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A Clinical Study of Low Molecular Weight Heparin Sodium Injection Combined with Magnesium Sulfate Injection and Labetalol Tablets in the Treatment of Severe Pregnancy-Induced Hypertension

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Abstract: *Objective:* To investigate the clinical effect of low molecular weight heparin sodium injection combined with magnesium sulfate injection and labetalol in the treatment of severe pregnancy-induced hypertension. *Methods:* A total of 48 patients with severe pregnancy-induced hypertension admitted from February 2021 to February 2023 were selected, and the patients were divided into two groups by simple sampling, with 24 cases in each group. Patients in the control group received labetalol orally and intravenous infusion of magnesium sulfate, whereas those in the observation group received subcutaneous injection of low molecular weight heparin sodium on the basis of the control group. The two groups of patients underwent 5 days of treatment, and the blood pressure control, vascular endothelial function, renal function, and blood coagulation were compared between the two groups. *Results:* Before treatment, there were no significant differences in blood pressure readings, endothelin-1 (ET-1) and nitric oxide (NO) levels, serum creatinine (SCr) and blood urea nitrogen (BUN) levels, and the four coagulation indices between the two groups (all $P > 0.05$). After treatment, the blood pressure readings in the observation group were lower than those in the control group ($P < 0.05$); ET-1 in the observation group was lower than that in the control group, and the NO level in the observation group was higher than that in the control group ($P < 0.05$); compared with the control group, the observation group had lower SCr and BUN ($P < 0.05$), longer prothrombin time (PT), activated partial thromboplastin time (APTT), and thrombin time (TT), and lower fibrinogen (Fib) level ($P < 0.05$). *Conclusion:* Low molecular weight heparin sodium injection combined with magnesium sulfate injection and labetalol in the treatment of severe pregnancy-induced hypertension can help control blood pressure levels, promote the recovery of vascular endothelial function and renal function, and effectively correct coagulation function.

Keywords: Severe pregnancy-induced hypertension; Labetalol; Magnesium sulfate; Low molecular weight heparin sodium; Pregnancy outcome

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1. Introduction

Pregnancy-induced hypertension (PIH) is a complication during pregnancy, usually occurring after 20 weeks of pregnancy and mainly manifested by hypertension, proteinuria, and edema [1]. PIH patients have symptoms of hypertension, along with proteinuria, edema, preeclampsia, and headache, which are the main

causes of maternal and fetal death [2]. Despite a low incidence of severe PIH, this condition has high risk of serious adverse outcomes, thereby garnering widespread clinical attention. At present, the management of severe PIH includes the use of antispasmodics, sedatives, antihypertensives, and diuretics, as well as volume expansion; hence, magnesium sulfate (MS) is often used in the treatment [3]. MS functions by lowering blood pressure, inhibiting uterine smooth muscle contraction, and increasing uterine artery blood flow. However, it is difficult to control blood pressure in severe PIH patients with MS monotherapy, and increasing the drug dose will lead to more adverse reactions, thus threatening the health of both mothers and infants [4]. Therefore, MS is often combined with labetalol (LBT) in clinical practice. LBT is a common antihypertensive drug that selectively blocks β-adrenergic receptors to relax blood vessels, balance myocardial oxygen consumption, and increase cardiac output [5]. As severe PIH is complicated with renal dysfunction, LBT can increase renal blood flow and promote renal function recovery to a certain extent [6]. However, even with the above drugs, it is still difficult to achieve a satisfactory therapeutic effect. Clinical studies have been exploring new treatment options, and research results in recent years have revealed that hypercoagulability is an important manifestation of PIH, and as the condition progresses, the state of hypercoagulability also worsens. Hence, anticoagulant therapy has become a novel approach for the treatment of PIH [7]. In this study, anticoagulation with low molecular weight heparin sodium (LMWH-Na) was added on the basis of MS + LBT treatment.

2. Materials and methods

2.1. General information

Forty-four cases of severe PIH admitted to our hospital from February 2021 to February 2023 were included in the study. The patients were divided into two groups by simple sampling, with 24 cases in each group. Control group: age 24–38 years old (mean 31.16 ± 3.86); body weight 55–78 kg (mean 63.95 ± 5.15 kg). Observation group: age 23–38 years old (mean 31.26 ± 3.78 years old); weight 54–79 kg (mean 64.25 ± 5.22 kg). The general data of the two groups of patients were compared, and the two groups were comparable ($P > 0.05$).

Inclusion criteria: (i) patients who met the diagnostic criteria of PIH and whose blood pressure was ≥ 160/110mmHg, in line with the diagnosis of severe disease; (ii) patients and their families who agreed to participate in the study and signed the consent.

Exclusion criteria: (i) patients with liver and kidney dysfunction, primary diseases of the blood system, essential hypertension, bleeding tendency; (ii) patients who had recently received anticoagulant therapy; (iii) patients with other complications during pregnancy; (iv) patients with abnormal fetal development on B-ultrasound.

2.2. Treatment methods

2.2.1. Control group

Oral LBT (Jiangsu Desano Pharmaceutical Co., Ltd. H32026119 0.1 g) with a dose of 0.1 g/time, twice daily and MS (Tianjin Jinyao Pharmaceutical Co., Ltd. H12020994 10 mL:2.5 g) intravenous drip, 15 g dissolved in 500 mL of 10% glucose solution for injection, and completed within 6–8 h, were prescribed to patients in the control group.

2.2.2. Observation group

On the basis of LBT + MS as aforementioned, LMWH-Na (Italian ALFASIGMA SpA National Pharmaceutical Approval HJ20140281 0.6 mL:6400 IUaXa) was added at a dose of 5000 IU, subcutaneously, every 12 h.

2.2.3. Treatment cycle

Both groups were treated continuously for 5 days, and the therapeutic effect was observed.

2.3. Observation indicators

(i) Blood pressure levels were compared between both groups of patients.
(ii) The vascular endothelial functions of both groups of patients were compared (ET-1 and NO were detected using a kit from Hefei Laier Biotechnology).
(iii) The renal functions of both groups of patients were compared (Scr and BUN were detected by radioimmunoassay).
(iv) The four coagulation indices were compared between both groups (coatron 1800 automatic coagulation analyzer was used).

2.4. Statistical analysis

Data were imported into SPSS 22.0 for analysis and processing. Measurement data were represented by mean ± standard deviation, and *t*-test was used. Count data were represented by percentage (%), and chi-square test was used. $P < 0.05$ indicates a statistically significant difference.

3. Results

3.1. Comparison of blood pressure readings between the two groups

Before treatment, there was no significant difference in blood pressure readings between the two groups ($P > 0.05$). However, after treatment, blood pressure readings in the observation group were lower than those in the control group ($P < 0.05$). See **Table 1** for details.

Table 1. Comparison of blood pressure readings between the two groups

Group	Number of cases	Systolic blood pressure (mmHg)		Diastolic pressure (mmHg)	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	24	169.51 ± 7.52	141.82 ± 8.11	124.06 ± 6.19	96.81 ± 6.52
Control group	24	170.46 ± 8.11	148.89 ± 8.26	123.71 ± 6.26	101.83 ± 6.84
t		0.421	2.992	0.195	2.603
P		0.676	0.004	0.846	0.012

Data are shown in mean ± standard deviation.

3.2. Comparison of vascular endothelial function indices between the two groups

Before treatment, there were no significant differences in ET-1 and NO levels between the two groups ($P > 0.05$). However, after treatment, the ET-1 level in the observation group was lower than that in the control group, and the NO level in the observation group was higher than that in the control group ($P < 0.05$). See **Table 2** for details.

Table 2. Comparison of vascular endothelial function indices between the two groups

Group	Number of cases	ET-1 (mg/L)		NO (mg/L)	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	24	88.86 ± 10.19	61.19 ± 6.81	52.49 ± 5.59	68.91 ± 6.15
Control group	24	89.51 ± 10.41	70.19 ± 7.59	53.11 ± 5.69	62.80 ± 6.29

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Group	Number of cases	ET-1 (mg/L)		NO (mg/L)	
		Before treatment	After treatment	Before treatment	After treatment
t		0.219	4.324	0.381	3.403
P		0.828	0.000	0.705	0.001

Data are shown in mean ± standard deviation. Abbreviations: ET-1, endothelin-1; NO, nitric oxide.

3.3. Comparison of renal function indices between the two groups

Before treatment, there were no significant differences in SCr and BUN levels between the two groups ($P > 0.05$). However, after treatment, the observation group had lower SCr and BUN levels than the control group ($P < 0.05$). See **Table 3** for details.

Table 3. Comparison of renal function indices between the two groups

Group	Number of cases	SCr (U/L)		BUN (mmol/L)	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	24	60.59 ± 785	41.19 ± 6.82	5.56 ± 0.82	3.22 ± 0.38
Control group	24	61.10 ± 7.91	47.90 ± 7.05	5.64 ± 0.80	4.02 ± 0.41
t		0.224	3.351	0.342	7.011
P		0.824	0.002	0.734	0.000

Data are shown in mean ± standard deviation. Abbreviations: BUN, blood urea nitrogen; SCr, serum creatinine.

3.4. Comparison of four coagulation indices between the two groups

Before treatment, there were no significant differences in the four coagulation indices between the two groups ($P > 0.05$). However, after treatment, the observation group had longer PT, APTT, and TT and lower Fib level than the control group ($P < 0.05$). See **Table 4** for details.

Table 4. Comparison of four coagulation indices between the two groups

Group	Number of cases	PT (s)		APTT (s)	
		Before treatment	After treatment	Before treatment	After treatment
observation group	24	11.52 ± 0.72	12.86 ± 0.71	25.86 ± 1.91	28.79 ± 1.71
control group	24	11.60 ± 0.74	11.85 ± 0.70	25.56 ± 1.85	26.11 ± 1.84
t		0.380	4.963	0.553	5.227
P		0.706	0.000	0.583	0.000
Group	**Number of cases**	**TT (s)**		**Fib (g/L)**	
		Before treatment	**After treatment**	**Before treatment**	**After treatment**
Observation group	24	16.81 ± 1.56	18.80 ± 1.49	4.25 ± 0.62	3.05 ± 0.45
Control group	24	16.74 ± 1.55	17.15 ± 1.59	4.31 ± 0.61	4.11 ± 0.48
t		0.156	3.710	0.338	7.893
P		0.877	0.001	0.737	0.000

Data are shown in mean ± standard deviation. Abbreviations: PT, prothrombin time; APTT, activated partial thromboplastin time; TT, thrombin time; Fib, fibrinogen.

4. Discussion

PIH is a complication during pregnancy. A continuous rise in blood pressure in patients can lead to

decreased cardiac and renal blood flow, which in turn can lead to heart failure, renal dysfunction, *etc*., and ultimately lead to serious adverse outcomes to both mother and fetus [8]. Previous epidemiological surveys have pointed out that severe PIH poses a significant threat to the life and health of mothers and infants; hence, it is necessary to actively seek more effective treatment options [9]. The conventional treatment for severe PIH is based on the control of blood pressure. As a calcium antagonist, MS can lower blood pressure and, at the same time, enhance the synthesis of prostaglandins and the contraction of skeletal muscle and smooth muscle as well as increase uterine blood flow to prevent eclampsia [10]. In order to achieve a more ideal blood pressure control effect, LBT is jointly used to strengthen the antihypertensive effect, reduce peripheral vascular resistance, and make up for the shortcomings of MS monotherapy.

However, it is still difficult to achieve a very satisfactory therapeutic effect when MS + LBT is used clinically. Hence, other more effective treatment methods are still being explored. Clinical reports have pointed out that the onset of PIH is not only accompanied by elevated blood pressure, but also coagulation dysfunction. The blood of patients with PIH is in a hypercoagulable state, which greatly affects the treatment [11]. Based on this theory, anticoagulant therapy has become a novel approach for the treatment of PIH in recent years. LMWH-Na is a new type of anticoagulant drug, which achieves ideal anticoagulant effect by inhibiting the intrinsic coagulation pathway and accelerating the synthesis of tissue factor pathway inhibitor (TFPI) [12]. Its main component is low molecular weight heparin, which can inactivate blood coagulation factors Xa and IIa and is an ideal anticoagulant drug widely used in recent years [13].

In this study, LMWH-Na was added to the conventional regimen of MS + LBT, and the results showed that a more ideal therapeutic effect was achieved. In the study, the blood pressure readings in the observation group were lower than those in the control group after treatment ($P < 0.05$), suggesting that blood pressure drops significantly after adding LMWH-Na on the ground that it could promote blood circulation and reduce circulatory resistance [14]. In addition, the vascular endothelial function of the observation group also significantly improved; the observation group had lower ET-1 and higher NO than the control group ($P < 0.05$). LBT can dilate blood vessels and promote the repair of vascular endothelial function. Therefore, adding anticoagulant therapy to LBT can reduce vascular resistance and vascular endothelial function damage as well as improve the therapeutic effect of LBT [15]. Renal dysfunction is the main complication of PIH. MS + LBT can lower blood pressure, increase renal blood flow, and promote the recovery of renal function. By adding LMWH-Na to the regimen, blood pressure control and renal function can be further improved. At the end of this study, the four coagulation indices were compared between the two groups. The results showed that the observation group achieved an ideal anticoagulant effect in terms of blood pressure control, vascular endothelial function, and renal function recovery.

In conclusion, adding LMWH-Na on the basis of MS + LBT in patients with severe PIH can further improve the therapeutic effect. Therefore, it should be advocated in clinical practice.

Disclosure statement

The authors declare no conflict of interest.

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