Potential Hyperglycemia In Type 2 Diabetes Mellitus Patients Due To Drug Interactions At Hospital

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ABSTRACT

Background: Hyperglycemia is a medical condition in the form of an increase in blood glucose levels beyond normal limits with a blood sugar concentration of ≥200 mg/dl. Hyperglycemia that is not well controlled can cause serious disorders of the body's systems, especially the nerves and blood vessels. Based on WHO data, the prevalence of type 2 DM with the potential for hyperglycemia in the world in 2019 was 5.3%. This figure is expected to increase to 6.3% in 2030.
Objective: This research was conducted to determine the potential for hyperglycemia in type 2 diabetes mellitus patients due to drug interactions at one of hospital in Jember.
Method: This research uses a quantitative design with retrospective data collection, namely research obtained based on information from patient medical records. The population in this study was 539 patients suffering from type 2 diabetes mellitus for the period January-December 2022. The sample from this study was type 2 diabetes mellitus patients who met the inclusion criteria. Sampling was calculated using the Slovin formula using random sampling techniques and the results obtained were 84 medical record samples. Analysis using univariate. Data is displayed in frequency and percentage form. Data processing uses Microsoft Excel and SPSS.
Results: Most of the drugs received by type 2 diabetes mellitus patients experienced interactions that had the potential to cause hyperglycemia with blood sugar levels ≥200 mg/dl (96.43%) and a moderate clinical significance level of 70.24%.
Conclusion: There is a potential for hyperglycemia caused by diabetes drug interactions. Monitoring drug interactions and effective treatment in patients with type 2 diabetes mellitus needs to be carried out to achieve optimal therapy targets and increase awareness of healthy lifestyles in diabetes management.

Key words: diaebetes mellitus; drug interactions; hyperglycemia

INTRODUCTION

Diabetes Mellitus (DM) is a major health problem whose prevalence continues to increase every year. Diabetes Mellitus can cause chronic complications and can reduce the quality of human resources (Hartanti, et al, 2019). Diabetes Mellitus is a series of metabolic disorders characterized by hyperglycemia due to disruption of insulin function, insulin production, or both. Hyperglycemia is a condition where blood sugar levels increase which often occurs in diabetes sufferers and can cause symptoms such as weakness, blurred vision and excessive thirst. Hyperglycemia can be caused by several factors such as consuming foods high in sugar, stress, lack of exercise, and use of certain medications. Untreated hyperglycemia can cause serious complications, even leading to death (Norma & Rumatiga, 2022).

DM patients with additional diagnoses of comorbidities or complications will have an impact on the use of more than three types of drugs (polypharmacy). Polypharmacy is the use of several drugs (three or more drugs) by a patient or administering drugs outside of clinical indications, which can cause drug interactions and ultimately have an impact on reducing the outcome of drug therapy (Dasopang, 2020). The impact of polypharmacy is an increased risk of drug side effects, increased risk of medical complications, psychological impacts, and cognitive impairment (Fauziah, 2020). This can be done by conducting a medication review by a doctor or pharmacist with the aim of identifying drugs that are unnecessary or whose dosage can be reduced. Consult a doctor or pharmacist to evaluate the effectiveness and safety of the medicines you are currently taking.

Drug interactions that hinder the achievement of optimal therapeutic results, thereby causing hyperglycemia in patients with type 2 diabetes mellitus, are still common. There were 186 potential drug interactions with 16.2% potentially causing hyperglycemia and the remainder causing hypoglycemia (Saibi et al, 2020). Currently, the potential for drug interactions is increasing because DM patients are accompanied by comorbidities or complications that have an impact on polypharmacy. Drug interactions occur when one drug affects the effectiveness, pharmacodynamics, pharmacokinetics or potential toxicity of another drug (Rahmatillah, 2020). The prevalence of Diabetes Mellitus (DM) sufferers in East Java reaches 2.6% of the population aged 15 years and over. In First Level Health Facilities (FKTP) in 38 districts/cities throughout East Java, there were 867,257 cases recorded or 93.3% of the estimated total DM sufferers receiving health services. Based on riskesdas data in 2021, diabetes mellitus cases in Jember were 1.4% (Zaini, 2020). Based on data from WHO, the prevalence of type 2 DM with the potential for hyperglycemia in the world in 2019 was 5.3%. By 2030 this figure is expected to increase to 6.3%.

The role of a pharmacist or pharmacist in drug interactions is to monitor drug use and provide solutions to clinical problems such as major, minor and moderate interactions (Prasetyawan, 2024)). In hospitals, pharmaceutical services consist of two main activities, namely managerial which includes management of consumable medical materials, clinical pharmacy services, medical devices and pharmaceutical supplies. Both of these activities require the support of adequate human resources, equipment and facilities (Kemenkes, 2016).

Initial research results at Jember Hospital show that during the period January to October 2022, there were 4,216 cases of patients with type 2 Diabetes Mellitus found in the Outpatient Installation. Jember Hospital, as one of the leading health facilities in the Jember area, has an important role in treating and managing diabetes patients. Internal hospital data shows an increase in the number of diabetes patients treated every year. This encourages the need for a more in-depth evaluation of risk factors, disease patterns, and the effectiveness of diabetes management programs that have been implemented. Several studies also show the potential for antidiabetic drug interactions.

A study at a hospital in Bandung reported that 26.83% of patients received drugs that had the potential to interact (Aulia et al, 2020). In Manado, drug interactions in type 2 diabetes mellitus were found to be the main problem, with a frequency reaching 60% (Sibi et al, 2020). A similar study at a hospital in Depok noted that 41.69% of prescriptions received by patients contained interacting drugs (Suryati,

2019). Several other studies also found similar interactions with antidiabetes mellitus drugs.

MATERIAL AND METHODS

Research with the title potential hyperglycemia in type 2 diabetes mellitus patients due to drug interactions at Hospital aims to identify the potential for hyperglycemia in type 2 diabetes mellitus patients due to drug interactions at Hospital. This research was conducted in March-April 2024 at Jember Hospital. The sample in this study is the medical records of type 2 DM patients at Hospital for the period January-December 2022. This research received ethical approval with No. 153/KEPK/UDS/II/2024.

This research was conducted at Jember Hospital. This type of research is quantitative research with retrospective data collection, research obtained based on information from patient medical record data sources. The population in this study was 539 medical record data from outpatients suffering from type 2 diabetes mellitus for the period January-December 2022 at Hospital. The sample from this study was medical record data from patients diagnosed with type 2 DM who met the inclusion and exclusion criteria. Sampling was calculated using the Slovin formula using random sampling techniques and the results obtained were 84 medical record samples.

The medical records are then examined for any drugs used by the patient. Next, the medication used by the patient is applied to Medscape and seen whether there are drug interactions. If there is a drug interaction, whether the interaction is in the minor, moderate or major category. Then we look at the patient's GDA from drug interactions and the patient's GDA can be concluded whether it causes hyperglycemia. The research instrument used in data collection was a checklist sheet. The analysis in this research is through univariate analysis, data is presented in the form of frequencies and percentages. Data processing uses Microsoft Excel and SPSS.

RESULT AND DISCUSSION

GENERAL DATA

Based on Table 1. Above, of the 84 patients suffering from type 2 diabetes mellitus, 23 (27.38%) patients were male and 61 (72.61%) patients were female. This percentage shows that the number of female patients is significantly higher than male, with a difference of 23 patients (27.38%). This research shows that women have a greater tendency to experience type 2 diabetes mellitus. This is in line with research in Manado which also shows that most people with type 2 diabetes mellitus are women, with a percentage reaching 63.5% (Herdiani, 2021). Several factors are thought to increase a woman's risk of developing type 2 diabetes mellitus including high levels of stress which can trigger an increase in blood sugar levels, obesity, use of oral contraceptives and a history of pregnancy (Kemenkes, 2020). The cause of the high prevalence of diabetes mellitus in women is also related to differences in body composition and sexual hormone levels between adult men and women (Kemenkes. 2019). Women have more adipose tissue than men. The difference in the percentage of fat content between adult women and men is around 20-25% for women and around

15-20% for men (Pibriyanti et al, 2022). A decrease in the concentration of the hormone estrogen in postmenopausal women causes an increase in fat reserves, especially in the abdominal area, which results in an increase in the release of free fatty acids. This condition is associated with insulin resistance (Isnaini, 2018).

Based on Table 2. Above, of the 84 patients suffering from type 2 diabetes mellitus, 12 (14.28%) patients were aged 17-49 years and 72 (85.72%) patients were aged 50-70 years. The study results show that the age group 49 years and over has a high risk of developing diabetes mellitus. Aging causes changes in the body's metabolic system that can inhibit glucose release (Rosita et al, 2022). Research at Hospital X Semarang found similar results in terms of female predominance and age group (Ussa, 2021). Physiological changes in humans experience a rapid and drastic decline after the age of 40 years (Betteng 2022). Diabetes often appears after a person enters a more vulnerable age, especially after the age of 45 years in overweight individuals, which results in the body becoming less sensitive to insulin.

Based on Table 3, the majority of treated type 2 diabetes mellitus patients, namely 24 patients (28.58%), received 5 types of medication. Meanwhile, the number of patients who received the smallest number of drugs, namely 3 and 10 types of drugs, was only 2 patients each (2.38%). This shows that the majority of patients are on therapy with a moderate amount of medication, while only a small proportion of patients receive therapy with a very small or very large amount of medication. This research shows that almost all patients received more than 5 drugs. The use of five or more medications may be considered polypharmacy.The predominance of type 2 diabetes mellitus patients who take more than 5 types of medication indicates that polypharmacy requires serious attention in clinical pharmacy services. Some of the reasons for this are the need for long-term treatment, low patient compliance with the use of prescribed medications, and diabetes mellitus which is often accompanied by various complications which result in patients needing to take many medications. Polypharmacy or use of multiple medications simultaneously especially in the elderly population may pose several serious risks and harms.

Based on researchers' assumptions, potential drug interactions are more common in the elderly group, so pharmacists and doctors need to increase vigilance to prevent or reduce the risk of drug interactions. Drug interactions are considered clinically significant if they increase the risk of toxicity or reduce the therapeutic effectiveness of the drug being used. Interactions between drugs can be avoided by reducing excessive drug use or polypharmacy. Pharmacists need to have the ability to treat, prevent and identify drug interactions, and ensure that patient therapy goals are achieved in order to achieve optimal therapy results.

SPECIAL DATA

Based on Table 4 above, of the 84 patients suffering from type 2 diabetes mellitus, 59 (70.24%) patients experienced moderate drug interaction severity and 25 (29.76%) patients experienced minor drug interaction severity. Moderate interaction is the type of interaction most often found in this study. Moderate interactions are drug interactions that are quite significant and can cause adverse effects or reduce the

effectiveness of therapy, but are not always dangerous or life-threatening. Moderate drug interactions can cause changes in the patient's clinical condition and require adjustments in therapy. Meanwhile, minor interactions are drug interactions that have minimal clinical impact and rarely cause serious side effects. This interaction usually does not produce significant side effects in drug therapy, but requires drug monitoring. These two conditions will certainly hinder the patient's achievement of therapeutic goals, but require monitoring of drug use. In implementing patient-oriented pharmaceutical care, pharmacists are expected to be able to prevent and handle drug interactions by monitoring drug interaction events effectively. In addition, pharmacists must also ensure that patients truly understand the information provided, such as how to use drugs, to minimize the potential for drug interactions and increase the effectiveness of therapy.

Based on Table 5 above, of the 25 patients who experienced drug interactions based on minor severity, the most frequently occurred with the combination of glimepiride with furosemide, 11 (44%) and the combination of glimepiride with Sucralfate, 3 (12%). Furosemide is used to treat volume overload and edema caused by exacerbation of congestive heart failure, kidney failure, or liver failure. Furosemide may reduce the effectiveness of glimepiride and other antidiabetic drugs and interfere with blood glucose regulation, potentially increasing the risk of hyperglycemia. Minor interactions may produce less significant effects and not affect therapeutic outcomes. Clinically, minor interactions are not considered particularly dangerous, but still require monitoring during use. For example, the interaction between glimepiride and furosemide. Pharmacists can monitor symptoms that arise due to interactions between the two drugs such as dizziness, nausea, diarrhea and monitor the patient's blood sugar results.

Based on Table 6. above, of the 59 patients who experienced drug interactions with moderate severity, the most frequent occurrence was with the combination of glimepiride with bisoprolol, 28 (47.45%), the combination of amlodipine with metfromin, 16 (27.10%) and as many as 8 (13.55%) namely the combination of glimepiride and neuroxanthin. Theoretically, this category shows that the effects of drug interactions can worsen the patient's condition, so it is necessary to consider the use of alternative drugs that do not interact with each other. The most frequent interactions with moderate severity were glimepiride and bisoprolol in 28 (47.45%) cases. This percentage shows that drug interactions with the combination of glimepiride and bisoprolol are quite high. Bisoprolol, as an antihypertensive drug, can inhibit or block β2 receptors in the pancreas when used together with glimepiride, thereby reducing the effectiveness of glimepiride and causing hyperglycemia. Patients should routinely monitor their blood glucose levels when using these two drugs together and ensure that there is a time interval between their use to reduce the possibility of interaction effects. The second drug combination that most frequently caused interactions was amlodipine and metformin, with a total of 16 cases (27.10%). Amlodipine can reduce the effects of metformin which causes hyperglycemia and has a pharmacodynamic mechanism with moderate severity. The recommendation given is to adjust the time interval between metformin and amlodipine to minimize the possibility of interaction effects. Another common interaction, namely the drug interaction of glimepiride and neuroxanthin, was found in 8 cases (13.55%) with moderate severity. Neuroxanthin

can cause weight gain which can increase insulin resistance and the risk of hyperglycemia.

Based on Table 7 above, 84 patients suffering from type 2 diabetes mellitus had blood sugar levels of more than 200 mg/dl. Hyperglycemia is a medical condition characterized by blood glucose levels that exceed normal limits, with blood sugar concentrations reaching ≥200 mg/dl . here are several factors that can influence the occurrence of hyperglycemia in diabetes sufferers. These factors include physical activity, illness, food and medications that are not related to diabetes. Ignoring the dose or not taking enough insulin or other drugs that function to lower blood sugar levels can also cause hyperglycemia. If hyperglycemia is not treated, this condition can result in the buildup of toxic acids known as ketones in the blood and urine. This condition is known as ketoacidosis. Symptoms include dry mouth, fruity breath, confusion, shortness of breath, stomach pain, decreased consciousness, nausea and vomiting. Chronic hyperglycemia and metabolic disorders in diabetes are associated with long-term damage, failure or dysfunction in several body organs, especially the eyes, kidneys, blood vessels and nerves.Hyperglycemia can also affect the functioning of entire body systems. High blood glucose levels indicate that glucose cannot enter the body's cells and be used as an energy source. In this condition, the body's cells will send hunger signals to the hypothalamus and cause the patient to experience polyphagia or feel hungry quickly. Continuous lack of energy will damage various affected body cells. Lack of glucose forces the body to compensate by using other carbohydrate sources, such as sorbitol. However, not all cells can metabolize sorbitol and convert it into energy. Sorbitol metabolism requires the enzyme sorbitol dehydrogenase, which is not available in Schwann cells, retinal cells and nephrons. Continuous lack of energy can cause damage and even cell death. As a result, the organs consisting of these cells also experience decreased function, and in cases of severe complications, the organs can die.

CONCLUSION

Based on the results of research entitled Potential Hyperglycemia in Type 2 Diabetes Mellitus Patients Due to Drug Interactions at one of hospital in Jember, it was concluded that out of 84 patients, the drugs received by type 2 diabetes mellitus patients at one of hospital in Jember experienced interactions that had the potential to cause hyperglycemia with blood sugar levels. blood ≥200 mg/dl with a moderate clinical significance level of (70.24%).

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Table 1. Frequency Distribution by Gender

Type 2 Diabetes Mellitus Patients

Gender	Frekuensi	Persentase (%)
Man	23	27,38
Woman	61	72,62
Total	84	100

Table 2. Frequency Distribution by Age
Type 2 Diabetes Mellitus Patients

Age	Frekuensi	Persentase (%)
17-49 years old	12	14,28
50-70 years old	72	85,72
Total	84	100

Table 3. Frequency Distribution based on Number of Drugs
Type 2 Diabetes Mellitus Patients

Amount Of Medication	Frekuensi	Persentase (%)
3 drugs	2	2,38
4 drugs	13	15,48
5 drugs	24	28,58
6 drugs	22	26,19
7 drugs	9	10,71
8 drugs	7	8,33
9 drugs	5	5,95
10 drugs	2	2,38
Total	84	100

Table 4. Frequency Distribution of Drug Interactions based on Potential Effects and Level of Clinical Significance

Level of Clinical Significance	Frekuensi	Persentase (%)
Moderate	59	70,24
Minor	25	29,76
Total	84	100

Table 5. Frequency Distribution of Drug Interactions based on Minor Severity

Drug Interactions (*Minor*)	Amount	Persentase %
Glimepiride + Furosemid	11	44
Glimepiride + Sucralfate	3	12
Tazovell + Adalat oros	2	8
Pioglitazon + Amlodipin	2	8
Levemir + Gabapentin	2	8
Glimepiride + Amlodipin	2	8
Glicklazide + Bisoprolol	1	4
Tazovell + Cefixim	1	4
Glimepiride + Domperidone	1	4
Total	25	100

Table 6. Frequency Distribution of Drug Interactions based on Moderate Severity Level

Drug Interactions (*Moderate*)	Amount	Persentase %
Glimepiride + Bisoprolol	28	47,45
Amlodipin + Metformin	16	27,10
Glimepiride + Neurosantin	8	13,55
Glimepiride + Simvastatin	1	1,70
Glimepiride + Gabapentin	1	1,70
Glicklazide + Glucosamine	1	1,70
Novomix + neurosantin	1	1,70
Fonylin + Neurosantin	1	1,70
Tazovell + Metformin	1	1,70
Furosemid + Acarbose	1	1,70
Total	59	100

Table 7. Frequency Distribution based on Blood Sugar Levels Type 2 Diabetes Mellitus Patients

Blood Sugar Levels	Amount	Persentase (%)
≥ 200 mg/dl	84	100
Total	84	100