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The analysis of the use a combination of metformin and glibenclamide drugs with blood glucose levels at diabetes mellitus patients

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ABSTRACT
Diabetes mellitus is a non-communicable disease which is a concern a national and global public health problem. Indonesia was ranks sixth in the world with a prevalence of 8,6% of the total population and it is estimated that in 2025 it will increase to 12,4 million sufferers. This research was conducted at the one of public health center. The purpose of this study was to determine changes at blood glucose levels of diabetes mellitus patients on administration of a combination of metformin and glibenclamide drugs. This research used a type of comparative, comparatively paired sample analytical research, with the design cohort retrospective. The instrument used in this research was a patient's medical record. The population in this study were all adults diabetes mellitus patients that over 18 years old at the period of March-Mei 2020.Samples were calculated using the total sampling technique during the research period. The Data was processed using SPSS version 18 and analyzed use Wilcoxon test.The results showed that random blood glucose levels before the use of a combination metformin and glibenclamide with an average of 292,80 mg/dl and after using combination metformin and glibenclamide drugs was had decrease of -76.1mg/dl. Conclusion: A combination of metformin and glibenclamide drugs provided changes in blood glucose levels decrease in diabetes mellitus patients, so it can be used as an antihyperglycemic recommendation according to the classification of patients in research.

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INTRODUCTION

Diabetes mellitus is defined as a chronic disease that occurs when the pancreas didn't produced enough insulin or when the body cannot properly effectively uses the insulin it produces. Insulin is hormones that regulated blood glucose. Hyperglycemia or increased blood glucose, is a common effect of uncontrolled diabetes over time causes serious damage to many body systems, especially nerves and blood vessel. Various complications can arise due to high blood glucose levels uncontrolled, eg neuropathy, hypertension, coronary heart disease, retinopathy, nephropathy, and gangrene [WHO, 2023].

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Based on 2013 Diabetes Atlas data, as many as 382,000,000 people worldwide or 8.3% of 4.6 billion adults (20-79 years) thought to have diabetes. Diabetes mellitus has becomed the fourth leading caused of death in the world and an estimated 5.1 million deaths in the world 2 are caused by diabetes and half (48%) are people under 60 years of age. Indonesia was ranks sixth in number largest diabetics in the world after China, India, United States, Brazil and Mexico [IDF, 2020].With a prevalence of 8.6% of the total population, it is estimated that in 2025 it will increase to 12.4 million patients, which previously reached 4.5 million in 1995. According to data from the Ministry of Health of the Republic of Indonesia in 2013, the number of inpatients and outpatients with diabetes in hospital ranks first of all diseases endocrine. Based on the results of the 2018 Riskesdas shows the prevalence of Diabetes mellitus in Indonesia has increased when compared to 2013, this is based on the results of blood glucose examinations for people aged 15 years and over in Indonesia, amounting to 6.9% (2013) and being 8.5% (2018). The results of the 2018 Riskesdas for East Java Province showed the prevalence of Diabetes mellitus in Banyuwangi was 1.5% higher than the nearest district, namely Jember, with a Diabetes mellitus prevalence of less than 1% [Kemenkes, 2020].

The goal of diabetes treatment was to maintained a balance of blood glucose levels and minimize the risk of complications. Maintaining a balance of blood glucose levels can be done by adopting a healthy diet or doing regular exercise. In addition, it requires special attention from the family or health workers involved in monitoring the condition of Diabetes mellitus patients [Kemenkes,2020].

The types and classes of oral hypoglycemic drugs (OHO) are available, including the insulin secretagogues (Sulfonylureas, D-phenylalanine derivatives, meglitinids, alpha-glycosidase inhibitors, thiazolidinedions and biguanids. In diabetes mellitus, the first choice drugs commonly used is the sulfonylurea group, namely glibenclamide and the biguanid group namely metformin. Glibenclamide or glyburide is a drug used in diabetes patients to control high blood glucose levels. In diabetes, the body can't use and store glucose properly, so it builds up in the bloodstream. Glibenclamide plays a role in stimulating the body to release more insulin from usually to bind glucose in the bloodstream. In addition to drugs, diabetics need to change their lifestyle to be healthier by eating a balanced nutritious diet and exercising regularly [Rambirirch, 2018].

In addition the use of glibenclamide, metformin is considered as first-line therapy in type 2 Diabetes mellitus patients with obese patients. Metformin can be used in combination with other classes of oral antidiabetic drugs or with insulin. When used at the optimal dose metformin can reduce fasting glucose levels estimated by 2-4 mmol / l, with a decrease in HbA1C levels 1-2%. Metformin is recommended as first-line therapy in type 2 diabetes mellitus, because metformin is useful as an insulin saver, and its use does not cause weight gain [5].

The combination of Metformin and Glibenclamide is a hypoglycemic drug oral (OHO) which is formulated for people with type 2 diabetes with criteria for random blood glucose levels> 200 mg / dl and patients with overweight conditions. Metformin and glibenclamide are drugs recommended according to the National Formulary (FORNAS) ,therefore these

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drugs are widely used in pharmacological therapy for Diabetes mellitus patients in health facilities first level.

Health Center is one of the providers of health development services at the sub-district level, plays a role in implementing health activities, providing a variety of services including medical examinations, health promotion and drug administration. Based on the aboved background, this study was conducted to analysis of the use a combination of metformin and glibenclamide drugs with blood glucose levels at diabetes mellitus patients at the Health Center (Indonesia).

METHOD

This study was designed to comply the criteria for ethical conduct and was approved by the Health Research Ethics Committee of STIKES dr Soebandi, with reference number 018/KEPK/SDS/III/2020. This research used a type of comparative, comparatively paired sample analytical research, with the design cohort retrospective. The instrument used in this research was a patient's medical record. The population in this study were all adults diabetes mellitus patients that over 18 years old at the period of March-Mei 2020.Samples were calculated using the total sampling technique during the research period. The Data was processed using SPSS version 18 and analyzed use Wilcoxon test.

RESULTS AND DISCUSSION

This research was conducted in the period March to May 2020, in this study 163 samples of diabetes mellitus patients were obtained, after paying attention to the sample criteria in the study, the samples that met the inclusion criteria in the study were 143 samples. The sampling technique was total sampling that met the inclusion criteria, namely, all of diabetes mellitis patients aged over 18 years who received combination drug therapy of glibenclamide and metformin, type 2 diabetes mellitus patients with random blood glucose levels> 200 mg / dl and diabetes mellitus patients without complications. who got treatment at the Health Center.

Demographic data include gender, age at the Health Center with the following details were name the sex of women is higher than men, namely a number of 91 samples (63.64%). In terms of age, the highest number was dominated by the age range of 48-58 years, namely 87 (60.84%) (Table 1).

Table 1: Demographic data sample of diabetes mellitus, as the inpatients of (health facilities first level)

Demographic data	Category	n	Percentage (%)
Gender	Male	52	36,36
	Female	91	63,64
Age (years)	18-28	2	1,40
	28 - 38	4	2,80
	38-48	20	13,98
	48-58	87	60,84
	58-68	30	20,98

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From the calculation with analyzed data from SPSS statistic that random blood glucose levels before the use of a combination metformin and glibenclamide with an average of 292,80 mg/dl and after using combination metformin and glibenclamide drugs was had decrease of -76.1mg/dl.

The results of the Wilcoxon statistical test showed that there was a decrease in the patient's blood glucose by giving a combination of metformin and glibenclamide which was indicated by a Z value that was negative 1, 899 and a p value of 0.000 (Table 2).

Table 2. Wilcoxon statistic test

	Before and After used of combination metformin & glibenclamide
Z	-1,899
Asymp.Sig	0,000

The prevalence of diabetes mellitus in Banyuwangi (East Java) increases with increasing years. Provision of appropriate therapy to patients and other supporting factors are necessary for the success of therapy. This study aims to analyze the use of a combination of metformin and glibenclamide drugs at the One of Health Center.

In this study, 143 samples were examined from the age range of 48-58 years, namely a number of 87 samples (60.84%). Diabetes mellitus can attack from various groups, but diabetes often occurs, especially after the age of 45 years, especially in those who are overweight, so that the body is not sensitive to insulin. The existing theory says that someone aged ≥45 years has an increase the risk of diabetes mellitus and glucose intolerance caused by degenerative factors, namely decreased body function, especially the ability of β cells to produce insulin to metabolize glucose [Katzung et al, 2018].

Gender is a factor that can also affect diabetes mellitus, diabetes mellitus patients at the One of Health Center are mostly female, as many as 91 samples (63,64%) of the total diabetes mellitus patients (Table 1). This data showed that the prevalence of diabetes mellitus in women is higher than men. Diabetes mellitus is a degenerative disease, changes in glucose levels are influenced by progesterone levels which begin to decline at menopause experienced by women in old age. Factors on the unhealthy lifestyle of women and possibly obesity can also affect the work of insulin in the body [Mayasari, 2020]. The accumulated fat tissue will inhibit the work of insulin in the body and muscle tissues, so that glucose cannot be transported into cells and accumulates in the blood, and blood glucose will increase [Menderik et al, 2020]; [Mayasari, 2023].

From the results of the study there were 143 samples with an average value of 292.80 mg / dl, and after using combination metformin and glibenclamide drugs was had decrease of -76.1mg/dl. Metformin, which is categorized as an insulin sensitizer, works by increasing the effectiveness of the body in suppressing increased blood glucose levels, and can reduce glucose absorption in the intestine so that it has a weight loss effect. Glibenclamide is categorized as a stimulant for insulin secretion, which acts to stimulate the body to release more insulin to bind glucose in the blood. The combination of Metformin and Glibenclamide is an effective combination to reduced blood glucose levels for people

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with type 2 diabetes mellitus with random glucose levels> 200 mg / dl, especially in patients whose hyperglycemia cannot be controlled with a single therapy (metformin or glibenclamide alone), diet and exercise. Besides, a combination this mutually reinforces the work of each drug, so that blood glucose regulation can be better controlled. This combination has fewer side effects when compared to side effects when using monotherapy (metformin or glibenclamide alone). Metformin can suppress the potential of glibenclamide in increasing body weight in diabetes mellitus patients, making it effective for diabetes mellitus patients who are overweight (80% of all type 2 diabetes mellitus patients are too fat with high glucose levels up to 17-22 mmol / l) [Katzung, 2018].

Diabetes mellitus is a degenerative disease that can be controlled with four pillars of management. Diet is one of the important things in the four pillars of diabetes mellitus management because patients do not pay attention to balanced food intake [Suyono, 2020]. Bad eating / drinking patterns result in increased blood glucose levels in diabet mellistus patients, acting as a cause of imbalance in the amount of insulin, therefore diet is one of the prevention so that blood glucose levels do not increase, with a proper diet can help control glucose levels blood [Dipiro, 2014].

The aim of this study, namely to analyze the use of a combination of metformin and glibenclamide with the blood glucose of diabetes mellitus patients at the One of Health Center so that there was a change in the form of a random decrease in blood glucoselevels after combination of glibenclamide and metformin, with an average value. -76.1 mg / dl. In other words, the use of these drugs gave significant results, namely as many as 106 samples (74%) of the total sample, experienced a decrease in GDA levels towards normal, while only 37 samples (26%) showed results that were not as expected, which occurred. increase in GDA levels, between before and after using the drug.

As for the limitation in the study, the researcher did not examine other factors that caused the patient's blood glucose to increase or decrease, so they could only assess the success of the study in terms of the drugs used.

CONCLUSION

Based on the results of research on the Analysis of the use a combination of metformin and glibenclamide drugs with blood glucose levels at diabetes mellitus patients, it can be concluded that A combination of metformin and glibenclamide drugs provided changes in blood glucose levels decrease in diabetes mellitus patients, so it can be used as an antihyperglycemic recommendation according to the classification of patients in research.

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