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Research article

Obesity-related cardiovascular risk factors after long- term resistance training and ginger supplementation

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Abstract
Obesity and its metabolic consequences are major risk factors for cardiovascular morbidity and mortality. However, lifestyle interventions, including exercise training and dietary components may decrease cardiovascular risk. Hence, this study was conducted to assess the effects of ginger supplementation and progressive resistance training on some cardiovascular risk factors in obese men. In a randomized double-blind design, 32 obese Iranian men (BMI≥ 30) were assigned in to one of four groups: Placebo (PL, n = 8); ginger group (GI, n = 8) that consumed 1 gr ginger/d for 10 wk; resistance training plus placebo (RTPL, n = 8); and 1gr ginger plus resistance exercise (RTGI, n = 8). Progressive resistance training was performed three days per week for 10 weeks and included eight exercises. At baseline and after 10 weeks, body composition and anthropometric indices were measured. To identify other risk factors, venous blood samples were obtained before and 48-72 hours after the last training session for measurement of blood lipids (LDL-C, HDL-C, TG), systemic inflammation (CRP), and insulin resistance (HOMA-IR). After 10 weeks both RTGI and RTPL groups showed significant decreases in waist circumference (WC), waist-to-hip ratio (WHR), body fat percent, body fat mass, total cholesterol, and insulin resistance ($p < 0.05$) and a significant increase in fat free mass (FFM) ($p < 0.05$), while it remained unchanged in PL and GI. Further, significant decreases in the mean values of CRP were observed in all groups except PL ($p < 0.05$). Our results reveal that resistance training is an effective therapeutic strategy to reduce cardiovascular risk in obese Iranian men. Further, ginger supplementation alone or in combination with resistance training, also reduces chronic inflammation. However more research on the efficacy of this supplement to reduce cardiovascular risk in humans is required.

Key words: Cardiovascular risk factors, resistance training, ginger supplementation.

Introduction

Obesity (body mass index ≥30 kg·m^{-2}) has been increasing in epidemic proportions in both adults and children (Poirier et al., 2006). Obesity and its metabolic consequences, hyperglycemia and dyslipidemia, are major risk factors of cardiovascular morbidity and mortality (Hofsø et al., 2010). In addition, several other cardiovascular risk factors, such as Metabolic Syndrome, insulin resistance, and chronic low-grade inflammation, are all closely associated with obesity (Lavie et al., 2009; Pischon et al., 2008). Chronic inflammation is thought to play a major role in the pathophysiological mechanisms of cardiovascular disease (CVD) and minor elevations in its levels are considered a strong, independent predictor of adverse cardiovascular events (Tzotzas et al., 2010). Recently, it was shown that obesity may be regarded as a state of chronic low-grade inflammation (Nascimento et al., 2010) and strong associations between C-reactive protein (CRP) and obesity have been found in epidemiological studies (Greenfield et al., 2004).

Physical inactivity is a primary cardiovascular disease risk factor (Ahmadizad et al., 2007). Improvement in cardiovascular function with physical activity has been attributed to exercise-induced positive changes in metabolic abnormalities and risk factors that are associated with atherosclerosis (Thompson et al., 2003). Nevertheless, while aerobic-based training has been extensively investigated and has been proposed as an effective mechanism for improving cardiovascular protection (Martins et al., 2010), the efficacy of resistance exercise training (RT) - also known as strength, or weight training - in reducing cardiovascular risk factors is less well studied (Alberga et al., 2010; Tresierras and Balady, 2009), and unknown in obese Iranian men. Published research to date indicates that RT is an effective therapeutic for the treatment of a number of chronic diseases and has been demonstrated to be safe and efficacious for the elderly and obese individuals (Arora et al., 2009). For example, a RT intervention has been shown effective in improving insulin action (Ibanez et al., 2010; Martins et al., 2010) and blood lipid profile (Ibanez et al, 2010; Misra et al., 2008) in obese and elderly individuals. Resistance training for six weeks has also shown to result in improved cardiac autonomic function and reduced inflammation in African-American men (Heffernan et al., 2009).

Separately, the use of herbal medicine as a pharmacologic modality in improving cardiovascular risk has warranted further attention from several researchers. Ginger is an underground rhizome of plant *Zingier officinal* belonging to the family Zingibeaceae, and now is available world wide (Elshater et al., 2009). For centuries, it has been an important ingredient in Chinese, Ayurvedic and Tibb-Unani herbal medicines for the treatment of different diseases (Badreldin et al., 2008), and it has been widely speculated that ginger might be beneficial to human health because it exerts anti-inflammatory and anti-lipidemic activity (Alizadeh et al., 2008). Ahmida and Abuzogaya (2009) suggest that consumption of ginger could aid in the treatment of obesity and other diseases

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related to cardiovascular disease in rats, whilst Alizadeh et al (2008) showed ginger to have a significant lipid lowering effects in patients with hyperlipidemia. Furthermore, the consumption of ginger produces a significant hypoglycemic effect in diabetic rats (Elshater et al., 2009), presumably via an improvement of the blood lipid profile.

The purpose of this study was to test the effects of ginger supplementation and progressive resistance training on indices of cardiovascular risk in obese Iranian men, and to investigate whether the interaction between these two interventions could provide additional benefits.

Methods

Participants

The study protocol and methodology were approved by the Clinical Research Ethics Committee of the Islamic Azad University of Iran. Thirty-two obese men (BMI≥30 $kg \cdot m^{-2}$, aged 18–30 years) volunteered for participation after receiving a detailed explanation of the study. Through a health screening questionnaire, all participants had to meet the following criteria before enrollment in the study: 1) no participation in regular physical activity; 2) no current chronic health problems; 3) non-smokers; 4) no cardiovascular, metabolic, or respiratory disease; and 5) no consumption any antioxidant supplements or drugs within the past 6 months. Informed consent was obtained from all subjects.

Study design

In this randomized double blind, placebo-controlled trial, interventions were administered over a 10-week period and subjects were evaluated at baseline and at the end of the study. Upon recruitment, the 32 participating obese men were assigned to one of four homogenized groups: ginger (GI; n = 8); ginger plus resistance training (RTGI; n=8); placebo (PL; n = 8); resistance training plus placebo (RTPL; n = 8). The groups were matched according to the age, physical status, body fat percentage, and BMI values. Thus, 16 obese men (GI and RTGI) orally received 4 capsules of ginger rhizome powder four times a day at regular intervals (breakfast, lunch, dinner, and at 10 pm) for ten weeks, while another 16 men (PL and RTPL) received 1g of maltodextrin in 4, 250mg capsules four times a day (placebo). Each ginger capsule contained 250 mg of ginger-root powder sold under the trade name Zintoma (Goldaroo Company, Tehran, Iran). Eight participants from each group also followed a resistance training protocol for the ten weeks. All participants were carefully instructed not to change their normal physical activity routines or dietary patterns during the course of the study.

Anthropometric measurements

The same trained technician performed all anthropometric measurements on the day that blood specimens were taken. Height (to nearest 0.1 cm), weight (nearest 100 g), waist and hip circumferences (to nearest 0.5 cm) were measured while subjects were without shoes. Waist circumference (WC) measured at the midpoint between the lower border of the rib cage and the iliac crest, and hip circumference (HC) were measured at the widest part of the hip region. Body mass index (BMI; body weight [kg]/height [m^2]) and waist-to-hip ratio (WHR) were calculated. Fat density (fat mass) was predicted from the skin folds measurements taken on the right side of the body using calipers (Baseline economy plastic 'Slim-Guide') at the triceps, abdominal, and super iliac sites after 10 h of fasting. Body fat percent was then calculated by using the methods of Brozek et al. (1963).

Training protocol

The progressive resistance training (PRT) program utilized in this study has been previously reported (Levinger et al., 2009). In brief, resistance training was performed three days per week for ten weeks, with 48–72 hours of recovery between training sessions. The training consisted of seven exercises: chest press, leg press, lateral pull-down, triceps pushdown, knee extension, seated row, and bicep curl. In addition, participants performed one abdominal exercise; the abdominal curl. Before the start of each training session, a gentle aerobic warm up for ten minutes was performed. During the first two weeks of training participants performed two to three sets of 15–20 repetitions at 40–50% of one repetition maximum (1RM = largest load that an individual can lift⁄move in a single maximal effort). From weeks three to six, participants performed each exercise for three sets, 12–15 repetitions at 50–75% 1RM. During the last four weeks of training, the number of repetitions in each set was reduced to 8–12 while the intensity was increased (75–85% of 1RM). Each subject's 1RM was reassessed every three weeks, and load training was adjusted accordingly. Exercise physiologists supervised all training sessions.

Blood samples and biochemical analyses

First, the subjects were required not to perform any physical activity two days before the test. Blood samples were collected from each subject at baseline and at 48-72 hours after the last training session in an overnight (12-hour) fasted state. A 5mL blood sample was collected via venipuncture of an antecubital vein. The samples were allowed to clot at room temperature for 10 min and then centrifuged for 15 min at 0° C. The serum was then pipetted into polystyrene tubes and the aliquots were frozen at −80° C for subsequent analysis.

Triglycerides (TG), CRP, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) were measured at baseline and end of 10 weeks. Total cholesterol, HDL-C and triglycerides levels were measured using by enzymatic assays, while LDL-C was calculated using the formula of Friedewald et al. (1972), where LDL-C=TC - [HDL-C + (TG/5)]. Plasma levels of CRP were measured by a highly sensitive enzyme linked immunosorbent assay (ELISA) technique as described previously (Wong et al., 2007). Insulin resistance in fasting state was estimated using a homeostasis model assessment (HOMA-IR) and was calculated as follows:

HOMA-IR= [fasting plasma glucose (mg/dl^{-1}) × fasting plasma INSULIN ($\mu U/dl^{-1}$) /405)] (Matthews et al., 1985).

Table1. Physical characteristics of the all groups. Values are means (± standard deviation).

Variable	GI (n=8)	RTGI (n=8)	PL (n=8)	RTPL (n=8)
Age (years)	23.66 (3.39)	23.65 (4.42)	25.38 (2.23)	23.71 (3.81)
Weight (kg)	93.51 (4.49)	98.95 (9.65)	97.93 (8.97)	101.97 (8.62)
BMI (kg·m^{-2})	31.24 (.67)	32.56 (2.37)	32.20 (2.33)	32.81 (2.10)
Body fat (%)	25.62 (2.20)	27.78 (3.60)	26.03 (2.96)	26.68 (3.59)
FFM (kg)	67.46 (3.64)	71.44 (8.71)	71.44 (8.71)	74.54 (8.47)
FM (kg)	25.82 (2.12)	27.50 (2.90)	26.27 (2.39)	27.34 (1.65)

Statistical analyses

Before statistical comparison, all data sets were tested for normal distribution by a Kolmogorov- Smirnov test. Data were expressed as Mean ±SD and analyzed by the two-way analysis of variance (ANOVA) and Tukey's post hoc tests using the SPSS statistical software package (SPSS version 16.0 for Windows, SPSS Inc., Chicago, IL, USA). Significance was set at $p < 0.05$.

Results

Physiological characteristics of the subjects at the beginning of the research are presented in Table 1. Before the interventions there were no significant differences in age, BMI and body fat % among the four groups ($p > 0.05$).

Anthropometrics, body composition and blood lipid profiles pre- post interventions were statistically compared and are shown in Table 2. In all groups, baseline mean LDL-C and triglycerides were above the desirable levels (normality rates were TC < 200 mg·dl^{-1}, HDL > 40 mg·dl^{-1}, LDL < 100 mg·dl^{-1}, and TG < 150 mg·dl^{-1}). In comparison with baseline values, mean cholesterol, body fat %, fat mass (FM), WC, and WHR decreased in the groups RTGI and RTPL ($p < 0.05$) independently of GI and PL groups after 10 weeks. In addition, there was a mean increase in fat free mass (FFM) in the groups RTGI, RTPL and ($p < 0.05$), while mean FFM remained unchanged in two other groups ($p > 0.05$). In addition, mean BMI, HDL, LDL and TG remained unchanged in all groups.

CRP levels were not different between groups at baseline (GI 2.9 ± 0.7 PL 2.4 ± 0.3, RTPL 2.6 ± 0.6 and RTGI 2 ± 0.6 ml·L^{-1}, $p = 0.28$). Subjects in GI, RTPL and RTGI groups showed significant ($p < 0.05$) decrease in CRP levels, while the PL group did not change over the course of the intervention (Figure 1). In percentage terms, RTGI, RTPL and GI groups showed 35.1, 28.3 and 21.2% reductions in CRP. Moreover, insulin resistance index, assessed as HOMA-IR, was reduced significantly by 29.5 and 31.2% following the 10 week of interventions in RTPL and RTGI groups respectively, with no significant changes in the GI and PL groups (Figure 2).

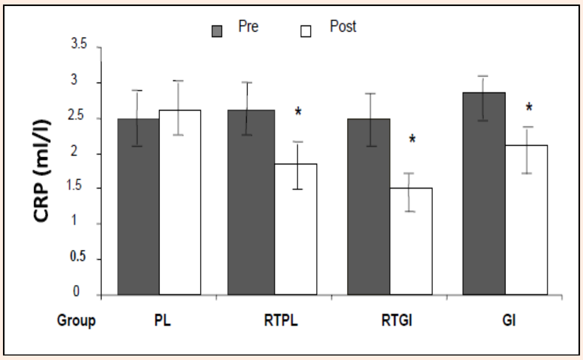

Figure 1. CRP pre- post exercise and supplement interventions. *Indicated significant ($p < 0.05$) difference vs. baseline.

Discussion

Obesity is a pro-atherogenic condition that predisposes to cardiovascular disease (CVD) via its major associated risk factors dyslipidemia, chronic low grade inflammation, insulin resistance, and type 2 diabetes mellitus (Tzotzas et al., 2010). However, lifestyle interventions, including

Table2. Anthropometrics, body composition and blood lipid profiles pre- post exercise and supplement interventions. Values are means (± standard deviation).

	PL		PLRT		GIRT		GI	
	Pre	post	pre	Post	Pre	post	Pre	Post
Anthropometrics								
Waist (cm)	104.9 (2.3)	105.0 (3.2)	108.3 (4.8)	105.0 (6.07)*	108.0 (5.3)	102.8 (3.6)*	107.0 (3.1)	105.7 (2.5)
WHR	1.05 (.04)	1.05 (.07)	1.06 (.03)	1.04 (.03)*	1.02 (.05)	1.0 (.05)*	1.08 (.04)	1.07 (.4)
Body composition								
BMI (kg·m^{-2})	32.2 (2.3)	32.3 (2.4)	32.8 (2.1)	32.5 (2.0)	32.5 (2.3)	32.2 (2.8)	31.2 (.6)	30.7 (.7)
Body fat (%)	26.0 (2.9)	25.9 (2.8)	26.6 (3.5)	23.5 (3.3)*	27.7 (3.6)	22.7 (2.8)*	25.6 (2.20)	25.2 (3.1)
FFM (kg)	74.4 (8.7)	74.8 (9.3)	74.5 (8.4)	76.2 (6.6)*	71.4 (8.7)	74.8 (9.3)*	67.4 (3.6)	68.3 (3.3)
FM (kg)	26.2 (2.3)	25.2 (2.2)	27.3 (1.6)	25.1(2.6)*	27.5 (2.9)	23.4 (2.8)*	25.8 (2.1)	24.6 (2.3)
Lipid profile (mg·dl^{-1})								
Tot Chol	192.5 (29.1)	193.2 (30.4)	181.1 (24.2)	159.1 (16.6)*	189.7 (41.4)	169.9 (33.1)*	186.0 (24.9)	175.1 (23.0)
LDL	116.9 (23.7)	118.8 (25.0)	104.2 (34.7)	90.8 (23.8)	112.5 (31.6)	98.8 (32.1)	108.6 (19.9)	100.4 (25.3)
HDL	42.2 (8.5)	42.5 (7.2)	45.0 (1.2)	48.0 (6.6)	43.2 (4.5)	47.6 (4.0)	46.6 (7.9)	47.8 (9.0)
TG	169.9 (38.1)	172.0 (35.1)	159.6 (63.9)	146.3 (72.7)	145.0 (23.0)	139.5 (3.2)	153.6 (54.5)	142.7 (28.4)
Gl (mg·dl^{-1})	87.3 (10.8)	88.7 (10.6)	86.6 (12.1)	85.7 (9.1)	86.4 (7.5)	85.0 (8.7)	92.8 (6.7)	91.2 (7.3)
Ins (μU·dl^{-1})	23.5 (3.5)	24.9 (3.6)	21.1 (9.5)	15.2 (10.9)*	22.7 (4.4)	15.7 (5.9)*	20.6 (6.8)	17.5 (3.2)

BMI: Body Mass Index, FFM: Fat Free Mass, FM: Fat Mass, Tot Chol: Total Cholesterol, TG: Trigliserid, Gl: Glukose, Ins: Insulin
* Indicated significant difference from baseline ($p < 0.05$).

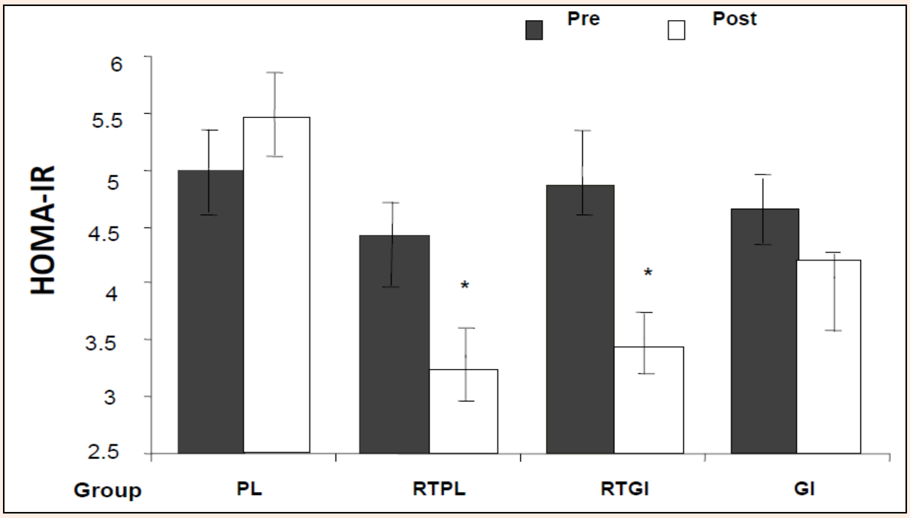

Figure 2. Changes (mean± S.D) in HOMA-IR before and after interventions. * Indicated significant ($p < 0.05$) difference vs. baseline.

exercise training and dietary components may eventually ameliorate their profile. Therefore, the present study investigated the effects of 10 weeks progressive resistance training and ginger supplementation on cardiovascular risk in obese men.

The most important finding of this study is that total cholesterol (TC), CRP and insulin resistance, as estimated via HOMA-IR, significantly decreased in obese Iranian men after 10 weeks of resistance training. Previous findings on the effects of resistance training on CRP and insulin resistance levels have been inconsistent, with some studies showing benefits (Brooks et al., 2007; Donges et al., 2010) and others showing no significant effect (Donges et al., 2010; Kwon et al., 2010). The lack of effects of training on CRP has been explained by the few concomitant metabolic risk factors of participants (Sillanpaa et al., 2009), and by a lack of changes in anthropometric variables (e.g., body weight, waist circumference) (Zoppini et al., 2006). The biological mechanisms by which these improvements in circulating CRP occur with resistance training are not fully understood, but probable mechanisms proposed to be responsible include reduction in visceral fat (Vieira et al., 2009), improved endothelial function (thus attenuating the secretion of pro inflammatory cytokines) (Gotto, 2007), and improved vagal activity (Heffernan et al., 2009). Also, although the mechanism responsible for the improvements in insulin resistance after resistance training cannot be deduced from the present study, it has been shown (Holten et al., 2004) that resistance training leads to increases in the protein content of GLUT-4, insulin receptors, glycogen synthase, and protein kinase B, without an increase in muscle mass.

Further, after the 10 week intervention, an increase in muscle mass percentage, corresponding to a gain of approximately 2-3 kg in muscle, was observed in the subjects engaged in resistance training with or without concomitant ginger supplementation. However, the fact that body fat %, WC, WHR, and total cholesterol significantly decreased in both GIRT and PLRT, permits us to confirm other published work (Martins et al., 2010; Ibanez et al., 2010; Misra et al., 2008) showing that RT is an appropriate and effective intervention for improving plasma lipid profile. . Further, the results of the present study are in accordance with those of others (Donges et al., 2010; Tresierras and Balady, 2009) who have observed improved measures of body composition following RT in previously sedentary individuals. However, aerobic-based exercise training maybe more beneficial than RT as a preventive measure in patients who are at risk of developing cardiovascular disease related to obesity (Chaudhary et al., 2010; Marques et al., 2009). Nevertheless, in some groups, RT may prove a more appropriate and popular mode of prescribed exercise; this may be the case for Iranian men.

Aromatic plants are invaluable sources of new drugs and have many applications in ethno medicine (Nogueira et al., 2011). An interesting finding from the present study is that CRP was improved with ginger supplementation in obese men. Although the mechanisms responsible for this improvement are not entirely clear, it has been suggested that anti-inflammatory properties of ginger may be due to a decrease in the formation of prostaglandins and leukotrienes (Grzanna et al., 2005). Also, Habib et al. (2008) reported that ginger might act as an anti-inflammatory and anti-cancer agent by inactivating NF-kappaB through the suppression of the pro-inflammatory TNF-alpha. Importantly, daily intake of ginger for a prolonged period will neither lead to side effects nor to complications as normally occurs with non-steroidal anti-inflammatory drugs (Thomson et al., 2002). The unique ability of ginger supplementation in decreasing CRP levels, and therefore preventing of cardiovascular complications, is potentially clinically very important.

Few studies have investigated the effect of ginger on blood lipids and insulin action in animals or humans. According to the present study, ginger supplementation seems to exert no effect on blood lipid profiles and insulin resistance in obese men (although the decrease in lipids and insulin resistance were not statistically significant, it did tend to decrease). These findings are in agreement with some previous studies (Bordia et al., 1997), however, hypolipidemic effects of ginger extract were demonstrated in some other studies (Alizadeh et al., 2008, Akhani et al., 2004). Akhani et al. (2004) suggest that; the reduction in serum lipid levels with ginger might be due to its antagonistic action on streptozotocin receptors, thereby increasing insulin levels. In addition, Fuhrman et al. (2000) reported that, the decreasing levels of plasma lipids following the intervention with ginger could have possibly resulted from the inhibition of cellular cholesterol biosynthesis after the consumption of the extract. One possible reason for the discrepancies between these and the present findings may be explained by differences in amount of given dose and length of supplementation. Other studies investigating the effect of ginger on lipid profiles have given doses of 3-4 g·day^{-1} (Alizadeh et al., 2008). Participants in the present study were given a lower dose (1 g/day) because ginger in doses higher may act as a gastric irritant and inhalation of dust from ginger may produce IGE-mediated allergy (Chrubasik et al., 2005).

Conclusion

Taken together, our data led us to conclude that progressive resistance training for 10 weeks significantly reduces chronic low grade inflammation, insulin resistance, body composition, and therefore has been an effective therapeutic devise to reduction cardiovascular risk factors in obese individuals. Similarly, ginger supplementation can also decrease chronic low grade inflammation in obese men. However, more research is required to elicit the effect of this supplement on cardiovascular risk factors in humans.

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Key points

- Long- term resistance training reduced cardiovascular risk factors in obese men.
- Ginger supplementation can also decrease chronic low grade inflammation in obese men.
- More researches are warranted to elicit the effects of these interventions on cardiovascular risk factors in humans.

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