ORIGINAL ARTICLE

Effects of Oral L-Carnitine Supplementation on C-Reactive Protein and Blood Sugar in Hemodialysis Patients: A Randomized Clinical Controlled Trial

Shima Dehghan Banadaki[1], Hassan Mozaffari-Khosravi[1,4]*, Sedighe Ahmadi[1], Mohammad Kazem Hajimirzadeh[2], Mohammad Hassan Lotfi[3]

1. Department of Nutrition, Faculty of Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
2. Assistant Professor of Medicine, Department of Internal Medicine, Islamic Azad University, Yazd, Iran
3. Associate Professor of Biostatistics and Epidemiology, Shahid sadoughi Medical Sciences and Health Services, Yazd, Iran
4. Yazd Diabetic Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

*Correspondence:
Hassan Mozaffari-Khosravi, Professor of Nutrition Sciences, Department of Nutrition, Faculty of Health, Yazd Diabetic Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
Email: mozaffari.kh@gmail.com
Tel: (98) 353 724 9333
Fax: (98) 353 725 8413

Received: 16 June 2015

Accepted: 25 August 2015

Published in September 2015

Abstract

Objectives: Inflammation is a common complication in patients treated with hemodialysis and increasing in inflammatory factors such as C-reactive Protein (CRP) is associated with increased cardiovascular disease and mortality in these patients. The purpose of this study was to investigate the effect of oral L- carnitine supplementation on serum CRP concentration and fasting blood sugar (FBS) in patients undergoing hemodialysis.

Materials and Methods: This study was a randomized clinical trial on 50 patients (30 males and 20 females) undergoing hemodialysis in the age range of 21-84 years from hemodialysis units of Yazd hospitals. Participants randomly divided into two groups, the Carnitine group (CaG) consumed daily oral syrup of L-carnitine containing 1000 mg of Carnitine for three months and the control group (CoG) did not use Carnitine. Serum levels of CRP and FBS were measured at baseline and at the end of the intervention. Statistical analysis was performed using the SPSS version 16.0.

Results: the mean difference in CRP concentration in CaG and CoG were, 1.95 ±9.4 and 0.6±10.8 (μg/l), respectively (*P*-value=0.7) and the mean of FBS at the baseline and after 12 weeks in the CaG were 118.7±51.4 mg/dl and 110.1±48.2 mg/dl, respectively (*P*-value=0.3) and in the CoG were 142.8±88.7 mg/dl and 131.8±68.9 mg/dl (*P*-value=0.26).

Conclusion: The oral administration of daily 1000 mg of L-carnitine for three months doesn't effect on serum CRP and FBS concentrations in patients undergoing hemodialysis.

Keywords: Blood sugar, Hemodialysis, Inflammation, L-carnitine.

Introduction

In recent years the number of patients with chronic kidney disease (CKD) increased that this trend seems to be rising due to an increase in diseases such as type 2 diabetes, blood pressure and cardiovascular disease and increase health awareness and timely detection of this disease (1). Common complication of the chronic renal failure disease, particularly in

[Downloaded from ijdo.ssu.ac.ir on 2026-11-20]

patients treated with hemodialysis is inflammation (2-4). Various studies have shown that inflammation occurs in 30 to 50% of these populaton (2-3) and inflammatory factors including serum C-reactive protein (CRP) concentration in these patients is higher than healthy people (3). In the patients treated with hemodialysis, inflammation is common, cause of reduced excretion of inflammatory cytokine, collision of the white blood cells with the dialysis filter membrane, pollution of hemodialysis solutions and the access to the location of the blood vessels to do hemodialysis (2,3,5,6). In patients with dialysis, inflammatory reactions release inflammatory mediators such as Interleukin -1, interleukin-b and tumor necrosis factor alpha ,lead to syntesis of CRP and increased homocysteine and endothelin types 1 that these changes can lead to progression of atherosclerosis in patients with chronic kidney failure (7-11). The inflammation in these patients can be caused several complications including anemia, atherosclerosis and cardiovascular disease (2-4). Cardiovascular disease is one of the most important causes of mortality in patients undergoing hemodialysis and the frequency of this disease in hemodialysis patients is 3-45 times of its frequency in the general population (12-13). In addition of the high prevalence of diabetes, blood pressure and dislipidemia in these patients, another factors such as, inflammation and oxidative stress can also be the causes of this high frequency (2) So in patients treated with dialysis, the prevention of the systemic inflammatory processes can by reducing morbidity and mortality in these patients (8,9,14).

L-carnitine (L-3-hydroxy-4-N-trimethylamino-butyrate) is an essential vitamin-like for human that is involved in many metabolic processes, such asketogenesis, mitochonrial energy compliance and long chain free fatty acids transference into the mitochondria for b-oxidation ,so carnitine is an essential compound in human (15). L carnitine reduces Acetyl-CoA syntesise and by this way the production of free radical is reduced.It also helps repairing phospholipid membrane oxidative damage and reduces heart arrhythmia and ischemia that has been created through apoptosis by decreasing the Acetyl-CoA.

L-carnitine is more effective in Krebs cycle during hypoxia because it stimulates the production of propionate which is converted to succinate without energy expenditure, while the consumption of propionate is toxic. L-carnitine increases the level of nitric-oxide synthase (NOS) and Heme oxygenase (HO-1), which are known as anti proliferative and anti inflammatory agent and these enzymes are protective against oxidative stress. Treatment with L-carnitine suppresses inflammation (16). In the end stage renal diseas (ESRD) patients are on choronic dialysis, carnitine deficiency is very common, so that carnitine deficiency (free carnitine< 40 micromol/liter) occurs in about half of women and one third of men undergoing continuous dialysis (17). Carnitine deficiency occurs in patients on hemodialysis due to reduce its syntesise and increase its loss during dialysis. Level of serum free carnitine during hemodialysis drop, but after an hour of hemodialysis its value be like its in the previous .Serum free carnitine levels in patients with ESRD who don't dialyze is higher than hemodialysis patients. L-carnitine enhances activity of pyruvate dehydrogenase by decreasing acetyl-CoA to coenzyme A proportion in mitochondrial to increased glucose catabolism (23-25).

Some study demonstrate that in type 2 diabetic patients serum level of carnitine is low and carnitine supplementation in these individuals is useful by improving the process of glucose catabolism (26,27) And continuous L-carnitine infusion in patients with type 2 diabetes results glucose uptake and insulin sensitivity in cells (28,29). However, studies on the effect of carnitine on blood sugar, especially in hemodialysis patients are limited (30).

According to the importance of inflammation as a risk factor of cardiovascular disease and mortality in hemodialysis patients,

[Downloaded from ijdo.ssu.ac.ir on 2026-11-20]

Considering the most studies have been done with intravenous form of the drug which is still not enough in our country, The present Study was conducted to evaluate the efficacy of oral L-carnitine on CRP and blood glucose levels in patients undergoing hemodialysis

Materials and Methods

Study participants: This study was a randomized clinical trial, The minimum sample size estimated for each group was 25 at a power of 80% and α = 0.05 fifty patients (30 males and 20 females) from hemodialysis units of Yazd hospitals who were undergoing hemodialysis at least one year enrolled in this study. The inclusion criteria were: the age range of 21-84 years, no inflammation diseases or use of antibiotics and non-steroidal anti-inflammatory drugs (NSAIDs) in the last month, no use of carnitine, vitamins E and C supplements 2 months before the start of the study. The change in the method of dialysis, kidney transplant and contracting to Infectious diseases were the exclusion criteria. All patients were undergoing hemodialysis 2-3 times per week for four hours by Hemofane and Polysulfone filters and only 2 patients were on hemodialysis one-time per week. Participants randomly divided into two groups (by random numbers table), the carnitine group (CaG) and control groups (CoG). The patients in CaG consumed daily oral syrup of L-carnitine containing 1000 mg of carnitine, at the evening and after a hemodialysis session And the CoG did not use carnitine. Patients are seen monthly in dialysis centers and supplements were delivered to them gradually and to ensure of syrup consumption, the completed drug recall forms were taken from patients.

Measurment: Patients were weighed at baseline and at the end of week 12 after hemodialysis with a minimum of cloths by using Seca digital scale made in Germany, with an accuracy of 100 grams and height was measured using a stadiometer with the accuracy of 0.05 cm without shoes. Participants were asked to don't change in physical activity, diet, medication and lifestyle during 3 months. To study diet style during the study dietary intakes of patients were assessed using a 24-hour dietary recall for 3 consecutive days at baseline and at the end of weeks 12 by an expert.

At the baseline and at the end of the study, blood sample was taken from patients before initiation of dialysis and transferred to the laboratory unit, After centrifugation of the samples, the serum was separated and frozen at -80 C. Serum CRP and FBS concentration were measured by latex immunoturbidimetric (LIA) and colorimetric method, respectively.

Statistical analysis: Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 16.0. Chi-square test was used to compare qualitative variables between the two groups. Because all quantitative parameters had normal distribution according to the Kolmogorov–Smirnov test, we used the student t-test and the paired t-test to compare parameters between and within groups respectively. Results are expressed as mean ± SD and differences are considered significant at $P \leq 0.05$.

Ethic concideration: According to the inclusion and exclusion criteria, supplementation in the present study were safe and completely ethical**.** In addition, at the baseline, the goals and methods of the study were explained to patients**.** The informed consent form was received**,** if they participated in this study. The patients could exclude at any time and any stage of the research.

Results

Of the fifty hemodialysis patients initially enrolled, one patient in CaG was withdrawn because of noncompliance, one patient because of lack of cooperation and two patients due to kidney transplant and four patients died. 23% 0f CaG and 36% of CoG were female. The baseline characteristics of patients did not differ significantly between the two groups In addition, body mass index did not significantly change within each group during the study. The mean of age and

[Downloaded from ijdo.ssu.ac.ir on 2026-11-20]

duration of hemodialysis in the CaG were 63.4±12.9 (year) and 3.47±2.35 (year), respectively, and these figures for CoG were 62.1±10.2 (year) and 3.35±1.9 (year), respectively and there was no significant difference between groups. There was no significant difference between two groups in history of diabetes and hypertension and hyperlipidemia, uses of drug and supplements, and the level of activity. Table 1 indicated baseline variables in both groups. There was no significant change in CRP concentrations at the beginning and the end of the study. The FBS concentration decreased in both groups, but the change was not significant.

Discussion

The present study showed that administration of 1000 mg daily oral L-carnitine for three months in hemodialysis patients have no Effect on CRP and FBS. Studies have shown that serum carnitine level decrease during hemodialysis so that this level diminished 70-75 % in each session of hemodialysis (18). Moreover, given that the kidney and liver are the main site of carnitine synthesis (19) in hemodialysis patients due to the loss of renal tissue, carnitine synthesis is impaired (18). Also, due to dietary restrictions and reduce the consumption of dairy products and red meat in hemodialysis patients, carnitine intake is less than the amount of required (18-20). A common complication in patients with chronic renal failure, including patients on hemodialysis, is inflammation and several studies have shown that 30 to 50 percent of these patients have inflammation so serum inflammatory markers such as CRP are higher than in healthy individuals in hemodialysis patients. Inflammation can increase cardiovascular diseases, malnutrition, anemia, the predisposition to infections, cancers in these patients (2,3) so decreasing inflammation in hemodialysis patients may have an important role in preventing these complications. CRP is an acute-phase proteins that increases in chronic dialysis and studies have demonstrated the association of CRP with risk of cardiovascular disease (21). Savica in 2005 and Duranay in 2006 showed that 20 mg/kg carnitine infusion after each hemodialysis session significantly reduce serum CRP concentrations (9,22) but In the present study, serum CRP was not significantly different between the two study groups. L-carnitine in diabetic patients

Table 1. The baseline characteristics of hemodialysis patients in the carnitine and control groups.

Variable	Carnitine group	Control group	*P*-value
Age(year)	63.4± 12.9	62.1±10.2	0.72
Weight(kg)	66.68±14	65.9±11.5	0.86
BMI (kg/m2)	24.4±3.4	24.6±3	0.82
Duration of dialysis(year)	3.47±2.35	3.35±1.9	0.86
History of diabetes			
yes	12(70%)	15(60%)	0.49
no	5(30%)	10(40%)	

Table2. Mean of serum CRP concentration (*µ*g/l) in the carnitine and control groups

Variable	Baseline	Week12	Change	*P*-value
Carnitine group	7.2±8.5	9.1±11.5	1.95±9.4	0.4
Control group	4.9±8.2	5.5±8.1	0.6±10.8	0.8
***P*-value**	0.4	0.2	0.7	

Table 3. Mean of fasting blood sugar concentration (mg/dl) in the carnitine and control groups

Variable	Baseline	Week12	Change	*P*-value
Carnitine group	118.7±51.4	110.1±48.2	-8.6±48.6	0.47
Control group	142.8±88.7	131.8±68.9	-11.04±80.9	0.5
***P*-value**	0.3	0.26	0.9	

[Downloaded from ijdo.ssu.ac.ir on 2026-11-20]

elevates pyruvate dehydrogenase activity that converts pyruvate into acetyl-CoA so increases the entry of glucose into the Krebs cycle and decreases blood glucose levels (29,31). A study in Patients with type 2 diabetes who had no symptoms of Neuropathy and retinopathy showed that the use of L-carnitine for 12 weeks reduced fasting blood glucose significantly (32). Other studies showed that different doses of L-carnitine are effective in lowering serum glucose levels (23-25,28,29). Derosa study of 94 diabetic patients showed that Prescription of 2 gram oral l-carnitine per day doesn't have Significant changes in serum levels of FBS, blood glucose and Hg A1c (33) in our study on hemodialysis patients, also no significant effect of taking 1 g of L-carnitine in reducing fasting blood glucose were observed. Our study showed that administration of 1 g L-carnitine daily as syrup in hemodialysis patients have no Effect on CRP and fasting blood sugar. Considering that, serum carnitine level should be low enough to observe the effects of L-carnitine on inflammatory markers and blood glucose levels, in this study we assumed that carnitine deficiency is common in hemodialysis patients so, serum carnitine levels were not measured and this is our study limitation. It is suggested that a large study with higher dose of L-carnitine should be done in the future.

Acknowledgment

This study was supported by Shahid Sadoughi University of Medical Sciences and Health Services of Iran and this manuscript is driven from MSc thesis. The authors thank the staff of the dialysis units in Yazd for their invaluable assistance, and the staff of the Day laboratory for their technical assistance. The authors also gratefully acknowledge the cooperation of the participating patients, without whom this investigation would not have been possible.

References

1. Hosseinpanah F, Kasraei F, Nassiri AA, Azizi F. High prevalence of chronic kidney disease in Iran: a large population-based study. BMC Public Health 2009;9:44.
2. Stenvinkel P. Inflammation in end-stage renal failure: could it be treated? Nephrol Dial Transplant 2002;17:33-8.
3. Stenvinkel P, Yeun JY. Role of inflammation in malnutrition and atherosclerosis in chronic renal failure. In: Kopple JD, Massry SG, editors. Kopple & Massry 's Nutritional Management of Renal Disease. 2nd ed. Philadelphia: Lippincott Williams & Wilkins 2004;199-212.
4. Horl WH. Oxidant stress. In: Kopple JD, Massry SG, editors. Kopple & Massry 's Nutritional Management of Renal Disease. 2nd ed. Philadelphia: Lippincott Williams & Wilkins 2004;99-110.
5. Tetta C, Biasiol S, Schiavon R, Inguaggiato P, David S, Panichi V, et al. An overview of haemodialysis and oxidant stress. Blood Purif 1999;17:118-26.
6. Kalousova M, Sulkova S, Fialova L, Soukupova J, Malbohan IM, Spacek P, et al. Glycoxidation and inflammation in chronic haemodialysis patients. Nephrol Dial Transplant 2003;18:2577-81.
7. De Mutsert R, Grootendorst DC, Indemans F, Boeschoten EW, Krediet RT, Dekker FW. Association between serum albumin and mortality in dialysis patients is partly explained by inflammation, and not by malnutrition. J Ren Nutr 2009;19(2):127-35.
8. Ferrari R, Merli E, Cicchitelli G, Mele D, Fucili A, Ceconi C. Therapeutic effects of L-carnitine and propionyl-L-carnitine on cardiovascular diseases: a review. Ann N Y Acad Sci 2004;1033:79-91.
9. Savica V, Santoro D, Mazzaglia G, Ciolino F, Monardo P, Calvani M, et al. L-carnitine infusions may suppress serum C-reactive protein and improve nutritional status in maintenance hemodialysis patients. J Ren Nutr 2005;15(2):225-30.
10. Bellinghieri G, Santoro D, Calvani M, Savica V. Role of carnitine in modulating acute-phase protein synthesis in hemodialysis patients. J Ren Nutr 2005;15(1):13-7.
11. Signorelli SS, Fatuzzo P, Rapisarda F, Neri S, Ferrante M, Oliveri CG, et al. Propionyl-Lcarnitine therapy: effects on endothelin-1 and homocysteine levels in patients with peripheral arterial disease and end-stage renal disease. Kidney Blood Press Res 2006;29(2):100-7.

[Downloaded from ijdo.ssu.ac.ir on 2026-11-20]

12. Singh SK, Brenner BM. Dialysis in the treatment of renal failure. In: Braunwald E, Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson JL ,editors. Harrison 's Principle of Internal Medicine. 15th ed. New York: McGraw-Hill 2001;1562-6.
13. Jungers P, Khoa TN, Massy ZA, Zingraff J, Labrunie M, Descamps-Latscha B, et al. Incidence of atherosclerotic arterial occlusive accidents in predialysis and dialysis patient: a multicentric study in the IIe de france district. Nephrol Dial Transplant 1999;14:898-902.
14. Calo LA, Pagnin E, Davis PA, Semplicini A, Nicolai R, Calvani M, et al. Antioxidant effect of L-carnitine and its short chain esters: relevance for the protection from oxidative stress related cardiovascular damage. Int J Cardiol 2006;107(1):54-60.
15. Arduini A, Bonomini M, Savica V, Amato A, Zammit V. Carnitine in metabolic disease: potential for pharmacological intervention. Pharmacol Ther 2008;120(2):149-56.
16. Mehrotra R, Kopple JD. Causes of protein-energy malnutrition in chronic renal failure. In: Kopple JD, Massry SG (eds). Kopple and Massry's Nutritional Management of Renal Disease. 2nd ed. Philadelphia: Lippincott Williams & Wilkins 2004;168-82.
17. Steinman TI. L-carnitine supplementation in dialysis patients: does the evidence justify its use? Semin Dial 2005;18(1):1-2.
18. Evans A. Dialysis - related carnitine disorder and levocarnitine pharmacology. Am J Kidney Dis 2003;41:13-6.
19. Hoppel C. The role of carnitine in normal and altered fatty acid metabolism. Am J Kidney Dis 2003;41:5.
20. Guarnieri G, Biolo G, Toigo G, Situlin R. Carnitine in renal failure. In: Kopple JD, Massry SG, editors. Kopple & Massry 's Nutritional Management of Renal Disease. 2nd ed. Philadelphia: Lippincott Williams & Wilkins 2004;357.
21. Kalantar-Zadeh K, Braglia A, Chow J, Kwon O, Kuwae N, Colman S, et al. An anti-inflammatory and antioxidant nutritional supplement for hypoalbuminemic hemodialysis patients: a pilot/feasibility study. J Ren Nutr 2005;15(3):318-31.
22. Duranay M, Akay H, Yilmaz FM, Senes M, Tekeli N, Yucel D. Effects of L-carnitine infusions on inflammatory and nutritional markers in haemodialysis patients. Nephrol Dial Transplant 2006;21:3211-14.
23. Di Donto S, Garavaglia B, Rimoldi M, Carrara F. Clinical and biomedical phenotypes of carnitine deficiencies. In Ferrari R, Di Mauro S, Sherwood G (ed):" L-cinitine and its Role in Medicine:From Function to Therapy."London: Academic Press. 1992;382-4.
24. Broderick TL, Quinney HA, Lopaschuk GD. Carnitine stimulation of glucose oxidation in the fatty acid perfused isolated working rat heart. J Biol Chem. 1992 25;267(6):3758-63.
25. Uziel G, Garavaglia B, Di Donato S. Carnitine stimulation of pyruvate dehydrogenase complex (PDHC) in isolated human skeletal muscle mitochondria. Muscle Nerve. 1988;11(7):720-4.
26. De Palo E, Gatti R, Sicolo N, Padovan D, Vettor R, Federspil G. Plasma and urine free L-carnitine in human diabetes mellitus. Acta Diabetol Lat. 1981;18(1):91-5.
27. Tamamogullari N, Silig Y, Icagasioglu S, Atalay A. Carnitine deficiency in diabetes mellitus complications. J Diabetes Complications. 1999;13(5-6):251-3.
28. Mingrone G, Greco AV, Capristo E, Benedetti G, Giancaterini A, De Gaetano A, Gasbarrini G. L-carnitine improves glucose disposal in type 2 diabetic patients. J Am Coll Nutr. 1999;18(1):77-82.
29. De Gaetano A, Mingrone G, Castagneto M, Calvani M. Carnitine increases glucose disposal in humans. J Am Coll Nutr. 1999;18(4):289-95.
30. eh GY, Eisenberg DM, Kaptchuk TJ, Phillips RS. Systematic review of herbs and dietary supplements for glycemic control in diabetes. Diabetes Care.2003;26(4):1277-94.
31. Capaldo B, Napoli R, Di B onito P, Albano G, Sacca L. Carnitine improves peripheral glucose disposal in non- insulin-dependent diabetic patients. Diabetes Res Clin Pract. 1991;14(3):191-5.
32. Rahbar A R, Shakerhosseini R, Saadat N, Taleban F, Pordal A and Gollestan B. Effect of L-carnitine on plasma glycemic and lipidemic profile in patients with type II diabetes mellitus. European Journal of Clinical Nutrition .2005;59:592-6
33. Derosa G, Cicero AF, Gaddi A, Mugellini A, Ciccarelli L, Fogari R. The effect of L-carnitine on plasma lipoprotein(a) levels in hypercholesterolemic patients with type 2 diabetes mellitus. Clin Ther. 2003;25(5):1429-39.

[Downloaded from ijdo.ssu.ac.ir on 2026-11-20]