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Prevalence of drug-related visits to the emergency department of King Chulalongkorn Memorial Hospital

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Problem/background : *Drug-related problems (DRPs) are major causes of patient visits to the emergency departments in several countries. However, there have not been sufficient publications on the prevalence and characteristics of this category of visits in Thailand.*

Objective : *To determine the prevalence and characteristics of drug-related visits (DRVs) to the emergency department.*

Design : *Descriptive study.*

Setting : *Non-trauma Emergency Department, King Chulalongkorn Memorial Hospital.*

Materials and Methods : *This cross-sectional study was conducted at the Non-trauma Emergency Department of King Chulalongkorn Memorial Hospital, affiliated with the Red Cross Society of Thailand and the Faculty of Medicine, Chulalongkorn University. All adult patients presenting to the Emergency Department during 7.30 a.m. and 3.30 p.m. over 4 months were evaluated. The emergency visits were identified as drug-related by a pharmacist and emergency physicians independently. DRPs were categorized according to Cipolle's classification confirmed by external expert opinion. Preventability of DRPs was determined using Schumock and Thornton criteria.*

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Results : *Of 1,000 patients, 369 patients (36.9%) were identified as having drug-related emergency department visits. Two hundred and fifty-five visits (69.1%) were preventable. Two hundred patients (54.2%) needed hospitalization and two patients (0.5%) died. The most common causes of DRVs were adverse drug reactions (32.52%), noncompliance (26.29%) and unnecessary drug therapy (14.36%). The most common drugs related to the emergency department visits were alcohol (5.53%), furosemide (3.95%), aspirin (3.75%), insulin (3.56%) and metformin (3.36%).*

Conclusions : *One-third of the patient visits at Non-trauma Emergency Department were drug-related. Two-thirds of these events were preventable.*

Keywords : *Drug-related visits, Drug-related problems, Emergency department.*

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เหตุผลของการทำวิจัย : *ปัญหาเกี่ยวกับยาเป็นสาเหตุที่พบได้บ่อยของการเข้ารับการรักษาที่หน่วยฉุกเฉินของผู้ป่วยในหลายประเทศ อย่างไรก็ตามยังไม่มีการศึกษาเกี่ยวกับความชุก และลักษณะของปัญหาเกี่ยวกับยาที่เป็นสาเหตุของการเข้ารับการรักษาตัวผู้ป่วยที่หน่วยฉุกเฉินในประเทศไทยมาก่อน*

วัตถุประสงค์ : *เพื่อศึกษาความชุกและลักษณะของปัญหาเกี่ยวกับยาที่เป็นสาเหตุของการเข้ารับการรักษาของผู้ป่วยที่หน่วยฉุกเฉิน*

รูปแบบการวิจัย : *การศึกษาเชิงพรรณนา*

สถานที่ทำการศึกษา : *หน่วยฉุกเฉิน Non-trauma โรงพยาบาลจุฬาลงกรณ์*

ตัวอย่างและวิธีการศึกษา : *ผู้วิจัยเก็บข้อมูล ณ จุดเวลาใดเวลาหนึ่ง (cross-sectional study) ในผู้ป่วยผู้ใหญ่ที่เข้ารับการรักษาที่หน่วยฉุกเฉิน Non-trauma โรงพยาบาลจุฬาลงกรณ์ ระหว่างเวลา 7.30 น. ถึง 15.30 น. เป็นเวลา 4 เดือน เภสัชกรและแพทย์ประเมินว่าการเข้ารับการรักษาที่หน่วยฉุกเฉินมีสาเหตุจากปัญหาเกี่ยวกับยาหรือไม่ ปัญหาเกี่ยวกับยาที่พบถูกจัดแบ่งประเภทโดยอาศัยเกณฑ์ของ Cipolle และคณะ โดยเภสัชกรในหน่วยและเภสัชกรผู้เชี่ยวชาญจากภายนอกและพิจารณาว่าปัญหาเกี่ยวกับยาเหล่านั้นสามารถป้องกันได้หรือไม่โดยอาศัยเกณฑ์ของ Schumock และ Thornton*

ผลการศึกษา : *จากผู้ป่วยที่เข้าร่วมงานวิจัยจำนวน 1,000 ราย ผู้ป่วยจำนวน 369 ราย (ร้อยละ 36.9) เข้ารับการรักษาที่หน่วยฉุกเฉินอันเนื่องมาจากยา ปัญหาเกี่ยวกับยาที่พบในผู้ป่วยจำนวน 255 ราย (ร้อยละ 69.1) เป็นปัญหาที่สามารถป้องกันได้ ผู้ป่วยจำนวน 200 ราย (ร้อยละ 54.2) จำเป็นต้องเข้ารับการรักษาตัวในโรงพยาบาลต่อ และมีผู้ป่วย จำนวน 2 ราย (ร้อยละ 0.5) เสียชีวิต ปัญหาเกี่ยวกับยาที่พบบ่อยที่สุด ได้แก่ การเกิดอาการไม่พึงประสงค์จากการใช้ยา (ร้อยละ 32.52) ปัญหาความไม่ร่วมมือในการใช้ยา (ร้อยละ 26.29) และปัญหาการได้รับยาโดยไม่จำเป็น (ร้อยละ 14.36) รายการยาที่สัมพันธ์กับการเข้ารับการรักษาที่หน่วยฉุกเฉินที่พบบ่อยที่สุด ได้แก่ แอลกอฮอล์ (ร้อยละ 5.53) furosemide (ร้อยละ 3.95) aspirin (ร้อยละ 3.75) insulin (ร้อยละ 3.56) และ metformin (ร้อยละ 3.36)*

สรุป : *1 ใน 3 ของผู้ป่วยที่เข้ารับการรักษาตัวที่หน่วยอุกเฉินมีสาเหตุจากปัญหาที่เกี่ยวกับยาและ 2 ใน 3 ของปัญหาเหล่านั้นเป็นปัญหาที่สามารถป้องกันได้*

คำสำคัญ : *การเข้ารับการรักษาอันเนื่องมาจากยา, ปัญหาเกี่ยวกับยา, หน่วยอุกเฉิน*

Drug-related problem (DRP) is an undesirable event, associated with drug use, that interferes with desired goals of the treatment for individual patients.[1, 2] Significant negative consequences of DRP include treatment failure, organ disability, new medication problem, hospital admission, or even death. Reports from various hospitals have shown that 5% to 10% of all hospital admissions are drug-related. [3] It was estimated that DRP comprise 28% of emergency department (ED) visits, 24% of which result in hospitalization. [4]

In Thailand, the incidence of hospital admission related to DRPs in hospitalized patients were 6.4% - 23.5%.[5] Patients seeking care only in ED were not included into these studies, the prevalence of ED visits related to DRPs was not known. We, therefore, conducted a cross-sectional study to determine the prevalence, category, medication involved and preventability of DRVs to the emergency department.

Material and Methods

Setting and participants

This cross-sectional study was conducted at King Chulalongkorn Memorial Hospital (KCMH) from November 2007 to February 2008. All patients who were 15 years of age and older who presented to the Non-trauma Emergency Department from Monday to Friday between 7.30 a.m. and 3.30 p.m. were selected based on the availability of the study pharmacist. Patients were excluded if they were transferred before data collection was completed.

Data collection and case definitions

Past and present medical history including past and current medication lists of individual patients and their allergy were gathered by interviewing patients or their relatives, and reviewing medical records. All related physical exam results, laboratory data and diagnosis were collected. The data were transcribed into KCMH Emergency Department Medication Reconciliation form (Appendix 1) for evaluation. Data verification was provided by visual check.

Drug-related ED visit cases were defined as a person who visited the non-trauma ED with chief complaint related to use or not to use drugs, including prescription medications, over-the-counter medicines, vitamins, nutritional supplements, alcoholic beverages, tobacco products, and illicit substances.

Outcome measures

A patient was identified as having drug-related visit only if other possible causes were ruled out. It was also mandatory that the attending physician agreed with pharmacist that the patient's visit was drug-related. When disagreements were found, a third opinion from ED senior staff would be required. DRPs were classified into 7 categories according to Cipolle's classification:[2] unnecessary drug therapy, need additional drug therapy, ineffective drug, dosage too low, adverse drug reaction, dosage too high and noncompliance. Categorizations were confirmed by an external expert pharmacist. Any disagreements found were resolved by consensus. In this study, allergic reaction, unintentional overdose, drug withdrawal, drug abuse and self-harm attempt using drugs were included into different categories of DRP (Table 1).

Appendix 1

KCMH Emergency Department Medication Reconciliation Form No □□□□

D.O.B_____ M/ F Ht _____cm. Wt _____kg. CC: _____

concomitant diseases _____smoking ( ) Y ( ) N alcohol ( ) Y ( ) N

allergy/ ADR	symptoms	allergy/ ADR	symptoms

( ) No known allergies ( ) Allergy history recorded ( ) No medication use before admission

Patient's medication lists prior to admission

Source of information: ( ) Patient/ Family ( ) Medical record ( ) Computer Data base ( ) Others_____

D/C HM	Drug/ Dose/ Route/ Freq	Indications	Last dose Date/ Time	Continue on Admission Yes	Continue on Admission No	Notes
				( )	( )	
				( )	( )	
				( )	( )	
				( )	( )	
				( )	( )	
				( )	( )	
				( )	( )	
				( )	( )	
				( )	( )	
				( )	( )	
				( )	( )	
				( )	( )	
				( )	( )	
				( )	( )	

Total number of medications used before ER admission_____items

Patient's medication orders during ER admission

D/C HM	Drug/ Dose/ Route/ Freq	Indications	Notes

Total number of medications used during ER admission_____items

Patient Status: ( ) Discharge ( ) Admit ( ) Refer ( ) Death ( ) others.....

Total number of take home/ discharge medications_____items

Reviewed and Transcribed: Pharmacist Signature_____ Date/Time_____

Table 1. Categories and common causes of DRPs defined by Cipolle et al.[2]

Drug related problems	Common causes of drug related problems
1. Unnecessary drug therapy	• There is no valid medical indication for the drug therapy at this time. • Multiple drug products are being used for a condition that requires single drug therapy. • The medical condition is more appropriately treated with non-drug therapy. • Drug therapy is being taken to treat and avoidable adverse reaction associated with another medication • Drug abuse, alcohol use, or smoking is causing the problem.
2. Need for additional drug therapy	• A medical condition requires the initiation of drug therapy. • Preventive drug therapy is requires to reduce the risk of developing a new condition. • A medical condition requires additional pharmacotherapy to attain synergistic or additive effects.
3. Ineffective drug	• The drug is not the most effective for the medical problem. • The medical condition is refractory to the drug product. • The dosage form of the drug product is inappropriate. • The drug product is not an effective product for the indication being treated.
4. Dosage too low	• The dose is too low to produce the desired response. • The dosage interval is too infrequent to produce the desired response. • A drug interaction reduces the amount of active drug available. • The duration of drug therapy is too short to produce the desired response.
5. Adverse drug reaction	• The drug product causes an undesirable reaction that is not dose-related. • A safer drug product is required due to risk factor. • A drug interaction causes an undesirable reaction that is not dose-related. • The dosage regimen was administered or changed too rapidly. • The drug product causes an allergic reaction. • The drug product is contraindicated due to risk factors.
6. Dosage too high	• Dose is too high. • The dosing frequency is too short. • The duration of drug therapy is too long. • A drug interaction occurs resulting in a toxic reaction to the drug product. • The dose of the drug was administered too rapidly.
7. Noncompliance	• The patient dose not understands the instructions. • The patient prefers not to take the medication. • The patient forgets to take the medication. • The drug product is too expensive for the patient. • The patient cannot swallow or self-administer the drug product appropriately. • The drug product is not available for the patient.

Drugs associated to ED visits were classified by generic name using the anatomical therapeutic chemical classification system with defined daily doses (ATC/ DDD). [6] Drugs not included in ATC/ DDD were classified into ATC/ DDD classes by their approval indications. Medical conditions leading to ED visits were categorized according to the international statistical classification of diseases and related health problems in the 10th revision version for 2007.[7]

Drug-related ED visits were subcategorized as preventable if one of these criteria [8] were met, namely: 1) drug was not appropriate for patient's conditions; 2) the dosage, route, or frequency were not appropriate for patient's age, weight, or renal function; 3) therapeutic drug monitoring or other necessary laboratory tests were not performed; 4) the patient had a history of allergy or previous reaction to the drug; 5) drug interaction was considered related to the a suspected drug reaction; 6) a drug level or laboratory test had shown a toxicity of drugs; and, 7) poor patient compliance.

Statistical analysis

The sample size was calculated by using an α of 0.05 and the assumed incidence of drug-related ED visits was 28%[3], at least 988 patients were planned to be enrolled. Inter-rater agreement (κ) was measured using kappa statistics. Chi-square and one way ANOVA test were used to compare variables. Differences were considered statistically significant when p-values were less than 0.05. Descriptive analyzes were performed with Statistical Package for the Social Sciences (SPSS) for Windows version 14.0.

Ethical criteria

The study has been approved by the Institutional Review Board (IRB) of the Faculty of Medicine, Chulalongkorn University. All patients were informed before documentation and received the standard treatments for their medical conditions even they denied to participate in this study.

Results

During the study period, a total of 1,019 outpatients visited the non-trauma ED, and they were eligible. Nineteen patients were, however, excluded: three declined to collaborate; four could not provide information about medication used, and twelve were transferred before completion of data collection. Ultimately, 1,000 patients were recruited into this study. Participated patients were 46.2% male patients and 53.5 $\pm$ 20.4 years of age. The mean number of concomitant diseases was 1.45 $\pm$ 1.26. The mean number of medication use was 4.27 $\pm$ 3.69.

Drug-related ED visits were detected in 369 patients (36.9%). Inter-observer variability was excellent[9], with a kappa statistic for the presence of drug-related ED visit being 0.81. Drug-related ED visit patients (n = 369) were 44.7% male patients and 55.5 $\pm$ 20.56 years of age. The mean number of concomitant diseases was 1.62 $\pm$ 1.21, the mean number of medication used was 4.72 $\pm$ 3.5. Mean age, number of concomitant diseases, and mean number of medications use in patients with drug-related ED visit were higher as compared to those without DRV ($p < 0.05$) (Table 2).

Table 2. Demographic information of the patients (n = 1,000)

Characteristics	With drug-related visit , n = 369	Without drug-related visit , n = 631	p-value
Male, number (%)	165 (44.7)	296 (46.9)	0.502[1]
Age (yr), Mean ± SD	55.5 ± 20.56	52.6 ± 20.26	0.029[2]
Alcohol use, number (%)	75 (20.3)	112 (17.7)	0.313[1]
Tobacco smoker, number (%)	72 (19.5)	113 (17.9)	0.528[1]
No. of concomitant disease, mean ± SD	1.62 ± 1.21	1.36 ± 1.28	0.002[2]
No. of medications, mean ± SD	4.72 ± 3.5	4.0 ± 3.77	0.003[2]

1 = Analyzed by Chi-square

2 = Analyzed by One way ANOVA

When classified patients who had DRV according to Cipolle's categorization, 32.52% of the patients had adverse drug reactions; 26.29% of the patients had noncompliance; 14.36% of the patients had unnecessary drug therapy; 8.13% of the patients needed additional drug therapy; 7.59% of the patients had ineffective drug; 7.59% of the patients had dosage too high; and 3.52% of the patients had dosage too low (Table 3). Inter-rater kappa statistic for DRP classification was excellent at 0.85.

When assessed by modified Schumock and Thornton criteria [8], 69.1% of DRPs leading to ED visits were preventable (Table 3). Top five underlying medical conditions most commonly associated with each category of drug-related ED visits were sought out. Hypertension was found the most frequently related to 4 of the 7 categories of DRPs that led ED visits. Diabetes mellitus was the second most common conditions related to 5 of the 7 DRP categories (Table 3).

A total of 506 drugs were implicated in the 369 visits to ED. When classified by ATC/ DDD: 23.32% were cardiovascular drugs; 16.21% were drugs used in nervous system; 14.82% were alimentary tract and metabolism drugs; 14.23% were anti-infection for systemic use; and 7.31% were musculo-skeletal system drugs. Alcohol, furosemide, aspirin, insulin and metformin were most commonly associated with DRVs to ED (Table 4).

Of the 369 patients with ED drug-related visits, 200 (54.2%) needed hospitalization and two patients (0.5%) died within 24 hours after discharged. One patient received intravenous cloxacillin and died of Stevens Johnson Syndrome. Another died from symptomatic HIV infection due to his noncompliance to drug therapy. Both deaths occurred during their hospitalizations.

Table 3. The seven drug-related problems and preventable DRPs.

Rank	Drug-related problems: Number (%)*	Preventable visits, number (%)	Top five medical conditions associated with each type of DRPs	Examples
1	Adverse drug reaction: 120 (32.52)	59 (49.17)	1. Hypertension 2. Diabetes mellitus 3. Cancer and neoplasm 4. Renal disease/ Hyperlipidemia 5. Cirrhosis	A patient developed myalgia with hyperkalemia associated with enalapril use for controlling his hypertension.
2	Noncompliance: 97(26.29)	97(100)	1. Hypertension 2. Diabetes mellitus 3. Hyperlipidemia 4. Epilepsy 5. Old CVA	A patient preferred not to take antihypertensive drugs. He visited ER due to severe headache from uncontrolled HT (BP 199/121).
3	Unnecessary drug therapy: 35 (66.03)	53 (14.36)	1. Psychosis 2. Hepatitis/ Cirrhosis 3. Hypertension 4. Diabetes mellitus 5. COPD/ Asthma	A patient was taking omeprazole together with rabeprazole for his gastric ulcer.
4	Need additional drug therapy: 30 (8.13)	13 (43.33)	1. Hypertension 2. Diabetes mellitus 3. COPD 4. Hyperlipidemia 5. Cirrhosis	A patient with history of ischemic stroke visited ER due to stroke. He was not received an aspirin for secondary prevention.
5	Ineffective drug: 28 (7.59)	19 (67.86)	1. Cancer and neoplasm 2. Hypertension 3. Diabetes mellitus 4. Gall stone 5. Chronic kidney disease	A cancer patient experienced uncontrolled pain during NSAIDs treatment.
5	Dosage too high: 28 (7.59)	28 (100)	1. Hypertension 2. Diabetes mellitus 3. Ischemic heart disease 4. Hyperlipidemia 5. Epilepsy/ Chronic kidney disease	An elderly patient with CKD developed bradycardia related to using 0.25 mg per day of digoxin for treating his CHF
7	Dosage too low: 13 (3.52)	4 (30.77)	1. Epilepsy 2. Diabetes mellitus 3. Hypertension 4. COPD	The patient's 250 mg daily dose of phenytoin is too low to provide adequate control of his seizure.
Total	369 (100)	255 (69.1)	-	-

* Percentages for frequency of case are calculated on the basis of the number of visits in each category

Table 4. Top ten drugs associated with ED visits.

Rank	Drugs	No. of visits associated with DRPs, n(%)*	Top DRP found associated to individual drugs
1	alcohol **	28 (7.59)	Unnecessary drug therapy
2	furosemide	20 (5.42)	Noncompliance
3	aspirin	19 (5.15)	Noncompliance
4	insulin	18 (4.88)	Dosage too high
5	metformin	17 (4.61)	Noncompliance
6	enalapril	16 (4.34)	Adverse drug reaction
7	pneumococcal vaccine	16 (4.34)	Need additional drug therapy
8	glipizide	15 (4.07)	Noncompliance
9	phenytoin	13 (3.52)	Noncompliance
10	atenolol	11 (2.98)	Adverse drug reaction
10	amlodipine	11 (2.98)	Noncompliance and Adverse drug reaction
	Total	184 (49.86)	

* Percentages of number of visits are calculated on the basis of 369 patients.

* * We included alcohol usage into unnecessary drug therapy category of DRPs only if it cause unwanted events, drug interactions, that interfere with outcomes of pharmacotherapy in individual patients. In our study, all 28 alcohol-related visits were associated with alcohol consumption. No DRVs related with alcohol contained medicine was found.

Discussion

In this study, about one-third of emergency department visits were drug-related. Among them, almost 70% were preventable. The prevalence of DRVs in this study was higher than in most previous reports. Two retrospective studies indicated the estimated frequency of DRVs was as low as 1.3% but as high as 10.6 %.[10, 11] Two prospective studies have shown a higher prevalence of DRPs (from 2.3% to 33.17%). [12, 13] This prevalence varies because of differences in methods of detection and variable study follow-up times. In order to get complete information of DRPs, we included also intentional overdose cases, drug-alcohol interaction, and pure alcohol intoxications. We believed that the cross-sectional design allows complete medication histories and related clinical findings to be obtained. And, by using therapeutic interventions as trigger tools for detecting DRPs, we were assured that the cases were clearly identified.

Proportion of preventable DRPs found in this study were consistent with other reports from various countries. In 2002, Patel P and Zed PJ [4] reviewed eight retrospective and four prospective literatures concerning DRPs that result in emergency department visits. They found that as many as 28% of all visits to emergency department were drug related. Of these, 70% were preventable, and as many as 24% resulted in hospital admission. In 2006, *Baena MI et al.* found that about 33% of the visits to a hospital emergency

department were caused by an undesired outcome of drug uses. More than 73% of those were considered to be preventable. [13]

In Thailand, most studies that were carried out on DRPs focused solely on adverse drug events that cause hospital admission. So far, it has been estimated that 2.43% - 23.5% of hospital admissions are drug-related. [4, 14, 15] Since, ED visit is one of the most undesired events, there was no study specifically investigated ED visit related to DRPs. The result of this study provides data on ED admissions associated with DRP cases in Thai population.

Since only DRPs are associated with chief complaints of the ED patients were determined in this study, the actual prevalence of DRPs in these patients was likely to be higher. DRP cases that were not related to their chief complaints were not included because they are less likely to be the actual cause of patients' emergency visits.

Nevertheless, our study has some limitations which include: first, times of study period (Monday to Friday between 7.30 a.m. and 3.30 p.m.) which did not allow exploration of all variations in drug-related presentations. Second, increased attention to the subject of DRVs from a pharmacist may have increased physicians' awareness of DRPs and added systemic bias. Finally, our study was limited to a single ED of a large university hospital and the prevalence of DRVs were based on the characteristics of patients presenting to our situation.

We suggest that future researches on the issue should sample patients presenting to emergency department 24 hours a day, on consecutive days and may focus on financial burden associated with DRP cases on basis of their clinical outcomes.

Conclusions

We have observed 36.9% prevalence of drug-related non-trauma ED visits in our study patients. Two-thirds of the DRP cases were associated with these ED visits were preventable (More than half of the patients who had drug-related visit needed hospitalization and less than 1% died). We recommended that the ED should be considered as a place where medication histories of patients should be systematically reviewed in order to identify and correct the route-causes of unwanted ED and hospital admissions.

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