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Original Article

Effects of vitamin C supplementation with and without endurance physical activity on components of metabolic syndrome: A randomized, double-blind, placebo-controlled clinical trial

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SUMMARY

Background & aims: Metabolic syndrome is a cluster of the most dangerous heart attack risk factors. The present study aimed to examine the effects of vitamin C supplementation with and without endurance physical activity on components of metabolic syndrome in a group of Iraqi adults.
Methods: In a parallel-randomized placebo controlled trial, 120 metabolic syndrome patients were randomly assigned into four groups. Fasting blood samples were taken at study baseline and after 12 weeks of intervention. All statistical analysis was performed using SPSS version 20.
Results: The mean vitamin C levels was increased significantly in both vitamin C and vitamin C plus physical activity groups (P value = 0.001). Vitamin C plus physical activity led to a significant reduction in systolic blood pressure compared to the placebo group (P value = 0.04). In addition, a significant changes in serum levels of total cholesterol were seen following vitamin C plus physical activity than that in the placebo group (P value = 0.04). Furthermore, vitamin C supplementation significantly affected BMI compared with the placebo group (P value = 0.02). No significant

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differences were found between the study groups in terms of triglyceride, LDL-C, HDL-C, fasting blood sugar, weight, waist circumference and diastolic blood pressure.
Conclusion: Daily supplementation of vitamin C (500 mg/day), for 12 weeks resulted in a significant reduction in BMI. However, the combination of physical activities and vitamin C supplements may improve systolic blood pressure and serum levels of total cholesterol in metabolic syndrome patients and this combination should be recommended.
Trial registration: WHO-ICTRP, IRCT20161110030823N2. Registered 01 February 2018, http://apps.who.int/trialsearch/Trial2.aspx?TrialID=IRCT20161110030823N2.

1. Introduction

Metabolic syndrome (MetS) is a collection of cardiovascular risk factors, which is related to increased risk of diabetes, stroke and mortality [1,2]. MetS has shown an increasing prevalence globally because of the constant increase of health-related factors such as obesity and physical inactivity [3,4]. Therefore, finding modifiable risk factors of MetS is of great importance. MetS is a multifactorial disorder; several factors including genetic, metabolic and environmental factors can contribute to the etiology of MetS [5]. Among the modifiable risk factors, dietary intakes have been highlighted as an effective approach for prevention and management of MetS [6]. Earlier studies have shown that antioxidant status was associated with lower prevalence of the MetS [7]. It has also been reported that oxidative stress is associated with most of the MetS features including diabetes mellitus, obesity, hypertension, dyslipidemia and inflammation [8]. Therefore, antioxidants supplementation especially vitamin C might be useful in the prevention of MetS. In addition, physical activity has also been shown to reduce obesity and other associated risk factors of MetS [9]. Therefore, physical activity plays a crucial role in the management of MetS. A cross-sectional study among general Korean population showed that physical activity and dietary vitamin C intake may be useful in MetS prevention [10]. To the best of our knowledge, there is no study that examined the effects of vitamin C supplementation on components of MetS. In addition, there is no study on the effects of vitamin C supplementation in combination with endurance physical activity in patients with MetS. This study, therefore, aimed to examine the effects of vitamin C supplementation with and without endurance physical activity on MetS features in a group of Iraqi adults.

2. Materials and methods

2.1. Study design and participants

This randomized, double blind, placebo-controlled clinical trial was performed between March 2016 and May 2016 in the Halabja hospital, Kurdistan region of Iraq. Sample size for this study was calculated based on suggested formula for parallel clinical trials [11]. We considered type 1 error of 5%, type 2 error of 20% (power = 80%) and fasting plasma glucose as a key variable and reached the sample size of 21 subjects for each group. To consider probable dropout throughout the study, we enrolled 30 patients in each group. A total of 120 patients with MetS, aged 30–60 years, were included in this study. Individuals who were using any kind of minerals, vitamins and medications, diabetic patients, smokers, alcohol users, pregnant or lactating women, post-menopausal women, patients with a history of bariatric surgery and those that were on a weight loss diet were excluded. We also did not include those with a high triglyceride (TG) levels (more than 400 mg/dl) and those with high systolic blood pressure (SBP) or diastolic blood pressure (DBP) (>140/90 mmHg). In the present study, MetS was defined according to the International Diabetes Federation (IDF) criteria [12].

2.2. Data collection

At study baseline, a standardized questionnaire was used to collect subjects' information on age, sex, marital status, smoking status, and family history of obesity, diabetes and hypertension. Then, participants were randomly divided into four groups: Group A received vitamin C supplements (500 mg/day) without endurance physical activity (n = 30); group B received vitamin C supplements (500 mg/day) with 30 min/day endurance physical activity (n = 30); group C received one placebo of vitamin C/day without endurance physical activity (n = 30); and group D received one placebo of vitamin C/day with 30 min/day endurance physical activity (n = 30) (Fig. 1). All investigators and participants were blinded to the random assignments. The vitamin C supplements and placebos manufactured by Osweh Company (Tehran, Iran). Placebos were on the same shape, odor and size of the vitamin C supplements. Participants were asked to use vitamin C supplements and placebos for 12 weeks. Compliance of study participants with the vitamin C supplements was assessed through quantification of serum vitamin C. To ensure maintenance of their habitual diets throughout the study, all participants provided 3-day dietary recalls (One weekend day and 2 weekdays). Then, we converted the reported portion sizes in the dietary records to grams using household measures. All dietary data were based on the average of three dietary recalls. The grams of food intake data were linked with Nutritionist IV software to derive nutrient intake data. In terms of ethics as well as to avoid any confounding effects from dietary changes throughout the study, dietary recommendation was given to all participants after final intervention. Physical activity recommendations were given to all participants at the end of the study.

2.3. Assessment of physical activity

Endurance physical activity with sun exposure without sun protective was eligible for participants. Two times a week around 2 h each time for climbing and two times of running a week around 1 h in the afternoon between 3 PM and 5 PM. Overall, approximately 6 h per week [13].

2.4. Assessment of anthropometric measurements

Weight was measured to the nearest 100 g using a calibrated digital scale while the subject wearing minimal cloths without wearing shoes. Height was measured using a wall mounted stadiometer Seca to the nearest 0.1 cm in standing position without wearing shoes while shoulders were relaxed. Body mass index (BMI) was calculated using the standard equation as weight in kilogram divided by height in meters squared (kg/m^2). Waist circumference (WC) was measured at the mid-way between the lower border of the ribs and the iliac crest, while the participants in standing position. Using an unstretched tape measure, without any pressure to body surface, measurement was recorded to the nearest 0.1 cm. To avoid subjective error, all measurements were taken by the same technician. Blood pressure was measured at morning time in the seated position using a standard mercury sphygmomanometer after at least 15 min of rest.

2.5. Biochemical assessments

Fasting blood samples were collected at baseline and 12 weeks of intervention, after 12 h overnight fasting to quantify serum levels of fasting blood sugar (FBS), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), TG, and vitamin C. The blood samples were taken using the protocol outlined in [14]. Serum Vitamin C was measured by the Model-vidas analyser (Biomerux, Italy) provided by the clinical laboratory, Slemani Hospital, Iraq. FBS was measured on the day of blood collection by enzymatic colorimetric method using glucose oxidase.

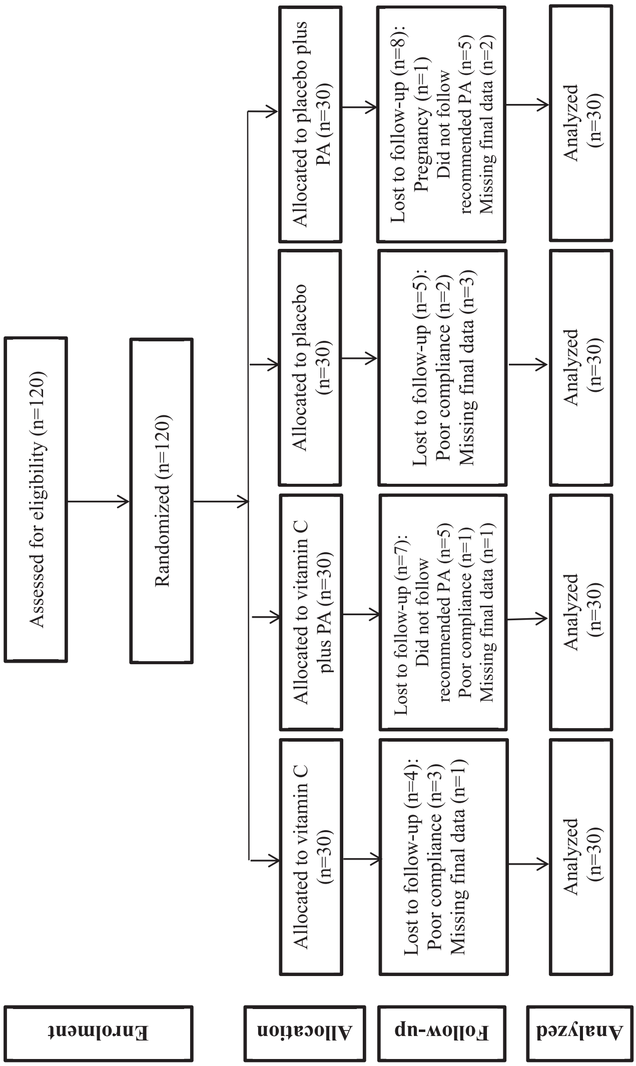

Fig. 1. Participant's flow diagram.

Serum TC and TG concentration were assayed using enzymatic colorimetric tests with cholesterol esterase and cholesterol oxidase and glycerol phosphate oxidase, respectively, by using standard kits following manufacturers' protocols. HDL-C was measured after precipitation of the apolipoprotein B containing lipoproteins with phosphotungistic acid. LDL-C was calculated from serum TC, TG and HDL-C based on relevant formula [15].

2.6. Statistical analysis

We used Kolmogorov–Smirnov test to examine the normal distribution of variables. The analyses were done based on intention-to-treat approach. Missing values were treated based on Last-Observation-Carried-Forward method. Baseline general characteristics among different groups were examined using one-way ANOVA for continuous variable and a chi-square test for categorical variables. To determine the effects of vitamin C supplementation and endurance physical activity on glucose metabolism, lipid profiles, and blood pressure, we used one-way ANOVA. We used Tukey's post-hoc comparisons to identify pairwise differences when we reached a significant finding in ANOVA. $P < 0.05$ was considered as statistically significant. Statistical analysis was performed using SPSS version 20.

3. Results

In this clinical trial, 120 MetS patients were enrolled and categorized into four intervention groups as follow: vitamin C ($n = 30$), "vitamin C plus 30 min/day physical activity" ($n = 30$), placebo ($n = 30$) and "placebo plus 30 min/day physical activity" ($n = 30$). The study procedure is shown in Fig. 1. Twenty-four participants were excluded from the study because of the following reasons: Pregnancy ($n = 1$), did not follow recommended physical activity ($n = 10$), poor compliance to vitamin C supplements ($n = 6$) and did not complete the study ($n = 7$). Finally, 96 subjects remained in the study. Using an intention-to-treat approach, the data for all 120 participants were included in the final analysis.

Baseline characteristics of study participants are presented in Table 1. The distribution of participants in terms of age, sex, marital status, smoking status, family history of obesity, diabetes mellitus and blood pressure was not significantly different among the four intervention groups (P value > 0.05 for all). Comparison of baseline serum vitamin C levels showed no significant difference among the groups. There were also no significant differences among the four groups in terms of weight, BMI, WC, SBP and DBP (P value > 0.05 for all). The baseline metabolic profile of study participants revealed no significant differences in FBS and TC levels among the four intervention groups. However, participants who received vitamin C supplements had higher serum levels of TG compared with those who received "vitamin C plus physical activity", placebo or "placebo plus physical activity" (272.7 ± 104.3 vs. 176.3 ± 81.3 and 152.9 ± 44.6 and 158.4 ± 65 mg/dl, $P < 0.001$). Participants in the placebo group had lower levels of HDL-C compared with those in the "placebo plus physical activity" group (30.8 ± 9.06 mg/dl vs. 40.9 ± 22.4 mg/dl, $P = 0.03$). In addition, participants in the vitamin C group had lower levels of LDL-C compared with those in the placebo and "placebo plus physical activity" groups (123.3 ± 42.2 mg/dl vs. 153.9 ± 38.8 mg/dl and 160.5 ± 38.8 mg/dl, $P = 0.001$).

On the other hand, end of trial means of anthropometric measures as well as blood pressure among study groups are provided in Table 2. The findings of the present study revealed that, "Vitamin C plus physical activity" could significantly decreased SBP compared with the vitamin C group (122.3 ± 9.8 vs. 130.3 ± 8.6 mmHg, $P = 0.02$). There were no significant effects of vitamin C on means of weight, BMI, WC and DBP at the end of the study. Furthermore, changes in means of anthropometric measures and blood pressure across four study groups are shown in Table 3. "Vitamin C plus physical activity" led to a significant reduction in SBP compared to the placebo group (-0.044 ± 0.07 vs. 0.01 ± 0.06, $P = 0.04$). Vitamin C supplementation significantly affected BMI compared with the placebo group (-0.016 ± 0.02 vs. 0.0002 ± 0.01, $P = 0.02$). Although we did not find any significant differences in weight change among the four groups, participants in the vitamin C group had slightly higher reduction in weight compared with the placebo group ($P = 0.06$). Moreover, end of trial means of biochemical indicators across four study groups are provided in Table 4. After intervention, subjects in vitamin C group had

Table 1
Baseline characteristics of study participants.[a]

Groups					
Variables	Vitamin C[b] (n = 30)	Vitamin C + PA[c] (n = 30)	Placebo[d] (n = 30)	Placebo + PA[e] (n = 30)	P-value[f]
Age (years)	41.2 ± 5.9	41.2 ± 6.1	42.7 ± 5.3	42.2 ± 6.2	0.68
Female (%)	19.0 (63.3)	20.0 (66.7)	16.0 (53.3)	17.0 (56.7)	0.73
Married (%)	26.0 (86.7)	25.0 (83.3)	26.0 (86.7)	25.0 (83.3)	0.99
Vitamin C (mg/dl)	0.87 ± 0.36	0.81 ± 0.33	0.92 ± 0.31	0.91 ± 0.34	0.56
Weight (kg)	83.1 ± 13.2	78.8 ± 14.7	80.6 ± 13.6	75.7 ± 12.2	0.19
BMI (kg/m^2)	32.9 ± 6.3	31.9 ± 5.9	32.5 ± 4.1	30.5 ± 4.9	0.35
WC (cm)	109.3 ± 10.1	106.9 ± 8.5	107.9 ± 9.9	110.5 ± 9.9	0.49
FBS (mg/dl)	107.7 ± 19.2	106.7 ± 15.2	109.9 ± 16.2	105.6 ± 17.4	0.78
TC (mg/dl)	180.4 ± 34	179.7 ± 38.6	190.7 ± 38.4	200.4 ± 36.7	0.06
TG (mg/dl)	272.7 ± 104.3†	176.3 ± 81.3	152.9 ± 44.6	158.4 ± 65	0.001
HDL-C (mg/dl)	32.04 ± 13.2	36.7 ± 10.1	30.8 ± 9.06‡	40.9 ± 22.4	0.03
LDL-C (mg/dl)	123.3 ± 42.2**	137.1 ± 38.4	153.9 ± 38.8	160.5 ± 38.8	0.001
SBP (mmHg)	131.2 ± 11.5	128.5 ± 11.4	124.3 ± 15	129 ± 10.3	0.18
DBP (mmHg)	81.0 ± 8.4	80.2 ± 7.6	78.7 ± 7.2	82.7 ± 5.5	0.19

*P < 0.05 compared with the placebo group, using Tukey's test.
†P < 0.05 compared with the other groups, using Tukey's test.
‡P < 0.05 compared with the placebo plus physical activity group, using Tukey's test.
**P < 0.05 compared with the placebo and placebo plus physical activity groups, using Tukey's test.
PA: physical activity; BMI: body mass index; WC: waist circumferences; FBS: fasting blood sugar; TC: total cholesterol; TG: triglycerides; HDL-C: high density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol; SBP: systolic blood pressure; DBP: diastolic blood pressure.
[a] Data are mean ± standard deviation (SD).
[b] Receiving 500 mg vitamin C per day.
[c] Receiving 500 mg vitamin C per day plus 30 min endurance physical activity.
[d] Receiving one placebo per day.
[e] Receiving one placebo per day plus 30 min endurance physical activity.
[f] Obtained from ANOVA or chi-square test, where appropriate.

Table 2
End of trial means of anthropometric measures and blood pressure across study groups.[a]

Groups					
Variables	Vitamin C[b]	Vitamin C + PA[c]	Placebo[d]	Placebo + PA[e]	P-value[f]
Weight (kg)	81.8 ± 13.4	77.4 ± 14.5	80.6 ± 13.5	74.8 ± 12.2	0.18
BMI (kg/m^2)	32.4 ± 6.3	31.4 ± 5.7	32.5 ± 3.9	30.2 ± 5	0.30
WC (cm)	108.2 ± 9.7	103.7 ± 8.1	106.8 ± 10	107.9 ± 10	0.23
SBP (mmHg)	130.3 ± 8.6	122.3 ± 9.8*	125.2 ± 13.2	124.8 ± 9.1	0.02
DBP (mmHg)	81.5 ± 5.7	80.3 ± 5.8	80 ± 7.3	81 ± 5.1	0.77

*P < 0.05 compared with the vitamin C group.
PA: physical activity; BMI: body mass index; WC: waist circumferences; SBP: systolic blood pressure; DBP: diastolic blood pressure.
[a] Data are means ± standard deviation (SD).
[b] Receiving 500 mg vitamin C per day.
[c] Receiving 500 mg vitamin C per day plus 30 min endurance physical activity.
[d] Receiving one placebo per day.
[e] Receiving one placebo per day plus 30 min endurance physical activity.
[f] Obtained from ANOVA.

higher serum levels of TG compared with the "vitamin C plus physical activity", placebo and "placebo plus physical activity" groups (253.3 ± 90.8 vs. 157.2 ± 56 and 162.2 ± 37.5 and 153.9 ± 55.3, P < 0.001). "Vitamin C plus physical activity" resulted in higher serum levels of HDL-C compared with the vitamin C and placebo groups (47.7 ± 19.8 vs. 32.1 ± 10.3 and 32.3 ± 7.8, P < 0.001). After vitamin C supplementation, participants in the vitamin C group had lower serum levels of LDL-C compared with the placebo and "placebo plus physical activity" groups (114.8 ± 48.6 vs. 160.8 ± 37.6 and 154.9 ± 34.5,

Table 3
Changes in anthropometric measures and blood pressure across study groups.[a]

Groups					
Variables	Vitamin C[b]	Vitamin C + PA[c]	Placebo[d]	Placebo + PA[e]	P-value[f]
Weight (kg)	−0.016 ± 0.02	−0.017 ± 0.04	0.0002 ± 0.01	−0.011 ± 0.01	0.06
BMI (kg/m^2)	−0.016 ± 0.02*	−0.014 ± 0.03	0.0002 ± 0.01	−0.012 ± 0.01	0.02
WC (cm)	−0.009 ± 0.02	−0.029 ± 0.05	−0.01 ± 0.03	−0.023 ± 0.02	0.05
SBP (mmHg)	−0.003 ± 0.06	−0.044 ± 0.07†	0.01 ± 0.06	−0.03 ± 0.05	0.04
DBP (mmHg)	0.012 ± 0.09	0.008 ± 0.09	0.022 ± 0.1	−0.018 ± 0.06	0.34

*P < 0.05 compared with the placebo group.
†P < 0.05 compared with the placebo group.
PA: physical activity; BMI: body mass index; WC: waist circumferences; SBP: systolic blood pressure; DBP: diastolic blood pressure.
[a] Data are means ± standard deviation (SD).
[b] Receiving 500 mg vitamin C per day.
[c] Receiving 500 mg vitamin C per day plus 30 min endurance physical activity.
[d] Receiving one placebo per day.
[e] Receiving one placebo per day plus 30 min endurance physical activity.
[f] Obtained from ANOVA.

Table 4
End of trial means of biochemical indicators across study groups.[a]

Groups					
Variables	Vitamin C[b]	Vitamin C + PA[c]	Placebo[d]	Placebo + PA[e]	P-value[f]
FBS (mg/dl)	106.3 ± 13.5	104.2 ± 12.6	107.8 ± 17.9	100.2 ± 12.4	0.19
TC (mg/dl)	175.7 ± 42.1	177.3 ± 38.7	199.8 ± 37.9	193.6 ± 33.2	0.05
TG (mg/dl)	253.3 ± 90.8*	157.2 ± 56	162.2 ± 37.5	153.9 ± 55.3	0.001
HDL-C (mg/dl)	32.1 ± 10.3	47.7 ± 19.8†	32.3 ± 7.8	39.5 ± 19.4	0.001
LDL-C (mg/dl)	114.8 ± 48.6‡	136.3 ± 35.7	160.8 ± 37.6	154.9 ± 34.5	0.001
Vitamin C (mg/dl)	1.31 ± 0.32+	1.48 ± 0.48+	0.86 ± 0.34	1.02 ± 0.31	0.001[g]

+P < 0.05 are significant.
*P < 0.0001 compared with the other groups.
†P < 0.0001 compared with vitamin C and placebo groups.
‡P < 0.02 compared with the placebo and placebo plus physical activity groups.
PA: physical activity; FBS: fasting blood sugar; TC: total cholesterol; TG: triglycerides; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol.
[a] Data are means ± standard deviation (SD).
[b] Receiving 500 mg vitamin C per day.
[c] Receiving 500 mg vitamin C per day plus 30 min endurance physical activity.
[d] Receiving one placebo per day.
[e] Receiving one placebo per day plus 30 min endurance physical activity.
[f] Obtained from ANOVA.
[g] Obtained from paired sample T test.

P < 0.001). There was a marginally significant favorable effect of “vitamin C plus physical activity” on serum levels of TC compared with the placebo group (177.3 ± 38.7 vs. 199.8 ± 37.9, P = 0.05). Additionally, we observed a significant increase in mean serum vitamin C concentrations in participants who received vitamin C (0.87 ± 0.36 mg/dl at study baseline vs. 1.31 ± 0.32 mg/dl at the end of the study, P < 0.001) or “vitamin C plus physical activity” (0.81 ± 0.33 mg/dl at study baseline vs. 1.48 ± 0.48 mg/dl at the end of the study, P < 0.001). No significant changes in serum levels of vitamin C were seen in participants in the placebo, and “placebo plus physical activity” groups after the intervention. Finally, changes in biochemical indicators across four study groups are presented in Table 5. Significant changes in serum levels of TC were seen following “vitamin C plus physical activity” than that in the placebo group (−0.004 ± 0.11 vs. 0.06 ± 0.21, P = 0.04). There was a marginally significant difference in changes of TG (P = 0.05), LDL-C (P = 0.09) and HDL-C (P = 0.05) among the four groups. No significant changes in serum levels of FBS were seen among the four groups.

Table 5
Changes in biochemical indicators across study groups.[a]

Groups					
Variables	Vitamin C[b]	Vitamin C + PA[c]	Placebo[d]	Placebo + PA[e]	P-value[f]
FBS (mg/dl)	−0.002 ± 0.09	−0.015 ± 0.11	−0.011 ± 0.14	−0.04 ± 0.11	0.63
TC (mg/dl)	−0.046 ± 0.15	−0.004 ± 0.11*	0.06 ± 0.21	−0.03 ± 0.07	0.04
TG (mg/dl)	−0.055 ± 0.09	−0.002 ± 0.33	0.09 ± 0.23	0.002 ± 0.14	0.05
HDL-C (mg/dl)	0.16 ± 0.78	0.34 ± 0.65	0.07 ± 0.21	0.014 ± 0.19	0.09
LDL-C (mg/dl)	−0.12 ± 0.25	0.02 ± 0.23	0.07 ± 0.25	−0.023 ± 0.1	0.05

*P < 0.05 compared with placebo group.
PA: physical activity; FBS: fasting blood sugar; TC: total cholesterol; TG: triglycerides; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol.
[a] Data are means ± standard deviation (SD).
[b] Receiving 500 mg vitamin C per day.
[c] Receiving 500 mg vitamin C per day plus 30 min endurance physical activity.
[d] Receiving one placebo per day.
[e] Receiving one placebo per day plus 30 min endurance physical activity.
[f] Obtained from ANOVA.

4. Discussion

This randomized, double-blind, placebo-controlled clinical trial on MetS patients showed that daily supplementation of vitamin C (500 mg/day), for 12 weeks resulted in a significant reduction in BMI. However, the combination of physical activities and vitamin C supplements may improve SBP and serum levels of TC, and this combination should be recommended. To the best of our knowledge, this is the first study that examined the effects of vitamin C supplementation plus endurance physical activity on components of MetS. We observed a significant reduction in serum levels of TC after 12 weeks of vitamin C supplementation plus 30 min' physical activity compared with the placebo group; however, there was no significant change in other metabolic variables including serum levels of FBS, TG, LDL-C and HDL-C after intervention. Over the past couple of decades, a number of nutritional compounds have shown some promise in reducing serum TC concentrations. One such compound is vitamin C, and a recent meta-analysis found that supplementation with at least 500 mg/day can reduce serum TC in both borderline-high and high hypercholeterolemic groups by 7.6 and 17.2 mg/dL, respectively [16]. Observational studies showed that MetS patients have lower levels of vitamin C in comparison to healthy subjects [17]. Thus, it is plausible to assume that oxidative stress may play a major role in the development of MetS [8]. Furthermore, considering the antioxidant effects of vitamin C, it seems that vitamin C supplementation may be useful in the management of MetS.

In our study, we found that, vitamin C supplementation could significantly affect BMI after intervention. No significant changes were seen in terms of other anthropometric measures including weight and WC. Johnston et al. in a cross sectional study show that, plasma vitamin C is inversely related to BMI in nonsmoking adults [18].

The inverse relationship between plasma vitamin C and BMI has been documented in several reports. Schectman et al. [19] noted a significant inverse relationship between BMI and plasma vitamin C concentrations among 11,592 participants of the NHANES II. The results of our study support these findings. Since, there is no previous study on the effects of vitamin C supplementation on anthropometric measures in MetS patients, further studies are required to reach a definite conclusion in this area. We found that vitamin C supplementation plus physical activity led to a significant reduction in SBP; no significant change was found in DBP. A clinical trial revealed that 500 mg vitamin C supplementation for 3 months resulted in decreased SBP in older persons [20]. However, 1.5 g daily intake of vitamin C for three weeks did not significantly affect blood pressure in patients with Type 2 diabetes [21]. There is growing body of evidence that oxidative stress contributes to the etiology of hypertension. Therefore, dietary antioxidants may beneficially influence blood pressure by reducing oxidative stress [22]. In the current study, we showed that physical activity has beneficial effects on components of MetS. Earlier studies demonstrated that physical activity can be used as a preventive approach for metabolic disorders [23]. The beneficial effects of physical activity on components of MetS including decreased weight and visceral fat accumulation [24–26], increased HDL-C and decreased TG levels [27,28], and decreased blood pressure [29] has been shown in previous studies. Given these findings, advising people to increase their physical activity levels can be used as a therapeutic approach for the management of MetS. Several possible mechanisms have been proposed for the effects of vitamin C consumption plus physical activity on serum levels of TC and SBP. Vitamin C can enhance or induce cytochrome P450 activity, and increase conversion of cholesterol to bile acids and HDL-C production [30]. As well as, vitamin C acts as an antioxidant protecting against oxidative damage leading to increase in the bioavailability of nitric oxide [31].

The strength of the present study is that this is the first study, which investigated the effects of vitamin C supplementation with and without endurance physical activity on components of MetS. However, this study has some limitations that must be considered. We used single measurement of metabolic variables instead of repeated measures. Since metabolic variables have day-to-day variation, taking multiple measurements would address these variations much more sufficiently. Current study has adequate power to detect the significant effects of vitamin C; however, further studies with longer duration of interventions might be needed to confirm the long-term effects of vitamin C supplementation in patients with MetS.

In conclusion, daily supplementation of vitamin C (500 mg/day), for 12 weeks resulted in a significant reduction in BMI. However, the combination of physical activities and vitamin C supplements may improve SBP, and serum levels of TC in MetS patients and this combination should be recommended.

Ethics approval and consent to participate

The Ethics Committee of Tehran University of Medical Sciences approved the study protocol, and the trial was registered at the World Health Organization, International Clinical Trails Registry Platform (Code: IRCT20161110030823N2). In addition, written informed consent was also obtained from each participant.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Authors' contributions

HAF, MJH, BAM and AHB participated in the design of the study, data collection, performed the statistical analysis and drafted the manuscript. MJH, AE and AHB supervising the study and participated in draft review. All authors have read and approved the final version of the manuscript and agree with the order of presentation of the authors.

Conflict of interest

The authors whose names are listed immediately below certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (Such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (Such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.yclnex.2019.05.003.

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