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Clinical study on the level of glucose metabolism and placental NO in patients with gestational hypertension.

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Abstract

Background: Gestational hypertension is a common syndrome of maternal, its clinical manifestations includes high blood pressure, proteinuria and edema. The aetiological agent was complicated that may be a more genes and is influenced by many environmental factors.
Objective: This research was to study the effect of sugar metabolism and the NO level of the placenta in patients with gestational hypertension (GHP).
Results: Both of the fasting blood glucose (FBG) and the fasting insulin (FINS) levels were tested between 40 patients with gestational hypertension (GH group) and 42 cases of normal pregnant women (NP group). And the HOMA-IR and HOM A-IS levels were compared. At the same time the NO level of placental villi homogenate in the pregnant women was tested with nitrate reduction method. The level of FINS, H OMA-IR, HOMA-IS were all increased compared with the NP group. There was no significant difference among each group on the level of FBG, however, the NO level was lower significantly than the NO level of NP group ($p<0.05$).
Conclusion: The gestational hypertension patients were resistant to insulin and they had secreted high level of insulin. The NO level and the level of sugar metabolism were important to the health of gestational hypertension patients.

Keywords: Pregnancy complications, High blood pressure, Nitric oxide, Placental, Blood sugar.

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Introduction

Gestational hypertension is a common syndrome of maternal, its clinical manifestations includes high blood pressure, proteinuria and edema. The aetiological agent was complicated that may be a more genes and is influenced by many environmental factors. Pregnancy-induced hypertension can cause serious complications of maternal vital organs. At the same time, it may cause fetal death. Gestational hypertension disease is the second cause of maternal death [1]. In recent years, researchers have shown that the person who has sugar metabolic abnormalities during pregnancy patients was attacked by gestational hypertension disease easily. It was serious impact on pregnancy [2-4]. Gestational diabetes mellitus refer to the merger of the pregnancies and diabetes or hidden diabetes prior to pregnancy and development to diabetes after pregnancy. It belongs to high-risk pregnancy. It have significant harm to pregnant women and foetus. Since insulin applied to clinical, diabetes maternal and perinatal death rate dropped significantly. The clinical process of gestational diabetes is relatively complex, and the mortality of pregnancy and infant is still high, so the gestational diabetes must be taken seriously. But the influence of the glucose tolerance decreased to gestational hypertension was less reported, and controversial.

Normal pregnancy, higher estrogen level, activate the increase of NO released into the blood, can play a role apparent diastolic blood vessels, and peripheral venous system resistance decreased, blood pressure decreased, and then adjust the matrix changes the system to adapt to the pregnancy, The level of nitrite detected increases which was stable metabolites of NO in the blood and urine of the pregnant women in the clinical. The discharge of cGMP which was second messenger of NO in the urine increased [5]. But there are also scholars opposed this idea, they think the NO level can increase blood pressure instead of lower blood pressure [6]. In this study, the influence and significance of NO level and glucose metabolism to the safe of the gestational hypertension was further analysis.

Subjects and Methods

Pregnant women were chose in hospital caesarean section with gestational hypertension, 40 cases, in our hospital obstetrics during January 2009 to January 2013. Among which mild gestational hypertension pregnancy, 10 cases, moderate gestational hypertension pregnancy, 10 cases, and severe gestational hypertension, 20 cases. Normal pregnant women (control group), 42 cases. Average age (28.5 ± 4.1), and the average gestational age (38.7 ± 1.52) for weeks, patients were gestational hypertension in the diagnosis of standard [7]. Randomly selected in the same period in hospital without

gestational hypertension, 30 cases of full-term pregnancy cesarean section delivery of pregnant women (control group), average age (27. 8 ± 3.4), and the average week gestational age (39.35 ± 1.06). Difference between two groups of age, pregnant weeks, no statistical significance (t, respectively is 1.180, 1.398, all P>0.05), and no other pregnancy complications and complications. Cesarean delivery are no labor, it is due to factors such as the pelvis, fetal or gestational hypertension.

Exclusion criteria (1) cesarean section after contractions; (2) the natural production; (3) the full-term pregnancy; (4) has a history of liver, heart, kidney and endocrine diseases; (5) two or more pregnancies; (6) hepatitis, tuberculosis, acute and chronic infectious disease nearly one month; (7) His spirit was abnormal.

Diagnostic criteria for sugar metabolic abnormalities [8] (1) DM: Diagnosed with diabetes before pregnancy or sugar metabolic abnormalities was found for the first time during pregnant, but blood sugar still apparently unusual postpartum and reached the diagnostic criteria for internal medicine diabetes during non-pregnant. (2) GCT (+):50 g glucose screening during 24 to 28 weeks of pregnancy and if the blood sugar was 7.8 mmol/L or more, it was sugar screening positive. A further 75 g oral glucose tolerance test, failed to meet the value according to the American diabetes association recommended standard of ADA [5] : Blood glucose were 5.3, 10.0, 8.6, 7.8 mmol/L when fasting and after take sugar 1, 2, 3 h respectively. (3) GDM: OGTT have two or more than two reach or exceed the standard above. (4) GIGT: OGTT only 1 item reach or exceed the standards or every item was failed to meet the criteria above, but the blood sugar reach or exceed 7.8 mmol/L after take sugar 2 h.

Sugar metabolism [9] Comparison blood sugar, glycosylated haemoglobin, and the difference degree of insulin resistance between the 3 groups. All pregnant women in the early morning fasting venous blood were taken and the serum was separated and stored in the -70°C. At the same time, fasting blood glucose (FBG) and fasting insulin (FINS) were Determined. Kits was bought from Beijing biological products company, batch variation within the <5%. FBG was determined by oxidase method. FINS was determined immunized with electrochemical method. The indexes of insulin resistance (HOMA IR) and insulin secretion index was calculated by a steady-state model analysis method (HOMA) Based on FBG and FINS. HOMA-IR=(FBG × FINS)/22.5; HOMA-IS=20 × FINS/(FBG -3.5), and calculating their nature logarithmic.

Detection of NO levels in placental villi homogenate after delivery of the placenta, immediately take the placenta and umbilical cord each under direct vision from maternal surface and avoid the calcification points, each 1 piece and about 2 mm^3, after RNA enzyme inactivation [10]. All subjects were fasting and taken from the peripheral blood of 5 ml with heparin anticoagulation tube. The plasma was kept at -30°C after 2000 rpm centrifugation for 10 min under 4°C. Blood samples of gestational hypertension e were collected without the treatment of magnesium sulphate and antihypertensive drugs. Because NO is very unstable, can be very fast generation of nitrite (NO^{2-}) and nitric acid (NO^{3-}) *in vivo and in vitro*. Therefore, NO^{3-}/NO^{2-} was used as an indicator to measure the level of NO, and the NO level in placenta was detected by copper plating cadmium reduction method (Griess method).

Results

Comparisons in both GH group and NP group

The FINS levels in GH group were obviously higher than that in NP group (p<0.01). The FINS levels in the middle and serious GH group were same when compared with the mild GH group. There were no statistical differences on the FBG level among each group (p>0.05). The level of HOMA-IR and HOMA-IS were significantly higher than NP group (p<0.01), was seen in Table 1.

Table 1. *Level of Sugar metabolism between GH and NP (□x ± s).*

Group	n	FBG (c/mmol▪L-1)	FINS (z/kU▪L-1)	HOM A-IR	HOM A-IS
NP group	42	4.2 ± 1.1	8.3 ± 2.5	1.18 ± 0.16	3.25 ± 0.49
GH group	40	4.6 ± 1.4	12.5 ± 2.8*	1.39 ± 0.14*	4.15 ± 0.51*
Mild	10	4.4 ± 1.6	9.7 ± 2.1	1.12 ± 0.11	3.31 ± 0.37
Middle	10	4.3 ± 1.5	11.7 ± 2.1	1.37 ± 0.13	4.14 ± 0.48
Serious	20	4.8 ± 1.2	12.5 ± 2.7	1.43 ± 0.15	4.34 ± 0.55

*There were significant differences on the level of FBG, FINS, HOM A-IR, HOM A-I between the NP group and GH groupp<0.01.

Detection of NO level of Placental villi homogenate [11].

From the Table 2, there was no difference between mild GH group and NP group, thus we could think that the NO level in this mild GH group should be also in normal range. However, after the comparison between middle GH group and Serious GH group, the NO level was significantly lower than the NP group. Nitric oxide synthase (NOS) which was used to catalyze the synthesis of nitric oxide mainly positioned on syneytiotrophoblast and villous vascular endothelial cell. The NOS activity in latter was higher than the former. Because the syneytiotrophoblast of human placental villiin in the late trimester of pregnancy. Thus, the syneytiotrophoblast is an important source of NO synthesis for the pregnancy.

Table 2. The NO level of Placental villi homogenate in NP and GH groups (x ± s, μmol/g).

Groups	n	NO
NP group	42	1.93 ± 0.42
Mild group	10	1.59 ± 0.44

Middle group	10	$1.13 \pm 0.24^{\#p}$
Serious group	20	$0.91 \pm 0.11^{\#q}$

indicated that when compared with NP Group, there were significant difference, and the p value was lower than 0.01; p indicated that when compared with mild GH Group, it showed mild differences. p value was lower than 0.05q indicated that when compared with mild GH Group, it showed obvious differences. p value was lower than 0.01.

Discussion

Gestational hypertension onset disaster is a specific disease, which threatened maternal and child health [12]. Although there were many studies of its etiology and pathology, physiology, but it is still not precisely clarified. Specification and reasonable application can reduce the hazards of preventive measures. In recent years, sugar metabolism disorder and the incidence of PIH relations become a research focus. Deep research were carried out from different levels including gene, molecule, and biochemistry, and found that high insulin can increase sympathetic sensitivity and activate adrenergic system. Elevated circulating system catecholamine concentrations, decreased -K^+-ATP Na^+ enzyme activity, and affect the sensitivity of vascular smooth muscle to the stimulation of vasoactive substance [13]. These factors could lead to high blood pressure. And PIH patients with high insulin phenomenon, this may be related with strong secretion of islet insulin increased, resulting in increased circulating insulin or PIH insulin target cells, or with placenta produces too much insulin, destruction of insulin related. Therefore, it plays an important role in the pathogenesis of PIH. Insulin secretion by pancreatic beta cell precursors, the main role is to promote the glucose oxidation and glycogen synthesis, inhibition of gluconeogenesis to maintain stable blood glucose.

When the insulin synthesis and utilization of the obstacles, it will directly affect the glucose metabolism, so PIH patients with impaired glucose metabolism. As for the OGTT screening time, the best time to prevent the discovery of the PIH problem, it is necessary to further epidemiological studies. 24 weeks of pregnancy is the best period for the screening of pregnant women's sugar, easy to find GDM in a timely manner, reasonable and timely treatment. However PIH can be as early as 20 weeks of pregnancy, early pregnancy screening positive rate will be missed, and its specificity, sensitivity is yet to be confirmed. In addition, the evaluation values of BG ISI and OGTT how to define, but also to consider the physiological situation of pregnant women [14].

NO by reducing sympathetic excitability to achieve the purpose of relaxing blood vessels, while NO can also reduce the weight of renal tubular Na to regulate blood pressure. Animal experiments showed that NO live enzyme inhibition can cause pregnancy induced hypertension [15]. Because NO is very unstable in the body, it is fast metabolism for a more stable metabolites nitrite (NO^{2-}), so often in the NO^{2-} concentration to indirectly reflect the level of NO in vivo. In normal pregnancy, the synthesis and release of NO increased, the peripheral vascular resistance decreased, and the blood vessel was in a state of relaxation. The increase of heart rate and cardiac output of pregnant women in pregnancy, maintaining the normal level of blood pressure, to ensure the nutritional supply of the foetus. But it was noted that the possibility of exogenous NO donor in clinical application may make patients with shock, cytotoxic and other dangerous, and the methods is quite complex, therefore, its clinical application should be cautious.

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