Prevalence and Patient Factors Associated with Non-steroidal Anti-inflammatory and Tricyclic Antidepressants Use among Elderly Inpatients at a District Hospital in the South of Thailand

Weerasak KHAMPHEERAPHAPKHUL, Wiyadee MATCHAROEN, Apinya KERDTALAY, Ammar DARAMA and Tanavij PANNOI[*]

School of Pharmacy, Walailak University, Nakhon Si Thammarat 80161, Thailand

([*]**Corresponding author's e-mail: tanavij.pa@wu.ac.th**)

Abstract

The Thai elderly population has rapidly increased; a number of diseases have been reported, which are mainly associated with overuse of medications. Evidently, Non-steroidal Anti-inflammatory drugs (NSAIDs) and Tricyclic Antidepressants (TCAs) have been commonly given to elderly patients, which might have caused adverse drug reactions (ADRs). It is essential to use screening tools in early detection of high-risk medications (HRM) which should be weighed by their benefits and risks. This study aims to identify the prevalence and patient factors associated with HRM. The HRM screening tool, developed by a Thai working group of drug system research, was applied in this cross-sectional study. 65-year-old and older inpatients that had at least one admission at the study hospital during the fiscal year 2013 were systematically sampled. Descriptive statistics were used for conducting prevalence. Logistic regression was used to analyze the association between patient factors and HRM with type I error = 0.05. Regarding exclusion criteria, the sample of the study group used 393 elderly inpatients. 30 out of 393 inpatients (7.6 %) received HRM. The prevalence of those receiving NSAIDs, TCAs, and both, were 3.8, 3.6, and 0.3 %, respectively. Patients who had a length of hospitalization of more than 6 days were likely to be at risk of HRM compared with those of 1 to 3 days. (OR = 3.704, 95 %CI = 1.242 - 11.041, p = 0.019). In conclusion, patients who had longer hospitalizations had a higher chance of being given HRM (NSAIDs and TCAs), so that the more medications were prescribed, the higher prevalence of HRM was observed.

Keywords: High-risk medication, elderly inpatients, prevalence, Patient factors, screening tool

Introduction

Thailand is an aging society since the rate of aging population has increased from 10.7 percent in 2007 to 25 percent or 17.8 million people in 2030 [1-3]. Polypharmacy was commonly given to those elderly patients with regard to their multiple diseases. The more medications were used by the elderly, the higher prevalence of adverse drug events (ADEs) were observed; approximately, 20.4 percent [4]. Having said that two common drug classes in relation to ADEs prescribed among the elderly were Non-steroidal Anti-inflammatory drugs (NSAIDs) and Tricyclic Antidepressants (TCAs) [5]. It is the fact that the major ADEs of NSAIDs and TCAs associated with the elderly use were gastrointestinal disturbances and orthostatic hypotension, respectively [5].

To prevent ADEs, many high-risk medications (HRM) screening tools were developed by researchers and clinicians, such as, Beers' criteria STOPP (Screening Tool of Older Persons' Prescriptions); START (Screening Tool to Alert doctors to Right Treatment); or MAI (Medication Appropriateness Index). In Thailand, criteria for high-risk medication use in Thai elderly patients were reported by Winit-Wajjana and his colleagues [5]. Potentially inappropriate medication was typically

replaced by "High risk medication" in the Thai criteria [6]. In recent years, a Thai drug system research initiated a country-specific list of elderly high-risk medication use, namely, "Lists of Risk Drugs for Thai Elderly" [7]. However, the criteria were not widely applied in the clinical practice, particularly for inpatient setting.

This study aimed to obtain the prevalence of and patient's factors associated with the use of HRM among elderly inpatients at a district hospital in the South of Thailand. Having developed formally by Thai researchers and medical specialist boards, included geriatricians, psychologists, and preventive medicine, the Lists of Risk Drugs for Thai Elderly, as a new country-specific tool, was selected as the screening tool with the only 2 classes of medication--NSAIDs and TCAs--in this study.

Materials and methods

A cross-sectional study was conducted by researchers. The retrospective data from a 120-bed hospital between October 1, 2012, and September 30, 2013, were retrieved. The whole population of 65 year old and older inpatients was 1,944, and their information was recorded in its entirety in the patient database. Sample size calculation for Logistic regression analysis was used in the study. To follow the calculated study samples with regard to a systematic sampling, 1,944 divided by 400 was 5, which was an interval sampling. The researcher picked a starting point randomly from 1 to 1,944, and sampled every fifth record until the researchers had reached 400 study samples. 400 out of 1,944 inpatient records were systematically sampled by their hospital numbers (HN).

Any inpatients were excluded if they had been given only intravenous fluid, medical devices, or medical procedures, regardless of medications used. The exclusion criterion also included an incomplete record of required data for study variables. Overall, 393 inpatients were included in the study. The prevalence of high-risk medication and patient factors- gender, age, health insurance scheme, duration of hospitalization, number of hospital visits, medications, and diagnosed diseases by ICD-10 codes- associated with the use of high-risk medication were analyzed by frequency count and percent/percentage. Logistic regression was applied in the analysis of association between categorical data (patient factors) and dichotomous outcomes (HRM/non-HRM), with a power of study at 80 percent and a significant level at 0.05. The study was ethically approved (approval code 060/2014) by the Walailak University Institution Review Board.

Results and discussions

The findings showed that 7.6 percent of all participants [30/393] were prescribed at least 1 high-risk medication- 3.8 [15/393] and 3.6 [14/393] percent for NSAIDs and TCAs used, respectively. There was more likelihood of receiving HRM in males (9.1 %, [16/30]) and those aged 70 - 79 years (7.8 %, [13/167]). Patients who were members of Universal Health Coverage (UHC) (80.0 %, [24/30]), as well as those who were given over 5 medications (8.9 %, [27/303]), were likely HRM users (see **Table 1**).

Additionally, there were 32 events of HRM given to those 30 HRM patients, of which 15 out of all HRM events could be matched to ICD-10 codes (46.9 %, [15/32]) by researchers. Those ICD-10 codes matched to HRM were mental and behavioral disorders, diseases of the nervous system, diseases of the circulatory system, diseases of the skin and soft tissues, diseases of the musculoskeletal system and connective tissue, and other injures of specified, unspecified, and multiple body regions.

Table 1 Characteristics of participants divided by receipt of high-risk medications or non-high-risk medications.

Patient factors	HRM* (%) [n = 30]	Non-HRM (%) [n = 363]	Total (%) [n = 393]
1. Gender			
- Male	16 (53.3)	159 (43.8)	175 (44.5)
- Female	14 (46.7)	204 (56.2)	218 (55.5)
2. Age (years)			
- 65-69	8 (26.7)	75 (20.7)	83 (21.1)
- 70-79	13 (43.3)	154 (42.4)	167 (42.5)
- > 79	9 (30.0)	134 (36.9)	143 (36.4)
3. Health Insurance Scheme			
-Universal Health Coverage (UHC)	24 (80.0)	258 (71.1)	282 (71.8)
- Non UHC**	6 (20.0)	105 (28.9)	111 (28.2)
4. Duration of Hospitalizations (days per person)			
- 1-3	10 (33.3)	203 (55.9)	213 (54.2)
- 4-6	10 (33.3)	110 (30.3)	120 (30.5)
- > 6	10 (33.3)	50 (13.8)	60 (15.3)
5. Frequency of Hospital Visits			
- 1-2	26 (86.7)	328 (90.4)	354 (90.1)
- > 2	4 (13.3)	35 (9.6)	39 (9.9)
6. Number of Medications (items)			
- 1-5	3 (10.0)	87 (24.0)	90 (22.9)
- 6-10	10 (33.3)	151 (41.6)	161 (41.0)
- > 10	17 (56.7)	125 (34.4)	142 (36.1)
7. Number of Diagnoses by ICD 10			
- 1-2	9 (30.0)	159 (43.8)	168 (42.7)
- 3-4	15 (50.0)	156 (43.0)	171 (43.5)
- > 4	6 (20.0)	48 (13.2)	54 (13.7)

*HRM: High Risk Medication,
**Non-UHC = Social Health Insurance, Civil Servant Medical Scheme, Accident Health Insurance, and out-of-pocket

     NSAIDs and TCAs were more often given to males (53.3 %, [8/15]) than females (46.7 %, [7/15]). Furthermore, 46.7 percent of all of the 70 - 79 age group received more NSAIDs, while 42.9 percent of all of the 65 - 69 age group received more TCAs. Five participants using NSAIDs and TCAs were evenly admitted to the hospital over 1 - 3, 4 - 6, and over 6 days, respectively. The number of hospital visits among NSAIDs and TCAs users were 1 - 2, and the number of diagnoses among NSAIDs and TCAs were 3 - 4. It was noticeably observed that half or more of NSAID and TCA users had over 10 medications (see **Table 2**).

Table 2 Patients who used either NSAIDs or TCAs or both, divided by patient factors (n = 30).

Patient factors	NSAIDs* (%) [n=15]	TCAs** (%) [n=14]	Both NSAIDs and TCAs (%) [n=1]	Total (%) [n=30]
1. Gender				
- Male	8 (53.3)	8 (57.1)	-	16 (53.3)
- Female	7 (46.7)	6 (42.9)	1 (100.0)	14 (46.7)
2. Age (years)				
- 65-69	2 (13.3)	6 (42.9)	-	8 (26.7)
- 70-79	7 (46.7)	5 (35.7)	1 (100.0)	13 (43.3)
- > 79	6 (40.0)	3 (21.4)	-	9 (30.0)
3. Health Insurance Scheme				
- Universal Health Coverage (UHC)	10 (66.7)	13 (92.9)	1 (100.0)	24 (80.0)
- Non-UHC	5 (33.3)	1 (7.1)	-	6 (20.0)
4. Duration of Hospitalizations (days per person)				
- 1-3	5 (33.3)	5 (35.7)	-	10 (33.3)
- 4-6	5 (33.3)	4 (28.6)	1 (100.0)	10 (33.3)
- > 6	5 (33.3)	5 (35.7)	-	10 (33.3)
5. Frequency of Hospital Visits				
- 1-2	12 (80.0)	13 (92.9)	1 (100.0)	26 (86.7)
- > 2	3 (20.0)	1 (7.1)	-	4 (13.3)
6. Number of Medications (items)				
- 1-5	2 (13.3)	1 (7.1)	-	3 (10.0)
- 6-10	5 (33.3)	5 (35.7)	-	10 (33.3)
- > 10	8 (53.3)	8 (57.2)	1 (100.0)	17 (56.7)
7. Number of Diagnoses by ICD 10				
- 1-2	6 (40.0)	3 (21.4)	-	9 (30.0)
- 3-4	6 (40.0)	8 (57.2)	1 (100.0)	15 (50.0)
- > 4	3 (20.0)	3 (21.4)	-	6 (20.0)

***NSAIDs**: Aspirin (> 325 mg), Diclofenac, Ibuprofen, Mefenamic acid, Meloxicam, Naproxen, Piroxicam, Celecoxib
**TCAs: Amitriptyline and Imipramine

In association analysis, duration of hospitalization was the only significant factor for receiving NSAIDs and TCAs (over 6 days vs 1 - 3 days, OR = 3.704, 95 %CI = 1.242 - 11.041, p = 0.019). Statistically, significant association between gender, age, health insurance schemes, number of hospital visits, medications, and diagnosed diseases by ICD-10 codes and receipt of HRM were not observed in this study (see **Table 3**).

Table 3 Patient factors associated with receiving NSAIDs and TCAs, analyzed by Binary logistic regression (n = 393).

Patient factors	Regression Coefficient (B)	Standard Error (S.E.)	Odds Ratio (OR)	95 % CI	p-value*
1. Gender					
- Male	-	-	1	-	-
- Female	- 0.425	0.398	0.654	0.300 - 1.428	0.286
2. Age (years)					
- 65-69	-	-	1	-	-
- 70-79	- 0.577	0.510	0.562	0.270 - 1.525	0.258
- > 79	- 0.800	0.548	0.449	0.154 - 1.314	0.144
3. Health Insurance Schemes					
- Universal Health Coverage (UHC)	-	-	1	-	-
- Non UC	0.569	0.494	1.767	0.672 - 4.650	0.249
4. Duration of Hospitalization (days)					
- 1-3	-	-	1	-	-
- 4-6	0.370	0.506	1.447	0.536 - 3.904	0.466
- > 6	1.309	0.557	3.704	1.242 - 11.041	0.019
5. Number of Hospital Visits					
- 1-2	-	-	1	-	-
- > 2	- 0.142	0.694	0.868	0.223 - 3.384	0.838
6. Number of Medications (items)					
- 1-5	-	-	1	-	-
- 6-10	0.407	0.709	1.503	0.375 - 6.027	0.565
- > 10	0.867	0.748	2.381	0.549 - 10.316	0.246
7. Number of Diagnoses by ICD-10 codes					
- 1-2	-	-	1	-	-
- 3-4	0.370	0.462	1.448	0.585 - 3.581	0.424
- > 4	0.341	0.669	1.406	0.379 - 5.218	0.610

*Significant at p-value < 0.05

The prevalence of NSAIDs were 3.8 percent, which had less observation than the study of Napolitano and colleagues [8], while, and the prevalence of TCAs users were 3.6 percent that ranged between 0.05 and 20.5 as Opondo and colleague study [9]. As a result, this was explained by the different list of NSAIDs and TCAs available in each of studied hospitals and by the differences of HRM screening tools.

In addition, the majority of elderly patients had less 2 visits per year as inpatient status and those were mainly diagnosed in relation to upper and lower respiratory disorders. It is implied that the prevalence of NSAIDs and TCAs use, which was not given in patients because of their serious side effects (e.g. respiratory tracts constriction and cardiovascular thrombotic events), were lower than the previous studies [8,9].

Although there were less male inpatients than female, male patients were at risk for receiving NSAIDs and TCAs rather than female. According the match between high-risk medications and diagnoses via ICD-10 by researchers, male inpatients were mostly given NSAIDs and TCAs with diagnoses of muscle pain and bone disorders. Therefore, the male might be given more NSAIDs and TCAs than female inpatients.

In this study**,** hospitalization was a statistically significant factor for receiving high-risk medication among the elderly inpatients. It was relevant to former studies that the longer those patients stay in the hospital, the more number of medications, included high-risk medications, were given to patients [9,10]. During patient's hospitalization; however, there were no any record of adverse drug events with regard to NSAIDs and TCAs.

The results are not able to anticipate that HRMs were inappropriate medication for the elderly; HRM is medication that poses more risks than benefits for the elderly [7]. It was recommended that the use of NSAIDs and TCAs among the elderly should be concerned with regard to any side effects, which highly reported in Thai Vigilance database that 81 and 37.4 percent of elderly who used NSAIDs and TCAs experienced in any ADRs. Others than that, elderly patients with multiple use of medications, which was a strongly significant factor associated with HRM in Thai outpatient and international inpatient study, are encouraged to monitor any adverse effects from those given medications [10,11].

A number of research limitations were also unveiled. For instance, random sampling error confounded the heterogeneity of participants that affected the generalizability of study result to other study sites. Because of retrospective data collection, the strength of exposure and initial time to expose some determinants were not existed in participants data, so that, the causation between covariates and outcome was not justifiable in the study. In addition, prescriber's factors, which are strongly potential determinants to HRM use, were not studied.

For further studies, a multi-center, prospective, cohort research is recommended in order to study the incidence of HRM and the strength of association between factors and serious adverse events of HRM. The full list of Thai HRM should be applied, as well as, the specificity and sensitivity analysis of this HRM screening tool should be evaluated.

Conclusions

It has been reported that 7.6 percent of elderly inpatients were given NSIADs and TCAs. Those patients who had longer hospitalizations, were likely to receive NSAIDs and TCAs. Prior to giving NSAIDs and TCAs to elderly inpatients, prescribers should weigh the benefits against the risks. Last but not least, hospital pharmacists should be aware of elderly patients who use HRM, in order to prevent any serious ADEs.

Acknowledgements

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