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Original Research Article

Serum IFI16 level in the prediction of preeclampsia

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Abstract

Purpose: To explore the correlation between serum Interferon Gamma Inducible Protein 16 (IFI16) and preeclampsia (PE), and to study the value of IFI16 in predicting preeclampsia.
Methods: 100 pregnant women with preeclampsia from February 2015 to October 2017 were chosen for experiments, simultaneously, 75 healthy pregnant women who underwent routine pregnancy test into the control group. Total protein (TP), albumin (Alb), blood urea nitrogen (BUN), uric acid (UA), creatinine (SCr), β2-microglobulin (β2-MG), α1-microglobulin (α1-MG), serum cystatin C (Cys C), lactate dehydrogenase (LDH) and other biochemical indicators were detected in the two groups. Serum IFI16, endothelin-1 (ET-1), anti-endothelial cell antibody (AECA) and the level of leptin (LP) were also detected. And then interactions between serum IFI16 and each indicator were analyzed. At last, the receiver operating characteristic (ROC) curve was used to evaluate the effect of serum IFI16 on forecasting preeclampsia.
Results: Levels of IFI16, ET-1, AECA and leptin in the research group were significantly promoted with significant differences (P<0.05). Serum IFI16 levels in PE pregnant women were positively correlated with SBP, DBP, 24h urine protein quantitation, ET-1, AECA, and leptin levels (r= 0.654, 0.435, 0.701, 0.563, 0.574, 0.561, P<0.01), respectively, negatively with Alb. (r= -0.398, P <0.01). The serum IFI16 concentration was 14.47 ng/ml, and the sensitivity and specificity of predicting PE were both 92%.
Conclusion: The elevated serum IFI16 level is associated with the onset of preeclampsia and can be used to predict the occurrence of preeclampsia.

Keywords: Serum IFI16, ET-1, AECA, Leptin, Preeclampsia, Correlation.

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INTRODUCTION

Preeclampsia (PE) seriously affects maternal and child health with elevated blood pressure and proteinuria, causing deaths of maternal and perinatal and systems are headache, vertigo, and vomiting, and so on []). The etiology of the disease has not yet been clarified. It has been reported that the central link in the pathogenesis of P is endothelial cell injury, and the "virulence factor" of placental tissue in PE pregnant women is considered to trigger endothelial damage [2#. The study found that serum interferon-induced protein 16 (IFI16) is mainly present in the cytoplasm or nucleus of epithelial cells, fibroblasts, endothelial cells and hematopoietic

cells [3]. Studies have shown that IFI16 can be intracellularly transferred to the outside of the cell under the stimulation of some factors [4]. And this study is mainly about the correlation between serum IFI16 level and some biochemical indicators and indicators related to endothelial cell injury, and then explore whether serum IFI16 is related to PE.

METHODS

General Information

Pregnant women (100) who presented with preeclampsia from February 2015 to October 2017 in Navy General Hospital, Beijing, China were the experimental group. Healthy pregnant women (75) who underwent routine pregnancy test formed the control group. Inclusion criteria were: subject met the diagnostic criteria for PE [5] and (in 2 groups) more than 20 weeks pregnant; presence of singleton, primipara; absence of hypertension, kidney disease, diabetes, autoimmune diseases before pregnancy; none smokers and signed informed consent form. Exclusion criteria: presence of oncological diseases; liver disease; and history of drug abuse. The study was approved by the Medical Ethics Committee of Navy General Hospital, Beijing, China.

The study group had the following characteristics: mean age: 32.12±4.23 years; the average blood collection gestation week was 34.02±1.56 weeks and the average body mass index: 27.61±5.23. In the control group: the average age was 31.62±4.51 years, average blood collection gestation week was 34.11±1.35 weeks, and the average body mass index was 26.89±6.13. Age, blood collection gestational age and body mass index between the two groups was comparable (P>0.05).

Procedure and related indicators

The age of the two groups of pregnant women, the gestational age of blood collection, systolic blood pressure (SBP), and diastolic blood pressure (DBP) were recorded. The 24h urine samples of the two groups were collected in a sterile container for 24h urine protein detection. Fasting venous blood (4ml) was taken in the morning from all subjects to avoid hemolysis. After standing for 30 minutes under natural conditions, his was centrifuged at 3000 rpm for 10-15 minutes and the serum obtained was stored at -80 °C [6]. Total protein (TP), albumin (Alb), blood urea nitrogen (BUN), creatinine (SCr), uric acid (UA), β2-microglobulin (β2-MG), α1-microglobulin (α1-MG), serum cystatin C (Cys C), lactate dehydrogenase (LDH) and other biochemical indicators were measured using the AU640 automatic biochemical analyzer manufactured (Olympus, China). Serum interferon-induced protein 16 (IFI16), endothelin-1 (ET-1), antiendothelial cell antibodies (AECA) and leptin (LP) were examined through enzyme-linked immunosorbent assay.

Statistical methods

All data were statistically analyzed using SPSS 21.0 statistical software and the Receiver Operating Characteristic (ROC) curve was analyzed using SPSS 22.0 software. Data were expressed in mean ± standard deviation and percentages as appropriate and the group comparison was based on χ^2 test. The Correlation was done using Spearman correlation analysis. The area under the ROC curve (AUC) was used to judge the diagnostic value. At 95% confidence interval, $P < 0.05$ was considered to have statistical significance.

RESULTS

SBP, DBP, 24h urine protein, BUN, UA, SCr, β2-MG, α1-MG, Cys C, LDH in the study group were much higher than those of the control group (P<0.05). TP and Alb were significantly lower (P<0.05, Table 1).

There was significant elevation of the IFI16, ET-1, AECA and leptin levels in the study group compared to the controls (P<0.05, Table 2).

Serum IFI16 levels in PE pregnant women were positively correlated with SBP, DBP, 24h urine protein quantitation, ET-1, AECA, and leptin levels, conversely negatively correlated with Alb, and there was no significant correlation between IFI16 and BUN, UA, SCr, β2-MG, α1-MG, Cys C, and LDH (Table 3).

Results of ROC curve analysis indicated that the sensitivity and specificity (92% and 92%, respectively) of PE were highest when the concentration of IFI16 was 14.47 ng/ml. The area under the ROC line was 0.975. When the concentration of AECA was greater than 57.7 pmol/L, the sensitivity and specificity was 86% and 89.33%, respectively while the ROC underline area was 0.952. When the leptin concentration was greater than 17.05 μg/L, the sensitivity and specificity were 77% and 88%, respectively and the ROC underline area was 0.902 {Figure 1).

Table 1: Comparison of related indicators between the study and the control (mean±sd)

Variables	Study group (n=100)	Control group (n=75)	*t*	*P*
Age (year)	32.12±4.23	31.62±4.51	1.136	0.548
Blood collection gestation week (weeks)	34.02±1.56	34.11±1.35	0.399	0.689
SBP (mmHg)	156.98±11.02	116.21±10.89	24.342	<0.001
DBP (mmHg)	105.14±8.32	75.23±7.98	23.948	<0.001
24h urine protein quantitation (mg)	498.97±14.32	80.25±13.98	193.372	<0.001
TP (g/L)	55.93±6.78	62.87±6.69	6.739	<0.001
Alb (g/L)	29.56±4.18	33.82±4.01	6.788	<0.001
BUN (mmol/L)	4.05±0.81	3.45±0.76	4.978	<0.001
UA (umol/L)	341.45±75.12	251.14±69.87	8.107	<0.001
SCr (umol/L)	54.21±9.15	43.65±7.98	7.974	<0.001
β2-MG (mg/L)	2.35±0.62	1.87±0.51	5.459	<0.001
α1-MG (mg/L)	27.85±6.87	23.45±5.96	4.434	<0.001
Cys C (umol/L)	1.62±0.41	1.02±0.39	9.781	<0.001
LDH (U/L)	269.65±59.82	181.53±51.68	10.213	<0.001

SBP, systolic blood pressure; DSP, diastolic blood pressure; TP, Total protein; Alb, albumin; BUN, blood urea nitrogen; SCr, creatinine; UA, uric acid; β2-MG, β2-microglobulin; α1-MG, α1-microglobulin; Cys C, serum cystatin; LDH, lactate dehydrogenase

Table 2: Serum IFI16, ET-1, AECA, and leptin levels (mean±sd)

Group	n	IFI16 (ng/ml)	ET-1 (ng/L)	AECA (pmol/L)	LP (μg/L)
Study group	100	18.02±2.59	43.65±7.34	47.98±15.49	23.57±5.25
Control group	75	10.21±2.42	10.01±6.98	28.21±15.23	14.23±5.18
t		20.299	30.637	8.415	11.713
P		<0.001	<0.001	<0.001	<0.001

Table 3: Correlation between serum IFI16 levels and various indicators

Variable	*r*	*P*
SBP (mmHg)	0.654	<0.001
DBP (mmHg)	0.435	<0.001
24h urine protein quantitation (mg)	0.701	<0.001
TP (g/L)	0.035	0.829
Alb (g/L)	-0.398	0.007
BUN (mmol/L)	0.256	0.076
UA (umol/L)	0.121	0.425
SCr (umol/L)	0.221	0.151
β2-MG (mg/L)	0.049	0.754
α1-MG (mg/L)	0.219	0.152
Cys C (umol/L)	0.291	0.055
LDH (U/L)	0.154	0.331
ET-1 (ng/L)	0.563	<0.001
AECA (pmol/L)	0.574	<0.001
LP (μg/L)	0.561	<0.001

SBP, systolic blood pressure; DSP, diastolic blood pressure; TP, Total protein; Alb, albumin; BUN, blood urea nitrogen; SCr, creatinine; UA, uric acid; β2-MG, β2-microglobulin; α1-MG, α1-microglobulin; Cys C, serum cystatin; LDH, lactate dehydrogenase; ET-1, endothelin-1 (), AECA, antiendothelial cell antibodies; LP, leptin

DISCUSSION

PE is a disease unique to pregnancy, which can further develop into eclampsia, symptoms such as convulsions and coma, leading to serious maternal and child complications, it had to terminate pregnancy and seriously affect maternal and child health [7]. At present, it is believed that the important link of PE is vascular endothelial cell dysfunction, which is related to genetic factors, insulin resistance, inflammatory reaction of vascular endothelial cells and placental shallow implantation [8-10]. It has been reported that serum IFI16 is mainly present in

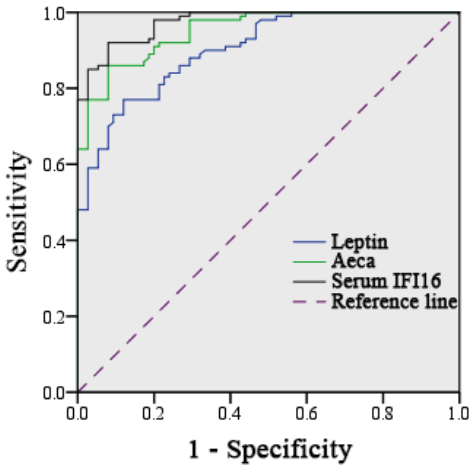

Figure 1: ROC curve of prediction of PE by serum interferon-induced protein 16

endothelial cells and may be associated with the pathogenesis of PE [11]. Present research analyzed the correlation between serum IFI16 and the pathogenesis of PE, and explored the value of serum IFI16 in the diagnosis of PEIFI16, an innate immune receptor for intracellular DNA, is vital in cell growth, apoptosis, angiogenesis, and tumorigenesis [12]. IFI16 is mainly expressed in vascular endothelial cells and can be moved from vascular endothelial cells to extracellular cells under the stimulation of some external factors, resulting in high concentration of IFI16 in serum. Studies have found that high levels of IFI16 in serum may cause damage to vascular endothelial cells [13-15]. ET-1 can be synthesized from vascular endothelial cells and released into the extracellular space when vascular endothelial cells are damaged, which is one of the indicators of vascular endothelial cell damage [16]. AECA has a cytotoxic effect on vascular endothelial cells, participating in inflammatory reactions, and promoting thrombosis, which is one of the causes of PE [17]. Leptin can damage the normal redox homeostasis of the human body, doing damage to the vascular endothelium, and causing paralysis of the body's small arteries and increasing blood pressure [18]. Results of this study revealed distinctly increased serum IFI16, ET-1, AECA, and leptin levels ($P<0.05$), indicating that the elevation of serum IFI16, ET-1, AECA, and leptin levels is related to PE. To further explore the relationship between serum IFI16 and PE, this study analyzed the correlation between serum IFI16 levels and various indicators in PE pregnant women. Moreover, serum IFI16 levels in PE pregnant women were positively correlated with SBP, DBP, 24h urine protein quantitation, ET-1, AECA, and leptin levels, conversely negatively correlated with Alb. Hypertension and proteinuria are the main clinical manifestations of PE, suggesting the damage of vascular endothelial cells to some extent [19]. It is suggested that high levels of IFI16 in serum may damage vascular endothelial cells and participate in the pathogenesis of PE. PE placenta tissue is in a state of high inflammatory response and strong oxidative stress, which can cause increased expression of IFI16 in vascular endothelial cells [20]. Stimulation by external factors further causes elevated levels of IFI16 in the serum, which damages vascular endothelial cells, leading to damage to renal capillaries, resulting in decreased glomerular filtration function and a change in renal parameters. Vascular endothelial injury leads to increased synthesis of ET-1, which is released into the peripheral blood and aggravates vasospasm, which forms a vicious circle and promotes the development of PE. ROC curve analysis indicated that PE were predicted to be the highest in sensitivity (92%) and specificity (92%), when the concentration of IFI16 was 14.47 ng/ml, respectively, the area under the ROC line was 0.975.When the concentration of AECA was greater than 57.7 pmol/L, the sensitivity and specificity was 86% and 89.33%, the ROC underline area was 0.952.When the leptin concentration was greater than 17.05 μg/L, the sensitivity and specificity were 77% and 88%, and the ROC underline area was 0.902.The results indicate that appropriate serum IFI16 levels have the highest sensitivity and specificity in predicting PE occurrence.

CONCLUSION

IFI16 is significantly elevated in PE serum of pregnant women, and has a certain correlation with PE, which may be used as an indicator to predict the occurrence of PE, so as to prevent disease diagnosis and control further development.

DECLARATIONS

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Tong Dong and Wen Jiang are co-first authors.

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