Study on the relationship between the expression of IGF-1 in umbilical cord blood and abnormal glucose metabolism during pregnancy

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Abstract. – OBJECTIVE: To explore the relationship between the expression of insulin-like growth factor-1 (IGF-1) in neonatal umbilical cord blood and abnormal glucose metabolism during pregnancy.

PATIENTS AND METHODS: We have selected 63 cases of delivery randomly, term birth and maternal from January 2015 to January 2016 in our hospital, gestational diabetes mellitus for Group A, abnormal gestational glucose tolerance for Group B and normal for Group C with 21 cases in each group. The venous blood samples were collected from all the pregnant females 2 weeks before delivery, and the levels of HbA1c in serum were detected by Elisa method. During the delivery, the umbilical cord blood was collected and the levels of IGF-1 were measured by double site immune enzyme analysis. The neonatal weight was recorded and the correlation analysis was made in respect of the measurement results.

RESULTS: The level of HbA1c in Group A was significantly higher than that in Group C (p < 0.05); IGF-1 level and neonatal weight of Group B were significantly higher than that of Group C (p < 0.05), IGF-1 has a significant correlation with neonatal weight in Group C, and HbA1c and IGF-1 were positively correlated (p < 0.05); IGF-1 was positively correlated with neonatal weight in Group A and Group B (p < 0.05). There was a significant positive correlation between the IGF-1 level of neonatal umbilical cord blood and the neonatal weight (p < 0.05). Also, the level of HbA1c was positively correlated with the level of IGF-1 in neonatal umbilical cord blood at the end of pregnancy (p < 0.05).

CONCLUSIONS: The expression level of IGF-1 in the final stage of pregnant females can be detected to predict the expression level of IGF-1 in newborn infants and then the growth status of the fetus can be obtained.

Key Words: Neonatal weight, IGF-1, HbA1c, Late pregnancy.

Introduction

Abnormal maternal glucose metabolism during pregnancy is a common complication of pregnancy. Accordingly, it is divided into Gestational Diabetes Mellitus (GDM) and Gestational Impaired Glucose Tolerance (IGT). Some patients are likely to be subject to other serious complications due to their reasons, which may not only affect the normal growth of the fetus but also threaten the mother and child’s life. Clinically, it is identified according to fasting plasma glucose (FPG) and oral glucose tolerance test (OGTT). HbA1c can reflect the average level of blood glucose in the past 6-10 weeks and has nothing to do with the blood glucose fluctuations, so the expression level of HbA1c can be regarded as a reliable indicator of abnormal glucose metabolism during pregnancy. Insulin-like growth factor, IGF in short, is composed of 70 amino-acid and divided into IGF-1 and IGF-2. Recently, the study showed that IGF-1 had a vital role in the growth of skeletal organs and the expression level of HbA1c in pregnant women with abnormal glucose tolerance during pregnancy may also be abnormal; at meanwhile, the expression level of IGF-1 in umbilical cord blood of newborns will be abnormal and the expression level of IGF-1 is closely related to the growth and development of newborn. There have been few domestic reports on the effects of HbA1c and IGF-1 on neonatal growth. This study aimed at studying the relationship between the expression of IGF-1 in umbilical cord blood and abnormal glucose metabolism during pregnancy.
Patients and Methods

Patients

63 cases of delivery, term birth and maternal were selected randomly from January 2015 to January 2016 in our hospital (Henan Provincial People’s Hospital, People’s Hospital of Zhengzhou University, Jinshui, Zhengzhou, Henan Province, P. R. China). As to the inclusion criteria, formal examination, no other serious complications, single living. The exclusion criteria were: birth abnormalities, serious organic disease, B-show stillbirth. Gestational diabetes mellitus for Group A, abnormal gestational glucose tolerance for Group B, normal for Group C, 21 cases in each group. Pregnant females of Group A were aged from 25 to 32 years old, (28.32 ± 2.34) years old on average with the gestational age of (38.11 ± 3.45) weeks on average; the pregnant females of Group B were aged from 26 years old to 33 years old, (29.99 ± 2.97) years old on average with the average gestational age of (38.19 ± 3.18) weeks; the pregnant females of Group C were aged from 27 years old to 33 years old, (29.93 ± 2.81) years old on average with the gestational age of (38.34 ± 3.12) weeks on average. The difference in gestational age among the three groups was not statistically significant (p < 0.05). The study has been consented by the pregnant females and their families.

Methods

3 ml venous blood was collected from all pregnant women two weeks before birth and immediately sent to the Hospital’s Biochemistry Laboratory. The ELISA method (Beijing Connaught Yajie Biological Technology Co., Ltd. Beijing, China) was used to detect HbA1c in serum. Upon the childbirth, 3 ml, neonatal cord blood was collected and sent to the laboratory for serum separation. Two sites ELISA analysis method (Beijing Perlong New Technology Co., Ltd. Beijing, China) was used to measure the IGF-1 levels record the birth weight and carry out correlation analysis on the measurement results.

Statistical Analysis

The data involved in the test was processed by SPSS19.0 software (SPSS Inc., Chicago, IL, USA); use mean ± standard deviation $x \pm s$ as measurement data. The comparison among the groups was analyzed by multi-way ANOVA, and the Bonferroni method was adopted in the comparison within each group and then analyze the bivariate correlation with the Pearson system according to the inspection standard $a = 0.05$.

Results

Comparison of HbA1c, IGF-1 Levels in Umbilical Cord Blood and Neonatal Weight at the End of Pregnancy

The differences of the levels of HbA1c, IGF-1 in umbilical cord blood and neonatal weights were statistically significant ($p < 0.05$). In pair comparison, the differences of the HbA1c level at the end of pregnancy between group C and group B ($p > 0.05$), and between group B and group A ($p > 0.05$) had no statistical significance. The level of HbA1c in Group A was significantly higher than that in Group C ($p < 0.05$); IGF-1 level and neonatal weight of Group B were significantly higher than that of Group C ($p < 0.05$), but the difference compared to group A was not significant ($p > 0.05$). Moreover, the difference of IGF-1 level in neonatal umbilical cord blood between group B and group A was not statistically significant ($p > 0.05$); the neonatal weight in group B was significantly higher than that in group C ($p < 0.05$), but the differences of neonatal weights between group B and group A and between group A and group C were not significant ($p > 0.05$) (Table I).

Correlation Analysis of HbA1c, IGF-1 Levels in Umbilical Cord Blood and Neonatal Weight at the End of Pregnancy

In Group C, Group B, and Group A, HbA1c and neonatal weight were not significantly correlated ($p > 0.05$); IGF-1 has a significant correlation with

Table I. Comparison of HbA1c, IGF-1 levels in umbilical cord blood and neonatal weight of pregnant women in the end of pregnancy in each group ($x \pm s$).

<table>
<thead>
<tr>
<th>Group</th>
<th>The number of cases</th>
<th>HbA1c/%</th>
<th>IGF-1/[μg/L]</th>
<th>Neonatal weight/g</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group C</td>
<td>30</td>
<td>6.11 ± 0.51</td>
<td>59.66 ± 18.97</td>
<td>3457.15 ± 306.55</td>
</tr>
<tr>
<td>Group B</td>
<td>30</td>
<td>6.52 ± 0.78</td>
<td>82.31 ± 19.62*</td>
<td>3795.64 ± 356.35*</td>
</tr>
<tr>
<td>Group A</td>
<td>30</td>
<td>7.13 ± 1.15*</td>
<td>71.24 ± 18.45</td>
<td>3636.45 ± 368.31</td>
</tr>
</tbody>
</table>
neonatal weight \((p < 0.05)\); the expression level of HbA1c and IGF-1 in Group C was positively correlated \((p > 0.05)\) (Table II).

**Correlation Analysis of Related Detection Indexes between all Groups**

There was not any significant correlation between HbA1c level of late pregnancy and the neonatal weight \((p > 0.05)\); and there was positive correlation between IGF-1 level in neonatal umbilical cord blood and neonatal body weight \((p < 0.05)\), in addition, the level of HbA1c in late pregnancy and IGF-1 level in neonatal umbilical cord blood was positively correlated \((p < 0.05)\), as shown in Table III.

**Discussion**

With the deepening of scientific research, the role of IGF-1 in pregnancy is gradually revealed, IGF-1 detection can provide more beneficial help to maternal, fetal and neonatal disease prevention, diagnosis and treatment.

IGF-1 is widely distributed in the human body and can promote the cell proliferation and differentiation, which has exerted great influence on the development of the fetus during pregnancy\(^{11}\). IGF-1 is composed of 70 amino acids, and the spatial structure is a single chain polypeptide, among them, 45\% of the amino acid sequence is the same as the insulin, so it has the function of insulin\(^{12}\). Through the receptor IGF-1, IGF-1R can complete most of its biological effects. IGF’s combination with IGF-1R will start the two signal transmission pathways as involved in the process of cell growth\(^{13}\). Its biological role has the role of insulin-like: stimulate the tissue cells to accelerate the absorption of glucose, and then play a role in promoting the fermentation of sugar; promote mitosis\(^{14}\), which promotes the synthesis of DNA and RNA, stimulate the cell proliferation rate, play an important role in the \(G_0 \sim G_1\) and \(G_1 \sim S\) stages. Previous researches showed\(^{15}\) that IGF-1 has a certain correlation with neonatal weight.

The content of IGF-1 in umbilical cord blood of premature, late birth and term birth is obviously different, and the content of IGF-1 in umbilical cord blood is the lowest\(^{16}\). The growth state of the fetus can be inferred by the content of IGF-1. HbA1c is a product of the production of non-enzymatic reaction between sugars and hemoglobin. Under normal circumstances, the hemoglobin is generated by the reaction of glycosylated hemoglobin 1, HbA1, and HbA1 is divided into HbA1a, HbA1b, and HbA1c. Researches showed\(^{17}\) that HbA1c could represent the average expression level of blood glucose in patients within 6-8 weeks. The red blood cell life is 120 days while the hemoglobin of the reaction is completed during this period and the blood glucose level during the period of HbA1c has a greater impact on HbA1c, so in a blood test, 30\% of the HbA1c is produced by human body a month ago, 25\% is produced in human two months ago, and another 25\% is generated in 2-4 months before blood sampling; therefore, HbA1c concentration can be a judge for the average blood glucose level in the human body within several months.

Kew et al\(^{18}\) said that fetal overgrowth might be related to whether the mother was suffering from diabetes. The average weight of newborn of the diabetic pregnant mother was higher than that of normal levels, and the content of insulin and leptin in umbilical cord blood was also found higher than normal levels. López Caudana et al\(^{19}\) said that the formation of HbA1c represented an average of blood sugar levels in the past 120 days without correlation to the blood glucose levels during

<table>
<thead>
<tr>
<th>Item</th>
<th>Group C</th>
<th>Group B</th>
<th>Group A</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(r)</td>
<td>(p)</td>
<td>(r)</td>
</tr>
<tr>
<td>HbA1c-neonatal weight</td>
<td>0.214</td>
<td>0.273</td>
<td>0.195</td>
</tr>
<tr>
<td>IGF-1-neonatal weight</td>
<td>0.788</td>
<td>0.003</td>
<td>0.655</td>
</tr>
<tr>
<td>HbA1c-IGF-1</td>
<td>0.565</td>
<td>0.045</td>
<td>0.210</td>
</tr>
</tbody>
</table>

**Table II.** Correlation of HbA1c, IGF-1 levels in umbilical cord blood and neonatal weight in the end of pregnancy.

**Table III.** Correlation analysis of related detection indexes between all groups.

<table>
<thead>
<tr>
<th>Item</th>
<th>(r)</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c-neonatal weight</td>
<td>0.209</td>
<td>0.284</td>
</tr>
<tr>
<td>IGF-1-neonatal weight</td>
<td>0.817</td>
<td>0.009</td>
</tr>
<tr>
<td>HbA1c-IGF-1</td>
<td>0.557</td>
<td>0.047</td>
</tr>
</tbody>
</table>
the blood sampling or fluctuations due to food or movement. The study results showed that the level of HbA1c in Group A was significantly higher than that in Group C (p < 0.05); IGF-1 level and neonatal weight of Group B were significantly higher than that of Group C (p < 0.05), suggesting that in pregnant women with the worse blood glucose tolerance, fetal weight would be heavier, blood glucose and neonatal weight had a certain relationship. Nadif et al. said that the neonatal weight of Group B were significantly higher than that of Group C (p < 0.05). The expression level of HbA1c and IGF-1 in Group C was positively correlated (p < 0.05). It’s suggested that IGF-1 is positively correlated with the weight of the newborn, and there is no significant correlation with HbA1c.

Conclusions

There are certain researchers about the expression level of HbA1c in pregnant women and IGF-1 level of the newborn umbilical cord blood, but its uncertainty is more and demands further studies and discussion. Researches on the relationship between the expression level of HbA1c and IGF-1 level of the umbilical cord blood of newborn babies are still in shortage, which needs to be revealed by further scientific researches.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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