

# Clinical study on the influence of phloroglucinol on plasma angiotensin II and D-Dimer index in patients with severe pregnancy-induced hypertension

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**Abstract:** To observe the effect of phloroglucinol on plasma angiotensin II and D-dimer index when it was applied to patients with severe pregnancy-induced hypertension. 212 cases of severe pregnancy-induced hypertension patients diagnosed clinically were selected to be randomly divided into the research group and the control group. The research groups were given phloroglucinol, while the control group were given magnesium sulfate. The plasma angiotensin II and D-dimer index in patients were detected before treatment and after 7 days respectively with statistical analysis of results. The difference after treatment was statistically significant ( $P < 0.05$ ). Compared within the same group, the difference of each index before and after treatment in the research group was statistically significant ( $P < 0.05$ ), while the control group was not statistically significant ( $P > 0.05$ ). It showed that the research group could reduce the plasma D-dimer and angiotensin II index in severe pregnancy-induced hypertension patients, and its effect was significantly better than the control group. according to the plasma D-dimer and angiotensin II index changes in patients, it indicated that it was effective of phloroglucinol treatment for patients with pregnancy-induced hypertension disease and superior to the western medicine conventional treatment, worth clinical promotion.

**Keywords:** Phloroglucinol, pregnancy-induced hypertension disease, D-dimer, Angiotensin II, effect,

## INTRODUCTION

Severe pregnancy-induced hypertension disease is a severe obstetric complication that harms to the mother and child health. Its pathological basis is that there exist Hypercoagulable factors in the blood of puerpera, leading to the small-vessel spasm in womb. Especially the patients with severe pregnancy induced hypertension developing to the pre-eclampsia are risky in having the HELLP syndrome (pregnancy-induced hypertension combined with hemolysis, rise of liver enzymes, thrombocytopenia), threatening to the life of mother and child (Li and Lv, 2004). It was thought in research that vascular endothelial injury is the pathological basis of patients with pregnancy-induced hypertension disease combined with HELLP syndrome. Vascular endothelial injury cause protein fiber deposition, vasospasm and platelet activation, closely relating to the patients' blood plasma D-dimer and angiotensin  $\alpha$  index (Committee for Revision of the Guidelines for Prevention and Treatment of Hypertension in China, 2010; Feng, 2006). When small-vessel spasm in womb occurs in severe pregnancy-induced hypertension patients, D-dimer index often increases. And vascular endothelial injury can activate Renin- Angiotensin -Aldosterone system, leading to the rise of angiotensin  $\alpha$  index. And the continuous rise of

angiotensin  $\alpha$  index can cause the irreversible changes in heart structure (Dong *et al.*, 2010). Angiotensin  $\alpha$  can increase sodium absorption of the renal proximal tubules and stimulate the juxtaglomerular cells secreting renin, forming a vicious cycle of occurring factors in pregnancy-induced hypertension patients. Phloroglucinol is spasmolytics used to fetus protection in obstetrics, which is compatible with muscle spasm without affecting the normal smooth muscle (Sun, 2013). Therefore, phloroglucinol can remove abnormal uterine contractions, without the occurring of adverse reactions of anticholinergic activities. Since phloroglucinol has already be proven no teratogenic, mutagenic and carcinogenic, it is used in severe pregnancy-induced hypertension patients with a high safety coefficient. So it is clinically significant in studying the influence of phloroglucinol on D-dimer and angiotensin  $\alpha$  index.

## MATERIAL AND METHODS

### General information

212 patients, diagnosed with severe pregnancy-induced hypertension disease in clinic from January 2011 to November 2013 in Maternal and Child Health Care Hospital of Zhengzhou, were selected and divided randomly into the research group and the control group with 106 cases each. And the research group with an age ranging from 25 years to 42 years (an average age of  $31 \pm$

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7 years), gestational age of 31-35 weeks (an average age of  $31.26 \pm 6.77$  weeks) and the course of disease of 2-3 months; while the control group with an age ranging from 26 years to 42 years (an average age of  $32 \pm 7$  years), gestational age of 31-36 weeks (an average age of  $31.86 \pm 6.79$  weeks) and the course of disease of 2-3 months. The difference of illness state, education level and life style and so on in the two groups is not statistically significant ( $P > 0.05$ ), comparably.

Case standard (Wu and Lei, 2009) conforming to the diagnosis standard of severe pregnancy-induced hypertension: blood pressure  $\geq 160/110$ mmHg (1mm Hg = 0.133 kPa), lower limb ( $\geq + +$ ) and edema urine protein ( $\geq + +$ ).

Case standard not conforming: patients had already occurred pre-eclampsia/eclampsia, or with severe complications of secondary hypertension, diabetes, gout, heart failure, renal failure, bronchial asthma and chronic obstructive pulmonary disease etc.

Methods: the control group were given 60mL 25% magnesium sulphate, intravenous infusion (6-8h) of 500ml 5% glucose solution, 7 days in continue. The drug indications in each group were both stomachache (whether uterine contraction or not).

The detection of plasma D-dimer and Angiotensin  $\alpha$ : Fasting blood drawing before and after treatment were detected once respectively. The detection of plasma D-dimer adopted Latex-enhanced Immunoturbidimetry method (full-automatic biochemical analyzer of American Beckman LX20, reagent of Beijing Lideman Biochemical Co., Ltd.). The detection of Angiotensin  $\alpha$ : adopting Immunoradiometric method, with a strict operation according to the reagent specification (the reagent kit of Angiotensin  $\alpha$  was produced in Beijing North Biotechnology Institute, Lot No.20111023).

## STATISTICAL ANALYSIS

All data was recorded as (mean  $\pm$  standard deviation). Using Levene's test to test homogeneity of variance test data, and homogeneity of variance among groups is used One-Way ANOVA method. If there was a significant difference among groups, we use LSD test for pairwise comparison;  $P < 0.05$  showed that the data is statistically significant.

## RESULTS

### *Changes of D - dimer and Angiotensin II index in patients*

There was no statistical significance in the comparison difference of two groups before treatment ( $P > 0.05$ ), while

the difference after treatment was statistically significant ( $P < 0.05$ ). Compared within the same group, the difference of each group before and after treatment in the research group was statistically significant ( $P < 0.05$ ), while the control group was not statistically significant ( $P > 0.05$ ) (table 1).

## DISCUSSION

Once pregnancy-induced hypertension disease developed to pre-eclampsia, the occurrence rate of premature labor, placental abruption and fetal death would increase greatly (Zhen *et al.*, 2009). The serious would develop HELLP syndrome threatening to mother and child life. Therefore, it played a positive role in the early treatment for spasmodic and those complications. The pathological basis of pregnancy-induced hypertension disease was small-vessel spasm in uterus. And the higher of the blood pressure, the wider covered the vascular disease. The occurrence of HELLP syndrome often accompany with disseminated intravascular coagulation (DIC) (Le *et al.*, 2008). There might exist factors causing vasospasm in pregnancy-induced hypertension patients. With the continuous activation of these factors, the micro vascular endothelium would be damaged, and gradually affecting the small-vessel endothelium. The injure of vascular endothelium triggered the activation of blood coagulation system, leading to the rise of the D-dimer index (Lin and He, 2010), as well as the renin-angiotensin-aldosterone system leading to the rise of the Angiotensin  $\alpha$  (Yang and Zhai, 2007; Wei, Fan and Xie, 2011). And the keep rise of these index indicated that there continuously exist factors causing vasospasm in pregnancy-induced hypertension patients. If this could not be controlled effectively, the erythrocytes passing through micro vascular would be broken, and the number of the broken erythrocytes rise would cause hypoxia of the endothelium, which in turn aggravated the injure of vascular endothelium. The broken erythrocytes would release vasogenic factors, directly activating blood coagulation system, indicating the quick increase of the D-dimer index. And the erythrocytes breaking would also vasomotion factors, activating renin-angiotensin-aldosterone system. With those function, the bilirubin in blood would increase sharply, that would damage liver function. And the increase of hepatic enzymogram index would damage hemopoietic system, causing hemolysis and thrombocyte damage, developing to HELLP syndrome.

Phloroglucinol, also known as 1, 3, 5-trihydroxy benzene, is a kind of flavonoids, used in obstetric fetus protection treatment with a good effect and safety. Since it only acted on the smooth muscle, without anticholinergic function, so that it less affect cardiovascular and other vital organs. With the increase of its application, antioxidant function was found, inhabiting xanthine from oxidizing enzyme and decreasing the active oxygen level,

**Table 1:** Index changes of plasma D-dimer and Angiotensin  $\alpha$  in the two groups

Grouping	D-dimer ( $\mu\text{g/L}$ )	Angiotensin $\alpha$ (ng/L)	P value
Research group			
Before treatment	519 $\pm$ 62	535 $\pm$ 9	> 0.05
After treatment	356 $\pm$ 54*	323 $\pm$ 6*	< 0.05
Control group			
Before treatment	534 $\pm$ 64	536 $\pm$ 9	> 0.05
After treatment	513 $\pm$ 61*	534 $\pm$ 8*	< 0.05

which indicated that it could inhibit acute inflammation and the stress reaction of cellular damage (Wen, 2013; Li and Peng, 2013). The load increase of circulating pressure in pregnancy-induced hypertension disease, and Phloroglucinol could reverse the corresponding index, playing an anti-vascular-damage role. The animal experiment showed that Phloroglucinol could shrink the diameter of heart failure cells, remitting the secondary injury of heart failure (Li *et al.*, 2011). Therefore it could lower the blood pressure of pregnancy-induced hypertension patients. Moreover, it was often used for spasmolysis treatment in clinic and it also had antioxidant and myocardial protection function, protective effect on myocardial ischemia-reperfusion injury, at the same time it also could inhibit myeloperoxidase activity as well as inflammatory cells infiltration. The functions of Phloroglucinol mentioned above had protective effect on the preventing hypercoagulation state and the vascular endothelial damage cause by the activity of renin-angiotensin aldosterone system, by protecting cardiac muscle, relieving uterine small vasospasm, interrupting the link of activating blood hypercoagulability and renin-angiotensin aldosterone system, thus acting as a prevention role before pregnancy-induced hypertension developing to preeclampsia.

Magnesium sulfate is the traditional medicine used for spasmolysis and antihypertensive. However when it reaches to a certain dose, it can be at risk of respiratory depression (Liu and Huang, 2011), while there is no maximum limits in phloroglucinol. Although phloroglucinol is not effective on cardiovascular system but safe, it can not used as a routine treatment for depressurization. However it has irreplaceable advantages to be used as spasmolysis drug to treat pregnancy-induced hypertension than any other. It removed the uterine smooth muscle spasm, at the same time alleviated the state of placenta supply, fetal, small-vessel spasm in uterus, protected the normal metabolism of uterus and placenta and fetal blood. Therefore it had protective effect on pregnant women and fetus. This study confirmed that there was no statistical significance in the comparison difference of two groups before treatment ( $P>0.05$ ), while the difference after treatment was statistically significant ( $P<0.05$ ). Compared within the same group, the difference of each index before and after treatment in the research

group was statistically significant ( $P<0.05$ ), while the control group was not statistically significant ( $P>0.05$ ).

## CONCLUSION

It indicated that the research could lower plasma D-dimer and angiotensin  $\alpha$  index in pregnancy-induced hypertension patients and its curative effect is superior to the control group. It explained that phloroglucinol treatment was effective in patients with pregnancy-induced hypertension disease and was more reliable than conventional treatment. The research also suggested that it was clinically significant in timely monitoring plasma D-dimer and angiotensin  $\alpha$  index in the patients with severe pregnancy-induced hypertension to judge their prognosis and take protective measures as early as possible.

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