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EFFECT OF ADMINISTRATION OF RICE BRAN OIL EMULSION BEVERAGES ON TUMOR NECROSIS FACTOR-ALPHA (TNF-α) LEVEL

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ABSTRACT

Rice bran oil emulsion beverage is a functional food rich in antioxidants and beneficial for human health, particularly to prevent metabolic syndrome. Metabolic syndrome is defined by a waist circumference of > 90 cm and two additional criteria out of five, namely triglycerides (TG) > 150 mg/dL, HDL-C < 40 mg/dL, and/or 140/90 mmHg, blood pressure, and fasting blood sugar of 100 mg / dL. This research aimed to examine the level of tumor necrosis factor-α (TNF-α) after the intervention of taking rice bran emulsion and determine the parameter shifted on metabolic syndrome. This study was a parallel-group, double-blind study with randomized controlled trials. The subjects were divided into two groups: treatment and control. The first group (n=19) received two glasses of rice bran emulsion per day for four weeks, while the control group (n=17) received two glasses of placebo per day for four weeks. Different intakes of fat, iron, and vitamin B1 were present in the control group before and after the intervention (p=0.05). The data were analyzed using independent T-test samples against differences for each group from before and after interventions. The formulation of rice bran emulsion was prepared using bran oil, water, sugar ester, CMC, sucralose, salt, and flavor. The study demonstrated that TNF-α levels in both groups decreased from 6.8 ± 7.3 to 4.7 ± 0.6 (pg/dL) but were not significant (p>0.05). Nutrition changes influenced the intakes of fat, iron, and vitamin B1 but did not influence metabolic syndrome parameters of the treatment group. The level of nutritional adequacy-fat, iron and vitamin B1 pre-and post-intervention in both groups were significantly different. In conclusion**,** the levels of serum TNF-α on the treatment group had a decrease than those in the control group; however, it is not significant. Further study needs to be done to verify this finding.

Key words: TNF-α, metabolic syndrome, type 2 diabetes, nutritional intake, rice bran oil

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INTRODUCTION

Recently, the overall number of obesity cases has increased, particularly in developing countries, along with lifestyle and diet changes with high energy accompanied by a lack of physical activity. Indonesia's nutritional problems have shifted from malnourishment and nutrient shortages to overweight or obesity. The prevalence of national obesity tended to increase based on basic health research data [1], including data in 2013. The proportion of male obesity with an index of body mass (BMI) > 25, aged 18, rose from 13.9% to 19.7%. Male obesity increased from 14.8% to 32.9%, while central abdominal obesity increased from 18.8% to 26.6% in males, and females increased by 8% [1].

The increased prevalence of obesity has led to an increase in the number of Non-Communicable Disease (NCD) patients associated with insulin resistance, such as pre-diabetes, impaired glucose tolerance, diabetes mellitus, hypertension, and heart disease. In individuals with obesity, increased intracellular free fatty acid causes uncoupling of mitochondria and β oxidation, resulting in increased compound-free radicals called reactive oxygen species (ROS) [2]. High-fat diet causes increased ROS production, resulting in increased production of adipocytokines, namely, increased production of individual biological molecules and decreased adiponectin production resulting in the development of metabolic syndrome [3].

Reaven [4] first introduced metabolic syndrome in 1988 as a complex disorder associated with multiple cardiovascular risk factors, with each component of the risk factors having the ability to induce the incident individually. Weight gain is a predisposing factor for two major metabolic syndrome components, namely obesity and insulin resistance. Increased central obesity must be prevented to avoid cardiovascular disease, particularly in people with a family history of type 2 diabetes mellitus (DMT2), hypertension, and coronary heart disease, or atherogenic dyslipidemia, such as low levels of HDL-cholesterol (HDL-C) and hypertriglyceridemia [4,5].

High-density lipoprotein-C has molecules that may inhibit lipid oxidation. High-density lipid-cholesterol levels may decrease as a result of oxidative stress. Its capacity to remove cholesterol from peripheral tissues is inhibited by oxidative stress, such as excessive consumption of fat and carbohydrates, obesity, and increased inflammatory chronicity characterized by increased tumor necrosis factor (TNF-□). Therefore, maintenance must be either in the form of the quantity or quality of HDL-C. If it goes wrong, the cardiovascular disease develops [6,7].

Antioxidants in rice bran oil enhance the body's levels, potentially bringing a damper on ROS and oxidative stress. Antioxidants can reduce the oxidation status by adding electrons and capturing the redox homeostasis. In this way, antioxidants can suppress the chain reactions of free radical formation and ultimately prevent damage from oxidative cells, DNA, and tissues to prevent diabetes mellitus and cardiovascular disease [8].

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There are currently plenty of functional food ingredients that contain bioactive compounds that are useful for improving body functions to prevent disease. Some studies have shown that bioactive compounds of fiber-containing fruits and vegetables rich in antioxidants benefit health. Gamma oryzanol is one of the bioactive compounds in functional foods. Oryzanol in rice bran oil has been scientifically proven to improve underlying cholesterol and serum LDL levels for obese people [6]. Scientific evidence suggests an antioxidant-rich diet can protect the body against inflammation and obesity in metabolic syndrome [9,10]. This research aims to study the diet and serum levels of TNF-α before and after the administration of rice bran oil emulsion. In addition, the metabolic syndrome parameters were determined as well.

MATERIALS AND METHODS

Research Design

The study was a double-blind, randomized, placebo-controlled trial conducted in Mintohardjo Navy Hospital, Jakarta, Indonesia.

Materials

The formulation of rice bran emulsion was rice bran oil obtained from The Thai Company (Thailand) and sugar ester obtained from Bratachem, Indonesia, carboxymethyl cellulose (CMC), sucralose, salt, flavor, and water. The rice bran oil, water, sugar ester, and CMC were mixed for 30 minutes with a homogenizer at 2,000 rpm. After incorporating flavor, sucralose and salt, the homogenizer stirred the mixture for 30 minutes at 2,000 rpm. The emulsion was pasteurized for 30 minutes at 30°C and then packaged into tightly closed bottles. The amount administered was equivalent to 57.6 mg γ-oryzanol.

Subjects

Subjects were males with metabolic syndrome and a waist circumference ≥90 cm. The subjects were selected based on the criteria of metabolic syndrome by the International Diabetes Federation 2006, which are having a waist circumference > 90 cm and having two other criteria out of the five, namely triglycerides (TG) level > 150 mg/dL, HDL-C < 40 mg/dL, and/or 140/90 mmHg blood pressure and fasting blood sugar of >100 mg/dL. Subjects were randomly divided into two groups; 19 people were included in the treatment group and 17 people for the control group. The two glasses of rice bran oil emulsion or placebo were administered to the subjects on a daily basis in the morning and afternoon for four weeks. Figure 1 shows the selection flow of the subjects.

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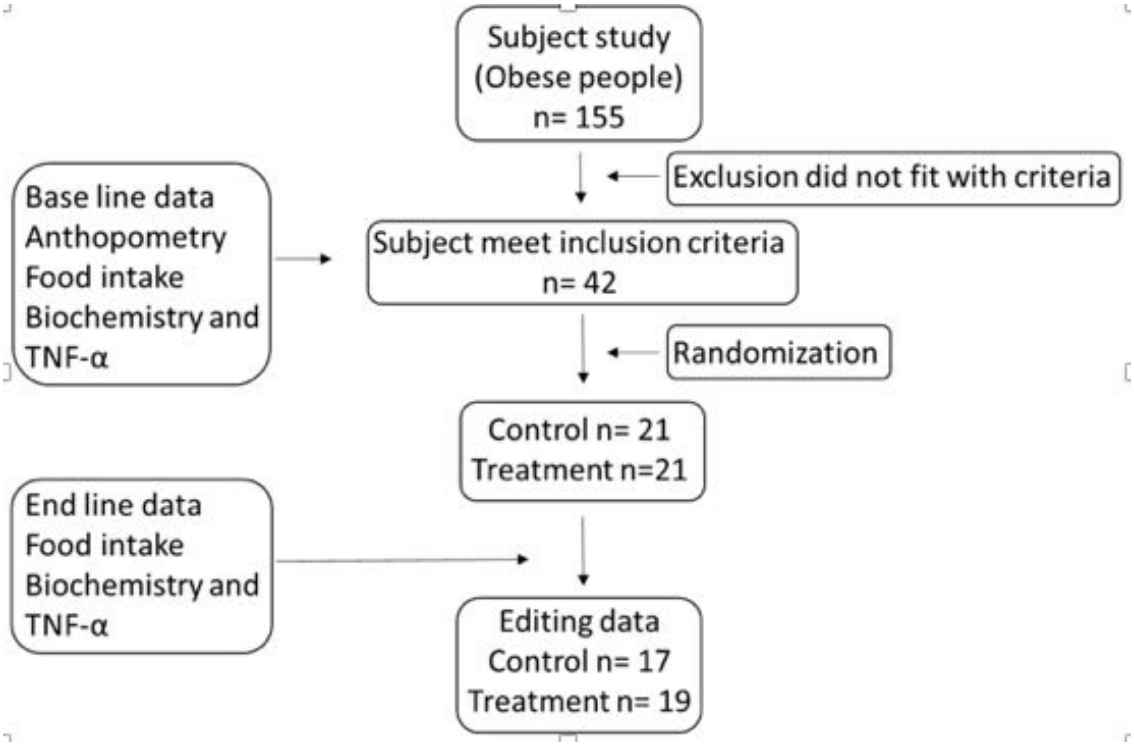

Figure 1: Selection Flow of Subjects

Ethical Approval

Prior to data collection, each subject was given a general description of the research purpose and benefits as well as the confidentiality of all data. Subjects who fulfilled the criteria for inclusion and were willing to follow the research activities provided signed informed consent. The research was approved by the ethical research committee of the University of Indonesia's Research Ethics Committee of the Faculty of Medicine with ethical review number: 870/UN2.FI / ETIK/2014.

Data Collection

During the study, nutrition education covered the consumption pattern. The subject was required to fill in dietary questionnaires and provide information on abdomen circumference, weight loss, and height. Venous blood collected by a paramedic in 2016 was used to evaluate the criteria for the metabolic syndrome.

The quality control of the data was carried out by contacting the subject by telephone each week, calibration of measuring instruments, and the collection of blood by experts. Bodyweight was measured and venous blood collected for TNF-α analysis after four weeks.

Serum analysis for TNF-α was undertaken at the University of Indonesia's Faculty of Laboratory Medicine by immunoassay ELISA kit D & DTA00C (USA) TNF-α.

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Data Analysis
Independent T-test was conducted to analyze the difference before and after the intervention in each group using the significance value (p=0.05). The data were not normally distributed, and the mean scores were analyzed using the Mann-Whitney test.

RESULTS AND DISCUSSION

Biochemical characteristics of the subjects based on the parameters of Metabolic Syndrome
Seventy-eight percent of subjects had elevated concentrations of blood TAG (>150 mg/dL), and 81.0 percent with low HDL-C (some 40 mg/dL) {**Table 1**}. Most subjects had glucose levels <100 mg/dL. Systolic blood pressure was largely in the normal category (≤120 mmHg), while the majority of the diastolic blood pressure above the normal category.

Adequacy and nutrition intake levels of the control and treatment group
Table 2 shows that there was a significant difference between the intake of fat, iron, and B1 vitamins before and after the intervention in the control group ($p \leq 0.05$). On the other hand, for the treatment group, there was no difference in nutrient intakes ($p \geq 0.05$). There was a significant difference between the nutritional adequacy of fat, iron, and B1 vitamins from before and after intervention in the control group with $p \leq 0.05$. There was no significant difference in nutritional adequacy levels from before and after the intervention for the treatment group with $p \geq 0.05$.

The study of the intervention products against TNFα levels of serum
The mean value of serum TNF-α levels in the control group before the intervention was lower than the treatment group (Table 2). After the intervention, the average levels of serum TNF-α in the treatment group were lower than those of the control group. The serum TNF-α levels between groups were not significant.

Nutrition Characteristics of the subject
The subject's features from the data suggest elevated concentrations of TG and diastolic stress, low concentrations of HDL-C, moderate levels of fasting blood sugar, and normal systolic blood pressure. All subjects had metabolic syndrome because they had ≥90 cm waist circumference that became the primary determinant. Central obesity with a waist circumference of ≥90 cm can trigger glucose resistance in metabolic syndrome, which can lead to the occurrence of certain illnesses, such as hypertension, type 2 diabetes, and coronary disease with increased body mass index and visceral fat [11]. Central obesity and visceral fat can induce proinflammatory adipokines, including the secretion of TNF-α, accompanied by a decrease in adiponectin [12]. It can contribute to an increase in the function of the heart pumping oxygen throughout the body, inducing stress [13].

There was no significant difference between the control and intervention groups in the nutritional intake of fat, iron, and vitamin B1, indicating that nutrition impacts did not influence the parameters treatment groups. Furthermore, this also indicates that the amount of dietary adequacy is adequate [1].

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The interplay of Rice Bran Emulsion at TNF-α level

Rice bran emulsion may have played a part against TNF-α levels, although it was not significant. These levels suggest that an intake of two glasses of rice bran emulsion beverages per day with an average of 57.6 mg oryzanol might deter a respiratory syndrome and eventually avoid cardiac illness, but more research is needed. Rice bran oil comprises not only oryzanol but also polyunsaturated fatty acids (n-3 PUPA). The consumption of n-3 PUPA is beneficial for patients with inflammatory illnesses with declining serum concentrations of TNFα and IL-6 [14,15]. Trebble *et al*. [16] stated that the production of TNFα and IL-6 decreased with increasing intake of n-3 PUFA in healthy men.

Acute inflammation in the body is related to cytokines, such as interleukin and C-reactive protein. Cytokines stimulate the liver to form proteins called acute phase proteins, including C-reactive protein and complement. The acute inflammatory response is an early response against inflammation. In some circumstances, when the process of acute inflammation is ineffective, it will develop into a chronic condition. Chronic inflammation will recruit TNF-α Cytokines since TNF-α plays an important role at the onset of insulin resistance in obesity and metabolic syndrome [17]. The levels of serum TNF-α will be increased in the case of chronic inflammation [18]. This pathway arises in blood vessels induced by elevated concentrations of serum triacylglycerol and cholesterol and a cardiac illness may develop.

Another study on inflammatory biomarkers in rats was conducted by Maigoda *et al*. [19] by administering food containing antioxidants. The findings of the study showed a decline in the inflammatory marker of TNF-α after the intervention. However, there was no significant difference between treatment groups after the intervention [19].

CONCLUSION

Rice bran emulsion did not show significant cardiac protection in the metabolic syndrome compared with the control group, which is defined by the reduction in TNF-α serum levels owing to its rich antioxidant content. This study implies that rice bran emulsion administration is not recommended for a duration of one month. Further study with a larger sample should be carried out, and the period of administration extended. In addition, the effect of the formulation of ingredient preparation on the absorption of rice bran emulsion should also be clarified. The limitation of this study was the difficulty of finding obese people with metabolic syndrome.

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Conflict of interest

The author declares no conflict of interest.

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Table 1: Biochemical characteristics of the subject regarding the parameters of the Metabolic Syndrome

Variable	*Cut off points*	*n (36 people)*	*%*	*Mean±SD*
TG (mg/dl)	≤ 150	8	22	217.3±106.8
	> 150	28	78	
HDL (mg/dl)	≤ 40	29	81	33.5±7.1
	> 40	7	19	
Glucose (mg/dl)	≤ 100	21	58	93.3±31.1
	> 100	15	42	
Systolic (mmHg)	≤ 120	21	58	127.8±16.1
	> 120	15	42	
Diastolic (mmHg)	≤ 80	5	14	85.8±9.1
	> 80	31	86	

Table 2: Intake and the level of adequacy of nutrients regarding a control and treatment group

		Control			*Treatment*		*p**
		Before	*After*	*p**	*Before*	*After*	
Energy (Kcal)	Intake	1469±478.6	1618±405.3	0.19	1367±362.0	1397±317.2	0.741
	% RDA	57	63		54	55	
Protein (g)	Intake	43.5±19.2	51.5±15.4	0.06	41.0±9.2	45.5±9.6	0.114
	% RDA	67	79	0.06	63	70	
fat (g)	Intake	40.5±22.7	49.74±15.2	0.032*	37.2±14.1	39.9±12.3	0.409
	% RDA	57	70	0.029*	53	56	
Carbohydrate (g)	Intake	228.8±67.8	232.5±61.0	0.82	213.1±74.5	207.35±59.26	0.721
	% RDA	60	61		56	54	
Calcium (mg)	Intake	261.6±132.7	240.2±116.1	0.56	194.8±115.7	240.88±149.43	0.349
	% RDA	26	24	0.56	19	24	
Phosphorus (mg)	Intake	453.4±190.5	456.4±214.7	0.96	395.3±127.7	427.69±149.9	0.50
	% RDA	302	304	0.96	264	285	
Iron (mg)	Intake	7.8±3.3	10.8±4.1	0.00	8.9±4.1	9.74±3.97	0.48
	% RDA	61	83	0.00	69	75	
Vitamin A (mcg)	Intake	876.0±958.3	451.8±322.8	0.11	497.4±334.2	764.01±1192.4	0.35
	% RDA	146	75		83	127	
Vitamin B1 (mg)	Intake	0.7±0.5	1.2±0.8	0.02	88.0±0.6	1.01±0.82	0.59
	% RDA	47	81		59	69	
Vitamin C (mg)	Intake	27.5±25.3	22.8±23.9	0.63	22.6±26.8	32.13±31.74	0.36
	% RDA	31	25	0.63	25	36	
PUFA (g)	Intake	0.5±1.7	1.5±3.4	0.33	0.4±0.4	0.54±0.85	0.66
	% RDA	3	8		2	3	

*Paired t-test (p<0.05) Recommended Dietary Allowance: RDA

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Table 3: Average levels of serum TNF-α before and after the intervention

Subject Group	*TNF-α serum concentration (pg/dL)*		
	Before The Intervention	*After The Intervention*	*Difference*
Control Group	6.6 ± 4.1	4.9 ± 0.9	-1.7 ± 4.3[a]
Treatment Group	6.8 ± 7.3	4 .7 ± 0.6	-2.1 ± 7.1[a]

Figures followed by the same letters in the different row showed no significant difference between groups (p>0.05)

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