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ACUTE MODERATE-INTENSITY STRENGTH EXERCISE INCREASES ANTI-INFLAMMATORY CYTOKINES IN OBESE FEMALES

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Authors' Contribution: A – Study design; B – Data collection; C – Statistical analysis; D – Manuscript Preparation; E – Funds Collection

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Abstract

The study purpose was to prove the effect of acute moderate-intensity endurance and strength exercise on increasing IL-6 levels in obese females.

Materials and methods. A total of 21 obese women aged 20-25 years were recruited from among university students and given two modes of acute exercise intervention, namely moderate-intensity endurance and strength exercise carried out for 35 minutes/session. Subjects were divided randomly into three groups, namely K_1 (control group without intervention; n = 7), K_2 (Acute moderate-intensity endurance exercise; n = 7), K_3 (Acute moderate-intensity strength exercise; n = 7). ELISA was used to analyze serum IL-6 levels before and after exercise. The data analysis technique used the One-way ANOVA test and continued with the Tukey HSD post-hoc test with a significance level of 5%.

Results. The results of the One-way ANOVA test showed that there was a significant difference between serum IL-6 levels after exercise and delta (Δ) in the three groups ($p \leq 0.01$). The results of the Tukey HSD post-hoc test showed that there was a significant difference between serum IL-6 levels after exercise and delta (Δ) at K_3 with K_1 ($p \leq 0.01$), K_3 with K_2 ($p \leq 0.01$), while there was no significant difference in serum IL-6 levels ($p \geq 0.05$) at K_2 with K_1.

Conclusions. Overall, our study concluded that 35 min/session of acute moderate-intensity strength exercise was effective in increasing anti-inflammatory cytokines, such as IL-6, in obese females.

Keywords: endurance exercise, anti-inflammatory, cytokines, obesity, strength exercise.

Introduction

Obesity is a health problems that occur in developed and developing countries (Friedman, 2009). Currently, around 13% of the adult population worldwide was obese in 2016 and the prevalence rate has almost tripled from 1975 to 2016 (WHO, 2021). The trend of obesity prevalence continues, it is estimated that by 2030 20% of the world's adult population will be obese (Kelly et al., 2008). The increase in the prevalence of obesity is directly proportional to the increases in morbidity and mortality worldwide (Abdelaal et al., 2017; Hruby & Hu, 2015). It is because obesity risk of chronic disease morbidities, like disability, depression, diabetes mellitus, hypertension, kidney failure, cardiovascular disease, and several types of cancer (Piché et al., 2020; Hruby & Hu, 2015; Friedman, 2009), so it can reduce the quality of life of obese people (Ogden et al., 2014; Hotamisligil, 2006), and increase the risk of death (Abdelaal et al., 2017; Hruby & Hu, 2015).

Obesity is a condition of increased accumulation of excess fat that can interfere with health (Panuganti et al., 2022). Increased adipose tissue can induce increased pro-inflammatory cytokine secretion and result in the initiation of low-grade chronic inflammation (Petersen & Pedersen, 2005; Ellulu et al., 2017; Zatterale et al., 2020). Increased pro-inflammatory cytokines are associated with metabolic dysfunction and glucose homeostasis (Raman et al., 2018). Exercise can be used as physical therapy in improving systemic metabolic disorders caused by obesity in peripheral tissues, including muscle, liver (Starkie et al., 2003; Pereira et al., 2017), and central nervous system, including hypothalamus (Ropelle et al., 2010). Besides that, exercise can as will be used to maintain homeostasis of pro and anti-inflammatory cytokines (Docherty et al., 2022; Ross et al., 2021).

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Exercise performed acutely has a positive effect on inhibiting the development of chronic disease through the post-exercise inflammatory response (Kramer & Goodyear, 2007). One of the inflammatory responses that increase post-exercise is muscle interleukin-6 (IL-6) levels (Fischer, 2006; Pedersen & Febbraio, 2008). Muscle IL-6 levels increase up to 100-fold during exercise and decrease rapidly after exercise (Docherty et al., 2022). The magnitude of the increase in muscle IL-6 levels during exercise depends on the mode of exercise, intensity of exercise, duration of exercise, and capacity of exercise in each individual (Ostrowski et al. 1999; Febbraio & Pedersen, 2002; Mendham et al., 2011). The American College of Sports Medicine (ACSM) explain that appropriate exercise doses can improve several health-promoting parameters, such as decreased systemic inflammation, by decreasing the secretion of proinflammatory cytokines (Garber et al., 2011; Theodorou et al., 2016; Dieli-Conwright, 2018).

Exercise has an anti-inflammatory effect by increasing the secretion of IL-6 in muscle to stimulate increased secretion of IL-10 (Starkie et al., 2003; Ropelle et al., 2010) hence inhibiting pro-inflammatory secretion, like TNF-α (Docherty et al., 2022). However, several studies reported inconsistent results (increase, decrease or no significant change) in IL-6 levels following moderate-intensity exercise (Mendham et al., 2011; Dimitrov et al., 2017; Windsor et al., 2018; Andarianto et al., 2022; Sugiharto et al., 2022). Factors that might influence the inconsistency of results at the IL-6 level, namely differences in exercise mode, exercise intensity, and duration of exercise (Fischer et al., 2006; Nindl et al., 2009; Mendham et al., 2011; Hennigar et al., 2017; Cerqueira et al., 2020; Andarianto et al., 2022). Therefore, the aim of this study was to prove the effect of acute moderate-intensity endurance and strength exercise on increasing IL-6 levels in obese females.

Materials and Methods

Research design

The design of this research is a randomized pretest-posttest control group design. A total of 21 obese female with inclusion criteria aged 20-25 years, body mass index (BMI) 27-35 kg/m^2, normal blood pressure, normal resting heart rate, normal oxygen saturation (SpO_2), normal fasting blood glucose (FBG), and normal hemoglobin (Hb) were recruited from among students and randomly divided into three groups, namely K_1 (n = 7, control group without intervention), K_2 (n = 7, acute moderate-intensity endurance exercise), dan K_3 (n = 7, acute moderate-intensity strength exercise). The Health Research Ethics Commission, Faculty of Medicine, Airlangga University, Surabaya has reviewed and approved all these research procedures with the registration number: 284/EC/KEPK/FKUA/2021.

Endurance and strength exercise program

The exercise program implemented in this study used two different exercise modes, namely endurance and strength exercise. Endurance exercise is running on a treadmill with an intensity of 60-70% HRmax for 35 minutes (Rejeki et al., 2022). Strength exercise was carried out using gym equipment with an intensity of 60-70% 1-RM which was carried out for 5 sets @12-15 reps and active rest between sets of 30 seconds. The exercise method used in strength exercise is circuit exercise which is divided into 2 (upper body and lower body). Upper body include, chest press, shoulder press, and tricep push-down, while lower body include leg extension, leg press, and leg curls. Warming up and cooling down out for 5 minutes each (Rejeki et al., 2022; Rejeki et al., 2021).

Anti-inflammatory cytokine measurement

Analysis of IL-6 levels before and after exercise was carried out using the ELISA kit (Catalog Number: E-EL-H6156; Elabscience, Inc., USA) method with a sensitivity level of 0.94 pg/mL and detection range 1.56-100 pg/mL.

Statistical analysis

The data in tables 1-2 are shown with mean ± SD. Paired Sample T-Test was applied to evaluate differences in serum IL-6 levels between before and after exercise in each group, while the One-way ANOVA test and Tukey's HSD post-hoc test were used to determine differences in levels intergroup serum IL-6. The level of significance applied in the statistical analysis used $p \le 0.05$. SPSS software versi 21.0 was used in the overall statistical analysis.

Results

Baseline data on the characteristics of study subjects between groups can be seen in Table 1.

The results of the One-way ANOVA test showed was no significant difference in the mean baseline data for the characteristics of study subjects between groups ($p \ge 0.05$).

Table 1. The results of descriptive statistical analysis of the characteristics of research subjects

Parameter	K_1 (n=7)	K_2 (n=7)	K_3 (n=7)	p-value
Age (years)	22.14±1.68	21.29±1.50	21.71±1.38	0.584
BW (kg)	76.88±6.42	74.39±7.07	74.88±8.35	0.799
BH (m)	1.58±0.06	1.57±0.07	1.55±0.07	0.566
BMI (kg/m^2)	30.56±3.36	30.22±2.52	30.98±2.90	0.890
FM (kg)	33.32±5.74	32.77±4.51	33.33±4.62	0.971
FM (%)	40.57±5.36	43.90±2.36	44.46±3.47	0.164
FMI (kg/m^2)	12.89±2.51	13.32±1.79	13.92±2.33	0.691
FFM (kg)	44.67±2.47	41.63±2.95	41.55±5.13	0.226
FFMI (kg/m^2)	17.82±1.17	16.90±0.90	17.22±0.96	0.257
SMM (kg)	20.11±1.36	18.52±1.45	20.08±5.30	0.590
SBP (mmHg)	114.00±7.35	109.72±9.23	114.29±10.27	0.579
DBP (mmHg)	76.86±7.38	77.86±8.19	82.14±8.53	0.443
RHR (bpm)	76.86±10.90	76.86±5.18	82.29±8.26	0.400
SpO2 (%)	98.26±0.49	98.00±0.82	98.00±1.15	0.777
FBG (mg/dL)	89.00±6.16	93.43±4.24	90.00±6.81	0.352
Hb (g/dL)	15.19±1.73	15.23±1.33	15.79±1.43	0.712

Description: Data are presented with mean ± SD. One-way ANOVA test was used to obtain the p-value.

Table 2. Results of analysis of mean serum IL-6 levels between groups

Period of Time	IL-6 (pg/mL)			p-value
	K_1 (n=7)	K_2 (n=7)	K_3 (n=7)	
Before exercise	246.06±99.59	276.07±146.83	257.26±75.71	0.879
After exercise	263.33±127.32	327.67±61.16	527.89±122.03*†	0.001
Delta (Δ)	17.27±122.25	51.60±138.85	270.63±144.85*†	0.005

Description: Data are presented with mean ± SD. One-way ANOVA test and followed by Tukey's HSD post-hoc test was used to obtain the p-value. (*) Significant with K1 ($p \leq 0.01$). (†) Significant with K2 ($p \leq 0.05$).

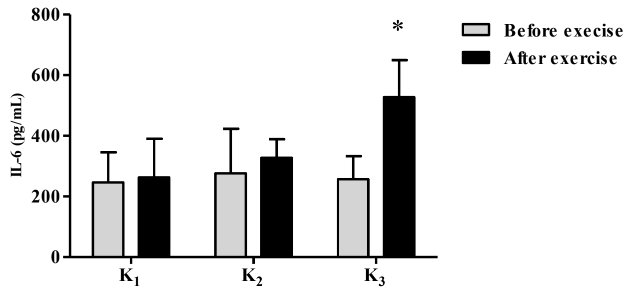

Fig. 1. The results of the analysis of IL-6 levels between before and after exercise intervention. Description: Data are presented with mean ± SD. Paired Sample T-Test was used to obtain the p-value. (*) Significant with before exercise ($p \leq 0.01$).

The analysis of the mean serum IL-6 levels between before and after endurance and strength exercise are presented in Figure 1.

The results of the Paired Sample T-Test showed was significant difference mean serum IL-6 levels between before and after exercise at K_3 ($p \leq 0.01$), whereas at K_1 and K_2 there was no significant increase ($p \geq 0.05$). The results of the analysis of the mean serum IL-6 levels based on the time period presented in Table 2.

Based on the One-way ANOVA test, there was no significant difference in the mean serum IL-6 levels before exercise ($p \geq 0.05$), while after exercise and delta (Δ) showed a significant difference ($p \leq 0.01$). The Tukey's HSD post-hoc test showed was a significant difference in the mean serum IL-6 levels after exercise between K_3 and K_1 (p=0.001), K_3 with K_2 (p=0.007), while K_2 and K_1 did not show a significant difference (p=0.516). The results of Tukey's HSD post-hoc test showed was a significant difference in mean delta (Δ) serum IL-6 levels between K_3 and K_1 (p=0.007), K_3 and K_2 (p=0.019), while K_2 and K_1 did not show a significant difference (p=0.516).

Discussion

The aim of this study was to prove the effect of acute moderate-intensity endurance and strength exercise on increasing IL-6 levels in obese females. The results showed that strength exercise significantly increased serum IL-6 levels, while endurance exercise did not show a significant. Griffen et al. (2021) reported that markers of systemic inflammation decreased after strength versus endurance exercise. Another study revealed that serum IL-6 levels were higher in strength exercise compared to endurances (Sabag et al., 2017). Docherty et al. (2022) in their research explained that strength exercise can increase muscle-derived (myokine), such as IL-6 which can help regulate anti-inflammatory responses. IL-6 can act as a pro-inflammatory and anti-inflammatory cytokine (Nara & Watanabe, 2021). Exercise has complex benefits for the body (Ruegsegger & Booth, 2018). This is because exercise involves not only skeletal muscle contraction but also systemic activity of the respiratory and circulatory systems (Nara & Watanabe, 2021). During exercise, muscle contraction increase so that it can stimulate myocytes to produce the myokines involved in autocrine regulation of metabolism in muscles as well as in paracrine/endocrine regulation of other organs and tissues, including the brain, liver, and adipose tissue through their receptors (Lee & Jun, 2019; Pedersen, 2019; Carson, 2017). This is one of the pleiotropic functions of IL-6 in various tissues and organs (Muñoz-Cánoves, et al., 2013). Muscles that move during exercise create stressors and secrete myokines, such as IL-6 (Lira et al., 2017). Increased IL-6 triggers the release of anti-inflammatory cytokines that will balance inflammation after exercise (Abd El-Kader & Al-Shreef, 2018). Muscle contraction will trigger the hypothalamic–pituitary–adrenal axis (HPA-axis) to be active so that cortisol levels (Bonato et al., 2017), and potent anti-inflammatory hormones in the blood increase (Ruijters et al., 2016). Muscle contractions also trigger activation of the sympathetic nervous system to increase catecholamine levels. Catecholamines can suppress the production of lipopolysaccharide (LPS) producing TNF-α and IL-1β (Gleeson et al., 2011), thereby reducing levels of pro-inflammatory cytokines (Cerqueira et al., 2020; Gleeson et al., 2011).

Obesity is the accumulation of excess fat in adipose tissue that can interfere with health (Panuganti et al., 2022). Obesity can be caused by an imbalance between caloric intake and long-term energy expenditure (Fan & Evans, 2017; Hruby & Hu, 2015). In addition, lifestyle, unhealthy eating patterns, and lack of physical activity can also trigger obesity (Rejeki et al., 2021; Sugiharto et al., 2022; Kim et al., 2015). Lifestyle modification recommended in obesity management (Gadde et al., 2018). Controlling energy expenditure and energy intake is one of the main mechanisms in regulating energy balance (Sugiharto et al., 2021; Gadde et al., 2018). Exercise can be used as an effective method of increasing energy expenditure, so exercise can be used as physical therapy in overcoming and preventing obesity (Rejeki et al., 2021, Sugiharto et al., 2021; Tsuchiya et al., 2014; Wiklund, 2016). Acute exercise can trigger an increase in the release of IL-6 (Andarianto et al., 2022) to activate the extracellular signal-regulated kinase 1/2 (ERK1/2) pathway, leading to increased lipolysis in visceral fat (Yang et al., 2020). Continuous increase in lipolysis can suppress adipose cell proliferation, resulting in a decrease in visceral fat tissue (Wedell-Neergaard et al., 2019). In addition, exercise is suspected to have an anti-inflammatory effect by increasing the secretion of IL-6 to stimulate an increase in IL-10 secretion (Starkie et al., 2003; Ropelle et al., 2010), so that it will inhibit the secretion of pro-inflammatory, such as TNF-α which will have an impact on reducing chronic systemic inflammation (Docherty et al., 2022; Ellingsgaard et al., 2019).

IL-6 is one of the most popular myokines being discussed in several previous studies (Zunner et al., 2022; Karstoft & Pedersen, 2016; Pedersen & Febbraio, 2012). IL-6 has a dual role namely, it can act as a pro-inflammatory cytokine, and act as an anti-inflammatory when released by contracting muscles (Zunner et al., 2022; Pedersen & Febbraio, 2008). IL-6 has regenerative and anti-inflammatory functions, especially when secreted by skeletal muscle during exercise (Kistner et al., 2022; Fischer 2006). As an anti-inflammatory cytokine, IL-6 has been reported to inhibit pro-inflammatory effects, like inhibiting TNF-α, increasing M2 macrophage polarization, and insulin sensitivity (Sindhu et al. 2015; Pedersen et al., 2001; Mauer et al., 2014). Increased levels of IL-6 mediated by exercise can reduce the risk of non-communicable diseases, such as diabetes mellitus, cardiovascular disease, and some types of cancer (Severinsen & Pedersen, 2020). This has proven that exercise has many health benefits, one of which can improve the body's metabolism (Thyfault & Bergouignan, 2020).

The limitation of this study is the number of subjects used in the study only amounted to 21 people, if the number of subjects used was greater it could describe the condition of obese women in Indonesia. This study did not observe the molecular mechanisms involved in increasing serum IL-6 levels, so only the results of increasing serum IL-6 levels were obtained without knowing the mechanism involved. During the intervention period, the subjects were not quarantined, so we could not control the activities of the research subjects in detail.

Conclusion

In general, it can be concluded that the 35 min/session acute moderate-intensity strength exercise was effective in increasing anti-inflammatory cytokines, like IL-6 in obese female. This study can be used as a basis in the management of preventing the increase in the prevalence of obesity and as an effort to reduce the impact of morbidity, mortality and improve the quality of life of obese.

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Conflict of interest

The authors do not have any conflicts of interest.

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СИЛОВІ ВПРАВИ СЕРЕДНЬОЇ ІНТЕНСИВНОСТІ ІЗ СИЛЬНИМ ФІЗИЧНИМ НАВАНТАЖЕННЯМ ПІДВИЩУЮТЬ РІВЕНЬ ПРОТИЗАПАЛЬНИХ ЦИТОКІНІВ У ЖІНОК ІЗ ОЖИРІННЯМ

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Авторський вклад: A – дизайн дослідження; B – збір даних; C – статаналіз; D – підготовка рукопису; E – збір коштів

Реферат. Стаття: 7 с., 2 табл., 1 рис., 66 джерел.

Метою дослідження було довести вплив силових вправ із сильним фізичним навантаженням і вправ на витривалість середньої інтенсивності на підвищення рівня інтерлейкіну-6 (IL-6) у жінок з ожирінням.

Матеріали та методи. Для участі в дослідженні була залучена загалом 21 жінка з ожирінням віком 20–25 років зі студенток університету, вони отримали два режими інтервенції у формі вправ із сильним фізичним навантаженням, а саме: вправи на витривалість і силові вправи середньої інтенсивності, які виконувалися протягом 35 хвилин/заняття. Учасниць випадковим чином розділили на три групи, а саме: K_1 (контрольна група без інтервенції; n = 7), K_2 (вправи на витривалість із сильним фізичним навантаженням середньої інтенсивності; n = 7), K_3 (силові вправи із сильним фізичним навантаженням середньої інтенсивності; n = 7). Для аналізу рівнів інтерлейкіну-6 у сироватці до та після виконання вправ використовували ферментний імуносорбентний аналіз (ELISA). У методиці аналізу даних використовували однофакторний дисперсійний аналіз із наступним розрахунком середнього Тьюкі за одержаними результатами за рівня значущості 5%.

Результати. Результати однофакторного дисперсійного аналізу показали наявність статистично значущої різниці між рівнями інтерлейкіну-6 у сироватці після виконання вправ та дельтою (Δ) у трьох групах ($p \leq 0,01$). Результати розрахунку середнього Тьюкі за одержаними результатами показали наявність статистично значущої різниці між рівнями інтерлейкіну-6 у сироватці після виконання вправ та дельтою (Δ) у парах K_3 з K_1 ($p \leq 0,01$), K_3 з K_2 ($p \leq 0,01$), тоді як у парі K_2 з K_1 статистично значущої різниці між рівнями інтерлейкіну-6 у сироватці не було ($p \geq 0,05$).

Висновки. Загалом, на підставі результатів нашого дослідження було зроблено висновок, що силові вправи із сильним фізичним навантаженням середньої інтенсивності по 35 хвилин/заняття були ефективними для підвищення рівня протизапальних цитокінів, таких як інтерлейкін-6, у жінок з ожирінням.

Ключові слова: вправи на витривалість, протизапальний, цитокіни, ожиріння, силові вправи.

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