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Improved Interleukin-10 Levels Through 8 Weeks of Moderate Intensity Combination Exercise in Obese Women

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ABSTRACT

Obesity is closely associated with chronic low-grade inflammation, which plays an important role in the development of various comorbidities and its prevalence continues to increase year by year. In obese individuals, IL-10 levels tend to be lower which is associated with increased insulin resistance, hyperinsulinemia, and increased risk of metabolic dysfunction, including type 2 diabetes, exacerbated by obstructive sleep apnea, contributing to systemic inflammation and cardiovascular risk. Physical exercise is believed to have beneficial effects on obesity and suppress inflammation followed by a decrease in fat mass and an increase in muscle mass. The aim of this study was to prove that combined aerobic and resistance training with moderate intensity increases anti-inflammatory cytokine production in obese women. This study used a true experimental method with a pretest-posttest control group design. 16 obese women aged between 20 and 30 years were divided into two groups: control group (K1; n=8), and combination exercise group (K2; n=8). The exercise intervention was moderate intensity combination exercise (60%-70% Hrmax; 60-70% 1-RM), with a frequency of 5x/week for 8 weeks. With a detection range of 0.78-50 pg/mL and sensitivity level of 0.49 pg/mL, inflammation levels were measured both at pretest and posttest using ELISA kit method. Data with a significant level ($p>0.05$) were evaluated with the Paired Samples T-test. The results of the analysis of IL-10 levels between pretest and posttest in K1 (1.74 ± 0.13 vs 1.75 ± 0.19 ng/mL; $p = 0.951$), and K2 (1.75 ± 0.19 vs 2.41 ± 0.72 ng/mL; $p = 0.016$). This study showed that obese women had higher levels of IL-10 after 8 weeks of combined exercise.

Keywords: women, obesity, IL-10, physical exercise, inflammation

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Introduction

Interleukin-10 (IL-10) is an anti-inflammatory cytokine secreted by activated monocytes/macrophages and lymphocytes and inhibits the expression of proinflammatory cytokines (Wang et al., 2011; Kim et al., 2021). Low IL-10 levels in obese individuals indicate a decreased capacity to produce anti-inflammatory cytokines (Kondo et al., 2018). Higher IL-10 levels are positively correlated with insulin sensitivity meaning that individuals with good IL-10 levels have a lower risk of developing inflammation (Kim et al., 2021). In reality, IL-10 levels tend to be lower in obese people compared to normal people (Carlini et al., 2023), which may contribute to an increase in pro-inflammatory cytokines (Medeiros et al., 2018). The increase is stimulated by dysfunctional adipocytes, which predispose macrophages towards a more pro-inflammatory profile. This crosstalk increases the inflammatory response in adipose tissue, which may ultimately promote chronic inflammation (Frühbeck et al., 2022).

Low IL-10 levels in obese individuals may lead to increased macrophage infiltration in adipose tissue, which contributes to obesity-related metabolic disorders (L. Wang et al., 2022). Macrophage infiltration in obesity leads to an increase in M1 macrophages, which secrete pro-inflammatory cytokines as well as suppress IL-10 production that may reduce anti-inflammatory responses (Heilbronn & Campbell, 2008). Low IL-10 levels that exacerbate metabolic disorders are associated with increased insulin resistance, hyperinsulinemia, and increased risk of metabolic dysfunction, including type 2 diabetes, contributing to systemic inflammation and cardiovascular risk (Leon-Cabrera et al., 2015; Liu et al., 2018; Oussaada et al., 2024). Increased IL-10 levels in obese individuals can be induced through physical exercise, by increasing IL-6 expression in skeletal muscle, which then increases IL-10 expression and reduces inflammatory infiltrates in adipose tissue, contributing to an anti-inflammatory response (Leal et al., 2018).

Physical exercise can lead to the release of IL-10 as part of the body's recovery process (Della Guardia & Codella, 2021). Moderate-intensity aerobic exercise performed for 6 weeks increased IL-10 levels by stimulating a significant decrease in fat mass among young passive women (Eizadi et al., 2018; Haji et al., 2023). Resistance training stimulates muscle contraction and increases skeletal muscle mass which contributes to increased IL-10 production in obese women, suggesting that resistance training enhances the anti-inflammatory response contributing to reduced inflammation in obese women (Phillips et al., 2012). Aerobic and resistance training combined for 6 weeks has been shown to effectively reduce fat mass and inflammatory cytokines and increase Free Fat Mass (FFM) which in turn may increase anti-inflammatory markers (adiponectin, IL-10) (Parhampour et al., 2019).

However, another study showed that acute aerobic-resistance combination training for 2 weeks did not significantly increase IL-10 levels (Ringleb et al., 2023). This is certainly a controversy, because there are inconsistent results. On the basis of this, the researcher wants to prove the effect of moderate intensity combination training on increasing IL-10 levels in obese women.

Methodology

This study used a true experimental design with a randomly selected pretest-posttest control group (Rejeki et al., 2023)1. This study was conducted for 8 weeks which was divided into 3 places, namely: 1) Sport Science Laboratory, Faculty of Sport Science, State University of Malang; 2) Atlas Sport Club Malang; and 3) Faal Science Laboratory, Faculty of Medicine, Universitas Brawijaya. In this study, 16 obese women aged 20-30 years had BMI 25-35 kg/m2, normal blood pressure, normal resting heart rate, normal hemoglobin, normal oxygen saturation, and normal blood sugar.

The participants were divided into 2 groups, namely: control group (K1; n=8) and combination exercise group (K2; n=8). Combination exercise (Aerobic and Resistance) was performed using moderate intensity (60-70% HRmax, 60-70% 1-RM), with a frequency of 5x/week for 8 weeks, which was divided into 3 parts, namely: 5 minutes warm-up, 4-6 sets; 10-15 repetitions of core exercises performed with resistance training; (1) upper body using chest press machine, shoulder press machine, and lat pull down machine. (2) lower body using leg press machine, leg extension machine and hip abduction machine. After that, continue the core exercise by walking on a treadmill using lifefitness and cybex brand gym equipment for 40 minutes, and 5 minutes of cooling down. The combination exercise intervention was carried out on Monday through Thursday and Saturday at 06.00-10.00 WIB. At pretest (before exercise intervention) and posttest (after 8 weeks of combined exercise intervention), blood samples were taken from the cubital vein as much as 4 ml. Blood samples will be centrifuged for 15 minutes at 3000 rpm, then serum will be separated and stored at -80°C to measure inflammation levels the following day using the ELISA kit method (Cat.No.: E-HSEL-H0005 Detection range: 0.78-50 pg/mL) with a sensitivity level of 0.49 pg/mL. Data analysis in this study was carried out after the pretest and posttest were collected. Furthermore, Statistical

Package for the Social Science (SPSS) version 21.0 to analyze the data that has been obtained. The normality test used the saphiro-wilk test with a significant level (p>0.05), the difference in inflammation levels at pretest and posttest in each group was tested with the paired sample t-test, and the independent sample t-test was used to measure the difference in IL-10 levels at pretest and posttest in each group.

Result

The results of descriptive analysis of data on the characteristics of research subjects with variables of age, height (TB), weight (BB), and Body Mass Index (BMI) systole blood pressure (SYS), diastole blood pressure (DYS), hemoglobin (Hb), resting heart rate (RHR), body temperature (ST), oxygen saturation (SpO2), fasting blood sugar (GDP). Table 1 shows that there was no significant difference in the data characteristics of the study subjects between the control group and the combination exercise group with a value of (p>0.05). Table 2 and Table 3 show the results of the analysis of mean inflammation levels between pretest and posttest in both groups.

Table 1. Characteristics of Research Subjects in Both Groups

Variabel	n	K1		K2		*p*-value
		Mean	SD	Mean	SD	
Age (years old)	8	24.75	2.31	25.50	2.50	0.544
Height(m)	8	1.56	0.54	1.55	0.58	0.828
Weight (kg)	8	80.66	6.67	83.78	12.45	0.546
BMI (kg/m^2)	8	33.25	2.78	34.63	3.51	0.400
SYS (mmHg)	8	123.50	3.66	121.25	5.59	0.358
DYS (mmHg)	8	72.50	9.97	74.13	5.02	0.687
HB (g/dL)	8	13.53	1.59	14.84	1.82	0.148
RHR (bpm)	8	84.25	9.70	88.38	9.50	0.405
Body Temperature (°C)	8	35.69	1.08	36.00	0.60	0.488
Fasting Blood Sugar (mg/dL)	8	98.38	9.28	100.75	7.36	0.580

Table 2. Results of Analysis of Pretest and Posttest IL-10 Levels in Each Group

Kelompok	n	*Pretest*		*Posttest*		*p*-value
		Mean	SD	Mean	SD	
K_1	8	1.74	0.13	1.75	0.19	0.951
K_2	8	1.75	0.19	2.41	0.72	0. 015*

Table 3. Table 3. Results of Analysis of Pretest and Posttest IL-10 Levels, in Both Groups

Kelompok	n	*Pretest*		*Posttest*		p-*value*
		Mean	SD	Mean	SD	
K_1	8	1.74	0.13	1.75	0.19	0.010
K_2	8	1.75	0.19	2.41	0.72	0.016*

Based on the results of the study, there was a difference in the average IL-10 levels in both groups between pretest and posttest. However, in the control group (K1) the difference in inflammatory levels was not significant compared to the combination exercise group (K2) (Table 2.).

Dicussion

This study used 16 obese female subjects who were randomly divided into 2 groups, namely K1 (n=8, control without intervention) and K2 (n=8, moderate intensity combination exercise). This study used a sample of obese women because women of productive age have higher rates of overweight and obesity and are more affected by obesity-related complications than men. The worldwide increase in overweight and obesity is greatest among women in the productive age group. Factors such as hormonal changes, lifestyle choices, and the increased prevalence of conditions such as polycystic ovary syndrome, which can lead to weight gain and reproductive health problems, make reproductive-aged women more susceptible to obesity (Andreeva et al., 2019). Many women have multiple work, family and household responsibilities, which limit their time for physical exercise. As a result, low physical activity levels are an important factor (Mehdiyeva et al., 2022). The problem becomes more severe due to dietary habits, such as reducing consumption of nutritious foods and consuming a lot of calories (Mosha et al., 2021).

Obesity has adverse consequences on reproduction, which can be categorized into gynecological and obstetric effects. (Ahmed & Konje, 2023). Women also have limited access to healthy food options and exercise facilities, especially in urban environments, which exacerbates obesity rates (Tan & Habib, 2021).

The results of this study showed that there was a significant increase in average IL-10 levels in the combination exercise intervention group, while the control group did not show a significant increase. This is in line with the findings of research conducted by Balducci et al. (2010), which showed an increase in IL-10 in the group given combined exercise and a significant decrease in pro-inflammatory cytokines (IL-1β). Muscle contraction caused by physical exercise stimulates the release of IL-6 with the main function of regulating cellular metabolic homeostasis and polarization to an anti-inflammatory environment through stimulation of anti-inflammatory and immunoregulatory cytokines (Pedersen & Febbraio, 2012). IL-10 increases after physical exercise due to compensatory secretion of anti-inflammatory cytokines, mainly driven by increased levels of IL-6 produced by working muscles, which promotes an anti-inflammatory environment during the early post-exercise recovery period (Proschinger et al., 2023).

The results of a previous study showed that HIIE (High Intensity Interval Exercise) caused a significant increase of systemic IL-6 in lean (30 min post) and severely obese subjects (immediate and 30 min post) indicating a role of HIIE in IL-6 modulation (Dorneles et al., 2016). In this context, IL-6 levels increased significantly during HIIE when compared to moderate continuous exercise in highly trained men (Peake et al., 2014). Regarding the chronic effects of high-intensity intermittent exercise, significant reductions in basal systemic CCL2 and IL-6 levels and adipose inflammation were demonstrated after two weeks (Leggate et al., 2012). These differences between studies may be related to metabolic and hormonal interactions during HIIE. The magnitude of the inflammatory response is inversely proportional to the quantity of glycogen, and is directly dependent on the intensity, duration and amount of muscle mass involved (Leggate et al., 2010).

Circulating IL-6 increases when muscle glycogen levels are low, and high levels of glycogenolysis during HIIE may facilitate an increase in IL-6 (Nieman et al., 2003). Previous studies have found that exercise increases muscle metabolism, resulting in increased IL-6 in blood and muscle, and increased IL-10 secretion in macrophages (Masoomeh et al., 2018). Long-term exercise can also reduce menonuclear cell production of atherogenic cytokines such as Tumor Necrosis Factor-alpha (TNF-α) and Interferon-gamma (INF-γ) (Taddei et al., 2000). One of the causes of increased anti-inflammatory cytokines such as IL-10 and decreased pro-inflammatory cytokines is increased fat oxidation, which ultimately correlates with decreased adipose tissue, along with reduced penetration of M1 macrophages into the M2 macrophage monocyte phenotype (Trayhurn & Wood, 2005). A change in the resting cytokine balance to an anti-inflammatory state is one of the effects of Exercise. Eizadi et al (2018) reported similar results in this regard. One of the mechanisms involved in the increase in IL-10 is the exercise-induced increase in IL-6. It has been shown that physical exercise increases muscle metabolism and leads to increased levels of IL-6 in both muscle and blood. Increased IL-6 increases IL-10 secretion in macrophages. By negatively regulating NF-kappa B activity, exercise increases IL-10 secretion by monocytes and T cells via Th2.

High-intensity exercise appears to be associated with a prominent anti-inflammatory environment mediated by Th2 lymphocytes and a decrease or lack of Th1 response (Walsh et al., 2011). This imbalance can lead to an increase in anti-inflammatory and regulatory cytokines, particularly IL-10, which helps control chronic low-grade inflammation (Gleeson et al., 2011). IL-10 is produced primarily by Treg cells and performs important immunomodulatory functions by inhibiting a variety of cells, including dendritic cells, macrophages, and T and B lymphocytes. In Dorneles' (2016) study, a significant increase in systemic IL-10 was observed. This suggests that acute high-intensity exercise is highly beneficial due to its inflammation-fighting regulatory properties. In accordance with this, it was shown that 8 weeks of physical exercise was able to increase IL-10 and decrease TNF-α systemic levels and lead to improvements in cardiac dysfunction (Kesherwani et al., 2015). Therefore, as obesity is a chronic low-grade inflammation with decreased frequency of Treg cells, increased levels of IL-10 after high intensity physical exercise may contribute to positive adaptation and immune cell-mediated regulation (McLaughlin et al., 2014).

Physical exercise has positive effects on metabolic variations such as insulin sensitivity and fat loss, even without overall weight loss, exercise (Langleite et al., 2016). Although overall weight loss does not occur, exercise can reduce abdominal and visceral subcutaneous fat mass. In the case of overweight individuals, visceral fat reduction is greater than subcutaneous fat reduction in response to physical exercise (Langleite et al., 2016). For overweight or obese individuals, exercise methods that combine acaerobic exercise and strength training, have been shown to be effective in fat loss. Aerobic exercise engages the muscles of the whole body, increases energy consumption, and reduces and suppresses fat accumulation. In addition, strength training added after aerobic exercise accelerates fat consumption and increases muscle proportion.

As a result, it has a positive impact of exercise, which has significantly changed body weight, BMI, and body fat levels. Secondly, the time and strength of exercise are related to the utilization rate of various nutrients during exercise. Exercise usually has a smaller strength and longer duration with respect to the percentage that depends on fat oxidation to calculate the overall energy metabolism of the human body (Li & Lorna, 2024).

the exercise intervention lasted for 5 weeks, four times a week. Exercise intensity was controlled by 60%-75% of the subject's maximum resting rate. During exercise, fat becomes the main source of energy, which leads to a reduction in adipose tissue in the body, and body weight, BMI, and body fat levels decrease. If physical exercise is accompanied by a decrease in total body weight, there is a greater relative decrease in visceral fat compared to a decrease in subcutaneous fat (Ross et al., 2000). Weight loss following caloric restriction has been shown to increase circulating anti-inflammatory cytokine IL-10 (Jung et al., 2008). Esposito et al (2003) showed that in obese women, IL-10 levels circulate higher and there is an association between metabolic syndrome and low cytokines. In the study of Formoso et al (2012) also found that the percentage decrease in visceral fat was significantly correlated with the percentage decrease in both TNF- α and IL-6 plasma levels and with the percentage increase in IL-10 levels and there was a significant correlation between the amount of visceral fat loss and increased insulin sensitivity.

This study was limited to a group of obese women selected based on body mass index (BMI). As such, the findings of this study may not apply to male people or people with normal or lower body weight. Also, the results of the study cannot be generalized to other age groups, such as adolescents or the elderly, as the study participants were adult females within the age range of 20 to 30 years. In this study, the combination exercises used included aerobic and resistance exercises with predetermined frequency, duration and intensity. To maintain consistency, the form, intensity or duration of the exercises were not changed. This means that the results of this study may have been different if these variables were changed. Before and after the exercise program, blood samples were taken for testing. As the study lasted for 8 weeks, the long-term effects of combination training on IL-10 levels may not have been fully seen in this study. The hormonal system, which is one of the factors that affect IL-10 levels, was also not considered in this study. Therefore, future research is expected to focus more on measuring the direct effect of combination exercise on IL-10 levels in specific groups as well as the factors that influence it, although these findings may not be generalizable to populations beyond those targeted in this study.

Conclusions

Based on the results of the study, it can be concluded that aerobic exercise by walking on a treadmill for 40 minutes with moderate intensity combined with moderate intensity resistance training with 4-6 sets, 10-15 repetitions with a frequency of 5x/week conducted for 8 weeks in obese women aged between 20-30 years proved to be able to significantly increase interleukin-10 levels. Moderate-intensity exercise can reduce inflammation and improve the body's anti-inflammatory system, which is very important in obesity control. An increase in IL-10 indicates this reaction. This study found that structured exercise is one of the non-pharmacological ways to improve overall public health specifically in obese individuals.

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