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The Effect of Methyldopa Combined with Rabelol Treatment on Patients with Pregnancy Induced Hypertension

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Abstract: *This paper aims to analyze the therapeutic effect of methyldopa combined with rabelol treatment in patients with pregnancy pregnancy induced hypertension. A total of 70 patients with gestational hypertension diagnosed in our hospital during the period from March 2021 to March 2023 were selected as the research objects. According to different treatment methods, 35 patients treated with magnesium sulfate were included in the reference group, while 35 patients treated with methyldopa combined with rabelol were included in the observation group. Blood pressure and urinary protein levels before and after treatment were compared, hemodynamic indicators,serum indicators and the pregnancy outcomes were compared between the two groups of patients. Result: Before treatment, there was no significant difference in various indicators between the two groups, with no statistical significance (P>0.05). After treatment, the blood pressure, urinary protein level, hemodynamic index, and serum indicators of the observation group were better than those of the reference group, with significant statistical significance (P<0.05). In terms of comparison of adverse pregnancy outcomes, the incidence rates of intrauterine distress, neonatal asphyxia, premature birth, etc. in the observation group were lower than those in the reference group, and the difference was statistically significant (P<0.05). The treatment effect of methyldopa combined with rabelol treatment in patients with gestational hypertension is significant positive, which can control blood pressure and urine protein to reach the ideal range, effectively improve hemodynamic indicators, protect patient vascular endothelial function, and reduce the probability of adverse pregnancy outcomes caused by hypertension. It has great medical significance for ensuring maternal safety and safe production.*

Keywords: *Methyldopa, Rabelol, Pregnancy induced Hypertension, Hemodynamics, Vascular Endothelium, Adverse Pregnancy, Magnesium Sulfate*

1. Introduction

Pregnancy induced hypertension is a common and unique disease during women's pregnancy, and its incidence rate accounts for 8% -10% of the total pregnant women. The clinical symptoms are that after 20 weeks of pregnancy, the pregnant women have pregnancy complications such as hypertension, edema, proteinuria, and when the condition is serious, dizziness, tinnitus, nausea, vomiting, and convulsions will also occur[1-3]. The etiology of pregnancy induced hypertension is currently unclear, but it is generally believed to be a multifactorial disease caused by excessive oxidative stress, activation of endothelial cells, inflammation, and immune systems in the body[4]. Clinical studies have shown that genetic factors and elderly postpartum women are also one of the causes of gestational hypertension. Pregnancy induced hypertension seriously damages the health of mothers and infants, and may even cause maternal and perinatal deaths[5]. Hypotension therapy is currently recognized as the main treatment for gestational hypertension in medicine. In the 2020 guidelines for the diagnosis and treatment of gestational hypertension in China, it was emphasized that pregnant women with systolic blood pressure greater than 140mmhg or diastolic blood pressure greater than 90mmhg are considered patients with gestational hypertension, and necessary blood pressure control measures should be taken to prevent maternal complications such as preeclampsia and cardiovascular and cerebrovascular accidents in pregnant women, as well as to prevent intrauterine distress in newborns Adverse pregnancy outcomes such as asphyxia and premature birth[6]. Magnesium sulfate is currently the primary choice for anti-hypertensive drugs, but it has obvious drawbacks such as slow treatment onset and large adverse drug reactions. Therefore, finding other more effective and safer anti-hypertensive drugs to replace treatment is the key to controlling gestational hypertension in clinical practice.

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Methyldopa is a central anti-hypertensive drug, while labelol is β-Receptor blockers and anti-hypertensive drugs are commonly used in patients with hypertension. In order to explore the therapeutic effect of methyldopa combined with rabelol on patients with gestational hypertension, our hospital proposed to conduct an experiment on 70 patients with gestational hypertension to explore the therapeutic advantages of the combination of the two drugs.

2. Research objects and methods

2.1. Research objects

Selecting March 2021 to March 2023 as the research period, 70 patients with pregnancy induced hypertension diagnosed in our hospital during the research period were randomly selected. According to different treatment methods, 35 patients in the reference group were treated with magnesium sulfate, while 35 patients in the observation group were treated with methyldopa combined with rabelol. The reference group, including 26 primiparous women and 9 multiparous women, had the oldest female at 36 years old and the youngest at 28 years old, with an average age of 31.5 ± 2.3 years old. The maximum gestational age was 29 weeks, while the minimum gestational age was 24 weeks, with an average gestational age of 24.5 ± 1.9 weeks. The highest systolic blood pressure was 175mmhg, the lowest was 162mmhg, the highest diastolic blood pressure was 115mmhg, and the lowest was 102mmhg. The oldest female in the observation group was 39 years old, while the youngest was 31 years old, with an average age of 32.6 ± 1.7 years. The maximum gestational age is 30 weeks, and the minimum gestational age is 25 weeks, with an average gestational age of 24.3 ± 1.7 weeks, and there are 25 primiparous women and 10 multiparous women in the observation group. The highest systolic blood pressure was 172mmhg, the lowest was 161mmhg, the highest diastolic blood pressure was 116mmhg, and the lowest was 103mmhg; There was no statistically significant difference between the two groups of patients in terms of gestational age, gestational frequency, diastolic blood pressure, systolic blood pressure, etc. ($P>0.05$). At the same time, our hospital's ethics committee is fully aware of the research and has approved it for implementation.

2.2. Inclusion and Exclusion Criteria

Inclusion criteria: ① Pregnant women with systolic blood pressure greater than 140mmhg or diastolic blood pressure greater than 90mmhg. ② The first diagnosis of gestational hypertension after 20 weeks of pregnancy, with no previous history of receiving any medication treatment. ③ Individuals who are not allergic to drugs such as magnesium sulfate, methyldopa, and rabelol. ④ Able to engage in effective verbal communication. ⑤ Nursing dependency is acceptable, and medication guidance and experimental data measurement can be conducted. ⑥ Single pregnancy. ⑦ There are no abnormal diseases during the initial visit and filing. ⑧ Informed and willing to participate in the study. ⑨ Not included in the same type of experimental research on gestational hypertension as the experimental subjects.

Exclusion criteria: ① Multiple pregnancy. ② Those who do not undergo regular prenatal examinations during pregnancy. ③ Individuals under the age of 18. ④ Individuals with mental disorders. ⑤ Those with lower cognitive abilities. ⑥ Deaf mute or physically disabled individuals. ⑦ Pregnant women with myocardial damage or heart conduction block. ⑧ Individuals with significant impairments in liver and kidney function. ⑨ Active liver diseases, such as acute hepatitis and active cirrhosis ⑩ Individuals with a history of coronary heart disease and angina pectoris. ⑪ Individuals with autoimmune diseases and a history of hemolytic anemia. ⑫ Direct anti globulin (Coombs) test positive individuals. ⑬ Pregnant depression. ⑭ Patients with concomitant pheochromocytoma. ⑮ Patients with bronchial asthma. ⑯ Patients with hypothyroidism. ⑰ Non allergic bronchitis patients. ⑱ Patients with congestive heart failure, diabetes and emphysema. ⑲ Those who have been included as experimental subjects of the same type.

2.3. Research method

After admission, both groups of patients were educated on relevant knowledge about pregnancy induced hypertension and instructed to lie on the left side, which is beneficial for uterine blood circulation. The researchers provided low salt intervention to the patients' diet and necessary oxygen

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inhalation, spasmolysis, and fluid replacement, while emphasizing the advantages of exercise intervention in controlling pregnancy induced hypertension.

The reference group patients were treated with magnesium sulfate: magnesium sulfate injection (Hebei Tiancheng Pharmaceutical Co., Ltd., National Drug Approval No.: H20033860, 10ml 2.5g) was mixed with 5g magnesium sulfate into a 100ml glucose solution with a concentration of 5% for intravenous infusion, and the infusion was completed within 30 minutes. Another 15g of magnesium sulfate was taken to mix into a 500ml glucose solution with a concentration of 5% for maintenance infusion. The infusion rate is 1-2g/h. During the infusion period, the patients' blood pressure, heart rate, breathing and other vital signs to prevent magnesium ion poisoning were closely observed. The same dose is continuously treated for 7 days.

Patients in the observation group were treated with methyldopa combined with rabolol: methyldopa (China Resources Shuanghe Pharmaceutical Co., Ltd., national drug approval number: H11020968, 0.25g * 12s/box, 0.25g * 30s/bottle), it was taken orally, 250mg/dose, 2-3 times/day, and the dosage was adjusted every 2 days until the treatment effect was satisfactory. Rabenol hydrochloride (Jiangsu Disenol Pharmaceutical Co., Ltd., National Drug Approval No. H32026120, 50mg * 15 tablets * 2 plates) is orally administered, 100mg, 2-3 times/day, and the dosage is adjusted every 2 days until the treatment effect is satisfactory. The combination therapy lasted for 7 days.

2.4. Observation indicators

① The blood pressure and urine protein levels of two groups of patients before and after treatment were compared, the patients' 24-hour urine were collected to measure urine protein using turbidity method. ② The hemodynamic indicators of two groups of patients were compared. Both before and after treatment, dynamic electrocardiograms were used to measure cardiac pulsatility index using surface electrode impedance cardiogram. Abdominal ultrasound was used to collect uterine resistance index and umbilical artery diastolic blood flow peak ratio before and after treatment. ③ The serum indicators of two groups of patients were compared. Before and after treatment, 3ml of fasting venous blood was taken from each patient. After centrifugation, C-reactive protein, homocysteine, angiotensin, and vascular endothelial growth factor were measured using enzyme-linked immunosorbent assay. ④ The pregnancy outcomes of two groups of patients were compared.

2.5. Statistical analysis

The data obtained in this study will be immediately included in the statistical SPSS 24.0 software for analysis. The econometric data will be compared using t-test method and represented by means, i.e. ($\overline{x} \pm s$), while the case and rate counting data will be analyzed using $\chi 2$ test method, expressed as a percentage(%). $P<0.05$ showed significant differences and statistical significance.

3. Results

3.1. Comparison of blood pressure and urinary protein levels

There was no statistically significant difference in blood pressure and urinary protein levels between the two groups before treatment ($P>0.05$). However, after treatment, the patients in the observation group had better systolic blood pressure, diastolic blood pressure, and urinary protein levels than the reference group, with significant differences ($P<0.05$), as shown in Table 1:

Table 1: Comparison of blood pressure and urinary protein levels between two groups of patients before and after treatment [$\overline{x} \pm s$]

Group (N =35)	Systolic blood pressure(mmhg)		Diastolic blood pressure(mmhg)		24h Urinary protein(mg/mmol)	
	Before	After	Before	After	Before	After
Observation group	168.5±7.6	137.3±2.6	113.2±5.7	85.7±1.1	3.18±0.2	1.02±0.2
Reference group	169.4±2.9	142.6±2.8	114.6±3.2	92.3±1.9	3.21±0.3	2.04±0.6
t	0.654	8.206	1.267	17.785	0.492	8.995
P	0.515	0.001	0.209	0.001	0.624	0.001

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3.2. Comparison of hemodynamic indicators

There was no statistically significant difference in treatment hemodynamics between the two groups of patients (P>0.05). After treatment, the heart beat index, uterine resistance index, and peak diastolic blood flow of the umbilical artery in the observation group were all better than those in the reference group, with statistically significant differences (P<0.05), as shown in Table 2:

Table 2: Comparison of hemodynamic indicators between two groups of patients[$\bar{x} \pm s$]

Group(N =35)	heart beat index(L/min/m2)		Uterine resistance index(cm/s)		Peak diastolic blood flow of the umbilical artery	
	Before	After	Before	After	Before	After
Observation group	0.91±0.11	0.62±0.3	0.71±0.1	0.31±0.07	3.45±0.2	1.21±0.3
Reference group	0.93±0.12	0.76±0.1	0.72±0.2	0.45±0.05	3.32±0.1	1.75±0.2
t	0.726	2.619	0.264	9.628	0.793	8.601
P	0.469	0.011	0.792	0.001	0.430	0.001

3.3. Comparison of serum indicators

In terms of serum indicators, there was no statistically significant difference between the two groups before treatment (P>0.05). After treatment, the C-reactive protein, vascular endothelial growth factor, homocysteine and other indicators in the observation group were better than those in the reference group, and the difference was statistically significant (P<0.05), as shown in Table 3:

Table 3: Comparison of the serum indicators of two groups of patients [$\bar{x} \pm s$]

Serum indicators	Time	Observation group(N=35)	Reference group(N=35)	t	P
C-reactive protein(mg/L)	Before	7.18±1.2	7.25±1.67	0.201	0.841
	After	3.25±0.62	4.35±0.75	6.505	0.001
Angiotensin(pg/ml)	Before	141.6±7.8	143.50±6.5	1.107	0.272
	After	102.5±5.6	112.3±4.2	8.282	0.001
Homocysteine (μmmol)	Before	24.9±2.9	24.6±3.6	0.383	0.702
	After	14.7±2.5	18.6±2.9	6.026	0.001
Vascular endothelial growth factor(ng/L)	Before	23.7±3.5	24.1±2.8	0.528	0.599
	After	16.57±2.9	20.3±2.7	5.569	0.001

3.4. Comparison of pregnancy outcomes

The incidence rates of intrauterine distress, neonatal asphyxia, premature birth, etc. in the observation group were lower than those in the reference group, and the difference was statistically significant (P<0.05), as shown in Table 4:

Table 4: Comparison of pregnancy outcomes between two groups of patients[n,(%)]

Group	N	intrauterine distress(case)	neonatal asphyxia(case)	premature birth(case)	Adverse event occurrence rate
Observation group	35	0(0%)	1(2.85%)	0(0%)	2.85%
Reference group	35	1(2.85%)	2(5.71%)	1(2.85%)	11.42%
$\chi 2$	-	-	-	-	5.542
P	-	-	-	-	0.019

4. Discussion

Pregnancy induced hypertension is a common reason for the increase of morbidity and mortality of pregnant women, which is mostly found in primipara. The highest incidence rate is in spring. It can be divided into pre-eclampsia, pre-eclampsia and eclampsia according to the severity of the condition. Failure to intervene in time may endanger the lives of mothers and children[7]. Xuexia Chen[8], a scholar, based on experimental research and domestic and foreign literature, concluded that compared to normal pregnant women, pregnant women with pregnancy induced hypertension have multiple times higher incidence rates of placental abruption, eclampsia, disseminated intravascular coagulation, pulmonary

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edema, stroke, and other complications, which poses great harm to the fetus and can lead to intrauterine growth retardation, premature birth, and iatrogenic premature birth after secondary hypertension complications. Magnesium sulfate is a common anti-hypertensive drug in clinical practice, mostly used to treat convulsions, eclampsia, uremia, tetanus, and hypertensive encephalopathy. It is also commonly used to treat sedation, anti spasms, and anti-hypertensive effects. The principle of hypotension is to release magnesium ions in the body after intravenous administration, inhibit the central nervous system, reduce the release of acetylcholine, and dilate peripheral blood vessels to have a hypotensive effect[9]. Clinical trials have shown that magnesium sulfate has a significant therapeutic effect on blood pressure reduction, but there are relatively many side effects. After injection, it can cause symptoms such as facial flushing, sweating, and dry mouth. During rapid intravenous infusion, there may also be adverse reactions such as nausea, vomiting, and minimal nystagmus. Before and during use, magnesium sulfate must undergo regular knee tendon reactions, monitor breathing times, and promptly observe whether there are symptoms of magnesium poisoning[10]. Dou Juan et al.[11] added that magnesium sulfate intravenous infusion poses certain risks and requires slow intravenous infusion. At the same time, it is necessary to prepare a 10% concentration of calcium gluconate injection to prevent poisoning in the body. Immediately use calcium gluconate for emergency rescue. Therefore, given that the low safety and high risk of use of this drug, the treatment of patients with gestational hypertension should consider their maternal and infant safety, and choose safer anti-hypertensive drugs for treatment.

Methyldopa also belongs to anti-hypertensive drugs and can be converted into methyl epinephrine in the central nervous system after medication. Methyl epinephrine is a strong central nervous system α Receptor agonists can excite heterogeneous neurons between the nucleus tractus solitarius, motor blood vessels, and motor center of the medulla oblongata, thereby inhibiting the impulse transmission of the heart, kidney, and peripheral blood vessels by inhibiting the peripheral sympathetic nervous system, reducing peripheral vascular resistance and vasorenin activity, and achieving stable blood pressure lowering. Rabelol is also an anti-hypertensive drug, serving as the central nervous system α Receptors and β. The pharmacological mechanism of receptor antagonists is to slow down sinus rhythm and peripheral resistance by blocking adrenergic receptors, achieving the goal of blood pressure reduction[12]. The combination of two drugs can increase blood pressure control, reduce diastolic and systolic blood pressure, and urinary protein levels. In the study by Hao Jianmin et al.[13], it was pointed out that gestational hypertension can cause vascular endothelial damage due to persistent hypertension, leading to the release of a large amount of C-reactive protein in the body, further exacerbating inflammatory damage, causing angiotensin to take effect, exacerbating blood pressure rise, and at the same time, homocysteine is also continuously increasing, causing the contraction and flaky shedding of vascular endothelial cells, exacerbating the damage of hypertension to the body and vascular endothelium. Rabelol and methyldoba can target the injury and disease mechanism of hypertension mentioned above, through the central nervous system contained in both drugs α. Receptors exert a blocking effect, reducing peripheral resistance, while inhibiting excessive activation of sympathetic nerves, restoring normal pressure receptors in the body, improving hemodynamics, and stabilizing blood pressure levels[14]. Methyldopa can reach its peak after 4 hours of administration, and in combination with rabolol, it inhibits vascular impulse output, alleviates peripheral vascular pressure, and corrects and adjusts serum abnormal indicators. In addition to the above advantages, methyldopa can also reduce blood viscosity and uterine resistance, increase placental blood supply, and create a favorable physiological basis for the normal development of fetuses in the uterus. At the same time, it can improve maternal and infant oxygen metabolism by improving hemodynamics and correcting abnormal serum indicators, which is beneficial for the mother to control ideal blood pressure levels while maintaining and stabilizing normal fetal development[15-16]. In this study, it can also be observed that the combination of methyldopa and rabelol has therapeutic advantages for patients with gestational hypertension, such as ideal control of blood pressure and urinary protein indicators, normal hemodynamics, stable serum indicators, and low incidence of adverse pregnancy outcomes.

To sum up, the treatment effect of methyldopa combined with rabelol in patients with gestational hypertension is very good. It can control blood pressure and urine protein to reach the ideal range, effectively improve hemodynamic indicators, protect patient vascular endothelial function, and reduce the probability of adverse pregnancy outcomes caused by hypertension. It has great medical significance for ensuring maternal safety and safe production.

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