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Anti-inflammatory responses to short-term high-intensity ergocycle training in healthy males

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Abstract

Introduction. Interleukin 10 (IL-10) is a cytokine with strong anti-inflammatory properties that plays an important role when produced during exercise, and has a role in limiting the body's immune response to pathogens and preventing tissue damage. Aim of Study. This study aimed to investigate the effect of high-intensity ergocycle training (HIET) on increasing IL-10 levels in healthy adolescent males. Material and Methods. A true-experimental design with pretest–posttest control groups was employed. The study involved 30 adolescent males aged 19–24 years, with a body mass index (BMI) of 19-22 kg/m^2 and no history of chronic disease. The participants were randomly assigned to two groups: G1 (n = 15, control group) and G2 (n = 15, HIET group). The HIET regimen involved pedaling an ergocycle for 40-60 minutes, including a 5-minute warm-up at 50-60% maximum heart rate (HRmax), 30-50 minutes of interval training at 80-90% HRmax (6 sets of 5 minutes each, with 2 minutes of active rest between sets), and a 5-minute cooldown at 50-60% HRmax. This intervention was conducted over the period of 4 weeks, with sessions held three times per week. IL-10 levels were measured via enzyme-linked immunosorbent assay (ELISA), using an ELISA kit. Statistical analysis was performed via the independent samples t-test with a significance level of 5%. Results. The results revealed no significant difference in pre-HIET IL-10 levels between G1 and G2 (7.64 ± 1.87 vs 8.41 ± 1.60 pg/mL; p = 0.239; ES: 0.442). However, post-HIET IL-10 levels were significantly greater in G2 than in G1 (8.33 ± 1.57 vs 14.35 ± 3.33 pg/mL; p = 0.001; ES: 2.312), and the change in IL-10 levels (delta) was also significantly greater in G2 (0.68 ± 0.48 vs 5.94 ± 0.68 pg/mL; p = 0.001; ES: 8.937). Conclusions. These findings indicate that HIET effectively enhances the anti-inflammatory response, as evidenced by increased IL-10 levels in healthy adolescent males.

KEYWORDS: adolescent health, anti-inflammation, cytokines, high-intensity training, IL-10.

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Introduction

Physical activity has profound positive effects on health [19]. In healthy individuals, both acute and chronic exercises are well recognized for their ability to modulate the concentration of circulating inflammatory markers, reduce infection incidence, and lower the risk of chronic diseases associated with morbidity [4]. Engaging in physical activity and/or exercise serves as a highly effective drug-free strategy for preventing and treating numerous chronic conditions [30]. The influence of physical activity and exercise on overall health, quality of life, and the prevention and management of specific diseases is remarkable [38]. As advocated by the World Health Organization (WHO) in 2020, promoting an active lifestyle and appropriate levels of physical exercise are essential for mitigating the risk of preventable adverse health outcomes for all individuals [38]. Consequently, research on physical activity and exercise remains a compelling and pertinent field of study.

The recently updated 2020 WHO guidelines on physical activity and sedentary behavior recommend engaging in at least 150-300 minutes of moderate-intensity physical activity or 75-150 minutes of vigorous-intensity aerobic exercise per week to achieve substantial health benefits [3]. Despite the well-established importance of long-term aerobic exercise for health, modern children and adolescents often struggle to find time for physical exercise outside of school due to academic and entertainment pressures [9]. In such cases, high-intensity interval training (HIIT) offers a time-efficient strategy to induce numerous beneficial physiological adaptations [21]. HIIT consists of repetitive high-intensity activities interspersed with short rest or recovery intervals [40]. HIIT has been reported to elicit strong metabolic and immunological responses, including an inflammatory reaction that alters the balance of pro- and anti-inflammatory cytokines, playing a crucial role in tissue repair and energy metabolism [4]. However, despite its proven benefits, research on the specific effects of HIIT on anti-inflammatory cytokines, particularly interleukin 10 (IL-10), shows inconsistent results. While some studies indicate a significant increase in IL-10 following high-intensity exercise [1, 11, 17], others suggest that such exercise might provoke an inflammatory response due to its stress-inducing nature, potentially leading to increased levels of pro-inflammatory markers [23, 35]. These conflicting findings highlight a need for further investigation into how short-term HIIT regimens influence IL-10 and other inflammatory markers in various populations, including healthy adolescents.

To ensure the validity of the findings, this study specifically included only male participants to minimize the potential confounding effects of hormonal fluctuations associated with the menstrual cycle, which can influence inflammatory responses and cytokine production. Previous research has shown that estrogen and progesterone levels modulate immune function and may alter IL-10 responses to exercise, making it challenging to isolate the direct impact of high-intensity ergocycle exercise (HIET) on inflammatory regulation in mixed-gender studies [6]. Additionally, sex differences in muscle metabolism, recovery rates, and exercise-induced cytokine responses suggest that the effects of HIET may vary between males and females. Future research should explore these differences to determine whether the observed anti-inflammatory effects of HIET extend to female populations.

Inflammation, as a biological response of the immune system, is designed to prevent, limit, and repair damage caused by pathogens or endogenous biomolecules [33]. Exercise-induced inflammation is mediated by cytokines such as interleukin-6 (IL-6), which inhibits tumor necrosis factor alpha (TNF-α) formation, leading to increased levels of IL-10 and interleukin-1 receptor antagonist (IL-1RA) [40]. The anti-inflammatory cytokine IL-10 plays a critical role in suppressing inflammatory processes [10]. However, exercise also acts as a stressor, which may exacerbate or mitigate inflammation depending on the intensity, duration, and population studied [5, 37]. These contrasting mechanisms suggest a complex interplay between exercise, inflammation, and recovery, making IL-10 a key focus in understanding the anti-inflammatory effects of HIET.

However, most existing studies on the anti-inflammatory effects of HIET have focused on athletes, older adults, or individuals with metabolic disorders, leaving a gap in research on healthy young males. Adolescence and early adulthood represent critical periods for establishing lifelong health behaviors, yet the specific inflammatory responses to short-term HIET in this demographic remain underexplored. Additionally, although the relationship between exercise and IL-10 has been studied, results remain inconsistent, particularly regarding the short-term effects of structured HIET programs on anti-inflammatory cytokines [36]. Understanding how HIET influences IL-10 levels in young males is crucial, as it may help optimize training regimens for both athletic performance and disease prevention. This study aims to address this gap by investigating the effects of a 4-week HIET program on IL-10 levels in healthy male individuals.

Aim of Study

Therefore, the implementation of physical exercise necessitates a well-structured program to ensure proper execution, particularly concerning the effects of exercise on inflammatory markers. Given this context, the aim of this study was to investigate the impact of HIET on IL-10 levels in adolescent males.

Materials and Methods

Research design

This study employed a true-experimental method with a pretest–posttest control group design. The participants included 30 adolescent males, aged 19-24 years, with a body mass index (BMI) ranging from 19-24 kg/m², normal blood pressure, normal heart rate, normal fasting blood glucose levels, normal hemoglobin levels, and no history of chronic disease. The subjects were selected via consecutive sampling, and the groups were randomly assigned into two groups: G_1 (n = 15, control group) and G_2 (n = 15, HIET group). All procedures in this study were approved by the Research Ethics Commission of Universitas Negeri Malang (KEP UM) (No:24.06.1/UN32.14.2.8/LT/2024).

High-intensity ergocycle training protocol
HIET was conducted by having participants pedal an ergocycle for 40-60 minutes. The training session included a 5-minute warm-up at 50-60% of the maximum heart rate (HRmax), followed by 30-50 minutes of core exercise at 80-90% HRmax, performed in intervals (6 sets). Each set lasted 5 minutes, with 2 minutes of active rest between sets. The session concluded with a 5-minute cooldown at 50-60% HRmax. The HIET intervention was applied over the period of 4 weeks, with a frequency of 3 sessions per week. Heart rate was monitored during the exercise via a Polar heart rate sensor.

Data collection
The data collection techniques involved various measurements. Height was measured via a Seca® stadiometer, whereas body weight (BW) was measured via an OMRON Model HN-289 digital scale [28]. BMI was calculated by dividing BW (kg) by height in meters squared (m^2) [24]. The participants' resting heart rate and oxygen saturation levels were measured using a pulse oximeter [27]. Systolic and diastolic blood pressures were measured via an OMRON Model HEM-7130 L digital tension meter [29]. Fasting blood glucose levels were measured via the ACCU-CHEK® Performa, reported in mg/dL, and hemoglobin levels were measured via the Easy Touch GCHb, reported in g/dL [29].

Blood collection and biochemical examination procedures
Blood samples were drawn from the cubital vein, with 3 ml collected each time. During blood collection, the subjects were in a supine position. Blood samples were taken twice: once before the intervention (week 0) and again 24 hours after the final intervention (week 4). IL-10 levels were measured via enzyme-linked immunosorbent assay (ELISA) (Cat. No. E-EL-H6154; Elabscience, Inc., USA).

Statistical analysis
The statistical analyses were conducted via the SPSS software (version 21). Normality was assessed via the Shapiro–Wilk test, whereas homogeneity of variance was evaluated via Levene's test, with significance thresholds of $p \geq 0.05$. Group differences were examined through both the paired samples t-test and the independent samples t-test, with statistical significance established at $p \geq 0.05$. In instances where the data failed to meet the assumptions of normality or homogeneity of variance, the Wilcoxon signed-rank test, a non-parametric alternative, was employed, maintaining the significance criterion of $p \geq 0.05$. Effect sizes were quantified via Cohen's d.

Results
Based on the research results, basic data such as age, anthropometry and vital signs were obtained and did not show any significant differences between the two groups which can be seen in Table 1. Meanwhile, the results of the analysis of IL-10 levels between pre-HIET and post-HIET in each group are presented in Figure 1

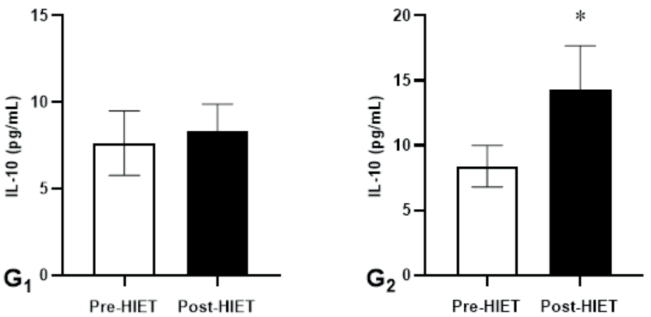
Table 1. Age, anthropometric, and vital sign data measurements

Variables	G1 n = 15	G2 n = 15	p-value
Age (years)	21.13 ± 1.19	20.67 ± 1.24	0.300
Height (m)	1.68 ± 0.06	1.67 ± 0.04	0.404
Body weight (kg)	63.19 ± 5.39	60.67 ± 3.59	0.144
Body mass index (kg/m^2)	22.41 ± 1.09	21.92 ± 0.92	0.193
Systolic blood pressure (mmHg)	115.07 ± 6.26	114.87 ± 3.99	0.918
Diastolic blood pressure (mmHg)	71.40 ± 3.44	72.13 ± 4.64	0.627
Resting heart rate (bpm)	72.33 ± 5.61	70.67 ± 6.39	0.454
Oxygen saturation (%)	96.67 ± 1.35	97.13 ± 1.41	0.361
Body temperature (°C)	36.13 ± 0.62	36.21 ± 0.57	0.715

Note: G_1 – control group, G_2 – high-intensity ergocycle training group
p-value was obtained using the independent sample t-test. Each data was presented as mean ± SD.

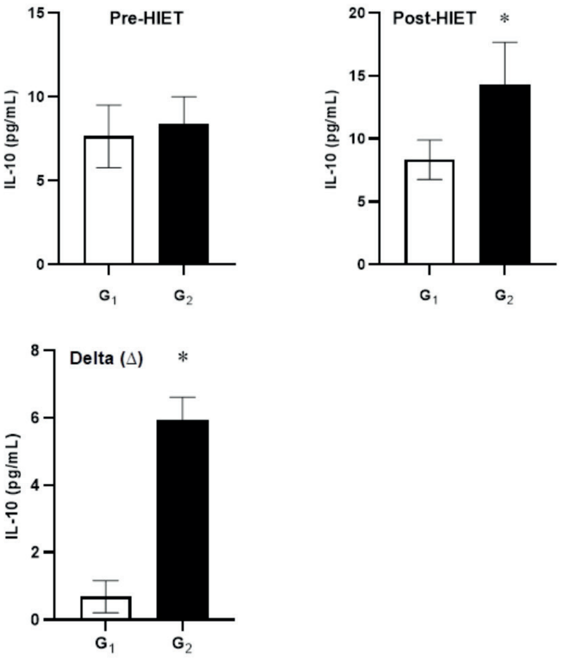
and Figure 2 presents comparative data on IL-10 levels between G_1 and G_2.

Based on Figure 1, it shows that there was no significant difference in (G_1) IL-10 levels between pre-HIET and post-HIET (7.64 ± 1.87 vs 8.33 ± 1.57 pg/mL; $p = 0.177$; ES: 0.399). However, (G_2) IL-10 levels were significantly greater in post-HIET than in pre-HIET (8.41 ± 1.60 vs 14.35 ± 3.33 pg/mL; $p = 0.001$; ES: 2.273).



G_1 – control group, G_2 – HIET group, HIET – high-intensity ergocycle training group, IL-10 – interleukin-10
* significant different from pre-HIET ($p \leq 0.001$)

Figure 1. Mean (± SD) measurement of IL-10 levels (pg/mL) in each group



G_1 – control group, G_2 – HIET group, HIET – high-intensity ergocycle training group, IL-10 – interleukin-10
* significant difference from G1 ($p \leq 0.001$)

Figure 2. Comparison of mean (± SD) IL-10 levels (pg/mL) between groups

Based on Figure 2, the results revealed no significant difference in pre-HIET IL-10 levels between G_1 and G_2 (7.64 ± 1.87 vs 8.41 ± 1.60 pg/mL; $p = 0.239$; ES: 0.442). However, post-HIET IL-10 levels were significantly greater in G_2 than in G_1 (8.33 ± 1.57 vs 14.35 ± 3.33 pg/mL; $p = 0.001$; ES: 2.312), and the change in IL-10 levels (delta) was also significantly greater in G_2 (0.68 ± 0.48 vs 5.94 ± 0.68 pg/mL; $p = 0.001$; ES: 8.937).

Discussion

This study aimed to investigate the ability of HIET to enhance the anti-inflammatory response, specifically through increased levels of IL-10, in healthy males. The primary finding demonstrated that a 4-week HIET protocol significantly elevated IL-10 levels, indicating an enhanced anti-inflammatory response. These results align with previous studies showing that structured and consistent physical exercise effectively increases IL-10, which plays a critical role in modulating immune responses by attenuating macrophage activity and suppressing pro-inflammatory cytokines such as TNF-α, IL-6, IL-8, and IL-12. IL-10 has also been shown to downregulate IL-1β production and inhibit inflammasome activation in immune cells, including microglia and tissue-resident macrophages [4, 25].

The anti-inflammatory effects associated with physical exercise are partly mediated by the release of IL-6, which typically peaks following aerobic exercise [26]. IL-6 acts as both a pro-inflammatory cytokine and an energy sensor, stimulating the production of anti-inflammatory cytokines such as IL-10 and (IL-1RA). The magnitude of IL-6 production depends on exercise variables like volume and intensity and is closely linked to energy regulation during exercise [31]. In this study, the observed changes in IL-10 levels may be attributed to IL-6 release from contracting muscle fibers, which helps sustain energy balance by limiting immune system energy expenditure [16]. This energy preservation mechanism is particularly evident when glycogen stores are depleted during high-intensity exercise [41]. These findings are consistent with studies demonstrating that IL-6 elevation induced by high-intensity exercise can subsequently increase IL-10 levels [2].

Additionally, previous research has shown that IL-10 levels increase significantly following intense exercise but remain unchanged after moderate-intensity exercise [20]. This suggests that high-intensity exercise, including HIET, is more effective in modulating inflammation. Immunologically, IL-10 inhibits the synthesis of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-8, while downregulating the expression of major histocompatibility complex class II molecules and costimulatory molecules on macrophages and monocytes [15]. IL-10 also blocks chemokine production, such as IL-8 and macrophage inflammatory protein-α, further contributing to its anti-inflammatory effects [32]. Moreover, IL-10 plays a role in metabolic regulation, protecting against insulin resistance in muscle tissue [8, 22].

While this study provides strong evidence of the anti-inflammatory benefits of HIET, it also highlights areas for further investigation. Previous studies have reported limited IL-10 responses to exercise protocols with lower intensities or shorter durations, likely due to insufficient IL-6 stimulation [12, 41]. Conversely, longer-duration protocols, such as ergocycle training for 60 minutes, have consistently shown significant IL-10 increases [39]. This aligns with our findings that 40-60 minutes of HIET effectively elevated IL-10 levels. However, shorter exercise durations often result in increased IL-6 without a corresponding IL-10 elevation [7]. For instance, studies involving adolescent males undergoing prolonged ergocycle training (e.g., 100 km or 40 km sessions) demonstrated substantial increases in IL-6 and IL-10, with IL-10 remaining elevated during recovery [18, 34].

Sex-specific differences in the inflammatory response also merit attention. Previous research has found that males exhibit a greater IL-10 response to exercise than females, potentially due to differences in muscle fatigue, inflammatory pathways, or hormonal influences [13, 14]. However, the limited number of studies comparing male and female responses precludes definitive conclusions. Future research should explore such differences in greater detail to develop more generalizable exercise protocols.

Future investigations should also address several limitations of this study. Firstly, incorporating a broader range of biomarkers, such as IL-1RA, TNF-α, and high-sensitivity C-reactive protein (hs-CRP), would provide a more comprehensive understanding of the anti-inflammatory effects of exercise. Secondly, longitudinal studies are needed to evaluate the long-term effects of HIET on inflammatory and anti-inflammatory markers, particularly in populations with chronic inflammatory conditions. Additionally, personalized HIET protocols tailored to individual characteristics, such as genetic predispositions, metabolic profiles, and exercise history, could optimize the anti-inflammatory benefits and improve clinical applications. Lastly, comparative studies between HIET and other exercise modalities, such as moderate-intensity continuous training or resistance training, could help determine the relative efficacy of various exercise approaches in modulating IL-10 and other markers.

In conclusion, this study demonstrates that HIET is an effective intervention for enhancing anti-inflammatory responses through the upregulation of IL-10. These findings support its potential as a therapeutic strategy in clinical and preventive health settings. However, further research is needed to explore the mechanisms, sex-specific differences, and long-term implications of HIET for broader and more diverse populations.

Conclusions

Based on the study results, a 4-week regimen of HIET was effective in enhancing the anti-inflammatory response, as evidenced by a significant increase in IL-10 levels. Specifically, IL-10 levels increased by 70.6% from pre- to post-HIET in the intervention group, highlighting the substantial impact of this training protocol. These findings suggest that HIET could be a promising therapeutic modality for improving anti-inflammatory responses. By enhancing IL-10 levels, HIET may contribute to reducing the risk of chronic diseases associated with inflammation-related morbidity. Further studies are needed to confirm these benefits across diverse populations and explore the mechanisms underlying these effects.

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Conflict of Interest

The authors declare no conflict of interest.

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