

Correlation Study of Color Doppler Examination of Deep Veins of Both Lower Extremities Combined with Fibrinolysis System in Hypertension during Pregnancy

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Abstract

Objective: To investigate the correlation between deep static color Doppler ultrasound of both lower extremities combined with fibrinolytic system detection in pregnancy-induced hypertension. **Methods:** A total of 70 normal pregnant women, 70 pregnant women with hypertension during pregnancy, and 50 healthy non-pregnant women in the same period were selected as the research objects. The deep veins of both lower limbs were examined by Rili Erlangshen's color Doppler ultrasound diagnostic instrument (CDU), and the fibrinolysis system was tested by enzyme-linked immunosorbent assay (ELISA) method and automatic hemagglutination analyzer. **Results:** Compared with the non-pregnant group, the inner diameters of the left/right femoral vein (CFV) and popliteal vein (POV) in the normal pregnancy group and the pregnancy-induced hypertension group were significantly widened, and the peak blood flow spectrum was significantly reduced. The difference was statistically significant ($P < 0.01$); FIB, PLG, t-PA, PAI, D-Dimer were significantly increased, the difference was statistically significant ($P < 0.01$); Compared with the normal pregnancy group, the inner diameter of the left/right femoral vein (CFV) in the hypertensive pregnancy group was significantly wider than that in the normal pregnancy group, and the peak value of the left/right POV blood flow spectrum was significantly lower than that in the normal pregnancy group, the difference was statistically significant ($P < 0.01$), while the left/right popliteal vein (POV) inner diameter, left/right CFV blood flow peak value did not change significantly from the normal pregnancy group,

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and the difference was not statistically significant ($P > 0.05$); FIB, PLG, PAI, D-Dimer of the hypertensive disease group during pregnancy significantly increased, the difference was statistically significant ($P < 0.01$), while t-PA was not statistically significant ($P > 0.05$). **Conclusion:** Normal pregnant women have a hypercoagulable state compared with healthy non-pregnant women, and pregnant women with hypertension during pregnancy are more likely to be in a pre-thrombotic state than pregnant women with normal pregnancy. Deep vein CDU examination of both lower extremities combined with blood fibrinolysis monitoring is of great value in the prevention and treatment of hypertension during pregnancy.

Keywords

Hypertension during Pregnancy, Prothrombotic State, Color Doppler Ultrasound, Fibrinolysis Index

1. Introduction

Hypertension during pregnancy is often in an abnormal hypercoagulable state. The body is often accompanied by hypoxia and injury of small blood vessel endothelial cells, as well as abnormalities in functions such as coagulation, fibrinolysis, and platelets. These abnormal pathological changes lead to the occurrence of prothrombotic state (PTS) in hypertensive disorders complicating pregnancy [1] [2]. The pre-thrombotic state of hypertension during pregnancy will also significantly increase the mortality of perinatal woman and child, which will have a significant negative impact on the survival and life of the majority of women and babies. With the comprehensive opening of China's second child policy, the number of pregnant women has increased significantly, and hypertension during pregnancy has increasingly attracted the attention of pregnant women [3] [4]. This study intends to explore the correlation between the results of deep venous color Doppler ultrasound examination combined with fibrinolysis system and hypertension in pregnancy. The results are reported below.

2. Information and Methods

2.1. Research Objects and Groups

2.1.1. Grouping Standards and Requirements

The diagnostic criteria for hypertension in pregnancy were based on the 8th edition of "Obstetrics and Gynecology" of the People's Medical Publishing House [5]. The pregnant group selected pregnant women with normal heart, liver, kidney, brain, blood vessels and coagulation function before pregnancy; In the non-pregnancy group, women with normal functions of heart, liver, kidney, brain and blood coagulation were selected, and they had not used procoagulant drugs such as contraceptives for half a year. All participants did not take drugs affecting heart, liver, kidney, brain function and coagulation function 1 week

before venous blood drawing.

2.1.2. Research Objects and Groups

Retrospective analysis of 70 cases of normal pregnant women hospitalized in obstetrics and gynecology from June 2018 to December 2019 (normal pregnancy group), 70 cases of pregnant women with hypertension during pregnancy (pregnancy-induced hypertension group) and 50 cases of healthy non-pregnant women (normal non-pregnancy group), including 19 cases of preeclampsia (mild), 26 cases of preeclampsia (severe) and 25 cases of eclampsia in the hypertensive disease group of pregnancy, aged 22 to 39 years, average 28 years old, the gestational week is 32 - 42 weeks, average 36 weeks; the normal pregnancy group is 20 - 38 years old, average 27 years old, the gestational week is 32 - 41 weeks, average 37 weeks; 50 normal non-pregnant women, age 21 - 38 years old, average 27 years old.

2.2. Instruments and Testing Methods

2.2.1. Apparatus and Method for Deep Vein Examination of Lower Extremities

Using the Rili series (Erlangshen) color Doppler ultrasound diagnostic apparatus to perform deep vein examination of the lower extremities of the three groups of candidates, detect the inner diameter of the left and right femoral veins, popliteal veins and peak blood flow spectrum and other indicators to observe the presence of thrombosis form. Calibration of wake-up equipment is before inspection.

2.2.2. Apparatus and Method for Detecting Blood Fibrinolysis Index

t-PA is measured by American Pacific company Eusa kit. The operation is determined according to the instructions. The rest of the items are tested by French STAGO-COMPACT hemagglutination instrument and the STAGO original kit is provided by Nanning Henghe Company; FIB uses steel ball coagulation method, D-Dimer determination using immunoturbidimetric method, PLG, PAI using chromogenic substrate method, t-PA determination using the quantitative method of enzyme-linked immunosorbent double antibody sandwich method (ELISA). All reagents are used within the validity period, and relevant indoor quality control is required before specimen testing.

2.2.3. Blood Specimen Collection and Processing

The venous blood of three groups of subjects was drawn into a vacuum anticoagulation tube containing 3.2% sodium citrate, anticoagulated according to the ratio of 9:1, and the plasma was centrifuged at 2700g for 10 min at room temperature to be tested.

2.2.4. Statistical Processing

SPSS19.0 statistical software was used for statistical analysis. The measurement data used two independent samples of t test, and the count data used χ^2 test or Fisher exact probability method. $P < 0.05$ was considered statistically significant.

3. Result

3.1. Compared with Non-Pregnancy Group

FIB, PLG, t-PA, PAI, D-Dimer in normal pregnancy group and pregnancy-induced hypertension group were significantly increased, the difference was statistically significant ($P < 0.01$); compared with normal pregnancy group, FIB, PLG, PAI, D-Dimer in pregnancy-induced hypertension group were significantly increased, the difference was statistically significant ($P < 0.01$), t-PA was not statistically significant ($P > 0.05$) (see **Table 1**, **Table 2**).

3.2. Comparison of the Results of Deep Vein Examination of Lower Extremities

The inner diameters of the left and right CFV and POV in the normal pregnancy group and the pregnancy-induced hypertension group were significantly larger than those in the non-pregnancy group, and the peak blood flow spectrum was significantly reduced, the difference was statistically significant ($P < 0.01$).

The diameter of the left/right femoral vein (CFV) in the hypertensive disorder pregnancy group was significantly larger than that in the normal pregnancy group, and the peak value of the left/right POV blood flow spectrum was significantly lower than that in the normal pregnancy group ($P < 0.01$). However, the inner diameter of the left/right popliteal vein (POV) and the peak value of the left/right CFV blood flow were not significantly changed from the normal pregnancy group, and the difference was not statistically significant ($P > 0.05$) (see **Table 3**, **Table 4**).

Table 1. Test results of three groups of fibrinolytic system indexes ($\bar{x} \pm s$).

Groups	Number of cases	FIB (g/L)	PLG (U/ml)	t-PA (U/ml)	PAI (U/ml)	D-Dimer (ng/L)
Non-pregnant group	50	2.26 ± 0.18	95.36 ± 2.94	1.30 ± 0.06	3.13 ± 0.23	0.22 ± 0.02
Normal pregnancy group	70	5.04 ± 0.18*	119.71 ± 3.41*	4.30 ± 0.12*	6.54 ± 0.23*	0.67 ± 0.03*
Pregnancy-induced hypertension group	70	6.47 ± 0.41**	156.63 ± 3.28**	4.34 ± 0.13*	10.70 ± 1.04**	1.44 ± 0.10**

Note: 1) The pregnancy-induced hypertension group is the abbreviation of pregnancy-induced hypertension disease group; 2) Compared with non-pregnancy group, * $P < 0.01$; Compared with normal pregnancy group, ** $P < 0.01$.

Table 2. T value and P value of three groups of fibrinolytic system indexes.

T value/P value	FIB (g/L)	PLG (U/ml)	t-PA (U/ml)	PAI (U/ml)	D-Dimer (ng/L)
T1	83.41	40.8	151.9	80.07	92.36
T2	68.01	105.27	153.92	50.54	84.96
T3	26.72	65.28	1.89	32.68	61.71
P1	<0.001	<0.001	<0.001	<0.001	<0.001
P2	<0.001	<0.001	<0.001	<0.001	<0.001
P3	<0.001	<0.001	>0.05	<0.001	<0.001

Note: The t and P values of normal pregnancy group and non-pregnancy group were T1 and P1. The t and P values of the hypertensive disease group during pregnancy compared with the non-pregnant group were T2 and P2. The t and P values of the hypertensive disease group during pregnancy compared with the normal pregnancy group were T3 and P3.

Table 3. Three groups of double lower limb CFV, POV inner diameter and blood flow spectrum peaking ($\bar{x} \pm s$).

Inner diameter of both lower limbs/Peak blood flow spectrum	Left/Right	pregnancy-induced hypertension group (70 cases)	normal pregnancy group (70 cases)	non-pregnancy group (50 cases)
CFV inner diameter (cm)	Left	1.37 ± 0.09**	1.09 ± 0.10*	0.70 ± 0.02
	Right	1.34 ± 0.11**	1.09 ± 0.09*	0.70 ± 0.03
CFV spectral peaks (cm/s)	Left	7.94 ± 1.83*	8.55 ± 2.08*	17.11 ± 1.93
	Right	7.97 ± 1.70*	8.60 ± 2.08*	17.39 ± 1.77
POV inner diameter (cm)	Left	0.69 ± 0.05*	0.68 ± 0.03*	0.48 ± 0.02
	Right	0.69 ± 0.04*	0.68 ± 0.02*	0.48 ± 0.03
POV spectral peaks (cm/s)	Left	5.04 ± 0.79**	7.09 ± 1.28*	12.45 ± 1.97
	Right	5.04 ± 0.75**	6.93 ± 1.33*	12.11 ± 1.99

Note: Compared with non-pregnant group *P < 0.01; compared with normal pregnant group **P < 0.01.

Table 4. Comparison of T value and P value of CFV inner diameter, POV inner diameter and blood flow spectrum peak value among the three groups.

T value/P value	CFV Inner diameter		CFV Spectral peak		POV Inner diameter		POV Spectral peak	
	Left	Right	Left	Right	Left	Right	Left	Right
T1	28.81	29.31	22.6	23.35	133.63	30.6	18.03	17.09
T2	49.12	39.64	26.42	30.94	29.43	31.34	28.46	27.17
T3	16.99	14.14	1.84	1.96	1.44	1.87	11.37	10.36
P1	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
P2	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
P3	<0.001	<0.001	>0.05	>0.05	>0.05	>0.05	<0.001	<0.001

Note: 1) The comparison of t value and p value of normal pregnancy group and non-pregnancy group are T1 and P1; The comparison of t value and p value of pregnancy hypertensive disease group and non-pregnancy group are T2 and P2; The comparison of t value and p value of pregnancy hypertensive disease group and normal pregnancy group are T3 and P3.

4. Discussion

Hypertensive disorder complicating pregnancy is a common complication in modern perinatal medicine and is one of the main factors of maternal and infant death. Hypertensive disorders complicating pregnancy are often accompanied by coagulation, fibrinolysis, platelet and vascular abnormalities. These changes are closely related to the occurrence and development of prothrombotic state (PTS) in hypertensive disorders complicating pregnancy [1]-[6].

Recent years, some scholars have proposed the laboratory index reflecting the activity of fibrinolytic system as the PTS specific experimental diagnostic index, while the detection value of deep vein diameter of both lower limbs and the change of its peak value of blood flow spectrum, hemodynamic index and blood screening index are basically consistent, which can be used as a reference for the diagnosis of PTS [7] [8] [9] [10].

FIB is one of the important factors of thrombosis, and the FIB amount in blood is positively correlated with the hypercoagulability of the body; the higher the amount, the easier it is to form a thrombus. Plasminogen only plays an active role when it is converted to plasmin, and tissue plasminogen activator (t-PA) is the key enzyme for the conversion of plasminogen to plasmin, which can cleave fibrin. It protolyzes and hydrolyzes a variety of activated coagulation factors, so when the amount of t-PA increases, the amount of plasmin also increases, and eventually the body's fibrinolytic activity is enhanced; while the role of PAI is opposite, PAI and t-PA form a complex which causes t-PA to lose activity [11] [12]. The results of this study showed that the levels of FIB and PLG in the normal pregnancy group and the pregnancy-induced hypertension disease group were significantly higher than those in the non-pregnancy group, and the pregnancy-induced hypertension disease group was significantly higher than the normal pregnancy group, and the differences between the groups were statistically significant, suggesting that normal pregnant women have increased FIB formation in the blood, the body is in a physiological hypercoagulable state, and patients with hypertension during pregnancy are in a pathological hypercoagulable state. The levels of t-PA and PAI in the normal pregnancy group and the pregnancy-induced hypertension disease group were higher than those in the non-pregnancy group. Because the increase in t-PA in the normal pregnancy group was greater than the increase in PAI, the fibrinolytic activity increased and the body was in high-level dynamic balance between coagulation and fibrinolysis. The levels of t-PA and PAI in normal pregnancy group and pregnancy-induced hypertension group were higher than those in non-pregnancy group; the increase of t-PA was higher than PAI in normal pregnancy group, which resulted in the increase of fibrinolytic activity, and the body was in high-level dynamic balance between coagulation and fibrinolysis. There was no significant difference in t-PA between normal pregnancy group and pregnancy-induced hypertension disease group, while PAI was further increased in patients with pregnancy-induced hypertension disease, and the increase of PAI exceeded the increase of t-PA, which led to the high-level dynamic balance of coagulation and fibrinolysis being broken again, resulting in blood hypercoagulability of the body further aggravated. The specific degradation product of fibrin is D-Dimer; the increased level of D-Dimer indicates that the body's fibrinolysis system is activated and reflects the secondary fibrinolysis enhancement; it can sensitively reflect the state of coagulation and fibrinolysis in the body.

The results of this study showed that the plasma D-Dimer levels of pregnant women in normal pregnancy were higher than those in healthy non-pregnant women and the difference was statistically significant, indicating that pregnant women were in a physiological hypercoagulable state, with increased fibrinolytic activity and increased fibrin degradation products (D-Dimer). The results of this study also showed that the level of D-Dimer in patients with hypertension during pregnancy was significantly higher than that in normal pregnant women, which was related to the ischemia, hypoxia, severe damage of vascular endothe-

lial cell structure and villon necrosis of placental capillaries in patients with hypertensive disorder complicating pregnancy; these changes prompted the release of a large number of tissue thromboplastin, resulting in the formation of intravascular microthrombus; at the same time, secondary fibrinolysis was also activated, which led to a significant increase in D-Dimer level. When the level of D-Dimer in patients with hypertension during pregnancy is significantly increased, it suggests microthrombosis and there may be asymptomatic chronic DIC [13] [14].

The results of ultrasonic examination showed that the deep diameter of both lower limbs was significantly larger than that of non-pregnant pregnant women, and the peak value of blood flow spectrum was significantly smaller than that of non-pregnant pregnant women; it suggested that normal pregnant women's lower limb vein diameter widened, vein velocity slowed down, and thrombosis was easy to occur; the results of deep color Doppler ultrasound in both lower extremities were basically consistent with the results of blood fibrinolysis index, indicating that pregnant women were more likely to be in the pre-thrombotic state than healthy non-pregnant women. The FIB, PLG, PAI, D-Dimers of hypertensive disorder complicating pregnancy were significantly higher than those of normal pregnant women, while the venous diameter of most lower limbs was significantly wider than that of normal pregnant women, and the peak value of some blood flow spectrum was significantly lower, indicating that patients with hypertensive disorder complicating pregnancy were more likely to be in PTS than normal pregnant women.

5. Conclusion

The examination results of this study showed that the detection value of deep vein diameter of lower extremities and the peak value of deep vein blood flow spectrum of lower extremities were basically consistent with the changes of fibrinolysis system detection index, which was consistent with the relevant research results [8]. However, the vascular ultrasound imaging diagnosis method is expensive and the imaging false negative causes the delayed diagnosis and other problems. At present, it is generally believed that fibrinolytic system detection index can be used as a sensitive index for screening thromboembolic diseases during pregnancy and postpartum. Under the condition of economic permission, the author thinks that deep vein examination of lower extremity combined with fibrinolytic system index detection will be more helpful to improve the diagnosis rate of prothrombotic state of hypertensive disorder complicating pregnancy, so as to detect early and intervene early, thus reducing the mortality rate of perinatal pregnant women and perinatal children.

Limitations of the Study

This study mainly observes a limited number of cases, which has certain limitations, and the number of cases can be expanded to obtain more powerful evi-

dence. In addition, the follow-up time of this study is relatively long, and the patient's compliance with follow-up has a certain complexity, which has a certain impact on the results.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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