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Evaluation of Rationality in Prescribing Antidiabetic in Outpatient with Type 2 Diabetes Mellitus at PKU Muhammadiyah Yogyakarta Hospital, Special Region of Yogyakarta - Indonesia

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Abstract

In the past few decades, the number of people with diabetes mellitus has steadily increased in various countries. Type 2 Diabetes Mellitus (DM) is the most common type of DM. An increase follows this significant increase in the number of patients in the use of antidiabetic drugs and the risk of irrational drug use, where drug use evaluation is one of the strategies to reduce it. This study aims to evaluate the rational use of antidiabetics in outpatients with type 2 DM at PKU Muhammadiyah Yogyakarta Hospital, Special Region of Yogyakarta - Indonesia. This study is a retrospective analytical observational study. The data used as reference is patient medical records from October 2021 to March 2022. Antidiabetic accuracy based on Indonesian Endocrinology Society guidelines and Drug Information Handbook ed. 22. A total of 155 medical records patients were included in this study. The result showed that patients with complications (50,4%) were higher than patients without complications (49,6%), with the most complication was nephropathy (67,9%) and the most comorbidity was hypertension (21,2%). The rationality of antidiabetics includes the right patient (94%), the right medicine (74%), the right dosage (100%), the right time administration (100%), and the right interval administration (97%). The rational drug use is expected to reduce the risk of drug side effects, reduce patient treatment costs, and improve patient life quality.

Keywords: diabetes mellitus, evaluation, rationality, antidiabetic

Introduction

DM is a chronic metabolic disease characterized by increased blood glucose levels, which, in the long term, might affect the damage to organs such as the heart, blood vessels, eyes, kidneys, and nerves. As the most common type of DM, type 2 DM shows a significant rise in diabetes sufferers in some countries. Indonesia is included in the ten countries with the most DM sufferers in 2019, with 10.7 million sufferers.[1] The increasing prevalence of DM in Indonesia showed 8.5% in 2018 compared to 2013, with only 6.9%.[2]

The use of antidiabetic drugs will follow a high ratio of DM cases. Antidiabetic drugs, which are divided into oral antidiabetic and insulin, have their respective advantages and disadvantages it is necessary to consider pharmacokinetics, pharmacodynamics, and side effects in their administration to optimize blood glucose control and to evaluate the use of antidiabetics.[3]

On the other hand, the use of irrational drugs will increase the risk of hypoglycemia and drug interaction, as well as reduce medication

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adherence, which both have an impact on increasing hospitalization length, mortality, and healthcare cost.[4,5] Rational drug use is a major implication of drug use studies. According to a WHO survey, irrational drug use is the cause of death for one-third of global patients.[6,7] Evaluation of drug use, the right diagnosis, and appropriate medication are important to reduce the risk of DM and improve the patient's quality of life. This study aims to evaluate the rational use of antidiabetics at PKU Muhammadiyah Yogyakarta Hospital, Special Region of Yogyakarta - Indonesia.

Methods

Data collection

This study is an observational analytic with a retrospective design using the total sampling method. We used all medical records of outpatients with type 2 DM from October 2021 to March 2022 in PKU Muhammadiyah Yogyakarta Hospital with a total of 155 medical records of outpatients with type 2 DM.

The data collected include patients' clinical data (allergies, diagnosis, and laboratory examination) and patients' medication (drug name, dosage, directions for use). This study has ethical exemptions from PKU Muhammadiyah Yogyakarta Ethics Committee, number 00059/KT.7.4/III/2022, 9 March 2022.

Data Analysis

This study analyzed complications, comorbid type 2 DM, and rationality evaluation. Rational evaluation is reviewed from the right patients, dosage, medicine, and time and interval drug administration based on the criteria for rational drug use, according to the Ministry of Health of the Republic of Indonesia.

The right patient is the accuracy of the drug given according to the patient's condition, such as allergic conditions and the condition of the patient who is contraindicated for anti-diabetes based on the 22nd edition of the Drug Information Handbook (DIH).

The right medication based on the Guidelines for the Management and Prevention of Type 2 DM from the Indonesian Society of Endocrinology, 2021. In contrast, the right dose, the right time administration, and the right interval of drug administration are the accuracy based on the Indonesian Society of Endocrinology 2021 and DIH 22nd edition.

Results and Discussion

The characteristics of clinical patients including complications and comorbidities are presented in Table 1. Complication is comorbidities related to the diagnosis of the main disease or diseases that occur during the treatment period and require additional treatment. Comorbidities is a coexisting health condition that can be related to the main disease or occur independently.[8] This study showed there were more patients with type 2 DM with complications (50.4%). Another study showed type 2 DM patients with complications at a ratio of 94.[9] The average type 2 DM patient is over 45 years old with uncontrolled blood glucose which tends to cause acute and chronic complications[1,10,11]

The most complications occured in this study were nephropathy (67.9%), followed by neuropathy (16.7%), and peripheral diseases (3.8%). Diabetic nephropathy used to be a chronic complication of type 1 diabetes and type 2 diabetes. Diabetic neuropathy is a multifactorial condition, which includes several risk factors, including elevated HbA1c, hypertension, smoking and obesity.[12] The distribution of outpatient type 2 diabetes comorbidities in this study is shown in Table II.

Table 1. Clinical Characteristics of Type 2 Diabetes Mellitus Patients

Characteristics	The number of patient (%)
Complications of Type 2 DM	
No Complications	77 (49,6)
Complications	78 (50,4)
Type of Complications	
Kidney	53 (67,9)
Neurology	13 (16,7)
Peripheral artery disease	3 (3,8)
Other	9 (11,6)

Table 2. Distribution of Comorbid Diseases in Type 2 Diabetes Mellitus Patients

Comorbid	The number of patient (%)
Hypertension	64 (21.2)
Nephropathy	54 (17.9)
Dyslipidemia	26 (8.6)
Neuropathy	26 (8,6)
Anemia	19 (6.3)
Congestive Heart Failure	18 (6)
Dyspepsia	14 (4.6)
Ulcer	9 (3)
Gout	8 (2.6)
stroke	7 (2.3)
Breast cancer	6 (2)
Erectile dysfunction	6 (2)
Covid	5 (1.6)
Vertigo	5 (1.6)
Depression	4 (1.3)
Heart failure	4 (1.3)
Lung cancer	3 (1)
Peripheral Artery Disease	3 (1)
Asthma	2 (0.7)
Bronchitis	2 (0.7)
Rheumatoid Arthritis	2 (0.7)
*Other	15 (5)
Total	**302 (100)**

Note: 1 patient can have more than one comorbid disease; *others: gastroparesis, hypoglycemia, insomnia, dementia, urinary tract infections, hyperkalemia, osteoarthritis, tuberculosis

Table 3. Rationality of Antidiabetic Use in Type 2 Diabetes Mellitus Patients

Criteria	The number of patient (%) n=155
The right patient	145(94)
The right medicine	115(74)
The right dose	155(100)
The right time administration	155(100)
The right interval administration	151(97)

Complication is comorbidities related to the diagnosis of the main disease or diseases that occur during the treatment period and require additional treatment. Comorbidities is a coexisting health condition that can be related to the main disease or occur independently.[8] This study showed there were more patients with type 2 DM with complications (50.4%). Another study showed type 2 DM patients with complications at a ratio of 94.[9] The average type 2 DM patient was over 45 years old with uncontrolled blood glucose which tends to cause acute and chronic complications.[1,10,11]

The most common comorbidities in type 2 DM patients were hypertension (21.2%), nephropathy (17.9%), dyslipidemia (8.6%) and neuropathy (8.6%). This result of this study supports the previous research which showed the most comorbid disease was hypertension (42.31%).[13]

Research in Japan states that the most comorbidities in DM patients are kidney disorders (35.4%).[14] Many studies show that hypertension and diabetes mellitus often occur together. Hypertension can cause atherosclerosis, which was a high-risk factor for microvascular and macrovascular disease.[15] Hyperglycemia can damage blood vessels and lead to atherosclerosis, and also might increase blood viscosity which will cause hypertension or ischemic stroke.[8]

The second biggest comorbidity is nephropathy (17.9%). Diabetic nephropathy is a clinical symptom in diabetics characterized by albuminuria and diabetic nephropathy which are the main causes of kidney failure disease.[16] Meanwhile, there are glomerular pathological changes in long-term DM patients.[17] DM patients have a higher glomerular filtration rate, which in the long term can lead to increased albumin, hypertension and decreased GFR.[18]

The evaluation of medication treatment based on the criteria for drug use that have been determined by the Ministry of Health of the Republic of Indonesia in 2011 regarding the rational use of drugs was showed in Table III.

The right patient

Drug contraindication is a condition where drugs should not be given to patient, so that the patient's accuracy can be seen from the patient's condition or allergies in the medical record.[19] In this study, it shows that 94% of the sample is the right patient. The previous study showed that drug administration was 100% right for the patient, because there was no drug contraindication found in the patient's clinical condition.[20,21]

The result on this point out that there are drugs that contraindicated in the patient's clinical condition. The drugs were gliclazide, gliquidone, and metformin. Gliclazide was contraindicated in patients with chronic

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kidney disease (CKD) stage 3, liver failure and type 1 DM.[22] Patients received gliclazide and gliquidone when the patient had coexisting CKD stage 3. The administration of antidiabetic sulfonylureas requires a dose adjustment in GFR below 30 ml/minute/1.73 m^2.[23]

Metformin was used by patients with GFR <30 ml/min/1.73m^2. Metformin was contraindicated in patients with renal failure GFR <30 ml/min/1.73m^2, Congestive Heart Failure (CHF) NYHA III-IV, diabetic ketoacidosis and lactation.[24,25] In patients with moderate to severe CKD, metformin Cmax increased, which may increase the side effects. In patients with kidney disorders, there was a decrease in the elimination of lactic acid from the kidneys, giving metformin will increase the risk of lactic acidosis.[26]

The right medicine

Appropriate and rational drug need to consider by doctor's diagnosis, benefits, level of safety and side effects. The results show that the right drug has 74 percentage. Previous study at PKU Muhammadiyah Gamping showed that the right drug had to be 33.33%.[27] In this study, inappropriate drugs include the use of a combination of oral antidiabetics with insulin novorapid. Novorapid insulin is an insulin aspart that works rapid-acting.[25] Based on Indonesian Endocrinology Society 2021 algorithm, the use of a combination iral antidiabetic with basal insulin. Rapid-acting or short-acting insulin used to control postprandial blood glucose, which is when the optimal dose of basal insulin has not been able to control blood glucose, and was used in combination with basal insulin.[25]

Another inappropriate drug is the used of monotherapy insulin novorapid. Based on the Indonesian Endocrinology Society 2021 algorithm, the use of insulin monotherapy was basal or premix insulin. Short/rapid acting insulin monotherapy was recommended for patients with kidney disorders,[28] also there were the administration of gliclazide, gliquidone, and metformin therapy in patients with CKD stage >3. The guidelines recommend the use of SGLT-2 or GLP-1 RA inhibitors which have been shown to reduce the progression of CKD. If SGLT-2 or GLP-1 RA was not available, safe therapy for CKD can be chosen, such as insulin.[25]

The right dose

The dosage needs to consider the patient's clinical condition, like kidney function. In patients with decreased kidney function, it very necessary to give the right dose or it will aggravate the disease.[29] Antidiabetics that require dose adjustment in conditions of renal failure are sulfonylureas (glipizide and glimepiride), glinides, and DPP-4 inhibitors. In this study, there were no drugs that required dose adjustment due to renal impairment.

In this study, the right dose ratio is 100%, which support the previous research from Ramdini et al (2020) that showed 100% of the correct antidiabetic dose based on the Indonesian Endocrinology Society 2015.[30] Dosage always be an important aspect that determines the efficacy or therapeutic effect of a drug. If the dose received by the patient is below the therapeutic range, the expected therapeutic effect will not be achieved. If the dose received by the patient is too high, it can cause hypoglycemia or the emergence of toxicity.[31,32]

The right time administration

Antidiabetic can be given before meals, with meals, or after meals. Drug administration can affect the effectiveness of a drug, related to the amount of drug that can be absorbed. The accuracy time administration has been regulated based on Indonesian Endocrinology

Society 2021, DIH 22nd, and information of drug. The result shows that the right time of drug administration was 100%.

In this study, novorapid insulin was given after meals. Novorapid insulin was a rapid-acting insulin analog that belongs to prandial insulin to control blood glucose after eating and was given at any time before eating or 5-15 minutes before eating, when necessary can be used immediately after meal.[25,28] Review articles showed that rapid-acting insulin was administered 15–20 minutes before meals with a good postprandial glucose control. The risk of postprandial hypoglycemia might increase when rapid-acting insulin distributed after meals.[33]

The right dose interval

The right dose interval for drug can affect the duration of drug effectiveness as it was the time difference between onset and the time required for the drug to fall back to the minimum concentration. Inappropriate drug intervals will also cause inappropriate drug frequency.[30] In table III, it can be seen that the time interval for drug administration was 97%. In the other hand, the study by Ramdini et al (2021) found that the time interval for drug administration was 100%.[30] Inappropriate time interval of administration was the use of acarbose. Acarbose was given 100-300mg/ 3 times a day.[25] In this study there were patients who received acarbose 1-2 times a day.

Conclusion

The rationale for the use of antidiabetics in patients with Diabetes Mellitus Type 2 outpatient at PKU Muhammadiyah Yogyakarta are include the right patient by 94%, the right drug by 74%, the right dosage regimen by 100%, the right time of administration by 100 % and interval administration of 97%. This study is expected to be used as a reference in the rational drugs administration, where can reduce the risk of drug side effects and patient treatment costs as well as improve the patient's quality of life.

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Conflict of Interest

Non declared

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