Relationship of Vitamin D deficiency with Lipid metabolism, micro-inflammatory response and endothelial injury in obese children

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ABSTRACT

Objective: To study the relationship of vitamin D deficiency with lipid metabolism, micro-inflammatory response and endothelial injury in obese children. Methods: a total of 68 cases of obese children who received examination in our hospital were chosen as obese group, 56 cases of overweight children who received examination in our hospital were chosen as overweight group, and 50 cases of normal children who received vaccination in our hospital were chosen as normal control group. The differences in peripheral blood 1,25-(OH)D3 content as well as serum contents of lipid metabolism, micro-inflammatory reaction and endothelial injury indexes were compared among three groups. Pearson test was used to evaluate the internal relationship between 1,25-(OH)D3 and the degree of environmental disturbance in obese children. Results: 1,25-(OH) D3 contents in obese group and overweight group were lower than that in normal control group, and 1,25-(OH) D3 content in obese group was lower than that in overweight group. Serum contents of lipid metabolism indexes TC, TG and LDL-C in obese group and overweight group were higher than those in normal control group while HDL-C content was lower than that in normal control group; contents of micro-inflammation indexes CRP, IL-6 and TNF-\(\alpha\) were higher than those in normal control group; serum content of endothelial injury index ET-1 was higher than that in normal control group while NO, CGRP and PGI2 contents were lower than those in normal control group; the changes in serum contents of above indexes in obese group were larger than those in overweight group. Conclusion: There is vitamin D deficiency in obese children, and the degree of deficiency is directly related to the degree of abnormal lipid metabolism, micro-inflammation and endothelial injury.

1. Introduction

Obesity of children continues to rise in recent years, it is closely related to their imbalanced diet, overnutrition, reduced physical exercise and so on, and the continuously increasing body weight not only increases the difficulty of the children’s daily activities, but can also cause the body’s endocrine disorder and even cause cardiovascular diseases\cite{1,2}. Vitamin D is a fat-soluble steroid derivative that has a variety of biological activities, it mainly exists in the active form 1,25-(OH)D3 in the blood, and it has multiple functions such as maintaining the calcium phosphate balance, regulating immune function and resisting cardiovascular and cerebrovascular diseases\cite{3,4}. Latest research suggests that vitamin D deficiency may be an important factor leading to occurrence and development of childhood obesity, but there is less research on the vitamin D level effect on children’s homeostasis. In the study, serum vitamin D levels in children with different weight status were detected, and the inner link of vitamin D levels with fat metabolism, micro-inflammation, endothelial injury and other internal environment indicators was further explored in order to clarify the role of vitamin D in obese children, now reported as follows.
2. Information and methods

2.1 General information

A total of 68 cases of obese children and 56 cases of overweight children who received examination in our hospital between May 2013 and May 2016 were chosen as the obese group and the overweight group, 50 cases of normal children who received vaccination in our hospital during the same period were chosen as normal control group, and the guardians of the enrolled children signed informed consent. There were 36 male cases and 32 female cases in the obese group, and they were 4-13 years old; there were 30 male cases and 26 female cases in overweight group, and they were 5-12 years old; there were 26 male cases and 24 female cases in normal control group, and they were 3-14 years old. There was no significant difference in gender and age distribution among three groups of children (\(P > 0.05\)), and the hospital ethics committee approved the study.

2.2 Inclusion and exclusion criteria

Inclusion criteria: (1) to group the body weight of children according to the growth curve of children's body mass index in China between 0 and 18 years of age; (2) not associated with hyperthyroidism, hypothyroidism and other endocrine diseases that might affect the body weight; (3) cooperating with the examination all the time. Exclusion criteria: (1) with long-term use of hormones and other drugs that might lead to significant weight gain; (2) associated with severe congenital diseases; (3) associated with systemic infectious diseases.

2.3 1,25-(OH)D3 content

1.0 mL of fasting peripheral venous blood was extracted from three groups of children, enzyme-linked immunosorbent assay (ELISA) was used to determine the 1, 25-(OH)D3 content, ELISA kits were purchased from Thermo Fisher Scientific, and the article number was JDH-1267.

2.4 Internal environment indexes

1.0 mL of fasting peripheral venous blood was extracted from all groups, anti-coagulated, let stand at room temperature for stratification and centrifuged at low speed (2 500 r/min, 10 min) to take supernatant and freeze it in -70 °C environment for test. SMT-100 portable automatic biochemical analyzer was used to determine serum contents of lipid metabolism indexes total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) content. ELISA was used to detect serum contents of micro-inflammation indexes C-reactive protein (CRP), interleukin-6 (IL-6) and tumor necrosis factor (TNF-α), ELISA kits were purchased from Thermo Fisher Scientific, and the article number was MDH-298, SGH-846 and MAH-155 respectively. RIA was used to determine serum contents of endothelial injury indexes endothelin-1 (ET-1), nitric oxide (NO) calcitomin gene-related peptide (CGRP) and prostacyclin (PGI2), RIA kits were purchased from Sigma Company in the United States, and the article number was AN-293, KDS-827, ND-371 and FH-742 respectively.

2.5 Statistical processing

Data in the study were recorded and calculated by specially-assigned person, and software was SPSS 20.0. 1,25-(OH)D3, lipid metabolism indexes, micro-inflammation indexes, endothelial injury indexes and other measurement data were in terms of (\(x \pm s\)). Comparison among groups was by variance analysis and pair-wise comparison between groups was by LSD. Correlation analysis was by Pearson test. \(P < 0.05\) was the standard of statistical significance in differences.

3. Results

3.1 1,25-(OH)D3 content

Peripheral blood 1,25-(OH)D3 content in normal control group was (67.38±8.19) nmol/L, peripheral blood 1,25-(OH)D3 content in overweight group was (54.92±7.53) nmol/L and peripheral blood 1,25-(OH)D3 content in obese group was (40.88±6.12) nmol/L. Differences in peripheral blood 1,25-(OH)D3 contents were statistically significant among three groups of children, 1,25-(OH)D3 contents in obese group and overweight group were lower than that in normal control group, 1,25-(OH)D3 content in obese group was lower than that in overweight group, and differences between groups were statistically significant (\(P < 0.05\)).

3.2 Lipid metabolism

Comparison of serum contents of lipid metabolism indexes TC, TG, HDL-C and LDL-C among three groups of children was as follows: differences in serum TC, TG, HDL-C and LDL-C contents were statistically significant among three groups of children (\(P < 0.05\)). Serum TC, TG and LDL-C contents in obese group and overweight group were higher than those in normal control group while HDL-C...
content was lower than that in normal control group; serum TC, TG and LDL-C contents in obese group were higher than those in overweight group while HDL-C content was lower than that in overweight group, and differences between groups were statistically significant \((P<0.05)\), shown in Table 1.

### 3.3 Micro-inflammation

Comparison of serum contents of micro-inflammation indexes CRP (mg/L), IL-6 (ng/L) and TNF-α (ng/L) among three groups of children was as follows: differences in serum CRP, IL-6 and TNF-α contents were statistically significant among three groups of children \((P<0.05)\). Serum CRP, IL-6 and TNF-α contents in obese group and overweight group were higher than those in normal control group; serum CRP and TNF-α contents in obese group were higher than those in overweight group, and differences between groups were statistically significant \((P<0.05)\), shown in Table 2.

### 3.4 Endothelial injury

Comparison of serum contents of endothelial injury indexes ET-1 (ng/L), NO (μmol/L), CGRP (ng/mL) and PGI2 (ng/L) among three groups of children was as follows: differences in serum ET-1, NO, CGRP and PGI2 contents were statistically significant among three groups of children \((P<0.05)\). Serum ET-1 contents in obese group and overweight group were higher than that in normal control group while NO, CGRP and PGI2 contents were lower than those in overweight group, and differences between groups were statistically significant \((P<0.05)\), shown in Table 3.

### 3.5 Correlation between 1, 25-(OH)D3 and homeostasis

Serum 1, 25-(OH)D3 content in obese group was negatively correlated with lipid metabolism indexes TC, TG and LDL-C contents, and positively correlated with HDL-C content; it was negatively correlated with micro-inflammation indexes CRP, IL-6 and TNF-α contents; it was negatively correlated with endothelial injury index ET-1 content, and positively correlated with NO, CGRP and PGI2 contents.

### 4. Discussion

Obesity is that long-term energy intake greater than consumption leads to the accumulation of fat in the body and to the extent that damages the health. Studies have shown that more than 82% of obese children will continue to be fat in adulthood, so the early identifying the factors of obesity and taking active intervention is an important

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### Table 1.

Comparison of serum lipid metabolism index contents among three groups of children (mmol/L).

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>TC</th>
<th>TG</th>
<th>HDL-C</th>
<th>LDL-C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>50</td>
<td>3.42±0.46</td>
<td>0.92±0.11</td>
<td>1.57±0.24</td>
<td>2.09±0.31</td>
</tr>
<tr>
<td>Overweight group</td>
<td>56</td>
<td>4.18±0.53</td>
<td>1.37±0.25</td>
<td>1.18±0.21</td>
<td>2.93±0.35</td>
</tr>
<tr>
<td>Obese group</td>
<td>68</td>
<td>5.79±0.74*</td>
<td>2.68±0.37*</td>
<td>0.89±0.09*</td>
<td>3.41±0.54*</td>
</tr>
<tr>
<td>(F)</td>
<td></td>
<td>7.381</td>
<td>6.093</td>
<td>6.872</td>
<td>7.182</td>
</tr>
<tr>
<td>(P)</td>
<td></td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Note: compared with normal control group, \(*P<0.05\); compared with overweight group, \(#P<0.05\).

### Table 2.

Comparison of serum micro-inflammation index contents among three groups of children.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>CRP</th>
<th>IL-6</th>
<th>TNF-α</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>50</td>
<td>0.38±0.05</td>
<td>109.27±13.27</td>
<td>146.37±20.85</td>
</tr>
<tr>
<td>Overweight group</td>
<td>56</td>
<td>2.11±0.34*</td>
<td>156.82±20.19*</td>
<td>179.62±20.84*</td>
</tr>
<tr>
<td>Obese group</td>
<td>68</td>
<td>3.89±0.54*</td>
<td>241.66±30.47*</td>
<td>225.47±25.82*</td>
</tr>
<tr>
<td>(F)</td>
<td></td>
<td>7.287</td>
<td>12.174</td>
<td>18.982</td>
</tr>
<tr>
<td>(P)</td>
<td></td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Note: compared with normal control group, \(*P<0.05\); compared with overweight group, \(#P<0.05\).

### Table 3.

Comparison of serum endothelial injury index contents among three groups of children.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>ET-1</th>
<th>NO</th>
<th>CGRP</th>
<th>PGI2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>50</td>
<td>34.37±4.59</td>
<td>91.27±10.09</td>
<td>24.38±3.19</td>
<td>74.28±9.17</td>
</tr>
<tr>
<td>Overweight group</td>
<td>56</td>
<td>51.29±6.34*</td>
<td>54.83±7.19*</td>
<td>16.19±2.64*</td>
<td>61.56±7.38*</td>
</tr>
<tr>
<td>Obese group</td>
<td>68</td>
<td>74.82±8.95*</td>
<td>30.72±4.18*</td>
<td>9.35±1.04*</td>
<td>40.82±5.91*</td>
</tr>
<tr>
<td>(F)</td>
<td></td>
<td>12.184</td>
<td>9.283</td>
<td>15.837</td>
<td>10.283</td>
</tr>
<tr>
<td>(P)</td>
<td></td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Note: compared with normal control group, \(*P<0.05\); compared with overweight group, \(#P<0.05\).
measure to optimize children’s health in our country. At present, it has been widely recognized that obesity can lead to decrease in vitamin D levels in blood, vitamin D exists in the active form 1, 25-(OH)D3 in the blood, and the study of LIANG Hong[5] has shown that as body weight gains by 1 kg, 1, 25-(OH)D3 decreases by 0.95 nmol/L in the blood. The concrete mechanism of obesity to lower vitamin D levels is unknown, and it is speculated to be associated with the following points: (1) vitamin D decrease produced by bad life habit and photochemical effect of skin; (2) hepatic hydroxylation abnormalities; (3) low biological utilization[6,7]. In the study, serum vitamin D levels were compared among children with different weight status, and it was found that 1,25-(OH) D3 contents in obese group and overweight group were lower than that in normal control group, and 1,25-(OH) D3 content in obese group was lower than that in overweight group, it confirms that serum vitamin D levels in children continue to decline with the abnormal increase of body mass index, but the effects of vitamin D levels on children’s homeostasis remain to be researched in following study.

Fat accumulation is the direct cause of obesity, abnormal lipid metabolism is the core cause of fat accumulation, expression levels of lipid metabolism indexes are abnormal in obese children, and the specific index levels are consistent with the degree of obesity[8,9]. TC and TG are the common indicators to reflect the overall lipid metabolism of the body, and the abnormal increase in their contents is the basis of occurrence of hyperlipemia and fat accumulation[10]. HDL-C and LDL-C is a pair of indexes playing an important role in the process of fatty acid metabolism, LDL-C is the blood existence form of cholesterol, and its level rise will increase the risk of coronary heart disease; HDL-C can drive inverse operation of cholesterol, decompose the excessive cholesterol by the liver and reversely discharge it out of the body, and can also inhibit LDL-C oxidation and protect endothelial function[11,12]. It was found in the study that serum TC, TG and LDL-C contents in obese group and overweight group were higher than those in normal control group while HDL-C content in obese group was lower than that in normal control group, and the changes in contents of above indexes intensified with the increase of body mass index, confirming that the there is abnormal lipid metabolism in obese children. Further Pearson study showed that blood 1,25-(OH)D3 content in obese children was negatively correlated with the contents of TC, TG and LDL-C, and positively correlated with the content of HDL-C, showing that lower expression of 1,25-(OH)D3 can lead to abnormal lipid metabolism in obesity children.

The adipose tissue accumulation process can synthesize the inflammatory factors such as CRP, IL-6 and TNF-α, which make the body in low inflammatory state as a whole[13]. Persistent inflammation can also aggravate abnormal deposition of lipid in blood vessels and increase the risk of long-term cardiovascular disease, so the serum inflammatory factor levels in children can also reflect the severity of obesity to a certain extent[14]. It was found in the study that serum CRP, IL-6 and TNF-α contents in obese group and overweight group were higher than those in normal control group, and serum CRP, IL-6 and TNF-α contents in obese group were higher than those in overweight group. Pearson test confirmed that blood 1, 25-(OH)D3 content in obese children was negatively correlated with the micro-inflammatory state, showing that 1, 25-(OH)D3 content can objectively reflect the level of systemic inflammatory response and obesity in obese children.

Endothelial injury is a common pathological basis of cardiovascular and cerebrovascular diseases, it has been made clear in the study that obesity can cause the body’s micro-inflammatory state, but the relationship between obesity and endothelial injury has not been fully understood. Studies have pointed out that many kinds of adipocytokines can activate the body's blood coagulation function and cause vascular endothelial damage, the specific manifestation is decrease of vasodilator contents and increase of vasoconstrictor contents, and the two can work together to lead to blood viscosity increase and local microcirculation disturbance[15,16]. Et-1 is the most powerful vasoconstrictor, it can be massively released into blood after endothelial injury, and its content is consistent with the degree of endothelial injury[17]. NO, CGRP and PGI2 have vasodilation effect, they keep dynamic balance with content of ET-1 under physiological condition, their expression decreases or functions are inhibited after endothelial injury, and the vasodilation/ vasoconstriction balance is broken[18,19]. In the study, endothelial damage index contents were compared among groups, and it was found that serum ET-1 contents in obese group and overweight group were higher than that in normal control group while NO, CGRP and PGI2 contents were lower than those in normal control group, and the changes in above indicators were more significant in obese children. Pearson test confirmed that blood 1, 25-(OH)D3 content in obese children was negatively correlated with the content of ET-1, and positively correlated with the contents of NO, CGRP and PGI2, confirming that the 1, 25-(OH)D3 level is negatively correlated with the degree of vascular endothelial injury in obese children.

The content of 1, 25-(OH)D3, the active form of vitamin D, reduces significantly in blood of obese children, and the specific 1, 25-(OH)D3 level is directly correlated with the degree lipid metabolism, micro-inflammation, endothelial injury and other internal environment disorder, and can be used as the auxiliary index for overall state judgment and clinical treatment guidance of obese children.
References


