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Original Article

The Effect of Sleeve Gastrectomy and Omentoplasty on HOMA BETA Value and Islets of Langerhans in Rats with Type 2 Diabetes Mellitus

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Abstract

Introduction : WHO predicts an increase in the number of people with diabetes in Indonesia from 8.4 million in 2000 to around 21.3 million in 2030. Another marker for measuring insulin resistance is the homeostasis model assessment-insulin resistance (HOMA-IR). Bariatric surgery is the most effective therapy for patients both in terms of weight loss and improvement in obesity-related diseases such as Type-2 Diabetes Mellitus (DM). This study aims to prove the improvement of HOMA Beta values and Diameter of the islets of Langerhans in type 2 diabetes mellitus rats that underwent Sleeve Gastrectomy and Pancreatic Omentoplasty.

Methods : This study is an experimental post-test control group design study with 18 male Sprague-Dawley rats. Samples are divided into 1 control group and 2 treatment groups (Sleeve gastrectomy and Omentoplasty). Rats' pancreas and glucose level were measured by using HOMA IR method and Hematoxylin eosin-paraffin block method. Data of islets Langerhans were measured using ANOVA, while HOMA Beta values were measured by Mann Whitney and Kruskall Wallis test.

Results : HOMA Beta values in treatment Group P1 (Sleeve gastrectomy) and Group P2 (Sleeve gastrectomy + omentoplasty) are statistically different compared to control group. Islets cells of Langerhans diameter in treatment groups 1 and 2 was not statistically different compared to control group. HOMA Beta Value and Langerhans diameter was correlated moderately.

Conclusion : Sleeve Gastrectomy and Pancreatic Omentoplasty in type 2 diabetes mellitus rats improved the HOMA Beta values and the diameter of the islets of Langerhans.

Keywords : Sleeve Gastrectomy; Omentoplasty; Diabetes mellitus; HOMA Beta; Langerhan's Islet

INTRODUCTION

The World Health Organization (WHO) shows data that globally, 422 million adults aged over 18 years were living with diabetes in 2014. WHO predicts an increase in the number of people with diabetes in Indonesia from 8.4 million in 2000 to around 21.3 million in 2030.[1]

Diabetes Mellitus is defined based on the diagnostic criteria according to the 2015 Indonesian Endocrinology Association (PERKENI) consensus: 1) Fasting plasma glucose examination 126 mg/dl. Fasting is a condition where there is no caloric intake for at least 8 hours, 2) plasma glucose examination 200 mg/dl 2 hours after the test 3) Oral Glucose Tolerance Test (OGTT) with a glucose load of 75 grams, or examination of plasma glucose while 200 mg/dl with classic complaints (polyuria, polydipsia, polyphagia, and unexplained weight loss), or 4) HbA1c examination 6.5% using the method standardized by the National Glycohaemoglobin Standardization Program (NGSP).[2]

Measurement of insulin resistance plays an important role in the development of basic science and in clinical practice. The gold standard for measuring insulin resistance is the euglycemic hyper-insulinemic clamp, but it has a complicated procedure that makes it difficult to apply to large-scale tests. Another marker for measuring insulin resistance is the homeostasis model assessment-insulin resistance (HOMA-IR).[3] Homeostatic model assessment (HOMA) is a method for assessing -cell function and insulin resistance (IR) of basal (fasting) glucose and insulin or C-peptide concentrations. The HOMA model compared to other models has the advantage of requiring only a single plasma sample to be tested for insulin and glucose.[4] The American Diabetes Association (ADA, 2009) criteria were used for the classification of glucose tolerance. The insulin resistance homeostasis index (HOMA-IR) and -cell function (HOMA-B) models were calculated using the HOMA model software (University of Oxford, Oxford, UK). HOMA-IR and HOMA-β are most widely used as methods to evaluate insulin resistance and insulin secretion in epidemiological studies.[5]

The hyperglycemic state tends to cause the effect of the formation of free radicals or reactive oxygen species through oxidation-reduction mechanisms by pushing more electron donors into the electron transport chain in mitochondria. Insulin plays an important role in the process of glucose metabolism because insulin is responsible for glucose breakdown into glycogen which serves as food reserves. Insulin is synthesized in pancreatic cells in the endoplasmic reticulum.[6]

Three categories of bariatric surgeries for diabetic patients fall into 3 categories: surgery for restriction of intake, surgery for poor absorption, and surgery with both effects. Bariatric surgery is the most effective therapy for patients both in terms of weight loss and improvement in obesity-related diseases such as type 2 diabetes mellitus. The most striking effect of this procedure is the rapid change in glucose homeostasis and insulin secretion.[7] Bariatric surgery procedure includes sleeve gasterectomy and omentoplasty. Sleeve Gastrectomy involves removal of the fundus and body of the stomach, Omentoplasty is a surgical procedure in which part of the greater omentum is used to cover or fill a defect, enlarge arterial or portal venous circulation, absorb an effusion, or improve lymphatic drainage.[8]

This study aims to prove the improvement of HOMA Beta and Diameter of the islets of Langerhans in rats with type 2 diabetes mellitus who underwent Sleeve Gastrectomy and Pancreatic Omentoplasty.

METHODS

This is a laboratory experimental study with a "post-test only group design". The research was carried out for one month on September 2020.

The treatment on rats was carried out at the Central Laboratory for Food and Nutrition Studies (PSPG) and the process of making paraffin blocks to Hematoxylin-Eosin staining was carried out at the Anatomical Pathology Laboratory, Gadjah Mada University, Yogyakarta.

This study used 18 Sprague-Dawley rats which were randomly divided into 3 groups using simple random sampling method, each group of 6, namely Group K (Control), Group P1 (Sleeve Gastrectomy), and Group P2 (Sleeve Gastrectomy + Omentoplasty). The inclusion criteria in this study were male Sprague-Dawley rats, 150–200 g in weight, and with no anatomical deformities.

Animal Treatment

Diabetes Induction

All rats were injected intravenously through the tail vein with a dose of 45 mg/kgBW Streptozotocin (STZ) and Nicotinamide (NA) 110 mg/kgBW single dose with a 1cc syringe, and were given 30% sucrose solution ad libitum to drink. Fasting blood glucose (4–6 hours) of rats (taken from tail vein/lateral vein) and rats weight were measured 5 days after the last STZ injection using a (GlucoDR Bio-sensor) glucometer and a digital scale (total 10 days of diabetes induction). Diagnosis of diabetes was established when rat's fasting blood glucose > 126 mg/dL.

Sleeve Gastrectomy and *Omentoplasty*

The rats were anesthetized using intramuscular ketamine hydrochloride with a dose of 20 mg/kg body weight. Group P1 had sleeve gastrectomy procedure, the abdominal cavity was opened with a midline supra-umbilical incision. In sleeve gastrectomy, identification

and clamps are carried out parallel to the direction of the greater curvature. Then, the hull is cut leaving 20–30% of its volume. Then, the hull is sewn back together.

Group P2 underwent sleeve gastrectomy and omentoplasty procedure. Omentoplasty begins with the identification of the omentum and pancreas of rats. The free omentum was sutured covering the pancreas with Polyglycolic Acid (PGA) 5.0 suture. After controlling the bleeding, the abdominal wound was sutured again after 10 days. Then, the wound was cleaned with 0.9% NaCl and smeared with povidone-iodine.

Calculation of HOMA Beta Value

Ten days after the Sleeve Gastrectomy – Omentoplasty procedure, all rats were fasted for 4–6 hours. A 0.5 cc blood sample was taken from tail vein. Measurement of plasma insulin levels was carried out with rat insulin ELISA kit and microplate reader (Bio-Rad, CA, USA). The blood samples obtained were centrifuged (Thermo-Fisher) at 40°C at a speed of 3000xg for 10 minutes and plasma samples containing insulin (antigen) were obtained. Then the plasma samples were reacted with monoclonal anti-rat insulin (antibodies) that had been coated on the bottom of the microplate wells and the reagents provided in the rat insulin ELISA kit. After going through some of these reactions, the sample was measured using a microplate reader (Bio-Rad, CA, USA) at a wavelength of 450 nm.

Pancreatic Langerhans Islet Diameter Measurement

Histological examination was carried out to determine the size differences of pancreatic tissue structure in each treatment between groups. Rats were euthanized using chloroform and the pancreatic tissue was made into paraffin blocks and stained with Hematoxylin–Eosin. Pancreatic histopathological preparations were observed under a microscope (Olympus) with 400x magnification and measured the diameter of the pancreas. Size was measured from the exposed islets and from number of sections of a pancreas.

Data Analysis

Statistical analysis was done for differences in Langerhans islet in pancreatic tissue diameter between each group using the One-Way ANOVA test because the data were normally distributed, and the HOMA Beta value analyzed using the Kruskal Wallis test followed with Mann Whitney post hoc test because the data were not normally distributed. The limit degree of significance is a p-value of 0.05 with a 95% confidence interval. Data processing was done with SPSS Ver. 26.0

Ethical Clearance

This research has obtained ethical clearance with No.84.1/EC/H/FK-UNDIP/IX/2020 from the Commission on Medical Research Ethics, Dr. Kariadi General Hospital.

RESULTS

Rat characteristic

Consort diagram showed on Figure 1, showing how the

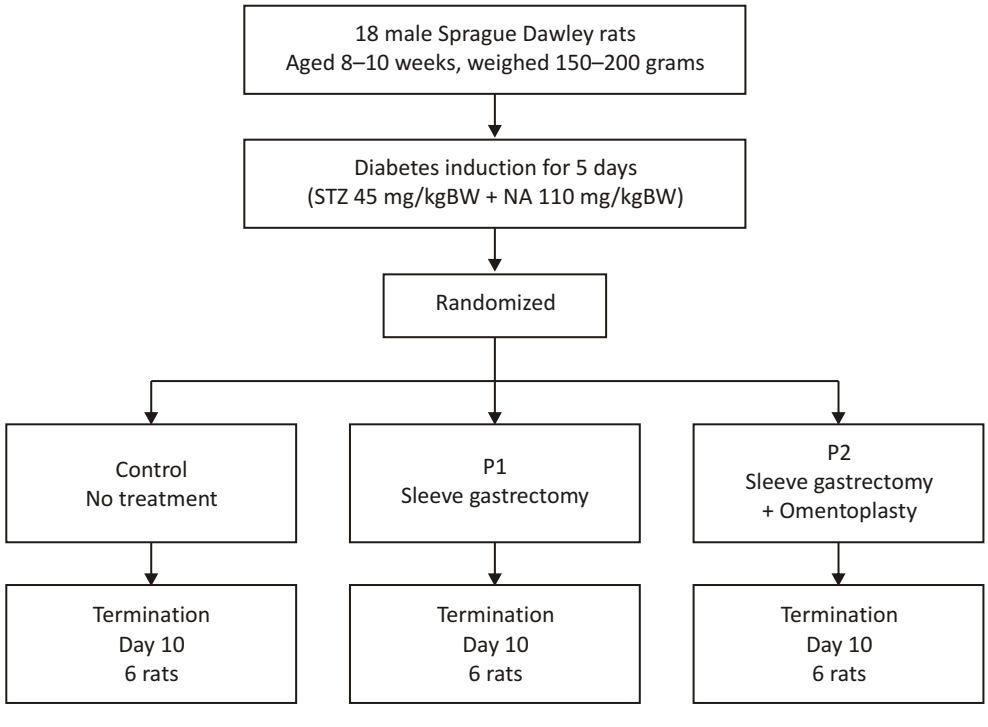

Figure 1. Consort diagram

TABLE 1
Mean of rat body weight and blood glucose a day before surgery, 5th, and 10th day after

Parameters	Group	Day 1	Day 5	Day 10
Mean Body Weight ± SD	K	177,17 ± 5,64	160,67 ± 4,50	144.17 ± 6.34
	P1	173,88 ± 4,26	156,88 ± 3,23	139,38 ± 3,58
	P2	173,63 ± 3,38	157,50 ± 4,04	142,75 ± 5,29
Mean Blood Glucose ± SD	K	266,54 ± 3,99	271,48 ± 2,27	273,48 ± 1,75
	P1	265,40 ± 5,79	193,66 ± 11,65	175,44 ± 6,97
	P2	265,47 ± 3,79	179,07 ± 4,78	172,63 ± 12,05
Mean Insulin Level ± SD	K	401,85 ± 10,78	396,15 ± 10,94	389,64 ± 9,60
	P1	411,40 ± 10,40*	458,99 ± 11,89	465,50 ± 11,00
	P2	407,34 ± 4,21*	432,55 ± 7,58	423,40 ± 7,86

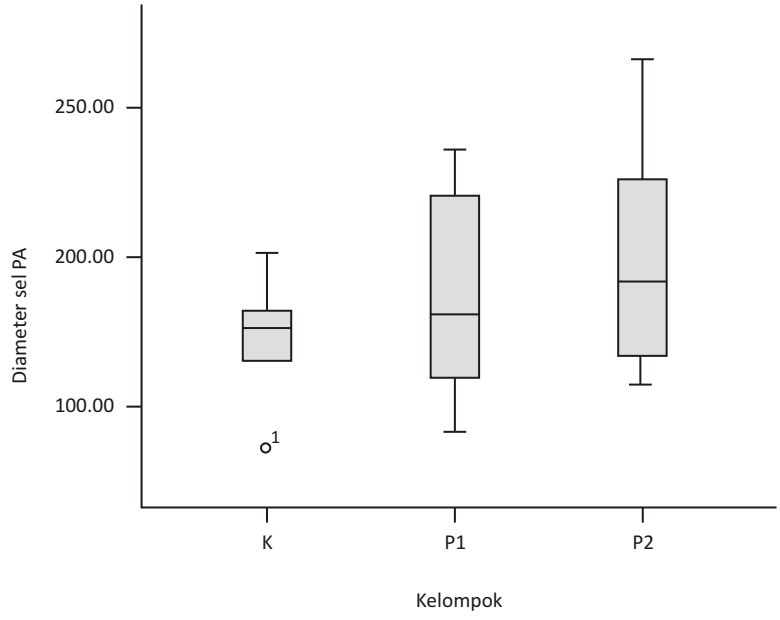

Figure 2. Diagram of Beta cell diameter between group

author conducted the experiment thoroughly.

Rat body weight
Rat body weight, blood glucose, and insulin level were assessed on a day before surgery, 5th postoperative day and 10th postoperative day (Table 1).

In this study, the body weight of rats in all study groups experienced a significant decrease on a day before surgery, 5th postoperative day and 10th postoperative day. Weight loss was found to be better in the P1 group (rats with sleeve gastrectomy procedure), then the P2 group (rats with sleeve gastrectomy and omentoplasty procedures), and then the control group.

Blood glucose levels in rats showed a decrease in the P1 and P2 groups but not in the control group which actually experienced a slight increase. The decrease in blood glucose was found to be better in the P2 group. In rat insulin levels, there was a significant difference in the mean insulin levels between the day before surgery, 5th postoperative day and 10th postoperative day.

Analysis Langerhan's Islet diameter
The diameter of the islets of Langerhans in each rat was measured and recorded at a day before surgery, 5th postoperative day and 10th postoperative day. It was found that the distribution of Langerhans Islet diameter data was normally distributed.

TABLE 2
HOMA Beta Value Analysis

Group	Median (min–max)	Normality Test	p
K	19,92 (19,20–20,99)	0,846¿*	0,004[K*]
P1	40,22 (37,76–48,59)	0,111¿*	
P2	43,11 (42,21–52,74)	0,007¿	

Description: *Significant; ¿Shapiro-Wilk; [K]Kruskal-Wallis

TABLE 3
Post Hoc Analysis on HOMA Beta Value

Group	Compared Group	p
K	P1	0.002[m*]
	P2	0.002[m*]
P1	P2	0.172[m]

Description: *Significant; [m]Mann-Whitney

TABLE 4
HOMA Beta Value and Islet Langerhans Cells Diameter Correlation

Variable	Median (min–max)	p	r	Description
Cell diameter	178,31 (136,69–265,39)	0,009[§*]	0,565	Significant, positive, moderate
HOMA β	41,23 (19,20–52,74)			

Description: *Significant; [§]Spearmann

Due to the normal distribution of the data, then the difference test is continued with the test One-Way ANOVA. This statistical test was conducted to determine whether there was a difference in the diameter of beta cells between groups in Figure 2.

In the one-way ANOVA test, a significance of p = 0.095 was obtained, which means that there was no significant difference between all groups in this study in terms of the diameter of the islets of Langerhans in all study groups. The beta cell diameter in both treatment groups was greater than control group, however, the difference is statistically not significant.

HOMA beta results analysis

In the HOMA beta value data, after the normality test using the Shapiro-Wilk test, the distribution of the HOMA beta data was not normally distributed (Table 2). Normality test result considered significant if p value > 0,05.

From the data on table 2, it can be seen that the HOMA beta value was found to be the highest in the P2 group (52,74) and was found to be lowest in the control group (19,20). Due to the non-normal distribution of the data, the different test was continued with the Kruskal Wallis test. This statistical test was conducted to determine whether there were differences in the HOMA beta data between the research groups. Kruskal-Wallis and Post Hoc test result considered significant if p value < 0,05.

From the results of the post-Hoc test, there were significant differences between the control group and treatment group 1 (0.002) and treatment 2 (0.002); there was a significant difference between the treatment group 1 and the control group (0.002) and a non-significant difference between the treatment group 1 and treatment 2 (0.172); there was a significant difference between the treatment group 2 and the control group (0.002).

Correlation analysis of HOMA beta values and the diameter of the islets of Langerhans

The HOMA beta values and the diameter of the islets of Langerhans in each rat were measured and recorded at

H+10 post with the mean beta cell diameter being 186.85 and a median of 178.31 while the mean value of HOMA beta was 37.10 and the median was 41.23.

In the HOMA beta value and beta cell diameter data, after the normality test with the Shapiro-Wilk test, the data distribution was not normally distributed, then continued with the non-parametric correlation test using the Spearman test (Table 4).

In the Spearman test, a significance of p = 0.009 was obtained, which means that there is a significant correlation and moderate strength (r = 0.565) of the relationship between the diameter of the islets of Langerhans and the HOMA beta value in this study.

DISCUSSION

Overweight and diabetes-associated obesity complicates long-term morbidity. The major chronic complications include micro/macrovascular disease, which causes an increased prevalence of coronary artery disease, peripheral vascular disease and stroke, and microvascular damage leading to diabetic retinopathy and nephropathy. Blood sugar control is essential in the management of Diabetes Mellitus.[9] In an effort to overcome insulin resistance, beta cells will increase insulin secretion, which is able to maintain a relatively normal glucose tolerance. Therefore, it is important to assess body weight, blood glucose and insulin levels in each DM patient in order to prevent further deterioration and complications.[10]

This study founds that insulin level on treatment groups are similar to those of Laiyuan et al, in their study of the effect of sleeve gastrectomy on DM rats, which reported that the weight loss of rats was found to be the best in the group of rats undergoing sleeve gastrectomy compared to the control group.[11] The rats fasting glucose and insulin levels also showed better results in the group of rats that underwent sleeve gastrectomy. Schauer et al, also stated that sleeve gastrectomy had a better effect on weight loss and glucose control than medication alone.[12]

Based on literature study, author believe that there are no significant literature that stated on how combination of ometoplasty and sleeve gastrectomy provide significant results in diabetic rats. While, this study showed remarkably results on blood glucose level parameter in diabetic rats that underwent sleeve gastrectomy and omentoplasty treatment.

Type 2 diabetes mellitus (T2DM) develops in response to multiorgan insulin resistance and inadequate insulin production from pancreatic cells. As has been noted in attempts to overcome insulin resistance, cells increase insulin secretion, resulting in hyperinsulinemia, which is able to maintain relatively normal glucose tolerance.[13] Insulin is a key hormone involved in glucose homeostasis as well as the release of chemical energy from food. Insulin is encoded by chromosome 11 and synthesized in the cells of the islets of Langerhans of the pancreas. The synthesis, intracellular processing, and secretion of insulin by cells is a characteristic pattern by which many other peptide hormones are produced.[14]

In this study, treatment group 1 (rats with sleeve gastrectomy procedure) affected beta cell diameter greater than the control group and treatment group 2 (rats with sleeve gastrectomy and omentoplasty procedures), but the difference was not statistically significant. The results of this study are in line with the study by Duoros et al, who reported no difference in beta cell mass in diabetic rats undergoing sleeve gastrectomy compared with controls.[15]

Likewise, the study by Camacho et al, who also stated that the mass of the islets of Langerhans showed no significant difference between diabetic rats treated with sleeve gastrectomy and Roux-en-Y gastric bypass compared to controls using the sham method, but neither group showed beta cell apoptosis.[16]

Camacho et al in their study stated that the mechanism for increasing morphology in beta cells could be caused by two mechanisms. First, that bariatric surgery causes food to reach the ileum more rapidly thereby increasing ghrelin secretion, this pathway also acts on -cell mass through the release of GLP-1, the -cell proliferative agent secreted by L-cells. the second mechanism is restriction of food transit in the jejunum, which indirectly causes a temporary modification of glucose tolerance, thereby stimulating beta cell proliferation due to high blood glucose.[16]

Seyfried et al, in their study of rats beta cell morphology after RYGB surgery, said that the expression of GLP-1 and PDX-1 (pancreatic duodenal homeobox-1) was found to be higher in the treatment group than the control group. This proves that PDX-1 expression is very important in the integration of GLP-1 receptor signals to regulate the growth, function and survival of cells. The increase in PDX-1 after bariatric surgery may be due to the release of GLP-1.[17]

Although there are no studies that combine omentoplasty and sleeve gastrectomy treatments on beta cell diameter, this study revealed that omentoplasty procedures gave a better effect on sleeve gastrectomy procedures as evidenced by the larger mean beta cell diameter than the control group and treatment group 1. This due to omentum properties of angiogenesis, mobility of pedicled omentoplasty and capillary ingrowth, resulting in an advantage in terms of survival and proliferation of the islets of Langerhans.[18]

Homeostatic model assessment (HOMA) is a method for assessing-cell function and insulin resistance (IR) from basal (fasting) glucose and insulin or C-peptide concentrations. This model has been widely used since it was first published. HOMA is one indicator to measure the level of strength of the islets of Langerhans that produce insulin. The greater the HOMA value, the better

the beta cell strength level. The HOMA-β calculation formula is (20 × Fasting insulin (mU/(L)) / (Fasting glucose (mmol/L)).[19]

The relationship between glucose and insulin under basal conditions reflects the balance between hepatic glucose output and insulin secretion, which is maintained by cyclical feedback between the liver and cells. Insulin resistance is a metabolic disorder characterized by elevated insulin levels. Insulin resistance increases mortality and morbidity due to metabolic syndrome, type II diabetes mellitus (DM) and cardiovascular disease.[20] A significant difference between the control group and treatment group 1 and treatment 2 showed that the function of insulin secretion by beta cells and blood glucose levels was higher. in both diabetic rats treated with bariatric procedures with and without omentoplasty.

The results of this study are similar to the study by Laiyuan et al, in his study of the effect of sleeve gastrectomy on glucose metabolism in rats, who reported that sleeve gastrectomy promotes better glucose homeostasis, as indicated by increased levels of GLP-1 in Sleeve Gastrectomy SG-treated rats compared to the control group; stimulates insulin secretion whereas GLP-1 levels stimulate insulin secretion; reduce fasting blood glucose levels, food intake and body weight; improve glucose tolerance; stimulates the growth of villi of the jejunum and ileum; and increased GLP-1 expression in the jejunum and ileum.[11] Laiyun et al stated that the mechanism underlying the metabolic changes produced by SG is due to an increase in postprandial GLP-1 levels and insulin sensitivity.[11] Specifically, the increase in glucose metabolism is further supported by increased expression of GLP-1 in the jejunal and ileal mucosa, which is consistent with increased plasma levels of GLP-1. Another mechanism, the hindgut hypothesis, suggests that incompletely digested food to the distal intestine after SG surgery causes greater GLP-1 secretion from L-cells, thereby increasing insulin action.[11]

Douros et al, in his study also found that cells showed greater sensitivity to glucose independent of food stimulation after SG. Second, the presence of increased insulin secretion contributes to the increased glucose tolerance seen in SG.[15] Although there has been no study combining omentoplasty and sleeve gastrectomy treatment on the HOMA beta value, this study revealed that omentoplasty gave a better effect on the sleeve gastrectomy procedure as evidenced by the higher mean HOMA beta value than the control group and the treatment group. High HOMA beta can trigger angiogenesis and capillary ingrowth, omentoplasty provides better vascularization of the pancreas so that the function of insulin secretion by the islets of Langerhans is getting better.[21]

In this study, there was a significant correlation with moderate strength of the islet of Langerhans diameter and HOMA beta values in rats. Where this shows that the morphology of the islets of Langerhans, especially cell diameter, has a synergistic effect on the function of beta cells in insulin secretion and blood glucose.

However, Duoros et al said that the morphology of beta cells (eg cell size and cell area consisting of - or cells, and the mass of - and cells) did not show differences in the research group, this indicated that the mass and morphology of beta cells did not contribute to differences in function. beta cells. Feng li et al, also stated in their study that although there was a significant increase in insulin in rats with SG, the morphology of beta cells remained unchanged.[15]

However, these results are in line with the study by Grong et al, who assessed the morphology of beta cells in rats after sleeve gastrectomy treatment reported that rats after SG treatment had lower fasting blood glucose levels than the duodenojejunostomy and control groups, where this result was in line with the assessment of the mass of the islets of Langerhans which was found to be significantly larger in the SG group. This is due to improved glycemic control, increased levels of GLP-1 and gastrin, two gastrointestinal hormones that function to increase the diameter and mass of beta cells.[22]

Although there are no related studies that combine omentoplasty and sleeve gastrectomy, as is known in this study, omentoplasty has a beneficial effect on sleeve gastrectomy procedures as evidenced by a larger mean beta HOMA value and better beta-cell diameter.

CONCLUSION

Sleeve Gastrectomy and Omentoplasty improve the HOMA Beta level in Sprague-Dawley rats induced by diabetes mellitus which was characterized by an increase in the mean HOMA beta value which was better than the control and sleeve gastrectomy alone.

Sleeve Gastrectomy and Omentoplasty did not affect the diameter of the Islets of Langerhans in Sprague-Dawley rats which was characterized by the absence of significant diameter changes in the islets of langerhans rats before and after treatment. The diameter of the islets of Langerhans and the HOMA beta values showed a significant correlation with a moderate strength relationship.

In conclusion, sleeve gastrectomy and pancreatic omentoplasty provide improvement of HOMA Beta value and Islets cell of Langerhans Diameter in Type 2 Diabetic Rats.

REFERENCES

1. Masayu Azizah, Fitri Ramadhanti, Agnes Rendowati. Gambaran Histopatologi Pankreas Mencit Diabetes Mellitus Setelah Pemberian Ekstrak Etanol Bonggol Buah Nanas

(Ananas comosus (L.) Merr). J Kesehat Saelmakers PERDANA [Internet]. 2019 Feb;2(1 SE-):53–8. doi:10.32524/jksp.v2i1.194 Available from: https://journal.ukmc.ac.id/index.php/joh/article/view/194
2. PERKENI. Pedoman Pengelolaan dan Pencegahan Diabetes Mellitus Tipe 2 Di Indonesia 2021 [Internet]. PB PERKENI; 2021. Available from: https://pbperkeni.or.id/wp-content/uploads/2021/11/22-10-21-Website-Pedoman-Pengelolaan-dan-Pencegahan-DMT2-Ebook.pdf
3. Tam CS, Xie W, Johnson WD, Cefalu WT, Redman LM, Ravussin E. Defining insulin resistance from hyperinsulinemic-euglycemic clamps. Diabetes Care [Internet]. 2012 Jul;35(7):1605–10. doi:10.2337/dc11-2339 Available from: https://pubmed.ncbi.nlm.nih.gov/22511259/
4. Elshall S, Hassan A, Ibrahim W, Hafez M, Erfan A. Study of Markers for Assessment of Insulin Resistance in Obese Children and Adolescents. J Adv Med Med Res [Internet]. 2021 Mar;89–95. doi:10.9734/jammr/2021/v33i430837 Available from: https://www.researchgate.net/publication/350132113_Study_of_Markers_for_Assessment_of_Insulin_Resistance_in_Obese_Children_and_Adolescents
5. Yu W, Zhou G, Fan B, Gao C, Li C, Wei M, et al. Temporal sequence of blood lipids and insulin resistance in perimenopausal women: the study of women's health across the nation. BMJ open diabetes Res care [Internet]. 2022 Mar;10(2). doi:10.1136/bmjdrc-2021-002653 Available from: https://drc.bmj.com/content/10/2/e002653
6. Phaniendra A, Jestadi DB, Periyasamy L. Free radicals: properties, sources, targets, and their implication in various diseases. Indian J Clin Biochem [Internet]. 2015 Jan;30(1):11–26. doi:10.1007/s12291-014-0446-0 Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4310837/
7. McGlone ER, Carey I, Veličković V, Chana P, Mahawar K, Batterham RL, et al. Bariatric surgery for patients with type 2 diabetes mellitus requiring insulin: Clinical outcome and cost-effectiveness analyses. PLoS Med [Internet]. 2020 Dec;17(12):e1003228. doi:10.1371/journal.pmed.1003228 Available from: https://pubmed.ncbi.nlm.nih.gov/33285553/
8. Abdallah E, Zakaria M, Fikry M, Abdelnaby M, Gado W, Elbaz SA, et al. Laparoscopic Sleeve Gastrectomy with T-Shaped Omentoplasty: Impact on the Early Postoperative Outcomes. Obes Surg [Internet]. 2020;30(10):3735–41. doi:10.1007/s11695-020-04743-6 Available from: https://pubmed.ncbi.nlm.nih.gov/32495075/
9. Cade WT. Diabetes-related microvascular and macrovascular diseases in the physical therapy setting. Phys Ther [Internet]. 2008 Nov;88(11):1322–35. doi:10.2522/ptj.20080008 Available from: https://pubmed.ncbi.nlm.nih.gov/18801863/
10. Chen C, Cohrs CM, Stertmann J, Bozsak R, Speier S. Human beta cell mass and function in diabetes: Recent advances in knowledge and technologies to understand disease pathogenesis. Mol Metab. 2017 Sep;6(9):943–57. doi:10.1016/j.molmet.2017.06.019
11. Li L, Wang X, Bai L, Yu H, Huang Z, Huang A, et al. The effects of sleeve gastrectomy on glucose metabolism and glucagon-like peptide 1 in Goto-Kakizaki rats. J Diabetes Res. 2018;2018. doi:10.1155/2018/1082561
12. Schauer PR, Bhatt DL, Kirwan JP, Wolski K, Aminian A, Brethauer SA, et al. Bariatric Surgery versus Intensive Medical Therapy for Diabetes - 5-Year Outcomes. N Engl J Med [Internet]. 2017 Feb;376(7):641–51. doi:10.1056/NEJMoa1600869 Available from: https://www.nejm.org/doi/full/10.1056/NEJMoa1401329
13. Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, et al. Pathophysiology of type 2 diabetes mellitus. Int J Mol Sci. 2020;21(17):1–34. doi:10.3390/ijms21176275
14. Röder P V, Wu B, Liu Y, Han W. Pancreatic regulation of glucose homeostasis. Exp Mol Med [Internet]. 2016 Mar;48(3):e219. doi:10.1038/emm.2016.6 Available from: https://www.nature.com/articles/emm20166
15. Douros JD, Niu J, Sdao S, Gregg T, Fisher-Wellman K, Bharadwaj M, et al. Sleeve gastrectomy rapidly enhances islet function independently of body weight. JCI Insight. 2019;4(6). doi:10.1172/jci.insight.126688
16. Pérez-Arana GM, Fernández-Vivero J, Camacho-Ramírez A, Díaz Gómez A, Bancalero de Los Reyes J, Ribelles-García A, et al. Sleeve Gastrectomy and Roux-En-Y Gastric Bypass. Two Sculptors of the Pancreatic Islet. J Clin Med [Internet]. 2021 Sep;10(18). doi:10.3390/jcm10184217 Available from: https://pubmed.ncbi.nlm.nih.gov/34575329/
17. Seyfried F, Miras AD, Rotzinger L, Nordbeck A, Corteville C, Li J V, et al. Gastric Bypass-Related Effects on Glucose Control, β Cell Function and Morphology in the Obese Zucker Rat. Obes Surg [Internet]. 2016;26(6):1228–36. doi:10.1007/s11695-015-1882-5 Available from: https://pubmed.ncbi.nlm.nih.gov/26377340/
18. Collins D, Hogan A, O'Shea D, Winter D. The Omentum: Anatomical, Metabolic, and Surgical Aspects. J Gastrointest Surg [Internet]. 2009 Apr;13:1138–46. doi:10.1007/s11605-009-0855-1 Available from: https://pubmed.ncbi.nlm.nih.gov/19291335/
19. Wallace TM, Levy JC, Matthews DR. Use and abuse of HOMA modeling. Diabetes Care. 2004;27(6):1487–95. doi:10.2337/diacare.27.6.1487
20. Diagnosis and classification of diabetes mellitus [Internet]. Vol. 32, Diabetes Care. 2009. p. S627. doi:10.2337/dc09-S062 Available from: https://diabetesjournals.org/care/article/32/Supplement_1/S62/25047/Diagnosis-and-Classification-of-Diabetes-Mellitus
21. Bartholomeus K, Jacobs-Tulleneers-Thevissen D, Shouyue S, Suenens K, In't Veld PA, Pipeleers-Marichal M, et al. Omentum is better site than kidney capsule for growth, differentiation, and vascularization of immature porcine β-cell implants in immunodeficient rats. Transplantation [Internet]. 2013 Dec;96(12):1026–33. doi:10.1097/TP.0b013e3182a6ee41 Available from: https://pubmed.ncbi.nlm.nih.gov/24056625/
22. Grong E, Kulseng B, Arbo IB, Nord C, Eriksson M, Ahlgren U, et al. Sleeve gastrectomy, but not duodenojejunostomy, preserves total beta-cell mass in Goto-Kakizaki rats evaluated by three-dimensional optical projection tomography. Surg Endosc. 2016 Feb;30(2):532–42. doi:10.1007/s00464-015-4236-4