

PLASMA FREE CARNITINE LEVELS IN CHILDREN WITH MALNUTRITION*

Fatoş Tanzer MD**, Selim Uzunsel MD***, Atilla Atalay MD****

SUMMARY: Tanzer F, Uzunsel S, Atalay A. (Department of Pediatrics, Cumhuriyet University Faculty of Medicine, Sivas, Turkey). Plasma free carnitine levels in children with malnutrition. Turk J Pediatr 1994; 36: 133-137.

In this study, plasma free carnitine and albumin levels were measured in children with protein-energy malnutrition (PEM). A total of 71 children with malnutrition were studied. The control group consisted of 20 healthy children. The mean plasma carnitine level was 78.4 ± 1.94 nmol/ml in the control group. Marasmus and kwashiorkor patients displayed lower plasma free carnitine values, which were found to be statistically significant when compared to those of the control ($P < 0.001$). However, the values were significantly lower in kwashiorkor patients than in marasmic cases ($29.7 > 5.46$). There was no correlation between serum albumin and free carnitine levels in cases with kwashiorkor. *Key words: malnutrition, plasma carnitine.*

L-carnitine plays an essential role in mitochondrial oxidation of long-chain fatty acids, facilitating their transfer across the mitochondrial membrane. The endogenous synthesis of carnitine from lysine and methionine occurs mainly in the liver, from which free and acylcarnitines are released into the blood and transported to other tissues. Cardiac and skeletal muscles depend greatly on fatty acid oxidation as an energy source and have a high requirement for carnitine¹⁻⁷.

Protein-energy malnutrition. (PEM) develops as a result of a lack of calories and protein and is usually associated with various infections⁸. Marasmus results mainly from an inadequate intake of calories in other words, starvation. A lack of calories causes an increase in catabolism, and naturally carnitine intake decreases in children with PEM.

In kwashiorkor, protein intake in particular is very limited. Likewise, the essential amino acids, such as lysine and methionine, are also deficient; consequently in sufficient endogenous synthesis of carnitine occurs. As a result, a fatty liver develops. Since carnitine plays an essential role in the oxidation of fatty acids, the deficiency of carnitine may provide an explanation for the accumulation of fats in the liver of these patients.

* From the Department of Pediatrics, Cumhuriyet University Faculty of Medicine, Sivas.

** Professor of Pediatrics, Cumhuriyet University Faculty of Medicine.

*** Pediatrician Malatya.

**** Professor of Biochemistry, Cumhuriyet University Faculty of Medicine.

There are limited data in the literature on carnitine metabolism in children with PEM⁶⁻⁷. Since studies of serum carnitine may aid in the understanding of metabolic changes occurring in PEM⁹⁻¹² and may be of potential value as regards therapy, the purpose of the present investigation was to determine carnitine and albumin concentrations in serum of children suffering from this disease in the Sivas region of Turkey.

Material and Methods

This investigation was carried out at the Department of Pediatrics at Cumhuriyet University Hospital on 71 children suffering from malnutrition and 20 healthy controls enjoying normal development.

Plasma carnitine and albumin levels were examined in 20 controls and 14 children suffering from kwashiorkor, 41 children suffering from marasmus and 16 children who were apparently healthy but had body weights which were 60-80 percent of the standard weight for Turkish children of that age¹³ and hence were judged as undernourished¹⁴. For all groups the age range was 9-24 months.

Plasma albumin fraction was estimated by Biotrol kits using RA 1000 autoanalyzer. Plasma free carnitine determination was made by an enzymatic method, using a Beckman model Spectrophotometer and recorder with electronic temperature control¹⁵.

Statistical evaluations were made in accordance with standard deviation, correlation Kruskal Wallis's analysis and real significance difference method.

Results

The mean ages, heights, weights and types of malnutrition of the 71 patients and 20 healthy controls are shown in Table I.

Table I: Mean Weights and Heights of Children with Malnutrition and Healthy Controls

Groups	n	Age (month)		Weight (kg)		Height (cm)	
		$\bar{X}$	Sx	$\bar{X}$	Sx	$\bar{X}$	Sx
Control	20	23.25	± 4.02	11	± 1.04	75.3	± 3.65
Undernourished	16	16.2	± 2.47	7	± 0.46	71.5	± 2.26
Marasmus	41	12.49	± 1.57	5.6	± 0.31	67.44	± 1.49
Kwashiorkor	14	9.6	± 2.62	6.4	± 0.57	69.4	± 2.52

Albumin levels were significantly lower in the plasma of children suffering from kwashiorkor as compared to control children (Table II).

Table II: Plasma Free Carnitine and Albumin Levels of Control and Malnourished Children

Groups	Number	Carnitine (nmol/ml)	Albumin (g/dl)
Control	20	78.40 ± 1.94	4.29 ± 0.15
Undernourished	16	67.75 ± 1.38	4.04 ± 0.09
Marasmus	41	58.97 ± 0.94	4.09 ± 0.08
Kwashiorkor	14	48.70 ± 1.91	2.10 ± 0.15
			KW = 36.76 p < 0.001

There was no correlation between serum albumin and free carnitine levels ($r=0.22$, $r=0.16$, $r=-0.05$, $r=0.45$, $p>0.01$).

Following measurements of plasma free carnitine values in marasmus and kwashiorkor patients, the mean values were found to be 69.75 ± 1.38 nmol/ml in undernourished children and 58.97 ± 0.94 in those with marasmus. The mean obtained in patients with kwashiorkor 48.7 ± 1.91 nmol/ml. All these values were significantly lower than those of the healthy controls (Table III, $P<0.001$). However, values were significantly lower in kwashiorkor patients than in marasmic cases ($29.7>5.46$, Table III).

Table III: Plasma Free Carnitine Levels of Control and Malnourished Children

Groups	Number	Carnitine (nmol/ml)	Analysis
Control ^a	20	78.4 ± 1.94	KW = 67.56 p > 0.001
Undernourished ^b	16	69.75 ± 1.38	
Marasmus ^c	41	58.97 ± 0.94	
Kwashiorkor ^d	14	48.70 ± 1.91	

Statistical Analyses: a vs b, a vs c, a vs d,
b vs c, b vs d, c vs d; $p<0.05$.

Discussion

Factors such as sex, age¹⁶⁻¹⁸, nutritional status¹⁹, fasting²⁰⁻²¹, and disease²²⁻²⁴ have been cited as influencing plasma carnitine levels in man. Recently there have

been several reports about the impact of diet on plasma carnitine levels in various species²⁵. Less has been published on plasma carnitine levels in man^{19,26}.

The present study clearly demonstrates a decrease in serum carnitine in children with PEM, especially kwashiorkor, as compared to well-nourished controls. This finding is consistent with the observations of Khan et al⁶ and Hammod et al⁷. The low levels of carnitine reported here for children with PEM, may be associated with reduced intake of carnitine itself, together with a deficiency of the precursor amino acids lysine and methionine, giving rise to inadequate endogenous synthesis²⁷⁻³⁰. Deficiency of other nutrients, such as iron and vitamin C, as well as enzymes required for the biosynthesis of carnitine may also be involved. This clearly accounts for the low level of carnitine leading to fatty liver in kwashiorkor.

This condition is an indicator of fatty acid catabolism disorder. In marasmic cases without fatty liver, the plasma free carnitine level was higher than that of the kwashiorkor cases. This finding stresses the significance of endogenous carnitine achieved by the liver.

The fact that no correlation between serum albumin and free carnitine levels was observed in the cases investigated in this study has been attributed to varying dysfunctions in the control mechanism in cases with kwashiorkor. The findings obtained clearly indicate that further investigations on carnitine concentration at the tissue level are essential in PEM for more effective oral management of carnitine deficiency.

REFERENCES

1. Lennon DL, Shrago ER, Madden M, Nagle FJ, Hanson P. Dietary carnitine intake related to skeletal muscle and plasma carnitine concentrations in adult men and women. *Am J Clin Nutr* 1986; 43: 234-238.
2. Stumpf DA, Parker WD Jr, Angelini C. Carnitine deficiency, organic acidemias, and Reye's syndrome. *Neurology* 1985; 35: 1041-1045.
3. Gilbert EF. Carnitine deficiency. *Pathology* 1985; 17: 161-171.
4. Bremer J. Carnitine metabolism and functions. *Physiol Rev* 1983; 63: 1420-1480.
5. Feller AG, Rudman D. Role of carnitine in human nutrition. *J Nutr* 1988; 118: 541-547.
6. Khan L, Bamji MS. Plasma carnitine levels in children with protein-calorie malnutrition before and after rehabilitation. *Clin Chim Acta* 1977; 75: 163-166.
7. Hammond KD, Toblansky R, Abrahams OL. Serum carnitine in children with kwashiorkor. *Ann Trop Paediatr* 1987; 7: 214-216.
8. Bhattacharyya AK. Protein-energy malnutrition (Kwashiorkor-Marasmus syndrome): terminology, classification and evolution. *World Rev Nutr Diet* 1986; 47: 80-133.
9. Rebouche CJ, Engel AG. Kinetic compartmental analysis of carnitine metabolism in the human carnitine deficiency syndromes. Evidence for alterations in tissue carnitine transport. *J Clin Invest* 1984; 73: 857-867.
10. Schiff D, Chan G, Seccombe D, Hohn P. Plasma carnitine level during intravenous feeding of the neonate. *J Pediatr* 1979; 95: 1043-1046.

11. Novak M, Wieser PB, Buch M, Hahn P. Acetylcarnitine and free carnitine in body fluids before and after birth. *Pediatr Res* 1979; 13: 10-15.
12. Battistella PA, Vergani L, Donzoli F, et al. Plasma and urine carnitine levels during development. *Pediatr Res* 1980; 14: 1379-1381.
13. Yalaz K, Epir S. Physical growth measurements of preschool urban Turkish children. *Turk J Pediatr* 1983; 25: 155-165.
14. McLaren. Protein energy malnutrition (PEM). Classification, pathogenesis, prevalence, prevention. *Textbook of Pediatric Nutrition*. London: Churchill Livingstone, 1976: 118.
15. Marquis NR, Fritz IB. Enzymological determination of free carnitine concentrations in rat tissues. *J Lipid Res* 1964; 5: 184-187.
16. Fritz IB. Carnitine and its role in fatty acid metabolism. *Adv Lipid Res* 1963; 1: 285.
17. Cederblad G. Plasma carnitine and body composition. *Clin Chim Acta* 1976; 67: 207-212.
18. Di Mauros, Scott C, Penn AS, Rowland LP. Serum carnitine. *Arch Neurol* 1973; 28: 186-190.
19. Khan-Siddiqui L, Bamji MS. Plasma carnitine levels in adult males in India: effects of high cereal, low fat diet, fat supplementation, and nutrition status. *Am J Clin Nutr* 1980; 33: 1259-1263.
20. Frohlich J, Secombe DW, Hahn P, Dodek P, Hynie I. Effect of fasting on free and esterified carnitine levels in human serum and urine: correlation with serum levels in human serum levels of free fatty acids and β -hydroxybutyrate. *Metabolism* 1978; 27: 555-561.
21. Hoppel CL, Genuth SM. Carnitine metabolism in normal-weight and obese human subjects during fasting. *Am J Physiol* 1980; 238: E 409-415.
22. Rudman D, Sewell CW, Ansley JD. Deficiency of carnitine in cachectic cirrhotic patients. *J Clin Invest* 1977; 60: 716-723.
23. Fuller RK, Hoppel CL. Elevated plasma carnitine in hepatic cirrhosis. *Hepatology* 1983; 3: 554-558.
24. Chen SH, Lincoln SD. Increased serum carnitine concentration in renal insufficiency. *Clin Chem* 1977; 23 (2 pt 1): 278-280.
25. Secombe DW, Hahn P, Novak M. The effect of diet and development on blood levels of free and esterified carnitine in the rat. *Biochim Biophys Acta* 1978; 528: 483-489.
26. Cederblad G. Effect of diet on plasma carnitine levels and urinary carnitine excretion in humans. *Am J Clin Nutr* 1987; 45: 725-729.
27. Tanphaichitr V, Broquist HP. Role of Lysine and ϵ -N-trimethyllysine in carnitine biosynthesis. II. Studies in the rat. *J Biol Chem* 1973; 248: 2176-2181.
28. Tanphaichitr V, Home DW, Broquist HP. Lysine, a precursor of carnitine in the rat. *J Biol Chem* 1971; 246: 6364-6366.
29. Strength DR, Yu SY, Davis EY. Biosynthesis of carnitine: dietary factors that influence concentration of carnitine in tissue. In: Wolf G (ed) *Recent Research on Carnitine. Its Relation to Lipid Metabolism*. Cambridge: M.I.T. Press; 1965: 45-46.
30. Wolf G, Berger CR. Studies on the biosynthesis and turnover of carnitine. *Arch Biochem* 1961; 92: 360-365.