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Response of Pro-Inflammatory Cytokines After A Single Bout of Moderate-Intensity Endurance Exercise in Obese

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Abstract

Reducing the complications of obesity by controlling the balance of inflammation and losing weight with physical exercise can be used as a strategy to overcome obesity problems. This study aims to prove the effect of moderate-intensity endurance exercise on the acute response of proinflammatory cytokines in obese women. A total of 22 obese women aged 20-24 years, with body mass index 27-33 kg/m2, and body fat percentage ≥30%, were selected to be respondents and given moderate-intensity endurance exercise intervention (60-70% HRmax) for 40 minutes. ELISA Kit was applied to evaluate TNF-α levels in all samples. The data analysis technique uses an independent sample t-test with a significance level of 5%. The results show the average TNF-α levels between the control (CON) vs endurance exercise group (END) in pre-exercise (5.47±2.19 vs 5.39±1.45 pg/mL, p=0.932), post-exercise (5.76±2.08 vs 3.68±2.10 pg/mL, p=0.039), delta (value of pre-exercise – post-exercise) (0.29±2.27 vs -1.72±1.04 pg/mL, p=0.020). This study consistently proves that one session of moderate-intensity endurance exercise for 40 minutes reduces TNF-α levels in obese women.

Keywords: *endurance exercise, obesity, pro-inflammatory cytokines, sedentary lifestyle*

Introduction

It has now been reported that obesity is at an alarming rate (Becetti et al., 2023). Data from the World Health Organization (WHO) (2021) reports that 39% of the world's population aged ≥ 18 years are overweight, and 13% are obese. Obesity in adolescents is a cause of long-term health problems and has become a major concern in the health sector, a wider medical problem, and a public health concern (Loux et al., 2023). Adolescence is an important phase of life for achieving human potential, as physical, cognitive, social, and emotional development occurs within a complex network of family, peers, schools, media, and broader sociocultural influences (Agung et al., 2023). In addition, adolescence can be used as a foundation for future health and well-being (Silvers & Peris, 2023). Therefore, obesity in adolescents is still a health problem that needs attention.

Obesity is a chronic disease characterized by excessive accumulation of adipose tissue (Basu et al., 2023). Adipose tissue is the largest endocrine organ in the body (Pallio et al., 2023). In recent years, adipose tissue dysfunction in obesity has been associated with metabolic changes (Santillana et al., 2023), and causes a low-grade inflammatory state in adipose tissue which is characterized by increased levels of tumor necrosis factor (TNF-α) (Guan et al., 2023), thus having an impact on the development of chronic diseases (Zhang et al., 2023), metabolic diseases, and complications at the tissue and organ

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level (Kawai et al., 2023). Currently, adolescents with obesity are at greater risk of morbidity and mortality, possibly appearing before the age of 30 in both sexes (Horesh et al., 2021). In addition, in individuals with obesity, there is also a decrease in quality of life related to health status, and an increase in obesity co-morbidities, including type 2 diabetes mellitus, and non-alcoholic fatty liver disease (NAFLD), this risk has the potential to occur in adolescents with severe obesity (Lister et al., 2023). This phenomenon makes obesity one of the most common non-communicable diseases and a major public health burden (Khanna et al., 2022).

Developing an appropriate exercise program is an integral part of a comprehensive obesity management approach (Rejeki et al., 2023). Obesity is a complex multifactorial disease (Lin & Li, 2021), meanwhile, programmed physical exercise also has complex biological effects, involving polygenic interactions within cells, tissues/organs, and systems (Ruegsegger & Booth, 2018). Physical activity is defined as any movement that requires energy (Qiu et al., 2023). Exercise that involves physical activity contributes to reducing excess calories in obesity by increasing insulin sensitivity which results in increased glucose uptake (Han et al., 2023). Evidence shows that losing weight has been shown to reduce circulating TNF-α levels in adults with obesity (Mulas et al., 2023; Pranoto et al., 2023a). However, weight loss cannot be done in a short time (Wharton et al., 2023). Meanwhile, the results of other studies show that heavy resistance training can suppress the immune system and cause inflammation and muscle damage (Cerqueira et al., 2020; Liu et al., 2023). Determining the intensity of exercise is important in compiling an exercise program. Therefore, reducing the complications of obesity by controlling the balance of inflammation (Callegari, et al., 2023), and losing weight with physical exercise (Borer, 2023) can be used as a strategy to overcome obesity problems. The study by Honkala et al. (2020), reported that endurance exercise can significantly reduce TNF-α levels. Makarewicz et al. (2022) reported that endurance exercise was less effective in reducing TNF-α concentrations in overweight and obese adults. However, a study conducted by Andarianto et al. (2022) reported different results that moderate-intensity endurance exercise was effective in reducing TNF-α levels in obese women. Based on several research results above, there are still gaps in the research results. Therefore, this study aims to prove the effect of moderate-intensity endurance exercise on the acute response of proinflammatory cytokines in obese women.

Methods

Study design

This study complies with the ethical principles of the Helsinki Declaration on medical research involving human subjects developed by the World Medical Association (WMA) and the protocol in this study was approved by the Health Research Ethics Commission (KEPK) Faculty of Medicine, Universitas Airlangga No. 16/EC/KEPK/FKUA/2022. This study used a true experimental method with a pretest-posttest control group design. A total of 35 prospective respondents underwent a screening process with several stages of examination, such as health status, body composition, anthropometry, and research demography. Thirteen people were declared not to meet the inclusion criteria. A total of 22 obese women aged 20-24 years, with body mass index 27-33 kg/m2, body fat percentage ≥30%, normal blood pressure, normal resting heart rate, normal oxygen saturation, and normal body temperature were selected to be respondents and carried out blood sampling. Information about the research has been conveyed to the participants clearly and the participants have stated consent to participate in the research by filling out and signing informed consent which was done consciously without any coercion. All selected respondents had no history of chronic disease, and for the last 5 years had no history of smoking or consuming alcohol. Group division was done randomly between the control group (CON; n=11), and the endurance exercise group (END; n=11).

Protocol of endurance exercise

All respondents came to the fitness center at 07.00 a.m. Before starting the endurance exercise, the subject underwent a 5-minute warm-up (dynamic stretching) and a leisurely walk on the treadmill for 5 minutes. Endurance exercise was applied once (acute exercise) with moderate intensity (60-70% HRmax), the duration of the exercise was 40 minutes/session using the Treadmill (Life Fitness 95t Inspire Treadmill., Schiller Park, Illinois 60176, U.S.A). Cooling down (static stretching) after resistance training was done for 5 minutes. While at the fitness center, each respondent was accompanied by a personal trainer to ensure that the respondent carried out the exercise program correctly, thereby minimizing the occurrence of injuries. During the intervention, exercise intensity was controlled using the Polar H10 Heart Rate Sensor. The environment used for training has a room temperature of 25°C with an indoor humidity level of 50%.

Blood sample collection and examination of TNF-α levels

Blood sampling (pre) was carried out after fasting overnight for 10-12 hours, while blood sampling (post) was carried out 6 hours after the intervention of 3 cc each. The collected blood samples were immediately centrifuged at 3000 rpm for 15 minutes, then the serum was separated and immediately examined for TNF-α levels. Examination of TNF-α levels using the ELISA Kit (Cat.No.: E-EL-H0109; Elabscience, Inc., USA) which has been validated by previous studies (Pranoto et al., 2023a).

Statistical analysis

The normality test with Shapiro Wilk was used to examine the distribution of the data. The parametric paired sample t-test was applied to see data differences per group, while the independent sample t-test was applied to see data differences per all groups. Data was declared to have a significant difference when 5%, and data was presented as mean ± SD. All statistical analyses used SPSS software version 20 for Windows 10.

Results

The results of the analysis of the demographic characteristics of the study subjects are shown in Table 1 which shows that there were no differences in the characteristics of the two groups ($p \geq 0.05$). Therefore, the two groups are confirmed to be on the same basis. Meanwhile, the results of the analysis of TNF-α levels between pre-exercise and post-exercise in each group are shown in Figure 1, while Table 2 presents the differences in TNF-α levels between the control group (CON) and the endurance exercise group (END).

Table 1. The characteristics of the study subjects

Parameters	Unit	n	CON	END	p-Value
			Mean±SD	Mean±SD	
Age	yrs	11	22.00±1.42	22.30±1.57	0.659
Weight	kg	11	74.10±6.83	72.05±6.98	0.514
Height	m	11	1.58±0.06	1.57±0.05	0.728
BMI	kg/m^2	11	29.61±2.82	29.04±1.76	0.595
FM	kg	11	33.65±6.19	30.48±4.76	0.218
FFM	kg	11	43.08±4.51	41.56±3.05	0.390
SMM	kg	11	20.31±4.27	18.43±1.89	0.226
SBP	mmHg	11	113.10±6.87	109.80±6.86	0.297
DBP	mmHg	11	77.40±7.26	77.70±5.34	0.917
RHR	bpm	11	78.30±10.02	77.50±6.87	0.838
SpO_2	%	11	98.10±0.74	97.90±0.99	0.616
BT	°C	11	36.27±0.29	36.29±0.18	0.856

Note: BMI: Body mass index; DBP: Diastolic blood pressure; FM: Fat mass; FFM: Free fat mass; RHR: Resting heart rate; SBP: Systolic blood pressure; SMM: Skeletal muscle mass; SpO_2: Oxygen saturation. the p-Value obtained by independent sample t-test.

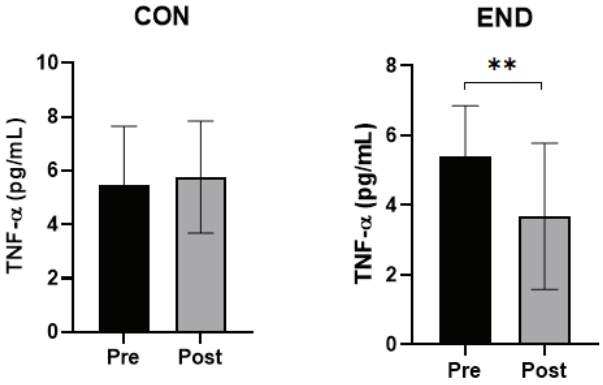

FIGURE 1. The comparison of TNF-α levels (pg/mL) between pre vs. post in each group; Note: (**) Significant at pre ($p \leq 0.001$). p-Value obtained by paired sample t-test.

Table 2. The comparison of TNF-α levels (pg/mL) between CON vs. END

Assessment	Unit	n	CON	END	p-Value
			Mean±SD	Mean±SD	
Pre-TNF-α	pg/mL	11	5.47±2.19	5.39±1.45	0.932
Post-TNF-α	pg/mL	11	5.76±2.08	3.68±2.10*	0.039
Δ-TNF-α	pg/mL	11	0.29±2.27	-1.72±1.04*	0.020
TNF-α changes from pre	%	11	15.08±47.44	-35.27±23.87*	0.008

Note: (*) Significant at CON ($p \leq 0.05$). the p-Value obtained by independent sample t-test.

Discussion

This study aims to prove the effect of moderate-intensity endurance exercise on the acute response of proinflammatory cytokines in obese women. The results of this study indicate that moderate-intensity endurance exercise significantly reduces TNF-α levels in obesity (Figure 1 & Table 2). This result is in line with the results by Accattato et al. (2017), which stated that endurance exercise can significantly reduce TNF-α levels. Likewise, a study conducted by Pranoto et al. (2023b) reported that moderate-intensity endurance exercise significantly reduced TNF-α levels in obese women. The study by Koh and Park (2017) also reported a reduction in TNF-α levels after endurance exercise in women with overweight and obese. Physical exercise plays a role in the treatment and prevention of various deadly non-communicable diseases because physical exercise has the potential to control inflammation in metabolic disorders due to obesity by reducing TNF-α levels, affecting macrophage infiltration and polarization (Callegari et al., 2023).

The training characteristics of elite/international and world-class athletes in endurance exercise have been extensively described in retrospective studies (González-Ravé et al., 2021; Casado et al., 2022; Staff et al., 2023). Endurance exercise is drawn by repeated isotonic muscle contractions of a large number of skeletal muscles (Morici et al., 2016). Various physiological functions are affected by time, such as

core body temperature, cardiovascular function, respiratory control, endocrine factors, and subjective alertness, which can affect physiological adaptation in response to exercise (Kusumoto et al., 2021; Bruggisser et al., 2023). Exercise induces signaling metabolites that act as stimuli and as substrates for cellular energy sensors and molecular signaling, as adaptive responses and transcriptional sequences in response to exercise (Bennett & Sato, 2023). Approximately 40% of the human body consists of skeletal muscle, which is responsible for 90% of glucose elimination after eating (Kohler et al., 2023). When insulin binds to the insulin receptor on the surface of skeletal muscle cells, activation of the phosphoinoside-3-kinase (PI3K)/protein kinase B (Akt)/Akt substrate of 160 kDa (AS160; also known as TBC1D4) pathway causes translocation of GLUT4-containing vesicles from the cytosol to the cell membrane and as a result glucose uptake occurs (Leto & Saltiel, 2012; Kohler et al., 2023). During endurance exercise, there is a shift in the use of energy sources from glucose to ketone-bodies and fatty acids, which has an impact on improving the dulling of metabolic flexibility observed in obesity and type 2 diabetes mellitus (T2DM) and improving mitochondrial function (Di Francesco et al., 2018; Stekovic et al., 2019; Song & Kim, 2023). Improving metabolic health conditions and weight loss can suppress inflammation in obesity which is characterized by decreased levels of the pro-inflammatory cytokine TNF-α (Mulas et al., 2023). It can be concluded that exercise is effective in restoring the inflammatory balance in obesity.

The limitation of this study is that sample size of participants is small, indicating the need for larger sample sizes in future studies. Besides that we only measured the response of endurance exercise to decreased TNF-α levels as an inflammatory marker in obesity, so we cannot explain exactly the physiological mechanisms involved in reducing TNF-α levels to maintain inflammatory balance. Further studies are suggested to examine other parameters, such as IL-6, IL-10, and adiponectin to elucidate the mechanisms involved in the inflammatory balance in obesity.

Conclusion

This study proves that one session of moderate-intensity endurance exercise for 40 minutes reduces TNF-α levels in obese women. Therefore, moderate-intensity endurance exercise can be used as an effective therapy in maintaining the balance of inflammation and is a recommendation in dealing with problems caused by obesity.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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