Comparison of Labetalol With Versus Without Magnesium Sulfate on Intraoperative Blood Pressure Variability During Cesarean Delivery in Hypertensive Disorders of Pregnancy: A Retrospective Cohort Study

Ann. Ital. Chir., 2026 97, 8: 1471–1479
https://doi.org/10.62713/aic.4542

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AIM: This study aims to investigate the effects of two medication regimens—labetalol combined with magnesium sulfate versus labetalol alone—on intraoperative blood pressure variability (BPV) and maternal-neonatal outcomes in patients with hypertensive disorders of pregnancy (HDP) undergoing cesarean delivery.

METHODS: This retrospective cohort study enrolled 170 HDP patients who underwent cesarean delivery at TongXiang Maternity and Child Health Care Hospital between January 2023 and June 2025. Based on perioperative medication regimens, patients were divided into a combination group (labetalol plus magnesium sulfate, n = 86) and a monotherapy group (labetalol alone, n = 84). After propensity score matching (PSM), a cohort of 54 patients was included in each group for analysis. All patients received oral labetalol for preoperative blood pressure control and postoperative management. Patients in the combination group additionally received intravenous magnesium sulfate. The primary outcome measure was the standard deviation of intraoperative systolic blood pressure (SD of systolic blood pressure (SBP)). Secondary outcomes included intraoperative blood pressure target attainment rate, incidence of severe hypertensive events, and maternal-neonatal complications.

RESULTS: After PSM, baseline characteristics were balanced between the two groups. The combination group exhibited a significantly lower intraoperative SD of SBP compared to the monotherapy group ($p < 0.001$), along with a higher intraoperative blood pressure target attainment rate ($p < 0.001$) and a lower incidence of severe hypertensive events ($p = 0.030$). Regarding maternal-neonatal outcomes, the combination group had significantly higher 1-minute and 5-minute Apgar scores ($p = 0.035$ and $p = 0.036$, respectively) and a lower rate of admission to the neonatal intensive care unit (NICU) ($p = 0.002$). There were no significant differences between the groups in the incidence of adverse drug events such as hypotension or bradycardia.

CONCLUSIONS: For HDP patients undergoing cesarean delivery, the perioperative application of a combined regimen of labetalol and magnesium sulfate, compared with labetalol alone, was associated with more stable intraoperative blood pressure, reduced variability under surgical stress, and improved early neonatal outcomes. This combined regimen provides valuable clinical reference for optimizing perioperative blood pressure management during cesarean delivery.

Keywords: blood pressure variability; hypertensive disorders of pregnancy; cesarean delivery; labetalol; magnesium sulfate

Introduction

Hypertensive disorders of pregnancy (HDP) include a range of conditions characterized by increased blood pressure during pregnancy. These disorders remain a leading cause of maternal and perinatal mortality worldwide, with both short-term and long-term complications for mothers and neonates. HDP affects about 5–10% of pregnancies worldwide, making it a critical risk factor for adverse perinatal outcomes [1,2]. In cases of moderate to severe preeclampsia or obstetric indications, cesarean delivery is often required. However, the perioperative phase of cesarean delivery presents a unique hemodynamic challenge. Factors such as surgical stimulation, anesthetic effects, pain, fluid shifts, and postpartum uterine contraction interact in complex ways, predisposing patients to abrupt elevations and marked fluctuations in blood pressure [3]. Poorly controlled acute hypertension during this period significantly increases the risk of life-threatening maternal complications, such as stroke, heart failure, eclampsia, postpartum hemorrhage, hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome, and posterior reversible encephalopathy syndrome (PRES) [4,5]. Simultaneously, uteroplacental circulation is highly sensitive to alterations in perfusion pressure. Pronounced fluctuations in maternal blood pressure can disrupt placental blood flow, exacerbating the risks of fetal distress, neonatal asphyxia, and even perinatal death [6,7]. Therefore, achieving stable and well-controlled perioperative blood pressure is a central objective in the management of HDP patients undergoing cesarean delivery.

Submitted: 12 January 2026 Revised: 25 March 2026 Accepted: 28 April 2026 Published: 13 August 2026
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Editor: Andrea Bondurri

While current national and international guidelines offer clear recommendations for the long-term management of HDP, there is still no standardized, unified protocol for managing acute blood pressure during the brief but physiologically high-stress perioperative period [8,9]. Labetalol is a first-line choice for treating acute hypertension in pregnancy due to its combined α1- and β-adrenergic blocking features, which reduce peripheral vascular resistance while slowing heart rate and lowering cardiac output. It has a rapid onset, a moderate duration of action, and minimal adverse impact on uteroplacental blood flow [10]. Magnesium sulfate, commonly used for preventing and treating eclampsia, acts primarily by antagonizing calcium ions and stabilizing neuronal and smooth vascular muscle cell membranes. Beyond its well-established neuroprotective and anticonvulsant roles, multiple studies suggest that magnesium sulfate has a mild vasodilatory effect that may contribute to smoother blood pressure control [11,12]. Given their distinct mechanisms, these agents are commonly used together in clinical practice, aiming to prevent eclampsia and achieve more consistent blood pressure regulation. However, whether combining magnesium sulfate with labetalol offers a significant advantage over labetalol monotherapy in managing acute perioperative blood pressure fluctuations remains uncertain, and current evidence is not yet conclusive [5,13].

In recent years, with the widespread adoption of ambulatory blood pressure monitoring and advancements in data analysis, blood pressure variability (BPV) has gained significant attention as an important cardiovascular risk predictor, independent of mean blood pressure levels [14]. BPV reflects the magnitude and frequency of blood pressure fluctuations over time. Studies have confirmed that both in hypertensive patients and the general population, increased BPV is independently associated with target organ damage, including left ventricular hypertrophy, renal impairment, and arterial stiffness, along with an elevated risk of cardiovascular events, such as stroke and myocardial infarction [15]. In the perioperative context, excessively high BPV is considered a key indicator of unstable tissue perfusion and an imbalance between oxygen supply and demand, contributing to complications such as postoperative acute kidney injury, myocardial injury, and postoperative neurocognitive dysfunction [15,16]. Therefore, when evaluating antihypertensive approaches in HDP patients during the perioperative period, assessing their impact on BPV—rather than relying solely on average pressure levels—may offer a more sensitive indicator of hemodynamic stability and organ protection.

Given this, the present retrospective cohort study aims to systematically compare the effects of a combined labetalol and magnesium sulfate regimen with a labetalol monotherapy regimen in HDP patients undergoing cesarean delivery. Particularly, the study focuses on perioperative blood pressure variability, evaluated using the standard deviation of systolic blood pressure, along with indicators of blood pressure and maternal and neonatal clinical outcomes. The findings are intended to guide more precise and personalized approaches to perioperative blood pressure management in this population.

Methods

Recruitment of the Study Participants

This single-center, retrospective observational cohort study collected clinical data of HDP patients who underwent cesarean delivery between January 2023 and June 2025. Patients were identified through the hospital's medical records management system using ICD-10 diagnostic codes for HDP.

Inclusion criteria for patient selection were as follows: (1) age ≥18 years; (2) singleton pregnancy with gestational age of ≥28 weeks; and (3) meeting the diagnostic criteria of HDP, including gestational hypertension or preeclampsia, according to the established criteria for the International Society for the Study of Hypertension in Pregnancy (ISSHP) and the American College of Obstetricians and Gynecologists (ACOG). Exclusion criteria included: (1) severely incomplete medical records; (2) comorbid severe pre-existing cardiac, hepatic, or renal disease; (3) intraoperative use of other antihypertensive agents; (4) fetal malformation or stillbirth.

Based on perioperative antihypertensive management, patients were categorized into a combination therapy group, which received both labetalol and magnesium sulfate, and a monotherapy group, which was treated with labetalol alone. The study protocol was approved by the Ethics Committee of TongXiang Maternity and Child Health Care Hospital (Ethics Review Research No. 001, 2026), and the requirement for informed consent was waived due to the retrospective study design.

Data Collection and Definitions

To systematically evaluate perioperative hemodynamic management, data were retrieved from electronic medical records and the anesthesia information management system. This section is divided into perioperative medication regimens and data collection with outcome definitions.

Perioperative Medication Regimens and Anesthesia Management

To isolate the effects of antihypertensive regimens from other perioperative factors and to ensure that observed differences primarily reflected pharmacological actions rather than variations in anesthetic practice, anesthetic and surgical protocols were standardized across all patients. All patients received a standardized anesthesia regimen: combined spinal-epidural anesthesia (CSEA) was the preferred technique, with 0.5% hyperbaric bupivacaine 8–12 mg plus fentanyl 15–25 μg administered intrathecally, and epidural supplementation with 2% lidocaine as needed to achieve a T4–T6 sensory block level. Depth of anesthesia was

carefully titrated to blunt hemodynamic responses to surgical stimuli (incision, uterine exteriorization, and peritoneal traction), while maintaining stable baseline hemodynamics. Intraoperative blood pressure fluctuations were managed through a dual-layer approach: (1) the assigned antihypertensive regimen provided baseline and sustained blood pressure control; and (2) standardized anesthesia adjustments (e.g., deepening anesthetic agents, optimizing fluid loading with balanced crystalloid at 8–10 mL/kg/h, and, when necessary, using small boluses of intravenous ephedrine or phenylephrine for refractory hypotension) were applied uniformly across groups. This distinction ensures that differences in blood pressure variability between groups can be attributed predominantly to the pharmacological actions of labetalol alone versus combined magnesium sulfate.

Patients received either labetalol monotherapy or combined labetalol and magnesium sulfate based on the attending physician's discretion. Labetalol (hydrochloride tablets; Jiangsu Desano Pharmaceutical Co., Ltd.) was administered orally for preoperative preparation and early postoperative control, with an initial dose of 100–200 mg every 8 hours, adjusted according to blood pressure levels. No additional oral labetalol was given for acute intraoperative hypertensive events. Magnesium sulfate (25% $MgSO_4$ Injection; Hangzhou Minsheng Pharmaceutical Co., Ltd.) was administered intravenously according to institutional protocol: a loading dose of 5 g in 100 mL of 5% glucose (Zhejiang Kangjier Pharmaceutical Co., Ltd.) over 30 minutes, followed by a maintenance infusion of 1–2 g/h, typically continued for up to 24 hours postoperatively. The infusion rate was titrated based on patellar reflex, respiratory rate (maintained at ≥16 breaths/min), and urine output (≥17 mL/h), with comprehensive clinical surveillance rather than using any single parameter as an isolated safety criterion. Of note, intraoperative acute hypertensive episodes (systolic blood pressure (SBP) ≥160 mmHg or diastolic blood pressure (DBP) ≥110 mmHg) were first managed by the standardized anesthesia adjustments described above; only if these measures failed to control blood pressure within 5 minutes would additional rescue intravenous antihypertensives be considered, but such rescue interventions were rarely required and were recorded separately.

Data Collection and Outcome Measures

Blood pressure monitoring and variability metrics. Preoperative blood pressure was measured using an automated electronic sphygmomanometer (Omron HBP-1300 professional device; Dalian, China). Intraoperatively, all patients underwent continuous non-invasive arterial pressure (cNIBP) monitoring via the anesthesia monitoring system (Philips IntelliVue MX450 patient monitor, Software Version V.3.0.1, Philips), and early postoperative data within the first 6 hours were collected from recovery records. One-minute interval trend data for systolic and diastolic blood pressure were extracted from the anesthesia information management system. For analytical purposes, the reference blood pressure target range was defined as SBP 130–139 mmHg and DBP 80–89 mmHg, consistent with major HDP guidelines [17]. Severe hypertension was defined as SBP ≥160 mmHg or DBP ≥110 mmHg; values exceeding SBP >140 mmHg or DBP >90 mmHg were considered inadequately controlled. A severe hypertensive event was recorded when blood pressure reached SBP ≥160 mmHg or DBP ≥110 mmHg for >5 minutes, requiring clinical intervention other than additional intravenous antihypertensive agents. The intraoperative period was defined from anesthesia induction to skin closure, and the early postoperative period was the first 6 hours after surgery.

Blood pressure variability (BPV) was evaluated using: (1) standard deviation of SBP (SD of SBP); (2) coefficient of variation of SBP (CVSBP = SD of SBP / mean SBP × 100%); (3) range of SBP (maximum – minimum); and (4) number of fluctuation events (SBP changes >20 mmHg lasting ≥2 minutes). The blood pressure target attainment rate was calculated as the proportion of intraoperative readings within the predefined target range.

Maternal-neonatal and safety outcomes. Maternal outcomes included perioperative eclampsia, HELLP syndrome, postpartum hemorrhage (estimated by suction volume and gauze weight), blood transfusion requirement, postoperative intensive care unit (ICU) admission, and total postoperative hospital stay. Neonatal outcomes comprised birth weight, Apgar scores at 1 and 5 minutes, umbilical artery pH, neonatal asphyxia diagnosis, the neonatal intensive care unit (NICU) admission, and NICU length of stay. Perinatal complications (fetal distress, placental abruption, preterm birth) were also recorded. Safety outcomes encompassed hypotension (SBP <90 mmHg or >30% reduction from baseline), bradycardia (heart rate <50 beats/min), and magnesium toxicity signs (loss of patellar reflexes, respiratory rate <12 breaths/min, need for assisted ventilation, or serum magnesium >3.5 mmol/L when available).

Statistical Analysis

Initially, normality of continuous variables was assessed using the Shapiro–Wilk test. Normally distributed continuous variables were presented as mean ± standard deviation and analyzed using the independent-samples *t*-test. Non-normally distributed variables were expressed as median with interquartile range and compared using the Mann-Whitney U test. However, categorical variables were presented as counts and percentages and compared using the χ^2 test or Fisher's exact test, as appropriate.

To reduce baseline differences between groups, propensity score matching (PSM) was conducted. Group allocation (combination therapy vs. monotherapy) was considered as the dependent variable, while key baseline characteristics, such as age, body mass index (BMI), gestational age, and baseline SBP, were included as covariates in the model bas-

Table 1. Baseline characteristics of the study population before and after propensity score matching.

	Pre-PSM				Post-PSM			
Variable	Monotherapy group (n = 86)	Combination group (n = 84)	*p*-value	SMD	Monotherapy group (n = 54)	Combination group (n = 54)	*p*-value	SMD
Age (years), Mean ± SD	30.62 ± 2.81	32.19 ± 2.62	<0.001	0.579	31.52 ± 2.55	31.48 ± 2.26	0.937	0.015
Gestational week (weeks), Mean ± SD	37.55 ± 1.53	37.31 ± 1.46	0.307	0.157	37.22 ± 1.56	37.31 ± 1.50	0.749	0.062
Parity								
Multiparous	55 (64.0)	41 (48.8)	0.066	0.309	30 (55.6)	31 (57.4)	1.000	0.037
Primiparous	31 (36.0)	43 (51.2)			24 (44.4)	23 (42.6)		
SBP (mmHg), Mean ± SD	154.76 ± 6.09	154.64 ± 5.12	0.896	0.020	155.19 ± 6.11	154.37 ± 4.73	0.440	0.149
DBP (mmHg), Mean ± SD	100.20 ± 4.00	99.60 ± 3.65	0.307	0.157	99.72 ± 3.55	99.46 ± 3.66	0.709	0.072
BMI (kg/m^2), Mean ± SD	28.05 ± 1.72	27.87 ± 1.95	0.541	0.094	27.96 ± 1.73	28.10 ± 2.07	0.709	0.072
Diabetes, n (%)								
No	77 (89.5)	62 (73.8)	0.014	0.415	46 (85.2)	45 (83.3)	1.000	0.051
Yes	9 (10.5)	22 (26.2)			8 (14.8)	9 (16.7)		
Adverse history, n (%)								
No	76 (88.4)	67 (79.8)	0.185	0.237	46 (85.2)	45 (83.3)	1.000	0.051
Yes	10 (11.6)	17 (20.2)			8 (14.8)	9 (16.7)		
Scar history, n (%)								
No	76 (88.4)	57 (67.9)	0.002	0.512	45 (83.3)	44 (81.5)	1.000	0.049
Yes	10 (11.6)	27 (32.1)			9 (16.7)	10 (18.5)		
Severe preeclampsia, n (%)								
Non-severe	77 (89.5)	76 (90.5)	1.000	0.031	49 (90.7)	49 (90.7)	1.000	<0.001
Severe	9 (10.5)	8 (9.5)			5 (9.3)	5 (9.3)		

BMI, body mass index; PSM, propensity score matching; SMD, standardized mean differences; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Table 2. Comparison of perioperative blood pressure management between the two groups.

Indicator	Total (n = 108)	Monotherapy group (n = 54)	Combination group (n = 54)	Statistic	*p*-value
Total surgery duration (min), Mean ± SD	44.58 ± 8.17	43.81 ± 8.71	45.35 ± 7.59	$t = –0.98$	0.330
Intraoperative SD of SBP (mmHg), Mean ± SD	13.13 ± 3.57	14.42 ± 3.63	11.84 ± 3.02	$t = 4.02$	<0.001
Intraoperative CVSBP (%), Mean ± SD	7.88 ± 2.14	8.89 ± 1.99	6.87 ± 1.79	$t = 5.53$	<0.001
Intraoperative mean SBP (mmHg), Mean ± SD	131.16 ± 7.52	132.98 ± 8.38	129.33 ± 6.11	$t = 2.59$	0.011
Intraoperative BP target attainment rate (%), Median (IQR)	32.80 (21.43, 44.02)	21.25 (17.25, 24.10)	44.05 (39.78, 49.32)	Z = –8.82	<0.001
Severe hypertensive events [n (%)]	16 (14.81)	12 (22.22)	4 (7.41)	$\chi^2 = 4.70$	0.030

BP, blood pressure; CVSBP, coefficient of variation of SBP.

ed on clinical relevance and prior literature. Propensity scores were estimated, and patients were matched using a 1:1 nearest-neighbor algorithm without replacement, with a caliper width of 0.2 standard deviations of the logit of the propensity score. Balance between groups was assessed using standardized mean differences (SMD), with SMD <0.2 indicating adequate balance. This process resulted in a balanced cohort of 54 patients per group, with greater comparability between treatment arms.

Statistical analysis was performed using R software (version4.5.2, R Foundation for Statistical Computing, Vienna, Austria). PSM was conducted using the "MatchIt" package, while standardized mean differences (SMD) were determined using the "tableone" package.

Results

Comparison of Baseline Characteristics Between Groups

After PSM, there were no statistically significant differences between the two groups in age, gestational age, baseline blood pressure (SBP/DBP), BMI, parity, or the presence of diabetes, or other baseline characteristics (all $p > 0.05$, SMD <0.2), indicating effective matching and good comparability between groups (Table 1).

Comparison of Perioperative Indicators Between Groups

There was no difference in total surgery duration between the two groups. However, patients in the combination group showed more stable hemodynamic profiles, indicated by lower blood pressure variability, favorable mean systolic pressure, and higher blood pressure target attainment rate (Table 2). Furthermore, intraoperative mean SBP, intraoperative blood pressure target attainment rate, and incidence of severe hypertensive events were all significantly improved in the combination group compared with the monotherapy group ($p < 0.05$).

Comparison of Maternal-Neonatal Outcomes Between Groups

Comparison of maternal-neonatal outcomes (Table 3) between groups revealed no significant differences in terms of postpartum hemorrhage volume, postoperative hospital stays, or the incidence of eclampsia/HELLP syndrome. In contrast, the combination group had higher Apgar scores at both 1 minute ($p = 0.035$) and 5 minutes ($p = 0.036$). The rate of NICU admission was significantly lower in the combination group ($p = 0.002$). However, no statistically significant differences between the groups were observed in birth weight or incidence of neonatal asphyxia.

Safety Analysis Across the Two Treatment Groups

Both treatment groups had a low frequency of drug-related adverse events, with no statistically significant differences between them (Table 4). The incidence of hypotension was 16.67% in the combination group and 9.26% in the monotherapy group ($p = 0.252$). The incidence of bradycardia was 1.85% and 3.70%, respectively, in both treatment groups, with no significant difference. In the combination treatment groups, two cases (3.70%) had adverse effects related to magnesium sulfate, which resolved after adjustment of the infusion rate. No similar events were observed in the monotherapy group ($p = 0.495$). Notably, none of the observed adverse events led to serious clinical consequences.

Discussion

The perioperative management of blood pressure in HDP patients during cesarean delivery remains particularly challenging. The perioperative phase is associated with rapid physiological shifts, such as surgical stimulation, anesthetic effects, fetal delivery, and placental extraction, which can all provoke significant hemodynamic fluctuations. These changes increase the risk of complications for both mothers and neonates. Therefore, effective blood pressure management during this critical period is especially important.

In the present study, we retrospectively compared the effects of labetalol combined with magnesium sulfate versus labetalol alone on intraoperative hemodynamic stability and maternal-neonatal clinical outcomes during cesarean delivery. The findings suggest that the combination treatment approach offers more consistent blood pressure control. Specifically, patients receiving the combination

Table 3. Comparison of maternal-neonatal outcomes between the two groups.

Indicator	Total (n = 108)	Monotherapy group (n = 54)	Combination group (n = 54)	Statistic	*p*-value
Postpartum hemorrhage (mL), Mean ± SD	342.45 ± 97.56	360.09 ± 112.37	324.81 ± 77.15	$t = 1.90$	0.060
Postoperative stay (days), Median (IQR)	5.00 (4.75, 6.00)	5.50 (4.00, 7.00)	5.00 (5.00, 6.00)	Z = –0.98	0.327
Eclampsia/HELLP [n (%)]	4 (3.70)	2 (3.70)	2 (3.70)	$\chi^2 = 0.00$	1.000
Birth weight (g), Mean ± SD	2928.38 ± 398.06	2936.80 ± 422.96	2919.96 ± 375.29	$t = 0.22$	0.827
1-minute Apgar score, Median (IQR)	8.00 (8.00, 9.00)	8.00 (7.00, 9.00)	9.00 (8.00, 9.00)	Z = –2.10	0.035
5-minute Apgar score, Median (IQR)	9.00 (9.00, 10.00)	9.00 (9.00, 10.00)	9.50 (9.00, 10.00)	Z = –2.10	0.036
Neonatal asphyxia [n (%)]	11 (10.19)	8 (14.81)	3 (5.56)	$\chi^2 = 2.53$	0.112
NICU admission [n (%)]	12 (11.11)	11 (20.37)	1 (1.85)	$\chi^2 = 9.38$	0.002

NICU, neonatal intensive care unit; HELLP, hemolysis, elevated liver enzymes, and low platelets.

Table 4. Incidence of drug-related adverse events between the two groups.

Adverse Event	Total (n = 108)	Monotherapy group (n = 54)	Combination group (n = 54)	Statistic	*p*-value
Hypotension Event, n (%)	14 (12.96)	5 (9.26)	9 (16.67)	$\chi^2 = 1.31$	0.252
Bradycardia Event, n (%)	3 (2.78)	2 (3.70)	1 (1.85)	–	1.000
Magnesium sulfate-related adverse reaction, n (%)	2 (1.85)	0 (0.00)	2 (3.70)	–	0.495

Note: Fisher's exact test was used when the expected frequency was small; "–" indicates that the chi-square statistic was not applicable.

treatment demonstrated reduced intraoperative blood pressure variability (manifested as lower SD and CVSBP), increased blood pressure target attainment rate, and fewer severe hypertensive events. Concurrently, the combined therapy was associated with some improvement in maternal-neonatal outcomes, including higher 1-minute Apgar scores and a lower rate of NICU admission, without increasing the risk of drug-related adverse events such as hypotension or bradycardia.

After PSM, the proportion of patients with severe preeclampsia was comparable between groups, suggesting that the observed differences in blood pressure variability were unlikely to be driven solely by baseline disease severity. During cesarean delivery, multiple stimuli such as surgical incision, visceral traction, and uterine contraction can lead to sympathetic excitation and catecholamine release, constituting the core cause of acute rises in blood pressure and significant fluctuations. The primary observational metric in this study—intraoperative blood pressure variability (BPV)—is a sensitive indicator for quantifying the degree of blood pressure fluctuation induced by surgical stress. Higher perioperative BPV has been linked to uneven organ perfusion and an increased risk of postoperative complications [18]. In the present study, patients in the combination group exhibited lower intraoperative SD of SBP and CVSBP, suggesting that during the high-stress process of cesarean delivery, the combination regimen was associated with more stable hemodynamic control during the perioperative phase. Recent research further emphasizes that the association between BPV and hypertensive target organ damage is independent of mean blood pressure levels, gaining particular attention in acute phase management [19,20]. Consistent with this context, the decreased SD of SBP and CVSBP found in the combination group indicates that magnesium sulfate may achieve smoother and more controlled blood pressure profiles when used along with labetalol.

Our findings are consistent with previous studies demonstrating the efficacy of magnesium sulfate in preventing eclampsia in patients with preeclampsia [11,12]. However, prior research has primarily focused on reduction in mean blood pressure rather than variability [13], while our study specifically examined blood pressure variability (BPV) as a primary endpoint, providing novel insights into the hemodynamic benefits of combination therapy during the perioperative period. In a 24-hour direct blood pressure monitoring study in hypertensive patients [13], labetalol significantly reduced both systolic and diastolic blood pressures by approximately 20%; however, it did not affect the coefficient of variation, indicating limited impact on BPV when used alone. In contrast, our study found that combining magnesium sulfate with labetalol was associated with a significant reduction in BPV, suggesting that combination therapy may offer advantages beyond blood pressure reduction alone. Previous randomized controlled trials have primarily evaluated the efficacy of magnesium sulfate in preventing eclampsia rather than its impact on acute blood pressure fluctuations during cesarean delivery [11]. In contrast, our study focused on the intraoperative period—a time of intense hemodynamic stress—and demonstrated that the addition of magnesium sulfate to labetalol was associated with lower BPV and a higher blood pressure target attainment rate. These results extend the existing knowledge by highlighting a potential role of magnesium sulfate in enhancing hemodynamic stability beyond its well-established anticonvulsant effects. While labetalol monotherapy remains effective for managing acute hypertension in pregnancy [10,21], the combination therapy may offer additional advantages in the surgical setting where sympathetic

activation and rapid hemodynamic fluctuations are more pronounced.

The underlying mechanism likely involves synergistic actions from multiple pharmacological pathways. In response to surgical stress, labetalol acts rapidly by antagonizing α- and β-adrenergic receptors, thereby effectively counteracting vasoconstriction and limiting reflex tachycardia induced by pain and tissue manipulation. This process makes it suitable for managing acute hypertension in the operative setting [21]. However, magnesium sulfate contributes through mechanisms that extend beyond its established role in preventing eclampsia.

The potential mechanisms by which magnesium sulfate may contribute to reduced blood pressure variability involve several complementary pathways. First, as a physiological calcium antagonist, magnesium sulfate inhibits voltage-gated calcium channels in vascular smooth muscle, reducing intracellular calcium influx and attenuating vasoconstrictor responsiveness to catecholamines and other stress-induced vasoactive substances [22,23,24,25]. The vasorelaxant effect of magnesium is endothelium-dependent and mediated in part through the nitric oxide-cyclic guanosine monophosphate pathway [25]. Additionally, magnesium sulfate acts as a non-competitive antagonist of the N-methyl-D-aspartate (NMDA) receptor, with demonstrated half-maximal inhibitory concentrations of approximately 0.4–0.6 mM for N-methyl-D-aspartate receptor (NR)1/NR2A and NR1/NR2B subunits [23]. This may help reduce central sensitization and attenuate sympathetic outflow in response to nociceptive stimuli, contributing to hemodynamic stability during surgical stress [23,24]. Furthermore, by reducing neuronal excitability and preventing seizure activity, magnesium sulfate may indirectly support overall hemodynamic stability [11]. Collectively, these mechanisms may synergize with the α/β-adrenergic blockade provided by labetalol [21] to achieve smoother hemodynamic control during the high-stress perioperative period, which explains the observed reduction in blood pressure variability and lower incidence of severe hypertensive events in the combination group.

Regarding clinical outcomes, the lower incidence of severe hypertensive events in the combination group carries significant clinical importance. Severe acute hypertension is a well-recognized trigger for critical complications in preeclampsia, including cerebral hemorrhage, heart failure, and PRES [26]. Combination therapy significantly reduced such events in our study. The lack of difference in the incidence of eclampsia and HELLP syndrome between groups may be because all patients received basic management with magnesium sulfate (combination group) or targeted labetalol (monotherapy group) for blood pressure control based on their allocation, and the sample size may have been insufficient to detect differences in these relatively rare events.

Notably, the combination therapy group had higher 1-minute Apgar scores and a lower NICU admission rate. This may be an indirect benefit stemming from more stable maternal blood pressure and improved uteroplacental perfusion. Stable maternal pressure helps maintain more constant placental blood flow, reducing the risk of fetal acute hypoxia and acidosis [27]. A meta-analysis indicated that good antenatal blood pressure control is associated with improved neonatal outcomes [28].

Beyond the 1-minute results, the combination group also demonstrated significantly higher 5-minute Apgar scores ($p = 0.036$). While the 1-minute Apgar reflects the immediate condition at birth, the 5-minute Apgar is a stronger prognostic indicator of neonatal neurological resilience and response to resuscitation [29,30]. The superior 5-minute scores in the combination group suggest that more stable hemodynamics not only reduced the initial hypoxic insult but also facilitated better early neurological adaptation. Additionally, given that magnesium sulfate readily crosses the placenta and possesses neuroprotective properties via NMDA receptor antagonism [31], direct fetal exposure may have provided supplementary neurological protection during delivery.

The markedly lower NICU admission rate in the combination group ($p = 0.002$) is consistent with evidence that higher blood pressure variability is independently associated with an increased risk of NICU admission [7]. The substantially lower admission rate likely reflects a compounding effect: smoother intraoperative hemodynamics led to better neonatal condition at birth, reducing the need for intensive monitoring. Since birth weight and gestational age did not differ between groups, the observed neonatal benefits are more attributable to peripartum hemodynamic management than to baseline fetal growth differences.

Although the rate of neonatal asphyxia did not reach statistical significance between groups, the reduction in NICU admissions is clinically relevant, suggesting that combined therapy was associated with a reduced need for higher-level neonatal care due to complications such as respiratory distress, infection, or feeding difficulties. The lack of difference in birth weight may relate to the similarity in gestational age and baseline condition between groups after matching.

In terms of safety, there were no significant differences between groups in the incidence of adverse events like hypotension or bradycardia. The few magnesium sulfate-related adverse reactions in the combination group were mild and easily managed. This indicates that, with careful clinical monitoring, such as evaluation of patellar reflexes, respiratory status, and urine output, the combination regimen is well-tolerated, with a safety profile consistent with prior clinical experience of these drugs in pregnancy [32].

This study has several limitations. First, as a single-center retrospective observational study, although PSM was used to reduce selection bias and confounding, resid-

ual confounding from unmeasured or unknown factors—particularly those related to disease severity (e.g., biochemical markers of preeclampsia, timing of disease onset) and perioperative management details (e.g., anesthetic agent selection, intraoperative fluid management)—may persist and could influence the observed associations. Second, the sample size is relatively limited, potentially affecting the statistical power to detect differences in some less frequent secondary outcomes (e.g., eclampsia) and possibly causing some clinically meaningful trends (e.g., 5-minute Apgar score) not to reach statistical significance. In addition, administration of magnesium sulfate in clinical practice is closely related to disease severity, and unmeasured indicators of disease severity may have resulted in residual confounding despite propensity score matching. Furthermore, due to the retrospective nature, despite PSM, details related to the cesarean delivery itself—such as anesthetic dosing, surgical technique, and use of uterotonic agents—may have differed between groups and were not uniformly recorded. These factors could influence intraoperative blood pressure fluctuations and some outcomes. Furthermore, intraoperative blood pressure data were obtained from the Anesthesia Information Management System. While based on continuous monitoring, its accuracy and completeness depend on clinical recording and device operation, potentially involving measurement errors or missing data. Lastly, this study primarily focused on perioperative and short-term maternal-neonatal outcomes, lacking follow-up data on long-term maternal cardiovascular health and child neurodevelopment, both of which are important directions in HDP research.

Despite these limitations, the findings carry potential clinical implications for perioperative blood pressure management in HDP patients undergoing cesarean delivery. The observed association between combination regimen and reduced blood pressure variability suggests that achieving target blood pressure ranges, rather than maintaining hemodynamic stability, may be an important therapeutic goal. For anesthesiologists and obstetricians, the use of labetalol combined with magnesium sulfate may offer a more comprehensive approach to mitigating the hemodynamic stress of cesarean delivery, potentially reducing the risk of acute hypertensive complications while improving neonatal outcomes. Future prospective studies are warranted to validate these findings and establish optimal dosing protocols.

Conclusions

In conclusion, this study demonstrates the significance of critical perioperative blood pressure management in patients with HDP. Compared with labetalol alone, the combined labetalol and magnesium sulfate treatment was associated with more stable intraoperative blood pressure, reduced variability under surgical stress, and may contribute to improvements in some perioperative maternal-neonatal outcomes. These findings provide valuable clinical reference for optimizing blood pressure management strategies in this high-risk population during the perioperative phase. Future large-scale, multicenter, prospective randomized controlled trials are warranted to further validate these findings and to investigate their impact on long-term maternal and neonatal outcomes.

Availability of Data and Materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions

JLL and CFG designed the research study. JLL performed the research. CFG analyzed the data. JLL drafted the article. Both authors contributed to the critical revision of the manuscript for important intellectual content. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study protocol was approved by the Ethics Committee of TongXiang Maternity and Child Health Care Hospital (Ethics Review Research No. 001, 2026), and the requirement for informed consent was waived due to the retrospective study design. All procedures followed the principles of the Declaration of Helsinki.

Acknowledgment

Not applicable.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

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