Relationship between expression of hepatocyte growth factor and apoptosis of trophoblasts in hypertensive disorder complicating pregnancy

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Abstract The aim of this study was to investigate the expression of hepatocyte growth factor (HGF) and Fas in placentas of uncomplicated pregnant women and those with hypertensive disorder complicating pregnancy (HDCP), and elucidate the possible relationship between HGF and apoptosis of trophoblasts. Reverse transcription-polymerase chain reaction (RT-PCR) was undertaken to examine the concentration of HGF mRNA and Fas mRNA obtained from 34 cases of HDCP and 30 cases of uncomplicated pregnancy. The expression of HGF mRNA in mild preeclampsia, severe preeclampsia and eclampsia cases was significantly lower than that in the uncomplicated cases (0.43 ± 0.12, 0.38 ± 0.09, 0.19 ± 0.17 versus 0.67 ± 0.19, P < 0.05), while the expression of Fas mRNA in mild preeclampsia, severe preeclampsia and eclampsia cases was significantly higher than that in the uncomplicated cases (1.58 ± 0.26, 2.96 ± 0.14, 5.98 ± 1.17 versus 1.01 ± 0.36, P < 0.05). For HGF mRNA and Fas mRNA, there was no difference between gestational hypertension cases and control cases. Decreased HGF mRNA or increased Fas mRNA was found along with the progress of HDCP. Negative correlation was found between the expressions of HGF and Fas. These results indicate that HGF inhibits the apoptosis mediated by Fas, and the reduced expression of HGF in HDCP may be responsible for the apoptosis of trophoblasts.

Keywords hepatocyte growth factor; pregnancy complications; cardiovascular; hypertension; trophoblasts; apoptosis

1 Introduction

Hypertensive disorder complicating pregnancy (HDCP) remains one of the leading causes of maternal and fetal morbidity and mortality. Although the etiology is unclear, a plenty of evidences show that increased apoptosis of trophoblast may be one of the causes of HDCP [1]. Cell apoptosis is under the influence of cytokine. Hepatocyte growth factor (HGF), known as a pleiotropic cytokine, plays an important role in inhibiting Fas-mediated cell apoptosis. We hypothesized that HGF had the same effect on placenta trophoblasts, and designed this study to examine the expression of HGF mRNA and Fas mRNA in both normal cases and HDCP cases, and explore the relationship between HGF and trophoblast apoptosis.

2 Materials and methods

2.1 Patients

The trial was conducted from September 2004 to April 2005, involved 34 women with HDCP and 30 pregnant women without any complications. The HDCP that was defined as systolic blood pressure is higher than 140 or diastolic blood pressure is higher than 90 mmHg, excluding chronic hypertension and other complications. All women with HDCP were divided into four groups: gestational hypertension (nine cases), mild preeclampsia (ten cases), severe preeclampsia (12 cases) and eclampsia (three cases).

The average age of women with HDCP was (29.4 ± 5.1) years, average gestational weeks were (35.7 ± 3.0) weeks. The ages and gestational weeks of uncomplicated women were matched with those of HDCP cases.
2.2 Tissue collection and processing

Placental tissues were obtained from the central portion of the decidua side plate without hemorrhage, necrosis or calcification. All these samples were collected immediately after the cesarean delivery then washed extensively in saline and store at −80°C until use.

2.3 HGF mRNA and Fas mRNA in placenta

Total RNA was extracted by Trizol (Invitrogen, USA), then reverse transcripted into cDNA. The primer used for the amplification of HGF had the following sequence: upstream: 5’AAG ATA TCC CGA CAA GG3’, downstream: 5’ATG CTC GTG AGG ATA CTG3’ and resulted in a 250 bp product. The primer used for the amplification of Fas had the following sequence: upstream: 5’ACA GCC CAG TCA ACT GC3’ and downstream: 5’CTT GCG CGA GAT CAG AG3’ and resulted in a 400 bp product. The GAPDH is used as an internal control to standardize the expression levels of Fas and HGF.

2.4 Gel electrophoresis

The polymerase chain reaction (PCR) products were loaded onto agarose gel for electrophoresis. The results were expressed as a ratio of sample RNA to GAPDH.

2.5 Statistical analysis

All data were analyzed by using SPSS 10.0 soft package and the results were generally expressed as $\bar{x} \pm s$. $F$-test was conducted to examine the difference between two groups and Pearson test was taken to analyze the correlation between HGF and Fas.

3 Results

3.1 Levels of HGF mRNA in placentas

The mean HGF mRNA level of the placentas from mild preeclampsia group, severe preeclampsia group and eclampsia group was significantly lower than that of the placentas of women with uncomplicated pregnancies. While, there was no difference between the gestational hypertension group and the control group. HGF mRNA decreased as this disease progressed (Table 1, Fig. 1).

3.2 Levels of Fas mRNA in placentas

The Fas mRNA expression of placentas of uncomplicated women was significantly lower than that of mild and severe preeclampsia women and eclampsia women ($P < 0.05$), which increased as this disease progressed. There was no difference between placentas of women with gestational hypertension and those without any complications ($P > 0.05$) (Table 1, Fig. 2).

3.3 Correlation between HGF and Fas

The expression of HGF mRNA had a negative correlation with that of Fas mRNA ($r = -0.018$, $P < 0.01$).

4 Discussion

The HDCP is a syndrome mainly characterized by hypertension and proteinuria in the second or third trimester of pregnancy. Although the etiology of HDCP is still unknown,