Effect of medical nutrition combined with exercise intervention on the placental ischemic hypoxic injury and serum angiogenesis factors in patients with gestational hypertension

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Objective: To discuss the effect of medical nutrition combined with exercise intervention on the placental ischemic hypoxic injury and serum angiogenesis factors in patients with gestational hypertension. Methods: A total of 90 patients with gestational hypertension who received antenatal care and gave birth in our hospital between July 2014 and July 2016 were collected and divided into control group and observation group according to random number table, 45 cases in each group. Control group of patients received routine therapy, observation group of patients received routine therapy + nutrition combined with exercise intervention, and the ischemic hypoxic injury index expression in placenta tissue and serum angiogenesis factor levels before delivery were compared between two groups of patients. Results: After intervention, ischemic hypoxic injury index NO level in placental grinding fluid of observation group was higher than that of control group while ET-1, HIF-1α, Bax, Caspase-3 and MDA levels were lower than those of control group; serum angiogenesis factors TGFβ1, HGF, bFGF, VEGF and Ang-2 levels were significantly higher than those of control group while sFlt-1 level was lower than that of control group. Conclusion: The combination of medical nutrition and exercise can effectively reduce the placental ischemic hypoxic injury and reduce the angiogenesis in patients with gestational hypertension.

1. Introduction

The incidence of gestational hypertension in pregnant women is about 9.4% in China, which is an idiopathic disease in pregnancy and one of the main reasons affecting maternal and child health in the perinatal period[1,2]. China nutrition and health survey in 2002 showed that in addition to the pregnant women in remote mountain village, the pregnant women in our country are in a state of excessive energy intake and weight gain, and overquick weight gain can significantly increase the incidence of hypertension during pregnancy; the deficiency of trace elements of pregnant women is very common in China, which is also one of the important causes of pregnancy complications[3-5]. Therefore, many scholars have thought at present that nutritional imbalance and lack of exercise are the direct causes of gestational hypertension in the pregnant women in China, and in addition to drug therapy, positive nutrition and exercise intervention is very necessary. At present, there is not much research on the effect of nutrition and exercise intervention on the condition of patients with gestational diabetes, and the change of illness in patients with gestational hypertension was explored in this study after increasing medical nutrition combined with exercise intervention in order to clarify the clinical value of the intervention, now reported as follows.

2. Information and methods

2.1 Case information

A total of 90 patients with gestational hypertension who received antenatal care and gave birth in our hospital between July 2014 and July 2016 were selected as the research subjects, and the
patients themselves or the family members signed the informed consent. According to random number table, the enrolled patients were divided into control group and observation group, 45 cases in each group. Control group were 23-37 years old, the gravidity was 1-4 and (1.94±0.36) in average, and the parity was 1-3 and (1.27±0.43) in average; observation group were 24-38 years old, the gravidity was 1-3 and (1.89±0.33) in average, and the parity was 1-3 and (1.31±0.42) in average. There was no statistically significant difference in the gender, gravidity or parity distribution between the two groups of patients, and the hospital ethics committee approved the study.

2.2 Inclusion and exclusion criteria

Inclusion criteria: (1) meeting the diagnostic criteria for gestational hypertension (2) with first attack; (3) not receiving systematic treatment before inclusion; (4) cooperating with the whole intervention contents and with complete clinical data. Exclusion criteria: (1) combined with gestational diabetes mellitus, heart disease during pregnancy and other pregnancy complications; (2) combined with placenta previa, placental abruption and other dangerous conditions of pregnancy; (3) combined with systemic infectious diseases; (4) combined with malignant tumor diseases.

2.3 Intervention

Control group of patients received conventional therapy for patients with gestational hypertension, including bed rest and oxygen intake, and meantime, they received magnesium sulfate (Tianjin Kingyork Pharmaceutical Co., Ltd., approved by H20064021) for anti-hypertension according to the condition.

Observation group of patients, on the basis of conventional treatment, received medical nutrition combined with exercise intervention, specifically as follows: (1) the nutritional intervention: balanced dietary structure, avoiding excessive fat and sugar intake, and the total pregnancy energy intake about 840 kJ/d more than that of non-pregnancy, which was mainly by increasing protein intake. The diet should be rich in fruits, vegetables, B vitamins, fish, whole grain food, dietary fiber, etc., and the intake of saturated fatty acids and trans-fatty acids should be controlled and reduced. Pregnant women with deficiency of trace elements received targeted supplementation of calcium iron zinc selenium, vitamin B2, folic acid etc. (2) Exercise intervention: pregnant women were encouraged to do fitting aerobic exercise according to different pregnancies. The exercise was conducted three times per week in mid pregnancy (16-31 weeks) and lasted for around 50 min each time, and the concrete content included the tension and flexibility training of abdominal muscle, thigh muscle, pelvic floor muscles and bladder muscle, increasing blood circulation and relieving edema of lower extremity, as well as reducing fertility lipid deposition in the above parts. The exercise was conducted 3 times/week in late pregnancy (32-40 weeks) and lasted for around 50 min each time, the pelvic floor muscle contractility training was added on the basis of the mid-term training intensity, and the patients were guided to master the method of pain-relieving by breathing. During the above exercise, the intensity was repeated from light to severe until the pregnant woman was slightly sweaty and tired.

2.4 Observation indexes

2.4.1 Ischemic hypoxic injury indexes

Placental tissue samples were collected from two groups of pregnant women after different intervention, the grinding fluid was taken, anti-coagulated and then centrifuged at high speed to get supernatant liquid, RIA kit instructions were followed to detect the contents of nitric oxide (NO), endothelin-1 (ET-1) and hypoxia-inducible factor-1 α (HIF-1 α ), and the ELISA kit instructions were followed to determine the contents of Bax, Caspase-3 and MDA. The RIA kit was purchased from Beijing Furi Runkang Biotechnology Co., Ltd., and the ELISA kit was purchased from Shanghai Westang Biological Co., Ltd.

2.4.2 Serum angiogenesis factors

2.0 mL of cubital venous blood was collected from two groups of pregnant women after different intervention and before entering delivery room, anti-coagulated, then let stand at room temperature for stratification and centrifuged at low speed to get upper serum, and the ELISA kit instructions were followed to determine the levels of angiogenesis factors, including transforming growth factor β 1 (TGF β 1), hepatocyte growth factor (HGF), basic fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF), soluble VEGF receptor (sFlt-1) and angiogenin-2 (Ang-2). The ELISA kits were purchased from Shanghai Westang Biological Co., Ltd.

2.5 Statistical processing

Data calculation software was SPSS 20.0, and the statisticians had professional background and passed the exam. Ischemic hypoxic injury indexes and angiogenesis factors belonged to measurement data and were in terms of (Mean ± SD), and comparison was by t test. Statistics P<0.05 was set as the standard of statistical significance in differences.
3. Results

3.1 Ischemic hypoxic injury indexes

Comparison of ischemic hypoxic injury indexes NO (μmol/L), ET-1 (pg/mL), HIF-1α (ng/mL), Bax (ng/mL), Caspase-3 (ng/mL) and MDA (nmol/L) levels in placental grinding fluid between two groups of patients was as follows: after intervention, ischemic hypoxic injury index NO level in placental grinding fluid of observation group was significantly higher than that of control group while ET-1, HIF-1α, Bax, Caspase-3 and MDA levels were lower than those of control group. Differences in ischemic hypoxic injury indexes NO, ET-1, HIF-1α, Bax, Caspase-3 and MDA levels in placental grinding fluid were statistically significant between two groups of patients after intervention (P<0.05), shown in Table 1.

3.2 Serum angiogenesis factors

Comparison of serum angiogenesis factors TGFβ1 (pg/mL), HGF (ng/mL), bFGF (pg/mL), VEGF (μg/mL), sFlt-1 (ng/mL) and Ang-2 (ng/mL) levels between two groups of patients was as follows: after intervention, serum angiogenesis factors TGFβ1 (pg/mL), HGF, bFGF, VEGF and Ang-2 levels of observation group were significantly higher than those of control group while sFlt-1 level was lower than that of control group. Differences in serum angiogenesis factors TGFβ1, HGF, bFGF, VEGF, sFlt-1 and Ang-2 levels were statistically significant between two groups of patients after intervention (P<0.05), shown in Table 2.

4. Discussion

The occurrence of gestational hypertension is associated with many reasons, and in addition to the generally accepted theories such as genetic susceptibility and immune maladjustment, a growing number of scholars have believed that artificial nutritional imbalance, i.e. lack of exercise, is an important cause leading to the increased incidence of disease year by year[6,7]. A large number of epidemiological data show that the obesity rate of women in the increased incidence of disease year by year[6,7]. In the study, the changes of illness in patients with gestational diabetes mellitus were compared after drug therapy alone and after nutrition + exercise intervention in order to clarify the clinical value of nutrition and exercise intervention.

The placental ischemia hypoxia and a series of resulting injuries in patients with gestational diabetes mellitus are the important causes of fetal intrauterine death or asphyxia after birth, which are specifically associated with the unbalanced expression of a variety of vasomotor factors and hypoxia-regulatory factors[10,11]. NO and ET-1 are the active components secreted by vascular endothelium, and the two antagonizes each other and maintain the normal vasomotor function together[12]. NO synthesis increases and ET-1 level declines in placenta of normal pregnant women, and the NO and ET-1 expression are unbalanced in patients with gestational hypertension, which are characterized by the decreased NO synthase activity and increased ET-1 expression, and eventually result in excessive placental vascular contraction and insufficient blood supply[13]. HIF-1α can sensitively reflect the hypoxia of the placenta. When vasoconstriction leads to the decrease of blood flow, HIF-1α expression increases rapidly and further regulates the overexpression of ET-1, and the two forms a vicious cycle. In the study, the levels of these ischemic hypoxia injury indexes in placental grinding liquid were compared between the two groups after intervention, and it was found that compared with the control group, the observation group were with higher NO level, and lower ET-1 and HIF-1α levels in placental grinding fluid after intervention, indicating that nutrition combined with exercise intervention can effectively reduce placent ischemic hypoxic injury in patients with gestational diabetes mellitus.

The placental ischemic hypoxic state can cause abnormal activation of apoptosis and oxidative stress response. Bax is an important molecule that regulates apoptosis, which is mainly expressed in mitochondrial membrane and can increase the permeability of mitochondrial membrane to cytochrome C; under ischemia hypoxia

Table 1.

Comparison of ischemic hypoxic injury indexes in placental grinding fluid between two groups of patients after intervention.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>NO (μmol/L)</th>
<th>ET-1 (pg/mL)</th>
<th>HIF-1α (ng/mL)</th>
<th>Bax (ng/mL)</th>
<th>Caspase-3 (ng/mL)</th>
<th>MDA (nmol/L)</th>
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<tr>
<td>Control group</td>
<td>45</td>
<td>84.36±9.11</td>
<td>195.42±22.38</td>
<td>83.26±9.51</td>
<td>25.58±3.52</td>
<td>12.42±1.75</td>
<td>74.55±9.83</td>
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<tr>
<td>Observation group</td>
<td>45</td>
<td>143.74±16.88</td>
<td>89.63±9.27</td>
<td>40.85±6.23</td>
<td>9.34±1.03</td>
<td>5.42±0.78</td>
<td>35.84±5.35</td>
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Table 2.

Comparison of serum angiogenesis factor levels between two groups of patients after intervention.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>TGFβ1 (pg/mL)</th>
<th>HGF (ng/mL)</th>
<th>bFGF (pg/mL)</th>
<th>VEGF (μg/mL)</th>
<th>sFlt-1 (ng/mL)</th>
<th>Ang-2 (ng/mL)</th>
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<tr>
<td>Control group</td>
<td>45</td>
<td>73.37±8.89</td>
<td>57.37±6.05</td>
<td>15.48±2.27</td>
<td>115.38±14.95</td>
<td>82.63±9.17</td>
<td>49.26±6.17</td>
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<tr>
<td>Observation group</td>
<td>45</td>
<td>108.66±12.17</td>
<td>79.66±8.23</td>
<td>21.69±3.15</td>
<td>207.62±23.17</td>
<td>50.94±6.15</td>
<td>68.57±7.14</td>
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state, Bax expression on mitochondrial membrane significantly increases, which can promote the cytochrome C release from mitochondria into the cytoplasm, then cause caspase-3 activation and lead to apoptosis through a series of cascade activation reactions. MDA is a direct product of oxidative stress response. The oxygen free radical generation in local tissues increases significantly under ischemia hypoxia state, which will react with lipid in the cell membrane structure and generate MDA. In the study, the levels of these apoptosis and oxidative stress response indexes caused by ischemic hypoxic injury in placental grinding fluid were compared between the two groups after intervention, and it was found that compared with the control group, the observation group were with lower Bax, Caspase-3 and MDA levels in placental grinding fluid after intervention, indicating that nutrition combined with exercise intervention can effectively relieve the apoptosis and oxidative stress response indexes caused by placental ischemia hypoxia in patients with gestational diabetes mellitus.

The smooth muscle cells and elastic fibers in uterine spiral artery disappear in early physiological pregnancy, the trophocytes change from proliferative type to invasive type, invade uterine spiral arteries and form new vascular wall in order to form the specific pregnancy blood flow state of low resistance and high output, and the balance of angiogenesis/anti-angiogenesis factors plays an extremely important role in the process[14,15]. There are trophocyte infiltration and placental vascular remodeling obstacle in patients with gestational hypertension, and studies have shown that in early stage of gestational hypertension, the expression of TGFβ 1, HGF, bFGF, VEGF, Ang-2 and other angiogenesis factors are decreasing, and the decreasing extent is negatively correlated with disease severity[16,17]. VEGF level reduces when its combination with receptor sFlt-1 increases, which reduces the stimulation to TGFβ 1, HGF, bFGF, Ang-2 and other downstream factors, and makes the overall placental angiogenesis in low levels. In the study, the serum levels of these angiogenesis factors were compared between the two groups after intervention, and it was found that compared with the control group, the observation group were with higher serum levels of pro-angiogenesis factors TGFβ 1, HGF, bFGF, VEGF and Ang-2, and lower level of anti-angiogenesis factor sFlt-1 after intervention, confirming that nutrition and exercise intervention on the basis of drug therapy can effectively reverse the imbalance of angiogenesis/anti-angiogenesis factors, and reduce placental vascular remodeling in patients with gestational hypertension.

Medical nutrition and exercise intervention on the basis of drug therapy can effectively reduce placental ischemic hypoxic injury and balance serum angiogenesis factor expression in patients with gestational hypertension, and it helps to improve the illness and is expected to optimize the long-term maternal-infant outcome.

References


