Detection and significance of serum insulin-like growth factor-1 in patients with type 2 diabetes, osteoporosis and type 2 diabetic osteoporosis

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ARTICLE INFO

Article history:
Received 3 Aug 2016
Received in revised form 17 Aug 2016
Accepted 14 Aug 2016
Available online 24 Aug 2016

Keywords:
Insulin-like growth factor-1
Type 2 diabetes
Osteoporosis
Complication

ABSTRACT

Objective: To investigate the content of insulin-like growth factor-1 (IGF-1) in serum and the relationship with type 2 diabetes, osteoporosis and type 2 diabetic osteoporosis. Methods: A total of 86 cases of patients with type 2 diabetes, 82 cases of patients with osteoporosis, 79 cases of patients with type 2 diabetic osteoporosis and 86 cases of healthy person were selected, the levels of IGF-1, diabetes related factors (fasting plasma c-peptide, FIN, HbA1c, GLU) and osteoporosis related factors (BMP, osteocalcin, β-CTx, P1NP, lumbar vertebra BMD) were detected, the relationship between the above indicators were compared with those of the disease. Results: In each group, content change of IGF-1 was not statistically significant; content changes of IGF-1, BMP and osteocalcin were control group>type 2 diabetes group>osteoporosis group>type 2 diabetic osteoporosis group. Diabetic osteoporosis enhanced the decrease of IGF-1 content. The contents of β-CTx and P1NP in osteoporosis group and diabetic osteoporosis group were similar, which were significantly lower than that in control group and type 2 diabetes group. The level of lumbar vertebra BMD in osteoporosis group and diabetic osteoporosis group were the lowest. Fasting plasma c-peptide in diabetes group and diabetic osteoporosis group were significantly lower than that in control group and osteoporosis group, and the content of fasting plasma c-peptide in diabetic osteoporosis group was the lowest. The contents of FIN, HbA1c and GLU in type 2 diabetes group and type 2 diabetic osteoporosis group were significantly higher than that in control group and osteoporosis group. Conclusion: IGF-1 was related with type 2 diabetes, osteoporosis and type 2 diabetic osteoporosis, and could offer help for predicting type 2 diabetes and osteoporosis in the future.

1. Introduction

With the improvement of people's living standard and the change of people's lifestyle, the incidence of type 2 diabetes presents the trend of increased year by year, and type 2 diabetes complications caused by osteoporosis is also increasing in the crowd at the same time, which seriously affects people's health and quality of life[1,2]. Insulin-like growth factor-1 (IGF-1) plays an important role in insulin metabolism, bone cell differentiation and proliferation[3,4]. This study provides clinical basis for the study of type 2 diabetes and osteoporosis by detecting IGF-1, osteoporosis related factors and type 2 diabetes related factors in serum of community residents.

2. Clinical data and methods

2.1. General data
This study was approved by the Ethics Committee in our hospital, all patients volunteered for the study and signed the informed consent. The research objects were from Xinchuan community in Shanghai Pudong New Area, which lived in the residential community for more than 10 years, the male patients were 40-64 years old, the average were (54.3±13.8) years, the female patients were 40-64 years old, the average were (55.6±12.7) years. 86 cases of patients with type 2 diabetes were confirmed according to the World Health Organization in 1999 diabetes diagnostic criteria, which were composed of 41 male and 45 female. 82 cases of patients with were selected according to ‘The Chinese osteoporosis recommended diagnostic criteria’ established by The World Health Organization of osteoporosis and Geriatric Society of China, which were composed of 41 male and 41 female. 79 cases of patients with type 2 diabetic osteoporosis which met the above diagnostic criteria of type 2 diabetes and osteoporosis were selected, which were composed of 40 male and 39 female. 86 cases of healthy person were selected, which were composed of 43 male and 43 female. The above crowd have detailed information without heart, kidney, liver, lung, and endocrine diseases, and have not conducted relevant treatment.

2.2. Correlative detection

All the research objects were conducted fasting for 12 h, 5 mL of elbow venous blood were extracted in the fasting state, fasting blood-glucose (ULG) was detected by FreeStyle Freedom (FreeStyle, USA), the related operations were conducted in strict accordance with the product manual. BMP, bone morphogenetic protein (BMP), fasting plasma c-peptide, fasting insulin (FIN) and glycosylated hemoglobin were detected by enzyme linked immunosorbent assay, the related kits were produced by Shanghai Sen-Xiong Technology Industry co., LTD, Wuhan Boster biological engineering co., LTD, Shanghai Mei-Yan biological technology co., LTD and Shanghai Mei-Lian biological technology co., LTD, respectively, and the related operations were conducted in strict accordance with the product manual. The average bone density of lumbar vertebra in each community residents (L2-L4) was detected by Dual X-ray Absorptiometry (Osteo KJ2000, South Korea), and the related operations were conducted in strict accordance with the product manual.

2.3. Statistics

SPSS 19.0 statistical software was adopted for data analysis. Measurement data were described as mean ± standard deviation, and inter-group comparison was carried out by t test, multiple groups were compared with analysis of variance, further pairwise comparison was conducted by SNK-q test. Values of P<0.05 were considered to be statistically significant.

3. Results

3.1. Serous IGF–1 contents of community residents

Serous IGF-1 contents were detected and analyzed by enzyme linked immunosorbent assay, the results showed that serous IGF-1 contents were statistically significant by analysis of variance (P<0.05), the changes of serous IGF-1 in male and female patients from each group were not statistically significant (P>0.05). Serous IGF-1 contents in control group, type 2 diabetes group, osteoporosis group and type 2 diabetic osteoporosis group were (168.23±6.81), (145.01±6.37), (116.39±6.34) and (105.3±7.41) μg/L, respectively, further pairwise comparison found that control group>type 2 diabetes group>osteoporosis group>type 2 diabetic osteoporosis group, serous IGF-1 content in type 2 diabetic osteoporosis group was the lowest, which was considered to be statistically significant (P<0.05). Diabetic osteoporosis enhanced the decrease of IGF-1 content, see Table 1.

Table 1. Serous IGF-1 contents of community residents (μg/L).

<table>
<thead>
<tr>
<th>Group</th>
<th>Male</th>
<th>Female</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>169.88±6.49</td>
<td>165.91±6.50</td>
<td>168.23±6.81</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>143.91±6.01*</td>
<td>145.41±5.78*</td>
<td>145.01±6.37*</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>117.17±7.30*</td>
<td>115.64±6.66*</td>
<td>116.39±6.34*</td>
</tr>
<tr>
<td>Type 2 diabetic osteoporosis</td>
<td>106.12±7.09*</td>
<td>107.13±7.69*</td>
<td>105.3±7.41*</td>
</tr>
</tbody>
</table>

Note: compared with control group, *P<0.05; compared with type 2 diabetes group, P<0.05; compared with osteoporosis group, P<0.05.

3.2. Expression levels of osteoporosis related factors of community residents

Analysis of variance showed that the comparison of BMP, osteocalcin, β-CTx, P1NP and lumbar vertebra BMD in the four groups were statistically significant (P<0.05), further pairwise comparison found that BMP and osteocalcin contents in each group were control group>type 2 diabetes group>osteoporosis group>type

Table 2. Expression levels of osteoporosis related factors of community residents.

<table>
<thead>
<tr>
<th>Group</th>
<th>BMP (μmol/L)</th>
<th>Osteocalcin (μg/L)</th>
<th>β-CTx (ng/mL)</th>
<th>P1NP (ng/mL)</th>
<th>BMD (g/cm2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>79.89±8.25</td>
<td>7.12±1.05</td>
<td>0.348±0.07</td>
<td>0.45±0.5</td>
<td>0.88±0.06</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>55.44±6.45</td>
<td>4.22±0.86</td>
<td>0.475±0.05*</td>
<td>44.73±5.92</td>
<td>0.82±0.08*</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>44.21±6.33*</td>
<td>3.10±0.87</td>
<td>0.543±0.07*</td>
<td>51.67±6.25</td>
<td>0.75±0.07*</td>
</tr>
<tr>
<td>Type 2 diabetic osteoporosis</td>
<td>37.38±4.50*</td>
<td>2.88±0.74*</td>
<td>0.548±0.08*</td>
<td>51.78±5.10*</td>
<td>0.74±0.06*</td>
</tr>
</tbody>
</table>

Note: compared with control group, *P<0.05; compared with type 2 diabetes group, P<0.05; compared with osteoporosis group, P<0.05.
2 diabetic osteoporosis group, which in the type 2 diabetic osteoporosis group was the lowest and considered to be statistically significant ($P<0.05$). $\beta$-CTx and P1NP contents in each group were control group $>$ type 2 diabetes group $>$ osteoporosis group $>$ type 2 diabetic osteoporosis group, and $\beta$-CTx and P1NP contents in osteoporosis group and diabetic osteoporosis group were similar and significantly lower than that in control group and type 2 diabetes group ($P<0.05$). The levels of lumbar vertebra BMD in osteoporosis group and diabetic osteoporosis group were the lowest. Type 2 diabetic osteoporosis enhanced the changes of osteoporosis related factors and significantly lower than that in type 2 diabetes group and osteoporosis group. See Table 2.

### 3.3. Expression levels of type 2 diabetes related factors of community residents

Analysis of variance showed that the comparison of fasting serum c-peptide, FIN, HbA1c and GLU in the four groups were statistically significant ($P<0.05$), further pairwise comparison found that fasting serum c-peptide in type 2 diabetes group and type 2 diabetic osteoporosis group were (1.48±0.27), (1.39±0.27) ng/mL, which were significantly lower than that in control group and osteoporosis group, and fasting serum c-peptide in type 2 diabetic osteoporosis group was the lowest. FIN, HbA1c and GLU content in type 2 diabetes group and type 2 diabetic osteoporosis group significantly improved and were higher than that in control group and osteoporosis group ($P<0.05$). The changes of fasting serum c-peptide, FIN, HbA1c and GLU contents in control group and osteoporosis group were not statistically significant ($P>0.05$). See Table 3.

### 4. Discussion

IGF-1 is a single polypeptide chain composed of 70 amino acids (7649 103), it acts on the related target cells through IGF-1 receptors to promote cell mitosis and differentiation[5], and plays an important role in type 2 diabetes, osteoporosis, cancer, oxidative stress[6]. Blood glucose, insulin, growth hormone, condition, nutrition could regulate the level of IGF-1[7]. This study found that serous IGF-1 contents in each male and female patients were not statistically significant. The IGF-1 contents were control group $>$ type 2 diabetes group $>$ osteoporosis group $>$ type 2 diabetic osteoporosis group, IGF-1 content in type 2 diabetic osteoporosis group was the lowest, and the decrease of IGF-1 content may be caused by the combined action of osteoporosis related factors and type 2 diabetes related factors, type 2 diabetic osteoporosis aggravates the disease and further causes the decrease of IGF-1 content.

With the improvement of people's living standard and the change of people's lifestyle, the incidence of type 2 diabetes presents the trend of increased year by year, and seriously affects people's health and quality of life[8,9]. Effect and mechanism of IGF-1 in type 2 diabetes attract wide attention by the broad masses of medical workers. It has significant homology with insulin structure[10]. This study showed that IGF-1 combined with insulin receptor could stimulate transportation of glucose in fat and muscle cells, inhibit the output of glucose and decrease blood glucose, and inhibit islet cells secreting insulin at the same time[11]. IGF-1 has a close correlation with insulin sensitivity, and serous IGF-1 level in type 2 diabetes patients with insufficient insulin is low. Patients with IGF-1 gene deletions showed severe insulin resistance[12,13]. Type 2 diabetes related factors were detected, and it was found that fasting plasma c-peptide contents in type 2 diabetes group and type 2 diabetic osteoporosis group were significantly lower than that in control group and osteoporosis group, and fasting plasma c-peptide content in type 2 diabetic osteoporosis group was the lowest. FIN, HbA1c and GLU contents in type 2 diabetes group and type 2 diabetic osteoporosis group were significantly higher than that in control group and osteoporosis group. Fasting plasma c-peptide, FIN, HbA1c and GLU contents in control group and osteoporosis group were similar. Type 2 diabetic osteoporosis enhanced the changes of type 2 diabetes related factors and were significantly higher than that in type 2 diabetes group and osteoporosis group. Type 2 diabetes related factors in type 2 diabetes group and type 2 diabetic osteoporosis group change along with the change of IGF-1.

Osteoporosis is one of the major complications of type 2 diabetes[14]. Osteoporosis patients prone to fracture, it has very high disability rate, the treatment and rehabilitation are more difficult particularly in elderly patients, which increased the economic burden of patients and affected people's living standards[15]. IGF-1, as the protein in bone formation, plays an important role in the process of bone rebuilding[16]. It was reported that IGF-1 has inhibitory to the secretion of osteocalcin, and can also decrease the activity of alkaline phosphatase, and achieve the purpose of suppressing osteogenetic differentiation[17]. IGF-1 receptors exist both in osteoblast and osteoclast, and IGF-1 is released which stored in the bone matrix.

### Table 3.

Expression levels of type 2 diabetes related factors of community residents.

<table>
<thead>
<tr>
<th>Group</th>
<th>Fasting serum c-peptide (ng/mL)</th>
<th>FIN (mU/L)</th>
<th>HbA1c (%)</th>
<th>GLU (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>2.45±0.24</td>
<td>10.91±3.57</td>
<td>5.03±0.45</td>
<td>5.01±1.32</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>1.48±0.27</td>
<td>16.01±3.61</td>
<td>6.87±0.52</td>
<td>7.41±1.41</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>2.43±0.26</td>
<td>11.03±3.78</td>
<td>5.20±0.49</td>
<td>5.19±1.29</td>
</tr>
<tr>
<td>Type 2 diabetic osteoporosis</td>
<td>1.39±0.27*</td>
<td>17.86±3.82</td>
<td>7.73±0.55</td>
<td>7.76±1.36*</td>
</tr>
</tbody>
</table>

Note: compared with control group, $*P<0.05$; compared with type 2 diabetes group, $P<0.05$; compared with osteoporosis group, $\tilde{P}<0.05$. 

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at the time of bone resorption, resulting in bone formation and bone resorption be tight coupling and maintain the balance of bone mass\cite{18,19}. Researches showed that serous IGF-1 content has a close relation with the incidence of fractures, IGF-1 content reduces the incidence of fracture, especially the spinal fracture and femoral fractures. The change of serous IGF-1 level has a close relation with osteocalcin, 1 type collagen cross-linking type C peptide, bone alkaline phosphatase, 1 type collagen N-terminal propeptide and bone mineral density, and it is affected by age, physical condition, etc at the same time\cite{20,21}. Further detection of osteoporosis related factor in serum found that BMP and osteocalcin contents in each group were control group>type 2 diabetes group>osteoporosis group>type 2 diabetic osteoporosis group, which were the lowest in type 2 diabetic osteoporosis group. β -CTx and P1NP contents in osteoporosis group and type 2 diabetic osteoporosis group were similar and significantly lower than that in control group and type 2 diabetes group. Lumbar BMD test results showed that bone mineral densities in osteoporosis group and type 2 diabetic osteoporosis group were the lowest. Type 2 diabetic osteoporosis enhanced the changes of osteoporosis related factors, which were significantly higher than that in type 2 diabetes group and osteoporosis group. Osteoporosis related factors in serum in type 2 diabetes group, osteoporosis group and type 2 diabetic osteoporosis group change along with the change of IGF-1.

In conclusion, IGF 1 as cytokine could regulate the levels of type 2 diabetes related factors (fasting plasma c-peptide, FIN, HbA1c and GLU) and osteoporosis related factors (BMP, osteocalcin, β -CTx, P1NP and lumbar BMD), and affect the condition of type 2 diabetes and osteoporosis. IGF-1 can be used as an important indicator for predicting type 2 diabetes, osteoporosis group and type 2 diabetic osteoporosis.

References


\[8\] De Felice FG, Ferreira ST. Inflammation, defective insulin signaling, and mitochondrial dysfunction as common molecular denominators connecting type 2 diabetes to Alzheimer disease. *Diabetes* 2014; 63(7): 2262-2272.