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The Effect of Eight Weeks Aerobic Training and Omega3 Ingestion on the Levels of Adipsin and Insulin Resistance in Overweight and Obese Women

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Abstract

Background: Exercise training and omega-3 supplementation are believed to have a positive effect on obese and overweight people. We conducted the present study in order to investigate the effect of aerobic training and omega3 ingestion on the levels of Adipsin and insulin resistance in overweight and obese women.
Methods: In this semi-experimental study conducted in Tehran, summer 2020, 40 overweight and obese women (aged from 20 to 35 years old, and BMI 29.6±1.93 kg.m2) were assigned in four equal groups, namely placebo (P), omega-3 (O), training (E), and training+omega-3 (OE) groups. The subjects in the training and training+omega-3 groups completed the eight-week (three sessions per week) aerobic training program. 2000 mg omega-3 supplement was consumed on a daily basis. Blood samples were obtained before and after completing the intervention and Adipsin and insulin levels were measured. The data were analyzed via repeated measures analysis of variance (ANOVA) test along with Tukey post-hoc test. The study was approved under the IRCT registration code of IRCT20200811048360N1.
Results: The findings of the present research shed light on a significant decrease in serum Adipsin levels in the E and OE groups compared to those in the P and O groups ($P<0.05$). Moreover, insulin resistance significantly decreased in E compared with that in the P group ($P=0.012$) and also in the OE group compared to that in the P ($P=0.001$) and O ($P=0.009$) groups.
Conclusion: The present study indicated that omega-3 supplementation could increase the effect of exercise training on the reduction in the Adipsin and insulin resistance; further effects may be observed by increasing the duration of exercise training period.

***Keywords*:** Obesity, Endurance training, Adipokines, Complement factor D

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1. Introduction

Obesity and overweightness are associated with increased health issues, including cardiovascular disorders and premature death. In addition, obesity leads to a variety of metabolic and hormonal disorders, such as the development of type 2 diabetes mellitus and impaired insulin function, which increase mortality in obese individuals (1). Adipocytes, through the secretion of proteins and other factors and by responding neurological, hormonal, and nutritional signals, are involved in energy homeostasis and energy sensitivity regulation. They also affect the neuroendocrine, cardiovascular, and immune systems (2). In fact, adipose tissue is recognized as an active endocrine organ, which secretes a numerous adipokines (adipose tissue secreted factors) into the bloodstream, such as Adipsin that exert different important functions (3). Adipsin is synthesized during lipolysis process and stimulates the hunger center (4).

Adipsin is known as an important adipokine firstly identified in 1987 (5). Although Adipsin is a major adipocyte-secreted protein, its expression and circulating level dysregulation has been reported under several conditions, including diabetes and overweightness/obesity (6). Adipsin catalyzes the breakdown of

complement factor C3 into C3a and plays an important role in activating the complement alternative pathway. Moreover, Adipsin, known as complement factor D, affects the immune system functions (7). Karajibani and colleagues (8) compared the serum levels of Adipsin in diabetic and healthy individuals and reported that Adipsin levels was significantly lower in diabetic patients compared to those in healthy individuals. They also observed higher levels of Adipsin in healthy men compared to those in healthy women (8). The negative correlation between Adipsin levels and insulin resistance has been reported in individuals with a low (less than 25 kg.m2) BMI and researchers have suggested that Adipsin may be involved in the pathogenesis of abnormal glucose metabolism (7).

In contrast, certain researchers have indicated that Adipsin level is positively associated with adipose tissue mass, fasting glucose levels, insulin resistance, and blood pressure and that Adipsin levels in women with metabolic syndrome are higher compared to those in healthy women, which emphasizes the pathological effects of Adipsin upregulation (9). Among various recommended strategies for combating obesity and its related consequences, exercise training has attracted a great deal of attention, owing to its capability to affect Adipsin levels. The results regarding the effect of exercise training on Adipsin levels are limited and contradictory. Decrease (10) and no change (11) in Adipsin levels with exercise training have also been reported. In addition to exercise training, it has been reported that certain nutritional interventions could affect obesity and its related disorders. In this regard, it has been observed that omega-3 supplementation can exert anti-obesity effects and minimize the pathological effects of obesity (12). However, the simultaneous effect of different exercise trainings and omega-3 ingestion on the level of Adipsin has not been investigated. Therefore, the present study aimed to determine the effect of aerobic training and omega-3 supplementation on Adipsin levels in overweight and obese females.

2. Methods

Study Design

The present study was semi-experimental approved by Islamic Azad University Ethics Committee with the code of IR.IAU.SRB.REC.1399.088. All conditions, limitations, disadvantages, benefits and side effects of the present study interventions, including aerobic training and omega3 supplementation or their combination (aerobic training+ omega3 supplement) were explained to the subjects. Ethical principles were considered at all the stages of the study and the subjects could withdraw from the study whenever they wanted to. The subjects who were still willing to participate in the present research signed the informed consent. After inviting people to participate in the investigation in public places, such as parks and gyms, and subject recruitments, 57 subjects were eligible for the study baseline conditions, among whom 40 subjects were chosen for conducting the present paper protocol. Subsequently, the subjects were randomly (according to random number table) classified into four equal groups (10 subjects in each group), including 1. placebo (no aerobic training program, no omega3 supplements), 2. omega3 supplement (omega3 supplement, no aerobic training program), 3. aerobic training (aerobic training program, no omega 3 supplements), and 4. aerobic training+omega3 supplement (omega3 supplement along with aerobic training program). We conducted this paper in summer 2020 in Tehran, Iran. The subjects were divided into placebo and omega3 supplement groups in a double-blind procedure and the researcher, trainer, or subjects were not informed about the consumed supplement or placebo until the end of the eight-week intervention. The present research was a randomized double-blind placebo-controlled trial documented in the Iranian registry of clinical trials (registration number: IRCT20200811048360N1).

Participants

Overweight and obese women from Tehran, aged between 25 and 40 years old, comprised the present study subjects; among the recruited volunteer subjects, 40 overweight and obese women were selected to for the study protocol. The sampling was carried out based on the available sample (region 5, Tehran) and after identifying the participants, they were assigned into different groups randomly using a table of random sampling numbers. We performed the sample size calculation according to the previously reported formula (13) and chose 10 subjects in each group.

Inclusion and Exclusion Criteria

The inclusion criteria were as follows: age range of 25 to 40 years old, no history of cardiovascular diseases, type2 diabetes, hypertension, or different types of cancer and malignancies, not having participated in any regular exercise trainings over the previous year, not consuming blood pressure and circulating lipid lowering medications, and finally, not taking nutritional supplements for at least six months before the beginning of the present study. The exclusion criteria were not participating in the blood sampling sessions (pretest or posttest), simultaneous participation in other exercise trainings or regular physical activity programs, no regular participation in designed exercise training programs, physician advice on interrupting or terminating the training program or omega3 supplementation, incidence of disease during the intervention, and subjects' injuries during training program.

Intervention

The interventions herein consisted of aerobic exercise training, omega3 supplementation, or their combination (aerobic training+omega3 supplementation), conducted for eight weeks according to the considered procedure.

Aerobic Training Program

The aerobic training program was conducted three sessions per week for eight weeks. The training intensity was 50-55% HRmax in the first two weeks, 55-60% HRmax in the second two weeks, 60-65% HRmax in the third two weeks, and 65-70% HRmax in the last two weeks (14). Each aerobic training session lasted about 20 minutes. Before and after each exercise session, 10 min warm-up and eight min cool down were performed. The control group subjects did not take part in any exercise training programs and continued their routine life.

Omega3 supplementation

Omega3 supplementation was considered to be 2000 mg daily for omega3 and aerobic training+omega3 supplement groups, which is an approved dose without any side effects for obese women (15). Omega3 supplement was consumed as two 1000 mg capsules in the morning and at night (with or after breakfast and dinner). The placebo group also consumed 2 g oral paraffin oil daily. Omega3 supplements were purchased from Karen Company.

Blood Sampling and Laboratory Assessment

The blood samples were collected at the baseline and after completing the eight weeks of intervention (training, omega3, training+omega3). The samples were centrifuged (15 minutes at 3000 rpm) and the obtained serum samples were frozen (-80 C) for laboratory assessment. Serum Adipsin (Cusabio, Sensitivity: 0.078 ng/ml, Catalog Number: CSB-E14369h) and insulin (Demeditec Company, Sensitivity: 1.76/IU/ml, Catalog Number: DE2935) levels were measured utilizing Elisa method. Pars Azmoon diagnostic kit was used for the measurement of glucose levels and body fat percentage was measured via BOCA-X1 body composition analyzer.

Statistical Analysis

The obtained data were analyzed with SPSS version 24. Since the Shapiro-Vilk test (16) indicated a normal data distribution ($P>0.05$), the differences between the groups were determined with repeated measures ANOVA along with Tukey post-hoc test. In addition, paired t test was employed for determining the intra-group difference. It should be noted that significance was considered at $P<0.05$ for all the analysis steps.

3. Results

The participants herein comprised 40 overweight and obese women, all of whom completed the present study protocol and none were excluded. Table 1 represents the physical characteristics (age, height, weight, and BMI) of the subjects in different groups. One way ANOVA test noted no significant differences concerning age, height, weight, and BMI between different groups ($P>0.05$).

Analysis of covariance test for body weight, BMI, and body fat percentage indicated a significant difference between the groups ($P<0.001$). In fact, a significant difference was observed between the E and OE groups, and P and O groups using Tukey post-hoc test ($P<0.001$). In addition, body weight, BMI, and body fat percentage significantly decreased in both E and OE groups ($P<0.001$). A significant difference was also observed

Table 1: Subjects' demographic characteristics (Mean ± SD)

	P	O	E	OE	P
Age (years)	28.3±3.63	26.7±3.19	26.2±2.98	27.8±3.35	0.492
Height (cm)	159.8±4.73	158.6±3.33	160.4±3.54	159.7±3.16	0.736
Weight (kg)	74.8±6.17	75.1±5.39	77.3±4.97	74.5±5.86	0.675
BMI (kg.m^2)	29.2±2.05	29.8±1.47	30.0±2.11	29.2±2.16	0.718

P: Placebo, O: Omega3, E: Aerobic Training, OE: Aerobic Training+ Omega3

between the groups concerning Homeostatic Model Assessment (HOMA-IR) (P<0.001). Additionally, there was a significant difference between the E group and the P (P=0.002) and O (P=0.012) groups, and between the OE group and the P (P<0.001) and O (P=0.002) groups. Moreover, paired t test indicated a significant decrease in Homeostatic Model Assessment (HOMA-IR) in the E and OE groups (P<0.001) (Table 2).

Adipsin data analysis indicated a significant difference among the P, O, E, and OE groups (P<0.001). Tukey post-hoc test demonstrated a significant difference between the E group and the P (P<0.001) and O (P=0.001) groups, and also between the OE group and the P and O groups (P<0.001). Intragroup analysis suggested that Adipsin levels significantly decreased in the E (P=0.001) and OE (P<0.001) groups (Figure 1).

Table 2: The variables levels (Mean ± SD)

Variables	Stage	P	O	E	OE	P value	Between group P value
Body Weight (kg.m^2)	**pre test**	6.17±74.8	5.39±75.1	4.97±77.3	5.86±74.5	0.675	
	Post test	6.08±74.9	5.47±75.3	4.68±75.9	5.52±73.2	0.429	<0.001
Paired t test		0.630	0.105	P<0.001	P<0.001	-	
BMI (kg.m^2)	**Pre test**	2.05±29.2	1.47±29.8	2.11±30.0	2.16±29.2	0.718	
	Post test	2.02±29.3	1.49±29.9	1.96±29.5	2.05±28.7	0.694	<0.001
Paired t test		0.596	0.177	P<0.001	P<0.001	-	
Body fat percentage(PBF)	**Pre test**	6.85±91.6	7.68±89.7	6.69±92.8	8.08±92.1	0.882	
	Post test	6.57±90.8	5.46±88.4	6.04±90.1	6.22±88.9	1.324	<0.001
Paired t test		0.280	0.231	0.040	0.004	-	
HOMA-IR	**Pre test**	0.35±1.95	0.27±1.87	0.16±2.08	0.27±1.99	0.412	
	Post test	0.29±1.90	0.22±1.81	0.22±1.86	0.23±1.76	0.638	<0.001
Paired t test		0.158	0.103	P<0.001	P<0.001	-	

P: Placebo, O: Omega3, E: Aerobic Training, OE: Aerobic Training+ Omega3

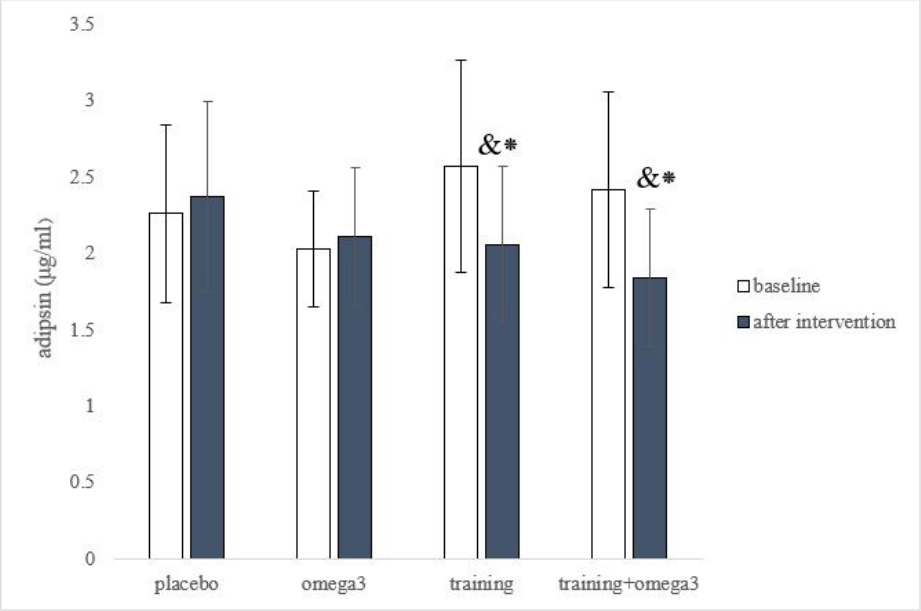

Figure 1: The figure shows serum Adipsin levels; significant decrease compared to placebo and omega3 group, and significant decrease compared to the pre-test stage.

4. Discussion

The obtained findings suggested that aerobic training alone or combined with omega-3 supplementation significantly decreased the serum level of Adipsin and insulin resistance. Even though the observed changes in Adipsin levels and insulin resistance in the aerobic training group along with omega-3 supplementation were more significant, no statistically significant differences were observed between the training and training with omega-3 supplement groups. This reported adipokines effect on various body functions and physical characteristics of individuals, including appetite and satiety, homeostasis, insulin sensitivity, energy expenditure, blood pressure, endothelial function, energy metabolism in insulin sensitive tissues, adipogenesis, fat distribution, and secretion of insulin from pancreatic beta cells (17, 18). Adipsin is believed to be one of the important adipokines secreted from adipose tissue, whose level changes in obesity. It can affect glucose metabolism and insulin resistance, yet the effectiveness of its mechanisms is still largely unknown (19). In this regard, researchers have suggested that Adipsin level is positively correlated with BMI and shown the highest levels of Adipsin in obese, overweight, and normal weight people, respectively. High levels of Adipsin in obese people have been attributed to impaired and increased production of Adipsin by adipose tissue (20). Accordingly, obesity has received a lot of attention as a main factor to increase Adipsin production and secretion (1).

A few studies have investigated the effect of exercise training on Adipsin levels. Nonetheless, the present findings showed that aerobic training alone or combined with omega-3 supplementation result in a significant decrease in Adipsin. Consistent with the present findings, Naderi and Sharifi (10) found that eight weeks of the combination of training (aerobic-resistance) and green coffee supplementation resulted in a significant reduction in serum levels of Adipsin and similar to the present study, no significant differences were found between training and training+green coffee groups (10). In addition, Naderi and Sharifi reported that the reduction in Adipsin level was associated with a decrease in insulin resistance and body fat percentage in training and training+green coffee groups (10). Despite similar findings, the conducted training program was different from our protocol, which emphasizes the importance of different types of exercise training for modulating Adipsin levels in obese individuals. Given that adipose tissue is one of the major sources for Adipsin secretion (21), the decrease in body fat percentage is a potential mechanism to downregulate Adipsin levels in this study. However, identifying the exact mechanism reported by a few conducted studies needs further investigation.

In contrast to our findings, certain researchers have reported that eight weeks of aerobic training in obese type 2 diabetic women did not affect the Adipsin levels significantly (11). This contradiction is probably related to different subjects' characteristics (obese versus diabetic), which represented that Adipsin in diabetes condition may exert a different effect. Researchers have shown downregulation of Adipsin levels in type2 diabetic patients compared to individuals with normal glucose tolerance and it has been suggested that Adipsin may improve beta cell function in type2 diabetes (4). According to our findings, the decrease in Adipsin level through exercise training is one of the potential mechanisms for insulin resistance improvement. Upregulation of the Adipsin level in obese and overweight individuals is known as the main risk factor increasing insulin resistance in these subjects (20). On the contrary to the present findings and above-mentioned results, some researchers have reported a high level of Adipsin in subjects with normal glucose tolerance, particularly decreased Adipsin levels in diabetic patients, and observed a negative correlation between Adipsin levels and insulin resistance (7). However, a negative correlation between Adipsin and insulin resistance was observed in individuals with a BMI less than 25 kg.m2 (7). Since our subjects were overweight and obese women with a BMI higher than 25 kg.m2, the above findings could not be compared to the results obtained herein and determining the effect of exercise training on Adipsin levels in people with different BMI needs further investigation. In contrast to our findings, Mohammadi Javid and co-workers (22) reported no significant changes in Adipsin levels following 16 weeks of home-based aerobic training in women with polycystic ovary syndrome (PCOS) (22). It seems as though the subjects' different characteristics, as well as the inability to perfectly control exercise training program intensity could be considered as possible reasons behind these contradictory findings.

In addition, the findings indicated that eight weeks of omega-3 supplementation did not affect Adipsin levels

and insulin resistance and that omega-3 supplementation did not increase the effect of exercise training on Adipsin levels and insulin resistance. Although the effect of omega-3 supplementation alone or combined with exercise training on Adipsin levels is unknown, Dadash Nejad and co-workers (15), consistent with the present findings, reported that Fetuin A (an inflammatory adipokine) and insulin resistance changes following eight weeks of combined training or combined training+omega-3 supplementation in obese women were not statistically significant, which represented that omega-3 supplementation could not increase the effect of exercise training on reducing Fetuin-A levels and insulin resistance (15).

However, it has been reported that omega-3 supplementations can enhance the effect of exercise training on improving metabolic (such as insulin sensitivity) and cardiovascular (further increase in HDL-c levels and further decrease in CRP) risk factors and that omega-3 supplementation can enhance the insulin-sensitizing effects of exercise training and have a synergistic effect (23). It seems that different conducted exercise trainings (high intensity interval training) as well as longer training period (16 weeks) compared to that of the present study could be noted as the main reason behind the contradictions. Although further decrease in Adipsin and insulin resistance was observed in the training+omega3 groups compared to the training group, it was not statistically significant. The decrease in insulin resistance in the training and training+omega-3 groups could be attributed to the decrease in Adipsin levels partly. Nevertheless, it has been reported that the improvement in insulin resistance following exercise training is owing to the changes in the expression and activity of the proteins involved in transmission of insulin signals in skeletal muscles, such as AMPK and protein kinase B (Akt), and also increased lipid oxidation (24). Due to the present study limitations, such as small number of subjects in each group, not having measured the other inflammatory (IL-6, TNF-α) and anti-inflammatory (adiponectin) adipokines, and inability to fully control the nutritional, economic, and motivational status of the subjects, the exact mechanisms of exercise training effects on Adipsin levels should be identified in future research. According to our findings, it could be recommended that obese and overweight subjects consume omega-3 supplement in order to maximize the positive effectiveness of exercise training, specifically over a long period of time.

5. Conclusion

The present findings revealed the positive effect of aerobic exercise training alone or in combination with omega-3 supplementation in modulating serum levels of Adipsin and insulin resistance. Based on the present results, the observed decrease in insulin resistance in training and training+omega-3 groups could be partly attributed to the decrease in serum levels of Adipsin.

Conflicts of interest: None declared.

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