Color Doppler ultrasound detection of uterine artery S/D, PI and RI in patients with preeclampsia and their correlation with disease severity

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ABSTRACT

Objective: To study color Doppler ultrasound detection of uterine artery S/D, PI and RI in patients with preeclampsia and their correlation with disease severity. Methods: Pregnant women with preeclampsia were selected as PE group, healthy pregnant women were the NOR group, color Doppler ultrasound detection was conducted to detect uterine artery S/D, PI and RI, serum was collected to detect the contents of angiogenesis-related cytokines, and placenta tissue was collected to detect the contents of proteases as well as inhibitors, oxidative stress molecules and anti-apoptotic molecules. Results: S/D, PI and RI of PE group were significantly higher than those of NOR group; serum PIGF, VEGF and PAPP-A contents of PE group were significantly lower than those of NOR group and negatively correlated with S/D, PI and RI while sVEGFR-1 and Kisspeptin-10 contents were significantly higher than those of NOR group and positively correlated with S/D, PI and RI; CTSB, CTSL, MMP3, MMP9, SOD, GST, VitC, VitE and coenzyme Q10 as well as Xiap and Survivin contents in placenta tissue of PE group were lower than those of NOR group and negatively correlated with S/D, PI and RI while TIMP1, TIMP2, TIMP3 and RECK contents were higher than those of NOR group and positively correlated with S/D, PI and RI. Conclusion: Uterine artery S/D, PI and RI significantly increase in patients with preeclampsia, and can assess the angiogenesis, cell invasion, anti-apoptosis and oxidative stress in patients.

1. Introduction

Hypertensive disorder complicating pregnancy is a common complication during pregnancy, and the main types include gestational hypertension, preeclampsia and eclampsia, etc., which causes serious harm to the maternal health. Preeclampsia is with higher incidence and bigger harm, will increase the risk of prematurity, intrauterine growth retardation and other complications, and also increases the risk of endocrine diseases and metabolic diseases when the newborns reach adulthood. At present, the pathogenesis and the inducement of preeclampsia are unknown, and the clinical methods and indicators that can early predict the disease are also needed. Studies have confirmed that in the pathological process of preeclampsia, the recasting of uterine artery is significantly abnormal, vascular resistance is higher and blood supply is relatively insufficient[1,2]. Color Doppler ultrasound is commonly used method for clinical evaluation of blood vessel function, which can determine the blood flow and resistance within the blood vessels[3]. In the following research, color Doppler ultrasound was used to detect uterine artery S/D, PI and RI in patients with preeclampsia and then the correlation of ultrasound-related indicators with disease severity was analyzed.

2. Subjects and methods

2.1 Result subjects

Included subjects were pregnant women with preeclampsia and...
healthy pregnant women giving birth in our hospital from August 2012 to October 2015, all women received antenatal care and gave birth in Obstetrics Department of our hospital and were informed of research matters, and then serum and placenta samples were collected. 52 cases of healthy pregnant women were included in normal group (NOR group), they were (31±4) years old and the gestational weeks was (38±4); 44 cases of pregnant women with preeclampsia were included in preeclampsia group (PE group), they were (30±4) years old and the gestational weeks was (37±4).

2.2 Color Doppler ultrasound detection methods

Philips ultrasound equipment was used for detection, probe frequency was set to 3.5 MHz, subjects took supine position, bladders were moderately full, blood flow frequency spectrum diagram of bilateral uterine artery at 1 cm of the internal iliac artery was obtained, and systolic to diastolic velocity ratio (S/D), pulsation index (PI) and resistance index (RI) were calculated.

2.3 Serum and placenta indicator detection methods

Peripheral blood was collected before childbirth and centrifuged to get serum samples; placenta tissue was collected after childbirth and homogenized to get tissue homogenate samples. Serum and tissue homogenate samples were collected, and ELISA kits were used to detect the contents of PIGF, VEGF, PAPP-A, sVEGFR-1, Kisspeptin-10, CTSB, CTSL, MMP3, MMP9, TIMP1, TIMP2, TIMP3, RECK, OD, GST, VitC, VitE, coenzyme Q10, Xiap and Survivin.

2.4 Statistical methods

SPSS 23.0 software was used to input and process data, measurement data analysis was by t test and differences were considered to be statistically significant at the level of P<0.05.

3. Results

3.1 Uterine artery S/D, PI and RI

Color Doppler ultrasound was used to detect systolic to diastolic velocity ratio (S/D), pulsation index (PI) and resistance index (RI) of two groups, and specific analysis was as follows: S/D, PI and RI of PE group were significantly higher than those of NOR group.

<table>
<thead>
<tr>
<th>Group</th>
<th>S/D</th>
<th>PI</th>
<th>RI</th>
</tr>
</thead>
<tbody>
<tr>
<td>PE</td>
<td>2.68±0.29</td>
<td>1.18±0.13</td>
<td>0.67±0.08</td>
</tr>
<tr>
<td>NOR</td>
<td>1.79±0.18</td>
<td>0.72±0.09</td>
<td>0.42±0.05</td>
</tr>
<tr>
<td>T</td>
<td>7.173</td>
<td>6.675</td>
<td>6.228</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

3.2 Contents of serum angiogenesis-related cytokines

Analysis of the contents of serum angiogenesis-related cytokines was as follows: serum PIGF, VEGF and PAPP-A contents of PE group were significantly lower than those of NOR group while sVEGFR-1 and Kisspeptin-10 contents were significantly higher than those of NOR group. Analysis of the correlation between the contents of serum angiogenesis-related cytokines and ultrasound indicators was as follows: serum PIGF, VEGF and PAPP-A contents negatively correlated with S/D, PI and RI while sVEGFR-1 and Kisspeptin-10 contents were positively correlated with S/D, PI and RI.

3.3 Contents of proteases and inhibitors in placenta

Analysis of the contents of proteases and inhibitors in placenta was as follows: CTSB, CTSL, MMP3 and MMP9 contents in placenta tissue of PE group were lower than those of NOR group while TIMP1, TIMP2, TIMP3 and RECK contents were higher than those of NOR group; analysis of the correlation of protease and inhibitor
contents with ultrasound indicators in placenta was as follows: CTSB, CTSL, MMP3 and MMP9 contents in placenta tissue were negatively correlated with S/D, PI and RI while TIMP1, TIMP2, TIMP3 and RECK contents were positively correlated with S/D, PI and RI.

3.4 Contents of oxidative stress molecules and anti-apoptotic molecules in placenta

Analysis of the contents of oxidative stress molecules and anti-apoptotic molecules in placenta was as follows: SOD, GST, VitC, VitE and coenzyme Q_{10} as well as Xiap and Survivin contents in placenta tissue of PE group were significantly lower than those of NOR group; analysis of the correlation of oxidative stress molecule and anti-apoptotic molecule contents with ultrasound indicators in placenta was as follows: SOD, GST, VitC, VitE, coenzyme Q_{10}, Xiap and Survivin contents were negatively correlated with S/D, PI and RI.

4. Discussion

In the process of pregnancy, the uterine artery blood flow determines the blood perfusion of the placenta. During normal pregnancy, trophoblasts start to invade uterine spiral artery from 5-7 weeks of gestation and gradually replace the vascular endothelial cells, make muscle elastic tissue remodeling within the vessel wall and turn to fiber structure, artery walls lose elasticity, tube cavity expands, resistance is reduced and blood flow increases significantly[4]. Uterine artery, meanwhile, will also change correspondingly from the state of high resistance and low output during non-pregnancy to the state of low resistance and high output after pregnancy, artery is gradually straightened, lumen is expanded, blood flow increases and flow rate is accelerated, ensuring the nutrients and energy supply necessary to the growth of fetus. But in the process of the onset of preeclampsia, trophoblast invasion ability is weakened significantly, can only invade the decidua layer and fails to invade and replace vascular muscle layer, uterine spiral artery remodeling is relatively insufficient and blood vessels are still in the state of high resistance and lower output[5,6]. In the research, color Doppler ultrasound was used to assess the blood flow and resistance in uterine artery, and results showed that S/D, PI and RI of PE group were significantly higher than those of NOR group. It indicated that color Doppler ultrasound could accurately assess the abnormality of blood flow in uterine artery of patients with preeclampsia.

In the process of the onset of preeclampsia, a variety of pro-angiogenesis cytokines and anti-angiogenesis factors are involved in the remodeling of uterine spiral artery. PIGF and VEGF are cytokines with pro-angiogenesis effect, and can promote the trophoblast invasion to spiral arteries and increase vascular permeability and the number of new blood vessels[7,8]. sVEGFR-1 can compete with VEGFR on cell membrane to be combined with VEGF and PIGF, inhibit the pro-angiogenesis effect of above cytokines and cause angiogenesis obstacles in placenta[9]. Kisspeptin-10 and its receptor GPR54 can directly inhibit endothelial cell proliferation and migration, thereby impeding the process of vascular remodeling and angiogenesis[10]. Pregnancy-associated plasma protein A (PAPP-A) is a newly discovered type of pregnancy-related insulin-like growth factor binding protein that can enhance the biological function of IGF and promote vascular remodeling[11]. In the research, the detection of the contents of serum angiogenesis-related cytokines of two groups showed that serum PIGF, VEGF and PAPP-A contents of PE group were significantly lower than those of NOR group and negatively correlated with S/D, PI and RI while sVEGFR-1 and Kisspeptin-10 contents were significantly higher than those of NOR group and positively correlated with S/D, PI and RI. It indicated that S/D, PI and RI detected by color Doppler ultrasound could reflect the contents of angiogenesis-related cytokines in pregnant women with preeclampsia.

The process of trophoblast invasion to decidua and blood vessels in placenta tissue is regulated by a variety of proteases. Cysteine cathepsins (CTSs) and matrix metalloproteinases (MMPs) are the key proteases degrading extracellular matrix and promoting cell invasion. Studies have confirmed that the CTSB and CTSL in CTSs family as well as MMP3 and MMP9 in MMPs family can induce trophoblast cells to invade spiral arteries and degrade smooth muscle layer and elastic layer of vessel wall, replace vascular endothelial cells and complete vascular remodeling[12,13]. At the same time there are a variety of inhibitors of proteases in the body, including tissue inhibitors of metalloproteinases TIMP1, TIMP2 and TIMP3 as well as matrix metalloproteinase inhibitor RECK. TIMPs molecules can directly inhibit the function of proteases, and RECK can inhibit the expression of proteases. In the research, the analysis of the expression levels of above proteases and inhibitors in placenta

<table>
<thead>
<tr>
<th>Group</th>
<th>SOD (U/L)</th>
<th>GST (U/L)</th>
<th>VitC (ng/mL)</th>
<th>VitE (ng/mL)</th>
<th>Q_{10} (ng/mL)</th>
<th>Xiap (ng/mL)</th>
<th>Survivin (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PE</td>
<td>56.2±6.6</td>
<td>33.1±39</td>
<td>103.2±12.9</td>
<td>85.6±9.3</td>
<td>135.2±15.2</td>
<td>58.2±6.5</td>
<td>76.3±8.5</td>
</tr>
<tr>
<td>NOR</td>
<td>124.2±14.9</td>
<td>76.7±8.5</td>
<td>184.9±22.5</td>
<td>145.2±17.8</td>
<td>241.2±31.4</td>
<td>99.3±10.4</td>
<td>153.4±17.6</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Table 4.
Contents of oxidative stress molecules and anti-apoptotic molecules in placenta of two groups.
tissue showed that CTSL, MMP3 and MMP9 contents in placenta tissue of PE group were lower than those of NOR group and negatively correlated with S/D, PI and RI while TIMP1, TIMP2, TIMP3 and RECK contents were higher than those of NOR group and positively correlated with S/D, PI and RI. It indicated that S/D, PI and RI detected by color Doppler ultrasound could reflect cell invasion in pregnant women with preeclampsia.

Insufficient trophoblast invasion and abnormal spiral artery recasting can lead to insufficient placental blood perfusion and local tissue ischemia hypoxia, thereby activating oxidative stress and cell apoptosis process. Oxidative stress is mainly characterized by excessive produced reactive oxide species and large consumption of antioxidants. The main antioxidants inside placenta include SOD, GST and other enzyme antioxidants as well as VitC, VitE, coenzyme Q10 and other non-enzyme antioxidants, and local hypoxia can cause large consumption of above antioxidants[14]. At the same time, placenta hypoxia can also inhibit the expression of a variety of anti-apoptotic molecules in the placenta, reduce anti-apoptosis ability of cells and induce cell apoptosis. Xiap and Survivin are two kinds of molecules closely related to trophoblast anti-apoptosis, and the decrease of their contents will induce trophoblast apoptosis[15,16]. In the research, the analysis of the contents of above oxidative molecules and anti-apoptosis molecules in placenta tissue showed that SOD, GST, VitC, VitE and coenzyme Q10 as well as Xiap and Survivin contents in placenta tissue of PE group were significantly lower than those of NOR group and negatively correlated with S/D, PI and RI. It indicated that S/D, PI and RI detected by color Doppler ultrasound could reflect oxidative stress and cell apoptosis in placenta of pregnant women with preeclampsia.

To sum up, uterine artery S/D, PI and RI significantly increase in patients with preeclampsia, and can assess the angiogenesis, cell invasion, anti-apoptosis and oxidative stress in patients.

References


