Carnitine Levels in Patients with Skeletal Myopathy due to Anorexia Nervosa before and after Refeeding

John Morton,[1]* Declan M. McLoughlin,[2] Stephen Whiting,[3] and Gerald F. M. Russell[2]

[1] Department of Clinical Pathology, The Maudsley Hospital, London, United Kingdom
[2] Department of Psychiatry, The Institute of Psychiatry, London, United Kingdom
[3] Department of Clinical Chemistry, The Royal Preston Infirmary, Preston, United Kingdom

Accepted 18 February 1998

Abstract: **Objective:** *To assess the role of carnitine in the skeletal myopathy present in anorexia nervosa.* **Method:** *Serum levels of free and total carnitine were measured in a group of severely underweight women with anorexia nervosa and skeletal myopathy before and after an inpatient refeeding program.* **Results:** *Carnitine levels were within the reference range before refeeding and remained unchanged despite significant weight gain in all the subjects.* **Conclusion:** *These findings suggest that carnitine plays no part in the muscle weakness seen in severe anorexia nervosa. © 1999 by John Wiley & Sons, Inc.* Int J Eat Disord 26: 341–344, 1999.

Key words: *carnitine levels; skeletal myopathy; anorexia nervosa*

INTRODUCTION

Extreme weight loss in anorexia nervosa (AN) causes weakness of the proximal limb musculature and the muscles which control head movements (Alloway, Shur, Obrecht, & Russell, 1988). The myopathy appears to be a metabolic myopathy and is characterized by Type 2 muscle fiber atrophy, abnormal accumulation of muscle glycogen, and an attenuated lactate response to ischemic exercise (Essen, Fohlin, Thoren, & Saltin, 1981; Lindboe, Askevold, & Slettebo, 1982; McLoughlin et al., 1998). In a recent case report of an anorexic patient with neuromyopathic complications, who was also found also to have a vitamin C deficiency, the authors speculated that a possible mechanism for the muscle weakness might have been reduced levels of carnitine (Woodruff, Morton, & Russell, 1994).

Correspondence to: John Morton, Department of Clinical Pathology, The Maudsley Hospital, London SE5 8AZ, United Kingdom.

 CCC 0276-3478/99/030341-04

Carnitine (β-hydroxy-γ-trimethylamino-butyric acid) is an indispensable cofactor for carnitine palmitoyl transferase (CPT). It catalyzes the transport of medium- and long-chain fatty acids into the mitochondria where they undergo β-oxidation to become involved in energy production (Rebouche & Engel, 1983). The highest concentrations of free carnitine are found in muscle where concentrations are approximately 40 times that found in serum. Red meat and dairy products are the main dietary sources of carnitine. Endogenous synthesis occurs predominantly in the liver and requires the two essential amino acids lysine and methionine plus the presence of vitamin C as a cofactor (Hughes, Hurley, & Jones, 1980). Hepatic production is normally sufficient to meet the metabolic needs of healthy adult vegetarians. Carnitine is excreted mostly unchanged in the urine. Carnitine deficiency, whether it be primary or secondary, manifests itself as proximal muscular weakness and is typically associated with lipid storage myopathy (Rebouche & Engel, 1983). Interestingly, in primary myopathic carnitine deficiency, a rare and probably autosomal recessive disorder, the concentration of carnitine is decreased in muscle but is normal or only slightly reduced in serum. This may reflect a primary defect in the active transport of carnitine into muscle. Primary systemic carnitine deficiency, which is also a rare and probably autosomal recessive disorder, is characterized by hepatic failure as well as a lipid storage myopathy. Both serum and muscle carnitine levels are markedly decreased, possibly due to a failure of the hepatic synthesis of carnitine (Anonymous, 1981).

In order to investigate and clarify the role of carnitine in myopathy caused by extreme protein-calorie malnutrition due to AN, serum levels were assayed in patients when severely weight reduced and again following an inpatient refeeding program.

METHODS

Eight women, mean age 24 years (*SD* = 3.0) and all vegetarians, admitted consecutively to the Eating Disorders Unit at the Maudsley Hospital were entered into the study. All patients fulfilled the criteria for AN outlined in the 4th ed. of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV; American Psychiatric Association, 1994) and had no intercurrent illnesses. A complete account of the patients' clinical status on admission is presented elsewhere (McLoughlin et al., 1998). Serum samples for estimation of free and total carnitine levels were obtained within 24 hr of admission (mean body mass index [BMI] = 13.1). They were obtained again when patients had completed the refeeding program and weight was restored to an acceptable level (mean BMI = 19.2). One of the patients discharged herself before completing the program (her data are shown in Table 1 but were not used in any statistical calculations). Sera were stored at -20°C for later analysis.

Carnitine levels were measured as follows: the samples were first deproteinized by centrifuging through a membrane (Intersep Filtration Systems, Wokingham, Berks, UK) and the ultrafiltrate used for subsequent analysis. Free carnitine was measured on a Cobas Fara (Roche Diagnostics, Welwyn Garden City, Herts, UK) by an enzymatic method (Seccombe et al., 1976). Total carnitine was measured by the same method but after an alkaline hydrolysis on the ultrafiltrates to convert all the esterified carnitine into the free form. Data were analyzed using paired *t* tests.

RESULTS AND DISCUSSION

Table 1 shows the BMI (kg/m^2), free and total carnitine levels (μmol/L), and the length of stay on the unit in days. Despite all subjects experiencing a significant weight gain,

Table 1. Body mass indices and carnitine levels before and after refeeding

Subject	BMI		Free Carnitine (μmol/L)		Total Carnitine (μmol/L)		Length of Stay (Days)
	Pre	Post	Pre	Post	Pre	Post	
1	15.02	19.66	34	24	47	34	119
2	13.32	21.14	32	51	58	65	95
3	11.59	18.61	22	35	39	53	144
4	13.45	18.99	41	43	56	66	130
5	12.82	18.43	35	40	47	45	87
6	12.86	20.20	45	47	54	59	88
7	12.64	17.61	36	35	50	42	77
8	(11.5)	—	(39)	—	(49)	—	Discharged
M	13.10	19.23	35.0	39.29	50.14	52.0	105.7
SD	1.04	1.19	7.26	8.96	6.52	12.17	25.3
t value	−13.0		−1.20		−0.50		
Significance	(<.0001)		(.13, NS)		(.31, NS)		

Note: Results and paired *t* test values. Data from Subject 8 shown, but not used in statistical calculations.

there was no change in carnitine levels. The total carnitine reference range for female subjects is 30 to 73 μmol/L (Rebouche & Engel, 1983). Our results clearly indicate that there was neither an absolute deficiency in serum carnitine nor was there a significant increase in levels upon refeeding. Serum-free carnitine levels, a good indicator of available carnitine (Veldee, 1986), were also normal (19 to 60 μmol/L) and remained unchanged upon refeeding. Furthermore, electron microscopic examination of muscle biopsies failed to show any lipid deposition, which is a characteristic of carnitine deficiency (McLoughlin et al., 1998).

Since carnitine is synthesized in the liver, liver function tests were monitored before and after the refeeding program. There were no significant changes in bilirubin, alkaline phosphatase, γ-glutamyl transpeptidase, aspartate transaminase (AST), or albumin. One patient had an elevated AST level (2.5 times the upper limit of normal) at the start of the study but this had returned to normal by the end of the refeeding program. Vitamin C, a cofactor of carnitine synthesis (Hughes et al., 1980), was not measured in any of our subjects, but none of them exhibited any signs or symptoms of a deficiency.

Little appears to be known about carnitine and AN. A case report in the Japanese literature describes carnitine deficiency in an 18-year-old female AN patient. However, this was a single case report of a patient with severe concomitant liver disease who was also receiving total parenteral nutrition (TPN; Fukusako, Negoro, Tsuda, Kato, & Morimatsu, 1995). Since TPN solutions contain little or no carnitine, combined with the patient's poor liver function, it was not too surprising that there was a carnitine deficiency. Furthermore, muscle biopsy from this patient demonstrated copious lipid accumulations, a feature typical of carnitine deficiency but not seen in any of the patients in the present study. In another study, one of three AN subjects investigated was reported to have had a low level of total carnitine (Bohmer, Ryding, & Solberg, 1974). Apart from stating that the AN subjects were otherwise healthy, clinical details were scant and carnitine levels after refeeding were not measured. To our knowledge, the present study is the first to systematically investigate the relationship between carnitine and myopathy in patients with severe protein-calorie malnutrition due to AN. We conclude that there is no evidence to support a major role for carnitine deficiency in the myopathy of AN.

REFERENCES

Alloway, R., Shur, E., Obrecht, R., & Russell, G.F.M. (1988). Physical complications in anorexia nervosa: Haematological neuromuscular changes in 12 patients. British Journal of Psychiatry, 153, 72–75.

American Psychiatric Association. (1994). Diagnostic and statistical manual of mental disorders (4th ed.), Washington, DC: Author.

Anonymous. (1981). Clinical nutrition cases. Nutrition Reviews, 39, 400–402.

Bohmer, T., Ryding, A., & Solberg, H.E. (1974). Carnitine levels in health and disease. Clinica Chimica Acta, 57, 55–61.

Essen, B., Fohlin, L., Thoren, C., & Saltin, B. (1981). Skeletal muscle fibre types and sizes in anorexia nervosa patients. Clinical Physiology, 1, 395–403.

Fukusako, T., Negoro, K., Tsuda, N., Kato, M., & Morimatsu, M. (1995). A case of secondary carnitine deficiency due to anorexia nervosa and severe liver damage. Rinsho Shinkeigaku, 35, 34–37.

Hughes, R.E., Hurley, R.J., & Jones, E. (1980). Dietary ascorbic acid and muscle carnitine in guinea pigs. British Journal of Nutrition, 43, 385–388.

Lindboe, C.F., Askevold, F., & Slettebo, M. (1982). Muscle changes in skeletal muscles of young women with anorexia nervosa. An enzyme histochemical study. Acta Neuropathologica, 56, 299–302.

McLoughlin, D.M., Spargo, E., Wassif, W.S., Newham, D.J., Peters, T.J., Lantos, P.L., Russell, G.F.M. (1998) Acta Neuropathol, 95, 632–640.

Rebouche, C.J., & Engel, A.G. (1983). Carnitine metabolism and deficiency syndromes. Mayo Clinic Proceedings, 58, 533–540.

Seccombe, D.W., Dodek, P., Frolich, J., Hahn, P., Skala, J.P., & Campbell, D.J. (1976). Automated method for L-carnitine determination. Clinical Chemistry, 22, 1589–1592.

Veldee, M.S. (1986). Nutrition. In C.A. Burtis, E.R. Ashwood (Eds.), Tietz Textbook of Clinical Chemistry (pp. 1236–1274), Philadelphia, Saunders.

Woodruff, P.W.R., Morton, J., & Russell, G.F.M. (1994). Neuromyopathic complications in a patient with anorexia nervosa and a vitamin C deficiency. International Journal of Eating Disorders, 16, 205–209.