Carnitine Serum Levels in Children with Iron Deficiency Anemia

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Abstract

Objective: To evaluate carnitine serum levels as a co-morbidity in children with iron deficiency anemia.

Patients and Methods: Fifty-four well nourished children (29 boys and 25 girls) with iron deficiency anemia were enrolled. Twenty-five healthy non-anemic age- and sex-matched children were included as a control group. For all anemic children and controls, we performed complete blood cell count, serum ferritin, serum iron, and total iron binding capacity. Carnitine levels were measured by spectrophotometric method.

Results: Serum carnitine levels were significantly lower in children with iron deficiency anemia than in the controls (p<0.001). There were strongly significant positive correlations between serum carnitine and hemoglobin, serum iron, and serum ferritin (p<0.001 for all).

Conclusions: Low serum levels of carnitine in those children may be due to iron deficiency. Therefore, iron fortification of diet of children seems to be essential not only to prevent anemia but also to avoid possible effects of iron deficiency in growing children such as secondary carnitine deficiency.

Key Words: Carnitine – Iron deficiency anemia – Children.

Introduction

ONE of the major causes of anemia in childhood period worldwide is iron deficiency [1]. In general, iron deficiency anemia is most common among children aged 6 months to 3 years, its prevalence drops among school-age children, but increases again during adolescence [2].

Carnitine is an amino acid derivative found in high energy demanding tissues (skeletal muscles, myocardium, liver and adrenal glands). Most carnitine is obtained from diet. It can be also synthesized endogenously by the liver and kidneys from the essential amino acids lysine and methionine [3,4]. Long-chain fatty acids penetrate the inner mitochondrial membrane as carnitine derivatives; activation of lower fatty acids, and their oxidation within the mitochondria, may occur independently of carnitine, but long-chain acyl coA or free fatty acids will not penetrate the inner membrane of mitochondria and become oxidized unless they form acylcarnitine [5].

Primary and secondary carnitine deficiency with decreased carnitine concentrations in blood and tissues have been described in humans [6]. Although primary deficiency is unusual, depletion due to secondary causes, such as a disease or medication side effect, can occur [7]. Primary carnitine deficiency is caused by a defect in plasma membrane carnitine transporter in muscle and kidneys [3]. Secondary carnitine deficiency in humans may result from excessive acyl coenzyme-A production, increased urinary losses, insufficient intake of carnitine or its precursors or decreased endogenous biosynthesis. Under these and related conditions, carnitine status may be compromised [6].

In children, abnormal plasma carnitine concentrations have been found associated with inborn errors of metabolism, Reye or Reye-like syndromes, treatment with valproic acid, parental nutrition, malabsorption, chronic dialysis, low syndrome, protein-calorie malnutrition or use of soy-based or carnitine-free formulas, thalassemia and prematurity [8-10].

L-carnitine has been administered in renal failure anemia and included in baby foods and milk [11]. Iron is required for the biosynthesis of carnitine and iron deficiency has been shown to cause depletion of liver carnitine in experimental animals [12-14].
This study aims to evaluate carnitine serum levels as a co-morbidity in children with iron deficiency anemia.

**Patients and Methods**

This study was conducted at the Pediatric Outpatient Clinic, Maternity and Children Hospital, Southwestern Region, Saudi Arabia between July 2008 and June 2010. The study was approved by the Ethical Committee of the hospital.

Fifty-four children (29 boys and 25 girls), aged ranged from 9 to 72 months with iron deficiency anemia were enrolled in the study after obtaining parental informed consent. Age- and sex-matched 25 non-anemic healthy children were included as a control group. All patients and controls were subjected to thorough history taking with special attention to nutritional history and full physical examination.

For all anemic children, we performed complete blood cell count (CBC) by an automated cell counter (Sysmex NE), including measuring hemoglobin (Hb) levels, hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC). Serum iron (SI) and total iron binding capacity (TIBC) levels assays [15] were performed by automated clinical chemistry, Dimension ES Delaware Depont Co.; additionally, serum ferritin [16] and C-reactive protein [17] were also performed. Iron deficiency anemia was confirmed in cases where Hb, Hct, MCV, serum ferritin and SI levels were considered when values were two standard deviations below their mean for age [18].

**Carnitine assay:**

Blood samples of 2mL were obtained by venipuncture from the patients and controls. Sera were separated and stored at 800°C until the assay. Serum total carnitine levels were measured according to Schafer and Reichmann’s spectrophotometric method [19].

**Statistical analysis:**

Data were expressed as means ± standard deviation (SD). Student ‘t’ test and χ² test were used to test significance of differences at 5% level. Pearson correlation coefficient was calculated to quantify the correlation between Hb, SI, Serum ferritin and serum carnitine levels in patients with iron deficiency anemia. Statistical analysis was performed using (SPSS) software.

### Results

A total of 54 children with iron deficiency anemia [29 males (54%) and 25 females (46%)] were enrolled in this study. Their mean age was 38.2±15.9 months. Hemoglobin, MCV, MCHC were significantly lower in patients than in controls (p<0.001), however, Hct values were lower in patients than in controls but this difference was statistically non-significant, as shown in Table (1).

Our results showed that serum iron and serum ferritin levels were significantly lower in children with iron deficiency anemia than in controls (p<0.001). Total iron binding capacity was significantly higher in patients than in controls, p<0.001 (Table 2).

Serum levels of carnitine showed significant positive correlations with hemoglobin, serum iron, and serum ferritin (r=0.84, p<0.001; r=0.91, p<0.001; r=0.90, p<0.001, respectively), as shown in Table (3).

#### Table (1): Some demographic characteristics and CBC results of patients and controls.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients (n=54)</th>
<th>Controls (n=25)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (months) (1)</td>
<td>38.2±15.9</td>
<td>34.8±17.2</td>
<td>0.38</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Male (2)</td>
<td>29 (54%)</td>
<td>14 (56%)</td>
<td></td>
</tr>
<tr>
<td>- Female (2)</td>
<td>25 (46%)</td>
<td>11 (44%)</td>
<td>&lt;0.85</td>
</tr>
<tr>
<td>Hb (g/dL)</td>
<td>10.0±2.1</td>
<td>13.8±0.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hematocrit % (1)</td>
<td>26±1.5</td>
<td>37±2.0</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>MCV (FL) (1)</td>
<td>60.2±5.0</td>
<td>87.2±6.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MCH (pg/cell) (1)</td>
<td>19±3.0</td>
<td>28±2.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MCHC (g Hb/dL RBC) (1)</td>
<td>26±2.5</td>
<td>33.0±3.0</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

(1): Mean ± SD. (2): Number (%).

#### Table (2): Serum levels of iron, iron binding capacity and carnitine in patients and controls.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients (n=54)</th>
<th>Controls (n=25)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum iron (µg/dL)</td>
<td>12.8±2.2</td>
<td>85±9.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total iron binding capacity (µg/dL)</td>
<td>551±60.7</td>
<td>308±40.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum ferritin (ng/ml)</td>
<td>4.9±2.3</td>
<td>82.1±31.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum carnitine (µmol/L)</td>
<td>13.9±2.2</td>
<td>40.4±3.4</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

#### Table (3): Correlation coefficient (r) between serum carnitine level and hemoglobin, serum iron and serum ferritin levels.

<table>
<thead>
<tr>
<th>Variables</th>
<th>r</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>0.84</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum iron</td>
<td>0.91</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum ferritin</td>
<td>0.90</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Iron deficiency has been shown to cause depletion of liver carnitine in experimental animals [11,12]. Furthermore, other evidence supports that some of the findings in severe iron deficiency anemia may be related to decrease tissue carnitine concentrations such as decreased exercise tolerance and muscle endurance [20,21]. Although many conditions are well known to cause secondary carnitine deficiency, its relation with iron deficiency has not yet been well studied. To our knowledge, there are few human studies in the literature documenting low carnitine concentration in healthy children with iron deficiency anemia. So, in this study, we evaluated carnitine serum levels as co-morbidity in children with iron deficiency anemia.

In our study, serum levels of carnitine were significantly lower in patients with iron deficiency anemia than in controls. These findings are consistent with those of Cemeroglu, et al. [22].

Moreover, our results showed that serum levels of carnitine were positively correlated with hemoglobin levels, serum iron, and serum ferritin. These findings are consistent with those of several studies, which indicated increased hemoglobin levels among groups receiving L-carnitine as compared with groups not receiving L-carnitine [22-24].

Moreover, it has been confirmed in animal studies that maternal iron deficiency leads to altered carnitine metabolism, causing a significant decrease in liver carnitine and a concomitant increase in liver triglycerides in rat pups [25]. Furthermore, it has been reported that liver iron-deficient rat pups contain significantly less carnitine than the liver of control pups [12,13]. In addition to these animal studies, it has been reported that patients with phenylketonuria have low serum carnitine concentrations, possibly due to inadequate iron availability in their diets [26].

Conclusions:

Lowered serum carnitine levels constitute a significant co-morbidity in children with iron deficiency anemia. Iron fortification of diet of children seems to be essential not only to prevent anemia but also to avoid possible effects of iron deficiency in growing children such as secondary carnitine deficiency. However additional studies are still needed to assess the need for carnitine supplementation in children with iron deficiency anemia. It will be interesting to measure the carnitine levels in those patients after normalizing their hemoglobin levels.

References


