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Nanoparticle bitter melon (*Momordica Charantia L.*) as the effort to reduce fasting plasma glucose in menopause women with type 2 diabetic mellitus

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ABSTRACT

Background

Clinically, the case of diabetic mellitus type two is the highest case of diabetic mellitus found, accounting there are > 90% of all diabetic cases. One of medicinal treatment of non pharmacology can be done is consume bitter melon. Bitter melon (*momordica charantia L.)* has antidiabetic and hypolipidemic activity so that it can be used coincide with chemical drugs to treat diabetic as well as inhibit diabetic complications. Nanoparticle are a technology that aims to make sizes (dosage forms) in range of 10nm-1000nm.

Objective

To prove that of nanoparticle bitter melon *(momordica charantia L.*) can reduce fasting plasma glucose in menopause women with type 2 diabetic mellitus for 30 days in the intervention group and the control group.

Methods

True experiment: with pretest - posttest control group design. The population is menopause women with diabetes mellitus type 2 who participated the prolanis program at the community health center Keruak. Sample technique use is *simple random sampling*. The sample consist of 30 respondents, each group consisted of 15 respondents. Each group was given the intervention for 30 days. The intervention group was given nanoparticle bitter melon (a daily dose of 1 gram) plus metformin (a daily dose of 1 gram), while the control group was only given metformin with a daily dose of 1 gram.

Results

The difference between the intervention group is 102,46 mg/dL with *p value* 0.000 and the control group is 20,47 mg/dL with *p value* 0.005.

Conclusion

Nanoparticle bitter melon (*momordica charantia L.)* can be used as an effort to decrease fasting plasma glucose in menopause women with diabetes mellitus type 2.

Keywords: Menopause Women, Diabetic Mellitus, Nanoparticle Bitter Melon

INTRODUCTION

Various types of diseases are caused by a person's unhealthy lifestyle, one of which is diabetes mellitus. The situation of a person's uncontrolled blood sugar levels is called diabetic. [1] Indonesia is one of the developing countries that has the largest DM patients in the world, which is as much as 80%. [2] Clinically cases of type 2 DM are the highest cases of DM, accounting for > 90% of all cases of diabetic. [3, 4] These cases are mostly experienced by older adults (*menopause)*. [5] Insulin resistance is a major factor that triggers type 2 diabetic. Insulin resistance has been defined as a condition of low insulin sensitivity, which is the ability of insulin to reduce blood glucose concentrations. [6]

Treatment for type 2 diabetic mellitus has been using insulin therapy, single hypoglycemic oral or combined with synthetic drugs such as metformin, sulfonylurea, biguanide, and alpha glycosidase inhibitors. [7] However, drugs using chemicals are known to be expensive, and have side effects (such as severe hypoglycemia, acidosis, liver cell injury, permanent neurological deficits, indigestion, headache, dizziness, and death). [8-9] Bitter melon *(momordica charantia L.)* has antidiabetic and hypolipidemic activity so that it can be used in conjunction with chemical drugs to treat diabetes as well as inhibit diabetic complications. The active principles in pare medicinal plants have pancreatic β cell regeneration, release insulin and fight insulin resistance problems. [10] The content of bitter melon which is useful for reducing sugar is charantin and p-polipeptide (polypeptides that are similar to insulin). Charantin serves to stimulate the pancreatic gland β cells of the body so that insulin production will be greater and increase glycogen reserves in the liver. While p-polypeptide can reduce blood sugar levels directly. [11]

Complex compounds contained in bitter melon extract are antioxidants, mimetic insulin (charantin, p-polypeptide and vicin), polyphenols, vitamins (B, C, and E) and minerals (zinc, mg, potassium, calcium, phosphorus). In bitter melon, there are also compounds including: flavonoids, terpenes, phenols, isoflavones, terpenes, glucosinolate and anthraquinone. [12] Obstacles that are often experienced in herbal medicines are difficult active substances to pass through body cell membrane lipids due to having large particle sizes, in low solubility water (causing poor absorption and bioavailability), because of that problem many plants have potential active substances but cannot be used in vivo even though the invitro test got good results. [13]

Nanoparticles are a technology that aims to make sizes (dosage forms) in the size range of 10nm-1000nm. Nanotechnology can make herbal preparations (atomic and molecular scale) so that changes in chemical, biological and catalytic activity occur. [14] The advantages of nanotechnology are modifying surface characteristics and molecular size so that herbal drugs can reach the targeted organs (brain, lungs , kidney, digestive tract) with selectivity and effectiveness, high safety, in the release of active compounds can be controlled to minimize side effects, and can be given in high concentrations (small size and high load capacity). [15]

Study Objective

To prove that of nanoparticle bitter melon *(momordica charantia L.*) can reduce fasting plasma glucose in menopause women with type 2 diabetic mellitus for 30 days in the intervention group and the control group.

Methods

This research used experimental method with randomized design of pre-post test control group design. The population is menopause women with diabetes mellitus type two who participated the prolanis program at the community health center Keruak. Sample technique use is *simple random sampling*. The sample consist of 30 respondents, each group consisted of 15 respondents. Each group was given the intervention for 30 days. The intervention group was given nanoparticle bitter melon (a daily dose of 1 gram) plus metformin (a daily dose of 1 gram), while the control group was only given metformin with a daily dose of 1 gram.

DATA ANALYSIS

Univariate analysis is done by calculating the mean, maximum, minimum and standard deviation of the indicator of inferential analysis instrument used to determine the significant differences between the two groups namely the intervention group and the control group. Data analysis using Paired t-test and Independent t-test ($p < 0.05$).

RESULTS

Data Presentation and Research Analysis. Giving Nanoparticles bitter melon and metformin are more influential than only given metformin in reducing fasting plasma glucose in menopause women with type 2 diabetic mellitus.

Table 4.1 Distribution of respondents characteristics based on education, employment, family history of DM, BMI, and number of respondents (n = 30 respondents).

Characteritics	Group				*p value*
	Intervention		Control		
	N	%	N	%	
Age					
45-59	6	40	6	40	0,970
60-74	9	60	9	60	
Total	15	100	15	100	
Education					
No School	6	40	5	33,3	
SD	5	33,3	9	60	0,160
SMP	1	6,7	-	-	
SMA	2	13,3	-	-	
S1	1	6,7	1	6,7	
Total	15	100	15	100	
Employment					
No Work	8	53,3	8	53,3	
Trader	6	40	3	20	1,000
Farmer	1	6,7	3	20	
PNS	-	-	1	6,7	
Total	15	100	15	100	
Family history of DM					
Nothing DM	6	40,0	7	46,7	
DM	9	60,0	8	53,3	0,448
Total	15	100	15	100	
BMI (kg/m^2)					
Abnormal (< 18 & >30)	-	-	-	-	
Normal (>18 & <30)	15	100	15	100	0,859
Total	15	100	15	100	

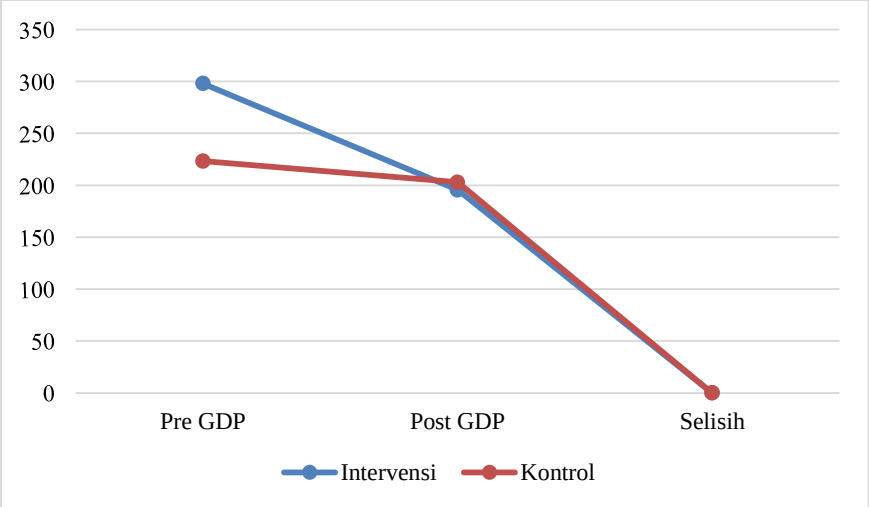
Table 4.1, the age variable illustrates that the highest age at the age of 60 years is 18 respondents (60%). The education level variable shows that the highest education is Primary School (SD) of 14 respondents (46.7). Employment variables indicate that the majority of respondents working as housewives (IRT) amounted to 16 respondents (53.3%). The results of the study on the history of diabetes mellitus showed the highest history of DM disease, there were 17 respondents (56.7%). Body mass index (BMI) variables indicate that all BMI respondents in the normal category are 30 respondents (100%).

Table 4.2 Descriptions the Value of Menopause Women Fasting Plasma Glucose with Diabetic Mellitus before and after treatment

Group	Variable		*t*	*P*	Δ	*Difference* Δ
	Pre_FPG	**Post_FPG**				
	Mean±SD	**Mean±SD**				
Intervention	297,93±74,608	195,47±41,648	5,170	0,000	102,47	82
Control	223,27±56,505	202,80±49,648	3,325	0,005	20,47	

* Paired t-test

** Independent t-test



Graph 4.1 Description of a decrease in fasting plasma glucose in the intervention group and the control group

Table 4.2 shows that the test results for differences in fasting plasma glucose before and after treatment in the study use the paired sample t-test and Indepent t-test. The intervention group the mean value before treatment was 297.93 ± 74.608, and after the treatment it was 195.47 ± 41.68 (there was a decrease in means value of 102.47) with a value of t = 5.170, p value of 0,000. Whereas, fasting plasma glucose in the means control group before being given treatment amounted to 223.27 ± 56.505, and after treatment to be 202.80 ± 49,648 (there was a decrease in means values of 20.47 mg / dL with a value of t = 3.325, p = 0,005 So that it can be concluded that there were differences before and after nanoparticle bitter melon were given for 30 days on fasting plasma glucose in menopause women with type 2 diabetic mellitus. The difference in fasting plasma glucose between the intervention group and the control group was 82 mg / dL. Giving metformin 2x500 mg added with 2x500 mg nanoparticle bitter melon for 30 days in the intervention group effectively lowered fasting plasma glucose compared to the group that only received metformin 2x500 mg.

DISCUSSION

Description of fasting plasma glucose before and after treatment of metformin

Research conducted on menopause women respondents with type 2 diabetic mellitus as many as 15 respondents as the intervention group and 15 respondents as the control group in Keruak Health Center showed a change in the value of blood sugar levels. Fasting plasma glucose changes in the control group (the group given only metformin) before the treatment of 223.27 mg / dL after administration of metformin for 30 days with a dose of 1 gram (2 x 500mg) the value of fasting plasma glucose decreased to 202, 80 mg / dL. So, the average difference between before giving metformin and after giving metformin is 20.47 mg / dL, with a value of *t* = 3.325, *p value* 0.005. That is, there is a difference in fasting plasma glucose in the control group between before and after administration of metformin. This study is in line with research conducted by Fuangchan for 4 weeks said that there was a decrease in fasting plasma glucose in patients given metformin dose of 2000

mg / dl at week 4 with a mean (95%) of 14.7 ± 15.4 (20.3, 9.4). [16] Another study conducted by Osot for 8 weeks said that administration of metformin with a dose of 6 grams can reduce fasting plasma glucose (A1C) in patients with type 2 diabetic mellitus with a value of p = 0.042 with an average difference of 2.84. [17]

Metformin is a biguanid antihyperglycemic drug. Control fasting plasma glucose by inhibiting glucose production *(gluconeogenesis)* in the liver is the main way of working metformin. Metformin has been used for a long time as a DM drug, which is useful in reducing the level of tissue resistance to insulin. The effect of metformin basically works post-receptor, influencing the improvement of the glucose transport (GLUT) mechanism. [18]

Description of the Effect of Nanoparticle Bitter Melon on Fasting Plasma Glucose of Menopause Women with Type 2 Diabetic Mellitus

Fasting plasma glucose changes in the intervention group (the group given nanoparticle bitter melon and metformin) before treatment amounted to 297.93 mg / dL after administration of nanoparticle bitter melon at a dose of 1 gram (2x500mg) plus metformin at a dose of 1 gram (2 x 500mg) for 30 days the value of fasting plasma glucose decreases the mean value to 195.47 mg / dL. So the average difference between before giving metformin and after giving metformin is 102.47 mg / dL, with a value of t = 5.170, *p value* 0.000. That is, there were differences in the value of fasting plasma glucose in the intervention group between before and after administration of nanoparticle bitter melon plus metformin. This study is in line with research conducted by Fuangchan for 4 weeks said that there was a decrease in fasting plasma glucose in patients given a pare extract dose of 2000 mg/dL at week 4 with a mean (95%) of 2.3 ± 15.5 (8.0, 3.5). [16] Another study conducted by Osot for 8 weeks said that administration of extract bitter melon could reduce fasting plasma glucose (A1C) in patients with type 2 diabetic mellitus with an average difference of 7.11. [17]

The results of previous tests with extract bitter melon were found to be components of flavonoids and charantin, which are considered as the largest components and which most influence the decrease in blood sugar levels. Flavonoids prevent complications or progression of DM in several ways, namely cleaning excessive free radicals, inhibiting the enzyme α glucosidase through hydroxylation bonds and substitution in the beta ring. Charantin are typical cucurbitane type triterpenoids in M. charantia and are potential substances with antidiabetic properties. Pitiphanpong et al. shows that charantin can be used to treat diabetes and potentially replace chemical treatment. Meanwhile, the results of the nanoparticle bitter melon test with SEM EDX analysis showed that the highest composition of components in bare nanoparticles was Potassium Oxide (K2O). Potassium is the main interacellular cation, and plays an important role in cell metabolism. The presence of calcium ions in the cytoplasm activates calmodulin enzymes in cells so that exocytosis of insulin occurs from the ventricles to be secreted out of the cell. [19]

One of the factors that cause insulin resistance is a lack of magnesium intake. The potential role of magnesium in diabetic mellitus is to improve insulin sensitivity. The importance of adequate magnesium intake especially in individuals with Diabetes Mellitus can be associated with its role in maintaining blood glucose homeostasis along with activation of factors involved in insulin sensitivity. Magnesium deficiency causes a decrease in insulin secretion in the pancreas and increases insulin resistance in body tissues. The same thing was stated by Larsson et al (2007) which states that the role of magnesium intake protection against type 2 diabetes can be caused by an increase in insulin sensitivity. Larsson who revealed that magnesium intake has a relationship inversely with Type 2 DM. Meanwhile, the results of the analysis using GCMS (Gas Chromatography-Mass Spectrometry) were obtained, namely the results of phytochemical nanoparticle bitter melon. The results of GCMS analysis have an effect on the process of Mitogen Activated Protein Kinase (MAPKs) which is associated with pancreatic β cells which influences insulin secretion. Increased hormone insulin results in an increase in glucose transporter 4 (GLUT 4). In addition, in the GCMS test it was found that bitter nanoparticles had the same working system in the body with metformin, which was able to suppress liver glucose production, improve glucose uptake (muscle, fat tissue) effect on cell membranes (specifically GLUT-4 stimulation, activation enzyme AMP-activated kinase). [20]

The combination of metformin plus nanoparticles bitter melon can be said to be an alternative treatment for the best type 2 diabetic mellitus to reduce fasting plasma glucose compared to the results of previous studies that were only given a single dose (only metformin or bitter melon *(momordica charantia L.)*.

CONCLUTION

The administration of nanoparticle bitter melon *(momordica charantia L.)* can be used as an effort to decrease fasting plasma glucose in menopause women with type 2 diabetic mellitus. There is a significant decrease in fasting plasma glucose in patients given metformin with a dose of 2x500 mg for 30 days with a value of p value = 0.005. There was a significant decrease in the value of fasting plasma glucose in patients given nanoparticle bitter melon at a dose of 2x500 mg plus metformin at a dose of 2x500 mg for 30 days with a p value = 0,000. The decrease in the value of fasting plasma glucose in patients given nanoparticle bitter melon plus metformin 5 times was higher compared to patients given only metformin.

RECOMMENDATION

For the next researcher can continue this research with developed using nanoparticle techniques (the latest nanotechnology) and use smaller particle sizes to reduce fasting plasma glucose. In addition, it can develop research on nanoparticle bitter melon with higher doses than metformin alone. Nanoparticle bitter melon can be used as an alternative treatment for patients who are not suitable for chemical drugs and reduce the use of drugs from chemicals.

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