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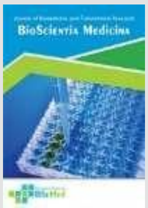

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The Effects of Pancreatic Omentoplasty on Weight Loss, Improvement of Triglyceride and Interleukin-1 Levels in Obese Rats with Type II Diabetes Mellitus Performed Sleeve Gastrectomy

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A B S T R A C T

Background: Obesity can trigger inflammation or inflammatory disease, which is one of the main features of adipose tissue dysfunction. Adipose secretes several different peptides called adipocytokines, which can induce several pro-inflammatory cytokines such as IL-6, TNF-α, and IL-1. Omentoplasty pancreas dan sleeve gastrectomy is a surgical technique that can treat overweight and metabolic syndrome in obesity and type II DM. This study aims to determine the effect of pancreatic omentoplasty on weight loss and improvement of triglyceride and interleukin-1 levels in rats obesity with type II diabetes mellitus performed sleeve gastrectomy. **Methods:** This study is an experimental study in vivo. Eighteen rats participated in this study and were grouped into the control group (KI) and the KII and KIII treatment groups. Triglyceride levels were assessed using the spectrophotometric method, and IL-1 levels were assessed using the ELISA method. Data analysis was carried out using SPSS univariate and bivariate. **Results:** The KII and KIII treatment groups experienced a decrease in body weight, triglyceride levels, and Interleukin-1 levels of rats after the treatment intervention, $p<0.05$. The KIII treatment group showed the most significant reduction in body weight, triglyceride levels, and Interleukin-1 levels compared to the KII treatment. **Conclusion:** Pancreatic omentoplasty is effective in reducing body weight, reducing triglyceride levels, and reducing IL-1 levels in obese rats with type II diabetes mellitus undergoing sleeve gastrectomy surgery.

1. Introduction

Obesity is one of the main risk factors for non-communicable diseases, where non-communicable diseases contribute >70% of premature deaths worldwide and are a major cause of premature mortality and disability. Obesity is a major health challenge because it increases risk factors for diseases such as type II diabetes mellitus, fatty liver, obstructive sleep apnea, hypertension, stroke, myocardial infarction, and several cancers. Obesity also reduces the quality of life, causes unemployment, unfavorable social impact, and causes a decline in socioeconomic productivity. The magnitude of the impact of obesity is a health problem that must be overcome. Obesity is strongly associated with dyslipidemia, mainly driven by the effects of insulin resistance and adiposopathy, which is characterized by increased triglyceride levels and decreased HDL levels. Insulin resistance causes enhancement lipolysis in adipose tissue due to the activation of hormone sensitive lipase (HSL) so that many FFA are released into the circulation and increase the secretion of very low-density lipoprotein (VLDL) in the liver. Circulating very low-density lipoprotein (VLDL) will be hydrolyzed into triglycerides (TG) with the help of lipoprotein lipase (LPL) so that insulin resistance will cause plasma clearance of TG-rich lipoproteins to be inhibited, resulting in hypertriglyceridemia. Obesity can trigger inflammation or inflammatory disease, which is one of the main features of adipose tissue dysfunction. Adipose secretes several different peptides called adipocytokines, which can induce several pro-inflammatory cytokines such as IL-6, TNF-α, and IL-1.[1-5]

The management of obesity consists of various therapies such as lifestyle modification, restricted diet, pharmacokinetics, and bariatric surgery. Despite acting as first-line therapy, nonoperative management is not a profitable method for obese patients because of poor adherence. Sleeve gastrectomy is one of the fastest-growing surgical techniques and is widely used because of its benefits for syndrome metabolic rate of severe obesity and a better risk of perioperative morbidity and mortality than other techniques. Technique Sleeve gastrectomy with the aim of cutting nearly 80% of the stomach, resection begins 3-6 cm from the pylorus cutting along the greater curvature to the gastric fundus to form a tube or banana. Mechanism Metabolically, sleeve gastrectomy is not known with certainty, but some explain that due to gastric mechanical restriction, decreased ghrelin levels due to fundus resection, changes in bile acid signals, hindgut effect causes weight loss due to reduced caloric intake, which ultimately improves adipose tissue and insulin sensitivity. The omentum is a broad layer of adipose tissue that is covered by the visceral peritoneum and hangs over the greater curvature of the stomach to the intraperitoneal organs. Omentum acts as an organ that has a role in controlling inflammation and promoting revascularization and tissue regeneration. Omental adipose tissue plays a role in local immunological responses and also contains a population of multipotent mesenchymal stem cells (MSCs) that facilitate tissue regeneration. Omentoplasty is a surgical procedure that attaches the omentum to certain organs to close the defect, repair tissue and improve portal arterial and venous circulation.[6-10] This study aimed to determine the effect of pancreatic omentoplasty on weight loss and improvement of triglyceride and interleukin-1 levels in obese rats with type II diabetes mellitus performed sleeve gastrectomy.

2. Methods

This study is an in vivo experimental study with a pre-post test approach with a control group design. The research subjects in this study were male rats (*Rattus norvegicus*) Wistar strain and around 6 weeks old. A total of 18 rats (each 6 rats/group) were included in this study, where the White Rats were grouped into 3 groups, namely group I: the control group, where the White Rats were induced by obesity and type II diabetes mellitus; Group II: Obese and type II diabetes mellitus rats have used sleeve gastrectomy; Group III: Obese and type II diabetes mellitus rats underwent sleeve gastrectomy and omentoplasty. Each rat was placed in its own cage with the temperature of the cage made at 25^{O}C, 55% humidity, and a 12:12 hour light-dark cycle. This study has received approval from the medical and health research ethics committee of the Faculty of Medicine, Universitas Diponegoro (No.118/EC/H/FK-UNDIP/XII/2020).

Each group was given a high-fat diet (comfeed pars 60%, flour 27.8%, cholesterol 2%, cholic acid 0.2%, lard 10%, and fructose 2 ml/head/day) for 4 weeks and then administration of injection of streptozotocin in sodium citrate buffer pH 4.5 intraperitoneal a single dose of 45 mg/kg BW. After 3 days, data collection was carried out pre-*test* and sleeve gastrectomy and omentoplasty surgery and maintenance for 10 days thereafter in analysis data *post-test*. The process of sleeve gastrectomy surgery is that rats have fasted for 10 hours before surgery, injection of ketamine at a dose of 0.5 mg/kgBB is carried out intramuscularly, abdominal hair is cleaned using hair clippers until the rat's skin is visible, asepsis and antisepsis of the operating area are carried out. Incision transversely starting from the xiphoid processus latera abdomen, deepen layer by layer cutis, subcutis, internal rectus abdominis muscle, external abdominis muscle, and peritoneum, identify gastrically, perform gastric removal along the curvatura major and treat bleeding, suture the stomach with polypropylene 3.0, clean the cavity abdomen with warm 0.9% NaCl, cover the surgical wound layer by layer. The surgical procedure for pancreatic omentoplasty was that the rats were fasted for 10 hours prior to the operation, injected ketamine at a dose of 0.5 mg/kgBB intramuscularly, the abdominal hair was cleaned using a hair shave until the rat's skin was visible, asepsis and antisepsis were carried out in the operating area, incision transversely from the xiphoid process to the lateral abdomen, deepen layer by layer cutis, subcutis, internal rectus abdominis, external abdominis muscles, and peritoneum, identify omentum and suture the omentum to the pancreas with polypropylene 3.0, clean the abdominal cavity with warm 0.9% NaCl, cover the surgical wound layer by layer. Measurement of triglyceride levels was carried out using the spectrophotometric method with the triglyceride FS kit®. IL-1 levels were assessed using the ELISA method using the Rat ELISA Kit Abclonal®. Data analysis was carried out using SPSS software version 21. Data analysis was performed univariately to describe the frequency distribution of each test variable. Bivariate analysis was carried out to determine the relationship between the test variables with a p-value <0.05.

3. Results

Table 1 presents a comparison of pre and post-test rats' body weight. The results of the study stated that in the KII and KIII treatment groups, there was a decrease in the weight of the rats after the treatment intervention, p<0.05. The KIII treatment group showed the most significant weight loss compared to the KII treatment.

Table 1. Comparison of pre-test and post-test rats' body weight.

Body weight	**Treatment**		**p-value***
	Pre-test	**Post-test**	
KI	252,90 ± 6,57	241,40 ± 6,75	0,001
KII	254,90 ± 5,44	207,80 ± 5,27	0,001
KIII	256,50 ± 5,25	194,50 ± 4,80	0,001

*Dependent T-test, p< 0,05.

Table 2 presents a comparison of pre and post-test rat triglyceride levels. The results of the study stated that in the KII and KIII treatment groups, there was a decrease in rat triglycerides after the treatment intervention, p<0.05. The KIII treatment group showed the most significant decrease in triglyceride levels compared to the KII treatment.

Table 2. Comparison of pre-test and post-test triglyceride levels.

Triglycerides	**Treatment**		**p-value***
	Pre-test	**Post-test**	
KI	134,29 ± 2,76	153,98 ± 3,17	0,001
KII	132,24 ± 1,93	114,86 ± 2,57	0,001
KIII	132,46 ± 3,75	94,25 ± 3,62	0,001

*Dependent T-test, p< 0,05.

Table 3 presents a comparison of Interleukin-1 levels in pre and post-test rats. The results of the study stated that in the KII and KIII treatment groups, there was a decrease in Interleukin-1 levels of rats after the intervention treatment, $p<0.05$. The KIII treatment group showed the most significant decrease in Interleukin-1 levels compared to the KII treatment.

Table 3. Comparison of Interleukin-1 pre-test and post-test levels.

IL-1	**Treatment**		**p-value***
	Pre-test	**Post-test**	
KI	91,38 ± 3,61	91,27 ± 4,06	0,897
KII	89,98 ± 3,12	73,67 ± 3,81	0,001
KIII	88,90 ± 2,73	60,20 ± 2,84	0,001

*Dependent T-test, p< 0,05.

4. Discussion

Sleeve gastrectomy surgery can reduce body weight significantly through restriction mechanisms due to reduced gastric volume and reduced ghrelin secretion, and increased secretion of intestinal hormones such as GLP-1 and PYY. In group KIII, where obese and type II DM rats underwent sleeve gastrectomy and pancreatic omentoplasty surgery, they showed greater weight loss than the other groups. This can be explained because the omentum can play a role in weight loss through the mechanism of restriction of leptin secretion mediated by CRP, IL-6, and activity-high lipolysis. Pancreatic omentoplasty will have the effect of reducing CRP and IL-6 levels which will increase leptin secretion and indirectly reduce body weight.[11-16]

Improvements in triglyceride levels in the group that underwent sleeve gastrectomy and pancreatic omentoplasty are related to the regeneration of pancreatic tissue by the effect of the omentum, which can increase activity insulin signaling in the pancreas thereby inhibiting lipolysis and reducing FFA secretion in plasma which is associated with reduced triglyceride hydrolysis. Improvements in interleukin-1 levels in the sleeve gastrectomy and pancreatic omentoplasty surgery group are related to weight loss which causes an increase in the hormone adiponectin so that adipocytokine secretion decreases. Reduced adipocytokine secretion leads to decreased induction of pro-inflammatory cytokines such as IL-6, TNF α, and IL-1 associated with a decrease in pro-inflammatory cytokines. This is in accordance with previous studies that omental stromal cells can reduce levels of pro-inflammatory cytokines such as IL-6, IL-1, and IL-12.[17-21]

5. Conclusion

Pancreatic omentoplasty is effective in reducing body weight, reducing triglyceride levels, and reducing IL-1 levels in obese white rats with type II diabetes mellitus undergoing sleeve gastrectomy surgery.

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