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Influence of 9-Weeks Aerobic Exercise and Multivitamin Supplement on Inflammation Biomarkers as Cardiovascular Risk Factor in Non-athletic Obese Women

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Abstract

Background: The aim of this study was to determine the effect of 9 weeks aerobic exercise and multivitamin supplement on plasma level of HCY, CRP and TNF-α in non-athletic obese women.
Materials and Methods: Total 30 sedentary and healthy obese women aged 25-50 year and BMI ≥30 Kg/m^2 volunteered for this study. The subjects were randomly categorized into three experimental groups, aerobic group, aerobic-supplement group, and a nonintervention control group. The experimental groups went through a 9-week (3 days per week) aerobic exercise program. Blood samples were taken of all subjects before and after the aerobic exercise program at overnight fast. The data were analyzed through paired t test, ANOVA, and Dant. The significance level was $p<0.05$.
Results: Aerobic and aerobic-supplement exercise decreased the rate of HCY (p=0.013), CRP (p=0.001) and TNF-α (p=0.006) in obese women significantly, also the reduction of basic rates of CRP and TNF-α in aerobic group (p=0.001) and aerobic-supplement group (p=0.001) were significant compared to control group. But reduction of basic HCY levels was not significant, though. This reduction was significant in aerobic-supplement group (p=0.036).
Conclusion: This prospective data indicate that aerobic exercise with definitive intensity and multivitamin supplement decreased cardiovascular risk factors in obese women. Therefore as a modifiable lifestyle factor should be encouraged in obese adults for prevention of cardiovascular events.

Introduction

Cardiovascular diseases, particularly athero sclerosis, have tremendously increased over the recent decade [1, 2]. These diseases, in Iran, are considered the first factor claiming people's lives, accounting for the 46 % of total death toll [3]. There are many factors which cause cardiovascular diseases, and in recent years independent risk factors such as fibrinogen, HCY (hyperhomocysteinemia), CRP, and TNFα are also detected [4, 5].

Along with the reduction of physical activity, change in the diet, increase in mental pressure, and being overweight, there is a great hike in the death toll and effects of cardiovascular diseases [6]. Manson et al showed in their study that active women are less exposed to cardiovascular diseases than non-active women [7, 8].

Moreover, fat texture discharges different cytokines such as TNF and may increase volumes of CRP in obesity [6, 8, 9]. Cytokines are discharged by different cells such as immunity cells, endothelial cells, fat cells, and muscles [10, 11]. It is shown that TNFα abound in the plasma levels of the obese, and it is considered as a warning for cardiovascular diseases [12, 13, 14]. The results of a study indicate that physical activity can be a mechanism for reducing inflammation a direct way by reducing cytokines production in fat texture, and in an indirect way by increasing insulin sensitivity, improving endothelial function, and reducing fat mass [12, 15]. Sloan et al. reported that 12 weeks of aerobic exercise in obese youngsters and adults can decrease TNFα significantly [16]. Lisa et al. showed that taking vitamin E and C along with sport activity can influence TNFα inflammation biomarker [17].

CRP is an acute-phase protein and an increase in its plasma levels leads to a 2-5 increase in the exposure to coronary artery diseases [10]. Gaeini et al. reported that among inflammation biomarkers that develop atherosclerosis, CRP is the most sensitive one and the independent predictor for this disease [18]. HCY is a newly known danger factor which is even called the biomarker of occurring heart stroke [19, 20]. Increasing in the amount of HCY has an undesirable effect on the cardiovascular system [21]. The HCY plasma level is determined by diet and genetic factors [22]. The reduction of HCY plasma level can be affective in the reduction of the exposure danger to cardiovascular diseases [23-26]. There are many newly recognized internal and external CRP, TNFα, and HCY modifiers. However, there is contradictory information about the effect of physical activity and taking multivitamin supplement on these biomarkers in obese women. Therefore, the main purpose of this study is to investigate the effect of 9 weeks aerobic exercise and multivitamin supplement on inflammation biomarkers in obese women.

Materials and Methods

This study is semi-empirical and its population consists of non-athletic obese women from 25 to 50 years old and with a BMI ≥30. Following the initial call up, 46 non-athletic obese women who visit Physical Education Organization’s sport clubs and gyms were volunteered to take part in this study. Then, from those who filled in the health questionnaire and another questionnaire determining the level of physical activity, 37 were selected for this study. During the training program, 7 women out of the 37 didn’t care about the researchers’ suggestions and didn’t participate regularly, so finally the population was formed using 30 participants [27].

During a session, the aims of the research, the way the exercises would be carried out, taking multivitamin supplement, and the schedule of the research were explained for the participants and they signed the voluntary participation form. The participants, then, were randomly categorized in 3 groups: aerobic exercise group, aerobic exercise-multivitamin supplement group, and the nonintervention control group.

Field variables were measured as such: age (year), height (cm, by the digital Seca machine, made in Germany with the accuracy of 0.1 cm), weight (by the weight-measuring Seca, made in Germany with the accuracy of 0.1 kg), the percentage of body fat and BMI (kg/m^2) by the digital Body composition logic/ Body fat analyzer, made in Korea), waist-hip ratio (cm, by a special stripe meter made in the U.S.), systolic and diastolic blood pressure (mmHg), resting heart rate (beat in min), by the wrist digital manometer MBO, made in Germany (model Digind 16).

The participants in aerobic exercise and aerobic exercise-multivitamin group did 9-week training program, three 45 to 60-minute sessions each week with the maximum heart beat of 60 to 65% for the obese. Each training session consisted of 5 minutes stretching, 10 minutes active warm up, 30 to 45 minutes main exercises including running, jogging, training with medicine ball, and different frequency trainings, and a final 5-minute cool down and returning to the initial state. In this study, in every stage of the training program, through the initial measurement of maximum heart beat for the obese, the intensity of the trainings was determined as 60 to 65% for each of the participants. Moreover, during the aerobic training program, whenever the increasing or decreasing of the intensity of trainings was required, the necessary feedback was given to the participants. To meet the relative accuracy of the participant’s food, reminding and food self-report method with a 3-day reminder was used [28].

500 mg multivitamin supplement capsules, made in Darou Pakhsh Iran Company, were provided for the participants of the aerobic exercise-multivitamin supplement group, and 60 capsules were given to each participant one day prior to the training program. These people were asked to take one capsule every day.

Blood sampling was carried out after 12 hours of overnight fast and in two phases. In the first phase, based on the instructions for blood sampling, the participants were asked to avoid any intense physical activity, stress-making situation, and listed foods or medicines, 3 days prior to the blood sampling. The participants, then, came to the medical laboratory and 10 ml of their blood was taken from their arm vein while they were sitting. The serums of these blood samples were frozen in the 20ºC until the experiment of the second phase. The blood sampling in the second phase was done 24 hours after the last training session in order to make the remove the effects of that session on the all participating groups. This phase was done in 24ºC. TNFα serum density was measured by ELISA kit (Bender Med system, TNFα England), HCY serum density was measured by Homocystein ELISA (IBL Hamburg Germany), and the serum density of CRP was measured by the high-sensitivity ELISA kits (R&D Systems, Oxon, U.K.).

To analyze the data for this study, descriptive statistics were used to measure the central biomarkers and the distribution, S-K test was used to determine the normality of the variables’ distribution, paired t test was used to investigate the changes in the groups from pre-test to post-test, ANOVA determined the difference between groups, and Dant test determined the significance of the differences. The data were analyzed by the SPSS-17 software and the level of significance was $p<0.05$.

Results

To evaluate the possible changes in physical features, body mixture, and the physiology of the participants in all three groups from the pre-test stage to the post-test, field variables such as age, height, BMI, WHR, systolic and diastole blood pressure and resting heart rate were measured table 1. After 9 weeks aerobic exercise with the 60 to 65% maximum heart rate for the obese, the serum density of TNFα (p=0.006), CRP (p=0.001), and HCY (p=0.013) in the aerobic exercise group and aerobic exercise-multivitamin supplement group decreased significantly compared to the basic state. In the non-intervention control group, however, there was not such a significant difference.

Also, the results of ANOVA and Dant tests showed that after 9 weeks training program, the level of TNFα and CRP plasma had a significant difference among the groups (aerobic exercise, aerobic exercise-multivitamin supplement, and non-intervention control). CRP and TNFα reduction in the aerobic exercise group (p=0.001) and the aerobic exercise-supplement group (p=0.001) was significant as compared to the control group. HCY reduction in the aerobic exercise, however, was not significant as compared to the control group while this difference was significant in the aerobic exercise-multivitamin supplement group (p=0.036) (Table 2).

Table 1. General features, body composition, and physiology of the participants in the three groups of the study, before and after 9 weeks training program

Variable	Aerobic exercise-multivitamin (Mean±SD)		Aerobic exercise (Mean±SD)		Control (Mean±SD)	
Group	pre-test	post-test	pre-test	post-test	pre-test	post-test
Age (year)	40.4±6.47		41±5.35		43.8±9.48	
Height (cm)	158.2±6.77		155.7±2.7		155.7±5.33	
Weight (kg)	78.2±14.7	77.2±13.3	71.7±8.85	70.1±9.05	75.7±9.64	75.6±11.03
BMI (kg/m^2)	31.2±6.66	30.3±6.34	30.2±3.84	29.9±4.23	31.1±4.24	31.2±4.61
Body fat (%)	36.7±7.21	35.1±6.93	36.4±3.77	35.3±3.96	37.9±5.14	38.05±5.43
Waist-hip ratio (cm)	11.15±5.20	11.22±3.54	8.56±0.52	8.39±0.47	8.39±0.6	8.47±0.47
Systolic blood pressure (mmHg)	12.3±1.24	11.5±1.10	11.9±1.15	11.06±1.29	11.3±1.04	11.52±1.34
Diastolic blood pressure (mmHg)	8.89±1.10	7.96±0.95	8.7±0.98	7.7±0.82	7.8±1.02	7.98±0.75
Resting heart rate (beat in min)	86.9±9.02	81.6±5.27	79.5±6.57	74.1±9.5	74.5±7.59	72.2±7.4

Table 2. The results of paired t test, variance analysis, and Dant test in determining the average difference of TNFα, CRP, and HCY among different groups

Variable	Group	Aerobic exercise-multivitamin (Mean±SD)	Control (Mean±SD)	Aerobic exercise (Mean±SD)
TNFα (Pg/ml)	pre-test	39.9±12.1	33.0±93.0	75.0±33.1
	post-test	28.0±79.0#	26.0±52.0#	78.0±39.1
	difference	11.9±33.0 *	07.0±41.0 *	03.0±06.0†‡
CRP (mg/l)	pre-test	68.0±37.6	32.0±45.6	87.0±23.6
	post-test	17.0±87.3 #	14.0±62.4#	26.0±61.6 #
	difference	51.0±5.2 *	18.0±83.1 *	61.0±38.0†‡
HCY (µmol/l)	pre-test	20.5±15.13	02.3±45.13	22.3±63.13
	post-test	54.3±22.11#	23.2±61.11 #	86.2±11.14
	difference	66.1±93.1*	79.0±84.1	36.0±48.0†

Significance as compared to the pre-test amounts
* Significance as compared to the control group
‡ Significance as compared to aerobic exercise group
† Significance as compared to aerobic exercise-multivitamin supplement group

Discussion

There have been many studies about the relationship of body activities and dangerous cardiovascular factors and in many cases a reversed relationship between these two has been reported [15, 22, 29]. However, there aren't any comprehensive studies investigating the impact of aerobic exercises and multivitamin supplement on cardiovascular biomarkers. Therefore, the purpose of the current study is to investigate the impact of 9 weeks aerobic exercises and multivitamin supplement on CRP, TNFα, and HCY serums (cardiovascular biomarkers) in obese women.

In the present study, there was a significant decrease in the HCY plasma density after 9 weeks of exercise, both in the aerobic exercise group and in the aerobic exercise-multivitamin supplement group as compared to the pre-test state. This reduction was reported 6.3% in the aerobic exercise group and 6.5% in the aerobic exercise-multivitamin supplement group. This small difference in the HCY plasma between these two groups shows the influence of multivitamin supplement. According to the previous studies, HCY plasma bears a relationship with diet, group B vitamin and folic acid [20, 30].

The results of this study accords with that of Gelecek et al., Uffelen et al., and Rousseau et al. [30, 32]. Also the current study showed that, when compared to the control group, aerobic exercise has no effect on the HCY plasma. Multivitamin supplement accompanied with aerobic exercise, however, decreases the HCY plasma as compared to the control group. Multivitamin supplement in the basic level decreases HCY in the obese women clearly [29]. Also the study of Papandreou et al. showed that there is a significant relationship between increasing HCY and decreasing vitamin B_{12} in the obese women [22]. It is pretty difficult, however, to conclude that positive effects of multivitamin supplement in decreasing HCY plasma is restricted to those who took these supplement, because there has been no significant difference between aerobic exercise and aerobic exercise-multivitamin supplement groups and the multivitamin supplement in the supplement group as compared to the non-supplement group (aerobic exercise) has not been affective. But, since in both groups, the intensity, duration, and sort of aerobic exercise was the same for the participants, it is most probable that the significant reduction of HCY plasma density in the aerobic exercise-supplement group has been due to the multivitamin supplement. Taking the HCY plasma reduction as 1.5 µm/l in the aerobic group and 1.17 µm/l in the aerobic exercise-multivitamin supplement group into consideration, it is expected that 6.18% of the heart attacks, 9.28% of heart strokes, and 9.66% of thrombosis be reduced. It is because of the fact that with the 3 µm/l reduction in HCY plasma, heart attacks, heart strokes, and thrombosis are reduced 12%, 24%, and 25% respectively [32].

TNFα encourages the production of IL-6 and IL-6 is a powerful motivator for the production of CRP. Therefore, the large number of fat textures in the obese leads to the acceleration of CRP production in a cascade manner. Hamedinia et al. reported in a study that in the basic state, CRP serum density is significantly more in the obese as compared to the thin [33]. In the current study, after 9 weeks aerobic exercise with the 60 to 65% of the maximum heart beat for the obese, both in the aerobic exercise and aerobic exercise-multivitamin supplement groups, CRP had a significant reduction as compared to the pre-test state. This significant difference, however, was not observed in the control group, while the other two groups encountered a significant reduction in their CRP. These results show a reversed relationship between sport activity and CRP inflammation biomarker. Gaeini et al. investigated the influence of 12 weeks aerobic exercise on the CRP of female obese old moles. They showed that regular aerobic exercise leads to the significant reduction of CRP and atherogenic process [34].

Kasapis et al. reported the increasing effect of TNFα, CRP, and HCY on the occurrence of cardiovascular diseases by producing free and motivating radicals for a planned death [35]. It is most probable that the influence of vitamin supplement on CRP plasma can be through the influence on high cytokines, particularly IL-1, TNFα, and IL-6, which are the main producers of acute stage response [36]. Christian et al. showed that vitamin supplement stops the expression of IL-6 gene and its release into blood circulation during the intense exercise. It also reduces the amounts of fat peroxidation during the training program [36]. Some researchers believe that fat percentage reduction and losing weight is necessary for improving CRP amounts, while some others declare that physical activity reduces the inflammation biomarkers significantly regardless of losing weight or a difference in body mixture [33].

TNFα is another cardiovascular risk biomarker. Some studies showed that the increase of TNFα density is a predictor for heart attack [10, 11]. Cesari et al showed, in a study of 2225 elders (70 to 79 years old), that there is a significant relationship between TNFα and heart coronary diseases [2].

In the current study, after 9 weeks aerobic exercise with the 60 to 65% of the maximum heart beat for the obese, both in the aerobic exercise and aerobic exercise-multivitamin supplement groups, TNFα had a significant reduction as compared to the pre-test state. This significant difference, however, was not observed in the control group, while the other two groups encountered a significant reduction in their TNFα. These results show a reversed relationship between sport activity and TNFα inflammation biomarker. The results accord with those of the studies by Sloan et al., Straczkowski et al., and David et al. [12, 16, 37].

Food diet and different medicines and vitamins are some of the factors that influence the changes of TNFα. Many of the vitamins and minerals work as anti-oxidants and protect the cells against oxidation threats caused by inflammation [17, 23]. There are only a few studies which investigate the influence of aerobic exercise and multivitamin supplement on inflammation biomarkers. While it has been shown that multivitamin supplement reduces IL-6 and CRP, the influence of vitamins on TNFα needs more studies. Ferries et al. showed that aerobic exercise accompanied with low-fat diet reduces TNFα [38]. It seems in this study, multivitamin supplement does not play a significant role as the TNFα modifier, because TNFα reduced more in the aerobic exercise group than the aerobic exercise-supplement one. This difference, of course, can be the result of the difference in the fat percentage and BMI of the two groups under study.

Given the relation between inflammation biomarkers such as TNFα and the amount of fat in the body, and since TNFα is produced in the fat texture, determining the exact amount of the body fat is necessary to determine the relationship between physical activity and inflammation biomarkers. This is more important for the obese because they have many fat textures [6, 8].

As the present study shows after the training program for the aerobic exercise group was done, fat percentage, BMI, and WHR decreased by 9.69%, 9.89%, and 9.80% respectively, while TNFα plasma decreased by 5.59%. In the aerobic exercise-multivitamin supplement group, fat percentage, BMI, and WHR decreased by 9.56%, 9.93%, and 1.006% respectively and TNFα plasma decreased by 7.05%.

This information shows that the reduction of body fat as result of regular exercises can lead to the reduction of the level of TNFα inflammation biomarker. The mechanism of these changes, however, is unknown yet. On the other hand, previous studies show that the relation between high physical fitness and less inflammation is independent of total obesity or stomach obesity [17, 39]. In this regard, Klein et al. showed that the improvement of endothelial function as a result of losing weight and reducing TNFα is independent of the change in the obesity and body fat distribution [40].

The results of the present study support this study because the reduction of TNFα is more than that of obesity and body fat percentage. Thus, it seems that the existing relationship between physical activity and inflammation is not completely caused by the reduction of obesity. Therefore, the reduction of body fat is a suggested mechanism to justify the reduction of TNFα.

In general, the result of the current study show that, by direct influence on fat texture and increasing lipolysis, selected aerobic exercises and multivitamin supplement can reduce the serum density of blood circulation inflammation biomarkers (CRP, TNFα, HCY) in non-athletic obese women

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