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Interval Exercise Decreases Inflammatory Markers In Obese Female

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ABSTRACT
Obesity was strongly associated with the level of inflammation indicated by the increase of pro-inflammatory cytokines such as Tumor Necrosis Factor-α (TNF-α). The exercise was an effective strategy to maintain an anti-inflammatory environment. This was because exercise could inhibit the production and the expression of proinflammatory cytokines such as TNF-α. This study aimed to analyze the decrease of the inflammatory marker after interval exercise in obese females. This study was experimental research with a pretest-posttest control group design on 12 adolescent girls aged 19-23 years old, body mass index (BMI) > 26.5 kg/m2, normal blood pressure, normal resting heart rate. The subjects were randomly divided into two groups, that were CO (n = 6, control group without intervention) and IE (n = 6, interval exercise group). The interval exercise was performed for 45 minutes on a treadmill. Blood samples were taken 30 minutes before exercise and 10 minutes after exercise. The ELISA method was used to measure the TNF-α level. Statistical analysis used the Independent Samples T-Test and Paired Sample T-Test with a significance level ($p<0.05$). The results of the Paired Sample T-Test on CO and IE showed that there were no significant difference in the mean of TNF-α levels between pre-exercise and 10 minutes post-exercise ($p>0.05$). The results of the Independent Samples T-Test showed that there were no significant difference in the mean of TNF-α levels on CO and IE in pre-exercise ($p>0.05$), while the mean of TNF-α levels in 10 minutes post-exercise between CO vs IE showed a significant difference ($p<0.05$) Based on the results of the study, it could be concluded that interval exercise performed for 45 minutes could decrease inflammatory markers in obese females.

Keywords: Interval Exercise, Inflammatory Markers, Obese Females

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BACKGROUND

Obesity was a serious problem in many countries, both developed and developing countries (Ng *et al.*, 2 014). Currently, there was proof that the prevalence of overweight and obesity had increased very sharply worldwide (Novitasary, 2014). In Indonesia, Basic Health Research (RISKESDAS) reported that in 2018 there were 21.8% of people aged over 18 were obese. The percentage of obesity in females aged over 18 years was 29.3%, while obesity in males was 14.5%, meaning that females were obese twice more than males based on body mass index (BMI) status (Riskesdas, 2018). The high prevalence rate of obesity was a serious problem that would threaten the quality of human resources and become health problems in countries around the world (Oto *et al*., 2014).

Obesity was a disease that had a high risk of complication occurrences, disability, and early death (Rosella *et al*., 2019; Akter *et al*., 2014). The reason was obesity increased the risk of non-contagious diseases, such as diabetes mellitus type 2, cardiac disease (Hruby & Hu, 2015), several types of cancer (Nimptsch *et al*., 2019), high blood pressure, and stroke (Agofure, 2017). Obesity was also systematically associated with low-level inflammation, indicated by abnormal adiponectin conditions so that could activate inflammatory pathway signaling (Jackson *et al*., 2016) which could lead to chronic inflammation (Bashashati *et al*., 2017) and risk of forming cancer cells (Heikkilä *et al*., 2008). That was proven by an increase in inflammatory markers like TNF-α in obese individuals which were higher than lean individuals (De Lorenzo *et al*., 2016). The exercise was an effective strategy in maintaining an anti-inflammatory environment (Gonzalez-Gil *et al*., 2020). This was because exercise could increase adiponectin levels as an anti-inflammatory marker (Achari *et al*., 2017; Bouassida *et al*., 2010) and decreased pro-inflammatory cytokines like TNF-α (Jahromi *et al*., 2014), so exercise could be used to balance the level of inflammation. However, the effect of exercise on changing TNF-α levels had not been clearly exploited. Research conducted by Sugama *et al*. (2013) reported that TNF-α levels increased after resistance exercise. Meanwhile, aerobic interval exercise significantly decreased TNF-α levels (Mokhtarzade *et al*., 2017). Research conducted by Salamat *et al*. (2016) reported that there was no significant decrease in TNF-α levels after endurance, resistance, and concurrent (endurance - resistance) exercises.

Based on this foundation, this study aimed to analyze the decrease of inflammatory markers after interval exercise in obese females. Researchers hypothesized that interval exercise might decrease inflammatory markers such as TNF-α.

METHODS

This study was an experimental study, by a pretest-posttest control group design, with 12 adolescent girls aged 19-23 years old, body mass index (BMI)> 26.5 kg / m2, normal blood pressure, normal resting heart rate. The subjects were randomly divided into two groups, that were CO (n = 6, control group without intervention) and IE (n = 6, interval exercise group). All research procedures had been approved by the Health Research Ethics Commission of the Faculty of Medicine, Universitas Brawijaya Malang.

The interval exercise was performed by running for 45 minutes on a treadmill with an intensity of 60-70% HRmax, The details were 5 minutes for warming up (50-60% HRmax), 35 minutes for the core exercise (5 minutes (60-70% HRmax) interspersed by active recovery on a treadmill for 2.5 minutes (50-60% HRmax) which were performed 5 times in repeat, and 5 minutes for cooling down (50-60% HRmax). Interventions were performed for 07.00-09.00 A.M using treadmills (Richter Treadmill Semi-Commercial Evolution (4.0 hp

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DC). The intensity of exercise was monitored by using polar (Polar H10 Heart Rate Sensor, Inc., USA) once each minute during exercise.

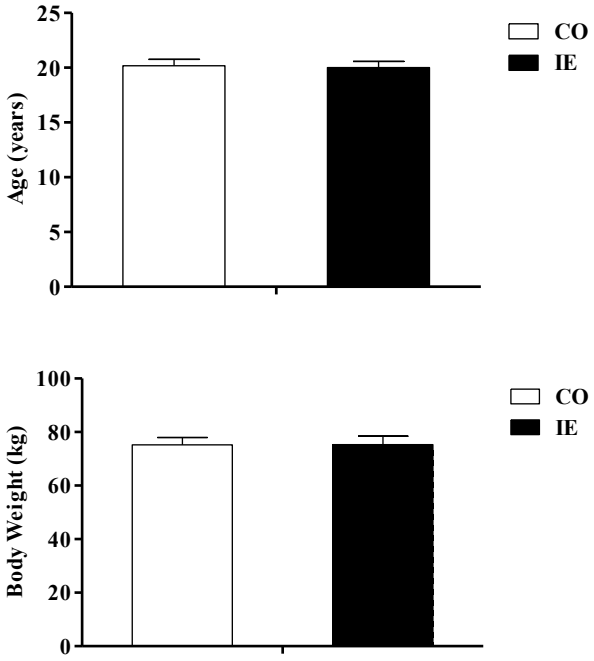
Body height was measured by using stadiometer (SECA, Chino, CA). Body weight was measured by using electronic scale (Tech 05®, China). BMI was measured through calculation weight divided by height in meter quadrat (m^2) (Nimptsch *et al*., 2019). Blood pressure was measured by using OMRON digital tensimeter (OMRON Model HEM-7130, Omron Co. Japan).

Blood samples were taken 4 ml from cubital veins in the subject's sleeping position. Blood samples were taken twice at 30 minutes before exercise and 10 minutes after exercise. Blood was centrifuged for 15 minutes at 3000 rpm. TNF-α level was measured by using Enzyme-Linked Immunosorbent Assay method (ELISA) kit (Catalog No. E-EL-H0109; Elabscience, Inc., China) with a standard curve range of 7.81–500 pg/mL and a sensitivity of 4.69 pg / mL.

Data were analyzed using the statistical software package for social sciences (SPSS) version 17 (Chicago, IL, USA). The normality test used the Shapiro-Wilk test. Normally distributed data were tested using the Independent Samples T-Test and Paired Sample T-Test with a significance level (p<0.05). All data were presented with mean ± standard error of mean (SEM).

RESULTS

The results of data analysis about the characteristics of research subjects including age, weight, height, body mass index, systolic blood pressure, diastolic blood pressure, and resting heart rate were presented in Figure 1.



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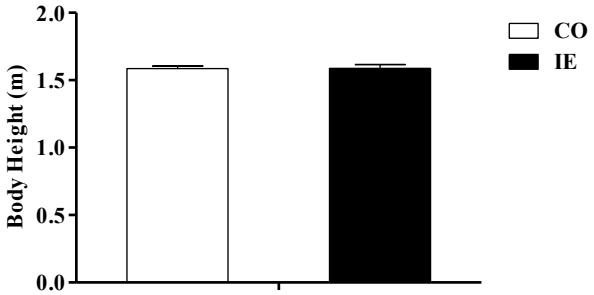

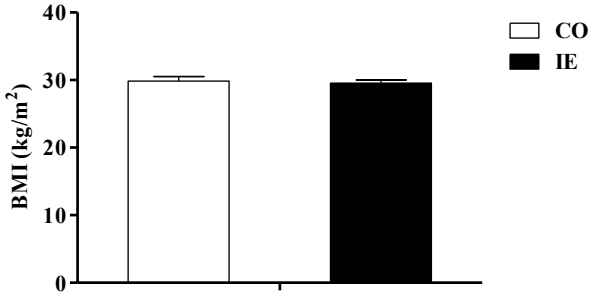

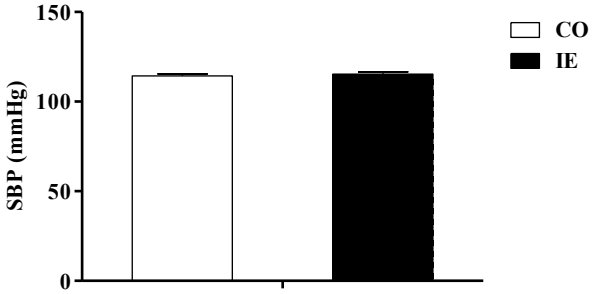

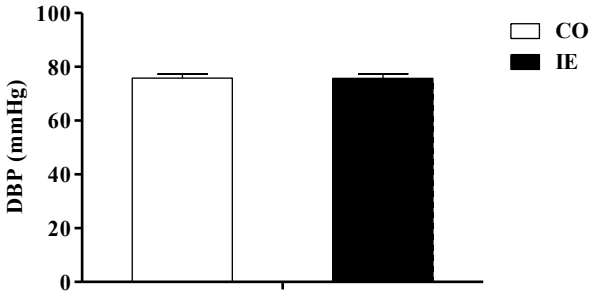

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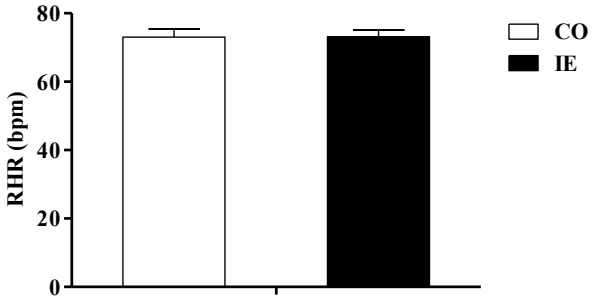

Figure 1. Characteristics of research subjects. CO: control group; IE: interval exercise group. p-Value were obtained using Independent Samples T-Test to compare CO and IE.

Based on the results of the Independent Samples T-Test (Figure 1), it showed that there was no significant difference between the mean on the characteristics data of the research subjects in CO and IE (p>0.05). The results of the TNF-α level analysis between pre-exercise and 10 minutes post-exercise could be seen in Figure 2.

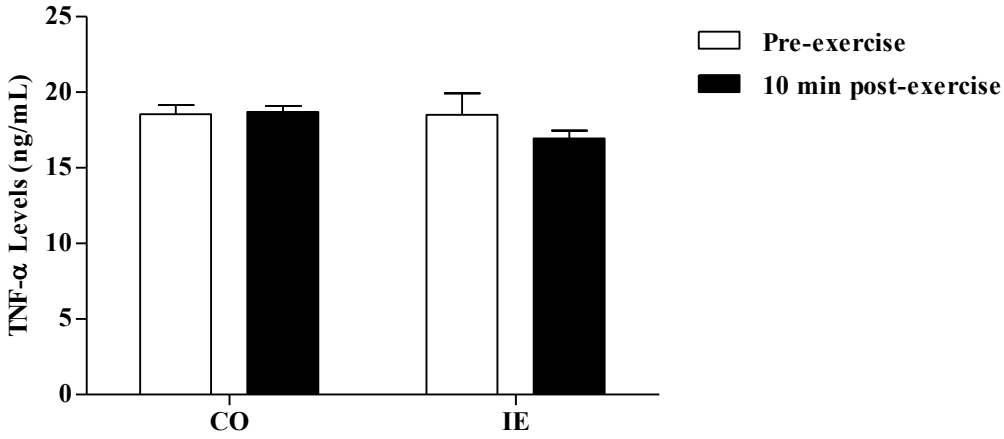

Figure 2. TNF-α levels pre-exercise vs. 10 min post-exercise. CO: control group; IE: interval exercise group. p-Value were obtained using Paired Sample T-Test to compare CO and IE pre-exercise vs. 10 min post-exercise TNF-α levels.

Based on the results of the Paired Sample T-Test on CO, it showed that there was no significant difference between the mean of TNF-α levels in pre-exercise and 10 min post-exercise (18.55±0.60 vs. 18.71±0.39 ng/mL, (p-value = 0.810). Likewise, IE showed that there was no significant difference between the mean of TNF-α levels in pre-exercise and 10 min post-exercise (18.51±1.42 vs. 16.95±0.52 ng/mL, (p-value = 0.186). The analysis results of TNF-α levels between CO and IE (Time x Group) were presented in Figure 3.

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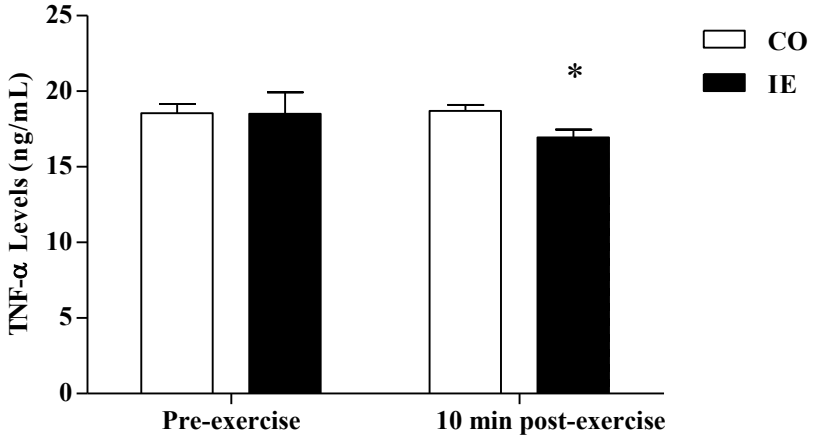

Figure 3. TNF-α levels on control group vs. Interval exercise group (time x group). p-Value were obtained using Independent Samples T-Test to compare control group vs. Interval exercise group (time x group) TNF-α levels.

The results of the Independent Samples T-Test (Figure 3) showed that there was no significant difference between the mean of TNF-α levels CO and IE in pre-exercise (18.55±0.60 vs. 18.51±1.42 ng/mL, (p-value = 0.977), while the mean of TNF-α levels between CO and IE in post-exercise showed significant difference (18.71±0.39 vs. 16.95±0.52 ng/mL, (p-value = 0.022).

DISCUSSION

Based on the results of the Independent Samples T-Test (Figure 1), it showed that there was no significant difference among all of the means on characteristics data of research subjects in the control group (CO) dan interval exercise group (IE) (p>0.05). That results were in line with the study conducted by Mokhtarzade *et al*. (2017) concluded that all of the characteristics data of research subjects consisted of age, body weight, body mass index, didn't show any significant difference between the experiments group and control group. Likewise, a study conducted by Salamat *et al*. (2016) showed that the characteristics data of research subjects consisted of age, body height, body weight, body fat, body mass index, also didn't show any significant difference among all of the groups. Therefore, if there was a change in TNF-α levels it was not due to the characteristics of the research subject, it might be due to the intervention factor of moderate-intensity interval exercise.

Tumor necrosis factor-α (TNF-α) was Pleiotropic cytokines produced mainly by active macrophages and other types of immune cells such as T lymphocytes, natural killer cells (NK cells), and neutrophils (Zhou *et al*., 2016). Macrophages on adipose were the main resources of TNF-α produced by white adipose tissues (Weisberg *et al.*, 2003). This could indicate indirectly that obese individuals had higher levels of TNF-α than individuals of normal weight (Salamat *et al*., 2016). It was proved by the increase in TNF-α levels as a pro-inflammatory indicator in obese individuals if compared to non-obese individuals (De Lorenzo *et al*., 2016). TNF-α didn't just participated in inflammation but also was autocrine and important paracrine of fat cell function which limited adipose tissues and skeletal muscles expansion by inducing lipolysis (Weisberg *et al*., 2003), insulin resistance (Dalziel *et al*., 2002), dan muscle apoptosis (Meadows *et al*., 2000). TNF-α had also correlated with the increase of leptin, thus could affect tissues growth inhibition (Argilés *et al*., 2005). Several studies had reported that exercise could inhibit the TNF-α production dan expression

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in healthy individuals (Gleeson *et al*., 2011; Steensberg *et al*., 2002). That was in line with the findings in this study that moderate-intensity interval exercise significantly decreased TNF-α levels compared to the control group ($p < 0.05$). Supported by research conducted by Jahromi *et al*. (2014) he reported that strength exercise significantly decreased pro-inflammatory cytokines, such as TNF-α. Likewise, the exercise with an intensity of 70% VO_2max significantly decreased TNF-α levels (Smart *et al*., 2011). Based on the Review Article conducted by Gonzalez-Gil *et al*. (2020), they explained that exercise could improve the anti-inflammatory environment thus decreased systemic inflammation which was indicated by the decrease of pro-inflammatory cytokines such as TNF-α and an increase on adiponectin as an anti-inflammatory marker.

The exercise was one of the effective strategies for maintaining the anti-inflammatory environment (Gonzalez-Gil *et al*., 2020). The reason was that exercise could increase the level of adiponectin as an anti-inflammatory marker (Achari *et al*., 2017) and decreased pro-inflammatory cytokines such as TNF-α (Bouassida *et al*., 2010), so that exercise could be used to balance the level of inflammation. The results of this research showed that moderate-intensity interval exercise significantly decreased TNF-α levels. The decreased of TNF-α levels were believed to be associated with the production and expression of interleukin-6 (IL-6) which induced by the exercise, resulting in activation of the anti-inflammatory response, which was affected by an increase in interleukin-10 (IL-10), interleukin-1 receptor antagonist (IL-1RA), and the level of tumor necrosis factor-soluble receptor (sTFr) which specifically caused a decrease of pro-inflammatory factor, such as TNF-α (Brandt and Pedersen, 2010; Cabral-Santos *et al*., 2015; Lira *et al*., 2015; Metsios *et al*., 2020). During inflammation condition, IL-6 was also proved that could limit the gen expression which coding the inflammatory cytokines (such as TNF-α, IL1β, NOS2) and activation of the terminal c Jun N kinase (JNK) which then increased the responsiveness of macrophages to interleukin-4 (IL 4), thereby strongly supported the idea that IL-6 could decrease the level of inflammation (Mauer et al., 2014). Also, exercise could result in the decreased activity of pro-inflammatory macrophages subtype 1 (M1) and increased activity of anti-inflammatory macrophages subtype 2 (M2) (Gordon *et al*., 2012). These observations had shown that exercise could increase the anti-inflammatory environment in the human body which resulted in the decrease of inflammation levels indicated by pro-inflammatory cytokines such as TNF-α.

CONCLUSION

Based on the results of this study, it could be concluded that interval exercise performed for 45 minutes could significantly decrease the inflammatory markers in obese females. Interval exercise could be one of the non-pharmacological methods which could effectively decrease pro-inflammatory cytokines such as Tumor Necrosis Factor-α (TNF-α) in obese females.

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