Effects of Pancreatic Omentoplasty

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Effects of Pancreatic Omentoplasty on Diabetes Mellitus with Obesity after Sleeve Gastrectomy: An In Vivo Study

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A B S T R A C T

Background: DM, especially type 2 diabetes mellitus (DMT2), is closely related to obesity. Insulin resistance and inflammation that occur in obese patients can be treated with SG procedures. Post-SG weight loss can reduce the lipo apoptotic process and can improve the function of pancreas β cells. The omentum is rich in potential mesenchymal stem cells and is rich in anti-inflammatory cytokines, and various growth factors, so the omentoplasty procedure is believed to be able to provide a regenerating effect on the pancreatic tissue so that the performance of the pancreas can be optimal. **Methods:** An experimental study with 18 rats which were divided into control and treatment groups. The treatments were sleeve gastrectomy and pancreatic omentoplasty. Furthermore, analysis of body weight and levels of IL-10 and HOMA IR was carried out with the help of SPSS software version 25 univariate and bivariate. **Results:** There was a difference in mean body weight, levels of IL-10, and HOMA IR before and after treatment, p<0.001. **Conclusion:** Omentoplasty is effective in improving the condition of diabetes mellitus with obesity after sleeve gastrectomy surgery in vivo.

1. Introduction

DM, especially type 2 diabetes mellitus (DMT2), is closely related to obesity. This disease has an influence on the incidence of cardiovascular diseases, such as coronary heart disease, hypertension, sleep apnea, stroke, gastroesophageal reflux, gallbladder disease, malignancy, and non-alcoholic fatty liver disease. In obesity, there is a low level of chronic inflammation in adipose tissue. Adipose tissue produces and releases various pro-inflammatory molecules such as interleukin (IL)-1, interleukin (IL)-6, TNF-α, and IFN-γ. IL-6 are pro-inflammatory molecules that predominate in obese patients. IL-6 is expressed by fat cells and adipose tissue matrix. Its expression and secretion in visceral fat tissue are 2-3 times higher than in subcutaneous fat. IL-6 expression in adipose tissue and circulating IL-6 levels are positively correlated with obesity and lead to insulin resistance. During the inflammatory process in obese patients, IL-6 will continue to be secreted.[1,2]

Currently, there are several managements in the treatment of obesity among lifestyle interventions such as increasing physical activity and reducing calorie intake and medical therapy. One of the treatments for obese patients in the surgical field is by means of Bariatric Surgery. Until now, there are several techniques in bariatric surgery, including gastric bypass (GBP), adjustable gastric band (AGB), biliopancreatic diversion (BPD), and sleeve gastrectomy (SG). And gastric bypass (GBP). Of the many bariatric surgery methods, SG is the fastest growing and most significant method of weight loss.[3,4]

Insulin resistance and inflammation that occur in obese patients can be treated with SG procedures. Post-SG weight loss can reduce the lipo apoptotic process and can improve the function of pancreas β cells. However, in obese patients, IL-6 and TNF-α levels that increase during inflammation affect the performance of pancreatic β cells. An intervention is needed to reduce inflammation in order to improve the function of pancreatic β cells to treat T2DM. Omentoplasty is a surgical procedure that attaches the omentum to certain organs. In this situation, omentoplasty is performed on the pancreas. The omentum has unique biological functions, namely initiation of neovascularization, anti-inflammatory, and tissue regeneration. The omentum is rich in potential mesenchymal stem cells and is rich in anti-inflammatory cytokines, and various growth factors. So that the omentoplasty procedure is believed to be able to provide a regenerating effect on the pancreatic tissue so that the performance of the pancreas can be optimal.[5,6]

This study is an attempt to explore the effect of pancreatic omentoplasty in improving pancreatic function and performance in conditions of diabetes mellitus and obesity in vivo. This study is the first study and aims to evaluate the effect of pancreatic omentoplasty related to the benefits of reducing body weight, IL-10 levels, and HOMA-IR values in diabetes mellitus with obesity conditions in vivo.

2. Methods

This study is an experimental study with a pre-post-only approach with a control group design. A total of 18 rats (*Rattus norvegicus*) strain were included in this study and met the inclusion criteria in the form of the male sex, weight between 150-200 grams, and of age 8-10 weeks first, the rats were acclimatized for 7 days, then divided into 3 groups (control, P1, and P2) randomly, where each group consisted of 6 rats. Control group: Rats were induced by diabetes mellitus and obesity and were sham-operated. Group P1: Rats induced by diabetes mellitus and obesity and receiving SG treatment. Group P2: Rats were induced by diabetes mellitus and obesity and received SG treatment and Omentoplasty. After each treatment, the rats were given wound care for 2 weeks. This study has been approved by the Health Research Ethics Commission of the Faculty of Medicine, Diponegoro University, with the number No. 63/EC/H/FK-UNDIP/VII 2020.

The induction of diabetes mellitus with obesity is carried out by giving a diet high in calories and fat for 25 days to achieve obesity. And 3 days with intraperitoneal administration of streptozotocin (STZ) at a dose of 60 ml/kg BW dissolved in citrate buffer pH 4.5 and 120 ml/kg BW nicotinamide dissolved in PBS (phosphate buffered saline). The SG operation was performed by first anesthetizing rats using ketamine (dose of 0.015 mg/g BW) intramuscularly and chlorate (dose of 0.0025 mg/g BW) intraperitoneally. Rats were subjected to asepsis and antisepsis at the operating area. Then, an incision is made in the midline, starting from the xiphoid process to the umbilicus. The incision is further deepened layer by layer cutis, subcutis, rectus abdominis internus muscle, musculus abdominis externus, and peritoneum. Next, identify the stomach, perform gastric removal along the greater curvature, and treat bleeding. Then, gastric suturing was performed with polypropylene 3.0 and cleaned the abdominal cavity with warm 0.9% NaCl. Finally, cover the surgical wound layer by layer. Pancreatic omentoplasty operation was performed by anesthesia in rats using ketamine (dose of 0.015 mg/g BW) intramuscularly and chlorate (dose of 0.0025 mg/g BW) intraperitoneally. Rats were subjected to asepsis and antisepsis at the operating area. Then, an incision is made in the midline, starting from the xiphoid process to the umbilicus. The incision is further deepened layer by layer cutis, subcutis, rectus abdominis internus muscle, musculus abdominis externus, and peritoneum. Next, identify the omentum, then take the size of 1x1 cm. Next, suture the omentum on the head of the pancreas with polypropylene 3.0 and clean the abdominal cavity with warm 0.9% NaCl. Finally, cover the surgical wound layer by layer.

Before treatment and after wound care for 2 weeks, 2 mL of blood was evacuated from the retro-orbital vein to check the levels of IL-10 and HOMA-IR. Examination of IL-10 and HOMA-IR levels was carried out using the enzyme-linked immunosorbent assay (ELISA) method, according to the instructions and guidelines of the ELISA Kit manufacturer's manual.

After the data is collected, data cleaning, coding, and tabulation are carried out. All results were assessed by means ± standard deviation accompanied by a normality test (Shapiro Wilk) and data homogeneity test (Levene Statistic). The test used in this study is the dependent T test or paired T-test to assess differences between groups before and after treatment. The results are said to be meaningful if $p \leq 0,05$. Data analysis was performed using SPSS version 25 for Windows.

3. Results

Table 1 shows that the P2 group had the greatest weight loss compared to P1 and control. Groups P1 and K also experienced weight loss before and after being given treatment. Table 2 shows that the P2 group had the greatest decrease in IL-10 levels compared to P1 and control. The P1 and K groups also experienced a decrease in IL-10 levels before and after being given treatment. Table 3 shows that group P2 had the greatest decrease in HOMA IR compared to P1 and control. Groups P1 and K experienced an increase in HOMA IR before and after being given treatment.

Table 1. Comparison of body weight between treatment groups

Body weight	Groups		p	Lost of body weight
	Pre-test	Post-test		
K	252.90 ± 6.57	241.40 ± 6.75	<0.001*	11.50 ± 1.27
P1	254.90 ± 5.45	207.89 ± 5.28	<0.001*	47.89 ± 0.93
P2	256.50 ± 5.26	194.50 ± 4.81	<0.001*	62.00 ± 1.41

*Paired T-Test, p=0.05

Table 2. Comparison of IL-10 levels between treatment groups

IL-10	Groups		p	Reducing IL-10 levels
	Pre-test	Post-test		
K	113.73 ± 3.49	80.30 ± 2.97	<0.001*	33.43 ± 1.20
P1	116.51 ± 1.07	27.68 ± 1.90	<0.001*	88.84 ± 1.46
P2	116.93 ± 0.68	12.82 ± 1.09	<0.001*	104.11 ± 1.43

*Paired T-Test, p=0.05

Table 3. Comparison of HOMA IR between treatment groups

HOMA IR	Group		p	Δ HOMA IR
	Pre-test	Post-test		
K	38.54 ± 0.34	121.66 ± 4 .07	<0.001*	83.12 ± 4.35
P1	39.67 ± 0.83	59.51 ± 2.79	<0.001*	19.83 ± 2.39
P2	38.24 ± 0.21	34.34 ± 2,09	0.028*	-3.90 ± 2.08

*Paired T-Test, p=0.05

4. Discussion

The results of the study showed significant weight loss in all groups of obese and DM rats type II. This is consistent with previous studies that sleeve gastrectomy surgery can significantly reduce body weight through a restriction mechanism due to a reduction in gastric volume and reduced secretion of ghrelin, and increased secretion of intestinal hormones such as GLP-1 and PYY.[7,8] In the P2 group, where obese and type II DM rats underwent sleeve gastrectomy and pancreatic omentoplasty, they showed a greater weight loss than the P1 and control groups.

Decreased levels of IL-10 in the control group, sleeve gastrectomy group, and pancreatic sleeve gastrectomy-omentoplasty group were found to decrease in value during pre-test and post-test examinations. This is consistent with previous studies, which stated that levels of anti-inflammatory cytokines, including IL-10, were decreased in morbidly obese patients with sleep apnea.[9,10] In the group with SG treatment, there was a significant decrease in IL-10. Decrease in adipose tissue due to gastric malabsorption mechanism affects IL-10 levels. In the group with SG treatment and pancreatic omentoplasty, there was also a significant decrease in IL-10. IL-10 is known to play a role in inhibiting inflammation by increasing the immune response to inflammatory events. In experimental animals, IL-10 deficit causes worsening of the inflammatory process. Plasma levels of adipokines such as adiponectin and leptin and inflammatory cytokines such as proteins CRP, IL-6, IL-10, and TNF-α are affected by adipose tissue mass. In addition, in obese patients, IL-10 was negatively correlated with body mass index and fasting glucose levels. In a previous study, it was found that IL-10 was also negatively correlated with insulin produced by the pancreas in obese subjects. In this study, the value of IL-10 in the SG group and the SG + pancreatic omentoplasty group experienced a significant decrease, where GDP levels in both groups also experienced a significant decrease.[11-14]

The HOMA-IR value of male rats decreased significantly, indicating an improvement in insulin resistance. HOMA-IR is calculated from the value of insulin and GDP (Fasting Blood Sugar). In the control group, it was found that the level of GDP increased. In obesity, there is an increase in the accumulation of body fat. Increased accumulation of body fat will increase fasting blood sugar levels. The value of insulin in the control group also found a significant decrease. The abundance of adipose tissue in obesity affects metabolism by secreting hormones, glycerol, and other substances, including leptin, cytokines, adiponectin, and pro-inflammatory substances, and by releasing non-esterified fatty acids (NEFA). This NEFA release is associated with insulin sensitivity. Based on the values of GDP and insulin, HOMA-IR was obtained in male rats. A significant increase in the HOMA-IR value was obtained, indicating insulin resistance in male rats. After performing SG, it causes minimal malabsorption effects due to reduced gastric volume, faster gastric emptying time, and increased intestinal motility, which can increase intestinal hormones that trigger anorexia. Cutting the gastric fundus, in addition to reducing the size of the stomach and the capacity for food, also causes a decrease in the hormone ghrelin. This is because the hormone is most widely produced in the gastric fundus. The decrease in the hormone ghrelin results in a decrease in the patient's appetite. Decreased appetite has an effect on weight loss which will result in decreased lipoapoptosis of the pancreas, and pancreatic β cells that survive will increase. This results in an improvement in the ability of insulin to metabolize glucose. In the SG treatment group and pancreatic omentoplasty, there was also a decrease in the HOMA-IR value. In the pre-test and post-test groups, significant values were obtained. When compared with the SG group, this group had a significant difference in decline. Omentoplasty has a regenerating effect due to the presence of mesenchymal cells. Omentoplasty is believed to be able to stimulate tissue regeneration through neovascularization, and anti-inflammatory and immunoregulatory effects. This is a mutually supportive mechanism resulting in improved function of the pancreas, resulting in a decreased HOMA-IR value.[15-17]

5. Conclusion

Omentoplasty is effective in improving the condition of diabetes mellitus with obesity after sleeve gastrectomy surgery in vivo.

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