

Measurement of Plasma L-Carnitine Levels in Patients with Chronic Renal Failure Undergoing Hemodialysis Treatment

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Abstract

Aim: This case-controlled study was planned to measure plasma L-carnitine levels of patients diagnosed with chronic renal failure (CRF) who received regular hemodialysis treatment.

Methods: Sixty-nine patients with CRF underwent dialysis treatment 3 times a week for 4 hours were included the study. 17 of 69 patients were given carnitine treatment. They were given L-carnitine 50 mg/kg/day, peroral (Carnitine®, Sigma-Tau, Milano, Italy). The remaining 52 patients received only dialysis treatment and they were divided into 3 groups according to the duration of dialysis treatment. Group 1; who have received dialysis treatment for a year, Group 2; those who have received dialysis treatment for 1-5 years, Group 3; those who receive dialysis treatment for 5 years or more. 27 healthy adults without kidney pathology were selected as the control group. Plasma L-carnitine levels were measured using the radioisotopic method. Normal range for carnitine was defined as 12.5 µmol/L to 200 µmol/L for total carnitine according to L-carnitine standart curve. The results were read on the beta liquid scintillation analyzer.

Results: The mean age of the patients who were given carnitine was 43.94 ± 2.3, and 46.98 ± 2.1 in subjects do not use carnitine and 30.70 ± 1.3 in control group. Predialysis (11.8 ± 7.6 vs 21.3 ± 5.4, p < .001) and postdialysis plasma carnitine levels were significantly lower in the carnitine free group compared to the control group (5.23 ± 5.0 vs 21.3 ± 5.4, p < .001). In patients using carnitine, predialysis plasma L-carnitine (43.5 ± 44.2 vs 21.3 ± 5.4, p < .001) levels were higher than the control group, while postdialysis carnitine levels (11.0 ± 13.5 vs 21.3 ± 5.4, p < .001) were significantly lower than control group.

Conclusion: Reduction in hemodialysis related plasma L-carnitine levels in CRF patients can be compensated with exogenous carnitine supplementation.

Keywords: Radioisotopic Method; Hemodialysis; L-Carnitine Support; Chronic Renal Failure

Introduction

Carnitine is an important molecule required to transport long chain fatty acids through the mitochondrial membrane. This feature puts it in an important place in energy homeostasis. Carnitine also plays a role in preventing apoptotic reactions. Moreover, it is a molecule that plays a role in oxygen balance by preventing erythrocyte destruction. The liver and kidney can synthesize carnitine using lysine and methionine amino acids [1-4].

It is a known fact that hemodialysis and peritoneal dialysis treatment reduce the levels of many amino acids, protein and carnitine used in energy pathways. In accordance with this, hypocarnitinaemia often occurs in patients with CRF who regularly undergoing hemodialysis treatment [1-4]. Reduction in plasma carnitine levels develops as a consequence of inadequate intake of carnitine and carnitine containing substances, reduced carnitine synthesis, and considerable losses of circulating carnitine secondary to hemodialysis procedure [5-7]. However, there is no study investigating the relationship between hemodialysis duration and plasma L-carnitine levels in CRF patients. Therefore, the prevalence of carnitine deficiency according to dialysis duration in CRF patients on hemodialysis needs to be investigated. The present study was, therefore, planned to evaluate the effects of L-carnitine supplementation on plasma carnitine levels of patients with CRF who underwent regularly hemodialysis treatment. Participants in carnitine free group were divided into three groups to determine the possible relationship between the duration of hemodialysis treatment and plasma carnitine levels.

Materials and Methods

The patients with CRF included in the study were selected among the patients who applied to Tepecik Training and Research Hospital Departments of Internal Medicine and Biochemistry for hemodialysis treatment. This prospective case-controlled thesis study was initiated after ethical approval and verbal informed consent. The study protocol and all procedures fully adhered to the Declaration of Helsinki. The exclusion criteria were local or systemic infectious disease, hepatic disease, history of peritoneal disease or malignancy and corticosteroid therapy.

Sixty-nine patients with CRF, comprising 52 participants receiving only hemodialysis treatment and 17 participants receiving L-carnitine plus hemodialysis treatment were included the study. Patients in carnitine group underwent regular hemodialysis treatment and they were given 50 mg/kg/day, peroral L-carnitine supplementation (Carnitine®, Sigma-Tau, Milano, Italy). The serum levels of total carnitine before and after hemodialysis treatment were analyzed and the results were compared. Hemodialysis treatment was given to the patients with CRF at least 3 times a week for 4 hours. Fifty-two patients who received only hemodialysis treatment were divided into 3 groups according to the duration of hemodialysis. Group 1; who have received hemodialysis treatment for a year, Group 2; those who have received hemodialysis treatment for 1 - 5 years, and Group 3; those who received hemodialysis treatment for 5 years or more. Twenty-seven healthy adults without kidney pathology were selected as the control group. Plasma carnitine levels were calculated using the radioisotopic method which is the most sensitive carnitine measurement technique. Normal range for carnitine was defined as 12.5 µmol/L to 200 µmol/L for total carnitine according to L-carnitine standard curve. The results were read on the Tri-carb-1600 TR-PACKARD beta liquid scintillation analyzer. Detailed information about L-carnitine measurement method is given in the thesis.

Statistical analysis

The Statistical Package for Social Sciences was used for statistical analysis. The conformity to normal distribution of the data was tested via the Shapiro-Wilk test. The quantitative data were expressed as mean \pm standard deviation (SD). The normality distribution of data was found to normal. The continuous variables were analyzed by Mann-Whitney U test. The categorical data were analyzed by the Pearson chi-square test. Statistical significance was accepted as $p < 0.05$.

Results

The mean age of the patients who were given carnitine support was 43.94 ± 2.3 and the mean age of the patients who did not use carnitine was 46.98 ± 2.1 . The average age of the healthy control group without CRF is 30.70 ± 1.3 and 13 of which are women and 14 are men. The predialysis carnitine levels of Group 1 were found as 13.4 ± 7.9 , Group 2 were 12.1 ± 8.6 and Group 3 were 8.13 ± 3.2 . Predialysis (11.8 ± 7.6 vs 21.3 ± 5.4 , $p < .001$) and postdialysis plasma carnitine levels were found to significantly lower in the carnitine free group compared to the control group (5.23 ± 5.0 vs 21.3 ± 5.4 , $p < .001$). In patients taking carnitine treatment, predialysis plasma carnitine (43.5

± 44.2 vs 21.3 ± 5.4, $p < .001$) levels were higher than the control group, while postdialysis carnitine levels (11.0 ± 13.5 vs 21.3 ± 5.4, $p < .001$) were significantly lower than the control group (Table 1).

Groups	Predialysis	Postdialysis	p value
L-carnitine plus hemodialysis (n=17)	43.5 ± 44.2	11.0 ± 13.5	.001
Hemodialysis only (n=52)	11.8 ± 7.6	5.23 ± 5.0	.001
Group 1 (n=23): on hemodialysis 1 year	13.4±7.9	6.53±6.9	.01
Group 2 (n=18): on hemodialysis 1-5 years	12.1 ± 8.6	4.8±2.4	.001
Group 3 (n=11): on hemodialysis > 5 years	8.13 ± 3.2	3.22±1.2	.01
Healthy control (n=27)	21.3 ± 5.4		NA
Carnitine results were given in µmol/L			

Table 1: Predialysis and postdialysis carnitine levels of patients with CRF.

Discussion

Our study showed the laboratory characteristics of carnitine deficiency in CRF patients on hemodialysis and healthy controls. In this case-controlled study, decreased levels of circulating carnitine were found in all CRF patients who were on hemodialysis. Interestingly, as the dialysis time extended, the reduction in carnitine levels was more pronounced. Give carnitine supplementation before hemodialysis leads to increase in the serum carnitine levels. However, hemodialysis lowered the carnitine levels of CRF patients again. In line with this, circulating carnitine levels after hemodialysis was lower than the control group. This finding supports idea that the continuation of carnitine treatment following hemodialysis in CRF patients who regularly undergoing hemodialysis is logical.

A clear conclusion from our study is that long-term dialysis treatment is seen as the most important factor leading to carnitine deficiency. Therefore, serum carnitine levels should be measured at regular intervals and replaced if carnitine is found low in patients undergoing chronic hemodialysis treatment. Different mechanisms of action may be involved in the development of carnitine deficiency in CRF patients on hemodialysis. One possible explanation is that carnitine synthesis decreases in the sick kidneys [6-8]. Second possibility is that CRF patients on dialysis have to intake of foods and beverages do not containing sufficient protein and carnitine because of failed renal function [6-8]. Whatever the results reduction in circulating carnitine levels is associated with many pathological disorders such as hepatic dysfunction, mild anemia, renal and cardiac dysfunction, and weakness carnitine turnover in many muscle types [8].

There are studies reporting that carnitine levels decrease in both patients on hemodialysis and peritoneal dialysis. Our results are compatible with other studies. The only feature that makes present study different from other studies is that our study showed that reduction in carnitine levels more evident as dialysis time increases. No significant side effects related to the use of L-carnitine have been reported when the literature is reviewed. Similarly, in our study, we found no special side effects related to carnitine use. The most important limitation of our study was that the number of participants were small and carnitine levels were measured only once. However, despite all these handicaps, our study has a critical importance since we demonstrated that long-term hemodialysis decreased plasma carnitine levels in proportion to the duration of dialysis. There is a clear need for more comprehensive studies investigating the loss of molecules other than carnitine.

Conclusion

L-Carnitine treatment in patients with CRF lead to increase in serum carnitine levels. This increase may be beneficial for energy production in the cardiac and skeletal muscles. Hence, it is important to detect carnitine deficiency and ensure appropriate carnitine supplementation in CRF patients on hemodialysis for one year and more.

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