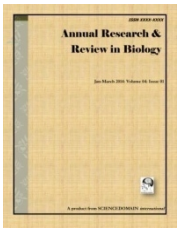

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Effects of Oral L-carnitine Supplementation on Lipid Profiles and Anemia in Patients under Hemodialysis in Gonbadkavoos, Iran

Samira Eshghinia[1], Abdoljalal Marjani[1*] and Behrouz Ebrahim Zadeh Kor[2]

[1]Department of Biochemistry and Biophysics, Metabolic Disorders Research Center, Gorgan Faculty of Medicine, Golestan University of Medical Sciences, Gorgan, Iran.
[2]Department of Nutrition, Gonbad Health Center, Golestan University of Medical Sciences, Gorgan, Iran.

Authors' contributions

This study was done in collaboration between all authors. Author SE gave the idea and designed the study, wrote the protocol, managed the literature searches and wrote the final paper. Author AM designed the study, performed the statistical analysis, managed the analyses of the study, managed the literature searches and wrote the final paper. Author BEZK was as the management of the patients and collection of medical assessment findings. All authors read and approved the final manuscript.

Original Research Article

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ABSTRACT

Aims: L-carnitine is an amino acid derivative, produced endogenously in the kidneys and liver or derived from meat and dairy products in the diet. Impaired L-carnitine synthesis by the kidneys contributes to the L-carnitine deficiency in dialysis patients. The aim of this study was to evaluate the effect of oral L-carnitine supplementation on lipid profiles and anemia in hemodialysis patients.
Study Design: Thirty and four eligible patients were assigned to either L-carnitine or placebo groups based on the random. The patients in the L-carnitine group received 1 vial 1g (10 ml) of L-carnitine oral supplement 3 day a week after dialysis, for 16 weeks and the patients in the placebo group received 10 ml distilled water as in the same manner and duration. Blood sample was collected at the onset and after 16 weeks intervention for laboratory evaluations of biochemical and hematological parameters.
Place and Duration of Study: Hemodialysis patients were chosen in Motahary Hospital in

**Corresponding author: Email: abdoljalal@yahoo.com;*

Gonbadkavoos, Iran, between September 2012 and March 2013.
Results: The concentration of very low density lipoprotein and triglyceride were significantly decreased in L-carnitine group, whereas, none of these differences were statistically significant in placebo group whereas other measured biochemical parameters were not shown significant changes in both group.
Conclusion: It seems that further experimental investigations are needed to clarify the effects of LC on lipid profiles, anemia and other factors in hemodialysis patients.

Keywords: L-Carnitine; lipid profiles; anemia; hemodialysis patients.

1. INTRODUCTION

According to the results of the resent study, the prevalence of chronic kidney diseases (CKD) stage 3–5 in Iranian population is higher than similar population based studies in the US, Europe and Japan [1]. These patients are at an increased risk for end-stage kidney disease and dialysis. It is well documented that one of the most common causes of deaths in patients with CKD is cardiovascular diseases. Atherosclerosis advances in renal failure and develops early in the course of renal dysfunction. In spite of medical advancements and increased survival rate of the patients, atherosclerosis and the subsequent cardiovascular diseases are still the most important causes of mortality in CKD patients and end-stage renal disease (ESRD) [2-5]. L-carnitine (LC) is an amino acid derivative, produced endogenously in the kidneys and liver or derived from meat and dairy products in the diet. It plays an essential role in the transfer of long-chain fatty acids into the mitochondria for beta-oxidation and therefore, its deficiency may lead to imbalance in fuel and energy homeostasis, abnormalities in fatty acid metabolism and some metabolic disorders such as insulin resistance [6]. L-carnitine because of small and not protein-bound molecule is removed from the circulation during hemodialysis. Impaired LC synthesis by the kidneys and poor nutritional status may also contribute to the carnitine deficiency in dialysis patients [7]. Some previous studies have reported that carnitine deficiency in patients on maintenance hemodialysis may contribute to dyslipidemia, anemia, muscle weakness, impaired exercise capacity, cardiomyopathy and inflammatory state [7-9].

Despite of some available studies have been conducted on the benefit of L-carnitine supplementation in patients under continuous hemodialysis, the clinical trial data are unconvincing. In this study, we evaluated the effect of oral L-carnitine supplementation on lipid profiles and anemia in hemodialysis patients.

2. MATERIALS AND METHODS

2.1 Patients and Setting

This randomized, placebo-controlled, double-blinded, clinical trial was carried out on end stage renal disease (ESRD) patients under continuous hemodialysis in Motahary Hospital in Gonbadkavoos, Iran. The inclusion criteria were the age range of 18–50 years, history of at least 12 weeks of hemodialysis, three times a week and each session almost 4 hours. The patients were not included into the study if they were on L-carnitine supplement, any drug or supplement that interacts with carnitine, lipid lowering drug, beta blockers, anti convulsion or other drugs influencing lipid metabolism and blood transfusion in the last 3 month. Sampling was performed with convenient nonrandomized method from among the patients referred to

the dialysis ward of the hospital. The sample size for each group was determined 17 (total 34 samples). A check list contained demographic data (age and body mass index (BMI)), the history of chronic kidney disease (CKD) and duration of dialysis was completed for each patient. Height and body weigh was measured as standard methods in first visit and every 2 weeks during study course with same instruments and were recorded. The study was approved by the Ethical Committee of Golestan University of Medical Sciences (No:1639), and all patients signed a fully informed written consent before including to the study.

2.2 Intervention

Thirty four eligible patients were assigned to either L-carnitine or placebo groups based on the random. The patients in the L-carnitine group received 1 vial 1g (10 ml) of L-carnitine oral supplement (SO.SE.PHARM–ITALY) 3 day a week after dialysis for 16 weeks and the patients in the placebo group received 10 ml distilled water as in the same manner and duration. L-carnitine and placebo were coded and the researchers and patients were blinded to the code of L-carnitine and the placebo. The patients were followed up for drug side effects and the compliance for drug consumption every week in the treatment centers. In our study, we did not reported complications associated with L-carnitine.

2.3 Laboratory Evaluations

Fasting blood sample was collected at the onset and after 16 weeks intervention for laboratory evaluations of serum concentrations of Albumin, total cholesterol, High Density Lipoprotein (HDL), Low Density Lipoprotein (LDL), Very Low Density Lipoprotein (VLDL), triglyceride (TG) and hemoglobin (Hb) and hematocrit (Hct), as well as the received erythropoietin dose was recorded at the onset of the study and 16 weeks after intervention.

2.4 Statistical Analysis

We used chi-square and independent sample t-test to compare baseline and demographical characteristics of the participants between two groups (Intervention with and without L-carnitine). For evaluation of variable changes in each group before and after intervention, we used paired t-test. Continuous variables are reported as means ± SD. The data was analyzed using SPSS software, version 16.0. The P-value less than 0.05 considered statistically significant.

3. RESULTS

Twenty patients for each group were joined. In the LC group, three patients were excluded (one underwent kidney transplantation and two were not willing to continue the study). In the placebo group, three cases refused to complete study. Therefore, 17 patients and 17 placebo group in each group completed 16-weeks trial. As it is shown in Table 1, demographical and baseline biochemical characteristics of two groups were not significantly different. After 16 weeks intervention, no significant differences were found between weight and BMI in both groups. Also as can be seen from the Table 2**,** the concentration of TG and VLDL were significantly decreased in L-carnitine group, whereas, none of these differences were statistically significant in placebo group. About other measured biochemical factors such as Hb, Hct, total cholesterol, HDL and LDL, comparison of changes were not statistically significant in both group. Because of no difference in hemoglobin concentration, dose of consumed erythropoietin was not changed after 16 weeks in two groups.

Table 1. Demographical and baseline of biochemical characteristics in two groups of hemodialysis patients

Parameters	L-carnitine(n=17)	Placebo (n=17)	P-value
	Mean ± SD	Mean ± SD	
Age (year)	45.1±12.7	43.12±15.09	N.S
Weight (kg)	61.08±3.67	57.55±2.81	N.S
BMI (kg/m2)	23.10±1.24	22.21±1.11	N.S
History of dialysis (year)	5.7±4.27	4.5±3.2	N.S
Hematocrit (%)	32.17±1.88	34.94±1.97	N.S
Hb (g/dl)	10.51±0.64	11.43±0.71	N.S
Chol (mg/dl)	150.47±8.08	152.12±9.15	N.S
TG (mg/dl)	188.24±30.99	184.88±15.53	N.S
VLDL (mg/dl)	37.64±6.19	36.97±3.11	N.S
HDL (mg/dl)	31.51±2.23	30.47±2.76	N.S
LDL (mg/dl)	77.10±5.96	84.76±7.96	N.S
Albumin (g/dl)	4.08±0.11	4.04±0.12	N.S

N.S: no significant

Table 2. The variation of Hb, Hct, lipid profiles, BUN, Cr and albumin in two groups of hemodialysis patients

Parameters	L-carnitine (n=17)			Placebo (n=17)		
	baseline	after 16th week	P-value	baseline	after 16th week	P-value
Hematocrit (%)	32.17±1.88	33.13±1.64	N.S	34.94±1.97	40.11±4.96	N.S
Hb (g/dl)	10.51±0.64	10.53 ± 0.58	N.S	11.43±0.71	11.41±0.59	N.S
TG (mg/dl)	188.24±30.99	147.44±20.78	P<0.05	184.88±15.53	175.65±13.28	N.S
Chol (mg/dl)	150.47±8.08	150.50±11.80	N.S	152.12±9.15	155.59±10.42	N.S
VLDL (mg/dl)	37.64±6.19	29.48±4.15	P<0.05	36.97±3.11	33.37±2.79	N.S
HDL (mg/dl)	31.51±2.23	30.12±1.53	N.S	30.47±2.76	29.76±2.59	N.S
LDL (mg/dl)	77.10±5.96	90.88±8.61	N.S	84.76±7.96	91.87±9.47	N.S
Albumin (g/dl)	4.08±0.11	4.13±0.24	N.S	4.04±0.12	4.16±0.10	N.S

N.S: no significant

4. DISCUSSION

High level serum TG is suggested as a CAD risk factor being common among hemodialysis patients. Carnitine causes transport of free fatty acids (FAs) from cytoplasm to mitochondria matrix and get oxidized. So more FAs go into the cells and the serum level of FAs reduces. Thus the hepatic uptake of FAs and their conversion to TG and presence of them as VLDL form decrease; therefore VLDL level lessens following serum TG reduction [10-11]. Whereas previous studies of LC effect on serum lipid profile in dialysis patients have been conflicting [7]. The results of this study show that supplementation with 1gr oral LC for 16 weeks reduced the 40 mg/dl concentration of TG in the serum. This finding is consistent with those of Shakeri, et al and Emami, et al. Nevertheless, another studies reported no statistically significant effect of carnitine on serum triglyceride [12-13]. Our result showed a reduction of mean VLDL serum level in those receiving L-Carnitine. This change was not supported in some other studies [14]. Effect of L-carnitine on LDL has been controversial in reports from several studies. Similarly to our findings, the results of some study showed no significant change on the LDL level after carnitine supplementation [12,13,15]. But there were some that reported its reduction following the L-carnitine administration [16]. Previous studies reported different effects of carnitine supplementation on serum HDL in hemodialysis patients [7,14]. In the current study the serum level of HDL did not change, that is consistent with other studies [12,15]. However, these findings do not support the result of some previous research that reported significant increase of HDL [13,17]. The heterogeneity of the findings in different clinical trials can be due to baseline lipid profile level, dose and rout of administered LC supplement. Taken together, these results suggest that LC supplementation in hemodialysis patients cannot control their dyslipidemia. Anemia is a common complication of hemodialysis. LC could enhance the response to erythropoietin through its anti-inflammatory and antiapoptotic effects [7]. Effect of L-Carnitine supplementation on anemia in patients undergoing continuous hemodialysis has been studied in previous work and showed variable results. In our study after 4 months supplementation with oral L-carnitine, no changes detected in Hb and erythropoietin dose in patients, which is in consistent with evaluation of a meta-analysis [14]. However, In some researches with small sample size reported increased of hemoglobin and reduced required dose of erythropoietin after 16 weeks supplementation with 1 g/d oral LC [13]. We showed that, 4 months supplementation of 1 gr oral LC 3 times a week did not change albumin level. These results differ from some published studies [18-20] that reported increased in albumin level. This difference may be due to a longer period of administration or the route of taking. In another study after 12 weeks receiving 1g/d LC orally, albumin serum level was reduced [1]. In general, it seems that further experimental investigations are needed to clarify the effects of LC on lipid profiles, anemia and other factors in hemodialysis patients. A limitation of this study is that the numbers of patients and controls were small. Secondly, the study did not evaluate the serum carnitine level before and after trial.

5. CONCLUSION

The present study was designed to determine the effect of LC administration on lipid profiles and anemia in CKD patients under hemodialysis. This research has shown that administration 1g oral L-carnitine 3 times a week for 16 weeks could decrease TG and VLDL levels without significant change in other lipids and anemic status of patients. More complementary researches with larger sample size, longer follow up; different dose and types of LC administration are needed to establish these findings.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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