Evaluation of the Success of OAD and Insulin Therapy on Blood Sugar in Type 2 Diabetes Mellitus Patients

Aghnia Fuadatul Inayah[1], Amaliyah Dina Anggraeni[2] and Irsan Fahmi Almuhtarihan[3]

Abstract

This research needs to be carried out because at the General Hospital of the University of Muhammadiyah Malang, especially in the Inpatient Installation, there has not been a comprehensive study of the evaluation of therapy. This research is a descriptive observational study and prospective data collection using time-limited sampling techniques. The number of samples that met the inclusion and exclusion criteria was 103 respondents. Analysis using SPSS Statistics 22. Based on the research results, it can be concluded that, of the 103 patients who met the inclusion criteria and received OAD and insulin therapy, who received either monotherapy or in combination, 57% showed a significant reduction in blood sugar. However, 39% can be said to be successful because they achieved the goals of therapy in T2DM patients. Meanwhile, 18% and 6% of the patients could say that the therapy was unsuccessful.

Keywords: *Type II DM, OAD, Insulin, Blood sugar, Therapy Evaluation.*

INTRODUCTION

Type 2 diabetes mellitus can be defined as a metabolic disorder characterized by increased blood sugar as a result of decreased insulin activity or insulin resistance and decreased insulin production by pancreatic beta cells.(PERKENI, 2015). The cutoff for T2DM is based on measurements of HbA1c, GDA, GDP, and GD2PP. A person is diagnosed with T2DM if the GDP level is ≥ 126 mg/dL, the GD2PP level is ≥ 200 mg/dL, the HbA1c level is ≥ 6.5%, and the GDA level is ≥ 200 mg/dL with typical symptoms and classic symptoms of diabetes.(Soelistijo, 2021). When T2DM occurs, symptoms often go unrecognized, and therapy is usually initiated several years after disease onset and complications have already occurred. However, generally DM sufferers often complain of polydipsia (excessive thirst), polyuria (frequent urination), polyphagia (often feeling hungry), weight loss.(Osende et al., 2001).

Pathophysiologically, T2DM is caused by two factors, including reduced sensitivity of peripheral tissues to insulin, also known as insulin resistance and decreased capacity of pancreatic cells to release insulin in response to high blood sugar.(Muhammad, 2018). According to(Katzung, Bertram Anthony, 2015), diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia coupled with abnormalities in carbohydrate, lipid and protein metabolism that cause chronic complications, such as microvascular and macrovascular problems. Acute complications include ketoacidosis, hyperglycemia and hypoglycemia. An immediate and potentially fatal complication of uncontrolled diabetes is hyperglycemia with ketoacidosis(de Sá-Ferreira et al., 2022). So this needs to be prevented so that complications do not occur that could endanger the patient's life. This is because T2DM patients themselves are more susceptible to complications because symptoms often appear without being noticed(Osende et al., 2001)

In general, insulin is divided into three types, namely short acting insulin (prandial insulin), rapid acting and long acting (basal insulin). Meanwhile, oral antidiabetics are divided into several types, including sulfonylureas (insulin secretagogue), biguanides and thiazolidinediones (increasing sensitivity to insulin), α glucosidase inhibitors (inhibitors of glucose absorption in the intestinal tract).(Soelistijo, 2021). The use of insulin therapy can be given to patients if the patient fails oral antidiabetic treatment or patients with HbA1c levels ≥7.5% and fasting blood glucose (GDP) levels ≥250 mg/dL(Ulhaq et al., 2023). Meanwhile, the combination of

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[1] Pharmacist Professional Program, Faculty of Health Sciences, University of Muhammadiyah Malang, Indonesia. E-mail: aghniainayah@umm.ac.id (Corresponding author).

[2] Department of Pharmacy, Faculty of Health Sciences, University of Muhammadiyah Malang.

[3] Department of Pharmacy, Faculty of Health Sciences, University of Muhammadiyah Malang

insulin with oral antidiabetics can be used if the HbA1c level is ≥9%(Soelistijo, 2021). T2DM patients also receive pharmacological treatment followed by diet, regular exercise and a healthy lifestyle.

Pharmacological treatment includes taking oral antidiabetic medication and also using insulin. However, in general the first line of T2DM therapy is OAD administration. According to the type 2 diabetes mellitus therapy algorithm, OAD monotherapy is given if the HbA1C level is 6.5-7.49 or < 7%, accompanied by healthy lifestyle modifications and this must continue to be monitored for approximately 3 months. (Soelistijo et al., 2019)The OAD that is generally recommended as first line treatment for type 2 diabetes mellitus is metformin (Riwu & Pujiati, 2018). However, it does not rule out the possibility that other OAD drugs could also be an alternative for the first line of T2DM prevention. The Perceptive Effect of Using an Antidiabetic Oral-Insulin Combination in Type 2 Diabetes Mellitus Patients in 2018 is the title of the research.

The combination of metformin (biguanide) and insulin will improve glucose levels after eating and during fasting so that blood glucose levels can always be controlled. In addition, oral-insulin combination therapy offers several advantages for patients with type 2 diabetes mellitus, including avoiding complications using smaller insulin doses and a lower risk of weight gain. A study conducted in March 2021 analyzed the effectiveness of metformin–insulin combination therapy. Proven by a better reduction in HbA1c and smaller weight gain than other combinations, the combination of metformin and insulin improves beta cell function better or more effectively than other combinations. In research conducted by Chen et al. (2022), a total of 217 patients were divided into two groups, namely the control group (receiving glimepiride therapy) and the study group (receiving glimepiride therapy and recombinant human insulin) then the data from the two groups were compared. The results of the study show that glimepiride combined with recombinant human insulin injection can effectively exert a synergistic effect which is able to correct metabolic defects in the patient's body so that it can control the patient's glucose and lipid metabolism within the normal range and also reduce the occurrence of oxidative stress, reduce vascular endothelial growth factor (VEGF) and reduces the formation of new blood vessels.

The combination use of glimepiride with recombinant human insulin injection is more effective than the use of glimepiride monotherapy. It can be concluded that the use of this combination therapy has a higher use value for therapy in patients with type 2 diabetes mellitus(Chen et al., 2022). One of them is an antidiabetic drug in the α-glucosidase inhibitor class. α-glucosidase inhibitors are a major class of antidiabetic drugs, among which is the drug acarbose (Rosak & Mertes, 2012). This group is given to T2DM patients when there is an increase in postprandial glucose levels (180 mg/dl or more) which are higher than fasting glucose levels by preventing or competitively inhibiting digestive tract enzymes-glucosidases, to prevent polysaccharides from becoming monosaccharides (Soelistijo, 2021) .Typical side effects of the α-glucosidase inhibitor group include gas in the stomach, which looks similar to an ulcer because this drug works in the digestive tract (Renaldi et al., 2021).

Based on the description above, this research needs to be carried out because at the General Hospital of the University of Muhammadiyah Malang, especially in the Inpatient Installation, comprehensive research has not been carried out on the evaluation of therapy. So patients need to get the right therapy to avoid complications and reduce the death rate experienced by T2DM patients. Type 2 diabetes mellitus patients must adhere to a treatment regimen with a high level of compliance (Soelistijo, 2021)The patient's blood sugar levels need to be controlled based on GDP, GDA, GD2PP data for approximately 3 months (ADA, 2019)Thus, carrying out a therapy evaluation can determine whether the therapy target has been met and blood sugar data can be used as material for evaluating the use of OAD and the insulin obtained by this patient is effective in reducing blood sugar levels in T2DM sufferers. Apart from that, it is also hoped that providing the therapy mentioned above can improve the patient's quality of life.

METHODS

This research is a descriptive observational study and prospective data collection using time limited sampling techniques. During the 2 months of data collection, researchers used total sampling. Data collection used

RMK data for all T2DM patients with OAD and insulin therapy who were hospitalized at UMM General Hospital for the period 19 September – 19 November 2023. The inclusion criteria for this study were all patients diagnosed with type 2 diabetes mellitus who received OAD and insulin and were undergoing hospitalization. At the Muhammadiyah University of Malang General Hospital. Meanwhile, the exclusion criteria were patients with type 2 diabetes mellitus who could not be followed up because they were referred to another hospital or died. The number of samples that met the inclusion and exclusion criteria was 103 respondents.

The blood sugar data obtained will be adjusted to the target therapy of T2DM patients. The success of OAD and insulin therapy is based on if blood sugar levels after therapy have reached the therapy goals recommended by Soelistijo et al. (2019) And ADA (2019) namely GDP 80-130 mg/dL, GDA <180 mg/dL, and GD2PP <180 mg/dL. Both examinations are based on GDS, GDP, and GD2PP parameters with complete blood sugar data before giving therapy and after giving therapy. The patient's blood sugar data obtained will be classified as having decreased and achieved goal therapy, experienced a decrease and not yet achieved goal therapy, indicating no success or inconclusive data. Blood sugar that experienced a decrease was analyzed using SPSS Statistics 22. To determine the significance of the decrease in value, it was analyzed using a paired T-test.

RESULTS AND DISCUSSION

Descriptive Analysis Results

Age

Table 1. Data on type II diabetes mellitus patients based on age.

Age Classification*	Number of Patients	Percentage (%)
< 45 years	7	7%
45 – 54 years old	23	22%
55 – 64 years old	46	45%
> 65 years	27	26%
Total	103	100%

Table 1 shows that the highest number of sufferers of type II diabetes mellitus are aged 55 - 64 years, namely 46 patients with a percentage of 45%. Research conducted by Talang Bakung Jambi shows that risk factors for DM often appear after the age of 45 years. At the age of 40 years and over, physiological functions in humans generally begin to decline. Likewise, the ability of the pancreas to produce insulin through its endocrine function may be threatened due to a decrease(Nasution et al., 2021).

Gender

Table 2. Data on type II diabetes mellitus patients based on gender.

Gender	Number of Patients	Percentage (%)
Man	55	53%
Woman	48	47%
Total	103	100%

Table 2 shows that the highest number of type II diabetes mellitus sufferers were male respondents, 55 respondents with a percentage of 53%. The risk factor for T2DM itself is not said to be influenced by gender but is caused by the unhealthy lifestyle of type II diabetes mellitus patients rather than being influenced by genetic factors. Meanwhile, men have a higher percentage of type II diabetes mellitus because it is more influenced by lifestyle. Men tend to follow unhealthy lifestyles such as frequent smoking, consuming alcohol, and lack of exercise(Kusuma et al., 2023).

Guarantor Status

Table 3. Data on type II diabetes mellitus patients based on guarantor status.

Guarantor Status	Number of Patients	Percentage (%)
General	9	9%
JKN	94	91%

Total	103	100%

Table 3 shows that the majority of patients' guarantor status is JKN at 91%. National Health Insurance (JKN) is a program from BPJS Health aimed at patients suffering from chronic diseases such as Diabetes Mellitus Type II, of which there are currently very many people suffering from this disease in Indonesia, with the aim of encouraging participants with chronic diseases to achieve an optimal quality of life.

Length of Treatment

Table 4. Data on type II diabetes mellitus patients based on length of treatment

Length of Treatment	Number of Patients	Percentage (%)
1 - 5 days	85	83%
>5 days	18	17%
Total	103	100%

Table 4 shows that the most patients who received inpatient treatment were in the range of 1 - 5 days with a percentage of 83%. Research conducted by Dian (2014) stated that the length of stay for Diabetes Mellitus patients is 1 to 8 days, therefore the length of stay for patients varies and really depends on the patient's condition, especially if complications occur that the patient experiences during treatment.

KRS Status

In table 5, during treatment at the Inpatient Installation, data on patients who left the hospital (KRS), that is, went home under control, was 99%. This shows that the therapy obtained can help control the patient's condition better.

Table 5. Data on type II diabetes mellitus patients based on KRS status

Guarantor Status	Number of Patients	Percentage (%)
Controlled	102	99%
Repair	1	1%
Total	103	100%

Patterns of Use of OAD and Insulin Therapy in Patients (T2DM)

Table 6.Patterns of OAD and Insulin Use in T2DM Patients

Therapy	Number of Patients*	Percentage (%)
Single	13	9%
2 Combinations	108	73%
3 Combinations	22	15%
4 Combinations	4	3%
Total	147	100%

Table 6 shows that the pattern of use of oral antidiabetic drug therapy (OAD) and insulin given to patients diagnosed with T2DM at the inpatient installation of RSU Muhammadiyah Malang has several models. The highest pattern of use is the use of two drug combinations, 73%. The two drug combinations in question are a combination of OAD-OAD, insulin-insulin and OAD-insulin. When single treatment is no longer effective, it is necessary to give a combination of 2 antidiabetic drugs which have different mechanisms of action. According to the ADA (2019), it is not recommended if given alone and recommends it as additional therapy in combination with other OAD drugs. The pattern of use of the 2 most common combinations is Insulin Glargine + Insulin Aspart with various variations in doses given subcutaneously. The two insulins are Long-acting Insulin + Rapid-acting Insulin. Giving basal rapid-acting insulin and long-acting insulin is one treatment strategy to improve fasting blood sugar levels or blood sugar before meals. Because blood glucose after eating is a condition that is influenced by fasting blood glucose levels, administering basal insulin is expected to reduce blood sugar levels after eating (Anggriani et al., 2020).

Perkeni (2019) states that a single therapy pattern for type 2 diabetes mellitus patients is given when the HbA1c value is checked, <7.5%, with healthy lifestyle modifications. If healthy lifestyle modifications cannot control blood sugar, first-line OAD monotherapy is started, usually metformin. The single pattern that

received the most therapy was OAD Metformin 1x500mg po and Acarbose 3x50 mg po. Metformin monotherapy is sometimes considered a first-line diabetes mellitus drug due to its relatively good effectiveness, low hypoglycemia side effects, and neutral effect on weight gain. Meanwhile, the use of acarbose in long-term comparative trials of drugs in the α-glucosidase inhibitor class resulted in less mortality and morality when compared with drugs in the biguanide and sulfonylurea classes, so most α-glucosidase inhibitor drug therapy was combined as additional therapy with one of the groups. Other types of antidiabetic drugs. However, α-glucosidase inhibitor drugs are effective in reducing the occurrence of postprandial hyperglycemia (AMH, 2014).

Apart from that, because this α-glucosidase inhibitor class of drugs has a relatively high percentage of side effects and a slight decrease in HBA1c, according to the ADA (2019), this α-glucosidase inhibitor class of drugs is not recommended if given alone and recommends it as additional combined therapy. With other OAD drugs, unless the patient is intolerant to other OAD drugs, then in certain conditions, acarbose can be given alone. Meanwhile, the 3 most common combinations are Insulin Glargine + Insulin Aspart + metformin. A combination of Rapid-acting Insulin + Long-acting Insulin + Oral Acquired Antidiabetic is administered.

According to Perkeni (2019), a combination of 3 types of drugs is needed if, after therapy with 2 types of drugs for 3 months, the Hba1c target is less than 7%. The pattern of use of 3 drug combinations; for example, the subject combines biguanide, long-acting, and rapid-acting insulin. For patients with type 2 diabetes who have a fasting blood glucose level of more than 250 mg/dL and a current blood glucose level of more than 300 mg/dL3, insulin is the first-line treatment option. The oldest diabetes drug, insulin, works best at lowering blood glucose levels. Because the pathophysiology of type 2 diabetes mellitus is complex, the advantage of using combination drugs is that we give drugs with different mechanisms of action, namely potentiating; because the dose of each drug is smaller, there will be fewer side effects. Type 2 diabetes mellitus is a chronic disease that cannot be completely cured which affects personal satisfaction (Dwijayanto & Isyarotullatifah, 2019). Giving a combination of drugs is of course not free from side effects considering that these drugs have different mechanisms of action, for example the occurrence of hypoglycemia during antidiabetic drug combination therapy.(AMH, 2014).

Concomitant Diagnosis in Type II Diabetes Mellitus (T2DM) Patients

Table 7. Concomitant Diagnosis in Type II Diabetes Mellitus (T2DM) Patients.

Concomitant Diagnosis	Amount	%
CAD	36	35%
CKD	8	8%
Strokes	10	10%
Hypertension	24	23%
Distal radius fracture	2	2%
Hyperuricemia	2	2%
Dyspnoea	2	2%
Abdominal pain	10	10%
Acute Fever	4	4%
S. ALO	4	4%
Cholecystitis	2	2%
Friday	104	100%

In table 7 it can be seen that the most common diagnoses are Type II Diabetes Mellitus patients with CAD complications of 35%. CAD is a macrovascular complication in patients diagnosed with Type II Diabetes Mellitus. According to WHO, the prevalence rate of heart disease in diabetes sufferers is between 26-35%

with a higher incidence in women and in many countries. CAD arises due to narrowing of the coronary arteries in the heart which causes the blood supply to the heart to become obstructed (Gray et al., 2016). The main risk factor for CAD is dyslipidemia, which has a strong correlation with CAD. Dyslipidemia, which includes increased LDL, triglycerides, and decreased HDL cholesterol, is a complication of type 2 diabetes mellitus caused by insulin resistance. Diabetes mellitus and its involvement are closely linked to future medical conditions and multi-organ damage. Changes in the microvascular system caused by diabetes lead to the melting of fibrous proteins and an increase in the thickness of the capillary basement membrane, which is a sign that the heart arteries are getting smaller. These changes are caused by the binding of sugar and fat, lack of antioxidants and free radicals, underlying inflammation, and the formation of small blood vessels in the walls of arteries and veins, leading to macrovascular complications.(Lyons & Jenkins, 1997)

Concomitant Therapy Received by Type II Diabetes Mellitus (T2DM) Patients

The most frequently used concomitant therapy is antihypertension (19%). Maintaining blood pressure adequately can be done using first line therapy, namely single use, low dose diuretics, beta blockers, angiotensin receptor blockers, ACE inhibitors, and calcium channel blockers. However, the combination of more than one antihypertensive drug often provides advantages over single therapy(Oktianti et al., 2017). ACE-I and ARB are the first choice in DM patients with hypertension because pharmacologically these two agents are nephroprotective which causes vasodilation in the renal efferent arterioles. ACE-I has benefits in inhibiting the development of DM and even preventing DM complications in patients with hypertension through the RAAS (Renin-Angiotensin-Aldosterone System) inhibition mechanism.(Ansa et al., 2012). Apart from that, according to the American Diabetes Association (ADA), the main drugs for DM accompanied by hypertension are ACE inhibitors and ARBs to achieve blood pressure of 130/80 mmHg in DM patients complicated by hypertension. In addition, the use of captopril with metformin may increase the effect of metformin in lowering blood sugar by a mechanism that is not yet known with certainty. ACE inhibitors may improve insulin sensitivity and glucose utilization (Nurlaelah et al., 2015) Hypertension treatment must be continued even though the target has been achieved. Controlled blood pressure after one year of treatment can be tried to reduce the dose gradually. The 2020 ADA recommendations suggest that DM patients with an increase in blood pressure ≥140/90 mmHg to take one type of antihypertensive drug, while the pressure blood ≥160/100 mmHg is recommended to take two types of anti-hypertension drugs to control blood pressure.

Data on the Success of α - Glucosidase Inhibitor Therapy In TYPE II Diabetes Mellitus (T2DM) Patients

Table 8: Data on the Success of OAD and Insulin Therapy in Type II Diabetes Mellitus Patients

Therapeutic Success	Number of Patients	Percentage (%)
Demonstrates decline and achieves therapy goals	40	39%
Shows decline and has not achieved goal therapy	19	18%
Indicates the absence of therapeutic success	6	6%
Results are inconclusive	38	37%
Amount	**103**	**100%**

Of the 103 samples that met the research inclusion and exclusion criteri, you can see Table 8 to see the percentage of success of the drug therapy. The parameters for checking blood sugar in type II diabetes mellitus patients here are based on GDA, GDP, and GD2PP values before and after therapy. The aim of providing therapy to type II diabetes mellitus patients is to be able to control the patient's blood sugar levels.

Type II Diabetes Mellitus patients are more prone to complications, so patients need to get the right therapy to avoid complications and reduce the death rate experienced by T2DM patients. Type 2 diabetes mellitus patients must adhere to a treatment regimen with a high level of compliance (Soelistijo, 2021). Goals Therapy in type II diabetes mellitus patients are based on Perkeni (2019) who states that blood sugar levels are controlled if they have reached the target A1C <7% (0.07; 53 mmol/mol Hb), GDP 80 – 130 mg/dL (4 .4-7.2 mmol/L) and GD2PP < 180 mg/dL (10.0 mmol/L) (1-2 hours after the start of the meal), and according to the ADA (2020) which states that the GDA value must be < 180 mg /dL.

For patients who could identify blood sugar data before and after therapy, there were 65 samples. Of the 65 samples, there were some patients who showed that they had achieved therapy goals in accordance with those recommended by Perkeni (2019) and ADA (2019), 39% of whom received various types of therapy such as getting a single therapy pattern, two combinations, three combinations, and four combinations. One therapy that can achieve goal therapy is a combination with insulin. Giving basal insulin rapid-acting insulin and long-acting insulin is one treatment strategy to improve fasting blood sugar levels or blood sugar before meals. Because blood glucose after eating is a condition that is influenced by fasting blood glucose levels, administering basal insulin is expected to reduce blood sugar levels after eating (Anggriani et al., 2020). However, of the 65 samples obtained, 18% experienced a decrease in blood sugar but had not reached goal therapy. The remaining 6% did not show any success in therapy, as it was known that the patient's blood sugar value increased after being given therapy. Achieving therapy goals in type 2 diabetes mellitus patients is aimed at ensuring that the patient's blood sugar levels can be well controlled and the patient's condition is also more stable so that later the disease does not progress and lead to other complications which can threaten the safety of the patient's life.

The results of this study can also be seen in that there were still 37% of patients whose results were inconclusive. This is because blood sugar data is measured only before or after therapy, and no further checks are carried out. Because the data is considered incomplete, the drug cannot be identified regarding whether the administration of the drug has shown success in controlling the patient's blood sugar levels; in other words, the results cannot be concluded.

Fifty-nine patients who showed decreased blood sugar, whether they achieved goal therapy or not, analyzed paired T-test samples. Where a significance result of 0.000 was obtained. This means that the significance value is <0.05, meaning the decrease in the patient's blood sugar levels before and after therapy is quite significant. Fifty-nine patients who had received various patterns of using OAD and insulin therapy showed that the therapy obtained was quite effective. Meanwhile, the other 44 patients still need further evaluation because they have not achieved therapeutic success, and complete data has not been obtained. It is necessary to evaluate the pattern of therapy given, which may require additional OAD or insulin. It may even need to adjust the dose and require blood sugar measurements to be taken after the therapy.

CONCLUSION

Based on the research results, it can be concluded that, of the 103 patients who met the inclusion criteria and received OAD and insulin therapy, who received therapy either monotherapy or in combination, 57% showed a significant reduction in blood sugar. However, 39% can be said to be successful because they achieved goal therapy in T2DM patients. Meanwhile, 18% and 6% of the patients could say that the therapy was unsuccessful. However, as many as 37% of patients who had received therapy could not be concluded regarding the success of the drug therapy because there were no follow-up examinations after the therapy was given. This data is in accordance with the therapy goals recommended by Perkeni (2019) and ADA (2020).

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