ORIGINAL ARTICLE

Effect of Magnesium Sulfate Combined with Phentolamine and Nifedipine for Gestational Hypertension and Serum Levels of LIF and Apelin

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ABSTRACT

Objective: To investigate the effect of magnesium sulfate combined with phentolamine and nifedipine for the treatment of gestational hypertension and on the levels of serum LIF and Apelin.

Study Design: An experimental study.

Place and Duration of Study: Obstetrics and Gynecology Clinics, The Affiliated Hospital North China University of Science and Technology, China, from September 2016 to February 2018.

Methodology: One hundred and sixty patients with gestational hypertension were randomly divided into a control group and an observation group, 80 patients in each group. Control group was given magnesium sulfate alone, while observation group was added with phentolamine and nifedipine on the basis of the treatment in control group. Curative effects, pregnancy outcomes, and levels of serum LIF and Apelin were compared.

Results: The total effective rate of treatment in the observation group was higher than that in the control group ($p=0.005$). After treatment, level of serum LIF in the observation group was higher than that in the control group ($p<0.001$), and level of serum Apelin in the observation group was lower than that in the control group ($p<0.001$). Incidence of premature birth, cesarean section and neonatal asphyxia in the observation group were all lower than those in the control group ($p=0.005$, $p<0.001$ and $p=0.005$, respectively), while there was no significant difference in the incidence of neonatal death between the two groups ($p=0.316$).

Conclusion: Magnesium sulfate combined with phentolamine and nifedipine has a better therapeutic effect on gestational hypertension, which can effectively regulate the levels of serum LIF and Apelin and improve pregnancy outcomes.

Key Words: *Gestational hypertension, Magnesium sulfate, Phentolamine, Nifedipine, LIF, Apelin.*

INTRODUCTION

Gestational hypertension is a common complication of pregnancy. It can cause miscarriage, placental abruption, premature birth and massive bleeding in pregnant women, which will pose a serious threat to the health and safety of pregnant women and fetuses.[1,2] The etiology and pathogenesis of gestational hypertension are not fully understood, and placental or trophoblastic ischemia and hypoxia is one of the many etiological theories. The theory holds that the declined trophoblastic infiltration during pregnancy in the placental formation stage in patients with gestational hypertension leads to vascular remodeling disorder, reduced placental perfusion, ischemia and hypoxia of trophoblasts, the release of large amounts of cytokines and eventually the occurrence of gestational hypertension.[3]

Studies have shown that leukemia inhibitory factor (LIF) is a multifunctional cytokine distributed in the uterine decidua and placental cells, which can affect the infiltration ability of trophoblast cells, and is related to the occurrence and development of gestational hypertension and perinatal prognosis to some extent.[4] Apelin is a small molecule active peptide newly discovered in recent years. It is collectively expressed in placental tissues of placental vascular endothelial cells, syncytiotrophoblasts, cytotrophoblasts, and villous interstitium.[5] Related studies have shown that Apelin has special physiological and pathological implications in the homeostasis of the placental vascular system during pregnancy.[6]

The basic purpose of treatment for gestational hypertension is to effectively prevent and control eclampsia, thereby reducing its perinatal prevalence and mortality and improving the prognosis of mother and child.[7,8] However, conventional antihypertensive and antispasmodic drugs have unsatisfactory results with different degrees of adverse reactions. Therefore, exploring safe and effective therapeutic drugs for gestational hypertension is of great value to improve the safety and health of pregnant women.

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Table I: Comparison of the clinical efficacy between the two groups.

Group	n	Significant	Effective	Improved	Invalid	Total effective	p-value
Control group	80	30 (37.50%)	28 (35.00%)	8 (10.00%)	14 (17.50%)	66 (82.50%)	0.005
Observation group	80	45 (56.25%)	26 (32.50%)	6 (7.50%)	3 (3.75%)	77 (96.25%)	

The purpose of this study was to investigate the curative effect of magnesium sulfate combined with phentolamine and nifedipine in the treatment of gestational hypertension and analyze its effect on the levels of serum LIF and Apelin, in order to provide reference for clinical treatment of gestational hypertension.

METHODOLOGY

This study was conducted at Obstetrics and Gynecology Clinics, The Affiliated Hospital North China University of Science and Technology, China, from September 2016 to February 2018. A total of 160 patients with gestational hypertension were selected as subjects. Inclusion criteria were patients diagnosed as gestational hypertension by blood pressure test, in combination with their clinical manifestations and signs, patients with treatment indications for magnesium sulfate combined with phentolamine and nifedipine; and patients and their families who understood the research content and treatment risk and were willing to cooperate. Exclusion criteria were patients with essential hypertension and a history of hypertension before pregnancy; and patients with severe comorbid conditions such as function abnormalities in liver, kidney, heart and lung, or malignant tumors. The patients were randomly divided into a control group and an observation group, with 80 patients in each group.

Both groups received routine symptomatic and supportive treatment, including oxygen uptake, sedation, and diuresis. The control group was given magnesium sulfate alone: 15 g 25% magnesium sulfate injection + 500 mL 5% glucose injection through intravenous infusion at a speed of 2 g/h. Another vein channel was opened in the observation group based on the treatment of the control group: 20 mg phentolamine injection +250 mL 5% glucose injection through intravenous infusion at a speed of 20 mg/h; and meanwhile, 30 mg nifedipine tablets was combined at 1 time/d sublingually. The two groups were treated continuously for 7 days.

The clinical efficacy of the two groups was compared. Significant: proteinuria and edema disappeared, and the mean arterial pressure index recovered. Effective: proteinuria and edema symptoms significantly improved, and the mean arterial pressure decreased by 20 mmHg or more. Improved: proteinuria and edema symptoms improved, and the mean arterial pressure decreased by 10 mmHg or more. Invalid: proteinuria and edema symptoms did not change or increased, and the mean arterial pressure decreased by 10 mmHg or less. Total effective rate = (significant + effective + improved cases) / total number of cases x 100%. The morning fasting cubital venous blood (3 mL) was collected from all patients before and after treatment. The levels of serum LIF and Apelin were detected by enzyme-linked immunosorbent assay (ELISA). The pregnancy outcomes of the two groups were compared.

Table II: Comparison of the levels of serum LIF and apelin before and after treatment between the two groups.

Index	Time	Control group (n=80)	Observation group (n=80)	p-value
LIF (ng/L)	Before treatment	676.94 ±38.24	675.51 ±28.64	0.789
	After treatment	706.30 ±47.79	763.06 ±27.03	<0.001
Apelin (ng/L)	Before treatment	376.32 ±23.87	377.15 ±33.41	0.857
	After treatment	263.86 ±22.05	214.78 ±25.55	<0.001

Table III: Comparison of the pregnancy outcomes between the two groups.

Pregnancy outcomes	Control group (n=80)	Observation group (n=80)	P-value
Premature birth	12 (15.00%)	2 (2.50%)	0.005
Cesarean section	49 (61.25%)	26 (32.50%)	<0.001
Neonatal asphyxia	12 (15.00%)	2 (2.50%)	0.005
Neonatal death	1 (1.25%)	0 (0)	0.316

SPSS 23.0 software was used for statistical analysis. Measurement data are expressed in mean ±SD and independent sample t-test was used. Count data was expressed in n(%) and Chi-square test was used. $P<0.05$ indicates statistically significant difference.

RESULTS

Among the 160 patients, the age ranged from 20 to 34 years, with an average of 28.75 ±2.36 years; the gestational age ranged from 28 to 39 weeks, with an average of 36.61 ±3.43 weeks; the systolic pressure was 140.84-180.57 mmHg, with an average of 143.86 ±12.52 mmHg (1 mmHg=0.133 kPa); and the diastolic pressure 78.55-102.46 mmHg, with an average of 95.74 ±9.38 mmHg.

The total effective rate of treatment in the observation group was 96.25% (77 cases), which was significantly higher than that of the control group 82.50% (66 cases) (p=0.005), as shown in Table I.

Before treatment, there was no significant difference in levels of serum LIF and Apelin between the two groups (p=0.789 and p=0.857, respectively). After treatment, the level of serum LIF in the observation group was higher than that in the control group (p<0.001), and the level of serum Apelin in the observation group was lower than that in the control group (p<0.001), as shown in Table II.

The premature birth rate in the observation group was 2.50% (2 cases), which was lower than 15.00% (12 cases) of the control group (p=0.005); the incidence of cesarean section in the observation group was 32.50%, which was lower than 61.25% (49 cases) of the control group (p<0.001); the incidence of neonatal asphyxia in the observation group was 2.50% (2 cases), which was lower than 15.00% (12 cases) of the control group (p=0.005); and there was no significant difference in the incidence of neonatal death between the two groups (p=0.316), as shown in Table III.

DISCUSSION

Effective control of blood pressure in patients with gestational hypertension is the key to ensure maternal and child safety as well as delivery quality. Magnesium sulfate is a commonly used antihypertensive agent in patients with pregnancy-induced hypertension syndrome. It is safer. After intravenous administration, it regulates the neuromuscular transmission mechanism by inhibiting peripheral nerve and muscle and the release of acetylcholine in peripheral vessels, relaxes the blood vessels as well as the bones, relieves the vasospasm, and improves the state of organ hypoxia and ischemia.[9] However, studies have found that the effect of pure magnesium sulfate is too short to guarantee a stable blood pressure in patients.[10]

Phentolamine is a novel alpha-blocker that reduces peripheral resistance by expanding smooth muscle of pulmonary artery and bronchi, and also has a reflex reinforcement effect on myocardial contractility to increase cardiac output.[11] At the same time, phentolamine can effectively improve renal blood flow by regulating the renal artery, and the efficacy of diuresis and detumescence is significant.[12]

Nifedipine is a calcium channel blocker drug that can relax systemic blood vessels, especially in the relief of coronary artery spasm. It is able to keep blood pressure low and blood concentration for as long as 24 hours, so its antihypertensive effect is stable and long-lasting.[13,14] This study found that the total effective rate of clinical treatment in the observation group was higher than that of the control group, which is consistent with the result of Xiao-Mei *et al*.[15] In terms of pregnancy outcomes, the incidences of cesarean section, neonatal asphyxia and premature delivery in the observation group were all lower than those of the control group, indicating that magnesium sulfate combined with phentolamine and nifedipine can ensure the quality of delivery and the health of newborns.

LIF, as a leukemia inhibitory factor, has a multi-directional regulatory effect on differentiation, proliferation, and infiltration of gestational trophoblast cells.[16] Insufficient secretion of LIF can cause incomplete trophoblastic invasion into the uterus spiral arterioles, and insufficient blood supply for the placenta. The hypoxic-ischemic state can stimulate the body to secrete related hormones with feedback, causing systemic arterial spasm and vascular endothelium damage, and hence the occurrence of pregnancy-induced hypertension.[17]

Apelin has two-way effects on blood pressure regulation in pregnant women: it not only promotes the synthesis of NO through the activation of nitric oxide synthase and exerts effective vasodilatory effects, but also has an effect of increasing blood pressure by directly acting on APJ receptors in vascular smooth muscle cells.[18,19] For patients with gestational hypertension, the over-expression of Apelin may further increase blood pressure and aggravate the condition.[20]

This study showed that after treatment, the level of serum LIF in the observation group was higher than that in the control group, and the level of serum Apelin in the observation group was lower than that in the control group, revealing that magnesium sulfate combined with phentolamine and nifedipine can more effectively regulate the levels of serum LIF and Apelin, and thus relieve hypertensive conditions in patients with gestational hypertension. The efficacy evaluation results showed that the curative effect of the observation group was significantly better than that of the control group, which is consistent with the more effective regulation of the levels of serum LIF and Apelin in the observation group.

CONCLUSION

Magnesium sulfate combined with phentolamine and nifedipine had a better therapeutic effect on gestational hypertension, which can effectively regulate the levels of serum LIF and Apelin and improve pregnancy outcomes. Therefore, it is suitable for treating gestational hypertension.

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