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Continuous Ambulatory Peritoneal Dialysis (CAPD) Adequacy Influences Serum Free Carnitine Level

A. E. GRZEGORZEWSKA,[1] I. MARIAK,[1]
A. DOBROWOLSKA-ZACHWIEJA[2]

Departments of [1]Nephrology and [2]Gastroenterology and Human Nutrition, Karol Marcinkowski University of Medical Sciences, Poznań, Poland

Objective: An evaluation of serum free carnitine level in CAPD patients in relation to dietary intake, nutritional status and CAPD adequacy and duration.

Study design: Food diaries, nutritional (total body mass, lean body mass, serum level of proteins, carnitine, cholesterol) and adequacy (Kt/V, PCR, tCcr, EN) parameters were obtained in 23 CAPD patients.

Results: Normal carnitine level (41.8±6.7 μmol/l) was found in 17 patients being on CAPD through 11.1±9.6 months, whereas in 6 persons treated with CAPD through 9.7±4.1 months carnitine level was 25.4±5.7 μmol/l. Significant differences between low and normal carnitine groups were in tCcr (82.7±16.7 v. 65.9±13.2 l/wk/1.73 m^2 BSA), effluent volume (10.9±0.8 v. 9.9±1.5 l/day), effluent glucose concentration (729±167 v. 530±220 mg/dl) and serum globulin level (22.6±6.4 v. 29.3±4.4 g/l). Significant correlation coefficients (for n=23) were found between serum carnitine level and effluent volume (r=−0.509) or plasma globulin level (r=+0.522).

Conclusion: Patients with higher CAPD adequacy show lower serum free carnitine levels and this is related to higher effluent volumes.

Introduction

Carnitine (exactly L-carnitine) is a very important nutritional constituent, partially generated in the human liver and kidneys. Carnitine facilitates the entry of fatty acids into mitochondria; serves an important metabolic cofactor in cardiac and skeletal muscles; may be involved in energy production from branched-chain amino acids [1]. Depletion of carnitine is characterized by mild to severe weakness of muscles and cardiomyopathy [2].

Earlier studies indicate that serum carnitine level depends on gender, age [3, 4], nutritional status [5], fasting [6, 7] and diet [8]. Uraemic patients are at high risk of carnitine deficiency due to inadequate food intake and significantly diminished carnitine synthesis in kidneys. In dialysed patients carnitine losses with dialysate substantially contribute to low serum and tissue (espe-

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cially muscle) carnitine content [9, 10]. Data on the influence of dialysis duration on serum or muscle carnitine concentration are not uniform [11, 12].

The aim of this study is to show differences in dietary intake, nutritional status and CAPD adequacy and duration in patients with normal or low serum free carnitine level.

Material and methods

Studies were performed in 23 uraemic patients (3 women and 20 men, aged 42±11 years), who were not supplemented with carnitine. The patients were treated with CAPD for 10.7±8.6 (range 0.7–30.6) months.

Food diaries (special attention for lysine, methionine, ascorbid acid, niacine, pyridoxine and ferrum as components important for carnitine endogenous synthesis), nutritional parameters (total body mass – TBM, ideal body mass – IBM, lean body mass – LBM, serum levels of protein, albumin, free, carnitine, cholesterol), peritoneal permeability and standard laboratory indices were obtained using previously described methods [13, 14]. CAPD adequacy was evaluated using Kt/V, protein catabolic rate – PCR, total creatinine clearance – tCcr and efficacy number – EN. Urea distribution volume (V) in Kt/V was calculated according to the Watson formula [15], PCR – according to the Randerson method [16], EN – according to Brandes [17]. Values of tCcr were obtained as a sum of peritoneal and renal clearances of creatinine. Renal creatinine clearance was the average of renal urea nitrogen and creatinine clearances. Clinical–laboratory status (CLS) of examined patients was evaluated using score assessment developed by Keshaviah et al. [18].

Serum concentration of free carnitine was estimated using an enzymatic method (Enzymatic UV test, Cat. No 1242008, Boehringer Mannheim, Germany). Other laboratory measurements were done with standard methods.

After obtaining results of serum free carnitine concentrations, all CAPD patients (n=23) were divided into 2 groups: with normal carnitine level (35–70 μmol/l) and with low carnitine level (<35 μmol/l). The groups were compared in relation to all examined parameters.

The Mann–Whitney test was used for statistical comparison of the results obtained in both groups of patients. Correlation analysis was made using the results of all patients (n=23) by the Spearman method. Value of $p<0.05$ was defined as statistically significant. All results are expressed as mean ± standard deviation.

Results

Normal carnitine level (41.8±6.7 μmol/l) was shown in 17 patients on CAPD for 11.1±9.6 months, whereas in 6 persons (26%) treated with CAPD for 9.7±4.1 months carnitine level was 25.4±5.7 μmol/l ($p=0.0003$). In 2 patients (9%) carnitine concentration was below 20 μmol/l. Differences in dialysis duration were insignificant.

Results of dietary intake, nutritional parameters, adequacy indices, peritoneal equilibration test (PET) and standard laboratory indices are summarized in Tables 1–5. Significant differences between low and normal carnitine groups were in tCcr (82.7±16.7 v. 65.9±13.2 l/wk/1.73 m^2 BSA), effluent volume (10.9±0.8 v. 9.9±1.5 l/day), effluent glucose concentration (729±167 v. 530±220 mg/dl), glucose content in daily effluent fluid (79.0± 18.0 v. 54.3±28.3 g) and serum total globulin level (22.6±6.4 v. 29.3±4.4 g/l). There were no significant differences between peritoneal (44.0±19.9 v. 46.5±14.2 l/wk/1.73 m^2 BSA) or residual renal (30.0±15.4 v. 16.9±12.3 l/wk/1.73 m^2 BSA) creatinine clearances in the low and normal carnitine groups.

Table I

Daily food intake in CAPD patients with normal (n=17) or low (n=6) serum free carnitine level

Parameter	CAPD patients with carnitine level: normal	CAPD patients with carnitine level: low
Total protein (g/kg IBM)	1.02± 0.35	1.08± 0.29
Animal protein (g)	47.7 ± 20.1	49.6 ± 9.0
Vegetable protein (g)	21.9 ± 9.6	22.9 ± 8.2
Lysine (mg)	4453 ±1708	4210 ±478
Methionine (mg)	1596 ± 628	1728 ±301
Carbohydrates (g/kg IBM)	3.89± 0.97	4.04± 1.63
Fat (g/kg IBM)	1.09± 0.56	1.32± 0.49
Saturated fatty acids (g)	29.9 ± 14.6	32.1 ± 9.3
Unsaturated fatty acids (g)	30.7 ± 16.6	33.6 ± 10.3
Combined polyunsaturated fatty acids (g)	8.33± 5.53	9.95± 5.89
Cholesterol (mg)	353 ± 259	495 ±262
Ferrum (mg)	11.8 ± 4.7	10.5 ± 2.4
Vit. B_1 – thiamine (mg)	1.37± 0.51	1.23± 0.51
Vit. B_6 – pyridoxine (mg)	1.69± 0.47	1.35± 0.43
Vit. C – ascorbid acid (mg)	42.0 ± 23.9	42.2 ± 24.0
Vit. PP – niacin (mg)	15.9 ± 5.2	12.0 ± 5.3
DEI with absorbed glucose (kcal/kg b. m.)	33.1 ± 7.8	36.6 ± 12.2

Significant correlation coefficients (for n=23) were found between serum carnitine level and effluent volume (r=−0.509, Fig. 1) or plasma globulin level (r=+0.522). Additionally, significant correlation was shown for effluent volume and glucose concentration (r=+0.462) or glucose content (r=+0.683) in daily effluent fluid.

There were no significant differences between the two groups of patients when total CLS or separate parts forming CLS were analyzed. For example, scores indicating "muscle weakness" showed worse results in the low carnitine group (2.33±0.47) than in the normal one (2.59±0.60) but the differences were not statistically significant.

Table 2
Nutritional status of CAPD patients with normal (n=17) or low (n=6) serum free carnitine level

Parameter	CAPD patients with	
	normal	low
	carnitine level	
Total body mass (TBM, kg)	73.7 ± 12.7	76.4 ± 17.6
TBM as % of IBM	109.3 ± 12.9	110.0 ± 13.1
Lean body mass (LBM)		
anthropometric (kg)	59.4 ± 9.9	59.5 ± 13.2
from creatinine kinetics (kg)	49.7 ± 14.6	57.6 ± 18.0
as TBW/0.73 (kg)	56.1 ± 8.3	56.7 ± 11.2
Body fat (kg)	14.2 ± 5.5	16.9 ± 6.4
BMI (kg/m^2)	25.1 ± 3.1	25.8 ± 3.7
BSA (m^2)	1.85± 0.19	1.89± 0.25
Plasma albumin (g/l)	38.0 ± 7.5	42.5 ± 8.4
Plasma total globulin (g/l)	29.3 ± 4.4	22.6 ± 6.4*
Plasma cholesterol (mg/dl)	211 ± 58	224 ± 28
Serum ferrum (µg/dl)	93.9 ± 26.3	83.7 ± 14.8
Total iron binding capacity (µg/dl)	320 ± 20	321 ± 20
Serum ferritin (ng/dl)	604 ±615	448 ±341

* $p<0.05$ compared to results obtained in patients with normal serum carnitine level

Table 3
Dialysis adequacy parameters in CAPD patients with normal (n=17) or low (n=6) serum free carnitine level

Parameter	CAPD patients with	
	normal	low
	carnitine level	
Kt/V	1.85± 0.50	2.19± 0.41
tCcr (l/week/1.73 m^2 BSA)	65.9 ±13.2	82.7 ±16.6*
EN (l/g cr/day)	7.51± 2.07	8.09± 2.73
PCR (g/kg IBM/day)	0.88± 0.23	0.97± 0.18
CLS (scores)	32.4 ± 2.4	31.8 ± 2.1

* $p<0.05$ compared to results obtained in patients with normal serum carnitine level

Table 4
Results of standard peritoneal equilibration test (PET) in CAPD patients with normal (n=17) or low (n=6) serum free carnitine level

Parameter (after 4 hour dwell)	CAPD patients with	
	normal	low
	carnitine level	
D/P for creatinine	0.80±0.14	0.79±0.09
D/D_0 for glucose	0.32±0.12	0.29±0.07
D/P for urea	0.89±0.21	0.84±0.08

Table 5
Standard laboratory measurements in CAPD patients with normal (n=17) or low (n=6) serum free carnitine level

Parameter	CAPD patients with	
	normal	low
	carnitine level	
Hb (g/dl)	10.3 ± 1.6	10.3 ± 1.3
Ht (%)	29.5 ± 5.5	30.4 ± 3.8
WBC (T/μl)	7.89± 2.66	8.03± 1.70
RBC (M/μl)	3.30± 0.66	3.28± 0.54
PLT (T/μl)	241.1 ±79.5	255.2 ±80.9
pH	7.37± 0.04	7.35± 0.02
pCO_2 (mmHg)	39.4 ± 4.4	39.2 ± 3.7
HCO_3^- (mmol/l)	22.1 ± 2.4	21.5 ± 2.0
BUN (mg/dl)	57.2 ±15.6	57.0 ±18.9
Urine volume (ml/min)	0.50± 0.42	0.84± 0.38

Discussion

Our results indicate that serum free carnitine levels are decreased in 26% of CAPD patients dialysed for less than 2 years but serum free carnitine depletion (concentration <20 μmol/l) [2] is observed only in 9% of patients. There were no significant differences in clinical-laboratory score assessment performed using the Missouri system [18] between the low and normal carnitine groups. It indicates that decreased serum concentration of free carnitine is not enough to induce symptoms or signs of clinical importance. However, low free carnitine level can precede carnitine depletion in serum and muscles, usually associated with muscle weakness and heart insufficiency.

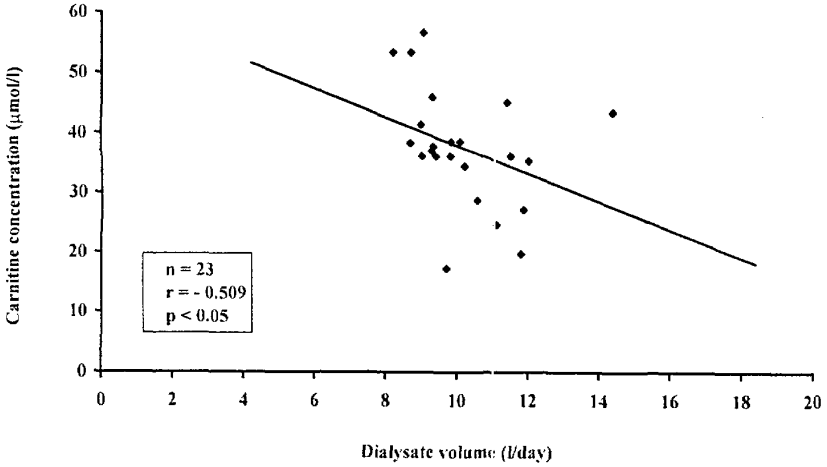

Fig. 1. Correlation between serum concentration of free carnitine and dialysate volume in CAPD patients

In our studies there is no significant difference in CAPD duration between patients with normal or low serum free carnitine level. It can be discussed that our patients were not dialysed so long as others [12, 19]. Chatzidimitriou et al. [19] have shown that patients who have been on CAPD for more than 2 years demonstrated significantly abnormally higher acylated carnitine to free carnitine ratios than those with shorter periods on CAPD treatment. An influence of increased levels of carnitine in pre-dialysis period observed by some investigators [20, 21] might still affect concentrations shown during short dialysis treatment. There are studies indicating that a depletion in serum free carnitine level can occur as late as 6–8 months of a regular haemodialysis (HD) program [22]. Savica et al. [11] suggest that there are still fairly high muscle free carnitine reserves in patients with short duration of dialysis.

Such factors as age [3, 4] and diet [8] are cited as influencing serum carnitine level in man. However, in our CAPD patients there were no differences in these factors between the normal and low carnitine groups, even if factors involved in carnitine synthesis (lysine, methionine, ascorbic acid, pyridoxine, niacin, ferrum) were separately analysed.

Due to low molecular weight of carnitine (161.2 daltons), the losses of this substance in dialysate during HD are much greater than that during CAPD [9, 10]. Thus, HD patients have generally low serum carnitine levels, whereas in CAPD patients this is not a consistent finding [9, 23]. In our studies a significant relationship between serum free carnitine level and effluent volume was shown, and patients with low carnitine level had better adequacy results than those with normal carnitine concentration. As expected, in our studies re-

lationship was also found between effluent volume and glucose concentration (and content) in drain fluid. Thus, relationship between serum carnitine level and glucose concentration (content) in dialysate can be related to a dependence of effluent volume on the osmotic gradient created by glucose. We postulate that patients with optimal CAPD adequacy should be regularly supplemented with carnitine because they are at risk of developing carnitine depletion with its clinical features.

In our studies peritoneal permeability (PET results) was not so strong a predictor of carnitine level as glucose concentration (and content) in dialysate. However, data of Chatzidimitriou et al. [19] have demonstrated that the high absorbers according to fast PET results lose significantly more free carnitine than the low absorbers. Zachwieja et al. [24] observed lower carnitine concentration in children on CAPD who had greater peritoneal permeability according to PET results.

Nutritional indices and standard laboratory measurements were not significantly different between the two groups except for serum globulin concentration. It is known that carnitine improves immunologic parameters in AIDS patients [25] but its relationship with serum globulin level was not established as yet. Pliakogiannis et al. [26] found a positive correlation between serum free carnitine level and total protein, but they did not show (like in our study) any correlations between carnitine and albumin, total cholesterol and triceps skinfold thickness.

In conclusion, patients with higher CAPD adequacy show lower serum free carnitine levels and this is related to higher effluent volumes.

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