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The Effect of Eight Weeks of High-Intensity Interval Training on C1q/TNF5 Serum Levels and Insulin Resistance in Obese Men

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ABSTRACT

C1q/TNF5 is a protein belonging to the C1q/TNF group, playing a role in glucose metabolism. The aim of this research was to investigate the effect of eight weeks of high-intensity interval training on C1q/TNF5 levels in obese men. In a semi-experimental study with a pre-test and post-test design, 24 obese men (BMI: 32.3 ± 1.1 kg/m², age: 34.7 ± 2.6 years) were purposefully selected. Participants were randomly divided into equal control and experimental groups. The experimental group underwent eight weeks of high-intensity interval training (three sessions per week). Blood samples were collected from both groups before and after the eight-week exercise intervention under fasting conditions. The data were analyzed using independent and paired t-tests ($p < 0.05$). After eight weeks of high-intensity interval training, a significant reduction was observed in serum levels of C1q/TNF5 ($p = 0.001$). Additionally, insulin resistance index significantly decreased ($p = 0.004$). Overall, it appears that eight weeks of high-intensity interval training can lead to improvements in insulin resistance and glucose metabolism in obese men.

1. INTRODUCTION

Today, more than 1.9 billion people worldwide are affected by obesity or overweight, leading to increased health problems such as insulin resistance, type 2 diabetes, cardiovascular diseases, liver diseases, and cancer [1]. Obesity is one of the most common metabolic disorders in industrialized and developing countries. The pathological consequences of obesity include cardiovascular diseases and metabolic syndrome. Metabolic syndrome, characterized by symptoms such as obesity, lipid disorders, their oxidation, increased blood glucose, inappropriate levels of dense and low-density lipoproteins, is a major factor associated with cardiovascular diseases [2].

Recent research has shown that skeletal muscle secretes proteins and various biological factors called myokines. These myokines play a role in physiological and metabolic adaptations that occur in response to physical activities in the body. Skeletal muscle, with the help of insulin, extracts over 70% of dietary glucose, playing a role in regulating the body's fat and glucose metabolism. Part of this extracted glucose is used for energy production, and any excess is stored as glycogen in muscles [3]. However, myokines involved in regulating the body's metabolism

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can have therapeutic effects on various metabolic disorders that improve with regular exercise. One of these myokines is C1q/TNF5. C1q/TNF5 is a protein belonging to the C1q/TNF family that can play a role in controlling metabolism (Henningsen et al., 2010). C1q/TNF5 protein was discovered in 2012 by Henningsen and colleagues. This protein is secreted from various tissues such as fat and muscles and, after entering the bloodstream, exerts its physiological effects [4].

Due to the molecular structure of C1q/TNF5 and other proteins in the larger C1q/TNF family and their similarity to adiponectin, they are classified into this group. C1q/TNFs are themselves a subset of the larger C1q family, characterized by the presence of a globular head at the end of C similar to the complement C1q function and structurally similar to the necrosis factor [5]. The level of C1q/TNF5 increases in conditions such as obesity and diabetes and can lead to increased insulin sensitivity, making it anti-diabetic. C1q/TNF5, by activating insulin-independent pathways such as adenosine monophosphate-activated protein kinase (AMPK), increases glucose uptake, induces GLUT4 mobilization to the cell membrane [6]. Additionally, with AMPK phosphorylation and activation, phosphorylated acetyl-CoA carboxylase (ACC) leads to increased fatty acid oxidation in mitochondria. Furthermore, C1q/TNF5 can activate the mitogen-activated protein kinase (MAPK) pathway, increasing glucose uptake and fatty acid oxidation [6]. Considering the biological function of C1q/TNF5 in activating AMPK and MAPK pathways and increasing fatty acid metabolism, C1q/TNF5 alone or in combination with drugs effective in metabolism can be used in the treatment of metabolic disorders such as obesity, diabetes, and metabolic syndrome [7].

Physical activity, as one of the most important and effective non-pharmacological therapeutic interventions, can significantly contribute to improving insulin resistance by initiating insulin-dependent and insulin-independent pathways. Lim et al. (2012) investigated the effect of 10 weeks of aerobic exercises on C1q/TNF5 levels in young and elderly women. Their results showed that aerobic exercises led to a reduction in C1q/TNF5 levels and improvement in insulin resistance and lipid profile in both age groups. Significant correlations were also observed between changes in C1q/TNF5 and insulin resistance in both groups [8]. Moreover, Choi et al. (2013) demonstrated that three months of combined aerobic-resistance exercises in overweight women and men resulted in improved insulin resistance and increased C1q/TNF5 levels [9].

Recent studies have shown that, in addition to aerobic and endurance exercises that have longer durations, high-intensity exercises with shorter durations can also be effective in improving the physiological conditions of overweight and obese individuals. These exercises, in addition to specific physiological adaptations, are influenced by factors such as intensity, duration, and repetitions of intervals and recovery periods. Research has shown that high-intensity interval training can have favorable effects on improving insulin sensitivity and reducing body fat mass in human subjects [10, 11]. However, very few studies have been conducted on the effects of various exercise modalities on C1q/TNF5, and to date, no study has investigated the impact of high-intensity interval training on C1q/TNF5 in obese men. Therefore, this study aimed to determine the effects of eight weeks of high-intensity interval training on serum levels of C1q/TNF5 and insulin resistance in obese men.

2. METHODOLOGY

This experimental study employed a pre-test and post-test design and was conducted in a field setting. The statistical population consisted of obese men (Body Mass Index ≥ 30 kg/m²) residing in Qom City in 2019, aged between 30 and 40 years. From eligible individuals, 24 volunteers were selected purposefully and conveniently as participants.

Inclusion criteria included: being within the age range of 30–40 years, having a BMI of 30 kg/m² or higher, not engaging in regular physical activity over the past three years, and having no cardiovascular disease. Exclusion criteria comprised cardiovascular, hepatic, or renal diseases, and smoking, which were verified through a medical history questionnaire.

After a briefing session explaining the study objectives and procedures and answering participants' questions, written informed consent was obtained from all subjects. The participants were then randomly assigned to two

equal groups (n = 12): a control group (maintaining their normal daily routines) and an experimental group (performing high-intensity interval training, HIIT).

The experimental group participated in HIIT sessions three times per week for eight weeks. The training protocol was designed based on the shuttle run test—a valid test for evaluating anaerobic performance (Gloster et al., 2009) [12]. Each session began with a 5–10-minute warm-up. Participants ran a 20-meter distance marked by three cones, alternating between 30 seconds of maximal running and 30 seconds of walking. The protocol started at the midpoint of the 20 m line toward the first cone and then continued to the far cone. During the first session, the participants performed three repetitions of this sequence (a total of 2 minutes of maximal running and 2 minutes of walking). The number of repetitions increased every two weeks, reaching seven repetitions by week eight. Each session concluded with a 5–10-minute cool-down period.

Blood samples (10 mL from the antecubital vein) were collected from both groups 24 hours before and 48 hours after the eight-week training intervention, following a 10-hour overnight fast. After coagulation, samples were centrifuged at 3000 rpm for 10 minutes to separate serum, which was then used for measuring C1q/TNF5, glucose, and insulin levels.

Insulin resistance was calculated using the following formula:

$$\text{Insulin Resistance Index} = \frac{\text{Fasting Insulin (μIU/mL)} \times \text{Fasting Glucose (mmol/L)}}{22.5}$$

Fasting glucose levels were determined using the glucose oxidase method and kits from Pars Azmoon Co. (Iran). Fasting insulin concentrations were measured via ELISA using kits from Mercodia Co. (Sweden), with a sensitivity of 1 μIU/mL and an intra-assay coefficient of variation (CV) of 6.5%. Serum C1q/TNF5 concentrations were assessed using a human-specific ELISA kit from Life Science (USA).

Data were analyzed using independent and paired t-tests with a significance level set at $p < 0.05$. All statistical analyses were performed using SPSS version 22.

3. Results

Table 1 presents the anthropometric characteristics of the participants at the pre-test stage. The mean and standard deviation of age, height, weight, and body mass index (BMI) in the control and experimental groups indicate that the two groups were comparable in baseline characteristics.

Table 1. Anthropometric characteristics of participants at pre-test

Variable Group	Age (years)	Height (cm)	Weight (kg)	BMI (kg/m²)
Control (n=12)	33.2 ± 2.7	178.2 ± 6.3	108.4 ± 9.8	32.1 ± 1.2
Experimental (n=12)	35.7 ± 2.9	173.6 ± 7.5	112.5 ± 7.6	32.5 ± 1.1

The results of within-group and between-group comparisons of the study variables, based on paired and independent t-tests, are presented in Table 2. In the experimental group, the intervention led to significant changes in weight, glucose, insulin, insulin resistance, and C1q/TNF5 ($p<0.05$). Furthermore, between-group comparisons revealed significant differences in all these variables, indicating the effectiveness of the intervention on the measured outcomes.

Table 2. Paired and independent t-test results for study variables

Variable	Group	Pre-test	Post-test	p (within)	p (between)
Weight (kg)	Control	102.4 ± 9.8	104.7 ± 9.6	0.02*	0.001*
Weight (kg)	Experimental	99.5 ± 7.6	97.9 ± 5.2	0.02*	
BMI (kg/m²)	Control	32.1 ± 1.2	32.2 ± 2.5	0.08	0.32

BMI (kg/m²)	Experimental	32.1 ± 1.1	32.3 ± 1.3	0.03*	
Glucose (mg/dl)	Control	92.4 ± 6.8	95.1 ± 8.5	0.01*	0.001*
Glucose (mg/dl)	Experimental	88.7 ± 6.2	80.2 ± 4.7	0.001*	
Insulin (mg/ml)	Control	5.6 ± 7.0	5.8 ± 6.0	0.02*	0.001*
Insulin (mg/ml)	Experimental	5.1 ± 5.0	4.8 ± 4.0	0.01*	
Insulin resistance	Control	1.26 ± 0.23	1.34 ± 0.44	0.07	0.004*
Insulin resistance	Experimental	1.29 ± 0.12	0.96 ± 0.18	0.072	
C1q/TNF5 (pg/ml)	Control	2634 ± 42,392	2711 ± 33,451	0.74	0.001*
C1q/TNF5 (pg/ml)	Experimental	2571 ± 64,539	2362 ± 75,422	0.002*	

*$p<0.05$ indicates a statistically significant difference.

4. DISCUSSION AND CONCLUSION

The findings of the current study demonstrated that eight weeks of high-intensity interval training in overweight men led to a significant reduction in C1q/TNF5 levels and improved insulin resistance. These results align with the study by [8], which reported a decrease in C1q/TNF5 levels following 10 weeks of aerobic exercises with 60-80% of maximum heart rate in both young and elderly women [8]. In contrast, the study by Choe et al. (2013) indicated an increase in serum C1q/TNF5 levels in overweight adult women and men after three months of combined aerobic and resistance exercises performed five times a week [9]. The differences in exercise types and frequency between the current study and Choe et al.'s study may contribute to the variations in results.

Various types of exercises can elicit different physiological responses, and factors such as exercise intensity, duration, and frequency of intervals and recovery periods can play a role. High-intensity interval training (HIIT) has been shown to have favorable effects on insulin sensitivity and fat mass reduction in human subjects (Gibala et al., 2012; Heydari et al., 2012) [10, 11]. In this context, the study by Gibala et al. (2012) and Heydari et al. (2012) suggested that high-intensity interval training could have beneficial effects on insulin sensitivity and reduction of body fat mass in human subjects.

One possible explanation for the changes in C1q/TNF5 levels could be related to blood viscosity or changes in serum volume. Previous studies have suggested that endurance exercises in different age groups can improve insulin resistance [13]. This improvement in insulin sensitivity is one of the effective mechanisms in reducing C1q/TNF5 levels, and the serum levels of C1q/TNF5 are associated with metabolic syndrome, obesity, and insulin resistance [14].

Moreover, changes in glucose and insulin levels can contribute to the improvement of insulin resistance [15]. The maintenance of normal blood glucose levels at rest and during exercise depends on the coordination and integration of sympathetic nerves and endocrine glands. Although muscular contraction increases the absorption of blood glucose into the muscles [16], high-intensity interval training can lead to a non-significant decrease in fasting blood glucose. The intensity and duration of exercise are essential factors in reducing glucose levels and insulin resistance. As exercise intensity increases, reliance on carbohydrates in the blood and muscle increases. In the initial stages of exercise, glycogen provides a substantial amount of fuel for active muscles, and the depletion of glycogen and the absorption of glucose from the blood, along with the release of free fatty acids from fat tissue, increase.

In conclusion, it appears that high-intensity interval training can improve insulin resistance, reduce C1q/TNF5 levels, and ultimately enhance glucose metabolism in overweight men.

Transparency Statement

The data supporting this study are available upon reasonable request to the corresponding author, subject to ethical and confidentiality considerations.

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Declaration of Interest

The authors declare that they have no competing interests.

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