



Effects of a Stanol-Enriched Yogurt on Plasma Cholesterol Levels

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ABSTRACT

Plant stanols have been recommended in combination with individualized dietary interventions to reduce plasma cholesterol concentrations. Even though yogurt is consumed in high quantities in Turkey, it is unclear whether yogurts with plant stanols will reduce high cholesterol levels in a Turkish population. We designed this study to settle this issue. We investigated the effect of plant stanols in yogurt, combined with the traditional Mediterranean diet (TMD), in subjects with high lipid levels. 100 patients were included: 50 in the intervention group and 50 in the control group. Neither the subjects nor the control group were taking any medication for cholesterol. The intervention group received 100 mls of stanol-enriched yogurt, while the control group received the same amount of yogurt without plant stanols. All subjects maintained TMD. Total cholesterol and LDL cholesterol levels decreased significantly in the stanol group (12.9%, 14.9%, respectively). In the control group, a slight decrease in LDL cholesterol (3.3%) was observed. The changes in total and LDL cholesterol between the two groups were significantly different ($p=0.01$). Intensive dietary intervention with the addition of plant stanols results in a clinically relevant reduction of total and LDL cholesterol in patients with high lipid levels.

Key words: Cholesterol, diet, stanol, Turkey, yogurt

Stenolden Zengileştirilmiş Yoğurtların Plazma Kolesterol Düzeylerine Etkisi

ÖZET

Plazma kolesterol seviyesini düşürmek için kişiselleştirilmiş diyet uygulamaları ile birlikte bitkisel stanoller tavsiye edilir. Türkiye'de yoğurt tüketimi çok fazla miktarda olmasına rağmen stanollü yoğurtların Türk milletinde yüksek kolesterol değerini düşürüp düşürmediği net belli değildir. Bu konuyu ortaya çıkarmak amacıyla bu çalışma planlanmıştır. Yüksek lipid seviyeli bireylerde, geleneksel akdeniz diyeti ile beraber bitkisel stanollü yoğurt kombinasyonunun etkilerini araştırdık. 50 kişi çalışma grubu 50 kişi kontrol grubu olmak üzere 100 hasta çalışmaya dahil edildi. Ne çalışma grubu ne de kontrol grubu kolesterol tedavisi için ilaç almıyordu. Çalışma grubu 100ml stanollü yoğurt alırken kontrol grubu stanolsüz yoğurt aldı. Bütün bireyler akdeniz diyeti yaptı. Stanol grubunda total kolesterol ve LDL kolesterol seviyesi bariz olarak düştü. (%12.9, %14.9 sırasıyla). Kontrol grubunda LDL kolesterolde hafifçe düşme görüldü (%3.3). İki grup arasında Total ve LDL kolesterol deki değişimler oldukça farklıydı ($p=0.01$). Yüksek lipid seviyeli hastalarda yoğun diyet tedavisine bitkisel stanollerin eklenmesi Total ve LDL kolesterol seviyelerinde düşmeye neden olur.

Anahtar kelimeler: Kolesterol, diyet, stanol, Türkiye, yoğurt

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INTRODUCTION

Cardiovascular disease (CVD) remains an important factor in morbidity and mortality. The incidence of CVD is directly related to blood cholesterol level. Hypercholesterolemia is one of the most important modifiable risk factors for atherosclerosis. According to many studies, every 1% drop in cholesterol level results in a 2% decrease in the CVD rate (1). Several randomized clinical trials have shown that reducing plasma cholesterol concentrations leads to a significant and clinically relevant decreased risk for atherosclerotic events (2). For this reason, various medications and lifestyle alterations have been suggested. Studies of statins have resulted in guidelines for reduced morbidity and mortality in at-risk patients (3). When LDL targets are not achieved with lifestyle interventions, statin medications are recommended. Some patients still do not reach target lipid levels with a combination of statin therapy and lifestyle interventions. Until recently, bile acid sequestrants or nicotinic acid were recommended in addition to statins and lifestyle interventions in these patients. However, these compounds are not ideal due to their side effect profiles. Alternatively, combination therapy with statins and fibrates is an option. However, this treatment brings the risk of elevated muscle enzymes and, potentially, rhabdomyolysis.

Among the alterations in lifestyle are consuming a healthy diet, exercise and dietary supplements, such as herbal sterols and stanols. Sterols and stanols have been known since the 1950's. Structurally, they are cholesterol analogues. Plant stanols and sterols have also been recommended in patients with mild hypercholesterolemia and in patients who do not reach their targets for lipid levels (4). Plant stanols decrease plasma cholesterol concentrations by reducing the intestinal absorption of cholesterol, thereby increasing the hepatic expression of LDL receptors and reducing the production of endogenous LDL cholesterol (5). This effect of stanols may reduce the risk of atherosclerosis (6). Combinations of plant stanols with antilipidemic drugs have been found to be more effective than individual usage, and an additional 17 % drop in serum cholesterol level was achieved using such a combination (7). We have investigated whether this intervention can reduce plasma cholesterol concentrations in a Turkish population.

MATERIALS AND METHODS

Patients

Patients were recruited at the Department of Internal Medicine of the Medical Park Goztepe Hospital, Istanbul. The Medical Ethics Committee approved the study, and all patients gave written informed consent. One hundred patients were included. The inclusion criteria were the following: primary hyperlipidemia and not currently receiving any medication for dyslipidemia. Exclusion criteria were the following: obesity (body mass index (calculated as kg/m²) >30), previous use of plant stanol or plant stanol-containing products, plasma cholesterol concentrations less than 200 mg/dL or more than 400 mg/dL, a recent (within 6 months) myocardial infarction or any other cardiovascular event, the use of any other drug that may affect intestinal cholesterol absorption (such as bile acid sequestrants or ezetimibe).

Study Design

All patients were screened and were randomly assigned to the intervention group (plant stanol enriched yogurt and TMD) or a control group (regular yogurt and TMD). The intervention period lasted for eight weeks. Fasting blood samples were taken at inclusion and after eight weeks of follow-up. A food frequency questionnaire (FFQ) was filled out at baseline, after one week and after eight weeks to assess adherence to the dietary guidelines (8). All participants visited the department at one and eight weeks and had an interview with a dietitian to enhance adherence. Anthropometric characteristics were recorded.

Yogurt

The intervention group received a plant stanol-enriched yogurt containing 2 gr of stanol (Benecol, Johnson & Johnson, Tilburg, the Netherlands) and TMD, while the control group received the same amount of regular yogurt without stanol and TMD. The intervention subjects were asked to use 100 mls of yogurt with 2 gs of plant stanols each day, which is the daily advised dosage to reduce LDL cholesterol (4).

Dietary Guidance

On the basis of their initial assessment, each participant was given personalized dietary advice by the dietician during a 30-minute session. Participants allocated to a low-fat diet were advised to reduce all types of fat and were given written recommendations according to

the American Hospital Association guidelines (10). The TMD includes the use of olive oil for cooking and dressing; increased consumption of vegetables, nuts, and fish products; consumption of white meat instead of red or processed meat; preparation of home-made sauce by simmering tomato, garlic, onion, and aromatic herbs with olive oil to dress vegetables, pasta, rice, and other dishes; and, for alcohol drinkers, following a moderate pattern of red wine consumption. No energy restrictions were suggested for the groups. One week after a participant's inclusion, the dietician delivered a one-hour group session for each group, with up to 20 participants per session. Each session consisted of an informative talk and written material with elaborated descriptions of typical Mediterranean foods, seasonal shopping lists, meal plans, and recipes. All participants had free and continuous access to their dietitian throughout the study.

Clinical Chemistry

Venous blood samples were collected after a 12-hour fast. Plasma cholesterol, triglycerides, and high-density lipoprotein cholesterol levels were measured by standard procedures in our laboratory (11). LDL cholesterol was calculated by the Friedewald Formula (12). We excluded those patients whose triglyceride level was so high that their Friedewald estimate of LDL was inaccurate.

Anthropometrics and Body Composition

Body weight without shoes or coat was measured and recorded in kilograms on a calibrated scale. Height was measured in centimeters using a measuring tape while the patient was standing straight with heels together,

feet angled about 45°, and the eyes and the top of the ears in a horizontal line (Frankfurter plane). Waist circumference was measured in centimeters over the patient's umbilicus, and hip circumference (also in centimeters) was measured at the largest points of the hips (trochanter height or symphysis height in patients with high subcutaneous fat tissues).

Statistical Analysis

Data are expressed as means±standard deviation. Differences between the intervention groups were tested by Student's t test and within each group by paired t test. Statistical significance was reached when $P < 0.05$ (two-tailed). Calculations were performed using SPSS/PC version 10.0 (SPSS Inc, Chicago, IL).

RESULTS

Table 1 shows the general characteristics, fasting plasma lipids, and apolipoproteins of the patients on experimental and control regimens in a study investigating the effect of plant stanols in yogurt in subjects on TMD. Age, gender, and BMI were not different between the two groups. Baseline lipid parameters were also not different between the two groups. Total cholesterol and LDL cholesterol decreased significantly in the stanol group (12.9 % and 14.9 %, respectively). A slight decrease in LDL (3.3%) was observed in the control group. The changes in total and LDL cholesterol between the two groups were statistically significant ($p=0.01$). There was no significant difference in HDL cholesterol and triglyceride levels between the two groups. The mean body weight in the control group decreased from 70.2 ± 11.3

Table 1. General characteristics, fasting plasma lipids, and apolipoproteins of the patients on experimental and control regimens in a study investigating the effect of plant stanols in yogurt in subjects on TMD.

	Experimental Group (n:50)		Control Group (n:50)		p value
	Before	After	Before	After	
Age (years)	41±9.9	—	41.7±12.3	—	0.55
Gender (male/female)	24/26	—	25/25	—	0.80
BMI (kg/m ²)	26.5±2.5	26.2±2.5	27.5±4.8	27.2±4.9	0.45
Body weight (kg)	70.2±11.3	69.2±11.9	72.2±14.3	72.2±14.5	0.07
Total Cholesterol (mg/dL)	256.3±29.7	223.1±26.7**	261.8±54.0	255.2±42.5	0.01
LDL-c (mg/dL)	164.8±25.4	140.3±19.2**	160.7±57.9	155.3±50.2	0.01
HDL-c (mg/dL)	39.7±11.6	39.8±11.2	39.4±14.3	40.6±16.6	0.25
Triglyceride (mg/dL)	194.7±44.9	188.2±38.4	180.5±70.8	170.2±88.5	0.36
Glucose (mg/dL)	88.4±10.4	88.6±9.8	89.4±10.2	88.8±10.3	0.74

BMI, body mass index; LDL-c, low-density lipoprotein cholesterol; HDL-c, high-density lipoprotein cholesterol; $p < 0.01$

kg to 69.2±11.9 kg (without reaching statistical significance ($p=0.07$)) compared with the plant stanol group (72.2±14.3 kg at inclusion and 72.2±14.5 kg at the end of the study).

DISCUSSION

The main finding of our study was a 12.9% extra reduction of total cholesterol and a 14.9% extra reduction of LDL cholesterol in hyperlipidemic patients given yogurt enriched with plant stanols. It has been reported that plant stanols reduce total cholesterol by 10% and LDL cholesterol by 10% to 15% (4). Our study confirms these results. Plant stanols are specific inhibitors of intestinal cholesterol absorption (4-13), which is a different mode of action than bile acid sequestrants. Bile acid sequestrants impede bile re-absorption, thereby indirectly reducing cholesterol absorption (14). Whereas the daily intake of cholesterol can be 300 mg, a larger proportion (900 mg daily) reaches the intestinal lumen due to bile secretion, as has been shown in a recent study (15). Plant stanols and sterols decrease intestinal cholesterol uptake by 40% (13,14). This would result in less hepatic delivery of exogenous cholesterol and therefore up-regulation of the hepatic LDL receptors. The consequence would be decreased hepatic very low-density lipoprotein (VLDL) secretion. It is likely that the decrease of blood lipids was caused by the plant stanols provided to the patients in the yogurt. Based on self-reports from the FFQ, it may be concluded that at least 85% of the patients adhered sufficiently to the dietary guidelines. The intake of plant stanols from foods other than the stanol yogurt is expected to be only approximately 40 mg per day and was probably not different between the intervention and the control group (16).

In control subjects, LDL cholesterol levels dropped only a very modest 3.3% from 160 mg/dL to 155 mg/dL. This finding was in agreement with studies in which the TMD has been applied (17). Yogurt and other milk products have been studied in the literature in the context of serum lipid lowering. It has been shown that low-fat milk products enriched with plant stanol esters lower both total cholesterol and LDL cholesterol significantly in subjects with mild or moderate hypercholesterolemia (17). In another study, the consumption of one yogurt serving per day containing 2 g of stanol significantly reduced cholesterol levels; this effect was not observed with placebo (18). In our study, a mean decrease of 12.9

% in serum total cholesterol and 14.9% in serum LDL cholesterol was observed. Thus, lowering cholesterol levels with a yogurt drink including stanols has been demonstrated in western countries, and similar results have also been obtained in a Turkish population.

The limitations of this study include its small size and short follow-up. Larger studies with a much longer follow-up period and a more representative sample will be necessary to establish the clinical significance of dietary education and the addition of plant stanols as first line therapy. Preferably, these trials should also include hard endpoints for cardiovascular disease.

In conclusion, the addition of a stanol-enriched yogurt to the diet of hyperlipidemic subjects resulted in a reduction of LDL-cholesterol compared with a control group. These findings should be considered when LDL target values are not reached with life style recommendations and before starting lipid lowering medications. A TMD improved serum lipid levels only slightly in this group of patients whose diet already complied with published guidelines.

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