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Response of TNF-α Levels and Blood Glucose Levels after Acute High-Intensity Intermittent Exercise in Overweight Women

Respuesta de los niveles de TNF-α y niveles de glucosa en sangre después del ejercicio agudo intermitente de alta intensidad en mujeres con sobrepeso

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Abstract. Sedentary behavior is a lifestyle that plays a role in the pathophysiology of obesity or overweight. TNF-α is an inflammatory cytokine that can affect glucose metabolism and can trigger insulin resistance. Acute HIIE is exercise with alternating periods of high-intensity exercise and periods of active recovery. The purpose of this study was to examine the changes of TNF-α and blood glucose levels after acute HIIE in overweight women. Subjects were overweight women, divided into 2 groups (K1=control group and K2=experimental group; n=7) with a body mass index between 23.00 and up to 24.99 kg/m^2. The acute protocol of HIIE with ergocycle consisted of a 3-minute warm-up (starting at 40 rpm), core exercise for 60 s at 80%-90% of HRmax, interspersed with 60 s of active recovery (40 rpm), and cool-down for 2 minutes. The pre-test was performed before treatment and the post-test was performed 60 minutes after treatment. Serum TNF-α levels were measured by the human enzyme-linked immunosorbent assay (ELISA) method. Blood glucose changing levels were taken by finger prick. The result showed that the change of TNF-α (the difference of pre and post) was a significant decrease in the K1 and K2 group ($p<0.05$), and the K2 group less decrease compared to K1. Blood glucose was significant ($p<0.05$). This study can be concluded that the TNF-α level is unchanged and the blood glucose levels is increase in overweight women with sedentary behavior performing acute HIIE.

Keywords: Interval exercise; TNF-α; Glucose; Overweight; sedentary lifestyle.

Resumen. El comportamiento sedentario es un estilo de vida que desempeña un papel en la fisiopatología de la obesidad o el sobrepeso. El TNF-α es una citoquina inflamatoria que puede afectar al metabolismo de la glucosa y puede desencadenar la resistencia a la insulina. El HIIE agudo es un ejercicio con periodos alternados de ejercicio de alta intensidad y periodos de recuperación activa. El propósito de este estudio fue examinar los cambios en el TNF-α y los niveles de glucosa en sangre después de un HIIE agudo en mujeres con sobrepeso. Los sujetos eran mujeres con sobrepeso, divididas en 2 grupos (K1=control y K2=experimento; n=7) con un índice de masa corporal entre 23,00 y hasta 24,99 kg/m^2. El protocolo agudo de HIIE con ergociclo consistió en un calentamiento de 3 minutos (comenzando a 40 rpm), ejercicio central durante 60s al 80%-90% de la FCmáx, intercalado con 60s de recuperación activa (40 rpm), y enfriamiento durante 2 minutos. La prueba previa se realizó antes del tratamiento y la prueba posterior se realizó 60 minutos después del tratamiento. Los niveles séricos de TNF-α se midieron mediante el método de ensayo inmunoabsorbente ligado a enzimas (ELISA) humano. Los niveles de glucosa en sangre se tomaron mediante una punción capilar en el dedo. El resultado mostró que el cambio de TNF-α (la diferencia de pre y post) fue una disminución significativa en el grupo K1 y K2 ($p<0,05$), y el grupo K2 menos disminución en comparación con K1. La glucosa en sangre fue significativa en el grupo K1 ($p<0,05$). Este estudio puede concluir que el nivel de TNF-α no cambia y los niveles de glucosa en sangre aumentan en mujeres con sobrepeso con comportamiento sedentario que realizan HIIE agudo.

Palabras clave: Ejercicio a intervalos; TNF-α; Glucosa; Sobrepeso; Sedentarismo.

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Introduction

Sedentary lifestyle in women is usually accompanied by overeating and a decrease in energy output. The consequence of less energy being burned from the body makes the remaining energy excess be stored as fats which lead to overweight, and then obesity. Overweight cases increased 20% in men and 23% in women in 1975 (As'ad, 2022). A high-fat accumulation in overweight person can cause an increase in the production of oxidative stress (Vigriawan et al., 2022) and increase the synthesis of proinflammatory cytokines, such as interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and IL-1β. Overweight and physical inactivity are associated with low-grade chronic inflammation. Chronic low-grade inflammation is one of the main metabolic changes associated with excessive caloric intake and adipose tissue formation.

An excess of adipose tissue in overweight and obese people can lead to insulin resistance (IR) (Cossio-Bolaños et al., 2020; Van Der Kolk et al., 2019). Adipose tissue produces and secretes cytokines such as TNF-α. Adipose tissue excess is also associated with increased inflammatory markers such as C-reactive protein (CRP), TNF-α cytokine, and IL-6. Adipose tissue undergoes hypertrophy and macrophage infiltration, causing chronic low-grade inflammation that continues to cause insulin resistance. TNF-α functions as a local initial mediator in the inflammatory process as well as an initiator of the systemic acute phase response (Ayubi et al., 2022). TNF-α interferes with insulin signaling indirectly and causes insulin resistance in several tissues (Susantiningsih & Mustofa, 2018). Increased TNF-α in overweight person is associated with insulin resistance in muscle and vascular

tissue. When there is an insulin resistance (insulin insensitivity), the glucose uptake will diminish and lead to an increase of blood glucose level (Hayes, 2020). Glucose is the predominant source of energy in exercise. When there is a condition that hinder glucose entering cells, it will lead to several health problems such as metabolic disorder that can cause a person to develop diabetes and heart disease (Salvador Soler, 2019).

Exercise has been known to contribute to lowering the risk of health problems in sedentary lifestyle and behavioral problem such as Attention Deficit Hyperactivity Disorder (ADHD) (Garzón Mosquera, 2021; Suárez Manzano, 2022). Acute High-Intensity Intermittent Exercise (HIIE) can increase energy expenditure. Exercise and physical activity also play a role in regulating the level of systemic inflammation because regular muscle contraction can suppress pro-inflammatory activities such as TNF-α (Kusnanik, 2022) through the release of myokines and cytokines. Acute HIIE has gained popularity as a time-saving exercise strategy, offering similar physiological benefits compared to continuous moderate-intensity, especially in patients with cardiometabolic disorders (Ferrandi et al., 2018; Segovia & Gutiérrez, 2020). Some studies focused on normal weight (not overweight) women. According to Dorneles (2016), acute HIIE (85-90 HR max, 10 intervals for 1 minute, interspersed with 75 seconds of recovery) using a treadmill ergometer (immediate post) can cause an increase of anti-inflammatory effects in overweight men. Obese male subject who did acute HIIE on a treadmill (10x60 seconds at 90% HRmax) interspersed with 60 seconds of active recovery showed an increase in anti-inflammatory effect (De Souza et al., 2018). However, the effect of acute HIIE (the ergocycle mode) on serum TNF-α level and blood glucose level in overweight women was unclear. Therefore, it is necessary to conduct a study of acute HIIE using the ergocycle method to create new workout variations that are more timesaving. The aim of this study was to analyze the effect of HIIE in minimizing the increase in TNF-α cytokines and blood glucose in overweight sedentary women with time-saving exercise. Ergocycle exercise was chosen to reduce the risk of injury that is more likely to occur in treadmill exercise.

Materials & Methods

Study Design

This study used cross-sectional experimental research with randomized pre- and post-test control group design. There were 2 groups in this study: the control group (without intervention/K1) and the experimental group (with acute HIIE/K2).

Participants

The research subjects were women aged 21-30 years old with BMI 23.1-24.99 (Asia Pacific) and sedentary activity category based on Questionnaire Adolescent Sedentary Activity Questionnaire (ASAQ) [Low (< 2 hours/day)]. The subjects were divided into 2 groups, control group (did not performed HIIE) and experimental group (performed HIIE). The sample size in each group was 7 females.

The inclusion criteria were women with low physical activity (less than 2 hours/day) and no physical exercise program; did not use anti-inflammatory drugs; were not in the pregnancy or menstrual phase; and did not have heart disease, hypertension, and kidney disease. The exclusion criteria in this study were women who were using non-steroidal anti-inflammatory medicine and had heart disease, hypertension, or kidney problem, pregnant women, and menstruating women.

In order to homogenize the status of the participants, before performing this study, all participants were asked to avoid meal and energy drink (such milk, tea, coffee) for about 12 hours. However, water was still allowed.

Blood sample was drawn from the median cubital vein. Blood sampling was done twice, when in fasting condition and 1 hour after the treatment was completed.

HIIE Protocol

The protocol of acute HIIE with ergocycle was: 1) Warming-up in for 3-min (start at 40 rpm); 2) The core exercise for 10 sets of 60 seconds at 80%-90% HRmax interspersed with 60 seconds of active recovery (40 rpm); 3) Cooling down for 2-min (De Souza et al., 2018) (Heydari, Freund, & Boutcher, 2012). This HIIE protocol was a single bout of exercise.

Blood Analysis

Blood samples were obtained in two session. The first session was before exercise under fasting condition (10-12 hours of fasting) and the second was 1 hour after HIIE. TNF-α serum was taken from an antecubital vein and measured by ELISA procedure using BT LAB E0082Hu, whereas blood glucose was taken through capillary puncture on a finger with a glucometer (Easy Touch GCU) (Abdelmotaleb, 2017). The collected samples were immediately transferred into blood collection tubes containing ethylenediaminetetraacetic acid (EDTA) for centrifugation. After centrifugation, serum was analyzed at the Blood Analysis Laboratory of the Airlangga University Hospital.

Data Analysis

The results of the data were analyzed using SPSS software.The Shapiro-Wilk Test was used for normality test. Levene's Test was applied for homogeneity test. If the data were normally distributed, paired t-test and independent test would be used, otherwise the Wilcoxon signed-rank test and the Mann Whitney u-test would be used.

Ethics

This research had received ethics approval from the Health Research Ethics Committee, Faculty of Medicine, Airlangga University, Surabaya, Indonesia with approval number 246/EC/KEPK/FKUA/2021.

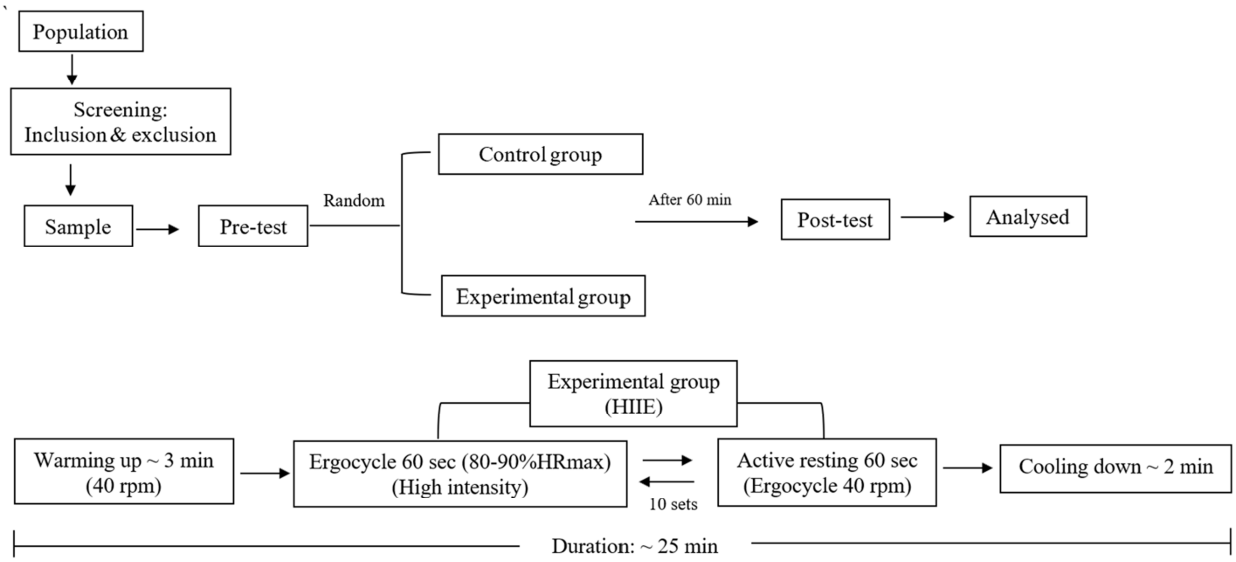

Figure 1. Research design

Table 1.
The characteristics of the subjects

Variable	Group	n	Mean ± SD	Shapiro-Wilk (p)	Independent T-Test (p)
Age (years)	K1	7	22.710 ± 1.799	0.292	0.187
	K2	7	24.000 ± 1.633	0.118	
Weight (kg)	K1	7	61.343 ± 5.564	0.580	0.151
	K2	7	57.371 ± 3.983	0.116	
Height (m)	K1	7	159.000 ± 6.055	0.369	0.197
	K2	7	155.000 ± 4.830	0.731	
BMI (kg/m^2)	K1	7	24.197 ± 0.558	0.358	0.387
	K2	7	23.914 ± 0.620	0.511	

K1=control group; K2=experimental group (HIIE)

The mean TNF-α levels in control and experimental groups decreased (Table 2). Since TNF-α was significantly different at pre-test, the delta or difference between pre-test and post-test was also analyzed. There were significant differences between groups ($p<0.05$).

Table 2.
TNF-α levels

Variable	Group	n	Mean ± SD (pg/mL)	Shapiro-Wilk (p)	Independent T-Test (p)
Pre-Test	K1	7	80.777 ± 18.084	0.845	0.006*
	K2	7	54.270 ± 10.891	0.868	
Post-Test	K1	7	51.948 ± 5.825	0.561	0.628
	K2	7	49.479 ± 11.788	0.329	
Delta	K1	7	-28.829 ± 15.304	0.539	0.025*
	K2	7	-4.791 ± 19.654	0.194	

K1= control group; K2 =experimental group (HIIE)

The blood glucose level decreased in the control group and increased in the experimental group

Table 3.
Blood glucose levels

Variable	Group	n	Mean ± SD (pg/mL)	Shapiro-Wilk (p)	Independent T-Test (p)
Pre-Test	K1	7	114.570 ± 8.696	0.201	0.593
	K2	7	111.710 ± 10.688	0.855	
Post-Test	K1	7	108.710 ± 4.751	0.532	0.107
	K2	7	117.430 ± 12.340	0.411	
Delta	K1	7	-5.860 ± 4.413	0.867	0.003*
	K2	7	5.71 ± 6.726	0.541	

K1= control group; K2= experimental group (HIIE)

Result

Based on the of result of Table 1, the characteristics of the research subject did not exhibit significant difference ($p>0.05$). All variables also showed normal data ($p>0.05$). There was an significant change in blood glucose level between group (Table 3).

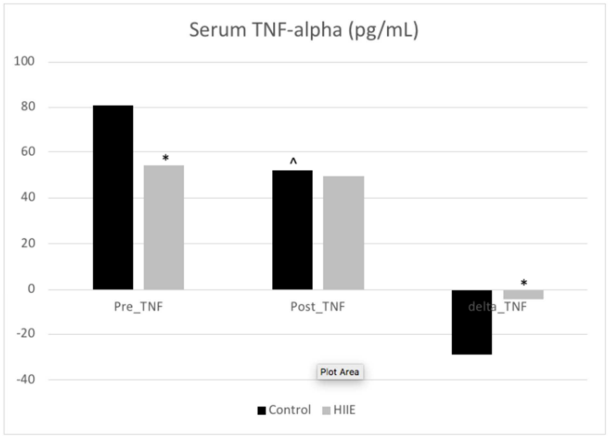

Figure 1. Mean TNF-α Serum Levels
^sig. difference ($p<0.05$) compared to the HIIE group (paired t-test)
*sig. difference ($p<0.05$) compared to the control group (independent t-test)

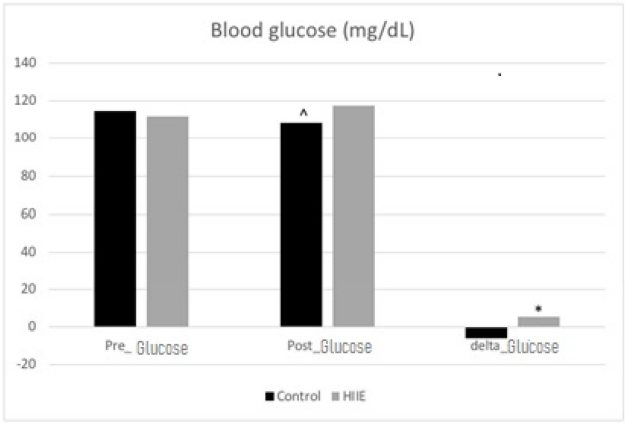

Figure 2. Mean Blood Glucose Levels
^sig. difference ($p<0.05$) compared to the HIIE group (paired t-test)
*sig. difference ($p<0.05$) compared to the pretest and posttest in each group (independent t-test)

Discussion

This study revealed that the TNF-α control group had more significant decrease compared to the experimental group. This finding is in accordance with the previous study by Dos Santos (2019) on obese female adolescents with sedentary behavior who were given a 30-minute intervention with an intensity equivalent to 75% of their treadmill VO2max. The insignificant decrease in TNF-α is associated with exercise intensity that is probably too high for the subjects. Previous research by Hawari (2021) on 14 obese women with BMI 27.5 – 35kg/m^2 applied an exercise using a treadmill with a moderate intensity of 60-70% HRmax for 30 minutes. Blood drawn 10 minutes after exercise showed a significant decrease in TNF-α. Dimitrov (2017) studied 47 healthy subjects who did treadmill exercise for 20 minutes at 65-70% VO2max and also confirmed a significant decrease in TNF-α.

Acute HIIE can increase circulating IL-6 levels in overweight subjects (Ferrandi et al., 2018). Muscle contraction releases large amounts of IL-6, which in this case has anti-inflammatory effect and stimulates the production of other anti-inflammatory cytokines such as IL-1ra and IL-10 (Eskandari, Asghari, Saghebjoo, & Kazemi, 2021). The anti-inflammatory effect of exercise offers protection against insulin resistance induced by TNF-α (Petersen & Pedersen, 2005). As a result, the rate of glucose uptake in muscles increases (Nie et al., 2012). Pre-exercise intramuscular glycogen content appears to be an important stimulus for IL-6 gene transcription, and muscle-derived IL-6 acts as an energy sensor. IL-6 will also induce lipolysis and oxidize fat (Petersen & Pedersen, 2005). Sympathetic nerves stimulated during exercise activates adrenal glands and secrete adrenaline. Adrenaline has been shown to inhibit TNF-α in response to endotoxin in vivo (Petersen & Pedersen, 2005).

The results of this study have proven that the decrease in blood glucose levels in the control group was more significant compared to that in the experimental group. This is in line with a study conducted by Antunes (2019) on 19 healthy male subjects who performed exercise using an ergocycle at 90% HRmax, which resulted in an increase in blood glucose. The decrease of blood glucose in control group also confirmed in the research of Yurida & Huzaifah (2019). A study conducted by Alfin showed that fasting had an effect on reducing blood sugar levels in patients with type 2 diabetes. Fasting (hunger) is a state of lack of energy and essential nutrient intake needed by the body for few days, which leads to changes in metabolic processes of the main elements in the body. Insulin will decrease and glucagon levels will increase as a result of increased blood glucose.

The increase in blood glucose level is also associated with an increase in catecholamines in physical exercise (87% VO2max for 15 minutes). It triggers 7-8 times more glucose production and 3-4 times higher glucose utilization. During vigorous physical exercise, decreased glucose utilization before glucose production can lead to more severe hyperglycemia. It requires a substantial increase in insulin over 40-60 minutes to recover to the pre-exercise level (Marliss & Vranic, 2002). The high concentration of glucose and insulin during recovery is useful for replenishing muscle glycogen that has been reduced during physical activity. The result of this study is similar with the results of research conducted by Bell (2010), "Short-term Sprint-interval Training and Regulation of Metabolism in Adult Humans", which stated that short-term physical exercise can affect metabolism in the body, namely, carbohydrate metabolism, which can increase blood sugar levels. Adrenaline increases plasma blood glucose concentration during exercise because the sympathetic nervous system is stimulated. Adrenaline has a very strong effect on glycogenolysis in the liver. It will release a large amount of glucose into the blood within minutes (Sherwood, 2016).

Conclusions

The effect of acute HIIE on an ergocycle on TNF-α level is unchanged and the blood glucose levels is increase in overweight women with sedentary behavior. This phenomena might be caused by the increased high intensity that will lead to secretion IL-6, increased stimultant of sympathetic nerves, and increased catecholamines. Further research regarding exercise intensity and other anti-inflammatory and pro-inflammatory mediators is needed to uncover the underlying mechanism.

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Conflicts of Interest

No potential conflicts of interest relevant to this article could be reported.

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