



Aerobic Interval training as non-pharmacological treatment in some coronary atherosclerosis indicators in inactive adult obese men



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ABSTRACT

Introduction: Accumulating evidence suggests that obesity is major risk factors for cardiovascular diseases and atherosclerosis and regular physical activity as a non-pharmacological treatment in obesity induced diseases. This study aimed to determine the effect of interval training on Interferon- γ (IFN- γ) and C Reactive Protein (CRP) as coronary atherosclerosis indicators in adult obese males.

Methods: For this purpose, 24 inactive adult obese males ($30 \leq \text{BMI} \leq 36$) were randomly divided into experimental (n=12) and control (n=12) groups. Then experimental subjects were participated in 8 weeks interval training (3 times/weekly) at %50–70 HRmax and subjects in control group continued inactive lifestyle. Fasting serum IFN- γ and CRP were measured before and 48 hours after lasting exercise session. Anthropometrical indices were measured before and after exercise intervention of groups. Data were compared with independent and paired sample t student using computer with SPSS Version 22.0. A p-value less than 0.05 was considered statistically significant.

Results: No significant difference were observed in all anthropometrical and clinical markers at baseline between groups ($p > 0.05$). Aerobic interval training resulted in significant decrease in anthropometrical indices ($p < 0.05$). Training intervention also led to significant decrease in serum IFN- γ ($p = 0.005$) and CRP ($p = 0.001$) in experimental group. All variables remained without change in control subjects ($p < 0.05$).

Conclusion: Based on our finding, it be concluded that aerobic interval training with be emphasis improvement in IFN- γ and CRP may be slow the onset of atherosclerosis in adult obese men.

Keywords: Obesity, Interval training, Atherosclerosis, Pro-inflammatory cytokine.

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Introduction

Obesity is associated with cardiovascular problems and oxidative stress or impaired vascular endothelial function (1,2). Recently, the chronic inflammatory nature of atherosclerotic disease has received widespread attention. Abnormal deposition of serum lipoproteins in arterial walls and their oxidative nature stimulate monocyte recruitment and transformation into foam cells, which leads to the induction of both innate and adaptive immune responses (3).

In response to this process, cytokines and growth factors produced as part of these responses lead to vascular wall remodeling, which is characterized by atherosclerotic damage and vascular smooth muscle aggregation and collagen matrix deposition (4). On the other hand, macrophages and T lymphocytes are the

predominant inflammatory cells in atherosclerotic plaques (5). In vitro studies have revealed that T lymphocytes play an important role in the development of inflammatory processes that lead to the development of atherosclerotic lesions (6). Most of these T cells have inflammatory phenotypic characteristics that are directly related to the development of atherosclerosis in laboratory mice (7). IFN- γ is the main cytokine secreted by T cells. IFN- γ , as a proinflammatory cytokine, is mainly produced and secreted by T lymphocytes and NK1 natural killer cells (8,9) and by binding to its receptors, it activates the intracellular STATE JAK signaling pathway and, on the other hand, binds to HS on the cell surface, which results in increased biological activity of intracellular IFN- γ (10). Its levels are increased in obese diabetic mice or type 2 diabetic mice, such

that induction of type 2 diabetes leads to increased levels (11).

This evidence is reported while inflammatory mediators CRP have been introduced as risk factors for death in coronary thrombosis (12). On the other hand, increased CRP in healthy or sick obese populations has been introduced as one of the predictive indicators of cardiovascular diseases, especially atherosclerosis (13). Also, IFN- γ -dependent signaling pathways are strongly activated in some clinical diseases accompanied by increased CRP levels, which points to the key role of inflammatory cytokine-dependent cascades in these diseases (12). This evidence points to a kind of joint and synergistic role of IFN- γ and CRP in the occurrence or increase in the severity of atherosclerosis and other cardiovascular abnormalities. Therefore, several therapeutic interventions are always being implemented to improve these conditions in heart disease or people susceptible to this disease with the aim of prevention.

In the meantime, the role of exercise and physical activity with cardiovascular goals is of great interest. As in the study of Smith et al, 6 months of aerobic training led to a decrease in serum levels of IFN- γ and TNF- α in middle-aged women and men (14). On the other hand, in the study of Zar et al (2012), 8 weeks of endurance training did not lead to a change in IFN- γ levels (15). However, in another study, IFN- γ concentration increased one hour after exercise but approached baseline levels 5 hours later (16). The available evidence suggests a contradiction in the response or adaptation of the variables of interest to exercise training. On the other hand, despite the lack of change in CRP following exercise training in some studies (17,18), Eizadi et al (2017) reported a significant decrease in CRP following relatively long-term aerobic training in obese individuals (13).

Materials and Methods

Subjects

The statistical population of this semi-experimental study that approved by the Research Ethics Committee of Islamic Azad University consists of inactive adult obese men ($30 \leq \text{BMI} \leq 36$). The statistical sample consisted of 24 obese adult men who met the inclusion criteria and were randomly divided into control and experimental groups. After the subjects were familiarized with

the objectives of the study by the facilitators, the consent form was completed by them.

Inclusion and Exclusion Criteria

Obesity is main inclusion criteria the study. The subjects were non-athletes, non-smokers, and non-alcoholics. The subjects also had not had a defined diet in the past 6 months, and their weight did not fluctuate by more than one kilogram. No history of other chronic diseases such as diabetes, asthma, respiratory, kidney, digestive diseases, and cancer, as well as the use of energy supplements, were other inclusion criteria. Failure to participate regularly and continuously in exercise sessions and having a disease that required medication during the exercise program were exclusion criteria.

Anthropometric indices

At the beginning of the study, the anthropometric indices of the subjects were measured. The weight of the subjects in the minimally covered state was measured using a digital height scale made in Taiwan with an accuracy of 100 grams. The height of the subjects was measured barefoot using a height scale. Body mass index (BMI) was calculated by dividing body weight (kg) by the square of height (m²). Using a non-elastic fabric meter, the abdominal circumference and hip circumference were measured at the most voluminous part. The percentage of body fat was also measured using a body composition measuring device (Omron model, England) (19). The measurement of anthropometric indices was also repeated after the training program.

Measurement of clinical indicators

Subjects were asked to refrain from any heavy physical activity for 48 hours prior to blood sampling. To measure biochemical variables in both conditions before and 48 hours after the last training session, blood sampling was performed after 10 to 12 hours of overnight fasting between 8 and 9 am. A 5 ml sample was taken from the left arm vein in a sitting position by a laboratory scientist. To separate serum, blood samples were centrifuged and the resulting serum was stored at -80°C until IFN- γ and CRP were measured. Serum IFN- γ and CRP were measured by ELISA using laboratory kits from Karmania Pars Gene and Diagnostics Biochem, Canada.

Interval training protocol

The experimental group performed aerobic interval training for 8 weeks, one session per week at an intensity of 50-70% of resting heart rate for

15-40 minutes. Each training session consisted of a 10-minute warm-up, main exercise, and 10-minute cool-down. The main exercise began for 15 minutes in the form of 3 sets of 5 minutes at an intensity of %50-55HRmax in the form of running on a flat surface in the first and second weeks and gradually increased to 2 sets of 20 minutes at an intensity of 65-70% HRmax in the final two weeks (Table 1) (2). Active rest between sets was in the form of walking. The target heart rate was monitored and recorded using a Polar heart rate monitor made in Finland.

Statistical analysis

All statistical analyses were performed through the use of a statistical software package (SPSS, Version 22.0, SPSS Inc., IL, USA). The Shapiro-Wilk Test was applied to determine the variables with normal distribution. Independent student t test was used for comparison of variables between two groups at baseline. Paired t test was used to determine the intra-group changes of variables in each group. A criterion alpha level of $P \leq 0.05$ was used for all statistical comparisons.

Results

The within-group changes in each of the anthropometric indices are summarized table 2.

The results of the independent t-test indicated that there was no significant difference in any of the anthropometric indices between the control and experimental groups. However, the results of the paired t-test revealed that in the experimental group, interval training significantly reduced weight and body fat percentage and other anthropometric indices after the exercise intervention compared to the pre-test. This is while none of these variables changed in the control group.

The main objective of the study was to determine the effect of interval training on IFN- γ and CRP in obese adult men. At baseline (pre-test), based on the results of an independent t-test, no significant difference was observed in IFN- γ ($p=0.527$) or CRP ($p=0.356$) between the experimental and control groups (table 3). However, statistical comparisons by paired t-test revealed that interval training in the experimental group led to a significant decrease in serum IFN- γ compared to the pre-test. In addition, interval training led to a significant decrease in serum CRP compared to the pre-test. However, no significant difference was observed in serum IFN- γ or serum CRP between the pre-test and post-test values in the control group.

Table 1: Distribution of exercise intensity while running during the training program

Weeks	Exercise intensity (%HRmax)	Time of running (min)	Active rest between sets (min)
First and second	%50 - %55	3 × 5	3
Third and fourth	%55 - %60	2 × 10	3
Fifth and Sixth	%60 - %65	2 × 15	5
Seventh and eighth	%65 - %70	2 × 20	5

Table 2: Pre and post-training of anthropometrical indices of 2 groups

Variables	Experimental group			Control group		
	Pre-training	Post-training	Sig	Pre-training	Post-training	Sig
Body weight (kg)	95.1 ± 2	92.1 ± 2	0.001	93.8 ± 3	94 ± 3	0.82
AC (cm)	101 - 2	98.5 ± 1	0.001	101 ± 4	102 ± 4	0.62
BMI (kg/m ²)	30.97 ± 0.46	30.03 ± 0.36	0.001	30.59 ± 0.76	30.68 ± 0.79	0.75
BF (%)	32.18 ± 1.26	27.94 ± 1.19	0.001	31.30 ± 1.39	31.43 ± 1.24	0.35

AC: Abdominal circumference, BMI: Body mass index, BF: Body fat percentage

Table 3: Pre and post-training of clinical markers of 2 groups

Variables	Experimental group			Control group		
	Pre-training	Post-training	Sig	Pre-training	Post-training	Sig
IFN- γ (pg/mL)	39.41 ± 2.98	40.19 ± 5.31	0.005	39.41 ± 2.98	40.23 ± 2.10	0.451
CRP (ng/mL)	5221 ± 205	4580 ± 293	0.001	5078 ± 528	5034 ± 621	0.698

IFN- γ : Interferon- γ , CRP: C Reactive Protein

Discussion

The decrease in serum IFN- γ and CRP levels following interval training compared to the control group is one of the main findings of the study. In other words, interval training for 8 weeks with 3 sessions per week resulted in a significant decrease in IFN- γ and CRP in obese adult men compared to those who did not participate in the training program. In this context, although some studies have reported no change in CRP following different training methods even in the presence of weight loss (17,18,20,21), but Eizadi et al (2017) have indicated a decrease in CRP accompanied by an increase in IL-10 in obese adult women following 3 months of aerobic training (13). On the other hand, in the study by Phillips et al. (2012), despite no change in IL-10 following 12 weeks of resistance training in obese mice, serum CRP levels decreased significantly (22).

Regarding the response or adaptation of IFN- γ to interval training in obese individuals, although limited studies have been reported, Zar et al (2012) reported no change following 8 weeks of endurance training in young men (15). On the other hand, Haydaryan et al (2020) also noted that resistance-endurance training does not lead to a change in the expression of IFN- γ and TGF- β in healthy and diabetic women (23). On the other hand, Silveira et al (2016) cited their findings and stated that long-term exercise training reduces the secretion of IL-12 as a stimulus for the synthesis and secretion of IFN- γ (24). The alignment of changes in IFN- γ and CRP in response to interval training in the present study supports the reciprocal effect of these two inflammatory components on each other. In this context, it was previously noted that systemic CRP levels are affected by IFN- γ -dependent signaling pathways in some clinical diseases (12).

In addition, immunohistochemical studies have shown that IFN- γ is present in human atherosclerotic plaques (25). Several studies in laboratory mice have pointed to the pivotal role of IFN- γ in atherosclerosis. On the other hand, exogenous IFN- γ administration is associated with increased severity of atherosclerosis (26). IFN- γ also has diverse biological effects, including increased antigen-presenting capabilities of endothelium and macrophages, increased recruitment of inflammatory cells through upregulation of endothelial adhesion

molecules, stimulation of proinflammatory cytokines and chemokine secretion by macrophages, production of reactive oxygen species (ROS) by macrophages, and inhibition of cholesterol efflux from foam cells, which increases the severity of atherosclerosis (27). IFN- γ directly increases the activity and proliferation of vascular smooth muscle (28), inhibits smooth muscle apoptosis, and increases neointimal proliferation after vascular injury (29).

In this context, ELISA measurements have shown a correlation between IFN- γ and IL-18 or IL-12. On the other hand, independent of IL-6 and CRP, a positive correlation has been observed between increased plasma levels of IL-12 and IFN- γ (12). In this regard, in vitro studies have revealed that inhibition of IFN- γ by repeated injection of a plasmid encoding IFN- γ , called sIFN γ R, helps reduce atherosclerosis damage. In vitro studies by Koga et al. have revealed that IFN- γ treatment with sIFN γ R leads to a reduction in the severity of atherosclerosis by reducing the expression of proinflammatory molecules such as IL-1 β , IL-6, VCAM1, MCP-1, and macrophage inflammatory protein (MIP) (12). To gather, aerobic interval training significantly reduced IFN- γ and CRP, inflammatory markers implicated in atherosclerosis, in obese adult men. This improvement may be attributable to weight loss or improvement in body fat percentage in response to interval training. Previous studies have suggested that a minimum 10% reduction in body weight following regular exercise training is required to improve inflammatory or metabolic markers in obese populations (30). Despite measuring IFN- γ and CRP as vascular function indicators in study but lack another importance hormonal or enzymatic variables such as IL-8, IL-12, NO, VEGF or other indicator are limitation of study.

Conclusion

Interval training reduces serum IFN- γ and CRP levels in obese adult men. Given the importance of these inflammatory components as effective inflammatory markers in coronary atherosclerosis, the implementation of this training method is associated with the prevention of coronary atherosclerosis in sedentary obese men. On the other hand, based on the findings of the study, the decrease in CRP as one of the predictors of cardiovascular function following

interval training may be attributed to the decrease in serum IFN- γ following this training method. Despite this evidence, understanding the mechanisms responsible for these changes indicates the need for further studies.

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Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no conflict of interest.

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