Serum total and free carnitine levels in children with asthma

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Background: **Serum carnitine is decreased in recurrent pulmonary infections. We aimed to evaluate serum carnitine levels in asthmatic children.**

Methods: **Study group consisted of children with stable asthma and those with acute asthma attacks, while control group included healthy children. Attack severity was determined by the pulmonary score system. Total and free carnitine levels were studied in one blood sample from the control group and stable asthmatics and in two samples from children with acute asthma exacerbation during and after the attack.**

Results: **All the 40 patients in the study group had moderate asthma including 30 with acute attack (13 mild and 17 moderate) and 10 with stable asthma. Carnitine levels were significantly lower in acute attack asthmatics than in the stable asthmatics and controls, while there was no significant difference between the latter two groups. Carnitine levels were not different between asthmatics with mild and moderate attack, and were similar during and after an acute attack.**

Conclusions: **Serum carnitine levels decrease in children with moderate asthma during exacerbation of asthma and shortly thereafter. Further studies are needed to evaluate the effect of carnitine treatment on serum carnitine level.**

World J Pediatr 2009;5(1):60-62

Key words: **asthma; carnitine; children**

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doi:10.1007/s12519-009-0011-8

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Introduction

L-carnitine, a cofactor that plays an essential role in the mitochondrial oxidation of long chain fatty acids, spares muscle glycogen, improves tolerance to physical activity, and reduces muscle fatigue.[1] L-carnitine administration is beneficial to exercise and respiratory strength training in outpatients with stable, moderate-to-severe chronic obstructive pulmonary diseases.[2] In addition, it has been demonstrated that carnitine supplementation can increase serum carnitine levels, improve exercise capacity and correct the obstructive pattern in breath function tests in maintenance hemodialysis patients.[3,4]

The bronchodilator effect of carnitine on asthma and asthma attacks is not known. In this study, we compared serum carnitine levels in children with asthma to those of healthy controls. We evaluated whether serum carnitine levels of asthmatic children are affected by acute exacerbations of asthma.

Clinical summary

The study group consisted of children with asthma who attended the Pediatric Allergy Clinic of Dokuz Eylül University Hospital during a 6-month period. The control group included children who were admitted to Pediatric Surgery Clinic or Otolaryngology Clinic for circumcision or tonsillectomy at the same period and who did not have a history of atopic disease in themselves or in their family. The study protocol was approved by the Ethics Committee for Human Research of the Dokuz Eylül University Medical Faculty and written consent was obtained from all participants.

Patients with asthma in the study group were diagnosed and classified according to the Global Initiative for Asthma (GINA) criteria.[5] In patients who presented with acute asthma attack, the severity of the attack was determined according to pulmonary score system. Pulmonary score was calculated with regard to breath rate according to age, wheezing severity and sternocleidomastoid muscle activity, which were scored between 0 and 3 each. Attack was considered mild if the pulmonary score was ≤3, moderate if it was 4-6,

and severe if it was 7 or more.[6]

Serum total and free carnitine levels were studied by the enzymatic spectrophotometric method (Shimadzu UV160A spectrophotometre, Japan) in peripheral blood samples. One blood sample was collected from the control group and the stable asthmatic children, but two were from the children presenting with acute asthma exacerbation during the attack and three weeks after the attack respectively. Then, the serum carnitine levels were compared 1) in asthmatic patients during and after an acute attack, 2) in asthmatic patients with different attack severity, and 3) between the control group and patients presenting with and without acute asthma attack.

Statistical analysis was performed with SPSS 10.0 software. Data were expressed as mean ± standard deviation. Dependent groups were compared by Wilcoxon's signed-rank test and independent groups by the Mann-Whitney U test. $P<0.05$ was considered statistically significant.

Forty asthmatic children (27 male) with a mean age of 9.4±2.9 years (range: 5-18 years) were included in the study group and 15 children (10 male) with a mean age of 9.1±4.3 years (range: 4-16 years) included in the control group. All the patients in the study group had moderate asthma according to the American Thoracic Society criteria and all were prescribed inhaled steroid therapy at doses of 200-400 μg/day. During the study period, 30 patients presented with acute asthma attacks, which was mild in 13 patients and moderate in the other 17. Serum samples were obtained from all the 30 patients during an acute attack, but samples three weeks after the attack could only be obtained from 17 of the 30 patients. One serum sample was obtained from the 10 stable asthmatics in the study group and from all the controls.

Serum total and free carnitine levels were similar during and three weeks after an acute exacerbation in the 17 patients (Table 1). Serum total and free carnitine levels were significantly lower in the asthmatics presenting with acute attack (30 patients) than those with stable asthma (10) and the controls. However, asthmatic children with a stable course and the control group showed no difference in carnitine levels (Table 2). Similarly, there was no significant difference between asthmatics with mild and moderate attacks (Table 3).

Table 1. Serum total and free carnitine levels in asthmatics with an acute attack

	During the attack (n=17)	3-week after the attack (n=17)	P
Total carnitine (μmol/L)	30.0±17.7	35.1±13.3	0.227
Free carnitine (μmol/L)	24.0±14.2	26.9±10.2	0.287

Table 2. Serum total and free carnitine levels in asthmatics with acute asthma attack, stable asthmatics and the controls

	Asthmatics with acute attack (n=30)	Stable asthmatics (n=10)	Controls (n=15)
Total carnitine* (μmol/L)	37.5±21.0	76.1±39.8	68.6±45.2
Free carnitine† (μmol/L)	29.9±16.7	60.9±31.9	55.0±36.2

*: P=0.005 for patients with acute asthma attack vs. stable asthmatics, P=0.014 for patients with acute asthma attack vs. controls, P=0.495 for stable asthmatics vs. controls. †: P=0.005 for patients with acute asthma attack vs. stable asthmatics, P=0.014 for patients with acute asthma attack vs. controls, P=0.531 for stable asthmatics vs. controls.

Table 3. Serum total and free carnitine levels in asthmatics with mild and moderate asthma attack

	Mild asthma attack (n=13)	Moderate asthma attack (n=17)	P
Total carnitine (μmol/L)	36.9±17.8	38.0±23.8	0.983
Free carnitine (μmol/L)	29.8±14.7	30.0±18.5	0.933

Discussion

Carnitine is found in the skeletal and cardiac muscle, kidney, liver and brain in addition to plasma.[2] The lung also contains more than 40 different cell types, most of them involved in lipid metabolism. Pulmonary surfactant, a complex of 90% lipids and 10% lung specific apoproteins, is synthesized and secreted from type II cells.[7] Serum carnitine level was found to be decreased in newborns with respiratory distress syndrome.[8] This was proposed to be associated with increased consumption of carnitine in the lung tissue for surfactant synthesis. During asthma exacerbations inflammatory cells release phospholipase A2 into the airway, which hydrolyzes phosphatidylcholine, the principal component of surfactant.[9] Thus, the low level of serum carnitine in our asthmatic children during or shortly after (3 weeks in this study) asthmatic attack might be attributed to decreased lung surfactant (during attack) and the use of body stores to replenish it (after attack). Moreover, serum free carnitine levels were reported to be decreased in children with recurrent pulmonary infections.[10]

We did not evaluate the effect of carnitine administration on our asthmatic patients. However, intravenous administration of carnitine after hemodialysis to the patients undergoing maintenance hemodialysis, who had decreased levels of serum

carnitine due to limited intake and dialytic loss, resulted in increased predialytic serum carnitine levels and prevented subclinical bronchospasm during hemodialysis.[4,11] Furthermore, carnitine treatment improved bronchoconstriction and bronchial inflammation by decreasing LTE4 levels in a rat model of asthma.[12] Another mechanism for the effectiveness of carnitine in asthma is related to the association of asthma to dietary fat. Proportion and the quality of dietary fat affect asthma prevalence which is correlated positively with saturated fat and negatively with unsaturated fat in adolescents.[13] Hence, diet rich in cholesterol increases levels of IL-5 and cysteinyl leukotrienes in the bronchoalveolar fluid in rats.[14] Supplementation with carnitine tends to normalize fatty acid profiles in dialysis patients.[3]

In conclusion, serum carnitine levels decrease in children with moderate asthma during exacerbation of asthma and shortly thereafter. Further studies are needed to evaluate the effect of carnitine treatment on serum carnitine level, bronchospasm and exercise tolerance in asthmatic children.

Funding: None.
Ethical approval: The study protocol was approved by the Ethics Committee for Human Research of the Dokuz Eylül University Medical Faculty.
Competing interest: There is no conflict of interest.
Contributors: Asilsoy S and Bekem Ö analyzed the data and wrote the article. Asilsoy S, Karaman Ö, and Uzuner N contributed to the design and interpretation of the study. Kavukçu S proposed the study and is the guarantor.

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Received July 10, 2008
Accepted after revision November 17, 2008