Original Article

Effect of Flaxseed Powder on Cardiovascular Risk Factor in Dyslipidemic and Hypertensive Patients

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Abstract

Background: Hyperlipidemia and hypertension are the most important causes of ischemic heart disease. There is evidence that flaxseed powder can improve lipid profile and blood pressure. In this study, we want to investigate the effects of flaxseed powder consumption on patients with hyperlipidemia and hypertension. **Methods:** This randomized double-blind placebo-controlled clinical trial was performed on 80 hyperlipidemic and hypertensive patients (men and women between 20 and 60 years old). In this study, participants were recruited from Imam Khomeini hospital clinics of Shiraz University of Medical Sciences in 2017 randomly allocated to flaxseed powder group and placebo group. The intervention group received 36 g of flaxseed sachet (n = 40), and control group received 12 g placebo sachet (n = 40) for 8 weeks. Serum lipid profiles, blood pressure, fasting blood sugar, and anthropometric indices were measured. Data were analyzed by using SPSS. **Results:** We found significant reduction ($P < 0.001$) in anthropometric indices (waist circumference and waist-to-hip ratio) and lipid profiles (triglycerides [$P = 0.015$], total cholesterol [$P = 0.018$], and low-density lipoprotein [$P < 0.001$]) within flaxseed group in comparison with placebo group. **Conclusions:** Based on beneficial effects of flaxseed on cardiovascular risk factors, it seems that flaxseed consumption can be considered as a useful therapeutic approach for reducing lipid profile and anthropometric indices.

Keywords: *Cardiovascular diseases, flax, hyperlipidemias, hypertension*

Introduction

Coronary heart disease is a leading cause of death throughout the world.[1-3] Hyperlipidemia and hypertension are the main risk factors of coronary heart disease.[4,5]

Three factors including – nutritional modification, incorporating exercise into our daily lives, and eliminating smoking are suggested as three major lifestyle modifications that can significantly reduce the risk of CAD.[6] Several studies have shown the cardiovascular protective effects of nutritional intervention of various foods and dietary factors such as omega3, fish, soy protein, and plant sterol.[7]

Due to its high content of lignans, fiber, and α-linolenic acid (ALA), flaxseed was recently recognized as a functional food that may reduce cardiovascular disease (CVD) risk factors such as hypertension and hyperlipidemia.[4,8,9] By regulation of inflammatory pathways, dietary phytoestrogens (isoflavones and lignans) may improve the risk of chronic diseases such as diabetes.[10] Some studies showed that flaxseed peptides may induce an antihypertensive effect through their rich arginine content.[11]

One study showed that 30% CVD incidence will be decreased by 10% reduction in serum concentrations of total cholesterol (TC).[12] Lucas *et al*. showed that flaxseed supplementation for 3 months could improve lipid profile levels.[13]

Due to inconsistency in available results, this study was designed to assess the potential effects of a new form of flaxseed powder (sachet) among individuals with high risk of cardiovascular disease. Therefore, the objective of the present randomized placebo-controlled clinical trial was to evaluate the effects of flaxseed sachet on serum levels of lipid profiles, blood pressure, anthropometric indices, and fasting blood sugar in hyperlipidemic-hypertensive patients.

Methods

Participants

This clinical trial was undertaken in 80 hyperlipidemic and hypertensive

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patients (men and women between 20 and 60 years old), in Isfahan University of Medical Science Clinics, Iran, during May 2016 to December 2016. Individuals were recruited through following inclusion criteria: no pregnancy and breast feeding, having established dyslipidemia (having an abnormality in one or more of lipid profile fraction, i.e., fasting TC >200 mg/dl, low-density lipoprotein cholesterol [LDL-C] levels >130 mg/dl, high-density lipoprotein cholesterol [HDL-C] <40–50 mg/dl, triglyceride [TG] >150 mg/dl) and being a well-known case of high blood pressure, i.e., consuming hypertensive drugs or have either systolic blood pressure equal or more than 140 mmHg or diastolic blood pressure equal or more than 90 mmHg. All of the participants have hyperlipidemia and hypertension simultaneously. Most of the individuals consumed prescribed related drugs for their hypertension and lipid profile disorders during the study period.

Participants were excluded if they had a history of renal diseases, cancer, infectious diseases, inflammatory diseases, endometriosis, fibroids, polycystic ovary syndrome, and impaired fasting blood sugar (more than 110 mg/dl). In addition, individuals who were in a specific diet during last 2 months were excluded as well. From 200 potentially eligible hyperlipidemic and hypertensive patients (approved by a cardiologist), 98 volunteers were enrolled based on inclusion criteria for this study. All of participants provided informed written consent. This study was approved by the ethics committee of Isfahan University of Medical Sciences (NO. 3941051) and was registered in Iranian Clinical Trials center (www.irct.ir; Code: IRCT2016081611763N28). According to a previous study, consuming a maximum dose of 50 g flaxseed is safe and could provide beneficial effects for adults. In this study, we used half of aforementioned dose for increasing the compliance of participants and easiness of consumption.[2]

Study design

This study is a randomized double-blind placebo-controlled clinical trial. We calculate sample size with power 80% and $\alpha = 5\%$ with the following formula. Forty participants were required for each group, which after considering 20% sample loss, fifty patients in each group were enrolled.

From the patients that were referred to Isfahan University of Medical Sciences clinics, 120 individuals were chosen for screening of the inclusion criteria. Ninety-eight eligible volunteers enrolled into the study. Participants were randomly (in a double-blind parallel manner from randomized number in an eighty-person list) allocated to two groups: (1) flaxseed powder group and (2) placebo group. Flaxseed and placebo sachet were coded randomly by someone other than investigator. Individuals, investigator, and statistician were blinded. The intervention group received 36 g of flaxseed sachet ($n = 49$) and control group received 12 g placebo sachet ($n = 49$). Flaxseed and placebo were produced in form of sachet with same shape, odor, color, and flavor by kamvar company, Isfahan, Iran. At first, healthy dietary recommendations for lowering blood lipid profiles and blood pressure were explained orally to both groups. Each flaxseed sachet contained 24 g flaxseed powder, 11 g isomalt, and 1 g stevioside and each placebo sachet contained 11 g isomalt and 1 g stevioside. Participants were asked to consume half of each sachet before lunch (with a cup of water) and half of it before dinner (with a cup of water). Participants were asked to use flaxseed and placebo for 8 weeks. To increase the compliance of participants, we made phone calls and sent text messages throughout the study period.

Dietary intakes and physical activity measurement

The average dietary intakes and physical activity rate of each individual were checked by records. All participants provided three physical activity records and three dietary records (3 days, 1 weekend day, and 2 weekdays) during the intervention at 0, 4, and 8 weeks. The presented portion sizes in each dietary record were converted to grams according to guide for household measures; Nutritionist IV software was used to evaluate the nutrients and energy intake of participants.

Physical activity was assessed using a physical activity questionnaire and was reported as metabolic equivalents per hour per day (MET-h/day). Three-day physical activity records were collected using 24-h physical activity record questionnaire (1 weekend day and 2 weekdays).

Anthropometric assessment

Weight was measured to the nearest 0.1 kg with minimal clothing and without shoes by digital scale (Seca, Germany). Height was measured to the nearest 0.5 cm in a standing position without wearing shoes by a wall-mounted stadiometer. Body mass index (BMI) was calculated as the weight in kilogram divided by the height in meters squared. Waist circumference (WC) was measured to the nearest 0.1 cm at the narrowest between the last rib and the top of the iliac crest over light clothing, by using a nonstretchable tape, without any pressure to the body surface. Blood pressure was measured on the left arm, after 15 min of rest, when participants were in the comfortable seat position, by the use of a mercury sphygmomanometer.

Biochemical assessment

After 12 h of fasting, blood samples were collected from patients at the baseline and the end of study (week 8 of intervention). Blood specimens were immediately centrifuged (Hettich D78532, Tuttlingen, Germany) at 3500 rpm for 10 min to separate serum and stored at −70°C before analysis. Commercial available kits were used to determine fasting blood sugar (FBS), TG, HDL and LDL (Pars Azmoon, Tehran, Iran). Both intra- and inter-assay coefficients of variation were <5% for all of the used measurement kits.

Statistical analysis

Normality of data distribution was evaluated by Kolmogorov–Smirnov test of normality probability plot. Nonnormal variables were also normalized by logarithmic conversion. Within-group comparisons were made by paired *t*-test, and between-group comparisons were made by analysis of covariance (ANCOVA). The difference of dietary intakes and physical activity measurements between two groups was analyzed by independent sample *t*-test. Biochemical assessment and anthropometric indices were adjustments for energy, carbohydrate, and fiber, resulted from ANCOVA. Data were analyzed by using SPSS (version 18, SPSS, Chicago, IL, USA), and a two-sided $P < 0.05$ was considered to be significant.

Results

A total of 120 hypertensive and hyperlipidemic patients in University of medical science clinics, Iran, were screened for inclusion criteria. Finally, 80 participants continued until the end of study and completed our study protocol [Figure 1].

Table 1 presents general features of study population. Based on the results of Table 1, there were no significant differences between two groups. No significant differences were seen between the two groups in terms of physical activity levels ($P = 0.348$, intervention mean: 32.58 Met. h/day; control group mean: 31.63 Met. h/day). Therefore, physical activity levels did not consider as a confounding factor.

Dietary intakes of participants are shown in Table 2. Based on obtained dietary records, no statistically significant differences were seen between two groups except for carbohydrate ($P = 0.005$) intake and a marginal significant difference for dietary fiber intake ($P = 0.059$).

Table 3 presents within-group and between-group comparisons of intervention and placebo group through 8 weeks of supplementation. We found significant improvement in anthropometric indices (WC and waist to hip ratio [WHR]) and lipid profiles (TG, LDL-C and total cholesterol [CHO]) within flaxseed and placebo groups. Furthermore, within-group significant reduction was observed in systolic and diastolic blood pressure, LDL, and HDL in flaxseed and weight and BMI in placebo group over 8 weeks of study. The full-adjusted model showed that there were significant differences in WC ($P < 0.001$), WHR ($P < 0.001$), TG ($P = 0.021$), CHO ($P < 0.001$), and LDL ($P < 0.001$) between two groups after flaxseed supplementation.

Discussion

In this study, we have demonstrated that incorporating whole flaxseed into the diet of hyperlipidemic and hypertensive patients along with healthy dietary recommendations for 8 weeks could reduce anthropometric measurements (WC and WHR) and improve lipid profiles (TG, CHO, and LDL) of participants.

Our findings are in agreement with some investigator who have made similar trials.[2,5] This study showed a decrease in anthropometric measurements (WC and WHR), in flaxseed group. Although the mean of weight and BMI had significant reduction in control group in compared with intervention group, there is no substantial differences

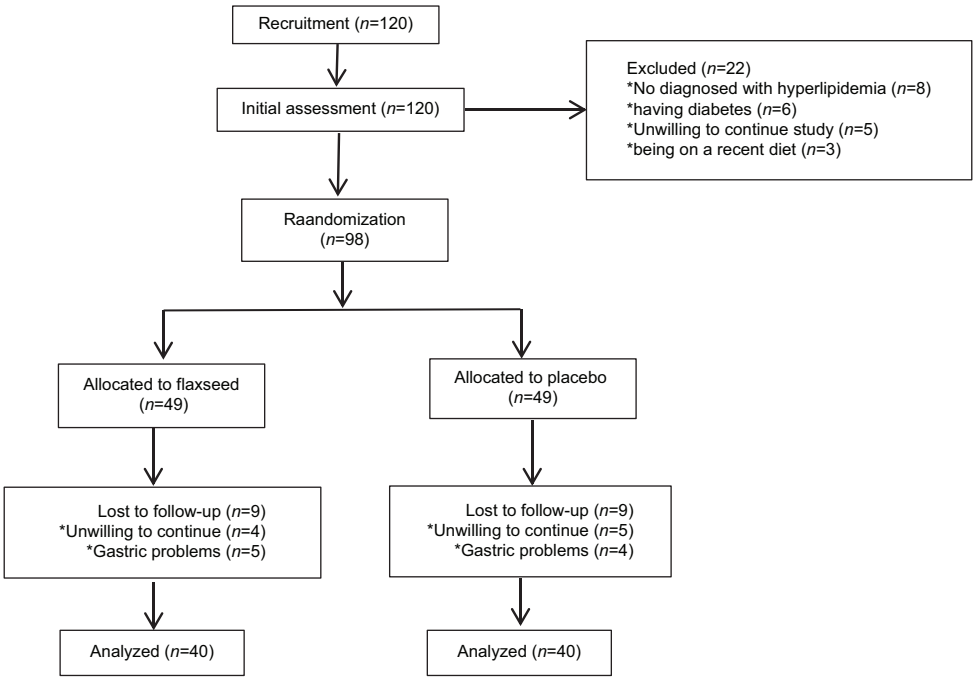

Figure 1: Trial flow chart

Table 1: General characteristics of study participants in two groups at baseline[a]

Variable	Intervention	Control	*P*[b]
Age (year)	44±10.07	42.7±10.09	0.929
Sex, male (%)	27.5	37.5	0.34
Medications			
Hypotensive drugs, yes (%)	90	93	0.899
TG-lowering drugs, yes (%)	85	82.5	0.762
Cholesterol-lowering drugs, yes (%)	95	92	0.644
Disease history			
Hypertension (month)	2.51±1.43	2.53±1.49	0.952
Hyperlipidemia (month)	1.84±1.02	1.81±1.03	0.897

[a]Data are mean±SD, [b]Resulted from independent sample *t*-test.
TG=Triglyceride, SD=Standard deviation

Table 2: Dietary intakes of study participants throughout the study[a]

	Intervention	Control	*P*[b]
Energy	2488.3±431.11	2311.8±341.1	0.702
protein	122.6±45.4	144.6±44.6	0.308
Carbohydrate	277.65±51.13	249.9±40.2	0.005
Fat	131.72±45.2	139.4±28.6	0.241
SFA	23.47±7.16	24.7±6.7	0.987
PUFA	42.12±10.57	36.2±8.6	0.828
Linoleic acid	28.3±9.9	26.58±5.7	0.465
Linolenic acid	0.6188±1.13	0.2075±0.498	0.601
Cholesterol	288.07±79.3	245.1±54.9	0.774
EPA	0.0075±0.021	0.0115±0.0406	0.605
DHA	0.0277±0.05	0.0033±0.0094	0.619
Fiber	22.2±7.3	23.83±5.17	0.059
Soluble fiber	1.33±0.85	1.62±0.67	0.360

[a]Data are mean±SD, [b]Resulted from independent sample *t*-test.
SFA=Saturated fatty acid, PUFA=Polyunsaturated fatty acids, EPA=Eicosapentaenoic acid, DHA=Docosahexaenoic acid, SD=Standard deviation

between two groups after controlling potential confounders. In this regard, available randomized control trials (RCTs) have reported conflicting results. Roberta Soares *et al*. showed that by receiving 35% of energy by carbohydrate and 60 g of flaxseed powder per day for 42 days, systolic blood pressure, weight, BMI, WC, and hip circumference will decrease significantly in men with cardiovascular risk factor.[9] The flaxseed is an oilseed that is a source of soluble and insoluble fiber, 20% protein, 41% fat, 6% carbohydrate, and 4% of waste. Due to high content of soluble and insoluble fibers, flaxseed could help to weight reduction.[14]

In the present study, systolic (flaxseed group = −5.55 mmHg reduction, placebo group = −3.63 reduction) and diastolic blood pressure (flaxseed group = −3 mmHg reduction, placebo group = −2.5 reduction) had more reduction within flaxseed group than control group. However, this difference did not reach to a significant level when comparing two groups. In line with our results, Stuglin *et al*. could not document a significant reduction in systolic and diastolic blood pressure of healthy adults after 32.7 g (per day) flaxseed consumption for 4 weeks.[15] However, there are some trials which have showed beneficial effects of flaxseed consumption on blood pressure (Caligiuri SP *et al*.).[11] The underlying mechanisms for antihypertensive effects of flaxseed on blood pressure are not entirely clear. However, some studies showed that flaxseed peptides may induce an antihypertensive effect through their rich arginine content.[16] Furthermore, each component of whole flaxseed including fiber, ALA, lignans, and peptides together might offer synergistic effects against hypertension.[17,18]

In this article, we could not show significant reduction in fasting blood sugar of participants. In contrast to our study, there are some trials which have proved the hypoglycemic effects of flaxseed. The results of one clinical trial study declared that 13 g and 26 g flaxseed intake lowers blood glucose and improves insulin sensitivity as a part of a habitual diet in overweight or obese individuals with prediabetes.[19] Although we could not prove the potential effects of flaxseed on FBS reduction, flaxseed and its components (ALA, lignans (secoisolariciresinol diglucoside, and peptides) have antioxidant, hypolipidemic, and hypoglycemic effects.[20]

The current study demonstrated that taking flaxseed sachet for 8 weeks had significant effects on lipid profiles (TG, CHO, HDL, and LDL) reduction of participants. These findings are in agreement with some investigators who have made similar trials, but in most of them, no change has been found in HDL-c levels.[2,5] One study showed that 10 g/d flaxseed powder supplementation in diabetic patients for 1 month resulted in reduction in TC (14.3%), TGs (17.5%), low-density lipoprotein cholesterol (21.8%), and apolipoprotein B and increase high-density lipoprotein cholesterol (11.9%).[21] As a source of dietary ALA, there are some studies which have shown beneficial effects of ALA consumption on serum TG levels of individuals.[21-23] Recently, flaxseed was identified as an alternative plant source of ω^{-3} fatty acids. Therefore, this component of flaxseed could also provide beneficial effects on lipid profiles improvement.[24] Flaxseed contains a high amount of fiber (28% by weight), and 25% of its fiber is, soluble fiber.[25,26] Dietary soluble fiber has cholesterol-lowering effects that lead to significant decrease in total and LDL cholesterol.[27] The result of one meta-analysis showed that whole flaxseed consumption could be more efficient in lipid profile improvement rather than flaxseed oil.[22]

However, this is the first study that has shown the effectiveness of flaxseed consumption in forms of sachet on lipid profiles and blood pressure improvement. This is an important clinical finding that by incorporating flaxseed powder in a regular diet of patients, such changes have been documented in cardiovascular risk factors.[2,4] It is possible that there are some unknown confounding factors which

Table 3: The effect of flaxseed and placebo on cardiometabolic risk factorsa

Variable	Treatment			Control			P^c	P^d
	Before	After	P^b	Before	After	P^b		
Weight (kg)	76.85±16.51	75±15.4	0.074	73.7±14.6	72.67±14.13	0.001	0.62	0.633
WC (cm)	98.3±11	94.3±11	<0.001	96±10.8	94.7±10.5	<0.001	<0.001	<0.001
Hip circumference (cm)	103.6±9.9	102.4±9.9	<0.001	99.5±8.8	98.42±8.7	<0.001	0.117	0.126
WHR (cm)	0.9501±0.0727	0.9225±0.0812	<0.001	0.9689±0.0626	0.9617±0.0592	0.039	<0.001	<0.001
BMI (kg/m^2)	29.18±4.6	28.5±4.4	0.087	26.8±3.8	26.55±3.7	<0.001	0.967	0.961
Systolic blood pressure (mmHg)	138.25±13.1	132±7.9	<0.001	136.5±12.8	132.87±8.1	0.056	0.312	0.295
Diastolic blood pressure (mmHg)	91.5±11.8	88.5±7.3	0.027	91±10.5	88.5±4.8	0.142	0.899	0.912
FBS (mg/dl)	94.22±8.3	94.22±7.6	1.000	92.2±8.2	92.6±8.9	0.563	0.923	0.833
TG (mg/dl)	207.9±101.37	173.7±57.12	0.011	195.5±64.6	189.65±6018	<0.001	0.015	0.021
TC (mg/dl)	202.47±46.07	186.5±41.15	<0.001	207.6±44.3	201.07±45.8	0.009	0.018	0.017
LDL (mg/dl)	127.27±36.98	115.9±36.6	<0.001	122.2±44.3	123.02±48.7	0.726	<0.001	<0.001
HDL (mg/dl)	46.65±8.6	48.4±8.06	0.048	45.7±10.03	46.06±9.5	0.574	0.054	0.057

[a]All values are mean±SD, [b]Resulted from paired sample t test; comparing before and after of each variable in each group, [c]Resulted from univariate analysis of variance; comparing the studied outcomes between two groups (adjustments were made for baseline values), [d]Resulted from univariate analysis of variance; comparing the studied outcomes between two groups (adjustments were made for baseline values, energy, carbohydrate, and fiber). WC=Waist circumference, WHR=Waist to hip ratio, BMI=Body mass index, FBS=Fasting blood sugar, TG=Triglycerides, TC=Total cholesterol, LDL=Low-density lipoprotein, HDL=High-density lipoprotein, SD=Standard deviation

we could not control in statistical analyses, and because of financial limitation, we could not measure more precise and relevant factors such as hsCRP or ppar gamma. Due to selected inclusion criteria for this study, the effects of flaxseed consumption were assessed in a specific group of people. Therefore, it is possible that we cannot generalize the results of this to the whole society. Moreover, this is the first time that flaxseed powder was provided in the forms of sachet to increase the compliance of participants. It is suggested that other studies apply such strategies to improve the flaxseed consumption compliance among participants.[23] It is strongly recommended that whole flaxseed should be used for future studies. In this study, we used brown flaxseed for intervention group. It is suggested that the potential effects of golden flaxseed should be determined in next surveys.

Conclusions

The present study proved significant reducing effects of flaxseed powder on anthropometric measurements (WC and WHR) and lipid profiles (TG, CHO, and LDL) of participants.

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Conflicts of interest

There are no conflicts of interest.

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