EXPERIMENTAL STUDY

Serum free carnitine in medium chain acyl-CoA dehydrogenase deficiency

Bzduch V, Behulova D, Salingova A, Ponec J, Fabriciova K, Kozak L

1st Department of Pediatrics, Comenius University Children's Hospital, Bratislava, Slovakia. **bzduch@inmail.sk**

Abstract

Medium chain acyl-CoA dehydrogenase (MCAD) deficiency is the most common disorder of fatty acid ß-oxidation and presents acutely with hypoglycemia, or a Reye-like illness with low free carnitine, often provoked by an infection or an excessive period of fasting. After acute attack these children are for the most time asymptomatic and may have normal plasma free carnitine concentrations. We observed a regularity in time course of serum free carnitine concentration during two attacks of Reye-like illness in patient with MCAD deficiency. Molecular investigation confirmed that the patient was homozygote for A985G mutation. Free carnitine was measured by enzymatic UV-test. First attack of severe hypoglycemia and Reye-like symptoms started at the age of 15 months and the second at the age of 25 months. In both episodes, treatment with intravenous glucose was given immediately, but without carnitine supplementation. Between the attacks patient was on a normal diet. In both attacks, low serum free carnitine concentration from the time of acute attack continually decreased for up to 8–13 days and then normalized at about 25 days after attack. We think that the time course of serum free carnitine may help in knowledge about carnitine depletion in MCAD deficiency. This is the first observation of this pattern during an acute attack and needs to be confirmed by other patients with MCAD deficiency. ***(Fig. 2, Ref. 7.)***

Key words: medium-chain acyl-CoA dehydrogenase (MCAD) deficiency, free carnitine, L-carnitine supplementation, Reye-like syndrome, disorders of ß-oxidation of fatty acid, time course.

The measurement of free carnitine and acylcarnitines is now a standard method for the investigation of children with disorders of fatty acid ß-oxidation (7). Medium chain acyl-CoA dehydrogenase (MCAD) deficiency is the most common disorder of fatty acid ß-oxidation and presents acutely as a Reye-like syndrome with low free carnitine in plasma (1). After an acute attack these children are asymptomatic and may have normal free carnitine concentrations.

Patient and method

During two acute attacks in a boy with proven MCAD deficiency (homozygote for A985G mutation with typical acylcarnitine profile) (2) we measured free carnitine in serum at regular intervals by enzymatic UV-test.

The first attack of severe hypoglycemia and symptoms of a Reye-like syndrome started at the age of 15 months. The second attack occurred at the age of 25 months. In both attacks, treatment with intravenous glucose was started immediately, but without carnitine supplementation. Between the attacks the patient was on a normal diet. During another (third) attack at the age of 27 months, intravenous supplementation with carnitine was given.

Results

In both attacks we observed a pattern in the time course of free carnitine concentration in the serum. From the time of the acute attack (day 0) free carnitine concentration in serum continually decreased up to 8–12 days and then spontaneously nor-

1st Department of Pediatrics, Comenius University Children's Hospital, Bratislava, Department of Clinical Biochemistry, Comenius University Children's Hospital, Bratislava, Department of Biochemical and Molecular Genetics, Research Institute of Child Health, Brno, Czech Republic

Address for correspondence: V. Bzduch, MD, PhD, 1st Dept of Pediatrics, Comenius University Children's Hospital, Limbova 1, SK-833 40 Bratislava 37, Slovakia.

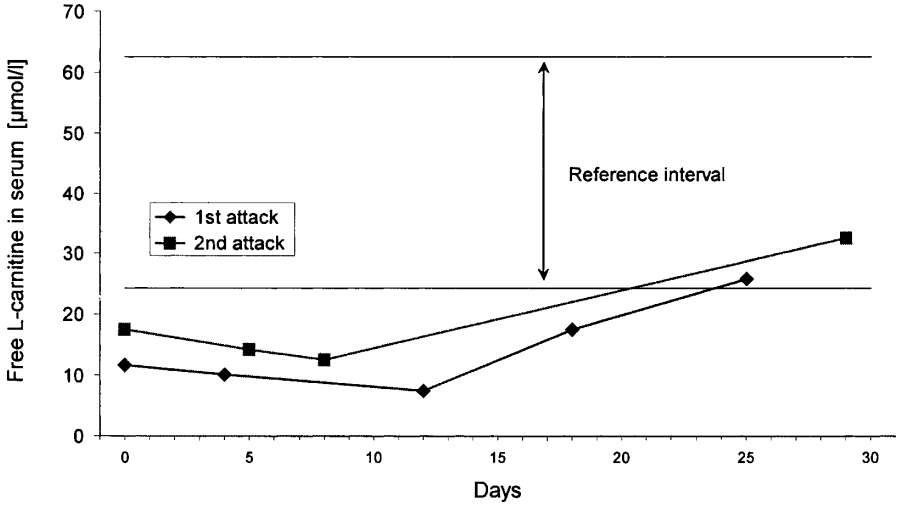

Fig. 1. Time course of free L-carnitine concentrations in serum from the time of attack to normalization.

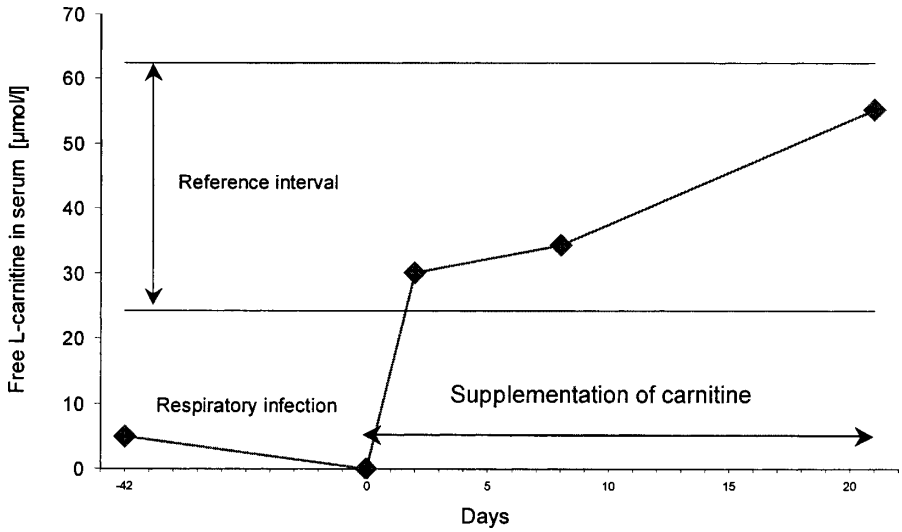

Fig. 2. Time course of free L-carnitine concentrations in serum during 3rd attack with carnitine supplementation.

malized approximately at 20–25 days after the attack (Fig. 1). During the third attack (day 0), proceeded by respiratory infection with low free carnitine concentration in serum, intravenous supplementation of carnitine normalized free carnitine concentration in the serum (Fig. 2). The patient has been on oral carnitine and a low fat diet for two years without acute episodes.

Discussion

Why is free carnitine concentration in plasma low during an acute attack in MCAD deficiency and when does it spontaneously normalize? A block in medium chain fatty acid oxidation creates an accumulation of acyl-CoA intermediates. Transesterification with carnitine leads to the formation of acylcarnitines, which are removed from mitochondria and excreted in urine and this mechanism accounts for a low free carnitine in plasma (6).

The clinical consequences of low free carnitine concentration in plasma with increased acylcarnitines concentration are poorly understood and it is difficult to distinguish between the effects of the disease and the carnitine deficiency. Supplementation of L-carnitine has not been recommended by some authors (3, 4) but by others it has been advocated on the basis of the biochemical role of carnitine in permitting conjugation and excretion of toxic intermediates (5). L-carnitine supplementation restores these levels at least in plasma and can allow normalization of mitochondrial energy production. The lowest concentra-

tion of free carnitine in plasma observed at 8–12 days after the attack shows that this period may be critical for the patients with MCAD deficiency. The observed regularity in the time course of free carnitine in serum during an acute attack may improve our knowledge about carnitine depletion. This needs to be confirmed in other patients with MCAD deficiency. Our case also shows that in MCAD deficiency exogenous carnitine supplementation might be beneficial when free carnitine levels in plasma are reduced.

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