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Evaluation of the Efficacy of Nifedipine Combined with Low-dose Aspirin in the Treatment of Pregnancy Induced Hypertension

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Abstract: *This study aims to explore the effectiveness of the combination of nifedipine and low-dose aspirin in the treatment of patients with pregnancy induced hypertension. Pregnancy induced hypertension patients who underwent treatment in our hospital from September 2022 to September 2023 were selected as the research objects. According to the random number table method, a total of 96 patients were divided into a control group and an observation group, with 48 cases in each group. The control group was only treated with nifedipine, while the observation group was treated with nifedipine combined with low-dose aspirin. The therapeutic effects of the two groups were compared. Result: After treatment with nifedipine combined with low-dose aspirin, the blood pressure indicators, coagulation function indicators, vascular endothelial function indicators, peripheral blood inflammatory response indicators, incidence of adverse reactions, and incidence of adverse birth outcomes in newborns and postpartum women in the observation group were significantly lower than those in the control group, and the differences were statistically significant (P<0.05). The combination of nifedipine and low-dose aspirin has an ideal therapeutic effect in the selection of treatment plans for patients with gestational hypertension, which can help maintain blood pressure stability and have a positive effect on the stability of their coagulation function and vascular endothelial function. At the same time, it can reduce peripheral inflammatory reactions, have high safety, and improve adverse outcomes for newborns and postpartum women.*

Keywords: *Nifedipine, low-dose aspirin, Pregnancy induced Hypertension*

1. Introduction

Pregnancy induced hypertension is a serious complication that may affect the health of pregnant women and fetal development during pregnancy. It refers to a situation where blood pressure increases during pregnancy, and if not treated in a timely manner, it may have a significant impact on the safety of the mother and baby. Allowing pregnancy induced hypertension to develop may lead to serious complications such as placental abruption, postpartum hemorrhage, eclampsia, premature birth, etc[1]. At present, clinical treatments such as sedation, hypotension, and termination of pregnancy are mainly used, but the efficacy of these methods is not very ideal. It has been found that there is a close relationship between coagulation dysfunction and pregnancy induced hypertension. Pregnant women are in a long-term hypercoagulable state with abnormal coagulation function, and the treatment method of nifedipine combined with low-dose aspirin is believed to improve this condition[2]. Nifedipine is a commonly used anti-hypertensive drug with vasodilation effects, while low-dose aspirin is a commonly used anticoagulant that can improve blood perfusion. The purpose of this research is to explore the clinical efficacy of nifedipine combined with low-dose aspirin in the treatment of patients with pregnancy induced hypertension.

2. Research information and methods

2.1. Information

96 patients with gestational hypertension who received treatment in our hospital from September 2022 to September 2023 were included in the research. Through a random number table method, they were divided into a control group treated with nifedipine and an observation group treated with additional low-dose aspirin, with 48 cases in each group. The age range of postpartum women in the

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control group is 21-41 years old, with an average age of 29.63 ± 3.07 years. The body mass index is 22-31kg/m2, with an average of 27.07 ± 2.56 kg/m2. The pregnancy cycle is 24-35 weeks, with an average of 29.73 ± 1.87 weeks. The age range of postpartum women in the observation group is 20-42 years old, with an average of 29.83 ± 3.12 years old. The body mass index is 22-32kg/m2, with an average of 27.10 ± 2.63 kg/m2. The pregnancy period is 24-36 weeks, with an average of 29.45 ± 3.02 weeks. After statistical analysis, the two groups of general data showed no statistically significant difference (P>0.05).

Inclusion criteria: ① The pregnancy is a single pregnancy, and the intrauterine condition of the fetus has been tested as good. ② All meet the corresponding standards in the Guidelines for the Diagnosis and Treatment of Pregnancy Induced Hypertension (2020)[3], and have been diagnosed through clinical relevant examinations. ③ Complete clinical data. ④ The patients and their families included in the study were informed of the research content and signed informed consent forms.

Exclusion criteria: ① Those with other pregnancy complications. ② Existence of reproductive system infections. ③ Individuals with severe organ dysfunction. ④ Individuals with mental illness. ⑤ Individuals with allergies or contraindications to the drugs used in this study. ⑥ Those with poor compliance.

2.2. Research methods

After admission, both the two groups of patients were given routine treatments such as sedation, spasmolysis, and oxygen inhalation, the maternal blood pressure were recorded and observed. Take measures such as observing the patient's condition, providing dietary care, and strengthening fetal intrauterine monitoring.

The control group was treated with nifedipine sustained-release tablets (I): The research institute used nifedipine sustained-release tablets (I) (Hunan Warner Pharmaceutical Co., Ltd., National Pharmaceutical Approval No. H20084558, 10mg/tablet), and was taken with warm water after meals, 10mg/time, twice a day; Patients in the observation group need to take a combination of low-dose aspirin enteric coated tablets on the basis of the control group: Aspirin enteric coated tablets used in the research institute (Shiyao Group Ouyi Pharmaceutical Co., Ltd., Guoyao Zhunzi H20153035 100mg/tablet), orally, 50mg/time, once a day. Both groups of treatments lasted for 2 weeks, and their therapeutic effects were observed after the treatment.

2.3. Observation indicators

2.3.1. Blood pressure indicators

To compare two groups of blood pressure indicators. The indicators include systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP). Using an ambulatory blood pressure monitor (brand: Swiss Schiller, model: BR-102 plusPWA, National Machinery Injection 20182211696), continuously monitor the patient in a quiet state for 3 times, take the average value, and record it.

2.3.2. Coagulation function indicators

To compare the coagulation function between the two groups. The indicators include four items: fibrinogen (FIB) and activated partial thromboplastin (APTT), prothrombin (PT), and thrombin (TT) time. 4ml of the patient's elbow vein blood were taken for anticoagulation treatment in the morning and centrifuge treatment at a speed of 3000r/min for 10 minutes. After separating the serum, store it at -20 ℃ for testing. The data was evaluated using a fully automated coagulation analyzer (brand: Leidu, model: RAC-030, Guangdong Food and Drug Administration 20142400170).

2.3.3. Vascular endothelial function indicators

To compare two groups of vascular endothelial function indicators. The indicators include two groups of levels of endothelin-1 (ET-1), nitric oxide (NO), soluble vascular cell adhesion molecule-1 (sVCAM-1), and receptor for advanced glycation end products (RAGE). 4ml of elbow vein blood from the patient were collected for anti-coagulation treatment and centrifuge treatment at a speed of 3000r/min for 10 minutes. After separating the serum, store it at -20 ℃ for testing. The ET-1 and NO levels were evaluated using a fully automated immune analyzer (brand: Boke, model: BKI1100, Shandong Medical Device Registration Approval 20202220932), evaluating by radioimmunoassay. The

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levels of sVCAM-1 and RAGE were evaluated using a full wavelength enzyme-linked immunosorbent assay (brand: Delang, model: DR-200Bc, Jiangsu Medical Device Registration Approval 20202220124), evaluating by enzyme-linked immunosorbent assay.

2.3.4. Peripheral blood inflammatory response indicators

To compare the inflammatory response of peripheral blood between two groups. The indicators include platelet lymphocyte ratio (PLR, ratio formula PLR=PLT/LYM), monocyte lymphocyte ratio (MLR, ratio formula MLR=MON/LYM), neutrophil lymphocyte ratio (NLR, ratio formula NLR=NEU/LYM), and coefficient of variation of red blood cell distribution width (RDW-CV). Two sets of RDW-CV, PLT, NEU, LYM, and MON levels were detected using a fully automated coagulation analyzer.

2.3.5. Incidence of adverse reactions

To compare the incidence of adverse reactions between the two groups. The indicators include decreased appetite, dizziness, headache, upper abdominal pain, and palpitations, and the incidence of adverse reactions is compared.

2.3.6. Incidence of adverse outcomes in newborns and postpartum women

To compare the incidence of adverse outcomes between two groups of newborns and postpartum women. Among them, adverse outcome indicators for newborns include fetal growth restriction, premature birth, neonatal asphyxia, and fetal distress. Maternal adverse outcome indicators include postpartum hemorrhage, uterine atony, and placental abruption.

2.4. Statistical Analysis

The research data was included in SPSS 20.0 software for statistical analysis, and the measurement data was represented as "$\bar{x} \pm s$", t-value for test. The counting data is represented as "n,%", with a x2 for test. There is a statistically significant difference between the data if P<0.05.

3. Research results

3.1. Comparison of blood pressure indicators

Analysis showed that the blood pressure indicators in the observation group were significantly lower than those in the control group, with statistical significance (P<0.05). As shown in Table 1:

Table 1: Comparison of blood pressure between two groups($\bar{x} \pm s$,mmHg)

Group	Cases	SBP	DBP	MAP
Observation group	48	129.27±6.30	80.35±4.58	93.08±4.35
Control group	48	138.51±6.53	89.04±4.92	99.54±4.80
t	-	7.055	8.957	6.909
P	-	0.001	0.001	0.001

3.2. Comparison of coagulation function indicators between two groups

The levels of APTT, PT, and TT in the observation group were significantly higher than those in the control group, while the levels of FIB were significantly lower than those in the control group. The comparison between groups was significant (P<0.05). As shown in Table 2:

Table 2: Comparison of coagulation function indicators between two groups($\bar{x} \pm s$)

Group	Cases	APTT(s)	PT(s)	TT(s)	FIB(g/L)
Observation group	48	28.74±2.55	12.44±1.33	15.94±1.16	3.72±0.82
Control grouo	48	26.21±2.33	11.45±1.13	14.91±1.12	4.55±1.06
t	-	5.075	3.930	3.581	4.426
P	-	0.001	0.001	0.001	0.001

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3.3. Comparison of vascular endothelial function indicators

The observation group showed significantly lower levels of ET-1, sVCAM-1, and RAGE compared to the control group, while the NO level was higher than the control group, with significant inter group comparison (P<0.05). As shown in Table 3:

Table 3: Comparison of vascular endothelial function indicators between two groups($\bar{x} \pm s$)

Group	Cases	ET-1(ng/L)	NO(μmol/L)	sVCAM-1(mg/L)	RAGE(ng/ml)
Observation group	48	58.33±4.82	41.20±4.32	537.20±53.32	5.55±1.06
Control group	48	65.21±5.24	35.25±4.73	665.25±62.73	6.56±1.25
t	-	6.695	6.435	10.776	4.279
P	-	0.001	0.001	0.001	0.001

3.4. Comparison of inflammatory response indicators in peripheral blood

The PLR indicators in the observation group were significantly higher than those in the control group, while the RDW-CV, MLR, and NLR indicators were significantly lower than those in the control group. The comparison between groups was significant (P<0.05). As shown in Table 4:

Table 4: Comparison of inflammatory response indicators in peripheral blood between two groups($\bar{x} \pm s$)

Group	Cases	PLR	RDW-CV(%)	MLR	NLR
Observation group	48	185.78±23.55	14.45±2.54	0.26±0.07	3.87±0.76
Control group	48	175.27±23.85	15.66±2.56	0.28±0.06	4.22±0.73
t	-	2.173	2.325	2.254	2.301
P	-	0.032	0.022	0.027	0.024

3.5. Comparison of incidence of adverse reaction

The incidence of adverse reactions in the observation group was significantly lower than that in the control group, and the inter group comparison was significant (P>0.05), as shown in Table 5:

Table 5: Comparison of adverse reaction incidence between two groups[n(%)]

Group	Cases	Loss of appetite	Dizziness and headache	Upper abdominal pain	Palpitate	Incidence
Observation group	48	1(2.08)	2(4.17)	1(2.08)	0(0.00)	4(8.33)
Control group	48	5(10.42)	4(8.33)	2(4.17)	1(2.08)	12(25.00)
x^2	-	-	-	-	-	4.800
P	-	-	-	-	-	0.028

3.6. Comparison of the incidence of adverse maternal and infant outcomes

Table 6: Comparison of the incidence of adverse outcomes in newborns between the control group and the treatment group [n(%)]

Group	Cases	Fetal growth restriction	Premature birth	Neonatal asphyxia	Fetal distress	Incidence
Observation group	48	1(2.08)	2(4.17)	0(0.00)	1(2.08)	4(8.33)
Control group	48	3(6.25)	5(10.42)	2(4.17)	2(4.17)	12(25.00)
x^2	-	-	-	-	-	4.800
P	-	-	-	-	-	0.028

After comparison, the incidence of adverse maternal and infant outcomes in the observation group

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was significantly lower than that in the control group, and the difference was statistically significant (P>0.05), as shown in Table 6:

Attached list of Table 6: Comparison of adverse outcomes between the control group and the treatment group [n(%)]

Group	Cases	Postpartum hemorrhage	Uterine inertia	Placental abruption	Incidence
Observation group	48	0(0.00)	0(0.00)	0(0.00)	0(0.00)
Control group	48	3(6.25)	1(2.08)	1(2.08)	5(10.42)
x^2	-	-	-	-	5.275
P	-	-	-	-	0.022

4. Discussion

Pregnancy induced hypertension (PIH) is a type of pregnancy complication characterized by clinical manifestations such as gestational hypertension, preeclampsia, and eclampsia. In recent years, epidemiological studies have shown that this disease has become one of the major public health issues worldwide[3]. The risk factors of pregnancy induced hypertension include elderly pregnant women, obesity, family history of hypertension, diabetes, chronic nephritis, etc. [4]. In recent years, the incidence rate of hypertensive disorder complicating pregnancy has gradually increased, but the pathogenesis of the disease has not yet been fully understood. Clinical studies have shown that the occurrence of this condition is related to changes in the endocrine and metabolic systems of women during pregnancy. Research has found that after 20 weeks of pregnancy, there is a corresponding increase in blood volume and calcium demand to meet pregnancy needs. However, the secretion of estrogen in women may lead to limited calcium absorption in the body, leading to a decrease in blood calcium levels[5]. Low blood calcium can cause vasoconstriction and hypertension, and increase vascular permeability. In addition, blood concentration and microvascular thrombosis may lead to insufficient blood supply, which may cause damage to the organs and organs of the mother, and in severe cases, directly threaten the life safety of the mother and baby. The main treatment method for this condition is medication, with the aim of reducing blood pressure, preventing convulsions, and protecting the fetus. Commonly used drugs include magnesium sulfate, nifedipine, etc. However, long-term use of magnesium sulfate poses risks to fetal bone development, and an increase in dosage can cause magnesium poisoning. The patient is in a pregnant state and needs to seek a safer treatment plan.

Nifedipine is a blocker that acts on calcium channels, and its unique effect lies in its ability to significantly dilate vascular smooth muscle. Its mechanism of action mainly lies in preventing calcium ions from entering the cells, reducing the loss of calcium components, and thus altering the electrophysiological characteristics of myocardial cells. It can increase blood flow and lower blood pressure. Aspirin, on the other hand, belongs to the category of platelet inhibitors and thrombosis inhibitors. It has the effects of improving vascular micro-circulation, dilating blood vessels, increasing blood flow, and reducing vascular resistance. It has also shown significant therapeutic effects in controlling blood pressure. Especially for patients with gestational hypertension, low-dose aspirin (50mg/d) can be quickly absorbed orally and reach the peak blood concentration in a short period of time, with a very long-lasting anti-hypertensive effect. When nifedipine is combined with aspirin, these two drugs can complement each other through different mechanisms, effectively controlling blood pressure[6]. In this study, the blood pressure indicators in the observation group were significantly lower than those in the control group, which indicates this point. In addition, the results of this research also showed that the levels of APTT, PT, TT in the observation group were significantly higher than those in the control group, while the FIB levels were significantly lower than those in the control group. This is because the pharmacological effect of low-dose aspirin is mainly to inhibit platelet cyclooxygenase. It can reduce the production of thromboxane A2, reduce the activity of cyclooxygenase, and prevent the conversion of arachidonic acid to thromboxane S2. As a result, the likelihood of platelet aggregation and thrombosis in the patient's body is significantly reduced, thereby achieving anticoagulant effects. This anticoagulant effect can prevent thrombosis and platelet aggregation, and achieve the goal of lowering blood pressure by reducing peripheral vascular resistance and making blood circulation smoother in the peripheral blood[7].

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Due to the effects of nifedipine on dilating blood vessels, restoring endothelial function, and reducing blood flow resistance. When combined with nifedipine and low-dose aspirin, it can reduce thromboxane production and protect vascular endothelial cells from damage. This is achieved by inhibiting the activity of cyclooxygenase and reducing vascular sensitivity. The combination of these two drugs can dilate arteries, reduce the damage of hypertension and hypercoagulability to the patient's vascular endothelium. Meanwhile, aspirin can block the conversion of prostaglandins to arachidonic acid, reduce the production of inflammatory mediators, and have anti-inflammatory effects, which can help patients alleviate endothelial damage caused by inflammation[8]. The comparison results of various endothelial function indicators in the observation group of this research also confirm that this combined medication can effectively reduce vascular endothelial injury in patients with gestational hypertension treatment. In the research, the PLR indicators in the observation group were significantly higher than those in the control group, while the RDW-CV, MLR, and NLR indicators were significantly lower than those in the control group. It also indicates that the combination of the two drugs can effectively reduce peripheral blood inflammatory reactions in patients with gestational hypertension. The reason for this is that aspirin, as a non-steroidal anti-inflammatory drug, can further inhibit the inflammatory response by inhibiting cyclooxygenase and limiting the release of inflammatory mediators[9]. At the same time, preventing the synthesis of prostaglandin E2 and white blood cell aggregation is also a step for aspirin to inhibit the inflammatory response. The anti-inflammatory mechanism of aspirin also includes regulating the release of lysosomal enzymes and reducing the formation of bradykinin, preventing nuclear factors by inhibiting the stimulation of inflammatory effector cells- κ B (NF- κ B) activation of NF- κ B cannot interact with the TNF gene promoter κ B sequence binding inhibits the release of inflammatory factors at the gene transcription level. In addition, aspirin can also reduce the ratio of thromboxane A2 to prostacyclin, helping to prevent excessive release of inflammatory factors, protect vascular endothelium, and thus alleviating peripheral blood inflammatory response. It can also prevent blood vessel contraction and lead to insufficient placental blood flow perfusion[10].

Meanwhile, by comparing the incidence of adverse outcomes in newborns and postpartum women between the two groups in this article, it was found that the observation group was significantly lower than the control group. It can be seen that the combination of nifedipine and low-dose aspirin in the treatment of gestational hypertension is safe and will not bring additional side effects to patients. Aspirin has a significant effect in relieving symptoms such as upper abdominal pain, dizziness, and headache, and can achieve rapid pain relief. Its main component, acetylsalicylic acid, is mostly metabolized in the liver at low doses, while salicylic acid bound to plasma proteins and free salicylic acid can achieve a binding rate of 65% to 90%. The metabolites formed by the combination of the two will be excreted through the kidneys, thus rarely causing adverse reactions[11]. In addition, research has shown that implementing combination medication in the treatment of gestational hypertension can improve adverse outcomes for newborns and postpartum women. After research, it has been confirmed that low-dose aspirin has no adverse effects on embryonic development. On the contrary, it can also reduce the risk of bleeding caused by taking high-dose aspirin. This drug has high biological activity and availability, and when apply combined with nifedipine, it can more effectively alleviate symptoms of vasoconstriction and improve uterine blood flow[12].

To sum up, in the clinical treatment of patients with pregnancy induced hypertension, the combination of nifedipine and low-dose aspirin can achieve better therapeutic efficacy. This method can effectively control the patient's blood pressure and help improve their coagulation function and vascular endothelial function. At the same time, it can also reduce peripheral inflammatory reactions and improve neonatal survival rate.

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