Journal of Clinical and Nursing Research, 2025, Volume 9, Issue 6
http://ojs.bbwpublisher.com/index.php/JCNR
Online ISSN: 2208-3693
Print ISSN: 2208-3685

Evaluation of the Improvement of Blood Pressure Levels in Patients with Hypertensive Disorders of Pregnancy Treated with Labetalol Combined with Aspirin

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Abstract: *Objective*: To evaluate the effect of labetalol combined with aspirin on improving blood pressure in patients with hypertensive disorders of pregnancy (HDP). *Methods*: Eighty-two patients with HDP who visited the hospital from August 2022 to August 2024 were selected as samples and randomly divided into two groups. Group A was treated with labetalol and aspirin, while Group B was treated with labetalol only. The efficacy, blood pressure, vascular endothelial function, coagulation indexes, and pregnancy outcomes were compared between the two groups. *Results*: The efficacy of Group A was higher than that of Group B ($P < 0.05$). The systolic blood pressure (SBP), diastolic blood pressure (DBP), and endothelin-1 (ET-1) in Group A were lower than those in Group B ($P < 0.05$). The prothrombin time (PT), thrombin time (TT), activated partial thromboplastin time (APTT), and fibrinogen (FIB) in Group A were all better than those in Group B ($P < 0.05$). The rate of adverse pregnancy outcomes in Group A was lower than that in Group B ($P < 0.05$). *Conclusion*: The combination of labetalol and aspirin for the treatment of HDP can stabilize blood pressure, optimize vascular endothelial function, improve coagulation indexes and pregnancy outcomes, which is highly effective and feasible.

Keywords: Hypertensive disorders of pregnancy; Aspirin; Labetalol; Blood pressure

Online publication: July 7, 2025

1. Introduction

HDP refers to hypertensive diseases that occur after 20 weeks of gestation. It is a common comorbidity during pregnancy with a high clinical incidence. The pathological features include edema and hypertension, which can affect mother and child outcomes. The pathogenesis of HDP is not yet fully understood, but it is believed to be associated with multiple factors, including intrauterine vascular disease, inflammatory response, vascular endothelial damage, and poor nutritional status. In particular, those with multiple pregnancies, first-time pregnancies, and pregnancy age > 40 years are more prone to HDP and should be actively diagnosed and treated

[1]. The clinical treatment of HDP mainly follows the principles of prolonging the gestational week, managing the disease, and protecting the health of the mother and child. If the disease is severe, termination of pregnancy may be considered to ensure the health of the mother. Labetalol is a commonly used drug for the treatment of HDP. It can block α and β adrenergic receptors, stabilize blood pressure, restore placental and renal blood flow, and also prevent platelet accumulation and optimize pregnancy outcomes. Aspirin is an antiplatelet drug that can reduce the risk of eclampsia and coagulation abnormalities [2]. This article explores the value of labetalol combined with aspirin in 82 patients with HDP who visited the hospital from August 2022 to August 2024.

2. Materials and methods

2.1. Materials

Eighty-two patients with HDP who visited the hospital from August 2022 to August 2024 are selected as samples and randomly divided into two groups. There was no significant difference in baseline data between Group A and Group B ($P > 0.05$). Refer to **Table 1** for details.

Table 1. Analysis of baseline data of HDP

Group	*n*	Age (years)		Gestational age (weeks)		BMI (kg/m²)	
		Range	Mean ± SD	Range	Mean ± SD	Range	Mean ± SD
Group A	41	23–38	31.42 ± 2.42	35–38	36.46 ± 0.81	21–28	26.81 ± 1.81
Group B	41	23–39	31.37 ± 2.39	35–39	36.49 ± 0.78	20–28	26.78 ± 1.78
X^2/t	-	0.0941		0.1708		0.0757	
P	-	0.9252		0.8648		0.9399	

2.2. Inclusion and exclusion criteria

2.2.1. Inclusion criteria

(1) Gestational age > 20 weeks with elevated blood pressure
(2) No history of hypertension before pregnancy
(3) Signed informed consent
(4) Singleton pregnancy with cephalic presentation
(5) Negative proteinuria results.

2.2.2. Exclusion criteria

(1) Normal liver and kidney function
(2) Normal immune function
(3) Placenta previa
(4) Congenital malformations.

2.3. Treatment methods

Restrict daily sodium intake, monitor blood pressure, supplement vitamins and calcium, and provide symptomatic treatment for underlying diseases.

(1) Group A: Oral administration of Labetalol Hydrochloride Tablets (Jiangsu Desano Pharmaceutical Co., Ltd.; National Medical Approval Number H32026120; 50mg), single dose of 50mg, 2 times/day; Oral administration of Aspirin Enteric-coated Tablets (Bayer Healthcare Co., Ltd.; National Medical Approval Number HJ20160685; 100mg), single dose of 100mg, 1 time/day. Administration continued until delivery.
(2) Group B: Oral administration of Labetalol Hydrochloride Tablets, single dose of 0.1g, 2 times/day. Administration continued until delivery.

2.4. Observation indicators

(1) Efficacy: Blood pressure returned to 90–140/60–90mmHg, 24-hour urinary protein quantitation < 0.15g, recorded as markedly effective; blood pressure and 24-hour urinary protein quantitation decreased by > 10–20mmHg and 0.03g, recorded as effective; small changes in blood pressure and urinary protein indicators, recorded as ineffective.
(2) Blood pressure and vascular endothelial indicators: SBP and DBP are recorded using an arm-type blood pressure monitor; 3ml of venous blood sample is collected and centrifuged (3000 r/min) for 15 minutes, the supernatant is taken, and ET-1 is detected by immunoturbidimetry.
(3) Coagulation indicators: 3ml of venous blood sample is collected and centrifuged (3000 r/min) for 15 minutes, the supernatant is taken, and PT, TT, APTT, and FIB are detected using an automatic coagulation analyzer.
(4) Adverse pregnancy outcomes: Record adverse pregnancy outcomes such as postpartum hemorrhage, fetal distress, fetal asphyxia, and premature birth.

2.5. Statistical analysis

SPSS 23.0 is used to process the data. Count data are recorded as percentages (%) and analyzed using the chi-square test (X^2 test). Measurement data are recorded as mean ± standard deviation ($\overline{X} \pm s$) and analyzed using the t-test. $P < 0.05$ indicated statistical significance.

3. Results

3.1. Efficacy

The efficacy of Group A was higher than that of Group B, $P < 0.05$, as shown in **Table 2**.

Table 2. Comparison of efficacy (n,%)

Group	Markedly effective	Effective	Ineffective	Effectiveness rate
Group A (n=41)	30 (73.17%)	10 (24.39%)	1 (2.44%)	40 (97.56)
Group B (n=41)	22 (53.66%)	12 (29.27%)	7 (17.07%)	34 (82.93)
X^2	-	-	-	4.9865
P	-	-	-	0.0255

3.2. Blood pressure and vascular endothelial function

After treatment, SBP, DBP, and ET-1 levels in Group A were all lower than those in Group B, with $P < 0.05$, as shown in **Table 3**.

Table 3. Comparison of blood pressure and vascular endothelial function ($\bar{X}$ ±s)

Group	SBP (mmHg)		DBP (mmHg)		ET-1 (ng/L)	
	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
Group A (*n*=41)	150.82 ± 2.88	126.44 ± 1.72	123.25 ± 6.28	100.42 ± 3.59	95.28 ± 4.29	50.94 ± 2.49
Group B (*n*=41)	150.79 ± 2.91	143.29 ± 1.98	123.31 ± 6.31	112.39 ± 4.14	95.21 ± 4.27	70.67 ± 3.88
t	0.0469	41.1373	0.0432	13.9870	0.0741	27.4027
P	0.9627	0.0000	0.9657	< 0.0001*	0.9412	0.0000

3.3. Coagulation indices

After treatment, the coagulation indices PT, TT, APTT, and FIB in Group A were superior to those in Group B, with $P < 0.05$, as shown in **Table 4**.

Table 4. Comparison of coagulation indices (±s)

Group	PT(s)		TT(s)	
	Before Treatment	After Treatment	Before Treatment	After Treatment
Group A (*n*=41)	8.22 ± 0.42	15.51 ± 1.25	11.27 ± 0.61	17.52 ± 1.36
Group B (*n*=41)	8.24 ± 0.39	11.33 ± 1.02	11.25 ± 0.65	14.11 ± 1.18
t	0.2234	16.5897	0.1437	12.1266
P	0.8238	0.0000	0.8861	0.0000
Group	**APTT(s)**		**FIB(g/L)**	
	Before Treatment	**After Treatment**	**Before Treatment**	**After Treatment**
Group A (*n*=41)	25.42 ± 2.43	35.42 ± 3.11	4.71 ± 0.44	3.01 ± 0.26
Group B (*n*=41)	25.39 ± 2.47	30.16 ± 3.02	4.73 ± 0.48	3.93 ± 0.37
t	0.0554	7.7694	0.1967	13.0267
P	0.9559	0.0000	0.8446	0.0000

3.4. Adverse pregnancy outcomes

The rate of adverse pregnancy outcomes in HDP patients in Group A was lower than that in Group B, with $P < 0.05$, as shown in **Table 5**.

Table 5. Adverse pregnancy outcomes in HDP patients (n,%)

Group	Postpartum hemorrhage	Fetal distress	Fetal asphyxia	Premature birth	Incidence rate
Group A (*n*=41)	0 (0.00%)	1 (2.44%)	0 (0.00%)	1 (2.44%)	2 (4.88)
Group B (*n*=41)	2 (4.88%)	3 (7.32%)	1 (9.76%)	4 ( )	10 (24.39)
X^2	-	-	-	-	6.2476
P	-	-	-	-	0.0124

4. Discussion

HDP is a common complication that occurs after the 20th week of gestation, which can cause elevated blood pressure, increased proteinuria, and even increase the risk of adverse pregnancy outcomes. Currently, the clinical cause of HDP is not yet clear, but it is believed to be related to multiple factors that synergistically damage the vascular endothelial function of pregnant women. Severe cases can lead to fetal intrauterine hypoxia, limiting fetal growth and development, and posing a threat to the health of both mother and child [3]. Analyzing the influencing factors of HDP, those with a family history of HDP are more prone to developing this disease. Abnormal immune system function in the mother can identify the placenta as a foreign object, triggering an immune response that can damage the blood vessel function of the pregnant woman, leading to disordered blood pressure regulation. Problems such as placental abruption or abnormal placental blood circulation can affect placental blood oxygen supply, or placental factors may infiltrate into the mother's blood circulation, which can aggravate vascular endothelial damage and increase the risk of HDP. Oxidative stress reactions in the mother's body can lead to the generation of a large amount of reactive oxygen species, which stimulates abnormal vasoconstriction, aggravating the degree of vascular endothelial damage and inducing HDP.

Poor nutritional status of the mother, such as insufficient intake of vitamins, protein, and calcium, cannot maintain the tension of vascular smooth muscle, leading to an increased incidence of HDP. Clinically, HDP is often treated with medication to reduce the risk of cardiovascular disease in the mother and adverse outcomes for both mother and child by regulating blood pressure. Labetalol is commonly used in the treatment of HDP. Its medicinal components can stimulate vasodilation, reduce systemic blood flow resistance, and lower blood pressure. Moreover, compliance with medication has minimal impact on the mother's cardiac output and renal blood flow, maintaining normal placental blood flow [4]. Additionally, the components of labetalol can also act on β-receptors, producing a non-selective blocking effect, which is beneficial for stabilizing heart rate and reducing myocardial oxygen consumption. Based on this, combined treatment with the antiplatelet drug aspirin can block platelet aggregation, achieving multiple effects such as antipyresis, analgesia, and microcirculation optimization. Furthermore, combined treatment of HDP can reduce complications related to abnormal blood pressure, which is beneficial for enhancing the efficacy [5].

After confirming the diagnosis of HDP, patients should be advised to increase their sleep time to more than 10 hours, and it is recommended to maintain a left lateral decubitus position to reduce uterine compression on the inferior vena cava, increase blood flow velocity, and maintain normal placental blood perfusion. It is also necessary to evaluate whether patients experience anxiety, decreased sleep quality, or abnormal mental state. If these issues occur, sedatives should be administered according to medical advice to reduce the impact of adverse factors on fetal growth and development. Patients' daily diet should be adjusted to control daily sodium intake and supplement calories, protein, calcium, and other nutrients to correct nutritional status and stabilize blood pressure.

Based on the data analysis in this paper, the efficacy of Group A is higher than that of Group B, with $P < 0.05$. The reason for this is that labetalol can block adrenergic receptors, reduce cardiac output, decrease blood flow resistance, and slow down heart rate, achieving a stable blood pressure-lowering effect. Combined with aspirin, it stimulates the release of nitric oxide from vascular endothelium, increases the level of vasodilators in patients, and thereby restores vascular tension. Additionally, the active ingredients of aspirin can reduce the level of thromboxane A2 in patients, further enhancing the blood pressure-lowering effect of labetalol [6]. Another set of data shows that Group A has lower SBP, DBP, and ET-1 than Group B, with $P < 0.05$. ET-1 stimulates vasoconstriction and is involved in the hemodynamic regulation process in patients. However, pregnant women

have an abundant blood supply and abnormally elevated ET-1 levels, which can affect pregnancy outcomes. In this paper, labetalol is chosen to treat HDP patients, which can stably regulate blood pressure while maintaining cardiac output. It can also increase CO production in patients, maintain vascular tension, and improve vascular endothelial function. However, labetalol has a short half-life, limiting its overall effect on blood pressure control. Therefore, it needs to be combined with aspirin for synergistic treatment to enhance the blood pressure-lowering effect [7]. Furthermore, aspirin can block the protein binding process, achieving an antiplatelet aggregation effect, which can further optimize vascular endothelial function, resulting in a decrease in ET-1 levels.

Another set of data indicates that Group A has better PT, TT, APTT, and FIB indicators than Group B, with $P < 0.05$. As HDP progresses, patients enter a state of hypercoagulability, with shortened PT, APTT, and TT indicators, which can increase the risk of massive bleeding during childbirth. Additionally, persistent hypercoagulability can worsen blood clots, reduce blood flow velocity, decrease placental blood flow, and even lead to reduced fetal blood supply and restricted growth and development. In this paper, labetalol combined with aspirin is chosen to treat HDP, which can improve oxygen utilization in pregnant women, relieve vascular spasms, reduce vascular damage, accelerate vascular endothelial recovery, and correct disorders of the body's coagulation and anticoagulation systems. This is beneficial for preventing and controlling hypertension-related complications. Additionally, combination therapy can reduce platelet activity in HDP patients, dilute the blood, correct microcirculation disorders, restore placental blood supply, improve HDP prognosis, and protect the health of mothers and babies [8].

The final set of data shows that Group A has a lower rate of adverse pregnancy outcomes than Group B, with $P < 0.05$. The combination therapy of labetalol and aspirin for HDP can reduce vascular resistance, correct blood circulation, and has high medication safety, which is beneficial for reducing adverse outcomes for both mother and baby [9]. During actual combined drug treatment, the active ingredients of labetalol and aspirin have minimal impact on placental blood circulation, which can reduce intrauterine distress events induced by antihypertensive drugs and compensate for the poor safety of labetalol monotherapy. Combination therapy can effectively reduce the symptoms of HDP patients and improve the prognosis of both mother and baby [10]. However, it should be noted that HDP patients are in a special physiological period, and medication management should be properly conducted. Medications should be taken strictly according to the prescribed dosage and time to avoid adverse drug events caused by forgotten or repeated administrations.

5. Conclusion

In summary, HDP patients receiving labetalol and aspirin therapy experience stable blood pressure, improved vascular endothelial function, optimized coagulation indicators, and high safety. This treatment approach can be widely promoted.

Disclosure statement

The author declares no conflict of interest.

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