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Change of hs−CRP, sVCAM−1, NT−proBNP levels in patients with pregnancy−induced hypertension after therapy with magnesium sulfate and nifudipine

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ABSTRACT

Objective: To investigate the change of the hs−CRP, sVCAM−1, NT−proBNP levels of the patients with pregnancy−induced hypertension (PIH) syndrome. **Methods:** A total of 200 patients with PIH were divided into mild, moderate and severe group, and 50 healthy pregnancy patients served as the control group. The serum sVCAM−1 levels were detected by enzyme−linked immunosorbent assay, hs−CRP were detected by immunity transmission turbidity, and NT−proBNP levels were determined by the colloidal gold method. Patients were treated with magnesium sulfate and nifudipine and the contrastive analysis was performed before and after treatment. And the pathological changes in placental of PIH patients were detected by hematoxylin−eosin staining at the same time. **Results:** The hs−CRP, sVCAM−1, NT−proBNP levels of patients in the mild, moderate and severe PIH group were significantly higher than that in the control group ($P<0.05$). The hs−CRP, sVCAM−1, NT−proBNP levels in the severe group were significantly higher than the mild group and the moderate group, the difference was statistically significant ($P<0.05$). The hs−CRP, sVCAM−1, NT−proBNP of the moderate group were significantly higher than the mild group ($P<0.05$). There was a positive correlation between hs−CRP, sVCAM−1, NT−proBNP expression levels and the degree of the PIH. The expression of hs−CRP, sVCAM−1, NT−proBNP levels of the moderate and the severe group were significantly decreased ($P<0.05$). The number of placental villi and interstitial blood vessel in the moderate and severe PIH group were significantly less than the control group ($P<0.05$). **Conclusions:** The increased levels of serum hs−CRP, sVCAM−1, NT−proBNP may be involved in the process of vascular endothelial cell injury of the PIH, and the hs−CRP, sVCAM−1, NT−proBNP can be used as the auxiliary index for diagnosis of PIH and determination of PIH severity.

1. Introduction

Pregnancy−induced hypertension (PIH) is common in patients with 20−week pregnancy and of 2−week postpartum. If the blood pressure can not be effectively controlled, it will be a serious threat to the health of maternal and newborn[1]. Although the cause is still not clear, the main pathological changes are the diastole of

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vessel and erosion defects of trophoblast. In recent years, magnesium sulfate and nifudipine is the main therapy, which not only has anticonvulsant effect, but also can change the level of the soluble vascular cell adhesion molecule 1 (sVCAM−1) and high−sensitivity C−reactive protein (hs−CRP) of patients with PIH. But the reports about *N*−terminal pro−brain natriuretic peptide (NT−proBNP) are few. In this study, we studied the effect of magnesium sulfate and nifudipine on expression hs−CRP, sVCAM−1, NT−proBNP in plasma and investigate the therapeutical mechanism of PIH to provide evidence for the clinical practice.

2. Materials and methods

2.1. General information

A total of 200 cases diagnosed as PIH from March 2009 to March 2012 in our hospital were enrolled. The patients were 22–33 years old, (28.5±9.6) years old on average. The average systolic pressure was (155.8±15.7) mmHg, and the average diastolic pressure was (91.5±6.5) mmHg. They were divided into mild, moderate and severe PIH group according to the "Obstetrics and Gynecology" standards. The inclusion criteria were as following: primipara; complete information; pregnant in our hospital. Exclusion criteria were as following: previous history of hypertension, diabetes, chronic kidney disease or cardiovascular disease; other pregnancy complications. A total of 50 cases were selected as normal control group at the same time, and there was proportionality in the age, gestational age and history between both groups (P>0.05).

2.2. Treatment

Routine examination such as blood and urine test, liver and kidney function, ECG, fundus examination, etc. were performed. Sixty mL 25% magnesium sulfate was added to 500 mL 5% glucose solution, then was injected into patients by intravenous drip, and the nifedipine controlled release tablet was given orally 30 mg/time, 1 time/d. For patients with the gestational age <37 weeks, drugs to promote lung ripe were also given.

2.3. Test and collection of specimen

2.3.1. Plasma specimens

Four mL of fasting venous blood were obtained from patients before and after 24 h of the treatment. Samples were immediately placed in 60 uL tube, then was mixed with 100 g/L edetate disodium, centrifuged at 4 ℃. The serum was obtained and then prepared at the −80 ℃ refrigerator. The serum sVCAM−1 concentrations were detected by enzyme−linked immunosorbent assay, the serum hs−CRP concentrations were detected by rate turbidimetric method, and the NT−proBNP concentration were detected by the colloidal gold stripes. hs−CRP, sVCAM−1, NT−proBNP kits were from Boehringer Mannheim company, and all measure operation steps were strictly followed.

2.3.2. Tissue samples

A 1 cm × 1 cm ×1 cm size tissue was obtained from the maternal side of the placenta and then placed in 10% neutral formalin for 24 h, embedded in paraffin, sliced and then was stained by HE staining. The histological changes of the placenta were observed. The 10 non−overlapping (×200) field was selected, the number of blood vessels of villous stroma and of villi was read, then the average value was calculated, respectively.

2.4. Statistical analysisx

The data was analyzed with SPSS13.0 software. Since the hs−CRP, sVCAM−1, NT−proBNP were not normally distributed, we applied Wilcoxon non−parametric test for statistical analysis. Correlation was analyzed with the Speraman correlation analysis, P<0.05 was regarded as statistical significance.

3. Results

3.1. Comparison of hs−CRP, sVCAM−1, NT−proBNP of patients with mild, moderate and severe PIH

hs−CRP, sVCAM−1, NT−proBNP levels of patients in the observation group were significantly higher than the control group (P<0.05), and were increased with the aggravation of PIH. The hs−CRP, sVCAM−1, NT−proBNP levels in the moderate group were significantly higher than in the mild group (P<0.05). The hs−CRP, sVCAM−1, NT−proBNP levels in the severe group were significantly higher than in the mild group and the moderate group (P<0.05) (Table 1).

3.2. Correlation between hs−CRP, sVCAM−1, NT−proBNP and the severity of PIH

There was a positive correlation between the hs−CRP, sVCAM−1, NT−proBNP expression levels and the degree of PIH, the correlation coefficients were r=0.569, P<0.05; r=0.489, P<0.05; r=0.592, P<0.05, respectively.

3.3. Change of hs−CRP, sVCAM−1, NT−proBNP expression levels after treatment in mild, moderate and severe PIH group

After the therapy with magnesium sulfate and nifudipine, the systolic blood pressure and diastolic blood pressure were significantly reduced, the average systolic blood pressure was (133.2±8.3) mmHg, and the average diastolic blood pressure was (82.1±5.2) mmHg. The hs−CRP, sVCAM−1, NT−proBNP levels were significantly decreased after treatment in the moderate group and the severe group (P <0.05). There was no significantly different of the hs−CRP, sVCAM−1 and NT−proBNP level before and after treatment for patients in the mild group (P>0.05) (Table 2).

Table 1

hs−CRP, sVCAM−1, NT−proBNP expression levels of different patients.

Groups	n	sVCAM−1 (mg/mL)	hs−CRP (mg/L)	NT−proBNP (ng/L)
Control group	50	664.1±172.3	2.6±1.2	62.0±12.0
Observation group	200	1 585.5±786.2*	42.7±7.8*	183.5±26.5*
Mild group	62	882.7±201.9*	8.3±2.1*	93.1±16.2*
Moderate group	57	1 654.8±652.6*△	32.1±7.3*△	175.0±23.2*△
Severe group	81	19 874.6±931.5*△▲	56.5±12.7*△▲	263.5±32.0*△▲

Note: * Compared with control group *P*<0.05; △compared with the mild group *P*<0.05; ▲compared with the moderate group *P*<0.05.

Table 2

Changes of hs−CRP, sVCAM−1, NT−proBNP before and after treatment in patients with varying degrees of PIH.

Groups	n	sVCAM−1 (mg/mL)		hs−CRP(mg/L)		NT−proBNP(ng/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Mild	62	882.7±201.9	798.2±152.8	8.3±2.1	7.5±1.2	93.1±16.2	83.7±10.2
Moderate	57	1 654.8±652.6	1 306.2±492.9*	32.1±7.3	16.9±4.7*	175.0±23.2	97.3±15.4*
Severe	81	19 874.6±931.5	1 282.6±622.6*	56.5±12.7	21.3±6.2*	263.5±32.0	105.3± 20.4*

Note: * compared with the level before treatment, *P*<0.05.

3.4. Pathological result

The number of placental villi and the interstitial blood vessel reduced with the severity of PIH, and the number in the moderate and severe group was significantly less than the control group and the mild group (*P*<0.05). The number of the placental villi and the interstitial blood vessel between the mild PIH group and the normal control group had no significant difference (*P*>0.05). The number of the placental villi and the interstitial blood vessel between the moderate group and the severe group had no significant difference (*P*> 0.05) (Table 3).

Table 3

Pathological changes of different levels PIH.

Groups	n	Number of placental villi	Number of interstitial blood vessel
Control group	50	15.5±1.8	41.2±3.4
Mild group	62	13.8±1.7	36.8±3.1
Moderate group	57	11.3±1.4*△	25.9±2.4*△
Severe group	81	10.5±1.3*△	22.8±2.0*△

Note: *Compared with control group *P*<0. 05; △compared with the mild group *P*<0. 05.

4. Discussion

PIH is a common obstetric disorders, accounting for 5%−10% of pregnancy[2–5]. It often occurred at 20 weeks of gestation and two weeks postpartum. The maternal mortality rate accounted for 10%−16% of pregnancy−related deaths, which is a high risk factor for maternal mortality. Patients are often associated with hypertension, proteinuria, edema, convulsions, coma, heart and kidney failure, etc. And other complications may also occur to patients such as pulmonary edema, acute heart failure, acute renal insufficiency herniation, cerebrovascular accident, aspiration pneumonia, placental abruption, fetal distress, fetal death *etc*. Timely and effective treatment must be taken to save the lives of pregnant women. It must be considered more during the course of treatment of PIH,not only to achieve the purpose of treatment of disease, but also to ensure that maternal and child health, and avoid adverse effects on the mother and child of the therapeutic interventions[6–8].

We use HE staining to observe the pathological changes of the placenta of patients with PIH. The number of the placental villi and the interstitial blood vessel reduced with the severity of PIH, and the number in the moderate and severe group was significantly less than the control group and the mild group, which suggested that there will be varying degrees of damage to the body if the blood pressure keep raising without timely control, and there may be life−threatening in severe cases. In this study, we adopted the therapy with magnesium sulfate and nifudipine as a treatment of PIH, which had a good effect. The hs−CRP, sVCAM−1, NT−proBNP levels in serum before and after treatment were detected by ELISA to predict the changes in disease.

hs−CRP are stress proteins synthesized by the liver and released into the blood, compared with CRP levels, it is more sensitive and more easily to be detected as stimulated. In this study, the experimental results show that the hs−CRP levels in the PIH group were significantly higher than in

normal pregnancy group, and increased with the aggravation of PIH. There is a positive correlation between the hs–CRP and the degree of PIH. hs–CRP is a marker of inflammation with high sensitivity and accuracy, which is closely related to tissue damage. The level of hs–CRP directly reflects the degree of inflammatory response, often as a reliable basis for the tissue damage[9–13]. After the therapy with magnesium sulfate and nifudipine, the blood pressure is significantly lower of patients with PIH. And the hs–CRP levels were significantly decreased of patients with PIH in the moderate and severe group, the difference was statistically significant. PIH is a special kind of inflammatory reactions. When the condition became more serious, the liver cells synthesized and secreted a large number of hs–CRP and released into the blood circulation because of the stimulation, and resulting in elevated concentration in the peripheral blood[15–18]. Therefore, hs–CRP can be used as the monitoring indicators of PIH.

sVCAM–1 belongs to the immunoglobulin superfamily which is soluble. It can binding with the T cells, NK cells and monocytes VLA–4 and mediated adhesion and migration of those cells, it also involved in inflammatory and immune processes[19]. The damage of hypoxia and oxidative can enhanced the expression of endothelial cell sVCAM–1, while the increase of endothelial cells SVCAM–1 can lead to the imbalance of vascular endothelial cell function. In this study, we compared the level of sVCAM–1 in mild, moderate and severe PIH group and found low sVCAM–1 expression in patients with mild PIH group, and the expression gradually increased in moderate and severe PIH group. The more severe the disease is, the higher the sVCAM–1 expression is.

In this study, we think that the serum sVCAM–1 expression levels increasing with the severity of the disease, it reflect the sVCAM–1 synthesis is also increasing in vivo of patients with PIH, which suggested that sVCAM–1 possibly involved in the development of PIH by damaging the vascular endothelial cells. After the therapy with magnesium sulfate and nifudipine, the sVCAM–1 expression in the moderate and severe group was significantly reduced. The treatment may reducing the blood vessel injury by controlling the patient's blood pressure, which suggested the therapy with magnesium sulfate and nifudipine to PIH had a good clinical effect.

Brain natriuretic peptide (brain natriurefic peptide, BNP) mainly synthesize and secreted by the ventricular muscle cells, which were expressed both in the ventricles and brain tissue. It had functions such as expand the arteriovenous, inhibit sympathetic activity and antagonize the renin–angiotensin–aldosterone system and some other

effects[20]. The plasma BNP expression levels did not change significantly at different stages of PIH, so it can not be used to determine the severity of PIH. NT–proBNP is the BNP precursor cleaved into the BNP N–terminal fragment. Studies have confirmed that NT–proBNP was with longer half–life and higher serum concentrations, and it is more easily to be detected[21–24]. It can be used as an indicator to assess the cardiac function of patients with PIH. The study of Chen[25] suggest that NT–proBNP had the high expression in PIH, so the NT–proBNP test can help to determine the severity of PIH. Our experimental results showed that the NT–proBNP are kept in a low and stable level in the normal control group, but the NT–proBNP levels in the patient group were significantly higher than in the control group. And the NT–proBNP expression level gradually increased with the aggravation of PIH. And the NT–proBNP level in the severe group was higher than that in the mild group and the moderate group, which suggested that the heart of healthy pregnant women can adapt to the increased load capacity during pregnancy, while the heart of PIH patient may have some disorder to adjust the change of heart volume load.

In summary, the hs–CRP, sVCAM–1 and NT–proBNP levels in the PIH group were significantly higher and increased with the aggravation of PIH, which suggested the hs–CRP, sVCAM–1, NT–proBNP levels can help to monitor the development of PIH. Early detection and early treatment can ensure the health of mother and child.

Conflict of interest statement

We declare that we have no conflict of interest.

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