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ARTICLE

Reduction of Serum Cholesterol in Postmenopausal Women With Previous Myocardial Infarction and Cholesterol Malabsorption Induced by Dietary Sitostanol Ester Margarine

Women and Dietary Sitostanol

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ABSTRACT: *Background* Reduction of serum cholesterol decreases mortality in primary and especially in secondary prevention. We investigated how effectively postmenopausal women with a previous myocardial infarction reduced their serum cholesterol with dietary means by using sitostanol ester rapeseed oil margarine, alone and in combination with statins, and to what extent cholesterol metabolism was affected.*Methods and Results* The first study group consisted of 22 randomly chosen women with angiographically documented coronary artery disease. Baseline studies on home diet were followed by double-blind, randomized, cross-over studies on margarine without and with sitostanol (3 g/d) ester for 7 weeks in random order. A second group of 10 women on simvastatin consumed sitostanol ester margarine for 12 weeks. Sitostanol ester margarine lowered serum total cholesterol by 13% (*P*<.05) and LDL cholesterol by 20% (*P*<.01). Sitostanol ester margarine reduced total cholesterol in all patients, LDL cholesterol <2.6 mmol/L (<100 mg/dL) in 32%, and <3.4 mmol/L (<133 mg/dL) in 73% versus none and 27% during the home diet (*P*<.01 for both). Combined with simvastatin, sitostanol still reduced total and LDL cholesterol by 11±3% and 16±5% (*P*<.01 for both). Sitostanol reduced absorption (−45%), increased fecal elimination (+45% as neutral sterols), and stimulated synthesis (+39%) of cholesterol. High cholestanol and plant sterol (high cholesterol absorption) and low baseline precursor sterol proportions (low cholesterol synthesis) predicted high decreases in serum cholesterol.*Conclusions* Dietary use of sitostanol ester margarine normalizes LDL cholesterol in about one third of women with previous myocardial infarction, especially in those with high baseline absorption and low synthesis of cholesterol, and in combination with statins reduces the needed drug dose.

Key Words: cholesterol ■ women ■ myocardial infarction ■ diet

Recent studies have convincingly shown that effective serum cholesterol reduction by about 25% with current cholesterol synthesis inhibitors decreases significantly total and coronary mortality in primary and especially secondary prevention[1 2 3] in both sexes.[2 3] This also indicates that women with coronary heart disease and increased serum cholesterol should be treated effectively with cholesterol-lowering measures. The findings also suggest that

hypolipidemic treatment with cholesterol synthesis inhibitors is beneficial for women with previous myocardial infarction ("coronary women") with relatively low serum cholesterol level (total cholesterol <6.2 mmol/L and LDL cholesterol from 3.0 to 4.5 mmol/L).[3] The respective mean decrease in the serum total LDL cholesterol concentrations were 20% and 28%.[3] On the other hand, serum cholesterol reduction can be achieved also by inhibition of cholesterol absorption. A combination of neomycin and sitostanol ester margarine almost totally inhibited cholesterol absorption, which resulted in a 37% reduction in the serum concentrations of total and LDL cholesterol.[4] By sitostanol ester alone, the respective decreases were 10% and 14% in a mildly hypercholesterolemic random population.[5] Sitostanol ester margarine lowers serum cholesterol by changing dietary fatty acid composition to less saturated and richer in monoenes and by causing cholesterol malabsorption. Accordingly, the purpose of the present study was to investigate how often optimal LDL cholesterol level can be reached with dietary measures by using only sitostanol ester margarine, alone or in combination with statins, in women with a previous myocardial infarction, and to which extent cholesterol metabolism is altered.

METHODS

Patients

The study population consisted of two groups of postmenopausal coronary women. The first group, selected randomly in 1993, consisted of 30 successive coronary women with no earlier estrogen therapy. Two of these patients were excluded because of hypolipidemic medication and 6 because of living too far away. Thus the study population included 22 women. Serum lipid levels were not an excluding factor. Angiography had been performed in all women, coronary artery bypass surgery in 8, and percutaneous transluminal angioplasty in 11. Our main focus is on this group not treated with lipid-lowering agents. The second group consisted of 10 coronary women who had been treated with simvastatin 10 to 20 mg/d over 1 year. All patients were 48 to 56 years old, and they had no thyroid, liver, or renal problems or diabetes mellitus. Myocardial infarction, angioplasty, or coronary bypass operation had occurred at least 3 months earlier. Some baseline data are shown in Table 1.

Study Procedure

After the run-in period on ad libitum home diet, the patients without previous hypolipidemic treatment were randomized to replace 21 g of their daily fat intake by rapeseed oil margarine without (n=11) or with sitostanol ester (n=11) for the next 7 weeks followed by switching of the margarines for another 7-week period. The amount of sitostanol in 21 g of the margarine was 3 g. The patients were advised to use the margarine daily in three divided doses, mostly on a piece of bread during the three major meals. The simvastatin group also replaced 21 g of their daily fat intake by sitostanol ester margarine for 12 weeks.

At the baseline home diet and at the end of both 7-week treatment periods, metabolic studies were performed in the first group. Two fasting blood samples were obtained at the end of a 7-day food diary. During that period, the patients consumed capsules containing Cr_2O_3 (200 mg), ^{14}C-cholesterol (4500±19 [SE] DPM), and ^{3}H-cholesterol (11 588±42 DPM), one with each of the three daily meals. Three-day stool collections were performed at the end of the week.

In the simvastatin group, serum and lipoprotein lipids were analyzed from two fasting blood samples at the beginning of the study on the home diet and simvastatin and at the end of 12

weeks on simvastatin and sitostanol ester margarine. No further metabolic studies were performed in this group.

The study protocol was accepted by the Ethics Committee of the Second Department of Medicine, University of Helsinki.

Methods

Serum and lipoprotein total and free cholesterol, triglycerides, and phospholipids and HDL cholesterol were determined enzymatically with commercial kits (Boehringer Diagnostica and Wako Chemicals). Means of two serum total cholesterol and triglyceride and HDL cholesterol determinations were used for each individual at each time point. Serum lipoproteins were separated once by density gradient ultracentrifugation at the end of each period in a Ti 50.4 fixed-angle rotor (Beckman Instruments) into the following density classes: VLDL <1.006 g/mL; IDL 1.006 to 1.019 g/mL; LDL 1.019 to 1.063 g/mL; and HDL 1.063 to 1.210 g/mL.

Serum sterols were determined twice at the end of each period by gas-liquid chromatography from nonsaponifiable serum material on a 50-m long SE-30 capillary column.[6 7 8] The procedure measures total cholesterol and noncholesterol sterols, including cholesterol precursors Δ^8-cholestenol, desmosterol and lathosterols (sterols reflecting cholesterol synthesis),[7 9 10 11 12 13 14] plant sterols, campesterol and sitosterol, and cholestanol (sterols reflecting cholesterol absorption).[14 15] To eliminate the effect of changing lipoprotein level, the noncholesterol sterol values are standardized and expressed in terms of 10^2×mmol/mol of cholesterol, that is, in proportions or ratios to serum total cholesterol.

Elimination of cholesterol from the body and cholesterol absorption efficiency were measured once in each period from the 3-day stool collections. Cholesterol absorption efficiency was calculated by the altered $^{14}C/^{3}H$ ratio in stools as compared with the fed ratio,[16] and the Cr_2O_3 measurement[17] was applied to the measurement of fecal flow. Fecal cholesterol as fecal neutral sterols (cholesterol, coprostanol, and coprostanone), bile acids, and plant sterols were quantitated by gas-liquid chromatography.[6 18 19] Dietary intake of fatty acids and cholesterol were determined from the 7-day diaries by a computer method applied to the country's dietary ingredients.[20]

Calculations

Cholesterol synthesis was calculated by the sterol balance technique as the difference between the sum of fecal neutral sterols plus bile acids and dietary cholesterol. Intestinal total influx of cholesterol was obtained by dividing fecal neutral sterol fraction (=fecal cholesterol) by (1-fractional cholesterol absorption). The total intestinal influx minus dietary cholesterol represents biliary cholesterol. Respective absorption of each intestinal cholesterol fraction is obtained by multiplication of each flux by absorption efficiency. Unabsorbed dietary and biliary cholesterol fractions are differences between the intestinal influxes and the respective absorbed fractions.

Statistics

The mean±SE values were calculated, and the changes were analyzed by the paired *t* test or ANOVA. The correlation coefficients were determined by the Pearson's product-moment correlation coefficient. Logarithmic transformations were used when appropriate.

RESULTS

The coronary women had been on a cholesterol-lowering diet since discharge from the hospital. Thus dietary cholesterol intake was low, 247 mg/d, and the diet contained 15 energy % (E%) of saturated, 13 E% of monoenic and 6 E% of polyenic fatty acids, and 36 E% of fat (Table 1). The polyunsaturated/saturated fatty acid ratio was 0.43. Replacement of 21 g of the baseline dietary fat by the same amount of the rapeseed oil margarine without or with sitostanol ester reduced dietary cholesterol intake slightly but significantly by about 15% ($P<.05$) and had no effect on fat intake but tended to increase the intake of monoenic and polyenic fatty acids and decrease saturated fatty acid intake so that the polyunsaturated/saturated fatty acid ratio increased significantly to 0.52±0.02. Body weight was not changed during the 14-week period.

Home Versus Margarine Diet

Serum lipids for the 22 coronary women with no previous hypolipidemic treatment are shown in Table 2. The shift from the home diet to the rapeseed oil margarine significantly reduced total, VLDL, and LDL cholesterol and HDL triglycerides (−5%; $P<.05$).

A relatively high campesterol content in the rapeseed oil margarine increased the campesterol proportion in serum by 13% ($P<.01$), but, in contrast to our earlier findings,[21] had no effects on the precursor sterol proportions (Table 3). Fecal steroid output and cholesterol absorption were not consistently changed (Table 4).

Sitostanol Ester Margarine Diet

Serum Lipids Table 2 shows that the rapeseed oil margarine with sitostanol ester lowered serum total and LDL cholesterol by 8% and 15%, respectively, from those without sitostanol, and 13% and 20% from the home diet values. The higher the home LDL cholesterol concentration, the higher was its decrease ($r=-.434$; $P<.05$). Thirty-two percent of the patients had their LDL cholesterol level <2.6 mmol/L (<100 mg/dL), a recommended level according to the NCEP guidelines,[22] and 73% <3.4 mmol/L (<133 mg/dL) during the sitostanol ester margarine treatment, the respective figures being none and 27% during the home diet ($P<.01$ for both comparisons). Even though the mean levels of VLDL, HDL, and total triglycerides only tended to decrease, the higher their home values, the higher were the changes ($r=-.553$ to $-.792$, $P<.01$ to .001). The ratio of HDL/LDL cholesterol was increased by 24% and 26% from the margarine and home diet periods, respectively. Fig 1 shows that 32% of the patients exhibited a decrease in serum cholesterol from the home values by margarine without sitostanol, the respective value being 100% when sitostanol was present.

In the coronary women treated with simvastatin over 1 year, sitostanol ester reduced total cholesterol by 11±3% and LDL cholesterol by 16±5% ($P<.05$ for both, Table 5). The respective simvastatin-induced reductions had been −23% and −35%, and the respective overall reductions, accordingly, were −32% and −46%. Seven of the patients exceeded 2.6 mmol/L during simvastatin, only two exceeded that during the combined treatment.

Noncholesterol Sterols The serum cholesterol reduction from the home period by the sitostanol ester margarine was associated with up to 33% decreases in the proportions of cholestanol, campesterol, and sitosterol and by up to 14% increases in those of the precursor sterols (Table 3). In fact, the higher the decreases in the plant sterol proportions, especially in that of sitosterol, the higher were the reductions in the total and LDL cholesterol (r=up to .676, $P<.01$). The higher the home or margarine period proportions of cholestanol and plant sterols, the higher were their sitostanol-ester induced reductions (Table 6). The higher the basal precursor sterol proportions,

the lower was the LDL cholesterol decrease, whereas the high cholestanol proportion, clearly less than those of plant sterols, predicted high LDL cholesterol lowering (Table 6).

Absorption and Fecal Output of Cholesterol Fecal steroids, shown in Table 4, revealed that cholesterol absorption efficiency was decreased by 45%, resulting in up to 45% and 28% increases in fecal elimination of cholesterol as neutral sterols alone or in combination with bile acids, respectively. Sitostanol ester increased fecal elimination of both dietary and biliary cholesterol (Table 4), which was balanced by enhanced synthesis, up to 39%, and turnover of cholesterol.

Cholesterol absorption was negatively correlated with cholesterol synthesis on the home, margarine, and sitostanol ester margarine diets (Fig 2). The sitostanol-induced change in LDL cholesterol was significantly associated with the change in cholesterol absorption efficiency (r=.443). In addition (Table 6), the high home proportions of the serum plant sterols and cholestanol and absorption efficiency of cholesterol predicted their high reductions by sitostanol ester margarine (r value ranged from −.678 to −.863, P<.001). On the other hand, the higher the synthesis at home, the smaller was the increase in synthesis and the smaller the decrease in cholesterol absorption. The changes in the plant sterol and cholestanol proportions were negatively related to those of fecal plant sterols shown for sitostanol (identical with dietary intake) in Fig 3 and cholesterol synthesis. However, the decrease of serum cholesterol was not related to the dietary intake of cholesterol, indicating that the total and LDL cholesterol concentrations were decreased similarly in subjects on diets low or high in cholesterol.

DISCUSSION

The present findings showed for the first time that sitostanol ester margarine effectively inhibited cholesterol absorption, which then reduced the LDL cholesterol levels in 32% of the patients to <2.6 mmol/L (<100 mg/dL) compared with none during home diet in postmenopausal women with coronary heart disease. Thus the 15% reduction of serum total and 20% of the LDL cholesterol level were reduced to about 5% by the rapeseed oil margarine and 10% to 15% by sitostanol ester present in that margarine. Combination of sitostanol ester margarine to simvastatin therapy further reduced serum total and LDL cholesterol by 11% and 16%, respectively, so that most of the women exceeding the 100 mg/dL limits were now below that value. These results indicate that one third of coronary women can be treated normolipidemic by dietary sitostanol ester margarine only. The simultaneous use of sitostanol ester and statin is more effective than statin alone, reducing the statin dose needed or even eliminating the drug.

The serum cholesterol lowering by sitostanol in the present coronary female patients is roughly similar to that obtained earlier in other mainly male subjects on scheduled 3 to 3.4 g/d of sitostanol.[23 24] The present findings in fecal elimination of cholesterol and serum noncholesterol sterols indicated that cholesterol absorption was markedly reduced by the sitostanol addition, increasing fecal output of cholesterol as neutral sterols, but having no effect on fecal bile acids and, accordingly, on bile acid synthesis. However, the increase in fecal elimination of cholesterol was balanced by a compensatory increase in turnover and synthesis of cholesterol, shown by the sterol balance data and cholesterol precursor sterols in serum, limiting the actual decrease in serum cholesterol. However, in view of the cholesterol-lowering diet, which the patients were using in home conditions, the advice to replace 21 g of their dietary fat by the sitostanol ester margarine further changed the diet to be more beneficial for cholesterol lowering so that the 15% usual fall in

LDL cholesterol by sitostanol itself was increased to 20% by the combined action of both margarine and sitostanol. This effect is about equal to that obtained by 10 mg of lovastatin or pravastatin,[25] [26] indicating that sitostanol ester margarine can be considered to be beneficial also from the economic point of view.

Sitosterol has been suggested to inhibit more effectively intestinal absorption of dietary than biliary cholesterol.[27] Accordingly, an unaltered serum cholesterol level by capsules, containing sitostanol in oil as suspension, was considered to be caused by ineffectiveness of sitostanol in subjects on a diet low in cholesterol.[28] We believe that dietary intake of sitostanol in fat-soluble form, as it is in our sitostanol ester margarine, was more effective than that in insoluble form (suspension). In the present series, the dietary intake of cholesterol was low, about 207 mg/d, with a range from 77 to 383 mg/d, yet there was no correlation between the decrease in the serum total or LDL cholesterol levels with the dietary intake of cholesterol. In addition, the calculations in Table 4 indicated that absorption of both dietary and biliary cholesterol were partly inhibited by sitostanol. Even if no dietary cholesterol were absorbed during the sitostanol period (fecal unabsorbable dietary cholesterol equaled dietary cholesterol intake of 207 mg), fecal output of biliary cholesterol was still significantly increased.

Who, then, is most responsive to the sitostanol ester margarine? The highest decrease in serum total and especially LDL cholesterol was obtained in patients with the highest respective baseline levels. These subjects also had the highest cholesterol absorption, as shown by absorption percentage or especially the serum cholestanol and plant sterol proportions, and the lowest precursor sterol proportions. The findings indicate that the basal serum precursor sterols predict the subjects mostly responsive to cholesterol malabsorption. Similar association between serum cholesterol decrease and noncholesterol sterol proportions has been observed earlier in sitostanol ester series of mainly male subjects.[23] [24] In addition, serum cholesterol value and cholesterol absorption efficiency are positively correlated with each other in a normal male population.[29] It is thus obvious that the higher the baseline total and LDL cholesterol concentrations and the serum cholestanol and plant sterol proportions and the lower the baseline precursor sterol proportions, the higher is the decrease in LDL cholesterol during sitostanol ester margarine also in postmenopausal coronary women. This would mean that sitostanol ester margarine, causing cholesterol malabsorption, is most effective in subjects in whom cholesterol absorption is high and cholesterol synthesis is correspondingly low.

As already noted, one third of the coronary women in this study obtained LDL cholesterol that was <2.6 mmol/L only with dietary means. Currently published studies[2] [3] clearly suggest that effective cholesterol lowering beneficially prevents recurrent coronary events. Accordingly, a combination of cholesterol malabsorption by sitostanol ester with statin could be beneficial, especially for the patients not responding satisfactorily to sitostanol ester margarine alone. As shown above, the subjects with high cholesterol synthesis are nonresponders to sitostanol ester and should be beneficially responding to statins. Recent preliminary studies of a 4S subgroup suggest, in fact, that subjects with low synthesis and high absorption of cholesterol did not respond, whereas those with high synthesis and low absorption responded to simvastatin-induced reduction of major coronary events.[30] A synergistic effect has been recently found[31] and observed also in the present study for cholesterol lowering by combined statin and sitostanol treatment. Thus it can be expected that a combination of sitostanol ester margarine to simvastatin treatment of coronary patients with high cholesterol absorption (detected by high baseline serum cholestanol and plant sterol and low precursor sterol proportions) will improve the response to reduced recurrence of coronary events.

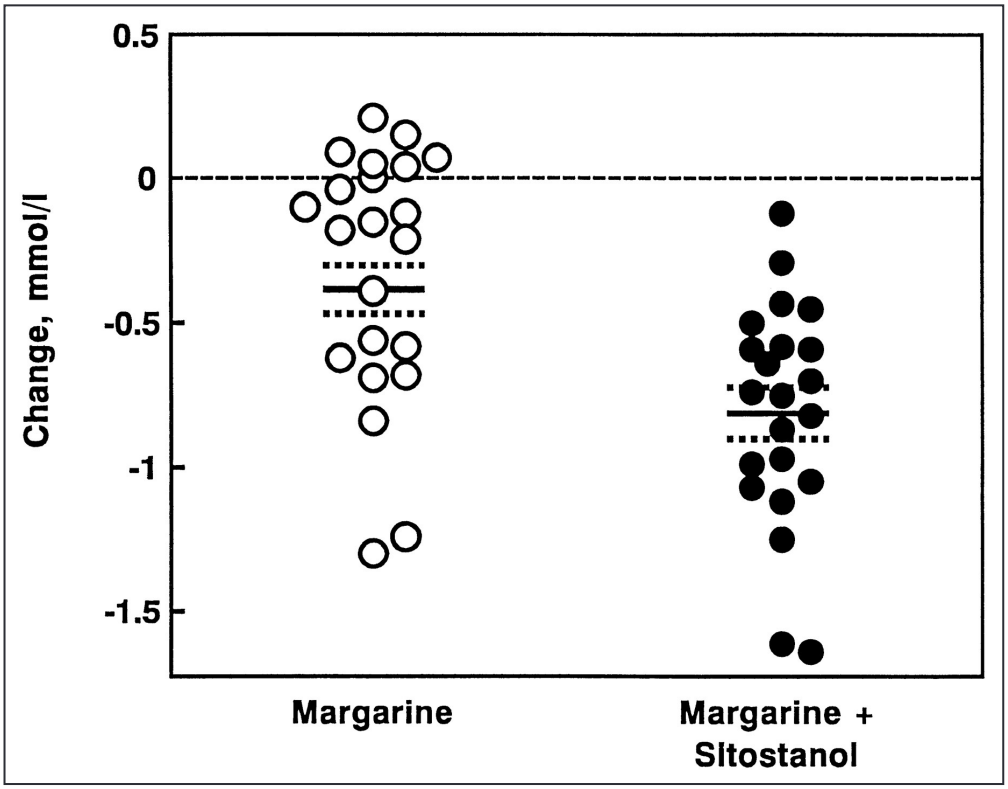

Figure 1. Serum cholesterol changes from baseline home values by margarine without (left) and with sitostanol ester (right) in women with previous myocardial infarction without previous hypolipidemic treatment. Mean±SE values indicated by horizontal lines.

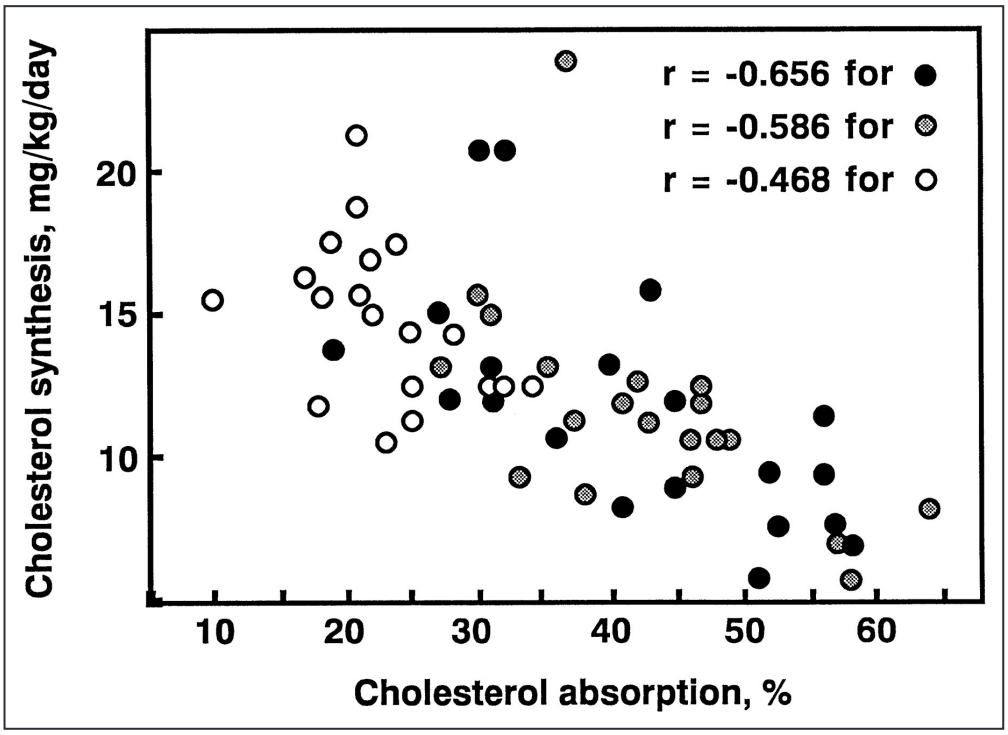

Figure 2. Correlation of relative cholesterol absorption with cholesterol synthesis on home diet (black circles) and margarine without (shaded circles) and with (open circles) sitostanol ester in women with previous myocardial infarction without previous hypolipidemic treatment.

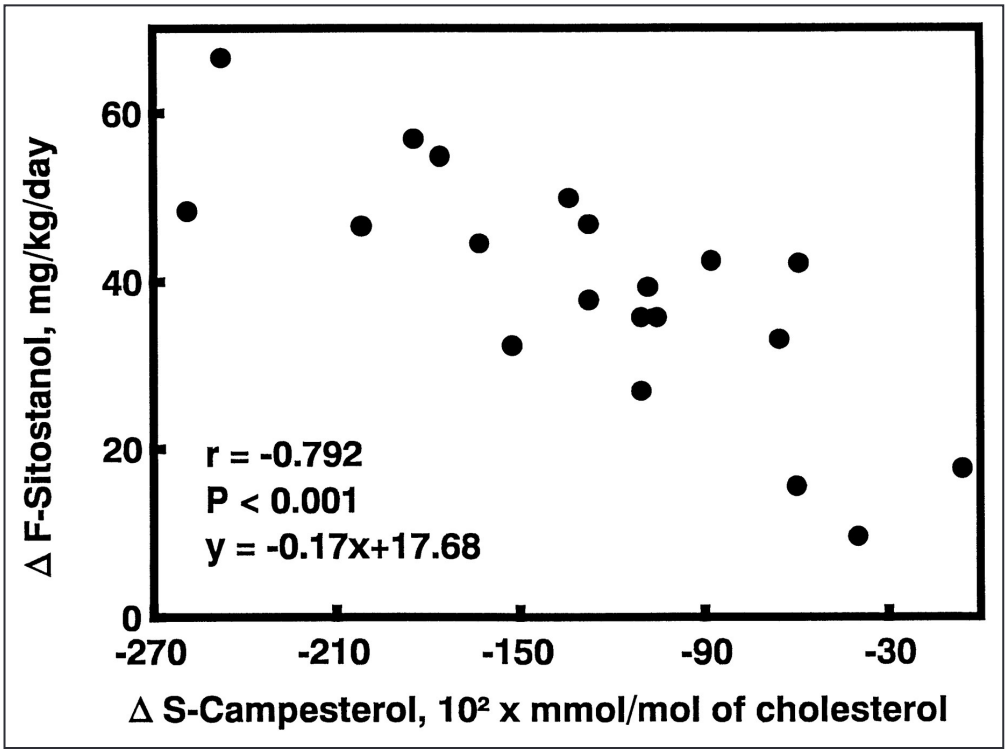

Figure 3. Correlation between changes in serum (S) campesterol and fecal (F) sitostanol in coronary women without previous hypolipidemic treatment.

Table 1. Study Population of Postmenopausal Women With Previous Myocardial Infarction Without Previous Hypolipidemic Treatment (n=22) (Table view)

Variables	Mean±SE	Range
Age, y	51 ±1	48-56
Body weight, kg	68±2	53 -86
Body mass index, kg/m^2	26.0±0.7	21-33
Dietary cholesterol, mg/d		
Home diet	247 ±17	96-431
Margarine	207±17[1]	77-383
Dietary fat, g/d		
Home diet	67±4	33-100
Margarine	65 ±4	33-102
Saturated fat		
Home diet	28±4	14-54
Margarine	24±2	15-39
Monoenes		
Home diet	23 ±3	9-37
Margarine	25±1	16-35
Polyunsaturated		
Home diet	11±1	6-16
Margarine	12±1	8-15
P/S ratio		
Home diet	0.43±0.04	0.29-0.66
Margarine	0.52 ±0.02[1]	0.31±0.77

P/S indicates polyunsaturated/saturated.
[1] *P*<.05 or less, margarine vs home diet.

Table 2. Serum Total and Lipoprotein Lipids (mmol/L) in Women With Previous Myocardial Infarction Without Previous Hypolipidemic Treatment (n=22) on Different Diets (Table view)

Variables	Home Diet	Rapeseed Oil Margarine	Rapeseed Oil Margarine+ Sitostanol Ester
	Total		
Cholesterol[1]	6.26 ±0.20	6.01±0.22[1]	5.46±0.21[1 2]
Phospholipids[1]	3.17±0.09	3.07±0.09	2.96 ±0.10
Triglycerides[1]	1.36 ±0.11	1.40±0.16	1.28±0.10
	VLDL		
Cholesterol, total	0.42±0.06	0.34 ±0.06[1]	0.35±0.04
Cholesterol, free	0.19 ±0.02	0.16±0.02	0.17±0.02
Cholesterol, esterified	0.23±0.03	0.18±0.03[1]	0.18±0.02[1]
Phospholipids	0.30±0.04	0.27±0.04	0.27±0.03
Triglyceride	0.78±0.10	0.74±0.12	0.74 ±0.08
	IDL		
Cholesterol, total	0.24±0.03	0.21±0.04	0.18±0.02[2]
Cholesterol, free	0.08±0.01	0.07±0.01	0.06 ±0.01[2]
Cholesterol, esterified	0.16±0.02	0.14 ±0.03	0.12±0.02[2]
Phospholipids	0.10±0.01	0.09 ±0.01	0.08±0.01
Triglyceride	0.10 ±0.01	0.09±0.01	0.08±0.01
	LDL		
Cholesterol, total	3.85±0.17	3.66 ±0.19[1]	3.13±0.17[1 2]
Cholesterol, free	1.07 ±0.05	1.01±0.05	0.86±0.04[1 2]
Cholesterol, esterified	2.78±0.12	2.64±0.14	2.27±0.13[1 2]
Phospholipids	1.27±0.05	1.20±0.05	1.05±0.05[1 2]
Triglyceride	0.29±0.01	0.26±0.01	0.25 ±0.02[2]
	HDL		
Cholesterol, total[1]	1.28±0.06	1.26±0.06	1.23±0.05
Cholesterol, free	0.20±0.01	0.20±0.01	0.20 ±0.01
Cholesterol, esterified	1.08±0.05	1.06 ±0.05	1.03±0.04
Phospholipids	1.26±0.05	1.21 ±0.05	1.22±0.06
Triglyceride	0.16 ±0.01	0.14±0.01[1]	0.14±0.01[1]

[1]Measured directly from serum by commercial kits. Other measurements from ultracentrifuge fractions (mean±SE).
[1] *P*<.05 from home values,
[2] *P*<.05 from margarine values. To get mg/dL, multiply cholesterol values by 38.7 and triglyceride values by 88.2.

Table 3. Serum Sterols (10^2×mmol/mol cholesterol) in Women With Previous Myocardial Infarction Without Previous Hypolipidemic Treatment (n=22) on Different Diets (Table view)

Variables	Home Diet	Rapeseed Oil Margarine	Rapeseed Oil Margarine+ Sitostanol Ester
Cholesterol, mmol/L	5.97 ±0.18	5.73±0.18[1]	5.21±0.17[1 2]
Δ^8Cholestenol	14.0±1.1	14.6±1.5	16.9 ±1.7[1 2]
Desmosterol	89.0±9.1	91.0±7.4	99.7±9.7[1 2]
Lathosterol	167.9±12.8	169.6±11.6	188.3±12.9[1 2]
Cholestanol	131.1±8.5	126.7±9.2	115.0±7.3[1 2]
Campesterol	265.3±28.2	300.7±30.6[1]	177.3±20.2[1 2]

Variables	Home Diet	Rapeseed Oil Margarine	Rapeseed Oil Margarine+ Sitostanol Ester
Sitosterol	141.0±12.1	147.4±12.7	113.7 ±9.5[1 2]

Values are mean±SE.
[1] *P*<.05 from home values,
[2] *P*<.05 from margarine values.
To get mg/dL, multiply cholesterol values by 38.7.

Table 4. Cholesterol Absorption, Fecal Steroids and Cholesterol Synthesis, and Turnover in Women With Previous Myocardial Infarction Without Previous Hypolipidemic Treatment (n=22) on Different Diets (Table view)

Variables	Home Diet	Rapeseed Oil Margarine	Rapeseed Oil Margarine+ Sitostanol Ester
Cholesterol absorption, %	40.8±2.4	42.2±2.1	23.4±1.3
Total cholesterol, mg/kg per day	7.37 ±0.62	7.17±0.52	4.03±0.27[1 2]
Dietary cholesterol, mg/kg per day	1.53±0.15	1.35 ±0.15	0.76±0.11[1 2]
Biliary cholesterol, mg/kg per day	5.84±0.53	5.22±0.45	3.27±0.20[1 2]
Intestinal flux, mg/kg per day	17.98±0.95	16.97±0.93	17.26±0.64
Dietary flux, mg/kg per day	3.70±1.28	3.10±1.23	3.17 ±1.45
Biliary flux, mg/kg per day	14.28±0.86	13.87 ±0.93	14.09±0.61
Neutral sterols, mg/kg per day	10.61 ±0.68	9.80±0.68	13.22±0.55[1 2]
Dietary unabsorbed, mg/kg per day	2.18±0.18	1.75±0.15[1]	2.41±0.22[2]
Biliary unabsorbed, mg/kg per day	8.44±0.60	8.05 ±0.67	10.83±0.53[1 2]
Bile acids, mg/kg per day	4.79 ±0.35	4.88±0.34	4.70±0.34
Total sterols, mg/kg per day	15.40±0.86	14.68±0.78	17.93±0.66[1 2]
Cholesterol synthesis, mg/kg per day	11.70 ±0.84	11.58±0.81	14.76±0.61[1 2]
Cholesterol turnover, mg/kg per day	13.22±0.78	12.93±0.75	15.52 ±0.58[1 2]
Dietary plant sterols, mg/kg per day	4.10 ±0.28	4.73±0.39	51.83±3.77[1 2]
Fecal sitostanol, mg/d	17±1	33±12	2568±178[1 2]

Values are mean±SE.
[1] *P*<.05 from home diet,
[2] *P*<.05 from margarine diet.

Table 5. Serum Lipids (mmol/L) Before and at the End of 3-Month Sitostanol Ester Margarine Period of Women With Previous Myocardial Infarction (n=10) Receiving Simvastatin (Table view)

Serum Lipid	Before	End	% Change
Cholesterol, total	4.94±0.43	4.38±0.35	−11.1 ±3.2[1]
LDL cholesterol	2.86±0.44	2.37 ±0.35	−16.3±5.0[1]
HDL cholesterol	1.35 ±0.08	1.37±0.05	+2.5±5.8
Triglycerides	1.63±0.15	1.43±0.15	−12.1 ±7.8

Presimvastatin cholesterol value was 6.45±0.17 mmol/L; LDL cholesterol, 4.42±0.35 mmol/L.

Values are mean±SE.
[1] *P*<.05 from before.
To get mg/dL, multiply cholesterol values by 38.7 and triglyceride values by 88.2.

Table 6. Baseline Home Values Correlated With Sitostanol Ester Margarine–Induced Changes in Various Variables of Cholesterol Metabolism in Women With Previous Myocardial Infarction Without Previous Hypolipidemic Treatment (n=22) (Table view)

Variables, Home Values	Changes From Home Values			
	Own Respective Values	Cholesterol Absorption, %	Cholesterol Synthesis, mg/kg per day	LDL Cholesterol, mmol/L
Serum Δ^8-cholestenol[1]	+0.325	+0.393	−0.555[1]	+0.466[1]
Serum desmosterol[1]	+0.212	+0.372	−0.517[1]	+0.167
Serum lathosterol[1]	−0.160	+0.468[1]	−0.675[1]	+0.449[1]
Cholesterol synthesis, mg/kg per day	−0.730[1]	+0.546[1]	−0.730[1]	+0.302
Serum cholestanol[1]	−0.678[1]	−0.502[1]	+0.656[1]	−0.440[1]
Serum campesterol[1]	−0.863[1]	−0.130	+0.554[1]	−0.263
Serum sitosterol[1]	−0.707[1]	−0.207	+0.552[1]	−0.271
Cholesterol absorption, %	−0.859[1]	−0.859[1]	+0.546[1]	−0.371

[1] 10^2×mmol/mol of cholesterol.
[1] *P*<.05 or less.

ARTICLE INFORMATION

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