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Original article

Carnitine in severely disabled patients: Relation to anthropometric, biochemical variables, and nutritional intake

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Abstract

Background: Carnitine plays a pivotal role in a variety of cellular functions. Carnitine deficiency often occurs in severely disabled patients, especially under valproic acid administration. However, the possible causative factors underlying carnitine deficiency have not been fully identified. The present study aimed at clarifying the association of various anthropometric and biochemical variables, including dietary intake of carnitine, with carnitine levels in severely disabled patients. *Methods:* Twenty-six severely disabled patients (mean age: 14.1 years; s.d. 7.8) were enrolled. Plasma carnitine levels were evaluated by an enzyme cycling assay. Estimation of the dietary intake of carnitine was made based on dietary records over a 3-day period. *Results:* Plasma total and free carnitine levels in patients were significantly lower than those in controls obtained from the previous report. However, the ratios of free carnitine to total carnitine did not change significantly. Free carnitine levels were well correlated with a nutritional intake of carnitine. Administration of not only valproic acid but also other anti-epileptic drugs was found to cause a significant decrease of free carnitine levels after adjusting the nutritional intake of carnitine. Among various anthropometric or biochemical variables, albumin and uric acid showed a significant correlation with free carnitine levels. *Conclusions:* Physicians should be aware of the fact that severely disabled patients are at risk for carnitine deficiency even in the absence of valproic acid administration, and pay more attention to the nutritional intake of carnitine.

Keywords: Carnitine; Disabled patients; Valproic acid; Dietary intake; Anthropometric measures; Biochemical variables

1. Introduction

Undernutrition or malnutrition is one of the serious problems in severely disabled patients [1,2]. Since these conditions may increase the risk of nutrition-related morbidity and mortality, it is necessary to carefully observe and, if necessary, intervene in the diets of patients [3]. With respect to the causative mechanisms underlying undernutrition or malnutrition, several factors including inappropriate dietary intake, oral motor dysfunction, increased nutrient losses and abnormal energy expenditure have been postulated [1]. Although oral feeding is preferable to tube or parenteral feeding at every clinical setting, oral intake is sometimes hampered in these patients because of their difficulty in chewing and swallowing or expressing their hunger or food preferences [1]. Consequently, tube feedings of

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enteral formula through different routes must sometimes be used [2,3]. During chronic tube feedings, especially in children, patients tend to suffer from selected nutrient deficiencies [4,5].

Carnitine (β-hydroxy-γ-N-trimethylaminobutyric acid) is one of the micronutrients that plays an important role in a variety of intracellular functions [6,7]. In humans, 75% of carnitine is thought to be obtained from the diet. The remaining 25% is synthesized endogenously from lysine and methionine mainly in the liver and kidney [7]. Secondary carnitine deficiency can be observed in various clinical situations, including inherited metabolic disorders, insufficient dietary intake, liver cirrhosis, hemo- or peritoneal dialysis and pharmacological therapy [7,8]. Among drug-induced causes, carnitine deficiency caused by valproic acid (VPA) is relatively common. Therefore, the prevalence and the mechanism of carnitine deficiency by VPA have been particularly well investigated [8–10]. Several hypotheses, i.e., increase of excretion in the form of valproylcarnitine, inhibition of tubular reabsorption, reduction of endogenous synthesis, and inhibition of the membrane carnitine transporter by valproylcarnitine, have been presented to explain the underlying mechanisms [8]. However, studies specifically targeting the association of clinical factors, including those considering the dietary intake of carnitine, are limited [11]. This fact led us to examine the relation of anthropometric, biochemical and nutritional factors to carnitine deficiency in severely disabled patients.

Table 1
Patient characteristics.

Total number	26
Gender	
Male	15
Female	11
Age (years)	
Mean [s.d.]	14.1 [7.8]
0–5	3
6–10	4
11–15	5
16–20	6
21–25	5
26∼	3
Diagnosis	
Perinatal abnormalities	10
Malformation syndromes	7
Epilepsy	2
Post-head trauma	2
Hypoxia	2
Others	3
Nutritional method	
Food only	15
Formula only	9
Both	2
Anti-convulsants	
VPA+*	10
VPA-AED+**	8
None	8

* Use of valproic acid (VPA) as a single drug or with other antiepileptic drugs (AED).
** Use of AED (carbamazepine, clobazam, or lamotrigine) without use of VPA.

2. Materials and methods

2.1. Study population

Twenty-six severely disabled patients admitted to Todaiji Medical and Education Center during April and September 2012 were enrolled. This facility specializes in the care and treatment of neurologically disabled patients mainly at age of less than 20 years old. The severity of disability in each patient was defined by using the Gross Motor Function Classification System [12]. Most patients had a disability level of 4 or 5. The patients had not received carnitine supplementation previously. The profiles of these patients are described in Table 1. This study was approved by both the ethical committee for epidemiological study at Nara Women's University and the ethical committee at Todaiji Medical and Education Center. Informed consent was obtained from the guardians of all patients.

2.2. Sample collection

Fasting blood samples were drawn from patients, and were immediately sent to a laboratory (Bio Medical Laboratories, Tokyo, Japan) for the measurement of plasma total carnitine, free carnitine, and acylcarnitine levels. These assays were done by an enzyme cycling assay [13]. Since it is difficult to get substantial numbers of samples from healthy children from ethical reasons at present in Japan, we used the data obtained from the previous report that measured carnitine levels by the same method, an enzyme cycling assay [14]. At the same time, the resting blood samples of the patients were used for evaluating the following biochemical variables: C reactive protein (CRP), creatinine, uric acid, glucose, HbA_1C, albumin, transthyretin, retinol-binding protein, and N-terminal pro-B-type natriuretic peptide (pro-BNP). At the time of blood sampling, patients had been free from any symptoms over the previous week, and their CRP values were less than 1.0 mg/dL in order to minimize the effect of inflammation.

2.3. Anthropometric measurement

Body height and weight were routinely measured by well-trained nurses at this facility. Spine height was measured to the nearest 0.1 cm, and weight was measured to the nearest 0.1 kg. Since most patients had severe spinal curvatures, their height was measured by the two split method, in which the whole body is divided into two