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Original Article

The Impact of High Intensity Intermittent Exercise (HIIE) on Serum Leptin Levels in Sedentary Overweight Adult Women

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ABSTRACT

The prevalence of a sedentary lifestyle is increasing, which can lead to overweight and subsequently obesity, potentially triggering metabolic diseases. The objective of this study is to analyse the HIIE impact on serum leptin levels in sedentary overweight adult women. Twenty-four adult women with a BMI falling within the overweight category (23-24.9 kg/m^2) were selected as subjects of this study. They were randomly divided into two groups: the control and the HIIE group. The HIIE group underwent static cycling, and the session lasted a total of 25 minutes which consisted of a 3-minute warm-up, 20 minutes of core exercise, and a 2-minute cool-down. The core exercise of the HIIE protocol followed a 1:1 ratio, involving 10 sets of high intensity cycling (80-90% of HRmax) for 60 seconds, alternated with low intensity cycling at a lower speed of 40 rpm without load. Blood samples for serum leptin measurement were collected before (pre-data) and 1 hour after the completion of the HIIE session (post-data). The post-data leptin levels (ng/mL) in both the control and HIIE groups showed a significant decrease compared to the pre-data levels ($p<0.05$; Cpre=74.521±16.658 vs. Cpost=68.178±19.367; HIIEpre=57.749±19.327 vs. HIIEpost=48.010±17.508). Based on these results, the study concludes that HIIE led to a greater reduction in serum leptin levels. From a physiological perspective, leptin is essential for appetite suppression. In overweight individuals, leptin levels tend to increase. However, due to the occurrence of leptin resistance, its ability to reduce appetite is compromised. Therefore, further research is needed to investigate leptin sensitivity.

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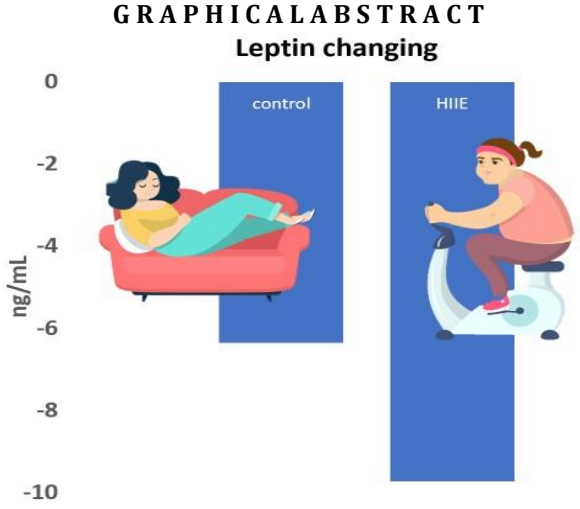
GRAPHICAL ABSTRACT



Introduction

Sedentary lifestyle, characterized by a lack of physical activity, is becoming increasingly prevalent in modern society [1]. It can reduce physical activity and increase the risk of becoming overweight and obese [2]. Overweight is a condition that arises from an imbalance between energy intake and expenditure, leading to the excessive accumulation of body fat. If left unaddressed, overweight can progress to obesity. This condition is known to trigger an increased production of oxidative stress [3]. According to the Asia Pacific criteria for Body Mass Index (BMI) classification, the overweight category corresponds to a BMI range of 23-24.9 kg/m^2, while obesity is classified as a BMI of 25-29.9 kg/m^2. In Indonesia, the overweight prevalence has been steadily increasing over the years. In 2007, the prevalence was 8.6%, which rose to 11.5% in 2013, and further increased to 13.6% in 2018 [4]. Overweight individuals are prone to experiencing oxidative stress and disruptions in adipokine production. Leptin, one of the adipokines, plays a crucial role in maintaining energy metabolism and overall homeostasis within the body [5].

Leptin is synthesized mainly by adipose tissue [6]. In today's overweight society, there is an observed increase in leptin levels. However, this increase is not accompanied by the expected physiological effects, leading to leptin resistance. Leptin resistance refers to a decreased sensitivity or failure of cells to respond to leptin, resulting in a reduced ability of leptin to suppress appetite or enhance energy expenditure. This ultimately leads to higher food intake and the development of overweight and obesity [7].

One effective preventive measure to decrease excessive calorie intake is engaging in physical exercise, which has been shown to benefit overweight women [8, 9]. Exercise, as a component of a healthy lifestyle, can serve as a non-pharmacological approach to mitigate health issues associated with overweight conditions [10].

According to Sirico [11], physical exercise in both men and women has been shown to decrease leptin levels after a 12-week intervention. The exercise regimen consisted of training sessions conducted three times a week at an intensity of 60%-65% of the maximum heart rate (MHR). de Souza *et al.* (2018) demonstrated that High Intensity Intermittent Exercise (HIIE) resulted in a decrease in leptin levels in adult men with obesity. The HIIE protocol involved treadmill exercises consisting of 10 sets of 60-second intervals, performed at 65%-75% of the individual's heart rate for 4 weeks, three times a week [12, 13]. HIIE has a role in brain activation [14].

However, the HIIE effect on serum leptin level on overweight sedentary women is unknown. Therefore, the objective of this research is to analyse the HIIE effect on reducing leptin levels in sedentary adult women with an overweight condition.

Materials and Methods

The ethical aspects of this study were reviewed and approved by the Health Research Ethics Committee, Faculty of Medicine, Universitas Airlangga (Approval No. 248/EC/KEPK/FKUA/2021). The study design employed an experimental approach with a pre- and post-control group design.

Study participants

A total of twenty-four sedentary adult women with overweight status were included in the study. They were randomly assigned to two groups: the control group and the High-Intensity Intermittent Exercise (HIIE) group. The inclusion criteria for the study were overweight females with an average BMI falling within the range of 23.1-24.99 kg/m^2 (Asia-Pacific criteria) and the age range of the participants in this study was 21-35 years old. Exclusion criteria included the use of anti-inflammatory medications and self-reported history of heart disease, hypertension, kidney conditions, and pregnancy.

Experimental protocol

All subjects in the study were required to fast for approximately 12 hours before the intervention to obtain blood samples for the pre-data measurements. Following the collection of pre-data, the control and HIIE groups were placed in separate rooms with identical environmental conditions.

In the control group, subjects were instructed to relax and sit comfortably, while in the HIIE group, subjects performed a single bout of exercise.

After 1 hour from the completion of HIIE session, or after 1 hour and 25 minutes for the control group, another blood sample was taken to obtain post-data measurements.

The High Intensity Intermittent Exercise (HIIE) protocol consisted of static cycling or ergocycle exercises performed in a 1:1 ratio. The exercise duration was 20 minutes, divided into 10 sets. Each set comprised 60 seconds (1 minute) of cycling at 80-90% of the maximum heart rate (HRmax) followed by 60 seconds (1 minute) of active rest with cycling at 40 rpm [12, 15]. Prior to the HIIE session, a 3-minute warm-up was conducted, and after the session, a 2-minute cool-down was performed. Therefore, the total duration of single bout of exercise was 25 minutes.

In this study, data including serum leptin levels were collected before (pre) and after (post) the intervention. Furthermore, changes in serum leptin levels were analysed by calculating the difference between the post-treatment and pre-treatment data. The measurement of serum leptin levels was performed using enzyme-linked immunosorbent assays (ELISA) with the CAN-L-4260 reagent.

Statistical analysis

The data obtained from the study were analysed using SPSS software. The normality of data distribution was assessed using the Shapiro-Wilk test. For data that followed a normal distribution, the paired t-test was employed for comparisons. In cases where the data did not exhibit a normal distribution, the Wilcoxon signed-rank test was used to analyse the differences.

Results and Discussion

The objective of this study was to investigate the effect of High Intensity Intermittent Exercise (HIIE) on serum leptin levels in sedentary overweight women, as previous studies have primarily focused on normal subjects or men. The collected data were analysed, and the baseline data of the research subjects were presented in Table 1. The statistical analysis indicated no significant difference.

Since Table 1 presents the baseline characteristics of the subjects, specifically overweight women, indicating that they were in a homogenous or similar condition at the beginning of the study.

Table 2 indicates the results of statistical analysis, specifically the difference test comparing the pre- and post-HIIE measurements. The analysis revealed significant differences within both groups, indicating a notable impact of HIIE on the serum leptin levels.

Table 1: The Characteristics of Subjects Before Treatment

Variables	Group		Sig. (p)
	Control Mean ± SD	HIIE Mean ± SD	
Age (year)	23.17 ± 1.850	24.33 ± 1.614	0.119
Height (cm)	158.67 ± 6.746	156.17 ± 6.746	0.319
Body weight (kg)	60.44 ± 5.931	58.53 ± 4.818	0.396
BMI (kg/m2)	23.957 ± 0.6155	23.933 ± 0.7584	0.935

The independent t-test was used.

Table 2: Serum Leptin Levels Before (pre) and After Treatment (post) for each group

Group	Variable	Mean ± SD (ng/mL)	Sig. (p)
Control	Pre -Leptin	74.521 ± 16.658	0,000
	Post Leptin	68.178 ± 19.367	
HIIE	Pre-Leptin	57.749 ± 19.327	0,000
	Post Leptin	48.010 ± 17.508	

The paired t-test were used.

The main outcome of this study was a significant decrease in the mean serum leptin levels between the pretest and posttest measurements in both the control group and the HIIE group, as listed in Table 2. Notably, the HIIE group exhibited a greater reduction in serum leptin levels compared to the control group. These findings are consistent with a study conducted by Keller (2005) on healthy men with a normal BMI, which also demonstrated a decrease in leptin levels following acute exercise using a 3-hour ergometer session at 60% of the maximal workload [16]. The research conducted by Rodrigues and Lucca (2020) also aligns with this study, as it demonstrated that performing High Intensity Intermittent Exercise (HIIE) for 30 minutes resulted in a significant reduction in leptin levels in normal weight young men and women. This aligns with the current study's observation of decreased leptin levels following HIIE in sedentary overweight women [6]. In a study involving pre-diabetic adult patients with overweight and obese conditions, it was observed that engaging in 60 minutes of exercise for 13 consecutive days led to a decrease in leptin levels. This finding supports the notion that regular exercise can have a beneficial impact on leptin regulation in individuals with prediabetes and overweight/obese conditions [17]. Similarly, in women with obesity, overweight, and normal BMI, a reduction in serum leptin levels was observed after performing a submaximal test using the Astrand-Rhyming procedures. This suggests that regardless of the BMI category, engaging in submaximal exercise can contribute to the decrease in leptin levels among women [18]. However, the results of this study contradict the findings reported by Fatouros *et al.* (2009), which indicated that intermittent exercise at low, medium, or high intensity for 60 minutes did not lead to a significant reduction in leptin levels in obese sedentary elderly men [19]. These contrasting results suggest that the impact of exercise on leptin levels may vary depending on factors such as age, sex, fitness level, and employed specific exercise protocols. Further research is needed to explore these discrepancies and better understand the relationship between exercise and leptin regulation in different populations.

According to the results of this study (as presented in Table 2), both the control group and the HIIE group exhibited significant changes in leptin levels between the pre-data and post-data measurements within each respective group. The significant decrease in leptin levels observed in the control group can be attributed to the influence of circadian rhythm of leptin. It has been observed that in individuals with normal weight or obesity, the peak levels of leptin occur around 10 pm, while the lowest levels occur around 10 am. This natural fluctuation in leptin levels throughout the day may explain the observed decrease in leptin levels in the control

group [20]. Blood sampling in this study was conducted in the morning for both the pre- and post-measurements, which may have influenced the observed reduction in serum leptin levels in the control group. In addition, all subjects, including the control group, were instructed to fast for approximately 12 hours prior to data collection. This fasting period could further contribute to the decrease in leptin levels observed in the control group. It is known that leptin levels can acutely decrease during periods of starvation, even before changes in body fat mass occur. Therefore, the combination of morning sampling and fasting likely played a role in the reduction of leptin levels in the control group [21]. The observed phenomenon can be attributed to the basal leptin secretion by adipocytes, which appears to be influenced by the availability of fat and metabolism of glycolytic substrates. Leptin secretion is known to be enhanced by glucose and insulin, and this effect is seen rapidly, typically within 2-4 hours. Therefore, if the availability of glucose is low, it can lead to a decrease in leptin levels [22]. Hence, Ruddick-Collins (2020) mentioned that leptin levels tend to be at their lowest point in the early morning until the midday, which can be estimated to be around 10 am or before 12 pm. Afterward, leptin levels gradually increase throughout the day, with the peak occurring during sleep [23].

The results of this study indicate that both the control and HIIE groups exhibited a significant decrease in leptin levels. However, when comparing the changes or differences between pre- and post-data (delta), there was no significant alteration in leptin levels in the control group, whereas the HIIE group showed a greater decrease in leptin levels (Table 3). This finding can be attributed to the leptin role as a hormone produced by adipose tissue to regulate and maintain the body's energy balance [24]. Leptin concentrations exhibit a consistent pattern of alteration that correlates with changes in fat stores [25]. HIIE has the potential to reduce fat stores. However, further exploration is necessary to fully understand its effects.

During HIIE, the activation of sympathetic nervous system can lead to an increase in blood glucose levels. This is due to the glycogenolysis stimulation by sympathetic signals, particularly through epinephrine. As a result, there may be a decrease in glycogen stores in the liver and skeletal muscle [26]. Therefore, it stimulates the gluconeogenesis mechanism [27], in an effort to meet the needs of glucose as an energy [28]. During HIIE, muscle contraction will increase the secretion of Interleukin 6 (IL-6) and increase glucose uptake through gp130Rβ/ IL-6Rα signaling and activation of phosphatidyl inositol 3-kinase (PI3-kinase) [29]. IL-6 secretion can also increase fat oxidation through activation of p38 Mitogen-Activated Protein Kinase (MAPK). The rise of energy expenditure may reduce leptin levels [29].

In addition, HIIE induces an increase in peroxisome proliferator-activated receptor gamma coactivator-1-alpha (PGC-1α) due to skeletal muscle contraction. This activation of PGC-1α leads to the production of fibronectin type III domain-containing protein 5 (FNDC5), which is subsequently released as irisin.

Table 3: The results of the different test of leptin levels before and after treatment between groups

Variable	Control Mean ± SD (ng/mL)	HIIE Mean ± SD (ng/mL)	Sig. (p)
Delta Leptin (Leptin changing)	-6.343 ± 4.396	-9.740 ± 6.793	0,160

The independent t-test was used.

Pre= before treatment; Post= after treatment; and Delta= the leptin changing.

Control= control group and HIIE= High Intensity Intermittent Exercise.

**sig. difference compared to pre data (in the same group) (p< 0.05).*

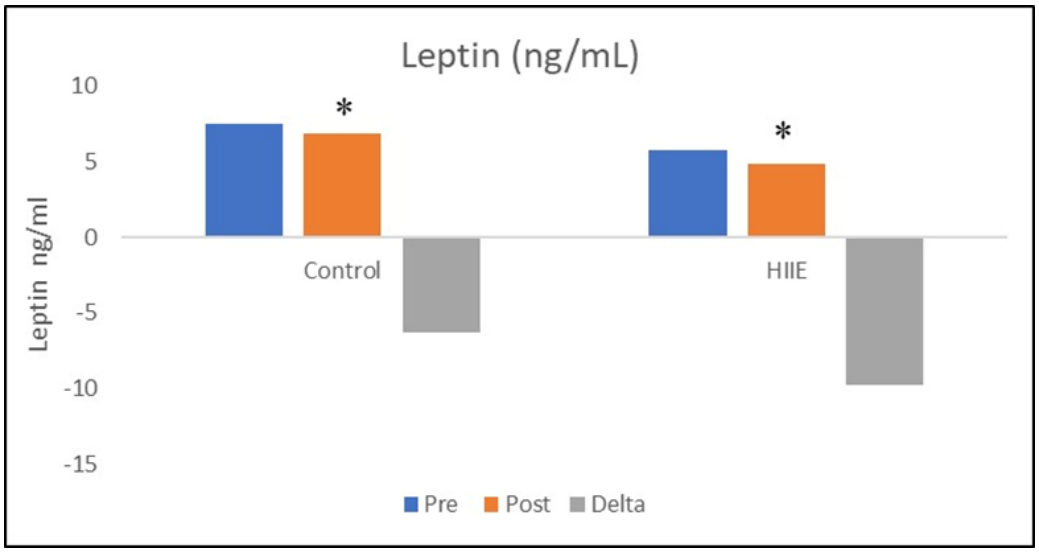


Figure 1: Mean of Leptin before and after HIIE in each group.

Irisin then circulates and reaches adipose tissue [30]. Once in adipose tissue, irisin stimulates fat browning through the promotion of mitochondrial biogenesis. This process leads to the conversion of white adipose tissue into a slightly brownish phenotype. As a result, the activation of Protein Uncoupling 1 (UCP1) is triggered, leading to an increase in thermogenesis (generation of heat) and energy expenditure [30]. The high energy expenditure will trigger a decrease in fat mass and reduce leptin levels [31].

Kao's (2021) study indicated that a single bout of high-intensity exercise in a short period and low-intensity exercise in a long time have beneficial effects on insulin resistance [32]. It has been known that leptin plays a role in insulin resistance and insulin sensitivity. Obese individuals generally exhibit higher levels of serum leptin and increased insulin resistance compared to individuals with normal weight [33].

Conclusion

Leptin plays a crucial role in regulating appetite by its suppression. However, in overweight individuals, despite increased levels of leptin, its effect on reducing appetite is diminished due to the occurrence of leptin resistance. In the current study, HIIE was found to lower leptin levels, although the decrease was not statistically significant. However, it is important to note that the leptin sensitivity was not examined in this study, and it remains unclear whether the decrease in leptin was accompanied by an improvement in leptin sensitivity. Further research is required to investigate leptin sensitivity and its implications.

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Authors' contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

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