

Original Article

The Impact of CX Training Combined with Inulin Consumption on Some Vascular Function Indices in Women with Metabolic Syndrome

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Abstract

Background and Aim: Recent studies have indicated the effectiveness of exercise training combined with antioxidant supplements on cardiovascular function in healthy and morbidly obese individuals. In the present study, the effect of CX Works training (CX) with and without inulin intake was evaluated on some markers of vascular function in women with metabolic syndrome.

Methods: In current semi-experimental study, 48 adult women with metabolic syndrome were randomly divided into 4 groups with 8 weeks intervention: CX training (every other day), inulin (10 grams/daily); combined (CX/inulin) and control (no intervention) groups. Serum Vascular endothelial growth factor (VEGF) and homocysteine after an overnight fast were measured in all groups (pre-training) and measurements were repeated 48 hours after the last exercise session (post-training).

Results: Compared to the control group, serum VEGF in the other groups increased significantly ($p < 0.05$). Serum VEGF in the combined group also increased compared to the CX and inulin groups ($p < 0.05$). Serum homocysteine in the combined group increased significantly compared to the other groups ($p < 0.05$).

Conclusion: Based on the findings, inulin consumption during CX exercises is associated with greater endothelial effects than either of them alone in patients with metabolic syndrome. Measurement of other markers of vascular function is recommended for better conclusions.

Keywords: Vascular Endothelial Function; CX Training; Inulin; Metabolic Syndrome.

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Introduction

In addition to its negative impact on mobility and mental health, obesity and increased body fat mass lead to metabolic disorders and changes in hormonal levels, leading to metabolic diseases such as type 2 diabetes, liver disease, and metabolic syndrome (1). Among obesity-related diseases, metabolic syndrome includes a set of metabolic and hormonal disorders. Metabolic syndrome patients have higher blood pressure, fasting glucose, TG, abdominal LDL, and insulin resistance than normal-weight individuals, and decreased HDL is another characteristic of these patients (2). Obesity and metabolic syndrome damage the vasodilation properties of the endothelium and lead

to impaired endothelial function, which is a precursor to the onset and progression of cardiovascular diseases (3). In laboratory studies, it has been shown that the positive effects of nitric oxide (NO) on endothelial function are associated with an increase in vascular endothelial growth factor (VEGF) (4). VEGF is a cytokine protein with a molecular mass of 45 kDa, which is known as the most potent angiogenic factor in endothelial cells and its effect on reducing blood pressure in conditions of overweight or obesity-related disorders is evident through stimulation of the VEGFR-2 receptor (5,6). As a result, the reduction of VEGF leads to vasoconstriction and increased blood pressure (7,8). Clinical studies have also introduced

high levels of homocysteine in obese individuals and related diseases as a predictive indicator of heart diseases such as atherosclerosis, coronary artery disease and endothelial dysfunction (9,10). This molecule accelerates the process of atherosclerosis and peripheral vascular disorders by causing damage to the inner lining of blood vessels, interfering with blood coagulation processes and stimulating oxidative processes of lipoproteins (11).

Based on this evidence, the development of therapeutic approaches that help improve vascular function in patients with metabolic syndrome and other obesity-related diseases is of great importance. Physical exercise and sports activities are considered as a non-pharmacological treatment that can be used alone or in combination with pharmacological interventions and changes in nutritional patterns. However, contradictory effects of different training methods, such as aerobic and resistance training, on vascular endothelial markers have been reported (12,13).

Among the new training methods, CX WORKS has been proposed as an emerging training method by Les Mills in the last decade. This type of training, which focuses on strengthening the upper body muscles and especially the core muscles, is currently receiving attention (14). Some studies have investigated the effect of this type of training on reducing body fat, improving the function of liver enzymes such as AST, ALT and ALP, as well as improving insulin resistance in overweight women (15). However, the direct effects of CX on endothelial health in people with metabolic syndrome have not yet been studied.

Recent research has shown that performing exercise training along with taking nutritional supplements, especially antioxidants, can be effective on markers effective in cardiovascular health. In this regard, inulin has been introduced as a herbal supplement. Inulin, which is a water-soluble fructan, is classified as soluble fiber and is found in foods such as onions, garlic, bananas, wheat germ, and chicory root (16). Research has revealed that using inulin supplements is effective in improving some antioxidant indices in women with diabetes and can also help reduce blood lipid levels and blood pressure. Inulin probiotic fibers have a positive effect on blood pressure control and help improve glycemic indices and increase insulin sensitivity (17). Despite its

antioxidant effects and effective role on metabolic factors affecting the glycemic profile, its role on vascular endothelium, especially in obese patient populations such as patients with metabolic syndrome, has not been reported.

Considering the effects of both CX exercises and inulin consumption on common metabolic components in obesity-related diseases on the one hand and the lack of sufficient evidence of the effects of both of them on vascular endothelial function indices in metabolic syndrome patients, the present study was conducted with the main aim of determining the effect of inulin consumption during CX exercises on serum levels of homocysteine and VEGF as indices affecting vascular endothelium in women with metabolic syndrome.

Methods

The statistical population of this semi-experimental study consists of obese adult women aged 30 to 45 years of old ($30 \leq \text{BMI} \leq 36$) with metabolic syndrome. The statistical sample consists of 48 inactive obese adult women with metabolic syndrome who are purposive sampling selected from the statistical population to participate in the study and are randomly divided into 4 groups: 1) CX group (CXWORKS) “8 weeks of CX training every other day”, 2) Inulin group “8 weeks of taking Inulin supplement, 10 g daily”, 3) combined group “8 weeks of CX with Inulin supplement, 4) control group “no intervention”.

Inclusion or Exclusion criteria: The main inclusion criteria for the study were obesity ($30 \leq \text{BMI} \leq 36$) and metabolic syndrome. In other words, those individuals who had at least 4 of the metabolic syndrome markers (waist circumference >88 cm, fasting glucose >100 mg/dL, systolic blood pressure >120 mm and diastolic blood pressure >90 mm, HDL <50 mg/dL, and TG >150 mg/dL) were included in the study.

The study participants were non-smokers, non-pregnant, and had no history of a controlled diet or regular exercise for at least the past 6 months. Individuals with a history of chronic diseases such as cancer, gastrointestinal and renal diseases, and orthopedic abnormalities were excluded from the study. Irregular participation in exercise training and failure to use inulin during the study were exclusion criteria.

Anthropometric measurements: Anthropometric indices were recorded both before and after intervention. Height was determined using a rigid tape measure, with participants barefoot, to a precision of 0.1 cm. Measurements of hip and abdominal circumferences were taken at their widest points following a normal exhalation, using a rigid tape measure with a measurement error of less than 0.1 cm. Weight was assessed using a Seca scale accurate to 0.5 kg. Body mass index (BMI) was calculated by dividing the weight in kilograms by the square of the height in meters. The percentage of body fat was ascertained using a body composition analyzer (OMRON-BF 508, Finland).

Interventions: The duration of the intervention for the study groups was 8 weeks. In the inulin group, participants consumed 5 grams of inulin twice a day, morning and evening (10g/daily, Pouyakabak Company).

In CX groups, the training program was conducted for 8 weeks (every other day) and each session lasting 45 minutes under the supervision of a tester. Each exercise session consisted of a 10-minute warm-up, 30-minute CX workout, and 5-minute cool-down. The exercises were divided into three levels: Level 1; 8 exercises, Level 2; 9 exercises, and Level 3; 6 exercises.

During the initial week, participants engaged in six Level 1 exercises, six Level 2 exercises, and two Level 3 exercises. Subsequently, each week saw the addition of one exercise per level. By the third week, participants had finished all Level 1 exercises, transitioning this level to a maintenance phase.

The completion of Level 2 exercises occurred in the fourth week, after which these exercises also moved to a maintenance phase for the remaining two weeks. By the fifth week, all Level 3 exercises were completed, and participants performed exercises from all three levels (18). Combined group (CX + Inulin) experienced eight weeks of CX exercise along with Inulin consumption. The control group maintained their usual lifestyle for eight weeks and did not engage in any physical activity program.

Laboratory and clinical measurements: Fasting blood samples (12-h overnight fast) was collected between the hours of 8 to 9 am (pre-training). Participants were asked to avoid doing any heavy physical activity for 48 hours before blood sampling.

Similar to the pre-training, fasting blood sampling was repeated 48 hours after the last training session (post training). After each blood sampling, serums were immediately separated and stored at -80° until the assays were performed. VEGF (Cusabio, China) and homocysteine (Zelbio, Germany) were measured by ELISA.

Statistical Methods & Analysis

Statistical comparisons were performed in SPSS software version 22. To ensure the normal distribution of data, the Kolmogorov-Smirnov test was used. To compare data between groups, the ANCOVA test was used with the Bonferroni post hoc test. The paired t-test was also used to determine the level of intra-group changes. It is performed at a significance level ($P < 0.05$).

Results

The levels of anthropometric indicators in the pre-test and post-test conditions of the study groups are summarized in Table 1. A paired t-test was used to determine within-group changes in each variable. Statistical comparisons revealed that each of the anthropometric indices in the CX, inulin, and combination groups decreased significantly in the post-training compared to the pre-training ($p < 0.05$). On the other hand, body weight and body mass index increased significantly compared to the pre-training in the control group ($p < 0.05$).

Pre- and post-training of serum VEGF in the study groups are shown in Table 2. Based on the findings of the ANCOVA test, significant difference was observed in VEGF changes between the study groups ($p = 0.001$). Also, the findings of the Bonferroni post hoc test showed that serum insulin increased significantly in all intervention groups compared to the control group ($p < 0.05$). In other words, CX training, inulin supplementation, and their combination resulted in a significant increase in VEGF compared to the control group.

No significant difference in VEGF levels was observed between the CX and inulin groups. On the other hand, serum VEGF in the combined group was significantly higher than the CX and inulin groups ($p < 0.05$). In other words, inulin consumption during CX training resulted in a significant increase in VEGF compared to the separate applications of each of them.

Table 1. Intra-group variations of anthropometric indices in the pre-test and post-test conditions in the studied groups.

Group	Time	Control	CX	Inulin	Combine
Weight (kg)	Pre-test	90.6 ± 3.59	88.7 ± 4.38	89.7 ± 4.82	88.3 ± 5.12
	Post-test	91.04 ± 3.26	85.88 ± 4.11	89.25 ± 4.86	82 ± 4.42
	Sig.	0.025	0.001	0.001	0.001
AC (cm)	Pre-test	107 ± 6	106 ± 7	108 ± 6	107 ± 6
	Post-test	107 ± 5	100 ± 8	107 ± 6	100 ± 5
	Sig.	0.689	0.001	0.001	0.001
BMI (kg/m ²)	Pre-test	33.03 ± 1.70	33.08 ± 1.33	32.71 ± 0.71	32.77 ± 1.04
	Post-test	33.21 ± 1.70	32.05 ± 1.48	32.54 ± 0.73	30.45 ± 0.98
	Sig.	0.022	0.001	0.001	0.001

- AC; abdominal circumference, BMI; body mass index.

- Data compared by paired t-test ($p < 0.05$).

Table 2. Pre- and post-training of serum VEGF in studied groups.

Group	Control	CX	Inulin	Combine
Pre-training	171 ± 9.8	173 ± 10	173 ± 9.5	174 ± 9.8
Post-training	173 ± 12.9	188 ± 10.5	189 ± 11.7	203 ± 8.5

Pre- and post-training of serum homocysteine in the study groups are shown in Table 3. The ANCOVA statistical test also indicated a significant difference in homocysteine changes between the studied groups ($p=0.001$). On the other hand, based on Bonferroni's findings, no significant difference in homocysteine was observed between the control group with the CX ($p=0.061$) and inulin ($p=0.088$) groups. In other words, CX training and inulin consumption alone did not lead to a change in serum homocysteine levels compared to the control group.

No significant difference was also observed in homocysteine levels between the CX and inulin groups ($p=0.999$). On the other hand, significant difference was observed in serum homocysteine in the combined group with the control, CX and inulin groups ($p=0.001$). In other words, inulin consumption during CX exercises led to a significant decrease in homocysteine not only compared to the control group but also compared to each of the CX and inulin groups.

Table 3. Pre- and post-training of serum homocysteine in studied groups.

Group	Control	CX	Inulin	Combine
Pre-training	44.7 ± 3.89	43.9 ± 2.80	43.5 ± 3.31	43 ± 3.31
Post-training	44.2 ± 4.90	41.4 ± 2.59	41.1 ± 2.48	33.9 ± 2.80

Discussion

So far, several studies have been conducted to determine the effect of different training methods alone or in combination with nutritional supplements,

especially antioxidant supplements, with therapeutic purposes on different healthy and diseased populations, but the effect of inulin consumption during exercise training on oxidative, antioxidant, and cardiovascular endothelial stress components has been less reported. In the present study, CX training combined with inulin consumption was associated with improved markers of vascular endothelial function in women with metabolic syndrome. In addition to the fact that each of CX training and inulin consumption separately led to a decrease in VEGF levels, the effectiveness of their combination led to a significant increase in VEGF compared to other groups. In this context, although Shekarchizadeh et al, reported no change in VEGF following 4 weeks of resistance training (19), Mehri-Alvar et al, (2016) indicated an increase in serum VEGF levels in young men in response to 5 weeks of resistance training (20). Although the effect of CX training combined with inulin on VEGF levels has not been reported so far, in a study by Valeh et al (2024), a significant increase in VEGF was reported following 8 weeks of Selen Plus antioxidant supplement consumption during aerobic exercise in women with metabolic syndrome (21). Jahangiri et al (2017) also reported an increase in VEGF along with a decrease in TNF- α in the heart of diabetic rats following 6 weeks of aerobic swimming training combined with arbutin consumption (22). The effectiveness of CX training combined with inulin on VEGF in the present study is reported while clinical studies have pointed to VEGF as an effective factor in vascular angiogenesis, which is dependent on an increase in NO (23). Thus, an increase in nitric oxide levels in response to internal or external stimuli by stimulating the PI3K-AKT-VEGFR-2 and VEGFR-2/ERJ1/2 signaling pathways and increasing VEGF

synthesis leads to improved vascular endothelial function and blood pressure (4,7,8).

Despite the potential effect of CX and inulin training on VEGF, serum homocysteine levels did not change in the groups that experienced CX training alone or inulin consumption. However, the implementation of both in the combined group significantly reduced homocysteine levels not only compared to the control group but also compared to either CX or inulin groups. In this regard, although Bahram et al (2013), Antunes et al (2015) and Rousseau et al (2005) have reported no change in homocysteine (24, 25, 26). However, Etemad et al, (2017) have pointed out a significant decrease in serum homocysteine in response to 8 weeks of resistance training (27).

On the other hand, a significant decrease in serum homocysteine in response to 10 weeks of aerobic training with 5 sessions per week in obese or overweight women has been reported by Soori et al (2016) (28).

Although no study has been reported regarding the interactive effect of CX and inulin exercises on homocysteine, in the study of Habibian et al (2017), although 8 weeks of aerobic exercise, vitamin C intake, and its combination together led to a decrease in homocysteine and insulin resistance in obese girls, the improvement in the combined group was much greater than the application of each of them alone (29). In the study of Rostami et al (2018), 8 weeks of resistance exercise combined with garlic supplementation significantly reduced homocysteine levels compared to the control group in male Wistar rats with metabolic syndrome. However, resistance exercise and supplementation alone did not affect homocysteine levels. The researcher stated that the possible reason for the effect of exercise on homocysteine is due to increased absorption of vitamins effective in homocysteine formation and reduced methyl group transfer for homocysteine formation (30).

In the present study, despite the lack of homocysteine changes in response to independent CX and inulin exercises, their combination, or in other words, inulin consumption during CX exercises, led to a decrease in homocysteine not only compared to the control group but also compared to each of them alone. The lack of homocysteine changes in response to CX and inulin exercises may be attributed to the small number of samples studied. On the other hand, it

is also possible that the baseline homocysteine levels before the interventions were not significantly different from normal levels, and the lack of a healthy control group is a limitation of the present study. In other words, the hypothesis is put forward to test that CX or inulin exercises affect homocysteine levels in those individuals who have higher baseline homocysteine levels than healthy individuals. In this regard, research has shown that exercise in individuals with high homocysteine levels has a significant effect on reducing it. For example, Okara and colleagues in 2006 observed that aerobic exercise significantly reduced homocysteine levels in individuals with homocysteine levels greater than 15 $\mu\text{mol/L}$ (31). Given that homocysteine is a known risk factor for heart disease, theories such as the Macaulay hypothesis suggest that high plasma homocysteine levels are associated with cardiovascular disease through increased LDL cholesterol oxidation and decreased nitric oxide (32). Other studies have also shown that combining physical activity with antioxidant supplements can be effective in reducing LDL and homocysteine concentrations, thereby preventing and delaying the progression of atherosclerosis (33, 34). Despite the available evidence, inulin consumption during CX training in the present study resulted in a significant reduction in homocysteine compared to the control group and the groups that only underwent CX training or consumed inulin, which points to the endothelial role of inulin during CX training, and based on laboratory evidence, this improvement may be attributed to the conversion of homocysteine to methionine. As the acceleration of coenzyme cobalamin and folic acid activity in response to these interventions provides the basis for the conversion of homocysteine to methionine (35).

Conclusion

Based on the available findings, eight weeks of CX training, three sessions per week, along with inulin consumption, relying on increasing VEGF and reducing homocysteine, leads to improved vascular endothelial function in women with metabolic syndrome. Given that similar studies on the effect of inulin supplementation and CX training on vascular endothelial function, especially in patients with metabolic syndrome, were not found, the present findings cannot be interpreted with certainty and the need for further molecular cellular studies to

understand the mechanisms responsible for these changes is emphasized.

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Conflict of Interest

The authors declare no conflict of interest.

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Ethics

This study was approved by Azad Marvdasht University (ethical code: IR.IAU.M.REC.1403.506).

Authors' contributions

All authors were involved in conception and design of the study as well as in data generation, data analysis, and drafting the manuscript. All authors approved the final draft.

Using AI Declaration

Artificial intelligence was not used in the writing of this article.

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