

Pharmacists Intervention Reduced Drug-Related Problems in the Treatment of Patients with Type 2 Diabetes Mellitus

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Abstract

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BACKGROUND: Type 2 Diabetes Mellitus (T2DM) remains as a global public health problem, including Indonesia due to its continuous increasing prevalence.

AIM: To analyze the impact of pharmacist intervention on drug-related problems (DRPs) occurred in the management of patients with T2DM admitted to Tebing Tinggi Hospital (TTH), Indonesia, period March through August 2018.

METHODS: This six-month retrospective prospective cohort study evaluated the impact of pharmacist intervention on the occurrence of DRPs in the management of patients with T2DM (n = 45) insured by Social Security Organizing Body in TTH, North Sumatera, Indonesia. The inclusion criteria were T2DM patients with age ≥ 18 years and under treatment of antidiabetic drugs. A questionnaire was used to assess the characteristics of the patients and antidiabetic drugs provided. The incidence of DRPs in groups with usual care for the previous three-month and with pharmacist interventions for the next three-month admissions were analyzed using Pharmaceutical Care Network Europe (PCNE) DRP classification system version 8.01 that consists of 3 primary domains for problems, 8 primary domains for causes, and 5 primary domains (PCNE, 2017) and trustable literatures. The obtained data were analyzed using descriptive statistics and paired t test in the program of Statistical Package for the Social Sciences version 19 ($p < 0.05$ was considered significant).

RESULTS: Most (66.7%) of the patients were female. Their mean age was 61.96 ± 6.45 (years). The three most widely provided drugs were metformin, glimepirid, and gliclazide. Total incidence of DRPs in groups with: usual care, 128; intervention, 39. There was a significant difference between the incidence of DRPs in groups with usual care and intervention, $p \leq 0.001$.

CONCLUSION: Pharmacist intervention reduced the incidence of DRPs in the management of T2DM patients.

Introduction

Diabetes mellitus (DM) remains as a serious global public health threat that is growing rapidly in developed as well as developing countries, including Indonesia. Based on the World Health Organization (WHO) finding, the global prevalence of diabetes has increased from 4.7% in 1980 to 8.5% in 2014. A fact indicated that 1.5 million deaths occurred in 2012 due to diabetes. Globally, morbidity of DM patients was 422 million adults in 2014 compared to 108 million in 1980 [1]. In Indonesia itself the morbidity of DM patients was 8.4 million in the year 2000 and was predicted to increase to 21.3 millions in 2030 [2].

Type 2 diabetes mellitus is a metabolic disorder due to insufficiency of insulin function marked

by high blood glucose levels and followed by carbohydrates, lipids and proteins metabolism interference due to failure or insufficient insulin production by the beta cells of the pancreatic islets [1], [3]. Lifestyle of the Indonesian population has been affected by the advancement of economic development. This condition has reduced their physical activities causing changes in patterns of diseases [4]. In addition, socioeconomic levels, including education, employment, and marital status also promote the increasing prevalence of the disease [2].

There are numerous factors associated with the successfulness of the treatment of diabetes, including sufficient health services provided by healthcare providers and the adherence of the patients to their medications [5]. Patients with T2DM

who do not adhere to their medications will in turn result in insufficient treatment, finally cause complications, including nephropathy which the risk for kidney disease, retinopathy with potential blindness, neuropathy causing nerve tissue damage, gastrointestinal symptoms, amputation, and impotency [2]. These conditions require complex management and multiple drug therapies which in turn tend to result in DRPs causing not only sub optimal therapeutic outcomes but also increase costs. These issues are the global challenges of the health care systems [6], [7]. The occurrence of DRPs in the management of diseases as well as T2DM may vary from one country to another.

Management of T2DM should always be monitored and studied to avoid negative clinical outcomes. Thus, active participation of pharmacists to identify, to prevent, and to resolve the incidence of DRPs in the management of T2DM is crucial to optimize outcomes. A systematic review conducted on 36 pharmacist intervention studies involving 5,761 participants indicated greater varied outcomes in the intervention groups compared to the groups without the involvement of pharmacists [8]. Another systematic review on 59 pharmacy-led intervention studies on the management of T2DM also indicated the significant enhancement of the patients' outcomes compared with usual care groups [9]. In contrast, a systematic review of randomized controlled trials and pre-post-test studies in the management of T2DM undertaken in South Asia revealed that there was only little improvement of the disease outcome in intervention groups compared with usual care [10]. There was a limited intervention study on DRPs in the management of T2DM patients undertaken in Indonesian health care facilities.

In light of these issues, the present study aimed to analyze the impact of pharmacy intervention in the management of T2DM patients admitted to TTH, North Sumatera, Indonesia.

Material and Methods

This six-month prospective cohort study was conducted to evaluate the DRPs in the management of outpatients with T2DM (n = 45) insured by Social Security Organizing Body in TTH, North Sumatera, Indonesia period March through August 2018. Before conducting this study, ethical clearance was obtained from the Health Research Ethical Committee of North Sumatera, School of Medicine, University of Sumatera Utara, Medan, Indonesia. The inclusion criteria were patients diagnosed with T2DM, age \geq 18 years, and under treatment of antidiabetic drugs.

The researchers explained the study to each of the patients and set up the schedule for the data

assessment. A self-designed questionnaire was used to assess the characteristics of the patients and antidiabetic drugs provided. The patients' characteristics were descriptively analyzed. The PCNE version 8.01 instrument [11] and trustable literatures were used to analyze the incidence of DRPs in the management of the T2DM patients in groups with usual care for the previous three-month and pharmacist intervention for the next three-month patients' admissions. The PCNE DRP classification system applied in this study is listed in Table 1. The significance of intervention was analyzed applying paired t test. All analyses were performed using Statistical Package for the Social Sciences (SPSS, version 19, Chicago, IL, USA) ($p < 0.05$ was considered significant).

Table 1: The PCNE DRP classification system version 8.01

	Code	Primary domains
Problems	P1	There is a problem with the effect of the pharmacotherapy
	P2	Patient suffers from adverse drug event
	P3	Others
Causes	C1	Inappropriate drug selection
	C2	Selection of inappropriate dosage form
	C3	Inappropriate dosage selection
	C4	Inappropriate duration of treatment
	C5	The cause of DRP is related to prescribing and dispensing process
	C6	The cause of DRP is related to the way patient gets the drug
	C7	The cause of DRP is related to the patient and his behavior.
	C8	Other
Planned Intervention	I0	No intervention
	I1	At prescriber level
	I2	At patient level
	I3	At drug level
Acceptance	A1	Intervention accepted
	A2	Intervention not accepted
	A3	Other
Status of DRP	O0	Problem unknown
	O1	Problem solved
	O3	Problem not solved

Results

Characteristics of the T2DM patients

Of the 130-target population, there were only 45 T2DM patients fulfilled the inclusion criteria. Thus, these patients were included into this study. Characteristics of the T2DM patients according to gender, age, and education are demonstrated in Table 2. In the present study, there were more female (67%) admitted to the hospital compared to male (33%) during the study period. Most (56%) of the patients were in the age group of 60 years or above. Only 44% of the patients were in the age of younger than 60 years. Overall, the mean age of the patients was 61.96 with a standard deviation of 6.45 years.

In terms of education, it was found, as shown in Table 2, that 17.8% and 15.6% of them graduated from primary school and Junior High School, respectively. As much as 28.9% of the patients graduated from senior high schools. It was found that more than one-third (37.8%) of the patients graduated from universities.

Table 2: Characteristics of the T2DM patients (n = 45)

Variable	Percentage (%)
Gender:	
Male	33
Female	67
Age (years):	
< 60	44
> 60	56
Education:	
Primary school	17.8
Junior High School	15.5
Senior High School	28.9
University	37.8

Utilization of antidiabetic drugs

The pattern of antidiabetic drugs provided to the T2DM patients in groups before and after education in decreasing order is listed in Table 3. During the six-month period of patients' admission, as shown in Table 3, it was obtained that the four most widely prescribed antidiabetic drugs in both groups were metformin 500 mg, glimepiride 2 mg, gliclazide 80 mg, and glimepiride 4 mg.

Table 3: Pattern of antidiabetic drugs provided to the T2DM patients (n = 45)

	Usual care		Intervention group	
	Number of units	Costs (in Rp)	Number of units	Costs (in Rp)
Metformin 500 mg	1444	414.428	1672	479.864
Glimepiride 2 mg	868	261.268	970	291.970
Gliclazide 80mg	320	93.760	430	125.990
Glimepiride 4 mg	130	50.050	272	104.270
Acarbose 50 mg	104	72.280	0	0
Glimepiride 3 mg	80	28.320	130	46.020
Glimepiride 1 mg	50	12.850	90	23.130
Apidra	46	4,802.354	37	3,862.763
Lantus	14	1,326.000	20	2,040.000
Humalog Mix	0	0	2	264.000

The two most expensive antidiabetic drugs provided to the T2DM patients were apidra and lantus. In fact these two drugs were least frequently prescribed to the patients.

Drug related problems

The incidence of DRPs in the management of T2DM patients is shown in Table 4. It was found that 44 incidences were related to diet and physical inactivity. The second highest incidence was that 39 patients did not reach the target of blood glucose level (≤ 200 mg/dL) in the group with usual care indicating the occurrence of ineffective treatment. However, in the intervention group, as indicated in Table 4, the occurrence of ineffective treatment measured from blood glucose level decreased to only 20 (44%) of the patients.

This study also revealed 6 cases with wrong dose timing instructions occurred in the group with usual care. Four patients took metformin before meals supposed to be provided after or at mealtime. One patient took acarbose before meal, while this drug has to be taken at meal time to reduce the absorption of simple carbohydrate in the GI tract. This study proved based on interview, one patient took glimepiride after meal, while this drug should be taken before meal.

Table 4: Incidence of DRPs in the management of T2DM patients (n = 45)

Primary domain	Code	Problem	Usual care	Intervention group
Treatment effectiveness	P1.2	Effect of drug treatment not optimal (number of cases)	39	20
	C3.5	Dose timing instructions wrong, unclear or missing (number of cases)	6	0
	C5.2	Necessary information not provided (number of cases)	1	0
Dose selection	C7.6	Patients stored drug inappropriately (number of cases)	1	0
	C7.7	Inappropriate timing or dosing interval (number of cases)	37	11
	C8.2	Other: Diet and physical activity (number of cases)	44	8
	Total		128	39

Another DRP identified in the group with usual care was one patient did not receive the necessary information from the health care provider regarding the storage of apidra, consequently the patient stored this medication inappropriately. This drug must be stored at temperature between 2-8°C to maintain its stability [12]. The later 2 cases were not obtained in the group with intervention. Additionally, as many as 37 patients took their medications at inappropriate dosing intervals in the group with usual care. This DRP category reduced to 11 incidences in the group with intervention. This study also proved that 44 out of 45 patients did not practice healthy diet and physical activity in the group with usual care, while this DRP has been decreased to 8 cases in the group with intervention.

Overall, the number of incidences of DRPs in the group with usual care were 128 has been reduced to 39 in the group with intervention. The incidences of DRPs in the management of T2DM with pharmacist intervention reduced significantly compared those with usual care, $p \leq 0.001$.

Discussion

The present study found that 66.7% of the patients were female. This finding supported similar studies undertaken in Indonesia and USA [13], [14], [15]. It was indicated that 56% of the T2DM patients were at the age of 60 years or above. Aging decreases the pancreatic β cell sensitivity to glucose and delay the mediation of glucose uptake by insulin into the cells [16]. The majority of the T2DM patients (62.2%) graduated only from senior high school and lower. This limited education may have an impact on a failure to understand the importance of adherence to prescribed medications [10].

With regard to antidiabetic utilization, this study indicated that metformin was the most frequently prescribed drug to the T2DM patients followed by glimepiride and gliclazide. Patterns of antidiabetic utilization vary widely depend on the medical condition of the patients, severity of the disease, and its complications [5].

The occurrence of DRPs can result in failure to achieve the targeted blood glucose level in patients T2DM and increase in resource consumption [7]. Thus, identification of DRPs is important to improve effectiveness and efficiency in the management of T2DM. The present study revealed that the most frequently occurred problems in the treatment of T2DM with usual care were unhealthy diet and insufficient physical activity followed by treatment effectiveness and inappropriate drug dosing interval. The latter problem is related to the irregularity of patients' visit to this secondary health center. The patients did not immediately visit the health centers when they ran out of their antidiabetic medications, missed doses for several days, which in turn decreased the treatment outcomes and developed complications. In the intervention group, these problems were significantly reduced. A study in Scandinavia proved that counseling through video conference conducted on T2DM patients had a positive attitude towards increasing physical activity [17].

This study indicated that pharmacist education significantly decreased the incidence of DRPs in management of T2DM patients. This result is consistent with the previous pharmacist intervention studies conducted in different countries. In 2016, Pousinho et al., conducted a systematic review on 36 studies in the management of T2DM consisted of 5,761 participants with and without pharmacist interventions. They proved that greater outcomes were obtained in the intervention groups compared to the groups with usual care [8]. More recent systematic review conducted by Presley et al., on 59 pharmacist intervention studies in the management of T2DM patients also indicated the significant increase in the patients' outcomes compared with usual care groups [9]. However, Bhurji et al., revealed, in their systematic review of randomized controlled trials and pre-post-test studies in the management of T2DM undertaken in South Asia, that there was only little improvement of the disease outcome in intervention groups compared with pre-test or usual care groups [10].

In conclusions, involvement of pharmacists in the management of T2DM patients could decrease significantly the incidence of DRPs. These findings should be highlighted and considered by the policy makers to improve the management of T2DM patients.

Study limitation

This study is limited by the small number of T2DM patients involved in this study.

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