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Effect of 12 Weeks Aerobic Training with Ginger Consumption on IL-18 and CRP in Obese Men

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Abstract

Introduction: The use of antioxidant and anti-inflammatory supplements is important in improving the function of obese people. The aim of this study was to investigate the effect of 12 weeks aerobic training with ginger consumption on the levels of IL-18 and CRP in obese men.

Methods: 40 men (mean ± SD: age 23.9 ± 5.90 years old, weight 87.61 ± 4.69 kg and BMI 32.69 ± 3.25 kg / m2) were randomly selected and divided into four groups of 10, including 1- aerobic training, 2- training with ginger consumption, 3-ginger consumption, 4-control. The first and second groups, had 12 weeks, 3 sessions per week and 40 minutes each session aerobic training selections with an intensity of 65%MHR; during this period, the second and third groups received one gram of ginger capsule daily and the control group received no intervention. Blood samples were taken before and after the study period. Paired sample t-test and one-way ANOVA were used for data analysis ($p \leq 0.05$).

Results: There was a significant difference in IL-18 and CRP before and after exercise in all three experimental groups ($p \leq 0.05$).. Also, the results of the bonferroni post hoc test showed a significant difference in the level of IL-18 and CRP in the Reaserch groups. The highest decrease in these variables was observed in the aerobic training group and training with ginger consumption group ($p \leq 0.05$).

Conclusion: Ginger supplementation with aerobic training seems to be a suitable method for reducing IL-18 and CRP and preventing metabolic, cardiovascular and inflammatory diseases in obese men.

Keywords: Aerobic Training, Ginger, IL-18, CRP, Obesity

Introduction

Research indicates that obesity is a major negative factor in the health and longevity of a community members. According to the latest World Health Organization (WHO) estimates, 1.6 billion adults are overweight and over 400 million are obese (1). The WHO has also predicted that the incidence of severe obesity will double in the years 1995 to 2025; according to the forecast in 2025, in developing countries, the prevalence of obesity and overweight is rising at a considerable pace (2). Obesity is associated with inflammation, and inflammation is the main mechanism of creating atherosclerosis and insulin resistance. In this situation, inflammatory markers such as pre-inflammatory cytokines and proteins in the acute phase of the blood increase (3). Research findings have shown that the production of large amounts of inflammatory cytokines, such as InterLeukin-6(IL-6), InterLeukin (IL-18), tumor necrosis factor-α (TNF-α), and C-reactive protein (CRP) by adipose tissue contributes to the development of insulin resistance, diabetes and metabolic syndrome (4). IL-18 is among the cytokines that are expressed and secreted in the adipose tissue and as a pre-inflammatory cytokine is capable of stimulating the production of IL-6 and TNF-α (5). In fact, IL-18 is a polyotropic pre-inflammatory cytokine (with multiple effects) with important regulatory functions in the inherent immune system, which increases the

production of adhesive molecules, nitric oxide synthesis and chemokines (6). It also plays a decisive role in the pathological angiogenesis and is an indicator for predicting cardiovascular disease in patients with cardiovascular disease (CVD) (7). Besides, CRP is an acute phase reactant that is directly related to obesity and its amounts are rapidly increased in response to inflammation in the circulation (8), and its increase in the bloodstream is a sign of inflammatory diseases or tissue damage (9). Increasing CRP increases the risk of cardiovascular events by 2 to 5 times. One of the most important drivers of CRP production is obesity (10). Serum levels of CRP are low in healthy people, but increase by up to 100 times when inflammation or acute illness occurs (6). Although this substance is produced in the liver, new research has shown that it can also be made into the intima layer of the vessels with atherosclerosis (11). Preventive role of the exercise against these diseases is attributed to the anti-inflammatory effect of the regular training because the effects of the in-vivo of the exercise directly play a role in the anti-inflammatory response of the cytokines. Based on the findings of some studies, physical activity can reduce inflammatory markers (12). Exercises that lead to weight loss seem to result in a decrease in serum levels of IL-18, IL-6 and CRP (13). Physical activity reduces the level of inflammatory cytokines (12-13).

Kohurt (2002) showed that after 10-month aerobic training, serum levels of IL-6, CRP and IL-18 decreased in males and females (14). Spositio *et al.* (2002) also reported that performing eight weeks of aerobic exercise in obese women reduces serum IL-18 levels; possibly lowered IL-18 levels is due to reducing CRP levels (15). The relationship between CRP and IL-18 has already been reported. It is likely that the reduction of CRP levels in the aerobic training group has its inhibitory effects on IL-18 (13). In addition to regular physical activity, the attention of researchers has been drawn to the use of herbal medicine as a cost-effective and minimal side-effect method. For a long time, ginger has been used to treat cold, rheumatism, neurological diseases, gingivitis, toothache, asthma, stroke, constipation, diabetes, and act as an anti-stress, anti-inflammatory and immune regulator, inhibitory tumor formation, anti-apoptosis and anti-nausea, Inflammation and an effective way to reduce the risk factors for cardiovascular disease (16). Recent research has shown that ginger has various medicinal effects due to the presence of various compounds, including gingerols and shogaols. It seems that the effect of ginger on the reduction of inflammation is through the effects of these compounds (gingerols and zerombon) on the inhibition of NFκB and TNFα. The inhibition of the TNFα gene by ginger reduces the activity of NFκB and, as a result, the production of acute-phase positive proteins, such as CRP, is also inhibited (17). Atashak *et al.* (2010) in a study showed that daily intake of 1 g of ginger powder for 10 weeks resulted in a 27% reduction in mean concentration of CRP in the ginger group in obese men. Also, the combination of exercise and consumption of ginger was observed to reduce the level of CRP in obese men (11). Nayebifard *et al*. (2016), found that 10-week interval training with ginger supplementation could reduce the risk of atherosclerosis in obese men (16). Vahdatpoor *et al.* (2018), examined the effect of ginger supplements on oxidative stress induced by exogenous outgrowth activity in overweight girls. The results of this study indicated that non-drug approaches such as ginger supplementation along with physical activity, are likely to contribute to improving the quality of life and health of overweight people by reducing inflammation and cellular stress (17). Therefore, due to the lack of comprehensive studies on the anti-inflammatory role of ginger with aerobic training on IL-18 and CRP, the present study was aimed to investigate the effect of 12-week aerobic training with ginger

supplementation on the levels of CRP and IL-18 in obese men.

Methods

As a semi-experimental and developmental research with a post-test design with control group, the present study was carried out in a fieldwork and applied in terms of the obtained results. The statistical sample of this study consisted of 40 obese (BMI> 30) who were selected from 60 volunteers by recall and purposefully. After completing the medical questionnaire and obtaining consent forms, they were randomly divided into four groups of 10, including 1-aerobic training, 2- training with ginger consumption, 3-ginger consumption, and 4-control. The criteria for entry into the study included no smoking and alcohol use, no participation in a regular exercise program during the past six months, having a BMI greater than 30, having a relatively similar dietary pattern and avoiding changing food habits during the conduct of the research, no history of any type of disease (cardiovascular, liver, kidney, lung, blood, diabetes, certain diseases, and hormonal, metabolic and motor disorders) and lack of any medication use that prevented participation in the study. Exit criteria included lack of regular engagement in training sessions, starting with exacerbations of pain or illness that cannot continue to work, non-consuming or irregularly consumed supplements, effective dietary changes, non-attendance at each blood sampling session and withdrawal of subjects for any reason. At first, the subjects were matched based on BMI (Table 1) and divided into 4 groups of training (n=10), training with ginger supplement (n=10), ginger supplement (n=10) and control (n=10). Also, the present study was conducted under the supervision of a specialist physiologist and athletics physiologists. The participants were introduced in one session with the methods of doing training and blood sampling. Pretest and posttest were performed 24 hours before and 24 hours after the last exercise session, at 8:00 am and after 12 hours of fasting. At each stage, 5 cc of blood was collected. Serum samples were used to measure the variables. The subjects of the aerobic training group and the training with ginger group did exercise for 12 weeks, each week 3 sessions and each session 40 minutes at the gym. The training of the first week were performed with low intensity (50% of maximal heart rate) and then in the following 11 sessions reached 65% of maximum heart rate. The intensity of exercise was monitored by means of a polar pulsating apparatus. In each session, 10 minutes was used to warm up, including walking with stretching techniques, and at the end, the cooling was performed for 10 minutes in the form of gentle walking and stretching movements. The target heart rate (exercise) was calculated based on the formula of age -220. It should be noted that 3 minutes of complete rest between each repetition and 5 minutes of active rest were taken between each turn. The training group and the training with ginger group received daily 1 g of ginger capsule (zinetuma) after lunch for 12 weeks. Ginger capsules were purchased from GolDarou Herbal Medicine Manufacturing Company under the sanitary license of 1228022777 from the Ministry of Health's Food and Drug Administration. In this study, to measure biochemical variables, at first, 24 hours before the beginning of the first training session, at 8:00 a.m, 5 cc fasting blood was taken from the anterior venous vein; samples were centrifuged at 1500 rpm for serum separation for 10 minutes and then the attained serum was distributed in special eppendrof dishes and immediately stored at -80 ° C for freezing for further analysis. Subsequently, 24 hours after 8 weeks, the subjects were retested in 5-cc fasting state and the blood was centrifuged in order to isolate the serum. To measure the IL-18 by ELISA, RayBiotec for human specimens from Georgia was used, with a sensitivity of 0.9, pg / ml and inter- and intra-processing variation of 6.5 and 8.1,

respectively. High-sensitivity CRP levels were measured by immunometric method using ELISA kit. The minimal operating sensitivity of the processor and kit was 0.01 mg / dL and the coefficient of variation between and within the processing was 1.5 and 2.5%, respectively.
The height of the subjects was measured using a wall height guage with accuracy of 0.1 cm and weight using a digital scale (SKA) with accuracy of 0.1. The body composition apparatus (inbody) was used to calculate the fat percentage of the subjects. This device uses an electrical body impedance (BI) and a weak electrical current that does not feel when working with the device, and evaluates and determines the percentage of body fat based on the conductivity of body tissues. Levene's test was used to test the homogeneity of variances in the pre-test. The Kolmogorov-Smirnov test was used to ensure the distribution of the variables was normal. After showing the normality of data, to analyze the data,paired sample t-test was used to compare the pre-test and post-test means within the group, and One-way analysis of variance (difference between test and post-test) was used to compare the groups. Also, in the case of significant findings, Bonferron's post hoc test was used. All data analysis was performed using SPSS software version 22 and at a significance level of $p \leq 0.05$.

Results

The demographic characteristics of the participants in the study, such as age, height, weight, fat percentage and BMI, are presented in Table 2. The results of paired sample t-test showed that IL-8 levels in the training group ($p = 0.002$) ginger consumption ($p = 0.04$) and training with ginger ($p = 0.001$) decreased significantly in posttest compared to pretest. IL-8 did not change significantly in control group compared to pre-test time ($p = 0.7$). Also, CRP levels in training group ($p = 0.001$), ginger consumption ($p = 0.001$), and training with ginger consumption ($p = 0.001$), decreased significantly in posttest compared to pretest. CRP did not change significantly in comparison with the pre-test time in the control group ($p = 0.4$) (Table 3). The results of one-way ANOVA showed that levels of IL-18 in the training, ginger and training with ginger groups were significantly lower than the control group ($p = 0.001$) (Table 3). The results of the Bonferroni post-hoc test of IL-18 showed no difference between training and training with ginger groups ($p = 0.9$), but there was a difference between ginger and training groups ($p = 0.000$), training and control groups ($p = 0.000$), training with ginger and ginger groups ($p = 0.001$), ginger and control groups ($p = 0.000$), and training with ginger and control groups ($p = 0.001$). Also, levels of CRP in training, ginger and training with ginger groups were significantly lower than the control group ($p = 0.001$). The results of Bonferroni post hoc CRP test showed no difference between training and ginger groups ($p = 0.9$). But differences were shown between training and training with ginger groups ($p = 0.005$), training and control groups ($p = 0.01$), ginger and training with ginger groups ($p = 0.009$), ginger and control groups ($p = 0.006$), training with ginger groups with control groups ($p = 0.001$).

Discussion

The results of this study showed that 12 weeks of aerobic training led to significant decrease in IL-18 and CRP in obese men. The results of this study are consistent with the research by Troseid *et al.* (2009), Mehrlouei *et al.* (2018), Vahdatpoor *et al.* (2016) and Arabloo and Ariaeian (2013) (18, 10, 17). However, they do not match with the results of Mahluji *et al.* (2013) and Christopher *et al.* (2006) (19, 20). Perhaps this discrepancy is due to the implementation of the protocol and its duration, the gender and age of the subjects as well as the physiological adaptations of the exercises. Based on many researchers, it is believed that sports have anti-inflammatory effects and have a positive effect on the

Table 1. Aerobic training program

Week	Protocol
One	4 minutes with 3 repetitions and 2 turns
Two	2 minutes with 4 repetitions and 2 turns
Three	4 minutes with 3 repetitions and 2 turns
Four	2 minutes with 4 repetitions and 2 turns
Five	7 minutes with 2 repetitions and 2 turns
Six	4 minutes with 3 repetitions and 2 turns
Seven	4 minutes with 3 repetitions and 2 turns
Eight	2 minutes with 4 repetitions and 2 turns
Nine	4 minutes with 3 repetitions and 2 turns
Ten	4 minutes with 2 repetitions and 2 turns
Eleven	7 minutes with 2 repetitions and 2 turns
Twelve	2 minutes with 4 repetitions and 2 turns

Table 2. Demographic characteristics of subjects at baseline

Group Variable	Control	Training with ginger	Ginger	Training
Age (Year)	24.60 ±2.77	23.2 ±8.15	22.18 ±7.78	24.9 ±4.91
Height (Cm)	164.65±4.3	167.17±6.2	165.14±2.04	160.1±2.79
Weight (Kg)	86. 5±4.9	88.8±5.51	90.9±3.69	89.05±4.68
BMI (kg/m^2)	32.80±1.77	31.19±3.77	33.40±3.18	33.29±4.31
Fat (%)	39.72±6.24	37.83±6.88	39.12±6.79	37.38±6.58

Table 3. Comparison of IL-18, CRP before and after training in subjects under study using paired sample t-test and one-way ANOVA

Variable	Stages	Groups				P (Between-Group)
		Control	Training with ginger	Ginger	Training	
IL-18 (pg/ml)	Pre test	240.6±21.29	263.98±27.02	248.37±26.91	263.32±35.5	*0.001
	Post tetst	239.21±22.7	229.73±20.98	232.7±28.96	234.8±34.9	
	P (within group)	0.8	*0.001	*0.04	*0.002	
CRP (mg / L)	Pre-	3.17±.93	3.82±.93	3.52±.71	3.17±.93	*0.001
	Post-	3.17±.93	3.17±..93	2.39±.45	2.6±.96	
	P (within group)	0.4	*0.001	*0.001	*0.001	

* Indicates significant level as compared to that of pre-test (p≤0.05)

internal organs of the body, which reduce the amount of many inflammatory mediators (5). Evidence suggests that continuous exercise can reduce fat percentage. Since adipose tissue is one of the main sources of IL-6 and IL-18 production, the serum levels of these two cytokines also decrease with decreasing adipose tissue (15). Reductions in serum levels of IL-6 will weaken the signaling pathways for CRP production. Physical activity reduces the level of inflammatory cytokines (21). Kohurt (2002) showed that after 10-month aerobic training, serum levels of IL-6, CRP and IL-18 decreased in adult males and females (14). Sposito *et al.* (2002) also reported that doing 8 weeks of aerobic exercise in obese women reduced the concentration of serum IL-18 (15). Reducing serum IL-18 in obese people can be attributed to the anti-inflammatory effect of exercise. Sport activity produces more anti-inflammatory cytokines such as IL-6, IL-1ra and IL-10. The production of anti-inflammatory cytokines reduces the production of pre-inflammatory cytokines such as IL-6 and IL-18 from adipose tissue (22). Also, reducing the concentration of this cytokine can be attributed to the reduction in body fat percentage. One of the reasons for reducing IL-18 may be a reduction in CRP values. The relationship between CRP and IL-18 has already been reported. Probably the reduction of CRP levels in the aerobic exercise group has its inhibitory effects on IL-18 (14,15). Adaptation to physical exercises, especially aerobic exercises, also affects the response of indicators of acute inflammation such as CRP. In this study, serum CRP levels in the aerobic training group decreased significantly (23). In this respect, the findings of this study are consistent with Lindegraard *et al.* (2008). They reported that 16 weeks of interval training in endurance and resistance groups reduced IL-18 in both groups and CRP only in the endurance group. To them, this reduction was thanks to improved immune function due to adaptation to low to moderate aerobic exercises. Reduced chronic inflammation has also been shown to be effective in reducing acute inflammation after adaptation to sports exercise (24).

The results of this study showed that 12 weeks of use of ginger lead to a significant reduction of IL-18 and CRP in obese men. It seems that the effect of ginger on reducing inflammation occurs through the effects of some active compounds (ginerols and zerombon) on TNF-α inhibition. Inhibition of TNF-α by ginger inhibits the production of IL-18 and CRP (25). Ginger also contains components that prevent the synthesis of prostaglandin (PG), which provides scientific justification for its anti-inflammatory effects (26). Therefore, because daily intake of ginger has less side effects than non-steroidal anti-inflammatory drugs (NSAIDS) for long periods, the unique ability of ginger to prohibit the synthesis and reduce the medical-inflammatory indexes is very important. (25). In the present study, the use of anti-inflammatory supplementation of ginger reduced the levels of IL-18 and CRP compared to the pre-training period. In general, ginger supplementation due to anti-inflammatory and anti-oxidant properties has led to inhibition of prostaglandin synthesis and to stop pre-inflammatory cytokines (27). It has also been reported that the anti-inflammatory effects of this plant by inhibiting the synthesis of leukotriene and prostaglandins inhibit cyclooxygenase and lipoxygenase, which inhibits the metabolism of arichidonic acid. It also inhibits platelet adhesion and suppresses the release of free radicals. Consequently, it can lead to a modification of immune responses that aggravate inflammation (28). Thomson *et al.* (2002) investigated that anti-inflammatory markers of IL-18 were reduced by the use of ginger (25). Also, Arabloo (2013) showed that consuming ginger supplementation for 12 weeks could significantly decrease CRP levels in patients with diabetes (29).

On the other hand, the use of ginger supplements with aerobic exercise, which is associated with the production of free radicals

and oxygen reactive species, has led to a reduction in the production of cytokines by affecting neutralizing the production of free radicals and oxygen reactive species (25). It also has the effect of inhibiting the activity of oxidation-sensitive signal transmission pathways, and is likely to lead to a reduction in the levels of these cytokines in the present study (29). Also, the results of this study showed that 12-week aerobic training with ginger consumption significantly decreased the IL-18 and CRP in obese men. Obviously, a combination of aerobic training and ginger consumption through disabling of the NFkB pathway (a nuclear factor that activates transcription of cytokines) acts as an anti-cancer and anti-inflammatory agent by stopping pre-inflammatory cytokines, and so prevents the production of IL-18 and CRP (30). Aerobic training and ginger supplementation have been associated with an increase in blood flow and weight loss and fat percentage, which has been shown to reduce the inflammatory factors of IL-18 and CRP (28). Atashak *et al.* (2010) showed that daily intake of 1 g of ginger powder for 24 weeks reduced the average CRP and IL-18 concentration up to 27% in the ginger group in obese men (11). Although the study found that daily intake of one gram of ginger for 12 weeks by obese subjects reduced inflammatory symptoms during exercise, and hence the use of this supplement is appropriate for obese people, it is necessary to do different studies in order to identify other effects as well. It is also suggested that researchers measure other inflammatory markers, such as IL-6, IL-10 and TNF-α, to conclude definitively. In addition, it is necessary to conduct a similar study with different doses of ginger. Since despite the dietary recommendations and the completion of the dietary questionnaires there is no complete assurance of compliance with the diet by participants, a similar study with full diet control will yield to clearer results. Overall, little research has shown the effect of aerobic training and ginger on inflammatory factors, especially in obese people, and further studies are needed to obtain more clear results.

Conclusion

In general, there is little research on the effect of combined training and ginger supplementation on serum levels of IL-18 and CRP in obese people women. Based on the findings of this study, training, ginger supplementation and training with ginger exercise and ginger reduced the levels of IL-18 and CRP in obese men. IL-18 and CRP levels in the aerobic training group and training the Training with ginger group showed the greatest reduction. Finally, the results of this study showed that aerobic training withginger consumption may be effective in reducing IL-18 and CRP serum and preventing metabolic, cardiovascular and inflammatory diseases in obese men.

Ethical issues

No applicable.

Authors' contributions

All authors equally contributed to the writing and revision of this paper.

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