Original Article
Efficacy of magnesium sulfate combined with nifedipine for pregnancy-induced hypertension syndrome and its relation to glucose and lipid metabolism

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Abstract: Objective: To determine the efficacy of magnesium sulfate combined with nifedipine for pregnancy-induced hypertension syndrome (PIHS) and its influence on glucose and lipid metabolism. Methods: The clinical data of 124 cases of PIHS treated in Jiangxi Jiujiang Maternal and Child Care Centers from March 2020 to June 2022 were collected and retrospectively analyzed. Among them, 58 patients who received magnesium sulfate alone were enrolled as a control group, and the other 66 given magnesium sulfate combined with nifedipine were enrolled as a study group. The two groups were compared for treatment efficacy, blood pressure, fasting blood glucose (FBG) and blood lipid indexes (triglycerides (TG), high-density lipoprotein-cholesterol (HDL-C), total cholesterol (TC), and low-density lipoprotein - cholesterol (LDL-C)). Multivariate logistic regression analysis was performed to analyze the factors affecting outcome. Results: The study group showed a significantly higher total effective rate than the control group (P=0.008). After treatment, the study group showed significantly lower systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels than the control group (P<0.001). After treatment, the study group also showed lower levels of FBG, TC, TG, and LDL-C and a higher HDL-C level than the control group (P<0.001). Additionally, the incidences of cesarean section and postpartum hemorrhage were lower in the study group than those of the control group (both P<0.05). The two groups were not significantly different in premature delivery or low neonatal birth weight (both P>0.05), and the incidence of adverse reactions of the two groups was also not greatly different (P>0.05). According to multivariate logistic regression analysis, higher BMI (OR: 3.087, 95% CI: 1.295~7.358) and higher SBP (OR: 1.220, 95% CI: 1.001~1.487) at admission were independent risk factors for poor efficacy, while combined therapeutic regimen (OR: 0.018, 95% CI: 0.001~0.228) was an independent protective factor. Conclusion: Magnesium sulfate combined with nifedipine can deliver a powerful clinical efficacy for patients with PIHS by lowering blood pressure and the incidence of adverse pregnancy outcomes and by improving glucose and lipid metabolism.

Keywords: Magnesium sulfate, nifedipine, pregnancy-induced hypertension syndrome, glucose and lipid metabolism

Introduction

Pregnancy-induced hypertension syndrome (PIHS) is the most common complication in pregnancy, which can give rise to insufficient blood supply to the fetus and lower the antioxidant capacity and immunity of pregnant women, resulting in adverse pregnancy outcomes [1]. According to statistics, PIHS affects 5-10% of pregnant women [2]. These pregnant women face higher risks of pre-eclampsia, cesarean section, premature delivery before 37 weeks of pregnancy, neonatal birth weight below 2500 g, neonatal hospitalization and perinatal death, and also face a higher risk of cardiovascular disease in later life [3]. Reportedly, the incidence of hypertension in patients increased five times in the first five years after preeclampsia [4]. One study has also pointed out that 25-45% of women with pregnancy-induced hypertension develop hypertension within five years after delivery [5]. Therefore, in order to reduce the harm of PIHS to patients, it is of practical significance to find a safe and effective treatment for pregnancy-induced hypertension.
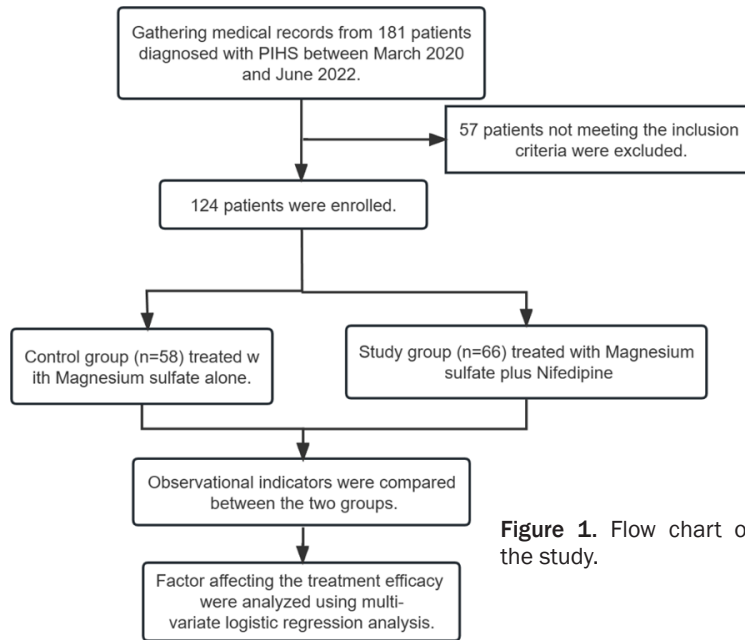
Figure 1. Flow chart of the study.

The pathogenesis of PIHS is complex and is still unclear, but the expression of various inflammatory factors and growth factors is considered to correlate with its development and progression [6]. Under the action of oxidative stress or lipid peroxide, a lipid metabolism disorder is correlated with inflammatory factors secreted by endothelial cells, followed by cell damage, which is one of the basic pathologic changes of PIHS [7, 8].

Drug therapy is a pivotal means to treat hypertension. It mainly aims at relieving vessel spasm and reducing blood pressure and heart load. However, some drugs may hurt the fetus, so it is necessary to carefully choose the treatment drugs [9]. Magnesium sulfate is a basic clinical treatment for PIHS, which can relieve small vessel spasm, but its blood pressure control effect is not satisfactory. It is unable to provide good efficacy for some patients when it is used alone, so it is usually used together with antihypertensive drugs [10]. Nifedipine is a calcium antagonist, which can strongly relax arterioles by inhibiting calcium ions from entering vascular smooth muscle and myocardial cells, thus rapidly and continuously reducing systemic blood pressure and increasing myocardial oxygen transport. Nifedipine has the characteristics of lowering blood pressure and resisting angina pectoris [11]. Prior research has reported the antihypertensive effect of magnesium sulfate and nifedipine in the treatment of preg-nancy-hypertension syndrome [12], but few studies have explored their effects on glucose and lipid metabolism and the factors affecting the efficacy. This study retrospectively evaluated the clinical effect of magnesium sulfate combined with nifedipine in the treatment of PIHS and analyzed the changes in glucose and lipid metabolism before and after treatment.

Materials and methods

Patient data

The clinical data of 124 cases of PIHS treated in Jiangxi Jiujiang Maternal and Child Care Centers from March 2020 to June 2022 were collected and retrospectively analyzed. Among them, 58 patients who received magnesium sulfate alone were enrolled as a control group, and the other 66 given magnesium sulfate combined with nifedipine were enrolled as a study group. This study was performed with approval from the Medical Ethics Committee of Jiangxi Jiujiang Maternal and Child Care Centres (Ethical approval number: 20200209). The process of the study is described in **Figure 1**.

Inclusion and exclusion criteria

Inclusion criteria: Patients who were diagnosed with PIHS according to the diagnostic criteria in the Guidelines for Hypertension and Preeclampsia in Pregnancy issued by the American College of Obstetricians and Gynecologists (ACOG) in 2019 [13]; patients with clinical manifestations of hypertension, proteinuria, and edema after 20 weeks of pregnancy, patients ≤40 years old, and those with detailed clinical data.

Exclusion criteria: Patients with abnormal glucose and lipid metabolism before pregnancy; patients with malignant tumor; patients with serious organic diseases or dysfunction of heart, liver or kidney; patients with hypertension before pregnancy; patients with nervous system diseases or severe cognitive dysfunction; and those who were allergic to drugs used in this study.

Index collection method

The clinical baseline data and laboratory index-related data of patients were collected from the electronic medical record system and LIS system. The collected data included age, gestational week, body mass index (BMI), fetal heart rate, uterine height, times of pregnancy, parity, place of residence, smoking history, SBP, DBP, triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), pregnancy outcome, and adverse reactions.

Evaluation criteria of clinical efficacy

Markedly effective: Within 12 weeks after delivery, the systolic blood pressure (SBP) and diastolic blood pressure (DBP) of patients returned to normal (SBP<140 mmHg (1 mmHg=0.133 kPa) and/or DBP<90 mmHg), and the clinical symptoms completely disappeared. Effective: Within 12 weeks after delivery, the SBP and DBP of patients decreased by ≥10 mmHg compared to before treatment, and the clinical symptoms were alleviated. Ineffective: Within 12 weeks after delivery, the patient's blood pressure had not changed significantly, and the clinical symptoms did not change or were even worsened. Overall response rate = markedly effective rate + effective rate.

Outcome measures

Primary outcome measures: (1) The treatment efficacy in both groups was assessed at the end of the 12th week postpartum. (2) The patients' SBP and DBP on the day before treatment initiation and at the end of the 12th week postpartum were documented. SBP and DBP were measured with a sphygmomanometer after keeping in a quiet state for 5 minutes without strenuous exercise.

Secondary outcome measures: (1) Fasting venous blood (3 mL) was collected the day before treatment initiation and 7 d after treatment, respectively, and the fasting blood glucose (FBG) and blood lipid indexes [triglyceride (TG), high-density lipoprotein-cholesterol (HDL-C), total cholesterol (TC), and low-density lipoprotein-cholesterol (LDL-C)] were detected by a Japanese OLYMPUS-AU600 automatic biochemical analyzer. (2) The pregnancy outcomes of patients were recorded, including cesarean section, preterm delivery, postpartum hemorrhage, or low birth weight. (3) The incidence of adverse reactions after treatment was counted.

Statistical analyses

SPSS 20.0 software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis of data. The chi-square test was used for comparing the rates, which was expressed as χ^2. Intra-group before-after comparison was conducted using the paired t test, and inter-group comparison was conducted using the independent t-test. For multiple group comparison, repeated measurement ANOVA was used, and Bonferroni test was used for post-test. Multiple logistic regression analysis was used to analyze the factors affecting the efficacy on patients. GraphPad Prism 7 (GraphPad Software, Inc., San Diego CA, USA) was adopted for figure drawing. P< 0.05 was considered a significant difference.

Results

Baseline data

According to the comparison of baseline data, the two groups were not greatly different in age, gestational week, body mass index (BMI), heart rate of fetus, uterine height, number of pregnancies, times of delivery, place of residence, or smoking history (all P>0.05, **Table 1**).

Comparison of efficacy between the two groups

According to comparison of efficacy, the observation group showed a higher overall response rate than the control group (93.94% *vs*. 77.59%, P=0.008, **Table 2**).

Comparison of blood pressure levels between the two groups before and after treatment

Before treatment, the two groups were not greatly different in SBP and DBP levels; while after treatment, the study group showed lower SBP and DBP levels than the control group (both P<0.001, **Figure 2**).

Comparison of glucose and lipid metabolism levels between the two groups before and after treatment

Before treatment, the two groups were similar in glucose and lipid metabolism levels (FBG, TC,

Table 1. Comparison of baseline data between the two groups

	Control group (n=58)	Study group (n=66)	t/χ²	P
Age (years)	29.7±4.1	29.5±4.5	0.257	0.797
Gestational weeks (weeks)	29.70±2.48	29.55±2.31	0.349	0.728
BMI (kg/m²)	24.45±1.19	25.03±1.37	0.991	0.324
Fetal heart rate	146.65±8.06	145.44±9.72	0.748	0.456
Uterine height (cm)	22.00±4.48	21.66±4.76	0.408	0.684
Times of pregnancies (times)			1.478	0.478
1	33 (56.90)	31 (46.97)		
2	20 (34.48)	26 (39.39)		
3	5 (8.62)	9 (13.64)		
Times of delivery			1.709	0.635
0	36 (62.07)	34 (51.52)		
1	16 (27.59)	21 (31.82)		
2	4 (6.90)	7 (10.61)		
3	2 (3.45)	4 (6.06)		
Place of residence			0.716	0.398
Urban area	40 (68.97)	50 (75.76)		
Rural area	18 (31.03)	16 (24.24)		
Smoking history			0.684	0.408
Yes	16 (27.59)	14 (21.21)		
No	42 (72.41)	52 (78.78)		

BMI: body mass index.

Table 2. Comparison of treatment efficacy between the two groups

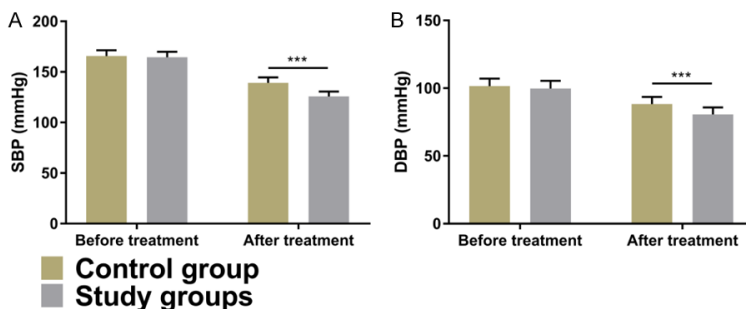|	Control group (n=58)	Study group (n=66)	t/χ	P
Markedly effective	28 (48.28)	43 (65.15)	7.560	0.023
Effective	17 (29.31)	19 (28.79)		
Ineffective	13 (22.41)	4 (6.06)		
overall response rate	45 (77.59)	62 (93.94)	6.979	0.008

Figure 2. Changes in blood pressure levels in the two groups before and after treatment. A. After therapy, the study group showed a lower SBP level than the control group (P<0.001). B. After therapy, the study group showed a lower DBP level than the control group (P<0.001). Note: ***P<0.001. SBP: Systolic blood pressure; DBP: Diastolic blood pressure.

TG, LDL-C and HDL-C), while after treatment, the study group showed lower levels of FBG, TC, TG, and LDL-C and a higher HDL-C level than the control group (all P<0.001, **Figure 3**).

Pregnancy outcomes of the two groups

According to statistics on the pregnancy outcomes, the two groups were different in the incidence of cesarean section and postpartum hemorrhage. The study group showed a lower incidence of cesarean section and postpartum hemorrhage than the control group (both P<0.05), but the premature delivery and low neonatal birth weight of the two groups were not greatly different (all P>0.05, **Table 3**).
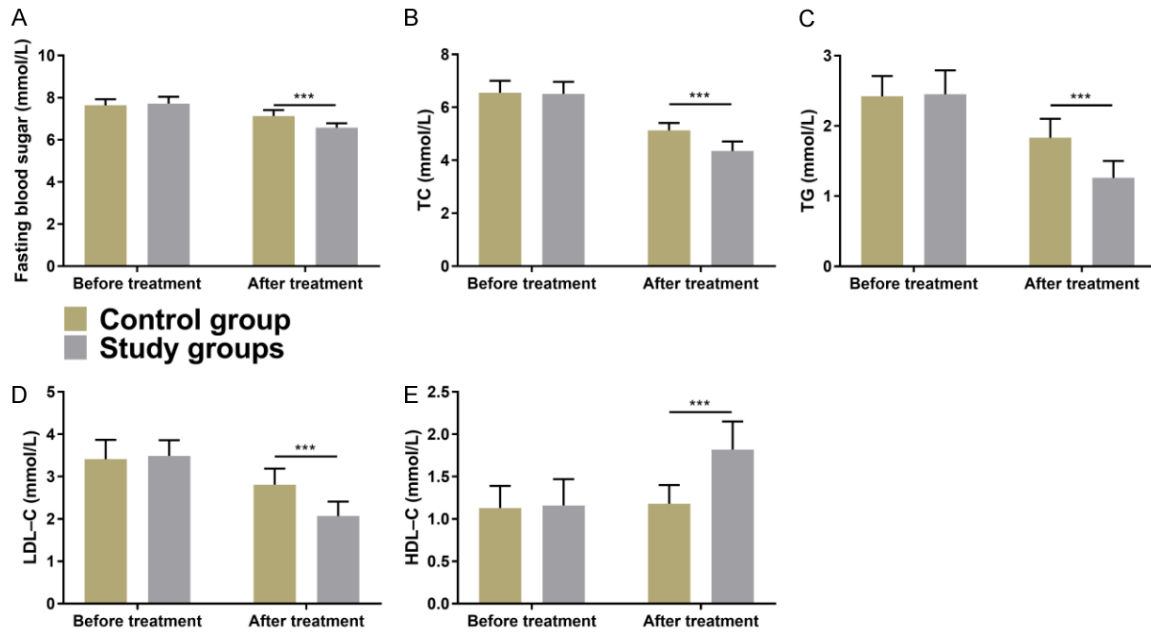
Figure 3. Changes in glucose and lipid metabolism in the two groups before and after treatment. A. After treatment, the study group showed a lower fasting blood glucose level than the control group (P<0.001). B. After therapy, the study group showed a lower TC level than the control group (P<0.001). C. After therapy, the study group showed a lower TG level than the control group (P<0.001). D. After treatment, the study group showed a lower LDL-C level than the control group (P<0.001). E. After treatment, the study group showed a higher HDL-C level than the control group (P<0.001). Note: ***P<0.001. TC: Total cholesterol; TG: Triglyceride; LDL-C: Low-density lipoprotein-cholesterol; HDL-C: High-density lipoprotein-cholesterol.

Table 3. Comparison of pregnancy outcomes between two groups

	Control group (n=58)	Study group (n=66)	χ^2	P
Cesarean section	15 (25.86)	8 (12.12)	3.858	0.049
Premature delivery	5 (8.62)	2 (3.03)	1.811	0.178
Postpartum hemorrhage	8 (13.79)	2 (3.03)	4.823	0.028
Low neonatal birth weight	6 (10.34)	3 (4.55)	1.542	0.214

Incidence of treatment-related adverse reactions in the two groups

The incidence of adverse reactions in the two groups was counted after surgery. According to the results, the incidence of adverse reactions was not significantly different between the two groups (P=0.580, **Table 4**).

Univariate analysis of facts affecting efficacy

According to the treatment efficacy, the patients were grouped into effective group (markedly effective + effective) or ineffective group. According to the results, the two groups were greatly different in age, BMI, SBP at admission, DBP at admission, fasting blood glucose at admission, TC at admission, TG at admission,

LDL-C at admission, HDL-C at admission, and therapeutic regimen (all P<0.05, **Table 5**).

Multivariate analysis of poor efficacy

According to multiple logistic regression analysis, higher BMI and higher SBP admission were independent risk factors for poor efficacy, and combined therapeutic regimen was an independent protective factor (**Table 6**).

Discussion

Pregnancy-induced hypertension syndrome PIHS shows a high incidence, but its pathogenesis is still under investigation. Some studies think the pathogenesis is related to old age, heredity, mental state, or high body mass index

Table 4. Comparison of adverse reactions between the two groups

	Control group (n=58)	Study group (n=66)	χ^2	P
Chest distress	3 (5.17)	3 (4.55)	0.026	0.871
Dizzy	2 (3.45)	4 (6.06)	0.458	0.499
Headache	1 (1.72)	3 (4.55)	0.787	0.375
Myasthenia	2 (3.45)	4 (6.06)	0.458	0.499
Total adverse reaction	10 (17.24)	14 (21.21)	0.312	0.577

Table 5. Univariate analysis of factors affecting treatment efficacy

	Effective group (n=107)	Ineffective group (n=17)	t/χ^2	P
Age (year)	29.1±4.1	32.5±4.2	3.166	0.002
Gestational weeks (weeks)	29.58±2.40	29.88±2.23	0.483	0.630
BMI (kg/m^2)	24.66±1.37	25.39±0.67	2.151	0.034
Fetal heart rate	146.15±9.30	145.00±6.62	0.490	0.625
Uterine height (cm)	21.61±4.70	23.17±3.89	1.298	0.197
Times of pregnancies			3.719	0.156
1 time	58 (54.21)	6 (35.29)		
2 times	39 (36.45)	7 (41.18)		
3 times	10 (9.34)	4 (23.53)		
Times of delivery			4.479	0.214
0 times	63 (58.88)	7 (41.18)		
1 time	32 (29.91)	5 (29.41)		
2 times	8 (7.48)	3 (17.65)		
3 times	4 (3.74)	2 (11.76)		
Place of residence			0.614	0.433
Urban area	79 (73.83)	11 (64.71)		
Rural area	28 (26.17)	6 (35.29)		
Smoking history			1.324	0.250
Yes	24 (22.43)	6 (35.29)		
No	83 (77.57)	11 (64.71)		
SBP at admission (mmHg)	164.37±5.27	168.71±5.64	3.125	0.002
DBP at admission (mmHg)	98.55±5.22	102.24±5.70	2.674	0.009
Fasting blood glucose at admission (mmol/L)	7.67±0.30	7.86±0.37	2.347	0.021
TC at admission (mmol/L)	6.49±0.49	6.87±0.40	3.037	0.003
TG at admission (mmol/L)	2.42±0.32	2.68±0.30	3.137	0.002
LDL-C at admission (mmol/L)	3.40±0.36	3.72±0.47	3.257	0.002
HDL-C at admission (mmol/L)	1.18±0.28	1.02±0.22	2.246	0.027
Therapeutic regimen			6.979	0.008
Magnesium sulfate alone	45 (42.06)	13 (76.47)		
Combined treatment	62 (57.94)	4 (23.53)		

BMI: body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; TC: Total cholesterol; TG: Triglyceride; LDL-C: Low-density lipoprotein-cholesterol; HDL-C: High-density lipoprotein-cholesterol.

[14]. Patients with PIHS have systemic vasospasm and slow blood flow velocity, which can easily give rise to ischemia and hypoxia of tissues and major organs, affecting fetal blood supply and finally resulting in adverse pregnancy outcomes [15]. Patients with PIHS have a relatively high blood Ca^{2+} level. A high blood Ca^{2+} level promotes parathyroid hormone secretion, and causes contraction of uterine smooth muscle, increase blood pressure and arteriole spasm, further increasing peripheral pressure of blood vessels, endothelial cell per-

Table 6. Multivariate analysis of factors affecting treatment efficacy

Factor	B	S.E,	Wals	Sig.	Exp (B)	95% CI of EXP (B)	
						Lower limit	Upper limit
Therapeutic regimen	-4.003	1.302	9.577	0.002	0.018	0.001	0.228
BMI	1.127	0.443	6.473	0.011	3.087	1.295	7.358
SBP at admission	0.199	0.101	3.900	0.048	1.220	1.001	1.487

BMI: body mass index; SBP: Systolic blood pressure.

meability, and proteinuria level, which finally promotes the development and progression of PIHS [16, 17]. Magnesium sulfate can prevent/reduce arteriolar spasm and prevent eclampsia by promoting the synthesis of prostacyclin in vascular endothelium. It can also improve coagulation and hemorheology indexes and alleviate blood stasis to help supply blood and oxygen to placenta and promote the continuation of pregnancy [18]. In the present study, the control group treated with magnesium sulfate showed better SBP and DBP levels after treatment, which further verified the mechanism of magnesium sulfate in patients with PIHS.

In this study, compared to the control group, the study group showed a higher overall response rate, and presented lower SBP and DBP levels after treatment, but the total incidence of adverse reactions was not greatly different between the two groups. The reasons may be as follows: Magnesium sulfate combined with nifedipine can play a synergistic role in dilating blood vessels, relieving spasm, and improving the hemodynamics of patients; besides, nifedipine will not be affected by gastrointestinal peristalsis, so the antihypertensive mechanism is in a constant state, which avoids serious fluctuations in blood pressure and contributes to a more stable antihypertensive effect [19]. The results are similar to those acquired by Xiang et al. [20]. They revealed that magnesium sulfate combined with nifedipine has a better antihypertensive effect than magnesium sulfate alone, with an overall response rate of 94.90%, and they also showed that the combination therapy could better reduce the plasma viscosity and urinary albumin of pregnant women. Yu et al. [21] found that magnesium sulfate combined with nifedipine can better alleviate the degree of oxidative stress and vascular endothelial cell injury in patients with pregnancy-induced hypertension, thus improving the level of blood pressure.

According to prior research [22], abnormal glucose and lipid metabolism can increase the risk of cardiovascular events in patients with PIHS. This study compared the glucose and lipid metabolism levels of patients before and after treatment. According to the results, the glucose and lipid metabolism and hemodynamic indexes of the two groups were improved, and the improvement in the group treated with nifedipine combined with magnesium sulfate was better. Reportedly, calcium antagonists can effectively inhibit the secretion of glucagon, improve the permeability of hepatocyte membrane and glucose, strengthen the inhibition of glycogen decomposition enzyme and gluconeogenesis enzyme activities, and thus improve the glucose metabolism ability of patients [23]. Nifedipine can also exert a strong effect on improving blood lipid. Houston et al. [24] pointed out that among 49 patients with mild/moderate essential hypertension, HDL-C increased significantly while TG decreased significantly after treatment with nifedipine. This suggests that nifedipine was effective in antihypertension, improving blood lipids, and reducing the risk of cardiovascular disease. Therefore, the combination with nifedipine provides a good effect of regulating glucose and lipid metabolism. Finally, this study analyzed the pregnancy outcomes and neonatal condition of the two groups and found significantly lower cesarean section rate and premature delivery rate in the group given combined drugs than those in the group who received single drug, suggesting the improvement effect of magnesium sulfate combined with nifedipine on the pregnancy outcomes. In order to explore the factors affecting the efficacy of treatment, multivariate logistic regression analysis was conducted. According to the results, higher BMI and higher SBP at admission were independent risk factors for poor efficacy, while combined therapeutic regimen was an independent protective factor. The reason may be that high BMI

and high SBP can increase the excitability of sympathetic nervous system and aggravate the contraction of arterioles, which increases the difficulty in effectively controlling blood pressure [25, 26]. The results also suggest that magnesium sulfate combined with nifedipine can improve the efficacy.

This study has some limitations. First, in such a retrospective study, there are some unavoidable biases. Second, limited to the follow-up time of the study, the long-term impact on postpartum women is not clear. Finally, this study has not collected data on the postnatal growth of the baby. We hope to explore the effects of this therapeutic regimen on the baby in the future.

In sum, magnesium sulfate combined with nifedipine can deliver a strong clinical efficacy for patients with PIHS by lowering blood pressure and the incidence of adverse pregnancy outcomes, and improving glucose and lipid metabolism.

Disclosure of conflict of interest

None.

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References

[1] Khedagi AM and Bello NA. Hypertensive disorders of pregnancy. Cardiol Clin 2021; 39: 77-90.

[2] Agrawal A and Wenger NK. Hypertension during pregnancy. Curr Hypertens Rep 2020; 22: 64.

[3] Kintiraki E, Papakatsika S, Kotronis G, Goulis DG and Kotsis V. Pregnancy-induced hypertension. Hormones (Athens) 2015; 14: 211-223.

[4] Engeland A, Bjorge T, Klungsoyr K, Skjaerven R, Skurtveit S and Furu K. Preeclampsia in pregnancy and later use of antihypertensive drugs. Eur J Epidemiol 2015; 30: 501-508.

[5] Veerbeek JH, Hermes W, Breimer AY, van Rijn BB, Koenen SV, Mol BW, Franx A, de Groot CJ and Koster MP. Cardiovascular disease risk factors after early-onset preeclampsia, late-onset preeclampsia, and pregnancy-induced hypertension. Hypertension 2015; 65: 600-606.

[6] Kametas NA, Nzelu D and Nicolaides KH. Chronic hypertension and superimposed preeclampsia: screening and diagnosis. Am J Obstet Gynecol 2022; 226: S1182-S1195.

[7] Wang Y, Liu RX and Liu H. Association of adiponectin gene polymorphisms with hypertensive disorder complicating pregnancy and disorders of lipid metabolism. Genet Mol Res 2015; 14: 15213-15223.

[8] Naviaux RK. Metabolic features of the cell danger response. Mitochondrion 2014; 16: 7-17.

[9] Abalos E, Duley L, Steyn DW and Gialdini C. Antihypertensive drug therapy for mild to moderate hypertension during pregnancy. Cochrane Database Syst Rev 2018; 10: CD002252.

[10] Reddy D, Fallah A, Petropoulos JA, Farrokhyar F, Macdonald RL and Jichici D. Prophylactic magnesium sulfate for aneurysmal subarachnoid hemorrhage: a systematic review and meta-analysis. Neurocrit Care 2014; 21: 356-364.

[11] Hosoda S. Clinical experience with nifedipine in the treatment of angina pectoris in Japan. Drugs 2006; 66: 4-6.

[12] Wang Y, Zhang X, Han Y, Yan F and Wu R. Efficacy of combined medication of nifedipine and magnesium sulfate on gestational hypertension and the effect on PAPP-A, VEGF, NO, Hcy and vWF. Saudi J Biol Sci 2019; 26: 2043-2047.

[13] ACOG practice bulletin No. 202: gestational hypertension and preeclampsia. Obstet Gynecol 2019; 133: 1.

[14] Hromadnikova I. Pathogenesis of pregnancy-related complications 1.0 and 2.0. Int J Mol Sci 2022; 23: 3020.

[15] Letourneur A, Freret T, Roussel S, Boulouard M, Divoux D, Toutain J, Bernaudin M, Schumann-Bard P, Bouet V and Touzani O. Maternal hypertension during pregnancy modifies the response of the immature brain to hypoxia-ischemia: sequential MRI and behavioral investigations. Exp Neurol 2012; 233: 264-272.

[16] Qu H and Khalil RA. Vascular mechanisms and molecular targets in hypertensive pregnancy and preeclampsia. Am J Physiol Heart Circ Physiol 2020; 319: H661-H681.

[17] Bukoski RD and Kremer D. Calcium-regulating hormones in hypertension: vascular actions. Am J Clin Nutr 1991; 54 Suppl: 220S-226S.

[18] Schauf B, Mannschreck B, Becker S, Dietz K, Wallwiener D and Aydeniz B. Evaluation of red blood cell deformability and uterine blood flow in pregnant women with preeclampsia or iugr and reduced uterine blood flow following the intravenous application of magnesium. Hypertens Pregnancy 2004; 23: 331-343.

[19] Yoshida K, Furuta K, Adachi K, Ohara S, Morita T, Tanimura T, Nakata S, Miki M, Koshino K and Kinoshita Y. Effects of anti-hypertensive drugs on esophageal body contraction. World J Gastroenterol 2010; 16: 987-991.

[20] Xiang C, Zhou X and Zheng X. Magnesium sulfate in combination with nifedipine in the treatment of pregnancy-induced hypertension. Pak J Med Sci 2020; 36: 21-25.

[21] Yu X and Zhou Q. Effects of nifedipine tablets combined with magnesium sulfate on blood coagulation index, oxidative stress, NO and ET-1 Levels in patients with pregnancy hypertension. Front Surg 2022; 9: 862676.

[22] Mai C, Hou M, Chen R, Duan D, Xu H, Lin X, Wen J, Lv L, Lei Q and Niu J. Cardiovascular risk factors in Chinese women with a history of gestational diabetes mellitus. Int J Clin Exp Med 2015; 8: 21694-21698.

[23] Salhanick SD and Shannon MW. Management of calcium channel antagonist overdose. Drug Saf 2003; 26: 65-79.

[24] Houston MC, Olafsson L and Burger MC. Effects of nifedipine GITS and atenolol monotherapy on serum lipids, blood pressure, heart rate, and weight in mild to moderate hypertension. Angiology 1991; 42: 681-690.

[25] Savitri AI, Zuithoff P, Browne JL, Amelia D, Baharuddin M, Grobbee DE and Uiterwaal CS. Does pre-pregnancy BMI determine blood pressure during pregnancy? A prospective cohort study. BMJ Open 2016; 6: e011626.

[26] Shawkat E, Mistry H, Chmiel C, Webster L, Chappell L, Johnstone ED and Myers JE. The effect of labetalol and nifedipine MR on blood pressure in women with chronic hypertension in pregnancy. Pregnancy Hypertens 2018; 11: 92-98.