The Effect of L- Carnitine on Cardiac Output in Patient with Chronic Kidney Disease on Regular Hemodialysis

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Abstract

Background: L- carnitine deficiency is common in patients with chronic kidney disease, especially those who are in regular dialysis. L- carnitine deficiency associated with high incidence of oxidative stress, dyslipidemia and impaired cardiac performance. The present study tends to evaluate the effect of L-carnitine supplement on cardiac output in patients with chronic kidney disease on regular hemodialysis.

Methods*:* the current study included 105 patients with chronic kidney disease, they were randomly selected from patients attending artificial kidney unit at Al-Hussein Teaching Hospital in Thiqar city for regular hemodialysis. They were divided into two groups, group I include 35 patients with chronic kidney disease who did not receive L- carnitine and considered as control group, group II include 70 patients with chronic kidney disease who receive L- carnitine. patients of group II further divided into two subgroups depending on dose of L- carnitine. Group II(A), include 35 patients with chronic kidney disease who received L- carnitine 10/kg body weight one time daily and group II(B): include 35 patients with chronic kidney disease who received L- carnitine 10/kg body weight two time daily. Ejection fraction was determined by transthoracic echocardiography. Frequency, percentage, association, paired t-test were used for analysis of variables. All variables represented by mean ± SD. P value of < 0.05 considered statistically significant.

Results: There was statistically significant increase in the mean of EF% (P<0.001) among patients with chronic kidney disease who receive L- carnitine in a dose of 10mg/Kg body weight twice daily (group IIB) after six months of treatment in comparison with the baseline values. There was a slight but significant (p< 0.05) increase in the mean of EF% in patients with chronic kidney disease who received single daily dose of L- carnitine 10mg/Kg body weight (group IIA) after six months in comparison with the initial values at the beginning of the study.

Conclusion: carnitine supplement in a suitable dose seem to improve cardiac performance among patients with chronic kidney diseases on regular hemodialysis.

Keywords: *l-Carnitine, hemodialysis, cardiac output.*

Introduction

L-Carnitine is a water soluble quaternary ammoniacal compound, the average body content of L-Carnitine in the human is about 300 mg/kg, which is stored intracellularly mainly in the skeletal muscle and to some extent in the cardiac muscle, while the circulating plasma carnitine represent only 0.5% of total body content of L carnitine [1-3]. The body requirement of L-Carnitine is provided either by ingested foods or by endogenous synthesis by the liver, kidneys and brain [4,5]. L-Carnitine play an essential role in the transport of long-chain fatty acids through the inner membrane of mitochondria which is critical for subsequent β oxidation and release of energy [6-8]. Chronic kidney disease (CKD) is one of the common health problems worldwide and despite of great advance in management of this syndrome it is still represent one of the main causes of morbidity and mortality [9]. Congestive heart failure is a common complication of CKD and it is the principle

cause of mortality among these patients [10-12]. A variety of factors may be considered as risk factors for heart failure like anemia, hypertension, and ischemic heart diseases [13]. Abnormality of lipid metabolism in cardiac myocyte and L-carnitine deficiency may predispose to heart failure in patients with CKD, by derangement of cardiac energy metabolism, increasing oxidative stress, and inflammation with subsequent cardiac myocyte necrosis [14,15]. An increasing number of studies have demonstrated that patients with CKD who are in replacement therapy with regular dialysis manifested L carnitine deficiency [16-18]. Many factors contributed to this abnormality in L carnitine level among CKD on regular hemodialysis, including decrease intake, impaired biosynthesis, and removal by dialysis [19,20]. The present study tends to evaluate the role of L carnitine in improving left ventricular function among patients with CKD maintained on regular dialysis.

Subjects, Materials and Methods

The present study is a randomized *controlled trial included* 105 patients (63 males and 42 females) with CKD on regular hemodialysis, they were selected randomly from patients who attending artificial kidney unit at Al-Hussein Teaching Hospital in Thiqar city during the period from August 2019 to March 2020. Their ages ranged from 22 - 65 years old. They were divided into two main groups:

1-Group I(control): include 35(22 male and 13 female) patients with CKD who did not received L-carnitine.

2- Group II: include 70 patients with CKD who received L- carnitine, they are further divided into two subgroups according to the dose of L- carnitine:

i- Group II(A): include 35(20 male and 15 female) patients with CKD who received L- carnitine 10/kg body weight one time daily.

ii. Group II(B): include 35(21 male and 14 female) patients with CKD who received L- carnitine 10/kg body weight two time daily.

L- carnitine (MEPACO) was given by i.v. infusion for patients of group II for six months. Cardiac performance was determined for all groups by measuring EF% utilizing transthoracic echocardiography at the beginning of the study and the same measurement repeated after six months by expert physician. All patients included in this study had two session of hemodialysis /week and each dialysis session last 3 hours.

The purpose and procedure of the study were explained to all patients included in this study and informed consent was taken from all.

statistical analysis of data done by using SPSS (statistical package of social science) version 25. Frequency, percentage, association, paired t-test were used for analysis of variables. All variables represented by mean ± SD. P value of < 0.05 considered statistically significant.

Results

The study included 105 patients with CKD divided into three groups each include 35 patients, the mean of their age and sex distribution are seen in figure 1and 2.

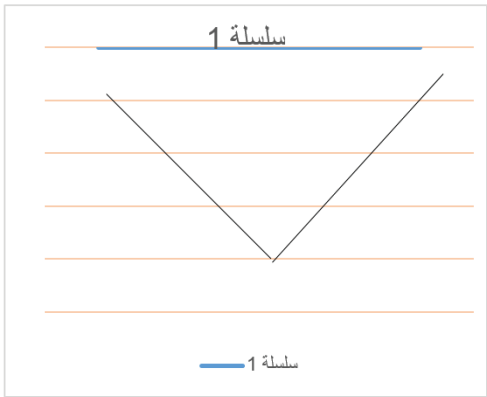

Figure1: the mean og ages of studied groups.

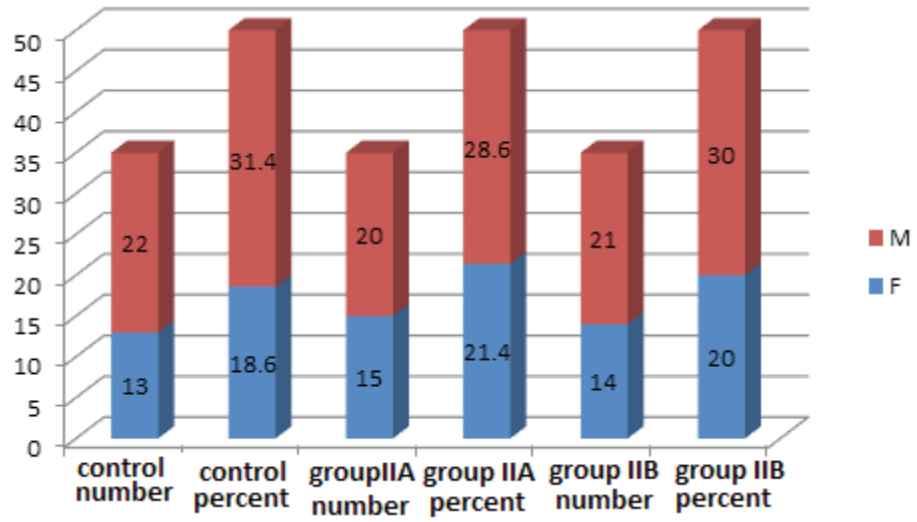

Figure2: sex distribution of studied groups.

The result of this study shows significant increase in the mean of EF% ($p< 0.001$) among patient with CKD who received L- carnitine in a dose of 10mg/Kg. body weight twice daily (group IIB) after six months of treatment in comparison with the initial values at the beginning of the study table 1 and figure 3.

Table 1: Mean SD of EF% in different studied groups before and after treatment with L carnitine.

		EF%		
Groups		**mean**	**SD**	**P value**
Group I (control)	Baseline	49.1	7.44	0. 471
	After 6 month	48.5	6.53	
Group IIA	Baseline	50.3	7.80	0.051
	After treatment	52.1	6.05	
Group II B	Baseline	49.9	5.33	0. 001
	After treatment	52. 5	5.77	

The increase in the mean of EF% among patients with CKD who received single daily dose of L- carnitine 10mg/Kg. body weight (group IIA) after six months in comparison with the baseline values at the beginning of the study was less than those who receive two doses but it was still significant ($p< 0.05$). However, there was no significant changes in the values of EF% in control group (group I) between baseline reading and that after six months.

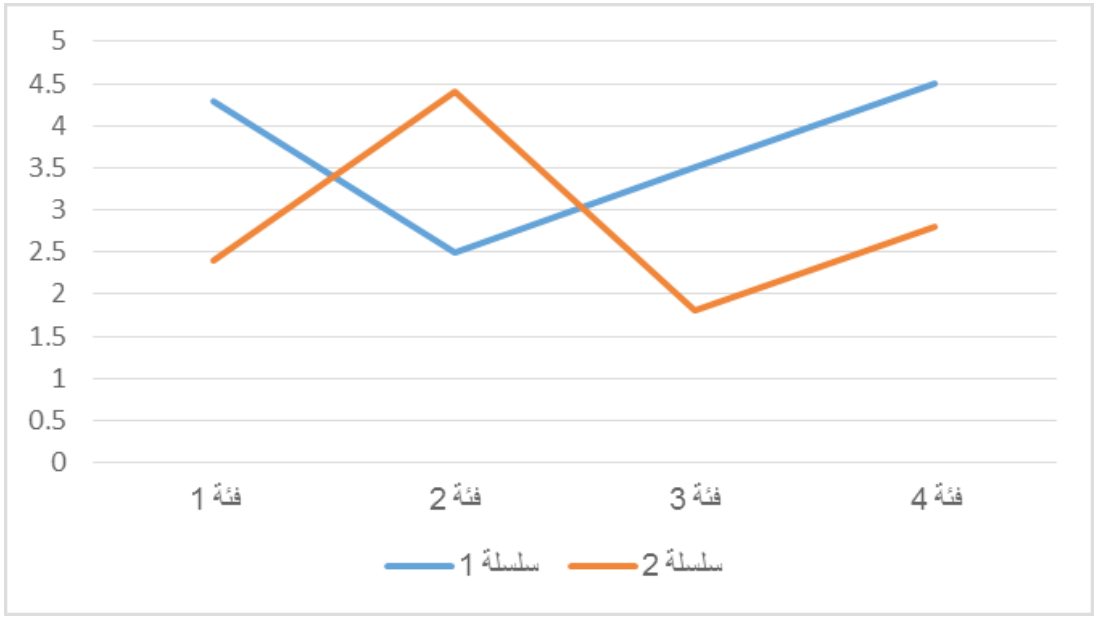

Figure 3: Means of the cardiac EF% in different studied groups at the start of the study(baseline) and after six months.

Regarding gender distribution there was no significant difference in gender between the studied groups. The mean ± SD of EF% at the start of the study(baseline) and after six months of treatment in different studied group according to the gender are shown in table 2. The values of EF% in both treated groups (IIA and IIB) were higher after six months of treatment with L- carnitine than baseline levels.

Table 2: Distribution of the means of the EF% according to the studied group and gender.

Sex		Group IIB		Group IIA		Control Group	
		Before	After	Before	After	Before	After
Female	Mean	51.71	53.8	51.13	52.93	48.92	49.23
	N	14	14	15	15	13	13
	Std. D	5.25	4.14	7.48	6.48	7.60	8.70
Male	Mean	48.71	51.52	49.65	51.55	49.22	48.18
	N	21	21	20	20	22	22
	Std. D	5.16	6.57	8.17	5.81	7.52	5.04
Total	Mean	49.914	52.45	50.28	52.14	49.11	48.57
	N	35	35	35	35	35	35
	Std. D	5.33	5.77	7.808	6.059	7.44	6.53
		.067	4.160	.573	.157	.020	5.799
		.798	.049	.454	.695	.888	022

Discussion

Heart failure considered as an actual challenge to treat, it affects millions of peoples all over the world, with great social and economic impacts on communities and high mortality rate [21-23]. Accordingly, a great deal of clinical trials and researches performed to identify an ideal treatment for heart failure, recently L-carnitine supplement attract attention in management of this disease [24,25]. The result of this study reviled considerable improvement in cardiac performance as manifested by significant increase in EF% among patients with CKD, after receiving L- carnitine in a dose of 10mg/Kg twice daily for six months (group IIB). However, there was a less significant increase in EF% values in those patients who receiving L - carnitine in a dose of 10mg/Kg once daily for six months (group IIA) when we compare the initial reading of EF% values with its values after six months of treatment.

In agreement with the result of this study Ali Reza Serati, etal. reported a significant improvement in cardiac performance among patients with diastolic cardiac dysfunction when they compare the base line echocardiographic parameters with that after three months treatment with 1.5 g/day L - carnitine [26]. Ioannis Rizos , study the effect of L-carnitine supplement on survival of patients with heart failure in comparison with placebo. Three years survival was significantly in favor ($P < .04$) of patients receiving L-carnitine in comparison with those who were given placebo [27].

The contraction of cardiac myocytes needs considerable energy, mitochondria play important role in this process as a principle site of oxidative phosphorylation [28]. the main substrates for cardiac myocyte are fatty acids, other substrate include amino acids, carbohydrate and ketones [29,30]. L - carnitine's play important role in βoxidation of fatty acid in the mitochondria, it also facilitates carbohydrate utilization [31,32]. Furthermore, L-carnitine is essential for maintaining normal lactate levels of in the cardiac myocyte [28]. In heart failure, the pattern of energy expenditure switch to other substrate in expense of fatty acid leading to increase plasma level of fatty acid which further deteriorate cardiac performance [33]. Heart failure is a multifactorial disease with a wide scope of pathophysiological mechanisms, it is believed that L-carnitine deficiency is one of the abnormalities which predispose to improper energy consumption due to impaired β oxidation of fatty acid in mitochondria [34]. Accordingly, L- carnitine supplement in patient with heart failure may act to correct the derangement of mitochondrial function by increasing fatty acid utilization and improve cardiac performance to some extent [35,36].

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Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the *College of Medicine* and all experiments were carried out in accordance with approved guidelines.

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