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How Ginger Influences Blood Lipid Levels in Individuals Who Were Suggested Lifestyle Change by Systematic Coronary Risk Evaluation?

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ABSTRACT

Objective: This study was performed to investigate the effect of powdered ginger supplemented to the diet on blood lipid indices in individuals with moderate physical activity that are recommended only lifestyle intervention by Systematic Coronary Risk Evaluation.
Methods: In this exploratory experiment, individuals were divided into 2 groups as ginger supplementation (n = 20) and control (n = 20). The ginger supplementation group received 1 ginger capsule (400 mg ginger extract, 80 mg gelatin) twice a day for a month. Blood lipid levels (total cholesterol, triglycerides, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol) and systolic blood pressure were measured, and Systematic Coronary Risk Evaluation values were calculated.
Results: The systolic blood pressure and Systematic Coronary Risk Evaluation values in the ginger supplementation group were decreased ($P < .05$). The systolic blood pressure values of the ginger supplementation group before and after the study were higher than the control group ($P < .05$). Systolic blood pressure values in both groups were decreased compared to previous levels. Before and after the study, the Systematic Coronary Risk Evaluation values of the ginger supplementation group were found to be lower than that of the control group ($P < .05$). The study showed that 85% of the ginger supplementation group remained in the category requiring a lifestyle change and possibly drug treatment, whereas 15% of the individuals moved to the category in which no intervention was required for lipid levels. However, 90% of the participants of the control group remained in the lifestyle change category.
Conclusion: The results of the current study implicate that consumption of ginger might be beneficial to reduce the risk of cardiovascular disease and further studies are needed to explore this effect in more detail.

Keywords: Blood lipid levels, coronary risk score, ginger

INTRODUCTION

Although progress has been made regarding the elucidation of coronary risk factors in the world, cardiovascular diseases (CVDs) are still among the most common causes of death. In 2012, 46.2% (17.5 million) of deaths were due to noncommunicable diseases (NCDs) worldwide, with 7.4 million deaths due to heart attack (ischemic heart disease) and 6.7 million due to stroke. Cardiovascular diseases are responsible for 37% of deaths due to NCDs under the age of 70 years. Deaths caused by CVDs are estimated to reach 22.2 million by 2030.[1] Hyperlipidemia is an important risk factor for the prediction of CVD. There is a strong and sustained relationship between total cholesterol (TC) or low-density lipoprotein cholesterol (LDL-C) level and CVD. In general, a 1% increase in LDL-C raises the risk of CVD by 2%-3%.[2] Controlling TC and LDL-C levels through dietary measures is the primary target of preventing CVD. Because skewed plasma lipid and lipoprotein levels, obesity, and high blood pressure are the main cardiovascular risk factors, the role of diet in CVD has been established; therefore, the diet should be modified in terms of components that increase and reduce these risk factors.[3] Ginger is a reliable, easy-to-tolerate

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herb used in the kitchen and also has an important place in the Ayurveda, Chinese, German, and Arabic medicine systems;[4,5] it contains phenolics such as shogaol and gingerol as potential active substances; sesquiterpenes such as bisabolene, zingiberene, zingiberol, sesquiphellandrene, curcurmene; and also[6] dehydrogingerdione, galanolactone, gigasulfonic acid, geraniol, neral, monoacyldiglycerides, glycolipids and gingerol as other active compounds. The active ingredient of ginger is in the essential oil part, and the main active ingredients are bisabolene, zingiberene, and zingiberol. Various mechanisms have been proposed to explain the positive effect of ginger on blood lipid levels. It has been suggested that ginger impairs and weakens the gastrointestinal absorption of cholesterol.[7-9] Phytochemicals (E)-8 β and 17-ep oxylabd-12-ene-15, 16-dial in ginger were reported to inhibit cholesterol synthesis in the liver in rats. Moreover, ginger supports the uptake and catabolism of LDL-C from the circulation; it inhibits LDL-C oxidation and aggregation.[7] It has been demonstrated that the addition of ginger to the diet reduces the expression of retinol-binding protein and fatty acid-binding protein genes in the liver and adipose tissue of rats.[10] In a study, 400 mg/kg ethanolic ginger extract was given to rats for 6 weeks. At the end of the study, the LDL receptor messenger ribonucleic acid level increased in the liver and decreased expression of 3-hydroxy-3-methylglutarylcoenzyme A reductase protein has been observed.[11] It has been claimed that ginger inhibits cellular synthesis of cholesterol by suppressing hydroxymethylgultaryl Co-A reductase, which is the rate-regulating enzyme in cholesterol metabolism. It inhibits cholesterol 7 alpha-hydroxylase, which is the key enzyme in the conversion of cholesterol to bile acids. It has been suggested that ginger increases the fecal excretion of cholesterol.[7,12] Although recent preclinical studies have shown that ginger reduces serum TC, LDL-C, and TG levels and simultaneously increases HDL-C levels, the results are still contradictory.[4-6]

Main Points

- This study showed that 85% of the individuals receiving 400 mg/day ginger extract remained in the category needing to make a lifestyle change and possibly will need drug treatment, whereas 15% of the individuals shifted to the category that did not require any intervention for lipid levels.
- Incorporating ginger into the diet reduces systolic blood pressure and Systematic Coronary Risk Evaluation values, possibly contributing to the prevention of cardiovascular disease.
- Consumption of ginger, 400 mg ginger extract might be beneficial to reduce the risk of cardiovascular disease risk factors such as systolic blodd pressure

For this reason, this intervention study was conducted to reveal the effect of incorporating ginger into the nutrition plan on anthropometric measurements, blood lipid levels, and Systematic Coronary Risk Evaluation (SCORE) values solely in individuals who were recommended lifestyle intervention depending on the results of SCORE.

METHODS

Participants and Study Design

To conduct a comprehensive power analysis, we first obtained the necessary information from the study of Alizadeh Navaei et al.[5]. In this case, the predetermined values for beta (β) and alpha (α) were 0.80 and 0.05, respectively, and the number of participants was calculated as 20 per group. Thus, this study was carried out with 40 volunteers showing moderate physical activity who applied to the Cardiology Outpatient Clinic of a Erciyes University between February 2017 and December 2018.

The ethics committee permission was obtained from a local ethics committee, the Erciyes University Clinical Research Ethics Committee (Date: March 3, 2017, Approval No: 2017/120), and informed consent forms were signed by the individuals. The mean age of the individuals was ≥40 (46.15 ± 3.70 years). The participants consisted of 50% women and 50% men. There were no participants with menopause, and only lifestyle intervention was recommended based on SCORE results.

In our study, we employed a simplified method for randomizing our patients into 2 distinct groups: the ginger supplementation group and the control group. This randomization was based on a specific criterion, namely, the last digit of patient barcode numbers. More specifically, patients whose barcode numbers ended with an odd digit were allocated to the intervention group, while those with an even final digit were assigned to the control group.

In previous studies, several doses of ginger were given to participants. According to a meta-analysis,[13] use of a low dose for a short time was effective in improving the lipid profile rather than higher ginger doses. According to the literature[5,14] the individuals in the ginger supplementation group (n = 20; 10 women and 10 men) received 1 ginger capsule (400 mg ginger extract, 80 mg gelatin capsule, Sepe Natural Ginger, Sepe Organic Natural Products Ind. & Trade Co., Turkey) twice a day after meals in the morning and evening for 1 month. Ginger capsules (32 mg gingerol as the active ingredient) were provided by the researcher and given to the participants free of charge. No supplements were given to the control group (n = 20; 10 women and 10 men), and they were asked to maintain

moderate physical activity. Both groups received a diet containing 300 mg of cholesterol per day during the study period. In order to observe the effect of ginger supplementation, no dietary intervention was made, the habits of the patients were questioned, and recommendations were made regarding the foods in the 300 mg nutrition model only. Therefore, dietary compliance was not followed. At the beginning and end of the study, anthropometric measurements and biochemical parameters of the participants were evaluated.

Sociodemographic Features

The sociodemographic information of the participants was obtained through face-to-face interviews with a questionnaire form created by reviewing the literature.[10] Information such as age, education, and smoking status were included in the questionnaire.

Anthropometric Measurements

At the beginning and end of the study, the body weight, height, waist circumference, and hip circumference of the participants were measured and body mass index (BMI), waist–hip ratio were calculated (kg/m²). Based on World Health Organization (WHO) adult BMI classification, those with a BMI below 18.5 kg/m^2 were classified as underweight, those with 18.5-24.9 kg/m^2 as normal, those with 25-29.9 kg/m^2 as slightly obese, and those above 30 kg/m^2 as obese.[16]

Fasting body weights and heights of individuals with light clothing and without shoes were measured in the morning using weight-length counter (150 IB, N, Turkey). The height of the participants was measured while the individuals were standing without shoes with their feet next to each other, with the head in the plane of Frankfort (the eye triangle and the auricle aligned). Waist and hip circumference values were measured while the individuals were standing, with arms open on both sides and feet adjacent to each other.

The waist circumference was measured with the non-stretchable tape measure between the lower rib bone and the caudal fin when the individual breathes out. Measurement was made by taking care that the tape measure is parallel to the ground and does not press on the skin. Hip circumference was determined by measuring the circumference from the side of the individual from the highest point of the hip. The waist−hip ratio was determined by dividing the waist circumference values by the hip circumference values.[15] The reference values determined by the WHO were used in the evaluation of waist circumference and waist−hip ratio measurements. Accordingly, a waist circumference of more than 80 cm in women and 94 cm in men was considered to be risky, and a waist circumference of 88 cm in women and 102 cm in men was considered obese.[16]

Blood Pressure Measurements

Before systolic blood pressure measurement, the researchers ensured that the participants did not smoke cigarettes, drink tea or coffee, consume caffeine and other nutrients within 30 minutes of measurement, and the measurement was performed by the nurse after at least a 5-minute resting period. The individual was asked to sit with their back leaned against the chair with the arm bare during the measurements. Measurements were made at least twice with an interval of 2 minutes and the average value was calculated.[17]

Biochemical Analysis

A 4 mL blood sample was taken from the participants after 12 hours of fasting. The TG, HDL-C, LDL-C, and TC levels were determined by an auto-analyzer (Architect/Aeroset 16000, Abbott, USA).[18]

Systematic Coronary Risk Evaluation

An electronic version, "HeartScore," specially adapted to Turkey is used for the SCORE calculation. HeartScore is the electronic and interactive version of the SCORE risk table of the European Clinical Practice Prevention of CVD, prepared by the Fourth United European Associations Working Group on the prevention of CVD in Clinical Practice.[19] A record for each individual was created in HeartScore. The SCORE values for each individual were calculated by entering the age, gender, smoking status, TC value and systolic blood pressure of the individuals to the system. Individuals with a 10-year calculated risk of cardiovascular death <1% were considered to be at low risk, from ≥1% to <5% were considered to be at moderate risk, from ≥5% to <10% were considered to be at high risk, and ≥10% were considered to be at very high risk.[19,20] Considering the LDL-C values, the low-risk group with a SCORE value of <1%, the medium-risk group with a value of ≥1%-<5%, and the high-risk group with a value of ≥5%-<10% were evaluated.[19] Individuals with SCORE values within the interval of recommended lifestyle intervention were included in the study.

International Physical Activity Questionnaire Short Form

In order to determine the physical activity levels of the participants, the IPAQ Short Form (88), consisting of 7 questions, was applied. Individuals were asked questions about heavy physical activity, moderate physical activity, duration and frequency of walking in the last 7 days. The sum of the values obtained via multiplying the number of days of activity type, daily duration, and the activity coefficient (heavy activity coefficient 8, medium activity

coefficient 4, and walking coefficient 3.3). Individuals with <600 metabolic equivalent of task (MET), those with 600-3000 MET, and those with >3000 MET were considered as inactive, moderately active, and very active, respectively. Individuals with moderate physical activity were included in the study.[14] Individuals were asked not to make radical changes in their physical activity status for a month.

Nutrition Plan

Training was provided to the participants in both groups to implement the nutrition plan including 300 mg of cholesterol per day.[19] The nutritional habits, sociocultural conditions, working conditions, and lifestyles of individuals were taken into consideration for preparing the nutrition plan for each individual. In nutrition education, portion sizes and amounts (grams) of foods were arranged according to the book named "Food and Food Photo Catalog: Measures and Quantities."[16] At the beginning of the study, 30-40 minutes of training was provided to each individual.

Exclusion Criteria

Individuals who were younger than 40; being obese (≥30kg/m²); having one of the diseases such as diabetes, familial dyslipidemia, atherosclerotic heart disease, and chronic kidney failure; using vitamin–mineral tablet, alcohol, or medication; having mild or heavy activity determined with the short form IPAQ[14] were excluded. And individuals who did not need any intervention or who were recommended drug treatment as a result of joint evaluation of SCORE and serum LDL-C levels (7) were not included in the study.

Statistical Analysis

Türkiye National cloud-based statistics software (TURCOUSA) was used for statistical evaluation of the data. The normality of the data was determined with Shapiro–Wilk test. When the data were normally distributed, Student's *t*-test was used for group comparisons and paired *t*-test was used for determination of the differences between the data obtained before and the after the study for each group. When the data were not normally distributed, Mann–Whitney *U*-test was used for group comparisons and the paired samples Wilcoxon test was used for the data obtained before and the after the study for each group. Categorical variables were analyzed with chi-square test. In addition, logistic regression analysis was performed. The results of the analysis were evaluated in the 95% CI and the significance level was accepted as $P < .05$.

RESULTS

The mean ages of the control and ginger supplementation groups were similar (44.80 ± 3.70 and 46.20 ± 5.08,

Table 1. Anthropometric Measurement Values and Smoking Status of the Participants in the Groups Before and After the Study

Anthropometric Measurements	Ginger Supplementation Group (n = 20)	Control Group (n = 20)	
	x ± S	x ± S	P**
Age (years)	44.8 ± 3.7	46.0 ± 5.1	.325
Body weight (kg)			
Before	70.74 ± 9.4	71.6 ± 8.3	.074
After	71.2 ± 9.273	71.52 ± 8.2	.558
P	.754	.902	
BMI (kg/m²)			
Before	26.1 ± 2.7	26.1 ± 2.6	.069
After	26.2 ± 2.7	26.0 ± 2.5	.490
P	1.000	.800	
Waist circumference (cm)			
Before	86.6 ± 8.1	86.3 ± 7.8	.163
After	86. 2 ± 8.1	86.0 ± 7.7	.083
P	.922	.952	
Hip circumference (cm)			
Before	99.1 ± 4.7	98.9 ± 4.1	.179
After	98.5 ± 5.1	98.6 ± 3.9	.069
P	.943	.945	
Waist–hip			
Before	0.87 ± 0.07	0.87 ± 0.09	0.748
After	0.88 ± 0.07	0.87 ± 0.09	0.666
P	.968	.921	
	n = 20	n = 20	Total (n = 40)
	n (%)	n (%)	n (%)
Smoking rate			
Nonsmoker	3 (15)	5 (25)	8 (20)
Regularly	8 (40)	14 (70)	22 (55)
Occasionally	6 (30)	0 (0)	6 (15)
Stopped	3 (15)	1 (5)	4 (10)
Total	20 (100)	20 (100)	40 (100)
	$\chi^2 = 9.1$, $P^* = .133$		

Student's *t*-test was used for group comparisons. Chi-square test was used for smoking status.
BMI, body mass index.
*Within the group. **Between the groups.

respectively) ($P > .05$), In terms of anthropometric measurements, there was no statistically significant difference between the groups before and after the study (Table 1, $P > .05$). In addition, the rate of nonsmokers in the control group (25%) was higher than the ginger supplementation group (15%) but the difference between groups was not significant ($P > .05$) (Table 1).

In the beginning of the study, concerning the TC, LDL-C, HDL-C, and TG levels, there were no significant differences between control and ginger supplementation groups. The systolic blood pressure in the ginger supplementation group before the study was higher than the systolic blood pressure value in the control group ($P < .05$). The SCORE value in the ginger supplementation group before the study was found to be lower ($P < .05$) than the SCORE value in the control group (Table 2, Figure 1, and Figure 2).

At the end of the study, the HDL-C level in the control group was found to be lower than that of the ginger supplementation group ($P < .05$). The systolic blood pressure decreased in both groups, but there was no significant difference between groups. Compared to the control group, the SCORE values in the ginger supplementation group decreased significantly ($P < .05$) (Table 2, Figure 2).

When the values obtained in the beginning and at the end of the study were compared, there were no significant differences in TC, LDL-C, HDL-C, and TG levels in the ginger supplementation group, whereas systolic blood pressure and SCORE values decreased. In the control group, TC and LDL-C levels decreased, but there were no statistically significant differences in HDL-C, TG, systolic blood pressure, and SCORE values.

At the end of the study, 85% of the individuals in the ginger supplementation group remained in the category needing to make a lifestyle change and possibly will need drug treatment, whereas 15% of the individuals shifted their category that did not require any intervention for lipid levels. In the control group, 90% of the participants remained in the category that require to make a lifestyle change, and if it is not controlled, possibly need drug treatment; the remaining 10% shifted to the category that did not require any intervention for lipid levels. Although not statistically significant ($P > .05$), the frequency (15%) of the participants in the ginger supplementation group who shifted to the category that did not need intervention for lipid levels was 10% higher than the control group (Table 3).

In addition, the frequency of individuals whose LDL-C was ≥100, <155 decreased from 90% to 70%. It was determined that the proportion of individuals with very high (≥190) LDL-C levels did not change. While the SCORE of 10% of the individuals remained the same, the LDL-C levels decreased to ≥70, <100 levels (Table 4).

When examining whether the ginger intervention improved blood pressure and blood lipid parameters, analyses showed that the intervention was likely to improve systolic blood pressure (B = 4.33, $P = .03$ for model 0; B = 5.05, $P = .03$ for model 1; Table 5).

Table 2. Serum Lipid Levels, Systolic Blood Pressure, and SCORE Values of the Groups Before and After the Intervention

Variables	Ginger Group (n = 20) x ± SD/Median (IQR)	Control Group (n = 20) x ± SD/Median (IQR)	P**
TC (mg/dL)			
Before	203.7 ± 24.5	194.5 (158-269)	**.570**
After	200.8 ± 25.7	183.5 (165-248)	**.256**
P*	.835	**.018**	
LDL-C (mg/dL)			
Before	127.9 ± 20.0	121.6 (103.4-198.4)	**.787**
After	124.8 ± 20.4	116.2 (92.4-170.8)	**.402**
P*	.869	**.021**	
HDL-C (mg/dL)			
Before	52.8 ± 11.9	43.5 (31-79)	**.140**
After	52.8 ± 12.2	40.9 (31.1-79)	**.027**
P*	.269	.064	
TG (mg/dL)			
Before	114.8 ± 45.6	116.5 (69-213)	**.285**
After	115.9 ± 41.9	129.5 (51-210)	**.323**
P*	.551	.247	
Systolic blood pressure (mm/Hg)			
Before	133.6 ± 17.7	112 (100-166)	**.005**
After	124.8 ± 15.6	117 (100-150)	**.062**
P*	**.012**	.361	
SCORE (%)			
Before	1.0 ± 0.0	1.4 ± 0.8	**.037**
After	0.8 ± 0.4	1.4 ± 0.8	**.005**
P*	**.036**	.682	

Student's *t*-test, Mann–Whitney *U*-test, and the paired samples Wilcoxon test were used.
*Within the group. **Between the groups.

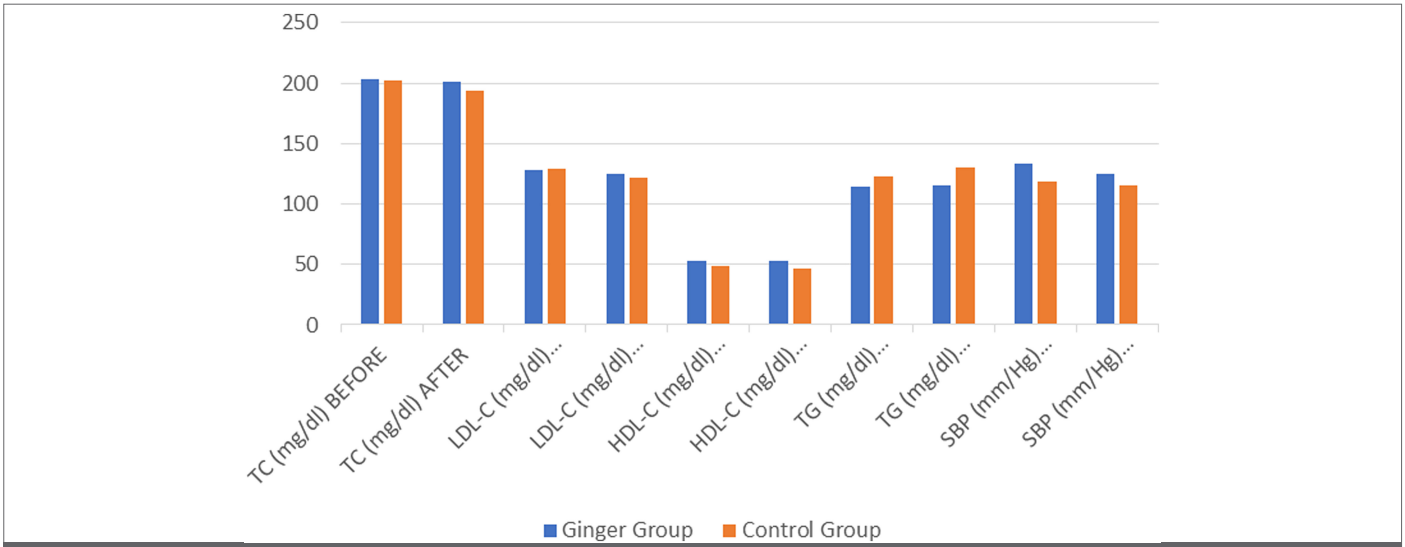

Figure 1. Serum lipid levels and systolic blood pressure values of the groups before and after the intervention.

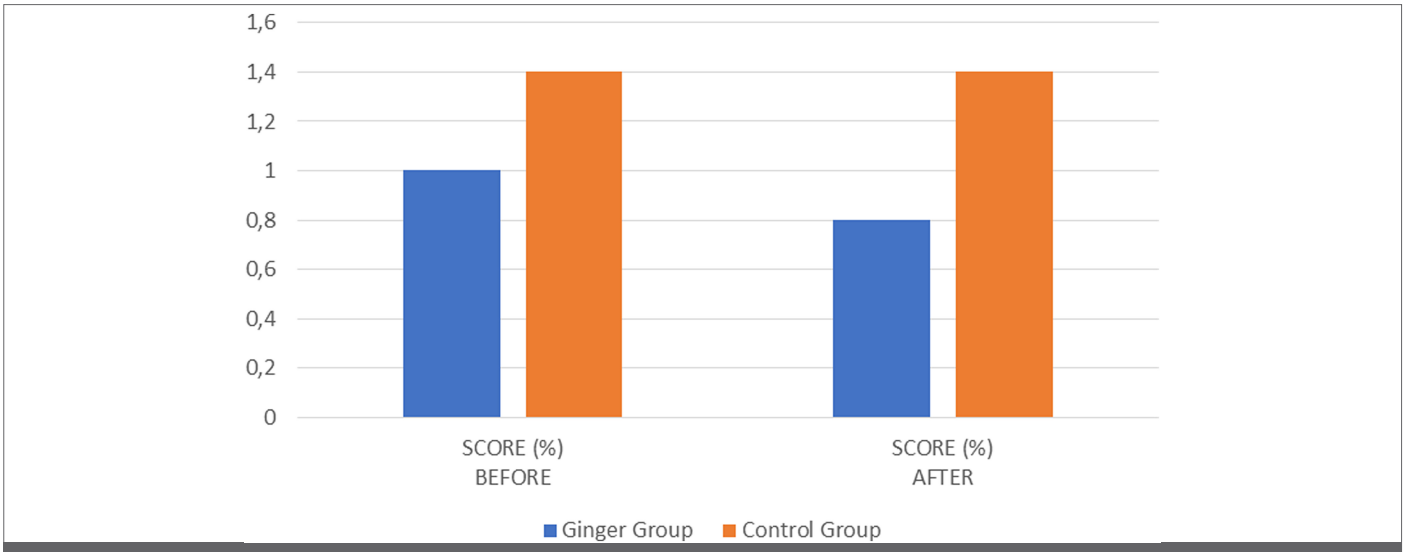

Figure 2. SCORE values of the groups before and after the intervention. SCORE, Systematic Coronary Risk Evaluation.

DISCUSSION

The CVD is a general nomenclature given to the group that includes diseases of the heart or blood vessels (arteries and veins) and is one of the leading causes of morbidity and mortality. According to the data of the WHO, CVDs rank first among global causes of death (31%) and 17.5 million people died in 2012. In Turkey, considering the 10

Table 3. Distribution of Interference Strategies Determined as a Function of SCORE and LDL-C at the End of the Study

	Ginger Group	Control Group	Total	
Interference Strategies	**n (%)**	**n (%)**	**n (%)**	
Lifestyle intervention, consider drug if uncontrolled	17 (85.0)	18 (90.0)	35 (87.5)	$\chi^2 = .663$ $P = .500$
No lipid intervention	3 (15.0)	2 (10.0)	5 (12.5)	
Total	20 (100)	20 (100)	40 (100)	

Chi-square test was used.
LDL-C, low-density lipoprotein cholesterol; SCORE, Systematic Coronary Risk Evaluation.

Table 4. Distribution of the Groups by SCORE and LDL-C Values Before and After the Study

	SCORE (%)							
	Ginger Supplementation Group (n = 20)				Control group (n = 20)			
	Before		After		Before		After	
	<1	1-5	<1	1-5	<1	1-5	<1	1-5
LDL-C	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
70-100 mg/dL				2 (10)				2 (10)
100-155 mg/dL		18 (90)	2 (10)	14 (70)		17 (85)		15 (75)
155-190 mg/dL		2 (10)		2 (10)		2 (10)		3 (15)
>190 mg/dL						1 (5)		

LDL-C, low-density lipoprotein cholesterol; SCORE, Systematic Coronary Risk Evaluation.

diseases that constitute the disability-adjusted life years, ischemic heart diseases (8%) occupy the second place.[21] The 40.4% of the death was due to CVDs in 2014, and the death rate due to CVDs in men was 35.83%, while in women it was 44.61%, with an increase of 0.8% when compared to the rate of 2013. Because increased plasma lipid and lipoprotein levels, obesity, and high blood pressure are explained as the main risk factors for CVD, the type of diet followed has proven to be beneficial for the amelioration of the lipid profiles. It has been shown that 10 g ginger reduced platelet aggregation in coronary artery patients when given at 4 and 10 g/day ginger for 3 months.[5]

The risk of CVD in smokers is 2-3 fold higher than that in nonsmokers. Smoking is responsible for half of the preventable deaths in long-term smokers, and 50% of these deaths are due to CVD. Smoking disrupts the lipid and lipoprotein profiles and causes endothelial dysfunction that results in the progression of atherosclerosis.[22] Cigarette smoking lowers HDL-C and increases the oxidation of LDL-C. The causal role of smoking in CVD has been demonstrated in over 20 million patients with a long time follow-up study.[23] It is known that there were 1.1 billion smokers in the world in 2012.[1] According to the WHO report in 2017, smoking rates in individuals over 15 years of age ranged from 21.9% to 25.9% in Turkey.[25] In the present study, the percentage of regular smokers was higher in the control group (70%) than in the ginger supplementation group (40%), which was considerably above the percentage stated in the WHO 2017 Turkey report. While there were no occasional cigarette smokers in the control group, the proportion of occasional smokers in the ginger supplementation group was 30% (Table 1).

Studies in individuals without CAD have shown that smoking cessation reduces the risk of death and reinfarction by 7%-47%.[25,26] Stopping smoking in patients without apparent disease ensures that the risk of CAD decreases to a nonsmoking level within 10 years.[27] In this study determining the risk of CVD with the SCORE system in healthy adults, although it was not statistically significant, the rate of those who used to smoke was higher in the ginger supplementation group than in the control group (Table 1). In this study, the number of cigarettes smoked per day was found to be significantly higher in the control group (15.21 ± 8.40) than in the ginger supplementation group (6.65 ± 6.1; $P < .05$) (Table 1). Smoking is a health problem that increases the risk and mortality of CVD and is therefore a unique problem.[25]

Exercise or regular physical activity has been shown to positively affect plasma lipid profiles, cardiovascular and pulmonary functional capacity, glucose tolerance, and blood pressure and prevent obesity.[23,25,28] In addition, increasing physical activity can prolong the total life expectancy of 1.3-3.5 years and life expectancy without CVD.[16,29] In a study investigating the effects of a 4-week intervention program consisting of diet restriction and walking activity on the lipid profile in sedentary individuals, significant decreases in TC (35 ± 37 mg/dL), TG (30 ± 68 mg/dL), and LDL-C (29 ± 41 mg/dL) levels were determined.[28]

Healthy individuals who have low physical activity are at twice the risk of CAD than the individuals who do regular physical activity. According to Turkey's Chronic Disease Risk Factors Incidence Study, 23% of men had adequate activity, 22% a moderate level, and 55% a low level of physical activity. These rates are even lower in women.[1] For these reasons, in order to prevent physical activity from affecting the risk of CVD and SCORE values in the present study, individuals with moderate physical activity were included in the study by applying the IPAQ Short Form[13] (ginger supplementation group: 1981.38 ±

Table 5. Effect of Ginger Intervention on Improvement of Blood Lipid and Blood Pressure Parameters

Improvements			Systolic Blood Pressure				Diastolic Blood Pressure				Blood HDL Levels			
			CI (B)	Lower	Upper		CI (B)	Lower	Upper		CI (B)	Lower	Upper	
Ginger intervention	Model 0		4.33	1.15	16.32	**0.03**	2.25	0.63	7.97	0.21	1.91	0.52	7.00	0.33
	Model I		5.05	1.71	21.82	**0.03**	2.25	0.64	7.97	0.20	2.33	0.54	10.16	0.26
		Blood LDL levels					**Blood triglycerides levels**				**Blood total cholesterol levels**			
	Model 0		1.08	0.26	4.43	0.92	1.86	0.52	6.61	0.34	0.67	0.15	2.92	0.59
	Model I		0.88	0.19	4.00	0.87	1.57	0.38	6.44	0.53	075	0.15	3.68	0.72

No adjustment has been made in model 0. Model I was adjusted for the parameters of age, gender, smoking, and physical activity levels. Logistic regression analysis was used.
HDL, high-density lipopotein; LDL, low-density lipoprotein.

837.97 MET and control group: 1536.75 ± 831.58 MET) ($P = .100$).

In a rat study, it was observed that serum TC decreased significantly whereas TG level was not affected by 500 mg/kg aqueous extract of ginger given for 4 weeks via oral route. Ginger suppresses the accumulation of bile and cholesterol in the body by increasing the secretion of bile salts and the activity of pancreatic lipase, thereby making a positive contribution to weight management.[30,31]

As BMI increases, the risk of CVD increases and if the waist–hip ratio also increases, this risk becomes more pronounced. Weight loss reduces the risk of developing CVD.[22] It has been claimed that ginger activates adrenaline secretion by activating beta-adrenoceptors, thereby increasing thermogenesis. Thus, the increase in lipolysis in adipose tissue results in decreases in body weight.[32] It has also been suggested that ginger increases fat catabolism by activating the peroxisome proliferator-activated receptors found in skeletal muscle. Thus, by increasing calorie burning, it provides weight loss.[30,32] In contrast, in our study, it was determined that there was no statistically significant difference ($P > .05$) between the groups in terms of anthropometric measurements as well as within each group before and after the intervention (Table 1).

Although the potential active ingredient of ginger 6-gingerol has been reported to prevent fat accumulation and weight gain,[33] and also 6-shogaol to decrease adiposity,[33,34] in the present study, the lack of statistically significant changes within and between groups in terms of all anthropometric measurements including body weight and waist–hip ratio may be due to the use of the powdered form of ginger, rather than its isolated active form. In addition, these results may be attributed to including the participants who are not obese (with 26.1 ± 2.7 kg/m² BMI).

Hyperlipidemia that can be corrected by diet is a predictor and an important risk factor for CVD. There is a strong, persistent, and high relationship between TC or LDL-C levels and CVD.[16] Controlling TC and LDL-C levels with dietary measures is the primary target of preventing CVD risk. Recently, although, some preclinical studies have shown that ginger reduces serum TC, LDL-C, and TG levels and simultaneously increases HDL-C levels,[4,5] in the present study, no statistically significant change was detected in the serum lipid levels of the ginger supplementation group at the end of the study (Table 2, Figure 1) ($P > .05$).

The amount of cholesterol taken by the diet is of great importance in the balance and regulation of cholesterol

synthesis.[33,34] In a study investigating the relationship between dietary cholesterol change and endogenous cholesterol synthesis, it was determined that when the diet contains 0.05% cholesterol, 70%-80% of TC was synthesized in the liver, small intestines, and adrenal glands.[35] In another study, it was shown that serum cholesterol level decreased by 0.13 mmol/L with the decrease of 100 mg of cholesterol in the diet.[33] Similarly, at the end of our study, it was found that the TC and LDL-C levels of the control group decreased significantly ($P < .05$) when compared to the levels prior to the study. These results may be attributed to the fact that the individuals in control group may be more compliant with the nutrition group containing 300 mg of cholesterol before the study than the ginger supplementation group.

When the studies evaluating the effect of ginger on TC in the literature were examined, it was seen that ginger reduced serum cholesterol levels in some studies.[5,25,36] However, in the present study, it was determined that before–after study TC levels did not differ statistically ($P > .05$) between groups (Table 2, Figure 1), similar to some previous studies.[13,37] According to the results of the present study and previous contradicting studies, it is not possible to make a definitive conclusion about whether ginger reduces serum TC or not.

In this study, it was determined that the differences in LDL-C levels were not statistically significant ($P > .05$) between groups before and after the study (Table 2, Figure 1). Different results have been obtained in studies investigating the effect of ginger on LDL-C levels. Confirming our results, there are also studies reporting ginger has no effect on LDL-C levels.[5,38] According to the results of studies especially in humans, ginger was found to be ineffective on HDL-C levels.[5, 33,35,37] Similarly, in the current study, it was determined that HDL-C levels were also statistically insignificant ($P > .05$) in the ginger supplementation group before and after the study (Table 2, Figure 1). This may be due to the fact that dietary factors are less effective on HDL-C.[36,39] Compared to the ginger supplementation group, a significant decrease was observed in the control group at the end of the study. However, there was no significant difference between the measurements performed before and after the study in the control group. This difference may be due to the lower but not significant HDL-C level in the control group that was determined before the study.

Looking at studies investigating the effect of ginger on TG levels, some studies[5,36,37,39] found that ginger reduced serum TG levels. However, in some other studies,[13,38] similar to the current study, it was concluded that ginger does not have a significant effect on serum TG. As in the present study, a study showing that ginger is ineffective on serum lipid levels has been carried out in Iran.[39] In another study investigating the effects of ginger use on serum lipid profile in coronary artery patients, ginger was added to the diet at 4 g/day for 3 months as a powder and 10 g/day for 3 months and no effects of ginger supplementation on the lipid profile was determined.[6]

In a meta-analysis evaluating the clinical study in humans, it was concluded that adding ginger to the diet did not have any significant effect on TC as in the current study. In the mentioned meta-analysis, a statistically significant decrease was found in serum TG level. However, high heterogeneity was detected in the studies that were included in the meta-analysis, and it remained in this heterogeneous subgroup analysis with the ginger dose, duration and quality of work used. Depending on the location and growing conditions of ginger, the active ingredients are likely to vary.[40] For these reasons, more studies are needed to determine the optimum dose. In addition to the amount of ginger used, its type, method of preparation, and the characteristic features of the participants may play a very important role in the effect of ginger on blood lipid levels.

Hypertension has a very important place among the risk factors of CVD. When taken under control, it has been shown that 8.6% of the total burden of disease can be prevented, thus reducing the risk of CVD.[14]

Considering the limited number of human studies on the effect of blood pressure and ginger in the literature, it was found that ginger used in different doses (50 mg/kg, 100 mg/kg) in healthy adults significantly reduced blood pressure[41] by reducing total peripheral resistance via directing the blood flow to the vessels in the periphery. Another possible mechanism has been suggested that the blood pressure lowering effect is due to the serotonergic antagonistic feature of ginger.[42,43] The vasodilator activity of the ginger was attributed to 6-shogaol and 6-, 8-, and 10-gingerol content.[44] In this study, the systolic blood pressure of control group was lower than the ginger supplementation group in the beginning of the study ($P < .05$). At the end of the present study, the systolic blood pressure in both groups were found to be lower than prior to the study and this result was found to be statistically significant ($P < .05$) However, there was no statistically significant difference between ginger supplementation and control groups ($\bar{x} = 124.8 \pm 15.57$ and $\bar{x} = 115.3 \pm 12.2$, respectively) (Table 2, Figure 1). Considering the limited number of human studies on the effect of blood pressure and ginger in the literature, similar to the current study, it was found that ginger used in different doses (50 mg/kg, 100 mg/kg) in healthy adults significantly reduced blood

pressure[41] by reducing total peripheral resistance via directing the blood flow to the vessels in the periphery. Another possible mechanism has been suggested that the blood pressure lowering effect is due to the serotonergic antagonistic feature of ginger.[42,43] The vasodilator activity of the ginger was attributed to 6-shogaol and 6-, 8-, and 10-gingerol content.[44] Therefore, it is thought that the current study may lead to future studies on this subject since it is a study that has determined the possible effect of ginger on hypertension in humans. Results from the aforementioned studies and our study indicate that ginger may be beneficial in reducing hypertension.

The SCORE system aims to make a risk estimate in individuals who are apparently healthy, with no clinical or preclinical symptoms. Considering this feature of SCORE system, its benefits and its primary target of primary protection, it is seen that the SCORE system is quite suitable for use in the detection of risky individuals in the primary level.[16,45] At the end of this, there was a significant ($P < .05$) decrease in the SCORE value in the ginger supplementation group ($\bar{x} = 1.0 \pm 0.0$ and $\bar{x} = 0.8 \pm 0.4$, respectively) compared to the prestudy value, and the difference between ginger supplementation and control groups was also significant ($P < .05$) (Table 2, Figure 2). Although there was no statistically significant effect of ginger on serum lipid levels in the current study, the statistically significant decrease in the risk level of the group using ginger as a result of the SCORE evaluation is important in terms of revealing the positive effect of ginger. When the distribution of the groups according to the SCORE and LDL-C values was examined, 10% of the individuals using ginger had reduced SCORE value below 1% at the end of the study, whereas the control group did not show the SCORE value below 1%. In addition, the proportion of individuals whose LDL-C was ≥100, <155 decreased from 90% to 70%. It was determined that the proportion of individuals with very high (≥190) LDL-C levels did not change. While the SCORE of 10% of the individuals remained the same, the LDL-C levels decreased to ≥70, <100 levels (Table 4). It is thought that these results may have been due to the effect of ginger. The present study is likely to contribute to the literature by evaluating the effectiveness of ginger on serum lipid levels and SCORE values. The results of the studies in the literature regarding the effect of ginger on serum lipid levels appear to contradict each other. The inconsistent results in clinical trials may be due to the comparison of study groups that are not similar to each other, the use of different types and doses of ginger preparations, and the duration of ginger supplementations as well as neglecting other factors affecting food intake. Therefore, clinical studies are needed where different amounts of ginger are used for longer periods. It is obvious that there is a need for human studies that would reveal the mechanism of the possible effects of ginger on serum lipid levels.

In many previous studies, the following variables were not evaluated. Physical activity, diet, and smoking status of the individuals included in the present study were questioned at the beginning of the study and individuals with moderate physical activity and smoking status did not change their behaviors during the study. Individuals were provided with nutritional training to stay in moderate physical activity for a month, not to make radical changes in their diet, and were informed about the sources of dietary cholesterol. Although in this study there is no significant relationship between ginger and serum lipids, it is hoped that the research will contribute positively to the literature in terms of physical activity, smoking, and dietary factors.

As a result, this randomized controlled intervention clinical study showed that supplementing 400 mg of ginger twice a day for 1 month showed no statistically significant effect on serum lipid levels in individuals who were at risk by SCORE evaluation. However, compared to the beginning of the study in the group using ginger, it was revealed that the systolic blood pressure and SCORE values decreased significantly at the end of the study. Since ginger is a safe, inexpensive, easily accessible, medicinal plant that does not have any serious side effects when used in routine doses, making it available for the treatment of CVD can reduce the use of common cardiovascular drugs and make treatments much more cost-effective. In this exploratory study, the results of regression analyses suggest that the ginger intervention contributed to the positive improvement of systolic blood pressure levels (OR: 4.33 for model 0; OR: 5.05 for model I) ($P < .05$). Current findings indicate that incorporating ginger into the diet reduces systolic blood pressure and SCORE values, possibly contributing to the prevention of CVD. However, it is obvious that large-scale, long-term further detailed studies are needed for confirmation of the results of the current study.

Study Limitations

This randomized study was summarized from a PhD thesis. The ginger used in the study was provided by the researcher. The limitations of the study were that the study could not be carried out for a longer period of time due to the burden of its cost and that it could not be carried out on a larger participant population even though the number of samples was calculated. In addition, it was a limitation that the individuals were determined to be moderately active, no dietary intervention was made, and the compliance with them could not be followed. In this exploratory experiment, the higher blood pressure in the ginger supplementation group than that of the control

group at the beginning of the study, and thus after the study, was another limitation of the study.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Erciyes University (Date: March 3, 2017, Number: 2017/120).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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