Effects of High-Intensity Interval Exercise on Interleukin 6 Levels in Healthy Male Adolescents

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Abstract

This study aims to prove the effects of high-intensity interval exercise on interleukin 6 (IL-6) levels in healthy male adolescents. Twenty healthy male adolescents aged twenty to twenty-five years with a body mass index (BMI) of 19-24 kg/m^2 were given one session of high-intensity interval exercise intervention by pedaling an ergocycle for 40 minutes. The ELISA method evaluated IL-6 levels between pretest and posttest in both groups. The data analysis technique uses a Paired Sample T-Test with a significance level of 5%. The results showed that there was an increase in the average IL-6 levels between the pretest and posttest in the high-intensity interval exercise group ($p \leq 0.05$). In contrast, in the control group there was no significant difference in the average IL-6 levels. 6 between pretest and posttest ($p \geq 0.05$). It is proven that one session of high-intensity interval exercise increases IL-6 levels in healthy male adolescents.

Keywords: High-intensity interval exercise; ergocycle exercise; IL-6 levels; metabolism

1. Introduction

Interleukin 6 (IL-6) is a cytokine that has pleiotropic functions in various tissues and organs (Muñoz-Cánoves et al., 2013). Skeletal muscle can produce and release IL-6 significantly after exercise (Muñoz-Cánoves et al., 2013; Lee & Jun, 2019). The increase in IL-6 after exercise depends on several factors such as age, body composition, and genetically expressed variations in the inflammatory response, including greater expression of toll-like receptor 4 (TLR4), which can induce greater transcription of inflammatory cytokines (Rogero & Calder, 2018). When released into the circulation, IL-6 can promote metabolic modulation in several organs like hormones, such as hepatic glucose production during exercise or lipolysis occurring in adipose tissue (Thyfault & Bergouignan, 2020). In skeletal muscle, IL-6 will also aid glucose metabolism in a manner dependent on signal transduction involving PI-3 kinase and the JAK-STAT pathway through enhanced expression of the major glycolytic enzymes, hexokinase 2 and PFKFB-3 (Kumari et al., 2016). This mechanism will also increase glucose transport by inducing the expression of glucose transporters 1 and 4

(GLUT-1 and GLUT-4), then translocating to the plasma membrane to increase glucose absorption (Kumari et al., 2016). In addition, IL-6 also causes activation of AMP-activated protein kinase (AMPK) phosphorylation, which is useful for increasing glucose uptake and lipid oxidation (Carey et al., 2006). The acute release of IL-6 after exercise can also produce anti-inflammatory effects characterized by increased production of anti-inflammatory cytokines, such as IL-1ra and IL-10 (Tajra et al., 2014).

Acute physical exercise has a positive effect in inhibiting the development of chronic diseases through post-exercise inflammatory responses (Pranoto et al., 2023; Kramer & Goodyear, 2007). One of the inflammatory responses that increases post-exercise is IL-6 levels (Fischer, 2006; Pedersen & Febbraio, 2008). IL-6 levels increase exponentially (up to 100-fold) in response to exercise and decrease rapidly in the post-exercise period (Docherty et al., 2022). The magnitude of the increase in IL-6 levels during acute exercise depends on the training mode, training intensity, training duration, and training capacity of each individual (Ostrowski et al., 1999; Ostrowski et al., 2000; Febbraio & Pedersen, 2002). Several studies reported inconsistent results (increase, decrease, or no change) in IL-6 levels after acute exercise (Dimitrov et al., 2017; Windsor et al., 2018; Mendham et al., 2011). Factors that are likely to influence the inconsistency of results on IL-6 levels, namely differences in training mode, training intensity, and training duration (Mendham et al., 2011; Cerqueira et al., 2020; Pranoto et al., 2023).

Based on this, this research aims to prove the effects of high-intensity interval exercise on interleukin 6 (IL-6) levels in healthy male adolescents.

2. Material and methods

This research uses a true-experimental method with a pretest-posttest control group design research design. Respondents in this study were twenty healthy male adolescents, aged twenty to twenty-five years, with body mass index (BMI) of 19-24 kg/m^2, normal blood pressure, normal heart rate, normal fasting blood glucose, and normal hemoglobin. Respondents were randomly divided into two groups, namely CTL (n = 10, control group), and HIE (n = 10, high-intensity interval exercise group).

High-intensity interval exercise is done by pedaling an ergocycle for 40 minutes with details of 5 minutes of warm-up (50% – 60% HRmax), 30 minutes of core (80 – 90% HRmax) which is done in intervals (6 sets) each set is done for 5 minutes with active rest between sets for 2 minutes and closed with 5 minutes of cooling down (50% – 60% HRmax). The high-intensity interval exercise intervention is applied once (acute exercise). Monitor heart rate during exercise using Polar H7.

Blood was drawn from the cubital vein for 3 ml. When taking blood, the subject was in a sleeping position. Blood sampling was carried out 2 times, namely 30 minutes before the intervention and 10 minutes after the intervention. IL-6 levels were measured using the Enzyme Link Immunosorbent Assay (ELISA) method (Cat.No.:E-EL-H6156; Elabscience, Inc., USA).

The data analysis technique used SPSS version 21 software. The Shapiro-Wilk test and Levene test were used to test normality and homogeneity with a significant level ($p \geq 0.05$). The difference test uses a Paired Sample T-Test and an Independent Samples T-Test with a significant level ($p \leq 0.05$). Data presentation is done as mean ± SD.

3. Results

The differences in the results of the analysis of the characteristics of research subjects in each group can be seen in Table 1.

Table 1. Differences in characteristics of research subjects in the two groups

Variable	n	Groups		Sig. (2-tailed)
		CTL	HIE	
Age, years	10	20.60 (1.17)	21.20 (1.03)	0.241
Weight, kg	10	1.65 (0.05)	1.68 (0.04)	0.221
Height, m	10	62.01 (5.66)	63.22 (6.40)	0.660
BMI, kg/m^2	10	22.74 (1.21)	22.50 (1.76)	0.729
SBP, mmHg	10	116.60 (7.91)	117.70 (5.74)	0.727
DBP, mmHg	10	72.10 (7.16)	68.40 (3.98)	0.175
HR, bpm	10	71.90 (10.39)	70.80 (9.705)	0.810
SpO_2, %	10	98.00 (1.06)	97.20 (1.23)	0.136
BT, °C	10	35.26 (0.56)	35.45 (0.83)	0.557

Description: BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; HR: Heart rate; SpO_2: Oxygen saturation; BT: Body temperature. Sig. (2-tailed) was obtained using the Independent Sample T-Test. Data are presented as mean±SD.

Based on the results of statistical analysis, it shows that there is no significant difference in the average data on the characteristics of research subjects in each group ($p \leq 0.05$). The results of the analysis of differences in IL-6 levels between the pretest and posttest in each group are presented in Figure 1.

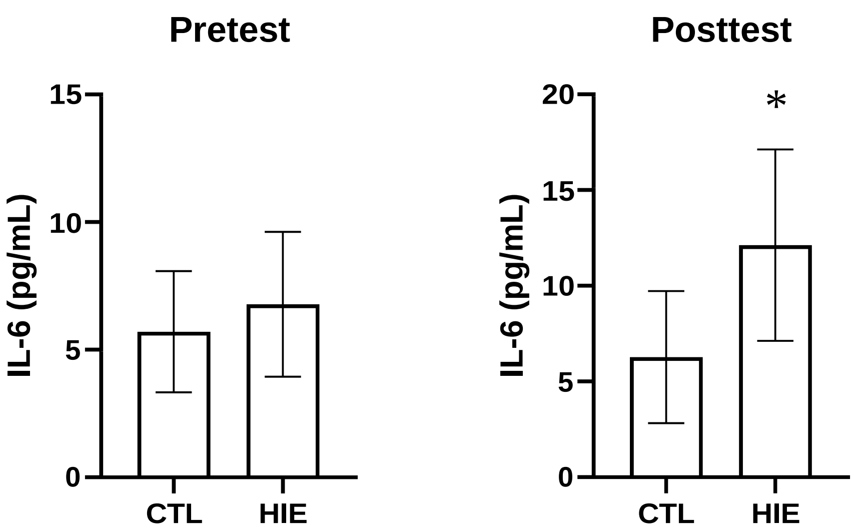

Figure 1. Differences in IL-6 level analysis results between pretest and posttest.
Description: Sig. (2-tailed) was obtained using the Independent Sample T-Test. Data are displayed as Mean±SD. (*) Significantly different from CTL ($p \leq 0.05$).

4. Discussion

Based on the research results, shows that high-intensity interval exercise (HIE) significantly increases IL-6 levels. These results are in line with the results of research conducted by Zwetsloot et al. (2014) who reported that a single session of high-intensity interval training (HIIT) induced an increase in IL-6 levels compared to pre-exercise in healthy young men. Another study reported that serum IL-6 levels in the HIIT group increased significantly in the one-hour post-HIIT phase in middle-aged men (Rohnejad & Monazzami, 2023). Exercise has complex benefits for the body (Ruegsegger & Booth, 2018). This is because exercise not only involves skeletal muscle contractions but also systemic activity of the respiratory and circulatory systems (Nara & Watanabe, 2021). During exercise, there is an increase in muscle contractions which will stimulate myocytes to produce myokines which are involved in the autocrine regulation of metabolism in muscles as well as in the paracrine/endocrine regulation of other tissues and organs including adipose tissue, liver, and brain through their receptors (Lee & Jun, 2019; Carson, 2017). This is one of the pleiotropic functions of IL-6 in various tissues and organs (Muñoz-Cánoves et al., 2013). Muscle movement during exercise creates stressors and secretes myokines, such as IL-6 (Lira et al., 2009). Increased IL-6 triggers the release of anti-inflammatory cytokines (IL-10 and IL-1R) which will balance the inflammatory events after exercise (Abd El-Kader & Al-Shreef, 2018). Muscle contraction will trigger the activation of hypothalamic–pituitary–adrenal axis (HPA-axis) to stimulate an increase in cortisol levels (Bonato et al., 2017), and increase potent anti-inflammatory hormones in the blood (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) which produces TNF-α and IL-1β (Gleeson et al., 2011), thereby reducing levels of the pro-inflammatory cytokine, TNF-α to maintain the balance of inflammation in the body (Cerqueira et al., 2020).

IL-6 is known to be the first myokine discovered and is one of the most popular myokines discussed in several previous studies (Zunner et al., 2022; Mahmoud et al., 2022; Mageriu et al., 2020; Gonzalez-Gil & Elizondo-Montemayor, 2020; Furuichi et al., 2018; Gmiat et al., 2017; Karstoft Pedersen, 2016). Although it is known that IL-6 is a pro-inflammatory cytokine, it also has anti-inflammatory capacity when released by contracting muscles (Zunner et al., 2022). IL-6 has regenerative and anti-inflammatory functions, especially when secreted by skeletal muscles during physical exercise (Kistner et al., 2022). As an anti-inflammatory cytokine, IL-6 has been reported to inhibit pro-inflammatory effects, such as TNF-α, promote M2 macrophage polarization, and improve insulin sensitivity (Sindhu et al., 2015). Increases in IL-6 levels mediated by physical exercise can reduce the risk of various non-communicable chronic diseases, such as diabetes mellitus, dementia, cardiovascular disease, and some types of cancer (Severinsen & Pedersen, 2020). This proves that exercise has many health benefits, one of which is improving the body's metabolism (Thyfault & Bergouignan, 2020).

5. Conclusion

The results of the study prove that one session of high-intensity interval exercise (HIE) increases IL-6 levels in healthy male adolescents. Therefore, HIE can be used to improve and maintain the body's metabolism.

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