

Identification of Drug Related Problems (DRPs) Based on Drug and Dosage Selection in Type 2 Diabetes Mellitus Patients at Karsa Husada Batu Hospital

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Abstract

Pharmacological therapy for type 2 diabetes mellitus involves more than one type of drug, this increases the potential for drug-related problems (DRPs) in terms of selecting the type and dose of the drug. This study aimed to determine the treatment profile and identify the occurrence of DRPs based on drug selection and dosage in patients with type 2 diabetes mellitus at Karsa Husada Batu Hospital. This descriptive observational study was conducted in October 2022 using medical records. The study sample was obtained by total sampling using 36 medical records of inpatients with type 2 diabetes mellitus without complications. Uncomplicated patients were chosen to optimize the assessment of diabetes treatment without concordance drug use for concomitant disease. Identification of DRPs based on The Pharmaceutical Care Network Europe (PCNE) V.9.1 guidelines. The results showed that glimepiride (6.45%), insulin (16.13%), a combination of metformin and glimepiride (3.23%), a combination of metformin and insulin (3.23%), and basal-bolus insulin (67.74%) were antidiabetic drugs used by patients. Based on the drug selection, 17 patients were identified as having DRPs where the use of drugs without indication (38.89%) was the most common case. DRPs based on dose selection were found in 6 patients with 13.89% of cases being too high a drug dose. Based on this study, it can be concluded that there are cases of DRPs based on drug selection and dosage in patients with type 2 diabetes mellitus so improved pharmaceutical services are needed to address this to improve patient safety.

Keywords: Dose Selection, Drug Associated Problems (DRPs), Drug Selection, Type 2 Diabetes Mellitus

Introduction

Type 2 diabetes mellitus is a metabolic disorder characterized by blood sugar levels too high that occurs due to the body's inability to produce or use insulin effectively or both¹. The causes of type 2 diabetes are not completely understood, but there is a strong link with overweight, and obesity, increasing age, ethnicity, and family history². Type 2 diabetes mellitus accounts for over 90% of all occurrences of diabetes worldwide.² The prevalence of type 2 diabetes mellitus in Indonesia will increase by 154% from 2000 prevalence to 2030¹. Type 2 diabetes mellitus is the sixth highest cause of death in Indonesia³.

Treatment of type 2 diabetes mellitus uses a variety and different mechanisms of action of drugs to maintain glycemic control⁴. Patients with type 2 diabetes mellitus also receive more medication due to the presence of other comorbid conditions or diagnoses⁵. Uncomplicated type 2 diabetes mellitus is a condition where blood sugar levels are too high because insulin cannot work effectively, but has not caused kidney, heart, eye, or nerve damage, so there are no other accompanying diseases. The prevalence of uncomplicated type 2 DM patients is still relatively high. Research conducted in Yogyakarta which states that the number of uncomplicated type 2 DM patients (63.5%) is higher than patients with complications (36.5%)⁶. Study in Jakarta also mentioned that of all type 2 diabetes mellitus patients evaluated, 90% were patients without complications and 10% with complications⁷. Treatment of type 2 diabetes mellitus generally requires a long time because it is a chronic disease that requires long-term treatment. The use of drugs over a long time causes an increased risk of side effects⁸. Therefore, patients with type 2 diabetes mellitus who receive more than one drug and for a long time are at high risk of experiencing drug-related problems (DRPs)⁹. The prevalence of DRPs

in diabetic patients can be found in several studies. A study conducted in Gadjah Mada University Academic Hospital states that out of 50 patients, 36 patients experienced DRPs and non-DRPs as many as 14 patients¹⁰. Research in India also mentioned that out of 110 patients, 91 patients experienced DRPs¹¹. DRPs also relate to patients' quality of life because it can reduce the quality of life of patients. DRPs can result in ongoing disease symptoms or new symptoms affecting the patient's quality of life¹². In addition, improper use of drugs may lead to harmful side effects and adverse events¹³.

DRPs may be categorized into 9 categories according to the PCNE Version 9.1. These areas include medication selection, dose selection, medication form, treatment duration, dispensing, drug use process, patient-related, patient transfer-related, and others¹⁴. The identification of DRPs in this study is based on drug selection and dosage because if using other domains such as treatment duration, it will take a long time because diabetes mellitus is a chronic disease that needs to take drugs throughout its life. DRPs in type 2 diabetes mellitus still occur frequently. The primary factors contributing to DRPs in patients with diabetes mellitus were mostly associated with medication selection (46%) and dosage selection (54%) identified based on PCNE V.05¹⁵. It is in line with the study in 2021, which stated drug and dose selection also the main cause of DRPs in type 2 diabetes mellitus patients identified based on PCNE V.8.03¹⁶. This study identified DRPs based on PCNE V9.1, which is the latest version of PCNE that has more codes in each domain. These DRPs could prevent patients from getting maximal therapeutic effects and increase the burden of health service costs.

Karsa Husada Batu Hospital is the only general government hospital that became the

referral health facility in the Batu, East Java area. Therefore, health services at this hospital must consider a rational therapy regarding drug and dose selection, so that patients can get effective treatment. However, In Batu City, diabetes mellitus is ranked fifth out of ten types of diseases with the highest number of cases in Batu City, namely 329 cases in 2018. In 2019, the number of diabetes mellitus cases increased to 1,874 cases¹⁷. Research related to the identification of DRPs in diabetes patients at Karsa Husada Batu General Hospital has never been published. Thus, it is essential to provide the assessment of these types of DRP to improve the rationality of the treatment and health quality of the patients. Therefore this study aims to determine the treatment profile and identify DRPs based on drug selection and dosage type 2 diabetes mellitus patients without complications at Karsa Husada Batu General Hospital.

Method

The research was conducted in October 2022 in Karsa Husada Batu Hospital Medical Record's room with the ethics number 072/2737/102.13/2022. This type of research is descriptive observational with a cross-sectional approach in the form of observations on the medical records of patients with uncomplicated type 2 diabetes mellitus who hospitalization at RSU Karsa Husada. Uncomplicated type 2 diabetes mellitus is a condition where blood sugar levels are too high because insulin cannot work effectively, but has not caused kidney, heart, eye, or nerve damage, so there are no other accompanying diseases. The population in this study were all medical record data of patients with type 2 diabetes mellitus without complications hospitalized at RSU Karsa Husada Batu in 2018-2021. A total sampling technique and was used to obtain 36 samples. Data collection was carried out from October 13-31, 2022.

The variables used were treatment profiles and identification of DRPs based on drug selection and dosage in patients with uncomplicated type 2 diabetes mellitus. The analysis of the medication profile was seen from the medical record data of pharmacological therapy prescribed to patients with uncomplicated type 2 diabetes mellitus. Drug characteristics included drug name, frequency, and dosage. Data were collected and presented in the form of a percentage table. The Drug Related Problems (DRPs) in terms of drug selection and dosage were assessed based on the guidelines from the American Diabetes Association in 2022 and the Indonesian Endocrinology Society (PERKENI) in 2021. Documentation of the Drug Related Problems (DRPs) incidence based on Pharmaceutical Care Network Europe (PCNE) V9.1. Data were processed using Microsoft Excel 2019 and data analysis was presented in tabular form, then described and percentages. The advantages of the PCNE classification compared to other classifications of Drug Related Problems (DRPs) are that PCNE is structured in detail and has coded subsections; appropriate duplication of a therapeutic group or active ingredient was a problem that was not found in this study. each category is clearly defined and has been validated through various studies in pharmacies and hospitals¹⁸.

Result and Discussion

Demographic of patients with type 2 diabetes mellitus without complications

Uncomplicated type 2 diabetes mellitus was identified in 36 people. Comparing men and women, we find that 61.11% of women and 38% of men have simple type 2 diabetes mellitus. The characteristics of patients with type 2 diabetes mellitus can be seen in Table 1. Among patients aged 55-65 years, the highest proportion (55.56%) had type 2 diabetes mellitus without any problems. The

prevalence of patients with uncomplicated type 2 diabetes mellitus according to age may be shown in Table 1.

In our study, diabetic type 2 occurred most in women. This is in line with the study at RSUP dr. M. Djamil Padang in 2022, type 2 diabetes mellitus was more common in women than in men, namely in 16 female patients (70%) and seven male patients (30%)¹⁹. Differences in adult male and female body composition and sex hormones are the reasons why type 2 diabetes mellitus is more common in women. Estrogen and progesterone levels in women are greater than in men. When menopause occurs, levels of estrogen and progesterone drop. A decrease in hormone levels causes the body to store fat, mainly around the middle. This causes free fatty acid release to spike, which in turn causes insulin resistance by interfering with insulin's ability to work properly within fat cells²⁰.

The finding shows patients above 56 years old are the larger class of patients with type 2 diabetes mellitus. The elderly are most susceptible to getting diabetes mellitus. Advancing age leads to alterations in carbohydrate metabolism and insulin secretion in the pancreas, resulting in the suppression of glucose release into the body. This leads to insulin resistance, which in turn produces fluctuations in glucose levels in the body, ultimately resulting in the development of diabetes mellitus²¹.

Antidiabetic drug use profile of type 2 diabetes mellitus patients without complications

According to the statistics provided, the most often used medication for diabetes treatment is a combination of basal-bolus insulin, accounting for 67.74% of usage. The other antidiabetic drugs are glimepiride (6.45%), insulin (16.13%), a combination of metformin

and glimepiride (3.23%), and a combination of metformin and insulin (3.23%). The antidiabetic drug use profile of type 2 diabetes mellitus patients without complications can be seen in Table 2.

Basal-bolus insulin is the most used medicine for the patients of the research. Basal-bolus treatment decreases the mean daily blood glucose levels²². Patients who were given basal-bolus treatment were more successful than those who were given prandial insulin therapy in keeping their blood glucose levels within the target range over the whole duration of their hospital stay. Hospitalized patients with type 2 diabetes mellitus who used a basal-bolus insulin regimen successfully controlled their hyperglycemia without an increased risk of hypoglycemia²³.

Identification of Drug Related Problems (DRPs) based on drug selection

Out of the 36 patients, 17 patients (47.22%) were found to have DRPs based on drug selection (Figure 1). Of these 17 patients, there were 42 cases of DRPs based on drug selection as shown in Table 3. The main reason for Drug-Related Problems in the area was patients did not get enough drug treatment although the right medicines were available. Meanwhile, non-DRPs occurred more in the sample, which was 52.78%. Inappropriate duplication of a therapeutic group or active ingredient was a problem thattable not found in this study.

In as many as 17 of 36 patients, DRPs are caused by inappropriate drug selection. Patients did not get sufficient drug treatment despite existing indications. The findings of this study in 2017, also showed that the greatest occurrence of drug selection DRPs was 25.3% due to the absence of a prescription medicine despite a clear indication²⁴. Other research in 2020, also revealed 10 instances

(6.41%) of individuals with diabetes mellitus who did not get treatment, despite obvious signs appearing²⁵.

The primary cause of DRPs related to medication selection is the failure to provide appropriate or full pharmacological therapy despite the presence of clear indications. Noncompliance or inadequate drug treatment despite existing indications is a medical problem that necessitates the commencement of pharmacological therapy²⁶.

The absence of drug administration despite clear indications results in indications or patient complaints not going away and can aggravate the disease, require longer treatment time result in cost overruns, therapeutic goals not being achieved, reduce quality of life, and increased mortality²⁷. Poor glycemic control in patients with diabetes mellitus can be caused by a lack of medication, thus the risk of complications microvascular and macrovascular increases²⁸.

Inappropriate drug according to guidelines is an incidence where a patient has an indication but receives the wrong or inappropriate medication. Inappropriate drug use is defined as drugs that have greater risks than benefits²⁹. In this study, was found 13 cases of DRPs because of inappropriate drugs according to guidelines. The consequences of treatment that is given not according to the guidelines are causing drugs to be ineffective so that they do not achieve the desired therapeutic goals, increasing the cost of treatment, and causing unwanted side effects³⁰.

No indication for a drug is when a patient takes a drug without a clear medical indication. In this study, was found 10 cases of DRPs because of no indication for the drug. The consequences of giving therapy without indication in addition to financially harming patients can

also harm patients with the possibility of unwanted effects. The more drugs that enter the body cause drug complexation in the body, increasing the risk of drug interactions, and unwanted effects, increasing the therapy cost, and can lead to other adverse effects³¹.

An improper amalgamation of pharmaceuticals, pharmaceuticals and botanical remedies, or pharmaceuticals and nutritional supplements is an interaction occurrence that might impact patient treatment. medicine interactions occur when the presence of one medicine changes the impact of another drug³². This study found 2 cases of DRPs because of Inappropriate combinations of drugs. Inappropriate drug combinations often result in an increased risk of drug-related problems.

Inappropriate duplication of a therapeutic group or active ingredient is defined as two prescribed drugs of the same drug class³³. In this study, there was no use of inappropriate duplication of therapeutic groups. Cases of duplication of drug use should be avoided because they can reduce the effectiveness of treatment, possibly increase side effects, cause toxicity reactions, and increase treatment costs³⁴.

The prescription of many medications or active components for a given reason is considered excessive and goes beyond what is clinically required³⁵. Only one instance was discovered in this investigation where DRPs occurred due to the excessive prescription of several medications or active components for a specific reason. Administering excessive medication for a single condition leads to escalated patient care expenses and heightens the likelihood of adverse effects or drug interactions³⁶.

Identification of Drug Related Problems (DRPs) based on dose selection

As many as 6 of 36 patients (16.67%) were found to have DRPs due to dosage selection, as seen in Figure 2. In the area of dose selection, there was the administration of medicine at a very high dose, affecting up to 5 patients. The remaining 83.33% of patients did not experience DRPs, especially in problems related to dosage regimens being too frequent and dose timing instructions being wrong, unclear, or missing. Of these patients, there were 8 cases of DRPs based on dose selection as can be seen in Table 4.

This study found as many as 16.67% of DRPs are based on dose selection and most of it is caused by the usage of high-dose medicine. Toxicity occurs when a patient is given a medication dosage that is too high, beyond the appropriate level of active substance. Administering medications at a dosage higher than the therapeutic dose may result in an elevated risk of adverse consequences³⁷.

In this investigation, the highest incidence of excessive medicine dosage of a single active component was seen in the administration of insulin. The recommended protocol for starting injectable therapy in individuals with diabetes mellitus involves administering basal insulin at a dosage of 10 IU before sleep, and prandial insulin at a dosage of 4 IU or 0.1 units/kg before each meal.³⁸ Giving too high a dose also results in therapeutic goals not being achieved, thus prolonging treatment time and hindering recovery³⁹.

A drug dose too low is a drug dose that is too low to produce the desired response. In this study, only 1 DRPS case generated by the drug dose was too low. Administering drugs with doses that are too low results in reduced efficacy or safety problems which leads patients to drug-related morbidity and

mortality.⁴⁰ Administering drugs with doses that are too low results in suboptimal therapy and prolongs treatment time⁴¹.

A dosage regimen not frequent is dosing intervals that are too infrequent to produce the desired drug response. One DRPS case was found in this study because the frequency of the drug regimen administration was not adequate. The accuracy of the dosage regimen and frequency of drug administration are indispensable to the success of patient therapy. The existence of an insufficient dosage regimen causes therapeutic failure, in this case not causing the desired therapeutic effect⁴².

Dose timing instructions wrong, unclear, or missing are defined as instructions on when to take medication that is inappropriate so as not to produce the desired therapeutic effect. In this study, the dosing instructions for the administration of antidiabetic drugs were correct and clear. There were no instances of incorrect, unclear, or missing dosing instructions.

This research only studies the patient's medical records retrospectively. Thus, the researcher cannot confirm to the physician the reason for the drug and dose selection pattern of the medicine for the patient. However, the findings of this study can be used as baseline data to increase interprofessional collaboration between physicians and pharmacists in medication decision-making and reduce DRPs incidence⁴³. Intentional communication and collaboration between clinical pharmacists and physicians can support patients with complex medication decisions and promote better health outcomes⁴⁴.

Conclusion

Based on our findings, basal-bolus insulin is the most used antidiabetic drug given to

patients with type 2 diabetes mellitus. The other antidiabetic drugs are glimepiride, insulin, a combination of metformin and glimepiride, a combination of metformin and insulin. As many as 47,22% of patients have DRPs related to improper drug selection, and 16.67 % related to dose selection. This finding indicates the need for efforts to improve the quality of prescriptions to provide effective therapy for patients.

Funding

The study was not funded by any source of grants.

Conflict of Interest

The author (s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Table 1. The Incidence of Type 2 Diabetes Mellitus Without Complications Based on Gender and Age

Variable	Frequency	Percentage(%)
Gender	22	61.11
Female	22	61.11
Male	14	38.89
Age	Frequency	Percentage(%)
36-45	2	5.56
46-55	6	16.67
56-65	20	55.56
>65	8	22.22

Table 2. Antidiabetic Drug Use Profile of Type II Diabetes Mellitus Patients Without Complications

Variation	Types of Drugs Used	Frequency
Monotherapy	Glimepiride	2
	Insulin	5
Two Combination	Metformin + Glimepiride	1
	Metformin + Insulin	1
	Glimepiride + Insulin	1
Insulin Initiation	Basal Bolus Insulin Combination (1-time basal insulin and 3 times prandial insulin daily)	21

Table 3: Drug-Related Problems (DRPs) Based on Drug Selection

Code	Cause	DRPs Cases
C1.1	Inappropriate drug according to guidelines	13
	Glimepiride	2
	Ondansetron	6
	Glargine insulin	3
	Detemir insulin	1
	Aspart insulin	1
C1.2	No indication of drug	10
	Ranitidine	2
	Omeprazole	2
	Domperidone	1
	Cefixime	1
	Lansoprazole	1
	Paracetamol	1
	Vitamin C	1
C1.3	Inappropriate combination of drugs, drugs and herbal medications, or drugs and dietary supplements	2
	Paracetamol + Metoclopramide	1
	Glimepiride + Insulin	1
C1.4	Inappropriate duplication of a therapeutic group or active ingredient	0
C1.5	No or incomplete drug treatment despite existing indication	16
	Headache	3
	Cough with phlegm	1
	Type 2 diabetes mellitus	4
	Pain	2
	Low back pain	1
	Dyspepsia	1
	Nausea Vomiting	3
	Anemia	1
C1.6	Too many different drugs/ active ingredients prescribed for indication	1
	Domperidone and ondansetron	1

Table 4: Drug Related Problems (DRPs) Based on Dose Selection

Code	Cause	DRPs Cases
C3.1	Drug dose too low	1
	Codein	1
C3.2	Drug dose of a single active ingredient too high	6
	Glargine insulin	6
C3.3	The dosage regimen is not frequent enough	1
	Phenytoin	1
C3.4	Dosage regimen too frequent	0
C3.5	Dose timing instructions wrong, unclear or missing	0



Figure 1: The Incidence of Drug-Related Problems Based on Drug Selection in Type 2 Diabetes Mellitus Patients Without Complications

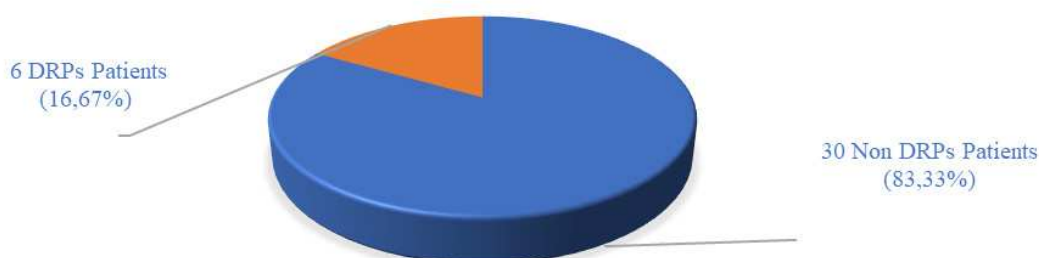


Figure 2: The Incidence of Drug Related Problems Based on Dose Selection in Type 2 Diabetes Mellitus Patients Without Complications