Detection of visfatin, Xiap and Survivin expressions in placenta tissue of preeclampsia and its correlation with serum indexes

Wei Zhong

Department of Obstetrics, People’s Hospital of Huangpi District, Wuhan City, Hubei Province, 430300

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ABSTRACT

Objective: To study the expressions of visfatin, Xiap and Survivin in placenta tissue of preeclampsia and its correlation with serum indexes. Methods: Preeclampsia patients who gave birth in our hospital and healthy volunteers during the same period were selected and enrolled in observation group and control group. Then placenta tissue was collected and mRNA contents of visfatin, Xiap and Survivin were detected; serum was collected and angiogenesis related factors, inflammatory cytokines were detected. Results: (1) Placenta index: compared with mRNA contents of target genes in placenta tissue of control group, mRNA content of Visfatin in placenta tissue of observation group was higher; mRNA contents of Xiap and Survivin were lower; (2) Serum angiogenesis related factors: compared with contents of serum angiogenesis cytokines of control group, serum PIGF and Glycodelin contents of observation group were lower; sEng, sFlt-1, PP13 and HtrA1 contents were higher; (3) Inflammatory cytokines: compared with serum inflammation related factor contents of control group, serum YKL-40, CXCL-10, Chemerin, IL-18, HMGB-1 and MIF contents of observation group were higher. Conclusion: Abnormal expressions of visfatin, Xiap and Survivin in placenta tissue are related to the occurrence of preeclampsia, and gene mRNA contents are related to the contents of serum angiogenesis related factors and inflammatory cytokines.

1. Objects and methods

1.1 Objects

Preeclampsia patients who gave birth in our hospital and healthy volunteers during the same period were selected by same group of doctors. Cases were enrolled time from May 2013 to September 2014. Preeclampsia patients were diagnosed through auxiliary examination. Total 45 cases were enrolled in observation group; healthy volunteers were healthy parturient women who gave birth in our hospital during the same period. They didn’t have pregnancy complications and total 45 cases were enrolled in control group. Both groups were informed of research matters and signed consents. Data of observation group was as follows: age range: 34.23±5.42, primipara/ multipara: 32/13 cases, gestational week range when giving birth: 35.58±4.58; data of control group was as follows: age range: 33.48±4.85, primipara/ multipara: 29/16 cases, gestational week range when giving birth: 33.94±4.27. There were no differences between two groups' general data (P>0.05).
1.2 Methods

1.2.1 Specimen collecting methods
(1) Serum collecting methods were as follows: after both groups were admitted to the hospital and when they were not about to give birth, peripheral venous anti-clotting blood was collected and centrifuged. Then serum was collected, transferred into 1.5ml EP tube and preserved at -80°C freezer; (2) Placenta tissue collecting methods: within half an hour after giving birth, placenta tissue of both groups was collected, washing away the blood with normal saline and sucking out the water, then transferred into freezing tube, quickly frozen in liquid nitrogen and then removed and preserved at -80°C freezer.

1.2.2 Index detecting methods
(1) Serum index detecting methods were as follows: before detection, serum specimen was taken out and unfrozen. Then referring to Elisa kit manual, contents of various indexes were detected; (2) Detecting methods of related indexes in placenta tissue: placenta specimen was taken out and unfrozen. 70-80 mg tissue was weighed on the scale, adding Trizol lysate. Total RNA was extracted for RT into cDNA. Then PCR was carried out to amplify visfatin, Xiap, Survivin and β-actin respectively. mRNA contents were calculated.

1.2.3 Statistical methods
Detected data was input by SPSS18.0 software, measurement data comparison between two groups for t test and correlation analysis among different indexes for linear regression. Differences were considered to be significant at a level of P<0.05.

2. Results

2.1 mRNA contents of Visfatin, Xiap and Survivin in placenta
Placenta tissue of preeclampsia and normal placenta tissue were collected. Fluorescence quantitative PCR was used to detect mRNA contents of Visfatin, Xiap and Survivin in placenta tissue. T test was carried out to analyze mRNA content differences of target genes between two groups. Results showed that compared with mRNA contents of target genes in placenta tissue of control group, mRNA content of Visfatin in placenta tissue of observation group was higher; mRNA contents of Xiap and Survivin were lower. Differences had statistical differences (P<0.05).

![Figure 1](image-url)  
**Figure 1.** mRNA contents of Visfatin, Xiap and Survivin in placenta of both groups. Compared with mRNA contents of target genes in placenta tissue of control group, mRNA content of Visfatin in placenta tissue of observation group was higher; mRNA contents of Xiap and Survivin were lower. *: Observation group vs. Control group, differences had statistical differences, (P<0.05).

2.2 Serum angiogenesis cytokine contents
Shallow trophoblast cell invasion and abnormal placental vascular recasting are important pathological features of preeclampsia patients. Angiogenesis cytokines are important cytokines that regulate this process. The research detected and analyzed serum angiogenesis related factor contents of both groups and results showed that compared with serum angiogenesis cytokine contents of control group, serum PIGF and Glycodelin contents of observation group were lower; sEng, sFlt-1, PP13 and HtrA1 contents were higher. Differences had statistical differences (P<0.05).

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<td><strong>Analysis of serum angiogenesis cytokine contents</strong></td>
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2.3 Serum inflammation related factor contents
Inflammation hypothesis is one of the important hypotheses on mechanism of preeclampsia. Abnormal contents of inflammation related factors are key elements that cause uncontrolled inflammation. The research detected and analyzed serum inflammation related factor contents of both groups and results showed that compared with serum inflammation related factor contents of control group, serum YKL-40, CXCL-10, Chemerin, IL-18, HMGB-1 and MIF contents of observation group were higher. Differences had statistical differences (P<0.05).
3. Discussions

Preeclampsia is an idiopathic disease during pregnancy with expressions of high blood pressure, proteinuria and so on. Clinical symptoms and signs of most patients gradually ease or disappear after termination of pregnancy or delivery of placenta, which indicates that placenta is an important factor that results in the occurrence of preeclampsia[2]. Current studies have shown that shallow implantation, oxidative stress, endothelial injury, vascular inflammation, and so on are important pathological features of local placenta. Abnormal expressions of a variety of genes are involved in the pathological process[3]. Visfatin (VF) is a newly discovered adipokine. In placenta tissue, major roles of visfatin include[4-5]: (1) promoting the differentiation and maturation of B lymphocytes, inhibiting apoptosis of neutrophils, thus enhancing local inflammatory response and immune response; (2) increasing expressions of thromboxane synthase and interleukin, resulting in injury of endothelial cells. The research detected Visfatin content in placenta tissue of preeclampsia and found out that compared with mRNA contents of target genes in placenta tissue of control group, mRNA content of Visfatin in placenta tissue of observation group was higher. Besides, excessive apoptosis of trophoblast cells is related to the occurrence of preeclampsia, too. Abnormal regulation of multiple apoptosis in placenta will cause the occurrence of preeclampsia. Xiap is an apoptosis-inhibiting protein linked with X-chromosome, which can directly combine with Caspase3/7/9 of Caspase family to inhibit apoptosis[6]; Survivin is currently known to be the most powerful anti-apoptotic molecule, which can play the anti-apoptotic role through a number of ways, including blocking activation of Caspase family molecules, inhibiting cytochrome C release in mitochondria, inhibiting functions of p53, and so on[7]. The research detected Xiap and Survivin contents in placenta tissue of preeclampsia and found out that compared with mRNA contents of target genes in placenta tissue of control group, mRNA contents of Xiap and Survivin in placenta tissue of observation group were lower, which indicated that abnormal expressions of Visfatin, Xiap and Survivin in placenta tissue were related to the occurrence of preeclampsia.

In development of preeclampsia, shallow trophoblast cell invasion and abnormal placenta vascular recasting are important pathological features, based on which, generation of placenta derived toxic cytokines increases, injury of endothelial function aggravates, and so on. In the process of trophoblast cell invasion and placenta vascular recasting, multiple angiogenesis cytokines play important roles. Placental growth factor (PIGF) is a pro-angiogenesis related factor with effects of inducing endothelial proliferation, increasing vascular permeability and facilitating the development of placental vascular network [8]. Soluble endoslin (sEng) and soluble PIGFR-1 (sPIGFR-1) are two cytokines with anti-angiogenesis effect. Ligand of the former one is TGF-β and ligand of the latter one is PIGF. Both can inhibit proliferation and migration of endothelial cells, and also have the effect of injuring endothelial cell integrity[9]. Placenta protein 13 (PP13) is a soluble protein locating in cytoplasm, also known as galectin 13. In placenta, PP13 mainly locates in the cytoplasm of syncytiotrophoblast; in the case of insufficient angiogenesis or placental ischemia and hypoxia, apoptosis of trophoblast cells occurs and PP13 in the cytoplasm is largely secreted into bloodstream[10]. Pregnancy-associated endometrial protein (glycodelin) is a secreted glycoprotein from glands in the decidua basalis. When acting on trophoblast cells in placenta, it can promote PIGF expression, thus achieving regulation to the development of placental vascular bed[10]. HtrA1 is a serine protease locating in the membranes with the nature of heat shock protein. It is expressed on the surface of trophoblast cells and regulates invasive process of cells; excessive expression of the protein will inhibit trophoblast cell invasion to spiral artery, resulting in abnormal establishment of placental vascular bed[11]. The research detected serum angiogenesis cytokine contents and found out that compared with serum angiogenesis cytokine contents of control group, serum PIGF and Glycodelin contents of observation group were lower and sEng, sFlt-1, PP13 and HtrA1 contents were higher, which indicated that abnormal angiogenesis cytokine contents were related to the occurrence of preeclampsia.

Inflammation hypothesis is one of the important hypotheses on mechanism of preeclampsia in recent years. C-reactive protein and tumor necrosis factor are traditional inflammatory factors. But they have greater limitations in clarifying preeclampsia mechanism and predicting the risk of disease and prognosis. In recent years, more and more new types of inflammatory factors are considered to be closely related to the occurrence of preeclampsia. Cartilage glycoprotein 40 (YKL-40) is a secreted protein synthesized by inflammatory cells such as monocyte- macrophages, neutrophils and so on. It is related to the occurrence and development of acute inflammation and chronic inflammation[12]. Chemokine ligand 10 (CXCL10) is an inflammatory factor with double functions. It has the function of activating monocyte- macrophages and neutrophils, and can mediate injury of trophoblast cells. IL-18 was initially considered to be interferon-inducing factor. In recent years, it is thought to be able to mediate apoptosis process through inducing inflammatory response and cell toxic reaction. It is an important factor that causes injury of trophoblast cells and vascular endothelial cells[13]. Chemerin is an adipokine that can participate in the occurrence of inflammatory response and injury of vascular endothelial cells[14]. High mobility group box protein-1 (HMGB-1) is a DNA-binding protein that mediates advanced inflammatory response. It is regulated by inflammatory factors IL-1 and TNF-α.
When secreted, it can act on monocyte-macrophages and promote the synthesis of IL-1, IL-8, TNF-α and so on. It is a key factor that mediates inflammatory cascade. The role of macrophage migration inhibitory factor (MIF-1) is to recruit macrophages in local lesion, promote macrophage infiltration and secrete a variety of cytokines. The research detected contents of serum inflammation related factors and found out that compared with contents of serum inflammation related factors of control group, serum YKL-40, CXCL-10, Chemerin, IL-18, HMGB-1 and MIF contents of observation group were higher, which indicated that increased contents of inflammation related factors were related to the occurrence of preeclampsia.

Based on above analysis and discussions, it can be concluded that abnormal expressions of visfatin, Xiap and Survivin in placenta tissue are related to the occurrence of preeclampsia, and gene mRNA contents are related to the contents of serum angiogenesis related factors and inflammatory cytokines.

References


