Effects of Carnitine and Coenzyme Q10 on Lipid Profile and Serum Levels of Lipoprotein(a) in Maintenance Hemodialysis Patients on Statin Therapy

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Original Paper

Introduction. Dyslipidemia and high serum lipoprotein(a) are among the risk factors for cardiovascular diseases in hemodialysis patients. Statins as a first line of therapy in hyperlipidemia does not always reduce the serum lipoprotein(a) level. Several studies have reported the lipid-lowering effects of carnitine and coenzyme Q10 in hemodialysis patients. This study was designed to investigate the effects of carnitine and coenzyme Q10 on serum lipid profile and lipoprotein(a) level in maintenance hemodialysis patients.
Materials and methods. This was a randomized placebo-controlled trial. We studied on hemodialysis patients who were on treatment with atorvastatin or lovastatin to assess the efficacy of supplement therapy. They were divided into 4 groups to receive carnitine, coenzyme Q10, both carnitine and coenzyme Q10, and placebo. After a 3-month experiment, blood samples were collected to measure serum levels of lipoprotein(a), triglyceride, total cholesterol, high-density lipoprotein cholesterol and low-density lipoprotein cholesterol.
Results. Fifty-two hemodialysis patients, 27 men and 25 women, completed the course of the study. Three months after supplement therapy, serum levels of lipoprotein(a) reduced significantly in the carnitine, coenzyme Q10, and combination groups compared to the baseline values and the 3-month value of lipoprotein(a) in the placebo group (P = .01). Serum levels of triglyceride and other lipoproteins did not significantly alter.
Conclusions. Our study showed that supplementation with carnitine and coenzyme Q10 could reduce serum levels of lipoprotein(a) in maintenance hemodialysis patients treated with statins.

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INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in maintenance hemodialysis patients.[1,2] Dyslipidemia, elevated serum levels of low-density lipoprotein cholesterol (LDLC), triglyceride, and lipoprotein(a), and reduced serum levels of high-density lipoprotein cholesterol (HDLC), are among the prevalent risk factors of CVD in hemodialysis patients.[3,4] Lipoprotein(a) is a genetically determined low-density lipoprotein with a unique apolipoprotein(a) molecule, that predisposes individuals to thrombotic complications of atherosclerosis and CVD.[5] Generally, statins have no apparent effects (neutral

effect) on serum lipoprotein(a) level.[6,7] Niacin, a well-known lipid-lowering agent, may cause a few side effects such as flushing and dyspepsia that might be not tolerated by some patients.[8] It has been reported that carnitine and coenzyme Q10 shows lipid-lowering effects.[9,10] The aim of this study was to investigate the effects of carnitine and coenzyme Q10 as safe and useful supplement medications on serum lipid profile and lipoprotein(a) level in maintenance hemodialysis patients.

MATERIALS AND METHODS

Patients

In a randomized double-blind placebo-controlled clinical trial, 64 maintenance hemodialysis patients with moderately high serum lipoprotein(a) levels being on treatment with atorvastatin and/or lovastatin (both 20 mg/d) were enrolled in this study. Patients were informed of the purpose, procedures, and probable hazards of this trial, and written consent was obtained from all of the participants. The protocol of research was approved by the Ethics Committee on Human Experimentation of Tehran University of Medical Sciences. Acute inflammation and taking any type of anti-inflammatory or anti-oxidative medications were among the exclusion criteria of this study. We designed a data sheet to record any probable side effects by nurses and physicians through close monitoring of patients during the study.

Methods

The patients were divided into 4 groups, A to D, by the randomized permuted balanced block method. Group A, received intravenous carnitine, 1000 mg (L-carnitine, Carnivore, Sigma tau, Spain), 3 times per week, after each dialysis session; group B, oral coenzyme Q10, 100 mg/d (Pharmed-Tnt Inc, Canada); group C, a combinations of both carnitine and coenzyme Q10; and group D, as placebo group, normal saline injection or lactose capsules orally. All of the patients were on supplement therapy for 3 months. Based on previous studies, this protocol of a dosage and intervention period would be safe and effective.[11-14]

After 12 hours of overnight fasting, blood was drawn before the beginning and at the end of supplement therapy to assess serum total cholesterol (TC), triglyceride, HDLC, LDLC, apolipoprotein A-I, apolipoprotein B-100, and lipoprotein(a).

Intake of nutrients was estimated by using a standard dietary recall questionnaire during 24 hours at the beginning and at the end of this study. This was analyzed by the Food Processor II software (ESHA Research, Salem, Oregon, USA). The patients were asked not to alter their usual diets and physical activity throughout the study.

Laboratory Assessment

Serum lipoprotein(a) level was assessed by an enzyme-linked immunosorbent assay (Biopool US Inc, Ventura, California, USA). The blood samples were also assessed for serum levels of triglyceride (enzymatic GPO-PAP method), TC (enzymatic colorimetric CHOP-PAP method), HDLC and LDLC (direct enzymatic method), and apolipoprotein A-I and Apo B-100 (immunoturbidometric assay, DRG, USA). All these biochemical assays were performed using diagnostic kits made by Bioactiva Diagnostica (Homburg, Germany).

Statistical Analyses

All data are expressed as means ± standard deviation. The Kolmogorov-Smirnov test was used to assess normal distribution of independent and dependent variables. Differences between the four studied groups were assessed by the 1-way analysis of variance for continuous variables and the chi-square test for grouped variables. Post hoc comparisons were performed with the Tukey test. Adjustment for differences in baseline and changes in variables during the study were performed by the analysis of covariance analysis using general linear models. Differences between results of before and after intervention were determined by the paired t test. A value of P less than .05 was considered to be significant. All data were analyzed using the the SPSS software (Statistical Package for the Social Sciences, version 13.0, SPSS Inc, Chicago, Ill, USA).

RESULTS

Among 64 maintenance hemodialysis patients who were enrolled in this study, 12 patients were dropped out of the trial because of infectious disease, irregular taking of the oral supplements, and/or withdrawal from the course of study on their own choice. No side effects secondary to the supplementation with carnitine and coenzyme Q10

were reported. The mean age of the 52 patients who completed the course of study was 53.3 ± 14.2 years (range, 21 to 81 years). They were 25 men (mean age, 54.2 ± 14.3 years) and 27 women (mean age, 52.4 ± 14.2 years).

The baseline characteristics of the patients (age, sex, and body mass index) and dialysis adequacy (Kt/V) did not significantly differ among the studied groups (Table 1). Since all studied populations had a chronic disease, they did not have severe or fast physical activity and tended to rest most of the time; thus, only the average time of daily activities was asked and analyzed. There were no significant differences in physical activity and dietary intake of the studied population during the study (data are not shown). After 3 months of supplement therapy, serum levels of lipoprotein(a) showed a significant decrease in group A, B, and C compared to the baseline levels (-9.6 ± -6.4 [21.3%]; -12.2 ± -9.9, [25.1%]; and -10.6 ± -12.1, [21.1%], respectively), and the placebo group. Serum levels of the other lipids or apolipoproteins did not significantly alter after supplementation and between the studied groups (Table 2).

Table 1. Demographic Characteristics of Patients on Hemodialysis*

Characteristic	Study Groups				*P*
	Group A Carnitine	Group B Coenzyme Q10	Group C Carnitine + Coenzyme Q10	Placebo	
Number of patients	12	13	14	13	…
Age, y	55.3 ± 15.6	53.5 ± 11.5	52.8 ± 10.4	51.6 ± 19.2	.94
Male-female ratio	6:6	7:6	6:8	6:7	.95
Body mass index, kg/m^2					
Before study	24.3 ± 2.1	23.6 ± 2.4	23.3 ± 2.3	23.6 ± 2.6	.88
After study	24.1 ± 2.0	23.7 ± 2.5	23.3 ± 2.3	23.7 ± 2.7	.84
Kt/V					
Before study	1.10 ± 0.20	1.17 ± 0.17	1.19 ± 0.19	1.18 ± 0.23	.72
After study	1.19 ± 0.23	1.19 ± 0.27	1.17 ± 0.24	1.18 ± 0.21	.99

*Values are means ± standard deviations unless otherwise explained.

Table 2. Serum Levels of Lipids, Lipoproteins, and Lipoprotein(a) Before and After Supplementation With Carnitine and/or Coenzyme Q10 in Maintenance Hemodialysis Patients Treated With Statins*

Parameter	Study Groups				*P*
	Group A Carnitine	Group B Coenzyme Q10	Group C Carnitine + Coenzyme Q10	Placebo	
TC, mg/dL					
Before study	147.1 ± 28.8	150.9 ± 25.6	152.5 ± 23.5	156.5 ± 31.9	
After study	147.9 ± 26.3	149.9 ± 37.2	150.5 ± 22.0	160.6 ± 35.4	.83
HDLC, mg/dL					
Before study	41.9 ± 7.8	40.9 ± 3.2	39.4 ± 7.0	42.8 ± 5.7	
After study	43.3 ± 8.0	38.4 ± 5.5	39.4 ± 6.8	42.2 ± 8.1	.36
LDLC, mg/dL					
Before study	84.5 ± 26.5	89.5 ± 28.7	83.2 ± 32.2	84.0 ± 13.9	
After study	87.5 ± 14.8	83.9 ± 29.0	77.4 ± 15.7	85.5 ± 19.1	.42
Triglyceride, mg/dL					
Before study	149.2 ± 75.2	131.0 ± 53.2	155.9 ± 62.6	150.9 ± 76.9	
After study	143.7 ± 85.0	128.7 ± 55.4	152.5 ± 58.3	137.5 ± 61.1	.71
Apolipoprotein A-I, mg/dL					
Before study	87.2 ± 11.0	89.2 ± 21.0	78.1 ± 11.9	88.6 ± 9.3	
After study	98.4 ± 10.8	89.7 ± 15.0	82.9 ± 15.0	100.5 ± 17.8	.66
Apolipoprotein B-100, mg/dL					
Before study	83.8 ± 27.5	78.8 ± 21.3	84.2 ± 20.5	80.3 ± 14.4	
After study	85.4 ± 27.6	89.1 ± 30.8	84.5 ± 20.5	88.2 ± 21.0	.48
Lipoprotein(a), mg/dL					
Before study	45.0 ± 23.9	48.6 ± 22.8	50.3 ± 18.4	31.6 ± 7.7	
After study	35.4 ± 23.1	33.4 ± 20.4	39.7 ± 17.9	33.5 ± 8.6	.01

*TC indicates total cholesterol; HDLC, high-density lipoprotein cholesterol; and LDLC, Low-density lipoprotein cholesterol.

DISCUSSION

The present study showed that supplementation with carnitine for a period of 3 months can reduce serum lipoprotein(a) level in maintenance hemodialysis patients who were on treatment with statins before and during the supplement therapy. Our results are in agreement with the previous reports of Derosa and colleagues and Sirtori and coworkers, regarding a decrease in serum lipoprotein(a) level following carnitine supplementation.[9,15]

Derosa and associates administered 1-g tablets of carnitine, orally, to 46 diabetic patients with a serum lipoprotein(a) level gretare than 30 mg/dL, twice a day for 6 months. They found 3.5% and 20.9% reduced serum lipoprotein(a) levels comparing with the baseline level in the 3rd and 6th month of therapy, respectively. Low baseline level of serum carnitine in hemodialysis patients and intravenous administration of carnitine may be the reason of rapid and significant serum lipoprotein(a) reduction in our study.

Sirtori and coworkers prescribed oral carnitine, 2 g/d, to 36 individuals with high serum lipoprotein(a) level for 3 months. They showed a 7.7% decrease in serum level of lipoprotein(a) compared with the baseline serum level and a 11.7% decrease compared with the placebo group. The reduced amount was lower than that in our study (21.7% and 26.9% decreases compared to the baseline and placebo group). Different routes of administration and different studied populations might be the reasons of this discrepancy. On the other hand, Elisaf and colleagues did not find any effect of oral L-carnitine on serum lipoprotein(a) level in hemodialysis patients.[16] This disparate result may be partly related to the prescribed dose (5 mg/kg) or the baseline serum lipoprotein(a) level.

Our study also showed that supplementation with coenzyme Q10 in a dose of 100 mg/d (oral capsules), either alone or in combination with carnitine, is associated with a significant decrease in serum lipoprotein(a) level in maintenance hemodialysis patients who are on treatment with statins. Results of our study are in accordance with Cicero and coworkers' study[10] that showed coenzyme Q10 could reduce serum lipoprotein(a) level in patients with high serum triglyceride levels resistant to polyunsaturated fatty acids and fibrates. Moreover, it is in along with Singh and associates' study,[17] which showed coenzyme Q10 could reduce serum lipoprotein(a) level in patients with coronary artery diseases.

The mechanisms by which L-carnitine can decrease high serum lipoprotein(a) level is not well known. L-carnitine fascinates and stimulates fatty acids movement and breakdown into the mitochondria and may reduce serum levels of lipoprotein(a).[18] Coenzyme Q10 is a lipid-soluble molecule, and it is present in sufficient amounts in lipoprotein(a). Supplementation with coenzyme Q10 can inhibit expression of lipoprotein(a) receptor and result in decreased serum lipoprotein(a).[17]

Other than serum lipoprotein(a) level, we did not find any significant change in the serum level of the other lipids or apolipoproteins following to carnitine and/or coenzyme Q10 supplementation. One probable reason is concomitant statin therapy of the studied population. Duration of therapy is also of potential interest. It has been reported that the lipid-lowering effects of carnitine may take a long time to appear in patients with hypertriglyceridemia.[19]

CONCLUSIONS

Our study showed that supplementation with carnitine and coenzyme Q10 might reduce serum lipoprotein(a) level in maintenance hemodialysis patients who were resistant to statin therapy.

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CONFLICT OF INTEREST

None declared.

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