Effects of magnesium sulfate combined with labetalol on inflammatory stress and pregnancy outcome of patients with gestational hypertension

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Received September 22, 2023; Accepted December 21, 2023

DOI: 10.3892/etm.2024.12554

Abstract. Gestational hypertension (GH) is a common disorder during pregnancy that can cause adverse pregnancy outcomes. In the present study, magnesium sulfate ($MgSO_4$) combined with labetalol was used for clinical treatment. Randomized controlled trial was conducted in 100 patients with GH, documented in the Department of Obstetrics and Gynecology (Taicang TCM Hospital) grouped into the experimental (Expt) and control (Ctrl) groups (n=50 cases/group). The Ctrl group was treated with $MgSO_4$, whereas the Expt group was treated with $MgSO_4$ + labetalol. The systolic blood pressure (SBP) and diastolic blood pressure (DBP) in the Expt group were not significantly different from those in the Ctrl group (P>0.05). By contrast, the SBP and DBP were significantly lower after treatment than those before treatment in both groups (P<0.05). Whole blood viscosity, plasma viscosity and hematocrit were significantly lower in the Expt group compared with those in the Ctrl group after treatment (P<0.05). High mobility group box-1 protein, homocysteine and serum cystatin C levels in the Expt group were also markedly lower than those in the Ctrl group after treatment (P<0.05). In the Expt group, the rate of spontaneous vaginal delivery was much higher, whereas the rates of cesarean section and postpartum hemorrhage were markedly lower than those in the Ctrl group (P<0.05). The occurrence of fetal intrauterine distress, placental abruption, neonatal asphyxia, premature birth and neonatal death were also significantly lower in the Expt group than those in the Ctrl group (P<0.05). In conclusion, $MgSO_4$ + labetalol could improve inflammatory stress and the hemodynamics of patients with GH, and may have a marked antihypertensive effect. Thus, it may improve pregnancy outcome and reduce perinatal complications.

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Key words: magnesium sulfate, labetalol, gestational hypertension, high mobility group box-1 protein, fetal intrauterine distress, inflammatory stress

Introduction

Gestational hypertension (GH) is a unique condition that affects pregnant women, which predominantly occurs after 20 weeks of pregnancy and 2 weeks after delivery. Some patients with GH also exhibit proteinuria or edema, and severe cases are associated with headaches, blurred vision, upper abdominal pain, convulsion and coma (1-3). A pregnant woman is considered to have hypertension when their systolic blood pressure (SBP) exceeds 140 mmHg or their diastolic blood pressure (DBP) exceeds 90 mmHg. Being overweight, pre-pregnancy hypertension, pregnancy with multiple births, chronic diseases and/or poor diet (high salt and fat) are all risk factors for GH (4,5). GH not only harms the mother, but can also affect the growth and development of the fetus. Hypofunction of the placenta caused by GH can lead to various complications, such as intrauterine growth retardation, stillbirth, premature delivery or asphyxia, and can damage the organs of newborns to varying degrees (6,7). The fetal nervous system can also be affected, resulting in adverse long-term cognitive outcomes in infants (8). Therefore, if hypertension occurs during pregnancy, pregnant women and their families should pay attention to it and actively receive prenatal examinations, in order to ensure timely detection of the disease and reasonable treatment to minimize harm (9).

GH should be treated actively, whether hypertension is present before or after pregnancy. It is generally considered

that if DBP exceeds 12.0 kPa (90 mmHg), in two measurements of the same arm taken >6 h apart, it should be treated in a timely manner. If blood pressure is >21.3/14.6 kPa (160/110 mmHg), this is also an absolute indication for the use of antihypertensive drugs even without clinical symptoms (10-13). Clinical treatment measures generally include a low-salt diet, ensuring a balance between work and rest, elimination of mental over-stress and adequate sleep. The aforementioned general measures can restore the blood pressure of patients with mild hypertension to normal. If the aforementioned measures are ineffective, stepped care can be given according to blood pressure level (14,15). Calcium channel blockers, such as nifedipine, nicardipine and diltiazem, can be applied in the first and second trimesters of pregnancy, but should not be used ~2 weeks before labor. Since calcium channel blockers can inhibit the contractile force of the uterine smooth muscle and affect the progress of labor, they are not suitable for patients in labor. In developed countries, methyldopa (tablets, central sympathoinhibitor) is the first choice of treatment for GH syndrome, and is recognized as the safest and most effective therapeutic drug (16-18). At present, no fetal toxicity has been found in response to methyldopa, and it is the only drug that has been proven to be safe after long-term follow-up into childhood. The only disadvantage is that it has a strong sedative effect, which limits its use (19). Sodium nitroprusside is a powerful vasodilator, which is only suitable for pregnant women in hypertensive crisis for which other antihypertensive drugs are ineffective, and the prenatal application of this drug should not exceed 4 h (20). Labetalol is an α-adrenoceptor blocker, as well as a β-adrenoceptor blocker, which is utilized to treat hypertension. Its principle is to block the adrenoceptor, slow down ventricular rhythm and reduce peripheral vascular resistance (21). Notably, no antihypertensive drugs are completely safe for GH, but allowing blood pressure to rise is considered more dangerous. Thus, for the clinical treatment of GH, antihypertensive drugs targeted at the conditions of different patients should be selected on the basis of fully weighing advantages and disadvantages (22).

A careful decision should be made regarding the clinical medication of patients with GH, because the effects and side effects of drugs differ. Magnesium sulfate ($MgSO_4$) is the most commonly used drug for treating GH and preventing severe eclampsia (23). The clinical effects and toxicity of $MgSO_4$ are related to its concentration in the plasma. The disappearance of the patellar reflex in mothers at plasma concentrations between 3.5-5 mmol/l gives the first warning of impending toxicity. With careful management and monitoring of $MgSO_4$, maternal toxicity is very rare (24). The use of multiple drugs is a common strategy for clinical treatment, such as $MgSO_4$ + nifedipine (25). To identify an effective treatment option, a randomized controlled study of $MgSO_4$ in combination with Labetalol for the treatment of GH was performed. Subsequently, inflammatory factors, hemorheology, pregnancy outcome and perinatal complications of the two groups were assessed, and the effect of $MgSO_4$ + labetalol on the clinical treatment of patients with GH was further discussed. The present study may provide reference for the clinical treatment of GH.

Methods and materials

Research objects. A total of 100 patients with GH, who were registered in the Department of Obstetrics and Gynecology, Taicang TCM Hospital Affiliated to Nanjing University of Chinese Medicine between June 2020 and June 2022, were recruited to the present study. The present study adhered to The Declaration of Helsinki, and was approved and implemented by the Ethics Committee of Taicang Hospital of TCM (approval no. 2022026). All of the patients voluntarily participated and signed informed consent forms prior to the study. During the intervention, the patients' right of privacy and confidentiality was respected, and all information obtained from the patients was kept strictly confidential.

The inclusion criteria were as follows: i) The patients could provide complete clinical data; ii) they were 18-36 years old; iii) they were conscious and were able to communicate normally; iv) they had not received any drug treatment; v) they had a natural pregnancy; and vi) only a single fetus was observed.

The exclusion criteria were as follows: i) Patients had severe cardiac, liver or renal insufficiency; ii) they were severely malnourished; iii) they dropped out of the experiment and did not complete the treatment process; and iv) they had recently suffered from an infection.

Experimental instruments and reagents. The experimental instruments used were as follows: DHM-30D automatic height and weight scale (Zhengzhou Dingheng Electronic Technology Co., Ltd.), diving mercury sphygmomanometer (Yuwell Medical Equipment & Supply Co., Ltd.) and automatic hemorheology analyzer SH210A (Shanghai Langyi Medical Equipment Co., Ltd.).

The experimental reagents included: 5% $MgSO_4$ (Shandong Pingsen Biotechnology Co., Ltd.), 10% glucose solution (Guizhou Tiandi Pharmaceutical Co., Ltd.), 25% $MgSO_4$ (Shandong Pingsen Biotech Co., Ltd.), 5% glucose solution (Guizhou Tiandi Pharmaceutical Co., Ltd.), labetalol (Shanghai Acebright Pharmaceuticals Group Co., Ltd.) and ELISA kits for HMGB1 (cat. no. ml085468), homocysteine (Hcy; cat. no. ml092715) and CysC (cat. no. ml003222) all from Shanghai Enzyme-linked Biotechnology Co., Ltd.

Therapeutic methods. The patients in both groups were given routine basic treatment, including sedation, oxygen inhalation and sodium restriction. The patients' breathing, blood pressure and heart rate were closely monitored, and timely treatment was carried out in case of abnormal conditions of the mothers and infants.

In the Ctrl group, patients were administered $MgSO_4$. Briefly, 15 ml 5% $MgSO_4$ and 20 ml 10% glucose solution were mixed and administered via an intravenous drip (1-2 g/h $MgSO_4$) and, 50 ml 25% $MgSO_4$ and 800 ml 5% glucose solution were mixed and administered via an intravenous drip (1-2 g/h $MgSO_4$) later the same day, this was repeated daily, with a 1-week course of treatment.

In the Expt group, in addition to the drug administered to the Ctrl group, the patients were given an intravenous drip of 100 mg labetalol mixed with 250 ml 5% glucose solution. After the patients' blood pressure was reduced to the expected

value (DBP, 90 mmHg) and stabilized, oral labetalol 100 mg was administrated, three times a day until delivery (26).

Determination of basic parameters of patients. First, patients were asked to remove their hats and shoes, and their height and weight were determined according to the unified side-face standard. During the measurement, the patients were requested to stand in the center of the pedal of the DHM-30D automatic height and weight scale, and to maintain a standing position with eyes level ahead, arms down and heels together for 5 sec. Subsequently, the patients were allowed to rest for ~15 min, and their SBP and DBP were measured using the diving mercury sphygmomanometer. Notably, the blood pressure of both upper arms was measured during the first measurement.

In addition, overnight-fasting venous blood was collected from the patients in two groups before and after treatment in the morning, and the supernatant was obtained after centrifugation at 1,500 x g at 4˚C for 15 min. The inflammatory factor indicators, high mobility group box-1 protein (HMGB1), homocysteine (Hcy) and serum cystatin C (CysC), were detected by ELISA according to manufacturer's protocols. The automatic hemorheological analyzer SH210A was used to detect hemorheological indicators, including whole blood viscosity (WBV), plasma viscosity (PV), and hematocrit (HCT), of the two groups before and after treatment. The pregnancy outcomes in the two groups, including cesarean section, spontaneous vaginal delivery and postpartum hemorrhage, were followed up. Perinatal complications, including fetal intrauterine distress (FIUD), placental abruption, neonatal asphyxia, premature birth and neonatal death, were also recorded.

Statistical analysis. The research data were analyzed using SPSS 19.0 (IBM Corp.), with measurement data presented as the mean ± standard deviation and enumeration data as value (%). The patient's basic information was analyzed using unpaired t-tests. Comparison of pregnancy outcomes was analyzed using the χ^2 test, whereas comparison of perinatal complications was analyzed using the Fisher's exact test. A mixed ANOVA was performed in every indicator between Expt and Ctrl groups, pre and post treatment. $P<0.05$ was considered to indicate a statistically significant difference.

Results

Study design and patient enrollment. A total of 100 patients with GH were randomly divided into the Expt group and Ctrl group (n=50 cases/group). In the Expt group, the age of patients was 21-40 years, the mean age was 26.78±5.54 years, the gestational age was 31-38 weeks, and the average gestational age was 35.17±2.05 weeks. There were 32 primiparas and 18 multiparas. In the Ctrl group, the age, average age, gestational age and average gestational age were 20-38 years, 25.59±6.14 years, 30-37 and 36.28±2.24 weeks, respectively. There were 30 primiparas and 20 multiparas in the Ctrl group. There was no significant difference in age, gestational age and pregnancy history between the Expt group and the Ctrl group ($P>0.05$), indicating comparability between the groups (Table I).

Table I. Baseline data of the Expt and Ctrl groups.

Characteristic	Expt group	Ctrl group	P-value
Age, years	26.78±5.54	25.59±6.14	>0.05
Gestational age, weeks	35.17±2.05	36.28±2.24	>0.05
Pregnancy history			>0.05
Primiparas	32	30	
Multiparas	18	20	

Ctrl, control; Expt, experimental.

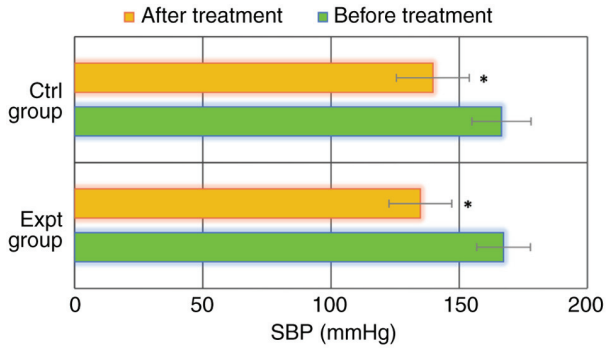

Figure 1. Comparison of SBP before and after treatment in two groups. *P<0.05 vs. before treatment. Ctrl, control; Expt, experimental; SBP, systolic blood pressure.

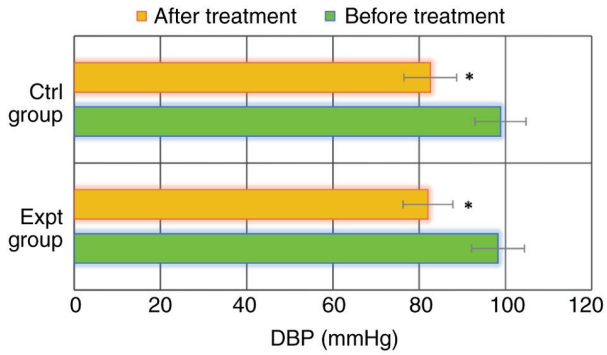

Figure 2. Comparison of DBP before and after treatment in two groups. *P<0.05 vs. before treatment. Ctrl, control; DBP, diastolic blood pressure; Expt, experimental.

Comparison of blood pressure values between groups before and after treatment. As shown in Figs. 1 and 2, SBP and DBP were 167.29±10.45 and 98.28±6.14 mmHg, respectively, in the Expt group before treatment. SBP and DBP after treatment reached 134.81±12.25 and 82.03±5.77 mmHg, respectively. In the Ctrl group, SBP and DBP were 166.51±11.53 and 98.84±5.93 mmHg before treatment, and 139.72±14.22 and 82.58±6.12 mmHg after treatment, respectively. SBP and DBP in the Expt group before treatment were not significantly different from those in the Ctrl group ($P>0.05$). In addition, SBP and DBP in the Expt group after treatment were also not significantly different from those in the Ctrl

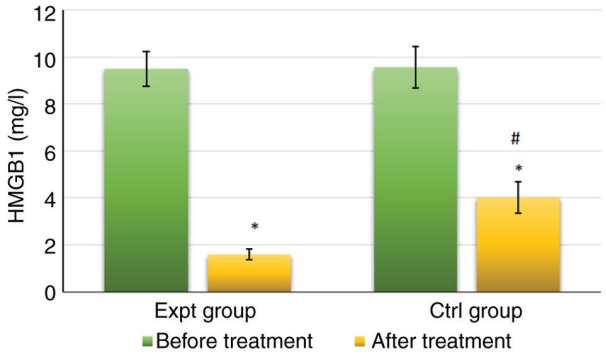

Figure 3. Comparison of HMGB1 levels between the two groups before and after treatment. *P<0.05 vs. before treatment; #P<0.05 vs. Expt group. Ctrl, control; Expt, experimental; HMGB1, high mobility group box-1 protein.

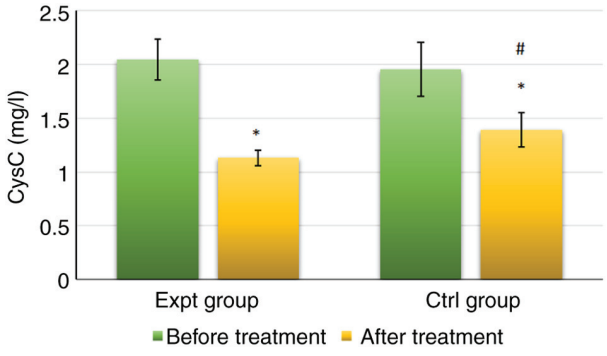

Figure 5. Comparison of serum CysC levels between the two groups before and after treatment. *P<0.05 vs. before treatment; #P<0.05 vs. Expt group. Ctrl, control; CysC, cystatin C; Expt, experimental.

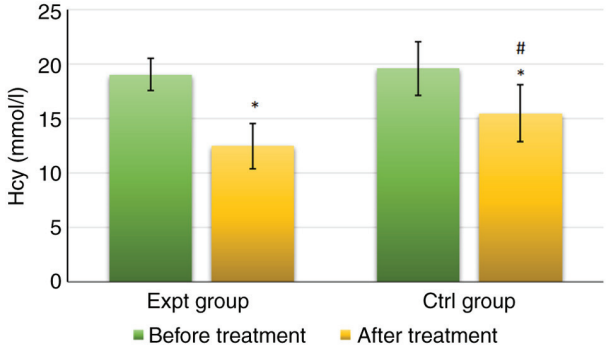

Figure 4. Comparison of Hcy levels between the two groups before and after treatment. *P<0.05 vs. before treatment; #P<0.05 vs. Expt group. Ctrl, control; Expt, experimental; Hcy, homocysteine.

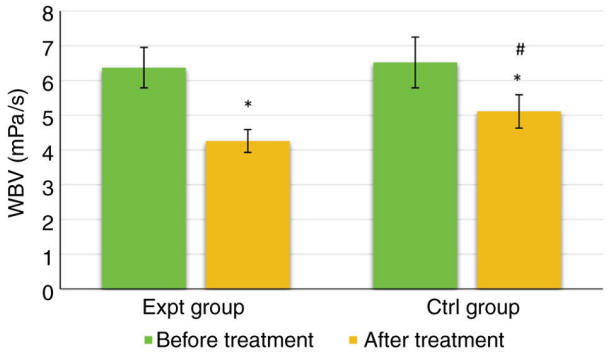

Figure 6. Comparison of WBV between the two groups before and after treatment. *P<0.05 vs. before treatment; #P<0.05 vs. Expt group. Ctrl, control; Expt, experimental; WBV, whole blood viscosity.

group (P>0.05). Notably, SBP and DBP after treatment were significantly lower than those before treatment in both groups (P<0.05). These data indicated that both SBP and DBP were significantly reduced in patients with GH treated with $MgSO_4$, regardless of whether they were also treated with labetalol or not.

Comparison of inflammatory factor indicators between groups before and after treatment. As shown in Fig. 3, the levels of HMGB1in the Expt group were 9.48±0.75 mg/l before treatment and 1.58±0.23 mg/l after treatment. The levels of HMGB1 in the Ctrl group were 9.57±0.88 mg/l before treatment and 4.02±0.68 mg/l after treatment. No significant difference was observed in HMGB1 levels between the Expt and Ctrl groups before treatment (P>0.05). By contrast, HMGB1 levels were significantly lower in the Expt group than that in Ctrl group after treatment (P<0.05). HMGB1 levels after treatment were also significantly lower than those before treatment in both groups (P<0.05).

As shown in Fig. 4, Hcy levels in the Expt group reached 19.02±1.48 mmol/l before treatment and 12.48±2.08 mmol/l after treatment. Hcy levels in the Ctrl group were 19.58±2.47 mmol/l before treatment and 15.44±2.61 mmol/l after treatment. There was no significant difference in Hcy levels between the groups before treatment (P>0.05). However, Hcy levels were significantly lower in the Expt group than those in the Ctrl group after treatment (P<0.05). Furthermore, Hcy levels after treatment were significantly lower than those before treatment in both groups (P<0.05).

As shown in Fig. 5, the serum CysC levels in the Expt group reached 2.04±0.19 mg/l before treatment and 1.13±0.07 mg/l after treatment. CysC levels in the Ctrl group reached 1.95±0.25 mg/l before treatment and 1.39±0.16 mg/l after treatment. No significant difference was detected in CysC levels between the groups before treatment (P>0.05). Conversely, CysC levels were significantly lower in the Expt group than those in the Ctrl group after treatment (P<0.05). In addition, CysC levels after treatment were significantly lower than those before treatment in both groups (P<0.05). Taken together, these data indicated that the addition of labetalol was more effective in reducing the level of inflammation in patients with GH.

Comparison of hemorheological indicators between groups before and after treatment. As shown in Fig. 6, the WBV of the Expt group was 6.37±0.58 mPa/s before treatment and 4.26±0.33 mPa/s after treatment. The WBV of the Ctrl group was 6.52±0.73 mPa/s before treatment and 5.11±0.48 mPa/s after treatment. There was no significant difference in WBV between the groups before treatment (P>0.05). However, WBV was significantly lower in the Expt group than that in the Ctrl group after (P<0.05). The WBV of both groups was significantly lower after treatment than those before (P<0.05).

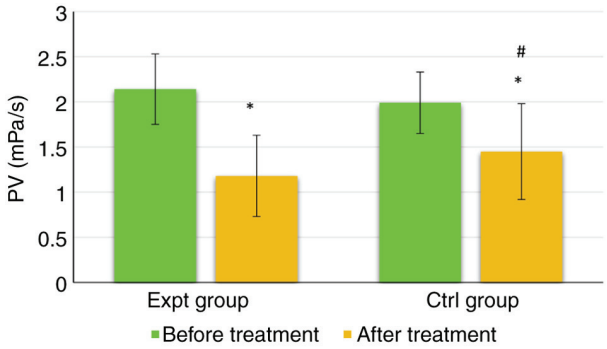

Figure 7. Comparison of PV between the two groups before and after treatment. *P<0.05 vs. before treatment; #P<0.05 vs. Expt group. Ctrl, control; Expt, experimental; PV, plasma viscosity.

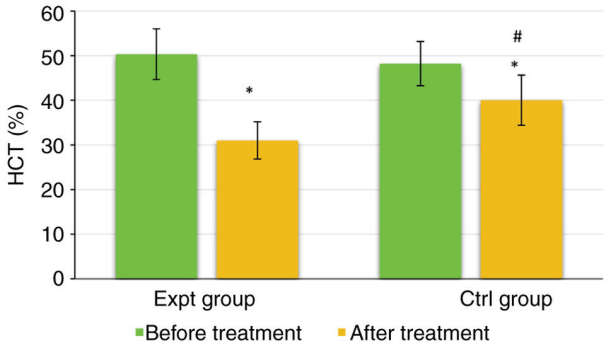

Figure 8. Comparison of HCT between the two groups before and after treatment. *P<0.05 vs. before treatment; #P<0.05 vs. Expt group. Ctrl, control; Expt, experimental; HCT, hematocrit.

As shown in Fig. 7, the PV of the Expt group reached 2.14±0.39 mPa/s before treatment and 1.18±0.45 mPa/s after treatment. The PV of the Ctrl group was 1.99±0.34 mPa/s before treatment and 1.45±0.53 mPa/s after treatment. Notably, there was no significant difference in PV between the groups before treatment (P>0.05). However, the PV was significantly lower in the Expt group than that in the Ctrl group (P<0.05). Furthermore, the PV of both groups was significantly lower after treatment than before treatment (P<0.05).

As shown in Fig. 8, the HCT of the Expt group was 50.34±5.68% before treatment and 31.02±4.17% after treatment. The HCT of the Ctrl group was 48.22±4.95% before treatment and 40.02±5.61% after treatment. There were no significant differences in HCT between the two groups before treatment (P>0.05). However, the HCT of the Expt group was significantly lower than that of the Ctrl group after treatment (P<0.05). The HCT in both groups was significantly lower after treatment than those before treatment (P<0.05). Taken together, these data indicated that the addition of labetalol was more effective in improving the hemodynamics of patients and producing antihypertensive effects.

Comparison of pregnancy outcomes between groups. As shown in Table II, there were 40 cases of spontaneous vaginal delivery (80%), 8 cases of cesarean section (16%) and 2 cases of postpartum hemorrhage (4%) in the Expt group. In the Ctrl group, there were 28 cases (56%) of spontaneous vaginal delivery, 15 cases (30%) of cesarean section and 7 cases (14%) of postpartum hemorrhage. The spontaneous vaginal delivery rate was significantly higher in the Expt group than that in the Ctrl group (P<0.05). By contrast, the cesarean section rate and postpartum hemorrhage rate of the Expt group were significantly lower than those in the Ctrl group (P<0.05). These data indicated that the addition of labetalol may improve pregnancy outcome.

Table II. Comparison of pregnancy outcomes between groups.

Outcome	Expt group, n (%)	Ctrl group, n (%)	χ^2	P-value
Spontaneous delivery	40 (80)	28 (56)	7.026	0.0298
Cesarean section	8 (16)	15 (30)		
Postpartum hemorrhage	2 (4)	7 (14)		

Table III. Comparison of perinatal complications between groups.

Complications	Expt group, n (%)	Ctrl group, n (%)	χ^2	P-value
FIUD	2 (4)	4 (8)	0.989	>0.05
Placental abruption	1 (2)	3 (6)		
Neonatal asphyxia	1 (2)	3 (6)		
Premature birth	5 (10)	12 (24)		
Neonatal death	0 (0)	1 (2)		

Ctrl, control; Expt, experimental; FIUD, fetal intrauterine distress.

Comparison of perinatal complications between groups. As shown in Table III, in the Expt group, there were 2 cases of FIUD (4%), 1 case of placental abruption (2%), 1 case of neonatal asphyxia (2%), 5 cases of premature birth (10%) and 0 cases of neonatal death (0%). In the Ctrl group, there were 4 cases of FIUD (8%), 3 cases of placental abruption (6%), 3 cases of neonatal asphyxia (6%), 12 cases of premature birth (24%) and 1 case of death (2%). The incidence of FIUD, placental abruption, neonatal asphyxia, premature birth and death was significantly lower in the Expt group than that in the Ctrl group. These data indicated that the addition of labetalol may result in fewer cases of perinatal complications.

Discussion

GH mainly refers to patients with normal blood pressure before pregnancy, whose blood pressure rises above normal values during or after pregnancy, with a series of related symptoms. GH is mainly associated with increased blood pressure, as well as edema, headache, dizziness and other phenomena in some patients, and even convulsions in severe cases (27,28). Long-term high blood pressure can result in serious harm

to the fetus and mother, and even prove fatal. Most patients exhibit symptoms of systemic arteriolar spasm, which can cause insufficiency of blood supply in the microcirculation of organs throughout the body. In severe cases, GH can even lead to failure and necrosis of all organs (29). At present, effective control of blood pressure is the key to clinical treatment of GH, and spasmolysis and pressure reduction are the basic principles of treatment. Both labetalol and $MgSO_4$ are commonly used drugs for treating GH (30-33). Therefore, the present study recruited 100 patients with GH, and randomly split them into the Ctrl and Expt groups. The Ctrl group was treated with $MgSO_4$, whereas the Expt group was administered $MgSO_4$ + labetalol. There were no statistically significant differences in age, gestational age and pregnancy history between the groups ($P>0.05$), which indicates that the groupings used were reasonable.

SBP and DBP of the Expt group after treatment were not statistically different compared with those in the Ctrl group ($P>0.05$); however, SBP and DBP in both groups were significantly lower after treatment than before treatment ($P<0.05$). The results of the present study are consistent with the findings of an open-label, randomized controlled trial (34). However, recent studies have reported the effect of labetalol on blood pressure control (35,36), though its potency has not been elucidated. Thus, the effectiveness of labetalol in controlling blood pressure needs to be evaluated in a separate study.

Further comparisons of inflammatory factors indicated that HMGB1, Hcy and serum CysC levels in the two groups were significantly lower after treatment, and those in the Expt group were also markedly lower than those in the Ctrl group after treatment ($P<0.05$). HMGB1 is a crucial late-stage pro-inflammatory factor, which has greater clinical significance than tumor necrosis factor (TNF), interleukin-1 and other early-stage immediate inflammatory factors (37). In addition, numerous studies have identified the close connection between HMGB1 and TNF-α (38,39). Hcy is a sulfur-containing amino acid in the human body, which is an intermediate metabolite of methionine and cysteine. Increased levels of Hcy can damage endothelial cells, disrupt the release and secretion balance of vasoactive substances, and promote the occurrence and development of hypertension (40). Serum CysC is a new endogenous biomarker which is regulated by transforming growth factor-β1 (41). As a sensitive and accurate indicator of early renal function damage, it also has been reported that high serum CysC levels are associated with abnormal cardiac diastolic properties in elderly Chinese patients with heart failure with a preserved ejection fraction (42), CysC also has the potential of tumor indication (43). Studies on the regulation of the inflammatory response by labetalol are rare. Xu *et al* (44,45) conducted several studies, which reported that labetalol can improve the TNF-α-induced separation of HTR-8/SVneo trophoblast cells from the endothelial cell network (44); furthermore, labetalol has been shown to reduce inflammatory factor inducible nitric oxide synthase levels by increasing the expression of endothelial nitric oxide synthase (45), thereby demonstrating that CysC was a key factor in inflammation. Notably, the present findings indicated that $MgSO_4$ + labetalol could effectively improve inflammatory stress in patients with GH compared with single $MgSO_4$ treatment.

WBV, PV and HCT of both groups were significantly lower after treatment than those before treatment, whereas WBV, PV and HCT after treatment were significantly lower in the Expt group than those in the Ctrl group ($P<0.05$). These were similar to the findings of Tooher *et al* (46), suggesting that $MgSO_4$ + labetalol could effectively improve the hemodynamics of patients and produce antihypertensive effects. Labetalol is a combined α- and β-adrenoceptor blocker, which is a non-selective antagonist of β-adrenoceptors and a competitive antagonist of postsynaptic α1-adrenoceptors. Labetalol acts more strongly on human β-adrenergic receptors than on α1-adrenergic receptors; the ratio of β-α antagonism is 3:1 and 6.9:1 after oral and intravenous administration, respectively (47). Unlike conventional β-adrenergic receptor blocking agents, which do not have intrinsic sympathomimetic activity, labetalol reduces peripheral vascular resistance and blood pressure during acute administration with minimal effect on heart rate or cardiac output (47). The potential mechanism by which labetalol improves blood pressure is that labetalol inhibits sympathetic nerve excitation, reduces catechol secretion, dilates blood vessels and reduces peripheral resistance by selectively blocking the effects of α- and β-adrenoceptor. Therefore, the hemodynamic indicators of patients can be improved (48-50).

Regarding pregnancy outcome, the spontaneous vaginal delivery rate was much higher in the Expt group than that in the Ctrl group, whereas the cesarean section rate and postpartum hemorrhage rate were markedly lower than those in the Ctrl group ($P<0.05$). These findings demonstrated that $MgSO_4$ + labetalol could markedly improve the pregnancy outcomes of patients with GH. In addition, the incidences of FIUD, placental abruption, neonatal asphyxia, premature birth and death of perinatal infants in the Expt group were markedly lower than those in the Ctrl group ($P<0.05$). This further indicated that $MgSO_4$ + labetalol could not only improve pregnancy outcomes of patients, but also reduce the harm of drugs to both mothers and fetuses (51).

In conclusion, in the present study, compared with single $MgSO_4$ treatment, $MgSO_4$ + labetalol effectively improved the inflammatory stress and hemodynamics of patients with GH during pregnancy, and exhibited a marked antihypertensive effect. Furthermore, $MgSO_4$ + labetalol could improve pregnancy outcomes and reduce perinatal complications. However, there were some limitations in the present study. The sample size of selected patients was quite small and all patients were recruited from a single source. In addition, there was no comparison of treatment effect in patients with different conditions, such as complications of diabetes mellitus. Therefore, more patients with GH should be included in a future study to explore the clinical application value of $MgSO_4$ + labetalol. In summary, the results of the present study offered a reference for drug treatment of patients with GH.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

The data generated and/or analysed during the present study are available from the corresponding author upon reasonable request.

Authors' contributions

ZG, WG and LZ conceived and designed the study. ZG, WG and GZ performed research. YT, MW and YG analyzed data. ZG, WG and LZ confirm the authenticity of all the raw data. MW and YG validated data. ZG and WG wrote the paper. WG and LZ reviewed the paper. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The present study adhered to The Declaration of Helsinki, and was approved by the Ethics Committee of Taicang Hospital of TCM (approval no. 2022026). Patients provided written informed consent.

Patient consent for publication

All participants in this study consented for publication.

Competing interests

The authors declare that they have no competing interests.

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