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Original Article

Effect of Interval Training and Melatonin Consumption on New Obesity Indices and Atherogenic Index in Overweight and Obese Women

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Abstract

Background: Obesity and being overweight elevate triglycerides, blood cholesterol, blood pressure, and LDL levels while decreasing HDL levels. This study aimed to examine the impact of eight weeks of interval training combined with melatonin consumption on novel obesity indicators and the atherogenic index in overweight and obese women.
Methods: This semi-experimental, applied research involved 40 women aged between 30 to 45 years. They were randomly divided into four groups of ten each: intense interval training plus melatonin consumption (Group I), intense interval training plus placebo (Group II), melatonin consumption only (Group III), and a control group. The high-intensity interval training was conducted over eight weeks, with three sessions weekly. The regimen progressed from 5 repetitions in the first and second weeks to 6 in the third and fourth weeks, 7 in the fifth and sixth weeks, and 8 in the final two weeks. Groups I and III consumed 3 mg of melatonin tablets (manufactured by Razak company, Iran) nightly, an hour before bedtime, for the study duration. Data were analyzed using SPSS version 22 at 0.05 significance level.
Results: The combination of eight weeks of interval training and melatonin consumption significantly impacted the visceral adiposity index (VAI), atherogenic plasma index (AIP), TC/HDL-c ratio, and HDL-c levels in overweight and obese women (P=0.001 for each). However, there were no significant effects on the ApoA-1/ApoB ratio, body adiposity index (BAI), or ApoA-1 and Apo B levels (P=0.089, P=0.053, P=0.696, P=0.156, respectively).
Conclusion: Intensive interval training coupled with melatonin supplementation positively influences obesity management, weight control, and cardiovascular disease risk reduction in overweight and obese women.

***Keywords*:** High-intensity interval training, Melatonin, Obesity, Atherogenesis

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1. Introduction

Today, individuals of all ages worldwide grapple with the issue of being overweight and obese. This problem has given rise to various diseases, prompting numerous studies to investigate the cellular mechanisms responsible for triglyceride metabolism in adipose tissue (1).

Overweight-induced blood lipid disorders play a significant role in cardiovascular diseases among overweight and obese individuals. An increase in body mass index (BMI) results in an 8% elevation in the risk of cardiovascular diseases. Conversely, increased physical activity decreases the risk of cardiovascular disorders by 8% (2).

Arteriosclerosis represents a chronic inflammatory disease and ranks as a significant cause of mortality globally. In this process, high-density lipoprotein cholesterol (HDL-C) functions as an anti-atherogenic factor and an effective antioxidant synthesized in the intestines and liver (3).

The synthesis and regeneration of HDL-C by blood factors involve a complex process necessitating enzymes such as lipoprotein lipase (LPL), lecithin cholesterol acyltransferase (LCAT), phospholipid transporter protein (PLTP), and ATP-dependent transporters (ABC) (4). Some studies indicated that apolipoprotein APO A-1 and APO-B, the principal apolipoproteins of HDL-C and low-density lipoprotein cholesterol (LDL-C), respectively, offer a more accurate assessment of heart disease risk compared to conventional lipid markers (5).

Behbodikhah and colleagues demonstrated that APO-B constitutes the primary structural component of LDL-C and very low-density lipoprotein cholesterol (VLDL-C). The interaction of APO-B with LDL-C receptors plays a crucial role in its uptake by peripheral cells and the liver (6).

In obesity, there is an elevation in plasma lipoproteins rich in triglycerides, notably VLDL. Plasma VLDL concentration is influenced by hepatic secretion and APO-B catabolism and determines plasma LDL-C levels (7).

Human studies established a substantial inverse correlation between HDL-C, particularly APO-A1 levels, cardiovascular disorders, and atherosclerosis (8). The APO B/APO A-1 ratio is a superior indicator for coronary artery disease risk compared to LDL-C alone, which is an inadequate predictor of cardiovascular risk (9).

The principal protein of HDL-C, APO A-1, possesses well-established antioxidant properties (10). HDL-C and APO A-1 play a crucial role in the reverse cholesterol transport (RCT) process, facilitating the transfer of cholesterol from lipid-laden macrophages to the liver and preventing the accumulation of cholesterol esters in macrophages, thereby averting the formation of foam cells (11).

Contemporary approaches to preventing and treating metabolic disorders and obesity include innovative methods. One such process involves melatonin, a hormone synthesized from the amino acid tryptophan in the pineal gland of vertebrates and secreted into the cerebrospinal fluid (12).

Due to its electron-rich cyclic structure, melatonin can directly scavenge free radicals. Furthermore, the presence of acetyl and O-methyl residues in its construction makes it a dual-friendly molecule, allowing it to traverse biological membranes and operate within the cell's inner compartments, including the mitochondria, cytosol, and nucleus (13). It is also known as a famous antioxidant due to its small molecule and non-toxicity. Melatonin has demonstrated its capacity to ameliorate oxidative damage, inflammation, proteinuria, and kidney damage in rats (14).

Research findings indicated that melatonin likely exerts its anti-inflammatory effects through various molecular pathways, influencing cytokines, chemokines, and cell adhesion molecules (15). Consequently, based on previous research examining the impact of intermittent exercise on both healthy individuals and those with obesity and diabetes, along with the role of exercise in weight management and the modulation of biological markers related to obesity, in conjunction with the anti-inflammatory effects of melatonin supplementation, an investigation has been embarked upon to answer the question: Does high-intensity interval training and melatonin supplementation affect novel obesity indices and the atherogenic index in overweight and obese women?

2. Methods

2.1. Participants

This study employed an applied, semi-experimental, and double-blind experimental design. Four experimental groups were subjected to comparison using a pre-and post-test method. The statistical population for this investigation consisted of all overweight and obese women residing in Ilam City, Iran, in the year of 2022. The statistical sample was selected based on specific inclusion and exclusion criteria. The eligibility criteria for participation in this research were as follows: individuals within the age range of 30 to 45 years, completion of a comprehensive medical history questionnaire (indicating the absence of cardiovascular diseases, diabetes, various cancers, kidney and digestive disorders, or any injuries or conditions that might hinder participation in physical activity), having a body mass index (BMI) falling within the range of 25 to 34, no engagement in physical exercise within the preceding 6 months, adequate sleep, non-smoking status, and abstention from the use of supplements, alcohol, caffeinated substances, or pharmaceutical therapies.

Conversely, exclusion criteria encompassed non-participation in two consecutive training sessions, concurrent involvement in other exercise regimens, medical advice to interrupt or discontinue the training program or melatonin supplementation, the onset of illness during the intervention, and any injuries incurred by subjects during the training program. All participants provided written informed consent. After participant identification, random assignment into different groups was executed using a random number table. Ultimately, they were randomly allocated to four equal groups, each consisting of 10 subjects: the intense interval training+melatonin consumption group (I), the fierce interval training + placebo consumption group (II), the melatonin consumption group (III), and the control group. The sample size was

determined using G*Power software to compute the required sample size for ANCOVA, with an effect size of 0.80, an alpha level set at 0.05, and a test power of 0.95 (16). To ensure homogeneity among the sample groups, 40 subjects were selected.

2.2. Interval training protocol

In the present study, a rigorous interval training protocol was employed: Each subject completed a designated 20-meter course at maximum speed in a round-trip manner within 30 seconds. Positioned along this course were two obstacles, each situated 20 meters apart. At the outset of the training, the subjects set themselves precisely at the midpoint between the two designated lines, thus maintaining a distance of 10 meters from each line. Subsequently, they sprinted from the center toward the first line, covering the 20-meter distance, and then retraced their steps back to the starting line. This sequence was repeated frequently in a back-and-forth fashion (17). The high-intensity interval training regimen was executed over 8 weeks, comprising three weekly sessions structured as follows: during the first and second weeks, participants completed 5 repetitions; in the third and fourth weeks, 6 repetitions were performed; the fifth and sixth weeks included 7 repetitions, and the seventh and eighth weeks involved 8 repetitions (Table 1). Before commencing the exercise routine in each session, participants engaged in a 5 to 10-minute stretching and warm-up routine, while after each session, a 5 to 10-minute cooling-down program was implemented. To ascertain exercise intensity, the maximum heart rate (HRmax=220 - age) was determined and ensured that throughout all phases of the intense interval training, exercise intensity remained consistently above 90% of the HRmax, with individualized calculations for each subject (17).

2.3. Melatonin Supplementation

In this investigation, melatonin supplementation was administered to the intense interval training group with melatonin consumption (I) and the melatonin consumption group (III). Participants in both groups were instructed to consume melatonin tablets produced by Razak Company in Iran, each containing a 3 mg dose. This supplementation regimen continued for 8 weeks (18), with participants taking the melatonin tablets every night one hour before bedtime.

2.4. Biochemical and Physiological Measurements of Variables

To assess the levels of TC, HDL-c, APOA-1, and APOB in the subjects' brachial vein before and after the intense interval training program, as well as following melatonin consumption and a 12-hour fasting period, 5 ml of blood was collected. Specialized kits were tailored for each index, and measurements were conducted using a photometric (colorimetric) autoanalyzer. Serum ApoA-1 and ApoB levels were determined using Pars Azmoun Company's specialized kits and the ELISA method, following manufacturer instructions.

2.5. Statistical Analysis

Data normality was assessed using the Shapiro-Wilk test, and homogeneity of variances was evaluated using Levene's test. In the inferential statistics section, a paired t-test was employed to compare group means before and after the intervention. Furthermore, analysis of covariance (ANCOVA) and Bonferroni's follow-up tests were utilized to examine intergroup changes. Statistical analyses were performed using SPSS version 22, with a significance level set at 0.05.

3. Results

Table 2 displays descriptive characteristics of the subjects across four groups before the initiation of the training protocol. The analysis of covariance for age (P=0.354), height (P=0.435), body weight (P=0.521), and BMI (P=0.368) did not reveal any

Table 1: Eight-week interval training protocol

Weeks	Duration of activity	Active rest period	Repetitions	Program duration	Total activity duration (main activity, warm-up and cool-down)
1-2	30s	30s	5	5 m	25 m
3-4	30s	30s	6	5 m	26 m
5-6	30s	30s	7	5 m	27 m
7-8	30s	30s	8	5 m	28 m

S: Second; M: Minutes

Table 2: Descriptive descriptions of subjects

Groups	Age (years)	Height (cm)	Weight (kg)	BMI (kg/m²)
Interval training (n=10)	40.32±3.85	169.38±4.53	75.41±6.39	26.28±1.29
Melatonin (n=10)	39.41±4.38	167.81±5.38	78.19±5.71	27.76±2.49
Interval training+melatonin (n=10)	38.63±5.21	168.45**±6.12**	76.35±4.80	27.04.±2.31
Control (n=10)	39.08±3.92	170.29**±5.74**	77.22±5.48	26.62±2.07
P value	0.354	0.435	0.521	0.368

BMI: Body Mass Index

Table 3: New obesity indices changes in pre and post-intervention

Variables	Groups				Between- group differences (P value)	
	Interval training	Melatonin	Interval training+ melatonin	Control	Pre-intervention	Post-intervention
Visceral obesity index (VAI)						
Pre-intervention	2.80±0.81	2.84±0.36	2.85±0.38	2.84±0.33	0.694	0.0001*
Post-intervention	2.56±0.57	2.64±0.54	2.51±0.38	2.81±0.13		
Within- group differences (P value)	0.001*	0.001*	0.001*	0.845		
Body Adiposity Index (BAI)						
Pre-intervention	40.59±4.86	40.68±4.93	40.92±5.32	40.53±7.29	0.452	0.241
Post-intervention	39.53±6.41	36.75±5.24	38.19±6.17	40.90±6.51		
Within- group differences (P value)	0.263	0.168	0.212	0.220		
Plasma ApoA-1						
Pre-intervention	1.75±0.034	1.78±0.031	1.76±0.33	1.75±0.043	0.371	0.228
Post-intervention	1.76±0.036	1.80±0.038	1.75±0.034	1.76±0.049		
Within- group differences (P value)	0.221	0.321	0.115	0.198		
Plasma ApoB						
Pre-intervention	1.274±0.026	1.282±0.040	1.285±0.023	1.274±0.036	0.528	0.251
Post-intervention	1.282±0.029	1.287±0.041	1.286±.024	1.280±0.38		
Within- group differences (P value)	0.156	0.210	0.118	0.193		
ApoA-1/Apo B ratio						
Pre-intervention	0.7216±0.023	0.7150±0.025	0.7290±0.012	0.7270±0.031	0.395	0.214
Post-intervention	0.7280±0.021	0.7200±0.034	0.7300±0.015	0.7260±0.034		
Within- group differences (P value)	0.089	0.098	0.115	0.124		
Plasma HDL-c						
Pre-intervention	43.59±6.62	44.98±6.35	45.96±5.18	46.84±5.21	0.287	0.006*
Post-intervention	55.04±7.14	55.40±6.73	56.34±7.24	45.65±6.09		
Within- group differences (P value)	0.001*	0.001*	0.001*	0.115		
TC/HDL-c ratio						
Pre-intervention	3.701±0.110	3.739±0.107	3.736±0.053	3.750±0.128	0.704	0.001*
Post-intervention	3.601±0.104	3.660±0.090	3.640±0.063	3.791±0.134		
Within- group differences (P value)	0.001*	0.001*	0.001*	0.061		
AIP changes						
Pre-intervention	0.499±0.031	0.487±0.024	0.501±0.026	0.512±0.029	0.132	0.001*
Post-intervention	0.470±0.029	0.478±0.020	0.458±0.030	0.517±0.027		
Within- group differences (P value)	0.001*	0.001*	0.001*	0.085		

Data are showed as mean±standard deviation. *Show a significant difference.

significant differences among the groups before commencing training.

Table 3 presents the results of paired t-tests, which demonstrate within-group differences for all variables. Notably, a significant difference was observed in the changes in the visceral obesity index (VAI) before and after the intervention (P=0.001).

Conversely, the changes in body obesity index (BAI) (P=0.241), ApoA-1 (P=0.228), ApoB (P=0.251) levels, and ApoA-1/ApoB ratio (P=0.214) before and after the intervention did not exhibit statistical significance (Table 3).

Furthermore, the alterations in plasma HDL-c (P=0.006), TC/HDL-c ratio (P=0.001), and AIP (P=0.001) before and after the intervention demonstrated a significant difference (Table 3).

4. Discussion

In the current study, the plasma atherogenic index (AIP) significantly decreased in the intermittent training group and the intermittent training group with melatonin compared to the control group. However, no significant difference was observed between the other melatonin and control groups.

Physical activity is associated with increased lipid oxidation, as the heightened energy demand in muscles enhances the accessibility of fatty acids. During physical activity, adipose tissue lipolysis provides most fatty acids, approximately 2 to 3 times more than during resting conditions (19).

An indirect increase in beta-adrenergic stimulation primarily mediates this process. Additionally, the re-esterification of fatty acids is halved during intense physical activity (20). Furthermore, vigorous sports elevate blood flow in adipose tissue by up to 2-fold and in skeletal muscles by up to 10-fold. This augmented blood flow can mitigate the toxic effects of lipid accumulation and improve atherogenic index values (21).

The results also indicated a significant increase in HDL-c serum levels in the intermittent training group and the intermittent training group with melatonin compared to the control group. However, no significant difference was observed between the other groups.

Exercise promotes the utilization of lipids over glycogen by skeletal muscles, thereby reducing plasma lipid levels (22). This lipid utilization mechanism involves an increase in the activity of an enzyme called cholesterol acyl lecithin transfer enzyme (LCAT) due to exercise. Simultaneously, it enhances lipoprotein lipase activity, which may also depend on the energy expenditure associated with the type of exercise (23). Additionally, the reduction in the TC/HDL-c ratio observed in the interval training and interval training with melatonin groups, in contrast to the control group in this study, suggests that a decrease in total cholesterol concentration or an increase in HDL-C concentration leads to a lower TC/HDL-c ratio, reducing the risk of cardiovascular diseases (24).

Researchers attributed the decrease in plasma concentrations of triglycerides (TG), total cholesterol (TC), and LDL-c, as well as the increase in HDL-c after exercise, to the heightened activity of the enzyme lipoprotein lipase (LPL) and a decrease in liver triglyceride lipase enzyme (25). In the present study, the strenuous muscular effort and the increased demand for free fatty acids as an energy substrate, along with the replenishment of triglyceride and phospholipid reserves instead of glycogen reserves for energy production, may have led to the hyperactivity of the lipoprotein lipase enzyme. Consequently, cholesterol absorption increases, reducing triglyceride and TC levels, denser and larger LDL particles, and decreased LDL plasma values. Accordingly, the levels of immature HDL increase, promoting cholesterol reverse transport (26). In the context of a reduced visceral obesity index (VAI) in the interval training group and the interval training with melatonin group compared to the control group in this research, it appears that intensive interval training causes a decrease in adenosine monophosphate, phosphocreatine, and glycogen reserves (27). This activates AMP-activated protein kinase (AMPK), ultimately leading to an upregulation of PGC-1α (28). Therefore, intensive interval training enhances the mitochondrial capacity of skeletal muscles by elevating PGC-1α (29).

Furthermore, regular, intense interval training significantly improves aerobic and anaerobic fitness, increasing the skeletal muscle's capacity for fatty acid oxidation and glycolytic enzyme content. Another possible mechanism is appetite suppression following intense interval training (30). This research indicated a significant reduction in visceral obesity after eight weeks of interval training combined with melatonin consumption. Tong and colleagues demonstrated that low-volume interval training reduces visceral obesity (31). Zhang and co-workers also showed that incorporating high-intensity training sessions, rather than high volume, is fundamental to lowering visceral obesity (32). In 2011, Koziróg and colleagues reported that long-term melatonin therapy can reduce cholesterol absorption in the small intestine, inhibit cholesterol biosynthesis, and impede LDL accumulation. These researchers suggested that melatonin substantially impacts

lipid profiles in the long term (33). Therefore, it can be inferred that when combined with intensive interval training, melatonin is complementary in reducing fat levels, promoting weight loss, and combating obesity (34).

The results showed that 8 weeks of training combined with melatonin consumption had no significant effect on ApoA-1, Apo B, and the ApoA-1/Apo B ratio in overweight and obese women. Naturally, as HDL-c levels increase, ApoA-1 levels also increase. However, the change was not statistically significant in the current research despite the increase in the ranks of this variable. Perhaps one reason for the lack of change in the APO A-1, Apo B, and Apo A-1/ApoB ratios was the interval training volume (35). Studies indicated that the magnitude and intensity of exercise have a more significant impact on apolipoproteins. Additionally, researchers noted that high-intensity and high-volume training have the most substantial effect on lipid indices, while low or moderate-intensity exercise with low volume primarily influences lipoprotein size (27, 31, 32, 36).

4.1. Limitation

The limitations of the current research encompassed the following aspects: a lack of control over the genetic characteristics of the subjects, an inability to precisely regulate the extracurricular activities undertaken by the issues outside their designated training hours, and an inability to modulate the subjects' levels of spirit and motivation for the implementation of the training program. It is recommended to explore the impact of rigorous interval training and melatonin supplementation on metabolic parameters such as glucose levels, insulin levels, and insulin resistance in forthcoming research endeavors.

5. Conclusion

The findings of the present study demonstrated that an 8-week regimen of high-intensity interval training in conjunction with melatonin administration among overweight or obese women yields improvements in lipid profiles and reductions in indices related to visceral obesity (Visceral Adiposity Index or VAI) and plasma atherogenicity (Atherogenic Index of Plasma or AIP). However, no discernible effects were observed on apolipoproteins A-1 and B and the Apo A-1/Apo B ratio. Nevertheless, the results underscored the favorable impact of intensive interval training in combination with melatonin supplementation on mitigating obesity, managing weight, and reducing the risk of cardiovascular diseases.

Ethical Approval

The Ethics Review Board of - Islamic Azad University, Ilam branch, approved the present study with the code of IR.IAU.ILAM.REC.1401.012. Also, written informed consent was obtained from the participants.

Authors' Contribution

Hadis Feyzi: Substantial contributions to the conception and design of the work; the acquisition, analysis, and interpretation of data for the work, drafting the work. Mahnaz Omidi: Substantial contributions to the design of the work, drafting the work and reviewing it critically for important intellectual content. Abdolhossein Taheri Kalani: Substantial contributions to the conception and design of the work; the acquisition, analysis, and interpretation of data for the work, drafting the work and reviewing it critically for important intellectual content. All authors have read and approved the final manuscript and agree to be accountable for all aspects of the work, such that the questions related to the accuracy or integrity of any part of the work.

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