STOPP is a more sensitive tool than Beers criteria for Thai older adults to detect PIMs. A higher number of medications are associated with greater numbers of PIMs based on STOPP. Healthcare pro-fessionals, especially physicians and clinical pharmacists play an important role by reviewing medications at every visit based on explicit criteria. Further research is required to study possible negative outcomes, diverse settings, and to develop a new medication reviewing tool that is appropriate for Thai older adults.

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