

Pharmacist Role in Drug Related Problems on Chronic Diseases Patients

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ABSTRACT

Chronic disease patients often receive multiple medications for their treatment that can lead to the occurrence of Drug Related Problems (DRPs). There was high incidence of DRPs occurrence and most of patients had at least one therapy problem case. It can contribute to significant morbidity, mortality, and prolonged hospitalization. The objectives of the study were to identify DRPs and explore the role of pharmacist in hospitalized chronic diseases patients. A prospective study was conducted at a hospital in Indonesia. There were 94 chronic disease inpatients included. DRPs were identified using Pharmaceutical Care Network Europe (PCNE) v.6.2. Classification system. A total of 89 DRPs cases were consisting treatment effectiveness (44.9%), adverse reaction (53.9%), and other (1.2%). Most common cause of DRPs was drug selection (84.1%). Pharmacists intervention were mostly at prescriber level (46.1%) and 39.2% of intervention were solved. The study demonstrated the importance of pharmacist role in treating DRPs of chronic disease patient.

Keywords: Drug Related Problems, PCNE Classification, chronic disease, pharmacist role, adverse reaction, treatment effectiveness, drug selection.

INTRODUCTION

Hypertension and Type 2 Diabetes Mellitus (T2DM) are two kinds of chronic diseases that cause a high morbidity and mortality (Adibe et al. 2014). Both are the leading cause of cardiovascular disease, stroke, renal disease, and mortality. A study indicated that 35% of adults in South-East Asia has abnormality of blood pressure and about 1.5 million deaths every year (Alyahawi et al., 2015; Adibe et al., 2014; Nasution et al., 2016; Neupane et al., 2014). Hypertension is the third leading cause of death in Indonesia while T2DM patients in Indonesia increased from 1.1% in 2007 to 2.1% in 2013 from population of 250 people (Badan Penelitian dan Pengembangan Kesehatan, 2013).

Several study performed high prevalence of DRP in T2DM patients. This is due to multiple drugs to control their medical problem. There were 77.11% of hypertensive

patients with T2DM in Indonesia experienced DRPs (Huri & Ling 2013; Alyahawi et al., 2015; Nasution et al., 2016). DRPs represent 4th-6th leading cause of death and adverse reaction are responsible for 3-6% of hospitalizations (Al-Azzam et al., 2016; Lenander et al., 2014; Silva et al., 2015). Identification of DRPs is important to reduce morbidity, mortality, and cost of therapy. It is necessary to increase the effectivity of therapy, especially in chronic disease that can develop progressively and require treatment throughout patients life. The identification of types, patterns of DRPs and factors related to DRPs assist clinician to prevent and manage the DRPs (Huri & Wee, 2013; Huri & Ling, 2013).

The existence of pharmacists is necessary in the health care system services as their competence on a rational medication and medication errors prevention. The role of pharmacist in improving treatment outcomes and patient's quality of life in many chronic diseases has been demonstrated by many studies (Pk & Adepu, 2014; Alyahawi, et al., 2015; Hammad et al., 2011; Furqani et al., 2015). Therefore the role of pharmacist in health care system is needed and would give a high contribution to the patients clinical outcomes (Silva et al., 2015). PCNE classification has been critically appraised as the most appropriate classification that reflects outcomes and the results are reproducible. The classification tool has been validated and was used in many other published studies to assess DRPs occurrence. Hierarchical design is the advantages of this instrument. There are separated codes for problem, cause, intervention and outcome domains (Huri & Wee, 2013; Ruths et al., 2007; Chan et al., 2012; Eichenberger et al., 2011; Silva et al., 2015). The objectives of the study were to identify DRPs and explore the role of pharmacist in hospitalized chronic diseases patients.

EXPERIMENTAL

This study was an observational study which done prospectively in Prof. Dr. Margono Soekardjo public hospital, one of tertiary care hospital in Indonesia. A total of 94 chronic disease inpatients were included in this study. Inclusion criteria were hospitalized patients diagnosed Type 2 Diabetes Mellitus (T2DM), hypertension and T2DM patients with hypertension, who received at least one antidiabetic drug or antihypertensive. Patient's age would be 18 years old or above and able to provide written informed

consent. Patients will be excluded from the study if they were pregnant and out of the hospital before meeting pharmacists.

DRPs were identified using Pharmaceutical Care Network Europe (PCNE) v.6.2. a classification system which involved the participation of both doctors and pharmacists to assess the role of pharmacist and their impact on DRPs identification. DRPs of each patients were assessed by author and discussed with the clinical pharmacist. The 4 primary domains for problems and 8 primary domains for causes were identified from patient's medical records with reference to standard guidelines and patients interviewing. The interventions were suggested by clinical pharmacist and the care plans were discussed with the physicians.

RESULTS AND DISCUSSION

A total of 94 patients consisted of Type 2 Diabetes Mellitus (T2DM), hypertension, and T2DM patients with hypertension. The data collected by observed the patients' medical record and interviewing them prospectively.

Table 1 demonstrates the demographic characteristic of subjects. There were 39.4% males and 60.6% females patients. The minimum and maximum ages of patients were 25 and 85 years old. Most common ages were between 45 to 64 years old.

Recent reports from developing countries have found that hypertension and T2DM more common in women. Similar studies shown that females were common in T2DM (81.1%) and hypertension (63%) (Marfo et al., 2014; Adem et al., 2014). Women have more cardiovascular risk factor than men, including hypertension, obesity, elevated total cholesterol, and low HDL. On average, women had a higher systolic blood pressure (Ong et al., 2008). There was increasing evidence that gender differences are important in T2DM. The evidence showed greater cardio metabolic risk in women, in terms of glucose and lipid abnormalities compared with males. Cardio metabolic similarities were described among women with androgen excess and men with androgen deficiency. Higher levels of androgens lead to increased body weight and visceral fat in women. The release of free fatty acids that can lead to excessive oxidative stress is a result of insulin resistance and relate to incident diabetes (Ardiani et al., 2015).

Aging is a risk factor for hypertension. The incidence of cardiovascular diseases in women increased with age and became higher than that in men after menopause (Ong et al., 2008). Consistent with this study, women aged 51-55 years old had a risk 1.4 times higher, while the age of 56-60 years old had 2 times higher risk and those aged 61 years and older had 2.7 higher risk of developing hypertension (Ardiani et al., 2015). A study in Bali, Indonesia showed that increasing age had a tendency of increasing T2DM frequency due to metabolic syndrome (Suastika & Dwipayana, 2011).

Table 1. Demographic characteristic

Characteristic	Number of Patients	Percentage (%)
GENDER		
Male	37	39.4
Female	57	60.6
Total	94	100
AGE		
25 – 44	10	10.7
45 – 64	66	70.2
≥ 65	18	19.1
Total	94	100
ANTIHYPERTENSION PRESCRIBED*		
Amlodipine	42	31.2
Furosemide	41	30.4
Captopril	11	8.2
Spironolakton	5	3.7
Irbesartan	19	14.1
Clonidin	5	3.7
Valsartan	8	5.9
Bisoprolol	4	2.9
Total	135	100
ANTIDIABETES PRESCRIBED*		
Insulin	48	40
Glimepiride	6	10
Glikuidon	1	1.7
Metformin	4	6.6
Pioglitazone	1	1.7
Total	60	100

There were 135 antihypertensive agent prescribed. Amlodipine (31.2%) were the most common antihypertensive prescribed. Antihypertensive agent can be used as

monotherapy or combination therapy. A total of 60 antidiabetic agent were prescribed. The percentages of insulin prescribed as antidiabetic agent were 40%, consisted of rapid acting insulin, combination insulin and long acting insulin. T2DM can be treated by monotherapy or combination therapy within dual insulin therapy or insulin and oral antidiabetic.

Amlodipine is a long acting, third generation dihydropyridine Calcium Channel Blocker (CCB). Amlodipine is an excellent first-line for hypertension. The efficacy of amlodipine as monotherapy in hypertension has proven. However less than 50% of stage I or stage II hypertensive patients were controlled adequately with monotherapy and initial treatment for hypertension require additional antihypertension. Combination therapy using different mechanism of antihypertension can lead to more effective blood pressure lowering. Using multiple agents can reduce side effect. Evidence from data trial shows that CCB with ACEI or ARB provide the best long-term outcomes (Fares et al., 2016; Medications & Changes, 2014). Recommendation of antihypertension should consider its comorbidities. According to the evidence, the first line therapy of hypertension associated with T2DM are ACEI or ARB or CCB (Medications & Changes 2014; White et al., 2010).

Insulin therapy is recommended for patients with T2DM and an initial A1C level greater than 9% or if T2DM is uncontrolled by using oral antidiabetics. Augmentation therapy include basal or bolus insulin. Comparative study between premixed and bolus insulin showed that more common weight gain in bolus insulin group (Petznick, 2011). The result of this study is in accordance with the recommendation therapy for hospitalized T2DM patients. UK Prospective Diabetes Study has publish evidence-based outcome in randomized addition of insulin or sulfonylurea treatment to lifestyle therapy after diagnosis of T2DM. Both of them gave similar degree of metabolic control long-term and reduce microvascular complications significantly, but failed to reduce macrovascular endpoints. They were burdened by significant weight gain and the risk of hypoglycemia (Standl & Schnell 2008).

Drug Related Problems (DRPs) identification was documented using PCNE version 6.2. This classification tool using hierarchical design, are separated into 4 basic classifications: problems, causes, interventions and outcomes.

A total of 89 problems occurred at treatment effectiveness, adverse reaction and others domains. The most frequently problems occurred was non allergic adverse event (53.9%). There were 89 causes associated with DRPs were identified among 10 categories of PCNE classification. The three leading causes were inappropriate combination of drugs (51.6%), new indication for drug treatment presented (26.7%) and drug under-used (8.9%).

DRPs identified were discussed with the clinical pharmacist and also concerned physician on the same day. Necessary intervention was made to 86.5% DRPs. The intervention implemented at prescriber level (45.9%), at patient level (4.6%), and at drug level (36%). Most of frequently outcome of pharmacist intervention were solved (70.8%). The interventions could be done by a clinical pharmacist or in collaboration with physicians. The outcomes were closely related to the effects of pharmacist interventions on DRPs event.

Drug Related Problems (DRPs) defined as any undesirable event experienced by a patients involving drug therapy that actually or potentially interferes with desired health outcome (Ruths et al., 2007). In the similar study, there were only 25% adverse reactions reported.

Table 2. Problems

Problems	Code	Frequency of DRPs	Percentage
Treatment Effectiveness			
Effect of drug treatment not optimal	P 1.2	12	13.5
Wrong effect of drug treatment	P 1.3	3	3.4
Untreated indication	P 1.4	25	28
Adverse reactions			
Adverse drug event (non-allergic)	P 2.1	48	53.9
Others			
Patient dissatisfied with therapy despite optimal clinical and economic treatment outcomes	P 4.1	1	1.2

In the case of hypoglycemia during Oral Antidiabetic Drug (OAD) or insulin usage, Amlodipine as Calcium channel Blocker, diuretics and ACEI were reported had cause

increased heart rate. Electrolytes imbalance were reported as adverse reactions of ACEI (Huri & Wee 2013).

Adverse drug reaction (ADR) is undesirable effect of a medication that occurs during usual clinical use. Adverse drug reactions were originally classified into two subtypes. Type A ADRs are dose-dependent and predictable. They are augmentations of known pharmacologic effects of the drug. Type B ADRs are uncommon and unpredictable, depending on the known pharmacology of the drug; they are independent of dose and affect a small population, suggesting that individual patient host factors are important. ADRs is a cause of patients low-adherence and consequently precipitate additional ADRs. It should be quickly identified and managed to limit their effects on the patients (Schartz & Weber 2015).

Table 3. Causes

Causes	Code	Frequency of DRPs	Percentage
Drug selection			
Inappropriate drug	C 1.1	3	3.4
Inappropriate combination of drugs, or drugs and food	C 1.3	46	51.6
Too many drugs prescribed for indication	C 1.6	1	1.2
Synergistic/preventive drug required and not given	C 1.8	1	1.2
New indication for drug treatment presented	C 1.9	24	26.7
Dose selection			
Dosage regimen not frequent enough	C 3.3	2	2.3
Drug use process			
Inappropriate timing of administration and/or dosing intervals	C 5.1	1	1.2
Drug underused/under-administered (deliberately)	C 5.2	8	8.9
Drug overused/over-administered (deliberately)	C 5.3	1	1.2
Other			
Other cause	C 8.1	2	2.3

There were many causes of DRPs. The most common was inappropriate combination of

drugs. It can lead to ADRs. Imbalance potassium serum occurred in the combination of irbesartan and furosemid. Furosemid as a diuretic are drugs that primary action is to reduce the reabsorption of sodium, chloride and water from the filtrate due to a direct action at different segment site of the renal tubular system. The action of loop diuretic indirectly increases potassium excretion. Combination of loop diuretics with ARB indirectly reduce plasmarenin activity, aldosterone secretion and decreases in serum potassium (Tamargo et al., 2014; Gunduz et al., 2004).

Table 4. Interventions

Interventions	Code	Frequency of DRPs	Percentage
No intervention	I 0.0	12	13.5
At prescriber level			
Intervention proposed, approved by prescriber	I 1.3	13	14.5
Intervention proposed, not approved by prescriber	I 1.4	28	31.4
At patient/carer level			
Patient (medication) counseling	I 2.1	2	2.3
Spoken to family member/caregiver	I 2.4	2	2.3
At drug level			
Drug changed to...	I 3.1	1	1.2
Dosage changed to ...	I 3.2	2	2.3
Drug stopped	I 3.5	3	3.3
New drug started	I 3.6	26	29.2

Table 5. Outcomes

Outcome of intervention	Code	Frequency of DRPs	Percentage
Not known			
Outcome intervention not known	O 0.0	26	29.2
Solved			
Problem totally solved	O 1.0	35	39.2
Partially solved			
Problem partially solved	O 2.0	1	1.2

Not solved

Problem not solved, lack of cooperation of patient	O 3.1	1	1.2
Problem not solved, lack of cooperation	O 3.2	26	29.2

Pharmacist role at prescriber level including proposed suggestion to the physician as prescriber. Unfortunately, not all of the pharmacist suggestion approved by prescriber because of administrative issues. A total of 13 from 41 suggestion approved. There were rapid acting insulin recommendation for untreated hyperglycemia and untreated hypoalbumin not approved.

This research showed that the role of clinical pharmacist in DRPs event strongly important. As much as 86.5% pharmacist intervention given to 89 problem and 81.8% of them were solved.

CONCLUSIONS

The study demonstrated the importance of pharmacist role in treating DRPs of chronic disease patients. Clinical pharmacist plays an important role on DRPs identification.

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