Analysis of the Clinical Effect of Nifedipine Combined with Labetalol in the Treatment of Hypertension during Pregnancy

Lingyan Zhang
Shaanxi Provincial People's Hospital, Xi'an 710068, China.

Abstract: Objectives: To investigate the role of labetalol in combination with nifedipine in patients with hypertension during pregnancy. Methods: A total of 120 pregnant women who underwent prenatal care and terminated pregnancy in our hospital were selected as the study subjects, and they were divided into two groups, 60 in each group, in which the control group was given nifedipine monotherapy orally to control blood pressure, and the experimental group was given nifedipine combined with labetalol to control blood pressure. Both groups were administered orally. The blood pressure, blood viscosity, hematocrit, and 24-hour urine protein content of the two groups were measured. Data on maternal delivery methods, delivery outcomes, fetal outcomes, complications, etc. were collected and compared and analyzed. Both groups had different degrees of systolic and diastolic blood pressure reduction after medication, and there were significant differences compared with the control group ($P<0.05$). The blood viscosity, hematocrit and 24-hour urine protein content of patients in the experimental group were significantly different from those in the control group ($P<0.05$); The rate of cesarean section, preterm birth and postpartum hemorrhage in the experimental group was significantly reduced ($P<0.05$). The incidence of postoperative complications in the experimental group was significantly lower than that in the control group ($P<0.05$), and none of them had perinatal death. Nifedipine combined with labetalol has a good therapeutic effect in patients with hypertension during pregnancy.

Keywords: Hypertension During Pregnancy; Nifedipine; Labetalol; Clinical Effect

Introduction

Hypertensive diseases during pregnancy are unique diseases of pregnancy, including hypertension during pregnancy, preeclampsia, severe preeclampsia, etc., if the disease is not well controlled, it will have an impact on pregnancy outcomes and is one of the main causes of maternal and perinatal mortality [1]. According to statistics, the incidence of hypertension during pregnancy in China is about 10%, and the incidence rate abroad is 7%~12%, which shows that pregnant women and clinically in China are facing a severe situation in the prevention and treatment of hypertension during pregnancy [2]. At 20 weeks of gestation and beyond, it is the high incidence of hypertensive diseases during pregnancy, and if not intervened in time, it will cause further deterioration of the condition, and even serious complications such as eclampsia convulsions, heart failure, stillbirth, placental abruption, etc., resulting in adverse pregnancy outcomes. Therefore, it is necessary to take reasonable measures as soon as possible to control the blood pressure level within a reasonable range and maintain the patient's blood circulation in a normal state. Labetalol can improve the affinity of heme with oxygen, and can also increase the concentration of oxygen in the blood; Nifedipine is a calcium antagonist with a relaxing effect, and the combination of the two can make the efficacy better. We enrolled 120 patients with hypertension during pregnancy and observed the efficacy of labetalol combined with nifedipine.

1. Information and methods

1.1 General Information

In this study, 120 patients with hypertension during pregnancy were selected from January 2019~January 2021, and

they were divided into two groups of 60 cases in each group by random number table method. Results: The general data and basal blood pressure of the two groups were analyzed and no significant differences were shown (P>0.05). Inclusion criteria: (1) meet the relevant diagnostic criteria in the *Guidelines for the Diagnosis and Treatment of Hypertensive Disorders in Pregnancy 2020*; (2) Systolic blood pressure greater than or equal to 140 mm Hg, or diastolic greater than or equal to 90 mm Hg, accompanied by dizziness, nausea, palpitations, fatigue, edema and other symptoms; (3) blood pressure was controlled through interventions such as diet and exercise, but the effect was not obvious; (4) None of the patients had contraindications to labetalol or nifedipine, nor did they have allergic reactions; (5) The patient's cognitive function and psychological state are basically normal, and he can cooperate well with the patient. Exclusion criteria: (1) Other serious comorbidities or complications (except hypertensive disorders during pregnancy) during pregnancy; (2) combined with autoimmune diseases; (3) Patients with missing or incomplete basic data; (4) The patient automatically withdraws during the trial; (5) Failure to go to the outpatient clinic on time for examination, resulting in the loss of test data.

1.2 Method

After hospitalization, according to the actual condition of the patient, corresponding symptomatic treatment is given. Patients are asked to take a left-sided decubitus position at rest, minimize activity, connect to a multifunctional ECG monitor, and receive oxygen inhalation, sedation, and other treatment measures according to the patient's specific situation [3]. The control group used labetalol hydrochloride tablets (Jiangsu Disano Pharmaceutical (D14202058819), the dose was 50-150mg, 3-4 times a day, and the dosage was 50-150mg. The observation group took labetalol combined with nifedipine sustained-release tablets as the main drug, and Qingdao Huanghai Pharmaceutical Co., Ltd. (H65020130) as the main drug, orally, 10mg each time, 3-4 times. The patient's blood pressure is closely monitored throughout the process. Both groups of patients received a week of treatment.

1.3 Observation indicators

(1) According to the relevant standards in the *Chinese Expert Consensus on the Management of Hypertension in Pregnancy (2019 Edition)*, the clinical effects of the two groups before and after treatment were evaluated. Efficacy: The patient's clinical manifestations have improved significantly compared with the previous one, but have not reached the standard; Ineffective: the patient's clinical manifestations did not improve or worsen, the patient's blood pressure did not change; (2) Electronic sphygmomanometer was used to detect changes in diastolic blood pressure (DBP) and systolic blood pressure (SBP), and the two groups were compared and analyzed. (3) Observe the changes of adiponectin (APN), leucine amine transpeptidase (LAP) and homocysteine amine (Hcy) in plasma before and after administration of the two groups, and collect about 5mL of fasting blood on this basis to make the blood clot on its own, and then centrifuge the 15min supernatant at a speed of 3500r/min under the condition of 3500r/min to obtain a 15min supernatant and detect it with an automatic biochemical machine. (4) The clinical manifestations of lower limb edema, dizziness, loss of appetite and fatigue of the two groups were compared and analyzed.

1.4 Statistical methods

SPSS23.0 was used to statistically analyze the data of this study, and the t-test was used to represent the measurement data with ($\overline{x} \pm s$), and the x^2 test was used to represent the counting data by [example (%)], and P<0.05 represented the statistical difference in the data.

2. Results

2.1 Comparison of systolic and diastolic blood pressure between the two groups before and after treatment

There was no significant difference in systolic and diastolic blood pressure between the two groups before treatment (P>0.05), and the difference in systolic and diastolic blood pressure between the two groups after treatment was statistically significant (P<0.05). See table 1.

Groups	Time	Systolic blood pressure/(SBP)	Diastolic blood pressure/(DBP)
Control group	Before treatment	169.97±11.91	106.27±5.19
	After treatment	155.48±10.83	101.74±4.92
Observation group	Before treatment	169.78±12.15	105.97±4.91
	After treatment	131.32±10.73	94.51±3.93
	t time after treatment	-8.214	-8.284
	p time after treatment	＜0.05	＜0.05

2.2 Blood viscosity, hematocrit and 24h urine protein levels of the two groups before and after treatment

Before drug treatment, blood viscosity, hematocrit and 24h urine protein level were not statistically significant (P>0.05), after drug treatment, the changes of the above three indexes were significantly reduced compared with before drug treatment (P<0.05), and after drug treatment, the changes of the above three parameters were also statistically significant compared with before drug treatment. See table 2.

Groups	Blood viscosity/mPa·m	Hematocrit/%	24h urine protein quantification/mg
Control group			
Before treatment	5.33±1.12	46.23±4.12	2.45±0.45
After treatment	3.62±0.63		1.78±0.24
Observation group			
Before treatment	5.11±0.85	45.88±3.82	2.42±0.41
After treatment	2.09±0.39	32.11±2.58	1.21±0.16
p time after treatment	＜0.05	＜0.05	＜0.05

2.3 Comparison of FIB before and after treatment in the two groups

After treatment, FIB values decreased significantly before administration (P<0.05) and after treatment (P<0.05). See table 3.

Groups	Time	FIB/(g/L)
Control group	Before treatment	6.03±0.77
	After treatment	4.28±0.79
Observation group	Before treatment	6.14±0.79
	After treatment	3.66±0.61
p time after treatment		＜0.05

3. Discussion

Hypertensive diseases during pregnancy are caused by abnormal regulation of immune function and damage to vascular endothelial function, which can lead to vasospasm, abnormal target organs due to ischemia, hypoxia, and adverse pregnancy outcomes such as premature birth and postpartum hemorrhage if not controlled in time. Magnesium sulfate and nifedidi are the average common therapeutic drugs, of which magnesium sulfate is the most common therapeutic drug, but it is not suitable for long-term use, and the safe dose of the drug cannot be accurately grasped. Therefore, a variety of antihypertensive regimens have been combined clinically, nifedipine and labetalol are one of the common antihypertensive drugs, and have the characteristics of high safety, so labetalol combined with nifedipine has become one of the common programs for the treatment of hypertensive diseases during pregnancy.

As a multiple clinical condition, hypertension during pregnancy can be divided into preeclampsia, eclampsia,

hypertension during pregnancy and other types, which occur more often after 20 weeks of pregnancy, with edema, proteinuria, hypertension, etc. as the main manifestations, endangering the health of mothers and infants. Therefore, it is necessary to effectively control blood pressure indicators to improve adverse pregnancy outcomes and protect maternal and infant health. Nifedipine is a commonly used calcium ion antagonist in clinical practice, which has the clinical effect of reducing arterial spasm, lowering blood pressure indicators, reducing endothelial cell damage, and reducing urine protein, and the drug also has the advantages of dilating blood vessels, relaxing smooth muscle, and preventing adverse reactions; Labetalol belongs to β receptor blockers, which can directly act on the patient's blood vessels, causing them to dilate, thereby reducing vascular resistance and lowering blood pressure indicators. Unlike simple β-blockers, they are effective in reducing perivascular resistance and generally do not reduce cardiac output. The results of this survey showed that the systolic and diastolic blood pressure indexes of patients in the experimental group were lower than those in the control group after the combination of nifedipine and labetalol drugs, indicating that the addition of labetalol drugs on the basis of nifedipine could effectively reduce blood pressure indicators, restore patients' blood pressure indexes to normal, and better protect the kidneys. Nifedipine is a commonly used drug for the clinical treatment of patients with hypertension during pregnancy, and its use alone can effectively reduce blood pressure, and it has also been reported that the combination of magnesium sulfate and phentolamine has a more prominent antihypertensive effect. However, the half-life of such drugs is relatively short, and it is very likely that blood pressure indicators will continue to fluctuate during medication, reducing blood flow and increasing nerve excitability. Labetalol has the effect of non-selective receptor blockade, which can fundamentally slow down heart rate, reduce oxygen consumption, stabilize blood pressure indicators after combined use, and prevent adverse reactions and adverse pregnancy outcomes. The results of this study showed that the incidence of postpartum hemorrhage in the experimental group was 7.0%, the incidence of neonatal asphyxia was 2.0%, the incidence of premature infants was 15.0%, and the incidence of eclampsia was 9.0%, which were lower than those in the control group of 20.0%, 12.0%, 32.0% and 30.0%. Moreover, the systolic blood pressure and diastolic blood pressure were significantly reduced after maternal medication, and the difference was statistically significant. Note: Compared with nifedipine alone, the effect of combining nifedipine and labetalol was more significant, which was basically similar to the neonatal asphyxia rate of 4.2% and postpartum hemorrhage rate of 12.5% in Zhu Cuijun's research report.

Nifedipine is a calcium channel antagonist, which can inhibit the transmembrane transport of calcium ions into cardiomyocytes and smooth muscle cells, thereby effectively reducing the blood pressure of patients. In addition, nifedipine can also increase coronary blood flow and reduce peripheral vascular resistance. The results of this study showed that nifedipine combined with labetalol treatment for hypertension during pregnancy can improve the treatment effect and improve blood pressure level. APN acts as vascular protection, which can inhibit atherosclerosis, regulate blood pressure, and prevent endothelial function damage; LAP can inhibit the levels of hormones such as angiotensin and oxytocin, and its elevated levels can effectively prevent the occurrence of maternal preterm birth; HCY can inhibit the synthesis of vascular endothelial cells, aggravate vascular endothelial damage, and increase the risk of angioatherosclerotic lesions; Nifedipine can reduce vasoconstriction response, regulate tubular sodium reabsorption, and then regulate serum APN, LAP and Hcy levels by dilating blood vessels and reducing vascular damage.

The results of this study showed that the systolic and diastolic blood pressure of patients in the observation group were significantly lower than those in the control group, and the incidence of cesarean section, premature birth and postpartum hemorrhage, fetal distress and neonatal asphyxia in the observation group were lower than those in the control group, indicating that the clinical safety of labetalol combined with nifedipine was significantly better than that of labetalol alone, confirming the superiority of labetalol combined with nifedipine treatment. The improvement of blood viscosity, hematocrit, 24h urine protein quantification and FIB indexes in the observation group was significantly better than that of the control group, suggesting that the treatment regimen of labetalol combined with nifedipine had excellent improvement in blood viscosity, erythrocrit, 24h urine protein quantification and FIB compared with labetalol alone, which proved that the clinical efficacy of labetalol combined with nifedipine was better than that of labetalol alone.

In summary, labetalol combined with nifedipine hypertension during pregnancy has a good safety profile by improving the therapeutic effect, improving blood pressure levels, reducing vascular damage and improving myocardial function.

References

[1] Huang XM. Analysis of the Implementation Effect of Labetalol in the Treatment of Hypertension Diseases during Pregnancy[J]. *Jilin Medical Journal*, 2020, 41(3): 615-616.

[2] Wu HR, Zhao N. Effects of Magnesium Sulfate Combined with Labetalol in the Treatment of Hypertension during Pregnancy on Homocysteine, Fetal Blood Flow and Pregnancy Outcome[J]. *Chinese Journal of Clinicians*, 2020, 48(2):220-223.

[3] Cui YT. Evaluation of the Effect of Magnesium Sulfate Combined with Nifedipine in the Treatment of Hypertensive Diseases during Pregnancy[J]. *Continuing Medical Education*, 2020, 34(1):142-144.

[4] Ning L. The Effect of Labetalol in the Treatment of Hypertensive Disorders during Pregnancy and Its Effect on Labor Outcomes[J]. *Famous Doctor*, 2020(1):267.

Author introduction: Lingyan Zhang (1984.12-), Title: Attending physician; Education: Master's degree; Research direction: The impact of recurrent miscarriage, gestational immune related diseases, gestational hypertension, and gestational blood glucose abnormalities on mothers and offspring.