Detection of serum iron and zinc levels in patients with type 2 diabetes mellitus and their relationship with glucose and lipid metabolism

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Objective: To study the blood iron and zinc levels in patients with type 2 diabetes mellitus and their relationship with glucose and lipid metabolism.

Methods: Patients with type 2 diabetes mellitus were enrolled in T2DM group and healthy people were enrolled in control group. T2DM patients were divided into low iron and zinc group and high iron and zinc group with the median of serum iron and zinc contents as the standard. Serum trace elements contents and glucose and lipid metabolism indicators were detected.

Results: T2DM patients’ blood iron contents were significantly higher than those of the control group while the zinc contents were significantly lower than those of the control group. Copper, calcium and magnesium contents had no significant difference between two groups of patients. HbA1c%, glucagon and HOMA-IR as well as apoB, apoE, ApoM, leptin and vaspin contents in high iron group were higher than those in low iron group while serum insulin, GLP-1, GIP, ApoA1, APN and HOMA-β levels were lower than those in low iron group. HbA1c%, glucagon, HOMA-IR, apoB, apoE, ApoM, leptin and vaspin contents in high zinc group were lower than those in low zinc group while serum insulin, GLP-1, GIP, ApoA1, APN and HOMA-β levels were higher than those in low zinc group.

Conclusions: the serum iron level was abnormally high and the zinc content was abnormally low in patients with type 2 diabetes mellitus. Serum iron and zinc levels were closely related to the glucose and lipid metabolism.

1. Introduction

Type 2 diabetes is the most common endocrine disease. The incidence continues to increase in recent years, which causes adverse effects to patients’ life quality, health and safety. Chronically elevated glucose levels will increase the incidence risk of the nervous, cardiovascular and renal complications[1]. The relative shortage of insulin secretion and insulin resistance in peripheral tissues are important pathological features of patients with type 2 diabetes. The factors that cause the pathological changes include genetic factors, environmental factors, dietary factors, and so on[2]. Recent studies have found that the body’s trace element iron (Fe) and zinc (Zn) content abnormality is closely related to the occurrence and development of type 2 diabetes[3,4]. Therefore, ascertaining Fe and Zn levels in patients with type 2 diabetes will help to provide a new target for the prevention and treatment of the disease. In the following study, we analyzed the serum iron and zinc levels in patients with type 2 diabetes mellitus and their relationship with glucose and lipid metabolism.

2. Objects and methods

2.1 Objects

A total of 35 patients first diagnosed with type 2 diabetes and 35 healthy individuals undergoing a medical examination from May 2013 to October 2015 in our hospital were enrolled in the study. Patients with type 2 diabetes mellitus were as T2DM group and...
healthy individuals were as control group. In T2DM group, there were 21 male cases and 14 female cases, whose age was (48±6) years old. In the control group, there were 20 cases of male and 15 cases of female, whose age was (47±5) years old. There were no significant differences between the two groups in the general information.

2.2 Methods

2.2.1 Detection of trace elements in serum
The contents of trace elements, including copper, zinc, calcium, magnesium and iron were determined by flame atomic absorption spectrometry. The instrument was BoHui flame atomic absorption spectrometry spectrograph in Beijing, and the model was BH5100plus.

2.2.2 Determination and evaluation of glucose and lipid metabolism indexes
Enzyme linked immunosorbent assay (ELISA) was used to determine insulin (INS), glucagon insulin-like peptide 1 (GLP-1), insulin dependent insulinotropic secretion of polypeptide (GIP), glucagon (glucagon), apoB, apoE, ApoM, leptin, vaspin, ApoA1 and APN contents. Glycosylated hemoglobin (HbA1c) content was detected by chemiluminescence method. Insulin resistance index (HOMA-IR) and insulin secretion index (HOMA-β) were calculated in accordance with the HOMA homeostasis model.

2.3 Statistical methods
Medians of T2DM patients’ serum iron and zinc contents were calculated. T2DM patients with serum iron and zinc contents below median were enrolled in iron and zinc low group while T2DM patients with those above median were classified as iron and zinc high group. T test was applied to the comparison of measurement data between two groups. The differences were statistically significant between groups when \( P < 0.05 \).

3 Results

3.1 Serum trace element contents
We measured and analyzed two groups of patients’ serum iron, zinc, calcium, copper and magnesium contents. Results were as follows: T2DM patients’ serum iron content was significantly higher than the control group’s while zinc content was significantly lower. Copper, calcium and magnesium contents had no statistical differences between the two groups, as shown in Table 1.

3.2 Glucose metabolism indexes of patients with different serum iron and zinc levels
Glucose metabolism indexes of patients with different serum iron levels were as follows: HbA1c, glucagon and HOMA-IR were higher in high iron group patients than those in low iron group while serum insulin, GLP-1, GIP and HOMA-β levels were lower, as shown in Table 2. Glucose metabolism indexes of patients with different serum zinc levels were as follows: HbA1c, glucagon and HOMA-IR were lower in high zinc group patients than those in low zinc group while serum insulin, GLP-1, GIP and HOMA-β levels were higher, as shown in Table 3.

3.3 Lipid metabolism indexes of patients with different serum iron and zinc levels
Lipid metabolism indexes of patients with different serum iron levels were as follows: ApoB, ApoE, ApoM, leptin and Vaspin levels were higher in high iron group patients while in low iron group and ApoA1 and APN levels were lower, as shown in Table 4. Lipid metabolism indexes of patients with different serum zinc levels were as follows: ApoB, ApoE, ApoM, leptin and Vaspin levels were lower in high zinc group patients while in low zinc group and ApoA1 and APN levels were higher, as shown in Table 5.

### Table 1
Comparison of serum trace elements in two groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Fe (mmol/L)</th>
<th>Zn (μmol/L)</th>
<th>Ca (mmol/L)</th>
<th>Mg (mmol/L)</th>
<th>Cu (μmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T2DM</td>
<td>35</td>
<td>2.29±0.25</td>
<td>0.68±0.08</td>
<td>0.029±0.004</td>
<td>1.39±0.17</td>
<td>1.78±0.19</td>
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<tr>
<td>Control</td>
<td>35</td>
<td>1.39±0.16</td>
<td>1.92±0.22</td>
<td>0.035±0.003</td>
<td>1.55±0.19</td>
<td>1.84±0.21</td>
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<tr>
<td>T</td>
<td></td>
<td>7.585</td>
<td>19.337</td>
<td>0.572</td>
<td>0.273</td>
<td>0.105</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
</tr>
</tbody>
</table>

### Table 2
Blood glucose metabolism indexes in patients with different serum iron levels.

<table>
<thead>
<tr>
<th>Group</th>
<th>HbA1c%</th>
<th>Ins (mmol/L)</th>
<th>GLP-1 (pmol/L)</th>
<th>GIP (pmol/L)</th>
<th>Glucagon (ng/L)</th>
<th>HOMA-β</th>
<th>HOMA-IR</th>
</tr>
</thead>
<tbody>
<tr>
<td>High iron</td>
<td>8.42±0.94</td>
<td>7.87±0.87</td>
<td>10.49±1.26</td>
<td>6.35±0.77</td>
<td>20.34±2.35</td>
<td>22.38±2.52</td>
<td>3.29±0.39</td>
</tr>
<tr>
<td>Low iron</td>
<td>7.39±0.88</td>
<td>13.86±1.68</td>
<td>16.79±1.84</td>
<td>10.23±1.36</td>
<td>13.29±1.45</td>
<td>40.59±4.48</td>
<td>1.68±0.22</td>
</tr>
<tr>
<td>P</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

### Table 3
Blood glucose metabolism indexes in patients with different serum zinc levels.

<table>
<thead>
<tr>
<th>Group</th>
<th>HbA1c%</th>
<th>Ins (mmol/L)</th>
<th>GLP-1 (pmol/L)</th>
<th>GIP (pmol/L)</th>
<th>Glucagon (ng/L)</th>
<th>HOMA-β</th>
<th>HOMA-IR</th>
</tr>
</thead>
<tbody>
<tr>
<td>High zinc</td>
<td>7.32±0.89</td>
<td>14.11±1.72</td>
<td>16.33±1.79</td>
<td>10.92±1.41</td>
<td>14.11±1.61</td>
<td>39.14±4.25</td>
<td>1.77±0.21</td>
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<tr>
<td>Low zinc</td>
<td>7.50±0.92</td>
<td>7.32±0.81</td>
<td>10.92±1.30</td>
<td>6.11±0.72</td>
<td>19.33±2.13</td>
<td>23.67±2.89</td>
<td>3.11±0.41</td>
</tr>
<tr>
<td>T</td>
<td>6.623</td>
<td>10.185</td>
<td>7.092</td>
<td>8.781</td>
<td>5.968</td>
<td>7.283</td>
<td>8.772</td>
</tr>
<tr>
<td>P</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
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</tr>
</tbody>
</table>
Epidemiological data shows that the incidence rate of type 2 diabetes is increasing year by year worldwide. Type 2 diabetes patients are expected to be over 360 million by 2030 in the world. High-risk population’s disease screening and prevention measures are becoming more and more important clinical problems[5]. Type 2 diabetes mellitus is a chronic metabolic disease, and the lifestyle and dietary changes are closely related to the increase of the incidence of disease[6]. Changes in dietary structure will not only directly affect the body's substances and energy metabolism, but also cause content and proportion changes of trace elements, and then cause the abnormal metabolism of glucose and lipid. Iron, zinc, manganese, iodine, fluorine, selenium, copper, molybdenum, chromium and cobalt are ten types of essential trace elements of the human body, which only account for 0.01% of the body weight, but have important physiological values. Trace elements are important parts of many hormones, nucleic acids and enzymes in the body, which determine the biological function of many kinds of molecules, and the contents will affect the metabolism and function of tissues and cells.

In recent years, more and more scholars have realized that trace elements are related to the occurrence and the development of type 2 diabetes. We detected and analyzed ten kinds of trace elements that were essential to human body. Results showed that serum iron content was significantly higher in patients with T2DM than that in the control group while zinc content was significantly lower than that in control group. Manganese, iodine, fluorine, selenium, copper, molybdenum, chromium and cobalt contents had no significant differences between the two groups. This indicated that the change of serum iron and zinc contents were related to the occurrence of type 2 diabetes mellitus. The excessively produced iron ion acts as biological catalysts for oxidative damage, it generates a large amount of oxygen free radicals by Fenton’s reaction and causes damage to cells. Pancreatic \( \beta \) cell function damage will directly cause insufficient insulin secretion and decreased sensitivity of peripheral tissues to insulin\[7,8\]. Zinc atom is an important part in insulin molecular structure, and also cofactor of 3-phosphoglycerate dehydrogenase, lactate dehydrogenase and malate dehydrogenase. Zinc deficiency can affect insulin synthesis and sugar decomposition metabolism\[9,10\].

Type 2 diabetes mellitus is characterized by the relative shortage of insulin secretion and the elevation of blood glucose level caused by insulin resistance in peripheral tissues. Incretin is recently discovered endocrine hormone closely related to type 2 diabetes mellitus (T2DM), including glucagon like peptide-1 (GLP-1) and insulin dependent insulinotropic polypeptide (GIP)\[11\]. GLP-1 is the incretin with the most significant insulintropic effect, which is mainly secreted by L cells in the small intestine, and can bind the G protein coupled receptor of pancreatic \( \beta \) cells and promote insulin secretion\[12\]. GIP, after binding with the receptor, can activate adenylate cyclase and increase the cAMP contents, and then enhance the insulin synthesis and secretion\[13\]. Our analysis on blood glucose metabolism indexes in patients with different levels of serum iron and zinc contents showed that HbA1c, glucagon and HOMA-IR were higher in high iron group patients than those in low iron group while serum insulin, GLP-1, GIP and HOMA-IR levels were lower. HbA1c, glucagon and HOMA-IR were lower in high zinc group patients than those in low zinc group while serum insulin, GLP-1, GIP and HOMA-IR levels were higher. This showed that in patients with type 2 diabetes, zinc and iron levels were related to glucose metabolism, the higher the zinc content and the lower the iron content, the more insulin and insulintropic hormone secretion and the higher the insulin sensitivity.

The course of the onset of type 2 diabetes mellitus is mainly complicated with abnormal lipid metabolism. The body’s contents of trace elements can affect the metabolism of blood lipid by affecting the secretion of insulin and insulintropic hormone. Apolipoprotein has the function of regulating the metabolism of lipoprotein, which is an important molecule to regulate the lipid metabolism in vivo. ApoA1 is the major protein component of high density lipoprotein, which can promote lipid metabolism and reduce the level of blood lipid. ApoB is the major protein component of low density lipoprotein. ApoB is the major protein component of low density lipoprotein.
lipoprotein, which can increase the serum lipid levels[14]. ApoE and apoM are two kinds of newly discovered lipoproteins, which participate in the regulation of glucose and lipid metabolism at the same time[15]. In addition to apolipoprotein, other kinds of adipocyte factors including leptin, adiponectin (APN) and Vaspin are also associated with lipid metabolism. Our analysis on blood glucose metabolism of patients with different levels of serum iron and zinc contents showed that: ApoB, ApoE, ApoM, Leptin and Vaspin levels were higher in high iron group patients than those in low iron group while ApoA1 and APN levels were lower. ApoB, ApoE, ApoM, Leptin and Vaspin levels were lower in high zinc group patients than those in low zinc group while ApoA1 and APN levels were higher. This showed that zinc and iron contents in patients with type 2 diabetes were related with lipid metabolism. The higher the zinc content and the lower the iron content, the more ideal lipid metabolism condition and the lower the level of blood lipid.

To sum up, patients with type 2 diabetes iron levels increased abnormally while the zinc contents decreased abnormally. Serum iron and zinc levels were closely related to glucose and lipid metabolism.

References