

Expression and meaning analysis of *HIF-1 α* and HSP70 in preeclamptic placenta.

Hua Lai, Huai Liu*

Department of Obstetrics, Jiang Xi Province Maternal and Child Health Care Hospital, Nanchang, Jiangxi, PR China

Abstract

Objective: To discuss the expression and meaning analysis of Hypoxia-Inducible Factor-1 α (*HIF-1 α*) and Heat Shock Protein 70 (HSP70) in preeclamptic placenta.

Method: Fifty patients (experimental group) with preeclampsia in our hospital and 50 normally pregnant women (control group) were recruited in this study, and then the expressions of *HIF-1 α* and HSP70 in placental tissues were compared between the two groups.

Results: Positive expressions of *HIF-1 α* and HSP70 in placental tissues in the experimental group were 80.00% (40/50) and 78.00% (39/50), respectively, whereas those in the control group were 28.00% (14/50) and 32.00% (16/50), respectively ($P < 0.05$). Furthermore, positive expressions were positively correlated with illness development ($P < 0.05$).

Conclusion: Among pregnant women with preeclampsia, *HIF-1 α* and HSP70 play significant roles in and have close relationship with the genesis and development of the illness, which have provided relevant reference data for the diagnosis and treatment of this illness.

Keywords: Preeclampsia, Placenta, Hypoxia-inducible factor-1 α (*HIF-1 α*), Heat shock protein 70 (HSP70).

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Introduction

There is no definite clinical conclusion over the specific pathogenesis of preeclampsia at present, and it is generally believed that vascular endothelial cells are damaged due to intrusion of abnormal trophoblastic cells into the myometrium of the human body [1,2].

Hypoxia-Inducible Factor (HIF) in placental tissues of patients with this kind of illness presents abnormal expression and corresponding products are produced through signal transduction pathway of trophocytes [3]. This process helps to provide relevant basis for pathogenic factors of preeclampsia. Many studies on Heat Shock Protein (HSP) have verified that stress factors can have an impact on substance synthesis and participate in activities of intracellular proteins, such as assembling and folding, so as to regulate signal transduction, growth, and differentiation [4,5].

Moreover, as a kind of endogenous protective substance, once damaged, HSP can realize self-protective effect. For analysis of *HIF-1 α* and HSP70 expressions in placental tissues of preeclampsia, detailed explanation is as follows.

Data and Methodology

General data

Fifty patients (experimental group) with preeclampsia in our hospital and 50 normally pregnant women (control group) were

recruited in this study. The inclusion period of subjects in both groups was identical, i.e., June 12, 2016 to June 12, 2017.

Twenty-eight patients in the experimental group had mild illness, whereas 22 had severe illness. Their ages ranged from 21 to 38 y, with the average age being 29.36 ± 2.20 y. The shortest and longest gestational weeks were 32 and 41 weeks, respectively, with the average value being 36.56 ± 1.22 weeks.

Conversely, in the control group, the patients' ages ranged from 22 to 37 y, with the average age being 29.12 ± 2.14 y. The shortest and longest gestational weeks were 32 and 40 weeks, respectively, with the average value being 36.35 ± 1.14 weeks.

No significant differences in age and gestational weeks were observed between the two groups through a comparison ($P > 0.05$), so favourable comparability existed.

Methodology

SP Immunohistochemistry (IHC) kit and polyclonal antibodies were used in this study. Materials were drawn within 0.5 h after placental expulsion. Tissue blocks (middle section of the maternal placenta) were cut, with their length, width, and height all being 1 cm.

Formaldehyde (10%) was used for specimen fixation, and after 24 h, specimen sectioning was carried out after embedding treatment through paraffin wax with thickness of 4 μ m. IHC staining treatment was given, and then the operation was implemented strictly according to the corresponding steps.

Criteria

Evaluation was made through the Shimizu method, and section staining status under a microscope was analyzed, where positive result indicated brown particle deposition phenomenon. Grading was conducted according to intracellular staining power and number of positive cells.

If intracellular staining was unclear or without staining phenomenon, showed even faint yellow staining phenomenon, or was consistent with the background, then it was given a value of 0. If there was a small quantity of faint yellow particles in plasma or nucleus with obviously higher power than the background, then a value of 1 was given.

If there was a large quantity of dark brown particles in plasma or nucleus, then a value of 2 was given. If there was a large quantity of brown or dark brown particles, then a value of 3 was given. If the percentage of positive cells was lower than 25%, then a value of 1 was given. If the percentage was 25%-50%, then a value of 2 was given. If the percentage was above 50%, then a value of 3 was given. Every two of the above were multiplied by each other, 0-1 score expressed (-), 2-3 scores expressed (+), 4-5 scores expressed (++), and above 5 scores expressed (+++).

Statistical analysis

SPSS 17.0 statistical software was used to record the data of the two groups. Enumeration data were expressed by percentages and rates, and χ^2 test was used for comparison. Measured data were expressed by mean \pm standard deviation ($\bar{x} \pm S$), and T-test was used for comparison. If difference of inter-group data is significant, then it is expressed by $P < 0.05$.

Results

HIF-1 α expression

As shown in Figure 1, positive expression of HIF-1 α showed yellowish brown particles filling the placental syncytiotrophoblast, cytoplasm, and karyon, which mainly existed in the cytoplasm, and positive expressions of syncytiotrophoblasts and cytotrophoblasts were (++) and (+++) and (+).

The positive rate of expressions in placental tissues of pregnant women in the experimental group was 80.00% (40/50), whereas that in the control group was 28.00% (14/50), so differences in positive rates of expressions were significant between the two groups ($P < 0.05$).

HSP70 expression

In Figure 2, particles with positive HSP70 were light to dark brown, and they mainly existed in the cytoplasm of syncytiotrophoblasts. Moreover, some presented cell nucleus staining. For pregnant women in the experimental group, positive rate of HSP70 expression reached 78.00% (39/50), whereas that in the control group reached 32.00% (16/50), so

differences in the positive rate of HSP70 expression were significant between the two groups ($P < 0.05$).

Correlation analysis

Based on analysis, HIF-1 α and HSP70 presented positive correlation, where $r_1 = 0.407$ and $P = 0.035$. The two had positive correlation in the experimental group, where $r_1 = 0.732$ and $P = 0.016$. The activation degree of HIF-1 α had positive correlation with the state of the illness, where $r_1 = 0.796$ and $P = 0.000$.

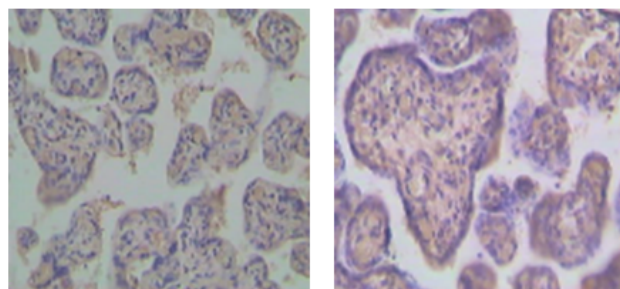


Figure 1. Normal placenta (left) and preeclampsia (right).

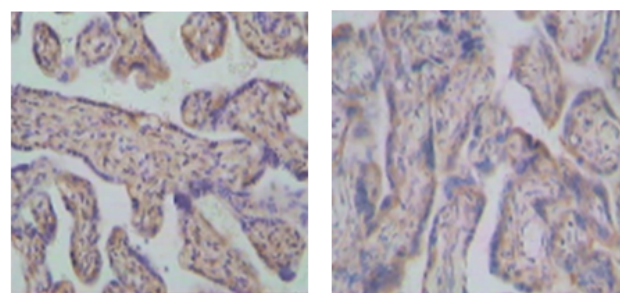


Figure 2. Normal placenta (left) and preeclampsia (right).

HIF-1 α staining results in placental tissues of patients in the preeclampsia group (experimental group) and control group

In Table 1, positive HIF-1 α expression in placental tissues was higher in the preeclampsia group than in the control group, and positive rate of HIF-1 α expression was higher in patients with severe preeclampsia than those with mild preeclampsia ($P < 0.05$).

HSP70 staining results in placental tissues of patients in the preeclampsia group (experimental group) and control group

In Table 2, positive HSP70 expression in placental tissues was higher in the preeclampsia group than in the control group, and positive rate of HSP70 expression was higher in patients with severe preeclampsia than those with mild preeclampsia ($P < 0.05$).

Table 1. HIF-1 α staining results in placental tissues of patients in the preeclampsia group (experimental group) and control group.

| Group | 0 | (+) | (++) | (+++) |
|----------------------------|------------|----------|------------|------------|
| Control group (n=50) | 10 (20.00) | 2 (4.00) | 2 (4.00) | 0 (0.00) |
| Mild preeclampsia (n=28) | 2 (7.14) | 2 (7.14) | 6 (21.43) | 6 (21.43) |
| Severe preeclampsia (n=22) | 0 (0.00) | 1 (4.55) | 11 (50.00) | 12 (54.55) |

Table 2. HSP70 staining results in placental tissues of patients in the preeclampsia group (experimental group) and control group.

| Group | 0 | (+) | (++) | (+++) |
|----------------------------|------------|----------|------------|------------|
| Control group (n=50) | 11 (22.00) | 3 (6.00) | 2 (4.00) | 0 (0.00) |
| Mild preeclampsia (n=28) | 1 (3.57) | 2 (7.14) | 5 (17.86) | 6 (21.43) |
| Severe preeclampsia (n=22) | 0 (0.00) | 2 (9.09) | 12 (54.55) | 11 (50.00) |

Discussion

For preeclampsia patients, local blood supply is reduced due to vasospasm; therefore, tissues are under anaerobic condition with increased HIF-1 α expression and obviously improved anoxic tolerance. Fifty patients (experimental group) with preeclampsia in our hospital and 50 normally pregnant women (control group) were recruited in this study. The results showed that positive expressions of HIF-1 α and HSP70 in placental tissues of patients in the experimental groups were 80.00% and 78.00%, respectively, both of which were higher than those in the control group. When the illness aggravates, positive expressions of HIF-1 α and HSP70 will gradually increase.

HIF-1 α is rapidly degraded through the pantothenic acid-proteolytic enzyme system under unstable oxygen partial pressure, which has a short half-life period of 5-10 min. Relevant studies have pointed out that in early pregnancy, there is a relative shortage of blood supply in the embryo, HIF has reached a corresponding level, and the embryo has favorable tolerance against hypoxic environment, which causes trophocyte development [6,7]. As gestational weeks increase, the embryo will be gradually under hyperoxic status, which is convenient for reducing the level of HIF. Based on analysis, HIF-1 has a heterodimer structure, and HIF-1 α and HIF-1 β jointly constitute this type of substance, where HIF-1 α can activate genetic expression and exert an effect on HIF-1 activity [8]. In the case of preeclampsia, vasospasm will reduce the blood supply, cause hypoxia of local tissues, increase HIF-1 α levels, and improve tolerance degree of tissues against anoxic conditions. The mechanism of action obtained through analysis is as follows [9,10]: Under histanoxia, the pathway for ubiquitin-proteasome degradation is blocked, which reduces HIF-1 α ubiquitination and degradation. Under hypoxic condition, HIF-1DNA binding activity will be induced. If EPO3 enhancer is bound, erythropoietin transcription will be enhanced so that oxygen carrying capacity of local tissues will be enhanced.

IHC scheme was used in this study to analyze HIF-1 α expressions in normal pregnant women and pregnant women with preeclampsia. The HIF-1 α level in the experimental group

was obviously higher than that in the control group. Through analysis, HIF-1 plays a significant role in regulating multiple cells and systems under anoxic and ischemic conditions. However, in the present clinical study, its effect on preeclampsia has not been fully elucidated. With further studies, this index may become a prevention and treatment approach for diseases such as preeclampsia and hypertensive disorder complicating pregnancy.

HSP70 plays a role in regulating cell proliferation, embryonic development, and bioactive molecules. Moreover, it is closely related to early embryonic development status. HSP70 immune positive reaction mainly occurs in endometrial stromal cells. With gradual increase in gestation, the number of positive cells will gradually increase. The expression of HSP70 in the secretory phase is stronger than that in the proliferative phase, and it can exert corresponding effect on compounds of technological steroid receptors. When the content of HSP70 continues to increase, it will help in the assembling and transportation activities of technological steroid receptor compounds. In addition, as estrogens are gradually enhanced, they will facilitate HSP70 synthesis, which increases cellular proliferation activity.

Conclusion

HIF-1 α and HSP70 play non-negligible roles in pregnant women with preeclampsia, so clinical study on these indexes should be strengthened so as to provide relevant criteria for the prevention, diagnosis, and treatment of illnesses.

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***Correspondence to**

Huai Liu

Department of Obstetrics

Jiang Xi Province Maternal and Child Health Care Hospital

Nanchang

Jiangxi

PR China