Investigation of the effect of ginger on the lipid levels

A double blind controlled clinical trial

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ABSTRACT

الأهداف: لمعرفة اثر البودرة النقية من الزنجبيل على مستوى الدهون لمجموعة من المرضى المتطوعين.

الطريقة: أجريت هذه الدراسة العشوائية المزدوجة السريرية خلال الفترة ما بين أبريل 2004م وحتى مايو 2005م، في مدينة بابول (شمال إيران). تم تقسيم المرضى الذين يعانون من فرط الدهون في الدم بشكل عشوائياً إلى مجموعتين، مجموع المعالجة: التي تلقت كبسولات الزنجبيل بمقدار 3g في اليوم على ثلاث جرعات، ومجموعة بلاسيبو: التي تلقت كبسولات لاكتوز بمقدار 3g في اليوم على ثلاث جرعات، 45 يوماً. تم استبعاد المرضى المصابين بداء السكري، نقص إفراز الدرقية، المتلازمة الكلوية، متعاطي الكحول، النساء الحوامل، و المصابين بالقرحة. قيست تركيزات الدهون قبل وبعد المعالجة بواسطة طريقة الإنزيمات.

النتائج: شارك في هذه الدراسة 45 مريضاً في مجموعة التحكم، و40 مريضاً في مجموعة بلاسيبو. كان هنالك انخفاض ملحوظ في: ثلاثي الغليسيرين، الكولسترول، ليبوبروتين منخفض الكثافة (LDL)، ليبوبروتين المنخفض الكثافة للغاية (VLDL)، ومستويات قبل وبعد الدراسة كل على حده في كل مجموعة ($p<0.05$). كانت التغيرات الفعلية في مستويات ثلاثي الغليسيرين والكولسترول لمجموعة الزنجبيل أعلى بشكل ملحوظ من مجموعة بلاسيبو ($p<0.05$). المستويات الفعلية لليبوبروتين منخفض الكثافة (LDL)، والزيادة في مستوى الليبربروتين عالي الكثافة (HDL) لمجموعة الزنجبيل أعلى من مجموعة بلاسيبو، ولكن مستويات (VLDL) لمجموعة البلاسيبو كانت أعلى من مجموعة الزنجبيل ($p>0.05$).

خاتمة: تشير هذه النتائج إلى أن لدى الزنجبيل أثر ملحوظ في تخفيض الدهون مقارنة بالبلاسيبو.

Objective: To study the effect of fine powder of ginger on lipid level in volunteer patients.

Method: This is a double blind controlled clinical trial study in 2 cardiac clinics Cardiac Disease Clinic, Babol, north of Iran, between April to May 2004. We randomly divided the patients with hyperlipidemia into 2 groups, treatment group (receiving ginger capsules 3 g/day in 3 divided doses) and placebo group (lactose capsule 3 g/day in 3 divided doses) for 45 days. All subjects with diabetes mellitus, hypothyroidism, nephrotic syndrome, and alcohol drinking, pregnancy and peptic ulcer were excluded. Lipid concentrations profile before and after treatment was measured by enzymatic assay.

Results: Forty-five patients in the treatment group and 40 patients in placebo group participated in this study. There was a significant reduce in triglyceride, cholesterol, low density lipoprotein (LDL), very low density lipoprotein (VLDL), levels of before and after study separately in each group ($p<0.05$). Mean changes in triglyceride and cholesterol levels of ginger group were significantly higher than placebo group ($p<0.05$). Mean reduction in LDL level and increase in high density lipoprotein level of ginger group were higher than the placebo group, but in VLDL level of placebo was higher than ginger ($p>0.05$).

Conclusion: The results show that ginger has a significant lipid lowering effect compared to placebo.

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Hyperlipidemia mirrors the onset of abnormality of lipid metabolism secondary to the manifestation and progression of the atherosclerotic disease. In addition to diet, the use of herbal medicine as a pharmacologic modality in preventing alteration in lipid metabolism has received a wide attention from several workers.[1] Ginger (Zingiber officinale, Zingiberaceae), a well-known spice plant, sweet, pungent, heating appetizer has been used in traditional oriental medicines for long time. Its extract and major pungent principles have been shown to exhibit a variety of biological activities.[2,3] It has been used to treat a number of medical conditions, including headache, colds, and arthritis.[4] Ginger reduces symptoms in patients with nausea of pregnancy, motion sickness, and postoperative nausea and vomiting.[5-8] Limited in vitro studies have shown that water and organic solvent extracts of ginger possess antioxidant active component in ginger properties.[9-11] The main antioxidant active materials in ginger are the gingerols and shogaols and some related phenolic ketone derivatives.[12] Ginger acts as a hypolipidemic agents in cholesterol-fed rabbits.[13] Ginger has been shown that can significantly reduce serum total cholesterol and triglyceride and increase the high density lipoprotein (HDL) cholesterol level as compared to pathogenic diabetic rats.[13] A combination of ginger and garlic has been reported to have hypoglycemic and hypolipidemic effects in albino rats.[14] Etanolic ginger extract consumption has also been shown to reduce plasma cholesterol and inhibit low density lipoprotein (LDL) oxidation in atherosclerotic, a-lipoprotein E-deficient mice.[15] It has been suggested that the aqueous extract of ginger might inhibit the intestinal absorption of dietary fat by inhibiting its hydrolysis.[16] On the other hand, one clinical study shows that ginger could not affect the blood lipid and sugar level,[17] but there are no adequate findings of clinical study of lipid lowering effect of ginger. Evidence continues to accumulate from epidemiological studies that elevated plasma concentrations of lipoprotein (a) [LP (a)] are a risk factor for a variety of atherosclerotic and thrombotic disorders.[18] High plasma levels of LP (a) are strongly associated with coronary artery disease, and LP(a) has been established as an independent risk factor and marker for atherosclerosis.[19] On the other hand, hyperhomocysteinemia is a risk factor for cardiovascular disease.[20] Plasma homocysteine predicts progression of atherosclerosis.[21] On the basis of this, in the present study we have investigated the effect of ginger on blood lipids and LP (a) and homocysteine in a double blind, placebo-control trail study.

Methods. This study was a randomized, double blind, placebo control trial performed between April 2004 and May 2005. All patients with hyperlipidemia that returned to 2 cardiac clinic in Babol (Iran) who had fasting triglyceride of >200 mg/dl or cholesterol >200 mg/dl were enrolled in this trial. Forty-five patients with hyperlipidemia in treatment group and 40 patients with hyperlipidemia in placebo group participated in this study. Exclusions criteria were diabetes mellitus, hypothyroidism, and nephrotic syndrome, alcohol drinking, pregnancy and peptic ulcer. We obtained written informed consent from all the subjects before the study period. Ethics committee of Babol University of Medical Sciences approved the study. Patients were randomized to receive ginger capsules (3 g/day in 3 divided dose) or lactose capsule (3 g/day in 3 divided dose) for 45 days. The dried rhizome of ginger was purchased from a valid market (Rezaeian, Tehran, Iran) and powdered as a fine particle. The fine powder was handed to a pharmaceutical Lab (Tehran, Iran) to prepare the capsules containing 500 mg ginger in each. Lactose (Merck, Germany) was used to prepare the placebo. Ginger (or placebo) capsules were given to all patients in one package including 6 bottles of drugs or placebo. Blood sample (5 ml) was taken before and after treatment and fasting serum triglyceride, cholesterol, HDL, LDL, and VLDL were measured by enzymatic assay and lipoprotein-a and homocysteine levels were measured using electro immunoassay and Enzyme-Linked Immuno-Sorbent Assay.

Statistical analysis was carried out using the Statistical Package for Social Sciences Version 10.5 software. Variations of lipids level were analyzed using paired sample student t-test. The differences between the groups were compared by unpaired sample student t-test, and Mann-Whitney U test and gender distribution between the 2 groups was analyzed using Fisher's exact test. Probability values of less than 0.05 were considered statistically significant.

Result. The mean ±SD age of patients in the treatment group was 53.8±11.8 years, and the control group was 53.5±11 years (p=0.905). The mean ±SD body mass index of patients in the treatment groups was 31±4.4 kg/m^2 and in the control group was 34.5±7.7 kg/m^2 (p=0.83). There were 16 (35.6%) males and 29 (64.4) females in the treatment group and 18 (45%) males and 22 (55%) females in the control group (p=0.387). **Tables 1 and 2** show the effects of administration of the ginger on the levels of lipid lipoprotein-a and homocysteine. **Table 1** demonstrates the serum lipid profile of ginger and placebo group at the beginning and at the end of the trial. Within the group analysis, the levels of triglyceride, cholesterol, LDL, VLDL, Lipoprotein-a and homocysteine were decreased in both groups at the end of the trial (p<0.05). The level of HDL increased in response to ginger (p<0.05) but not in the placebo

Table 1 - Fasting lipid, lipoprotein-a and homocysteine levels (Mean ±SEM) before and after treatment (mg/dl).

Variable	Ginger			Placebo		
	Before	After	*P*-value*	Before	After	*P*-value*
Triglyceride	320.2 ± 13.1	284 ± 11.5	0.000	331.4 ± 17.1	304.7 ± 15	0.004
Cholesterol	269 ± 4.9	241.5 ± 7.5	0.000	263.8 ± 5	249.2 ± 4.9	0.001
HDL	39.8 ± 0.7	42.6 ± 0.8	0.002	41.5 ± 1.3	41.3 ± 1	0.845
LDL	168.5 ± 5.4	151.2 ± 4.9	0.000	162.6 ± 5.3	152.7 ± 4.5	0.005
VLDL	28.9 ± 1.3	25.6 ± 0.9	0.001	31.5 ± 2.3	27.4 ± 1.4	0.008
Lipoprotein-a	23.1 ± 2	19.3 ± 1.6	0.000	29.6 ± 1.4	24.3 ± 3	0.009
homocysteine	10.7 ± 0.5	9.5 ± 0.4	0.012	10.8 ± 0.9	9.3 ± 0.5	0.012

* Paired t-test, HDL - high density lipoprotein, LDL - low density lipoprotein, VDL- very low density lipoprotein

Table 2 - Mean (±SEM) differences (mg/dl) lipids, lipoprotein-a and homocysteine between groups before and after treatment.

Variable	Ginger	Placebo	*P*-value
Triglyceride	36.2 ± 7.7	26.7 ± 8.6	0.039*
Cholesterol	27.5 ± 5.6	14.5 ± 4	0.027*
HDL	1.8 ± 0.5	0.17 ± 0.8	0.058†
LDL	17.3 ± 2.9	9.9 ± 3.3	0.093†
VLDL	3.3 ± 0.9	4 ± 1.3	0.638†
Lipoprotein-a	3.8 ± 0.9	5.2 ± 1.7	0.451†
Homocysteine	1.2 ± 0.4	1.5 ± 0.5	0.638†

* T-test, †Mann-Whitney, HDL - high density lipoprotein, LDL -low density lipoprotein, VLDL - very low density lipoprotein

group. There was a significant difference between the level of cholesterol and triglyceride in the ginger group compared to placebo (p<0.05). Some alterations were seen between the level of other parameters. Also, HDL was increased in the ginger group, but no significant differences were seen. However, the levels of LDL decreased, but the difference was not statistical significant. The dose of ginger (3 g/daily) had no effect on the concentration of VLDL, lipoprotein-a and homocysteine. Non-significant reduction in LDL was observed when ginger was administered at 3 g/daily for 45 days. The changes in the ginger treatment compared to the changes in placebo group are presented in **Table 2**. The mean changes in triglyceride and cholesterol levels of ginger receiving subjects were higher than placebo (p<0.05) (Table 2). There was no significant change in the ginger treatment group compared to placebo for lipoprotein-a and homocysteine.

Discussion. According to the result, there was a significant decrease of level of triglyceride and cholesterol after administration of ginger in comparison with placebo (p<0.05). These data were consistent with the previous studies.[17,22] Some investigations have been reported a decrease in levels of cholesterol and triglycerides in the serum of rats receiving oral and intraperitoneal administration of ginger.[23] There was a significant reduction in level of cholesterol was observed in the rats given a high dose of ginger (500 mg/kg) either orally or intraperitoneal. No significant change in triglyceride was observed in the serum of rats receiving either oral or intraperitoneal ginger. The anti-hypercholesterolemic effect of ginger was previously shown in rats fed with a high-cholesterol diet for 24 days.[24] These workers also reported that there was no immediate effect of ginger on serum cholesterol. This confirms our finding that ginger given daily for a period of 12 weeks orally significantly reduced the serum cholesterol in the patients (**Table 2**). The hypocholesterolemic effect of ginger could have possibly resulted, at least in part, from the inhibition of cellular cholesterol biosynthesis observed after consumption of ginger extract.[15] Reduced cellular cholesterol biosynthesis is associated with increased activity of the LDL receptor, which in turn leads to enhanced removal of LDL from plasma, resulting in reduced plasma cholesterol concentration.[25] These results are in agreement with previously reported data, showing that plant foods possess cholesterol-suppressive capacity.[26] It has been previously reported that the plant food-derived ingredients, ß-carotene and lycopene, also act as hypocholesterolemic agents, secondary to their inhibitory effect on cellular cholesterol biosynthesis.[27] It has been reported that consumption of 250 mg/day of ginger extract for 10 weeks resulted in reduction of triglyceride level in mice.[27] On the other hand, ethanolic extract of ginger (200 mg/kg for 10 weeks) shows reduce serum triglyceride levels in cholesterol fed rabbits compared with gemfibrozil.[1] Lipid lowering effect of ginger is possible that ginger decreased lipid by increasing pancreatic lipase and amylase,[24,28] inhibit lipid hydrolyze in intestinal tract[16] reducing lipid peroxidase[29] increasing intestinal peristaltism,[30] increasing cholesterol conversion to bile acids.[31] Feeding rats ginger significantly elevated the activity of hepatic cholesterol-7-hydroxylase, the rate-limiting enzyme in bile acids biosynthesis,

thereby stimulating cholesterol conversion to bile acids, resulting in elimination of cholesterol from the body.[31] In addition, a pure constituent from ginger [E-8 beta, 17 epoxylabd-12-ene-15, 16-dial (ZT)], was shown to inhibit cholesterol biosynthesis in homogenated rat liver.[32] However, Verma et al reported that air dried ginger powder (0.1 g/kg per os for 75 days) did not lower blood lipids to any significant extent in rabbits by cholesterol feeding (0.3 gr/kg per os).[33] In another study, patients with coronary artery disease, ginger failed to lower blood lipids when it was given in powdered form (4 g) daily for a period of 3 months.[31] In the present study, significant difference ($p<0.05$) in HDL response before and after ginger was considered after 45 days of daily intake of 3000 mg of ginger powder but there was no significant difference in placebo group. Bhandari et al[13] reported that the ethanolic extract of Zingiber officinale (200 mg/kg for 20 days) significantly increased the HDL-cholesterol level. Fuhrman et al[15] showed that consumption of 250 mg/kg of ginger extract resulted in reductions in LDL of apolipoprotein E-deficient mice.[15] Ginger extract consumption can result in accumulation of active ingredients within the cells, as well as in the cell plasma membrane, thus affecting cellular enzymes, and plasma membrane receptors. It has been shown that ginger extract consumption reduces the cellular uptake of oxidized LDL, possibly due to steric modification of plasma lipoprotein receptors.[15] We have observed no significant reduction in serum LDL levels in present study. However, the result of our study, regarding LDL level was not consistent with the previous study.[15] It may be due to the level of given dose of ginger to our patients. Since the equivalent dose of ginger extract with powder that was used in this study was 90 mg crude extract of ginger daily. That is in contrary with the previous study.[15] It was suggested that the study to be continue with different doses or different procedures. In this study, the finding of a non-significant HDL lowering effect lends itself to several possible interpretations; it is possible that ginger powder has no effect on LDL. The limitation of this study was having a single center and multicenter study with larger patients should be conducted.

In conclusion, the significant reduction in serum cholesterol by ginger could possibly play an important in the prevention and development of atherosclerosis. The unique ability of ginger to lower serum cholesterol and triglyceride levels is clinically important, because its daily intake for a prolonged period will neither lead to side-effects nor to complications as normally occurs with anti-hyperlipidemic drugs.

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