ANESTHESIOLOGY®

Efficacy and Safety of Preemptive Magnesium Sulfate Infusion during Pheochromocytoma and Paraganglioma Resection: A Randomized, Double-blind, Placebo-controlled Trial

Hao Kong, M.D., Yu-Xiu Zhang, M.D., Qiao-Li Yin, M.D., Shan Jiang, M.D., Jia-Hui Ma, Ph.D., Zhen-Zhen Xu, M.D., Zhen Zhang, M.D.

ANESTHESIOLOGY 2026; 144:301–13

ABSTRACT

Background: Hemodynamic instability frequently occurs in patients undergoing pheochromocytoma and paraganglioma (PPGL) resection. Magnesium sulfate has demonstrated efficacy in mitigating perioperative hemodynamic fluctuations. However, prospective clinical data confirming the safe and effective improvement of intraoperative hemodynamics by magnesium sulfate in PPGL patients are lacking.

Methods: This single-center, double-blind trial enrolled 92 patients who were scheduled for PPGL resection. The patients were randomly assigned to receive either magnesium sulfate (a loading dose of 50 mg · kg^{-1} followed by a continuous infusion of 15 mg · kg^{-1} · h^{-1}) or placebo (normal saline) with administration initiated 30 min before surgery and discontinued upon complete tumor resection. The primary efficacy outcome was a composite measure of intraoperative hemodynamic instability, defined as the cumulative time outside the blood pressure and heart rate target ranges (*i.e.*, systolic arterial pressure greater than 160 mmHg, mean arterial pressure less than 60 mmHg, and heart rate greater than 100 beats/min), expressed as a percentage of total anesthesia duration.

Results: A total of 88 patients were included in the modified intention-to-treat analysis. The cumulative time outside the blood pressure and heart rate target range was 4.3% (interquartile range, 2.4 to 9.6%) in the magnesium sulfate group compared to 8.3% (5.2 to 14.8%) in the placebo group ($P = 0.003$). Compared with the placebo group, intraoperative maximum systolic arterial pressure (185 [170 to 197] mmHg *vs.* 196 [185 to 215] mmHg; $P < 0.001$), proportion of patients requiring phentolamine (66% *vs.* 89%; $P = 0.011$), and phentolamine dose (3 [0 to 7] mg *vs.* 9 [2 to 15] mg; $P = 0.011$) were all lower in the magnesium sulfate group. In the magnesium sulfate group, the magnesium sulfate concentration peaked at 1.82 (1.47 to 2.14) mmol l^{-1} upon completion of the loading dose infusion. No significant differences were observed in safety outcomes between groups.

Conclusions: Preemptive magnesium sulfate infusion effectively reduced intraoperative hemodynamic instability in patients undergoing PPGL resection. The intervention regimen used in the trial was safe.

(ANESTHESIOLOGY 2026; 144:301–13)

EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- Magnesium supplementation has often been used to treat hemodynamics fluctuations in a variety of perioperative settings, often with limited supporting data
- Observational data suggest that magnesium supplementation may be of value in patients undergoing pheochromocytoma and paraganglioma resection, but randomized data are not available

What This Article Tells Us That Is New

- This randomized, double-blind, single-center trial utilized a loading dose and continuous infusion of magnesium sulfate started 30 min before surgery and discontinued at the time of complete tumor resection evaluating a primary composite efficacy outcome of intraoperative hemodynamics instability as a percentage of the total anesthesia duration
- Supplementation significantly reduced the primary outcome without difference in any of the safety outcomes between groups

This article is featured in "This Month in ANESTHESIOLOGY," page A1. This article is accompanied by an editorial on p. 260. Supplemental Digital Content is available for this article. Direct URL citations appear in the printed text and are available in both the HTML and PDF versions of this article. Links to the digital files are provided in the HTML text of this article on the Journal's Web site (www.anesthesiology.org). This article has a visual abstract available in the online version. H.K. and Y.-X.Z. contributed equally to this article.

Submitted for publication February 27, 2025. Accepted for publication September 23, 2025. Published online first on October 3, 2025.

Hao Kong, M.D.: Department of Anesthesiology, Peking University First Hospital, Beijing, China.

Copyright © 2025 American Society of Anesthesiologists. All Rights Reserved. ANESTHESIOLOGY 2026; 144:301–13. DOI: 10.1097/ALN.0000000000005778

Abbreviations: **IQR**, interquartile range; **ICU**, intensive care unit; **MAP**, mean arterial pressure; **PPGL**, pheochromocytoma and paraganglioma; **SAP**, systolic arterial pressure; **TWA**, time-weighted average

Copyright © 2025 American Society of Anesthesiologists. All Rights Reserved. Unauthorized reproduction of this article is prohibited.

<zdoi;10.1097/ALN.0000000000005778>

Pheochromocytoma and paraganglioma (PPGL) are rare catecholamine-secreting tumors posing unique perioperative risks due to severe hemodynamic instability and subsequent cardiovascular sequelae.[1] These tumors exhibit a biphasic hemodynamic pattern during surgery: hypertensive crises are commonly precipitated by anesthetic induction, endotracheal intubation, or direct tumor manipulation, while profound hypotension typically manifests after tumor resection and may persist into the immediate postoperative phase. Although preoperative optimization protocols including α-adrenergic blockade, selective β-blockade, and volume expansion are well established, optimal intraoperative management strategies remain a subject of ongoing debate.

Magnesium is the fourth most abundant cation and the second most prevalent intracellular cation in the human body. Serving as a cofactor for more than 300 enzymes, it plays a pivotal role in maintaining physiologic homeostasis.[2] Magnesium may stabilize hemodynamics through multiple mechanisms: inhibiting catecholamine release from adrenal medulla and peripheral adrenergic nerve terminals, direct blockade of α-adrenergic receptors, vasodilatory effects on vessel walls, regulation of cardiac output, and antiarrhythmic properties *via* L-type calcium channel antagonism.[3,4] Clinical trials have confirmed that magnesium sulfate—administered *via* intravenous infusion or single bolus dose—effectively attenuates hemodynamic fluctuations induced by procedures such as pneumoperitoneum creation or tracheal intubation.[5,6]

Given its physiologic effects, magnesium represents a compelling option for catecholamine modulation in patients undergoing PPGL resection. James first reported its clinical application in 1985.[7] Since then, multiple case series have demonstrated its utility in mitigating hemodynamic fluctuations during tumor resection and managing PPGL crises in adult patients.[8] Additionally, magnesium therapy has shown efficacy in PPGL resection among pediatric populations[9,10] and pregnant individuals.[11,12] However, evidence remains limited to case series due to the rarity of PPGLs.

In recent years, two retrospective cohort studies have associated the absence of intraoperative magnesium sulfate administration with increased intraoperative hemodynamic instability during PPGL resection.[13,14] Conversely, another retrospective study reported comparable hemodynamic parameters between patients who received intraoperative magnesium sulfate and those who did not.[15] Notably, no randomized controlled trial on this topic has been published to date. Therefore, we designed a randomized, double-blind, placebo-controlled trial to rigorously assess the efficacy and safety of magnesium sulfate in maintaining hemodynamic stability during PPGL resection.

Yu-Xiu Zhang, M.D.: Department of Anesthesiology, Peking University First Hospital, Beijing, China.

Qiao-Li Yin, M.D.: Department of Anesthesiology, Peking University First Hospital, Ningxia Women's and Children's Hospital, Yinchuan, China.

Shan Jiang, M.D.: Department of Anesthesiology, Nanjing Chest Hospital, Affiliated Nanjing Brain Hospital, Nanjing Medical University, Nanjing, China.

Jia-Hui Ma, Ph.D.: Department of Anesthesiology, Peking University First Hospital, Beijing, China.

Zhen-Zhen Xu, M.D.: Department of Anesthesiology, Peking University First Hospital, Beijing, China.

Zhen Zhang, M.D.: Department of Anesthesiology, Peking University First Hospital, Beijing, China.

Materials and Methods

Study Design and Ethics

This was a randomized, double-blind, placebo-controlled trial conducted at Peking University First Hospital (Beijing, China) between May 27, 2021, and June 30, 2023. The trial protocol was approved by the Clinical Research Ethics Committee of Peking University First Hospital (approval No. 2020-409; principal investigator: H.K.) on February 23, 2021. Written informed consent was obtained from patients or their legal guardians in the ward the day before surgery. The study was registered in the Chinese Clinical Trial Registry (www.chictr.org.cn; identifier: ChiCTR2100046067) and adheres to the Consolidated Standards of Reporting Trials (CONSORT) guidelines for randomized trials.

Participants

Potential participants were screened the day before their scheduled surgery. Patients were included if they met all the following criteria: (1) age 18 yr or older; (2) clinical diagnosis of resectable PPGL with planned elective surgical resection; (3) α-blockade for more than 7 days preoperatively; and (4) well controlled preoperative blood pressure (less than 140/90 mmHg) and heart rate (less than 90 beats/min). Exclusion criteria included: (1) severe hepatic dysfunction (Child–Pugh grade C) or renal failure (requiring renal replacement therapy); (2) allergy to study medications; (3) preoperative hypermagnesemia; and (4) attending physician or researcher judgment that the subject should be excluded from the study. Such exclusion was primarily based on patient safety considerations. The need for each subject's exclusion was jointly assessed by the attending physician and an independent research team member, ensuring decisions were not based solely on individual judgment.

Randomization and Masking

Random numbers were generated by a biostatistician independent of data management and statistical analyses using SAS version 9.2 software (SAS Institute, USA), with a 1:1 allocation ratio to assign patients to either the magnesium

Copyright © 2025 American Society of Anesthesiologists. All Rights Reserved. Unauthorized reproduction of this article is prohibited.

sulfate or placebo (normal saline) group. Randomization results were sealed in sequentially numbered envelopes and stored on-site. During the study, patients were consecutively recruited and randomly allocated to one of the two groups. A study nurse not otherwise involved in the trial opened the envelopes shortly before subjects entered the anesthesia preparation room and prepared study drugs according to the randomization sequence. Study personnel, the healthcare team, and patients remained masked to treatment group assignments throughout the study. In emergencies, such as unexpected rapid clinical deterioration, the anesthetist could request unmasking of treatment allocation or adjust/interrupt study drug infusion as clinically necessary.

Perioperative Care

After the diagnosis of PPGL, α-blockade was initiated 2 to 6 weeks (with a minimum of 7 days) before surgical resection, using blood pressure–guided dose titration to achieve a target blood pressure less than 140/90 mmHg. The choice of α-blocker (phenoxybenzamine or doxazosin) was left to the discretion of the urologists or endocrinologists. In cases of tachycardia, β-blockade was employed to maintain an heart rate less than 90 beats/min. Metyrosine was not used in any patient due to its unavailability in China. A high-salt diet was not mandated, as the average daily salt intake among Chinese individuals is already relatively high (11.8 ± 4.5 g).[16] Instead, participants were encouraged to drink plenty of fluids. All patients were treated by a dedicated team of urologists, endocrinologists, and anesthesiologists at the center.

In the anesthesia preparation room, the transverse abdominis muscle plane block or quadratus lumborum block was performed for postoperative analgesia. For participants assigned to the magnesium sulfate group, magnesium sulfate at a loading dose of 50 mg · kg^{-1}, diluted with normal saline to a total volume of 100 ml, was administered intravenously over half an hour; thereafter a continuous infusion of 15 mg · kg^{-1} · h^{-1} was delivered (5 g magnesium sulfate and saline mixed in a 50-ml syringe) and discontinued upon complete tumor removal. For those assigned to the placebo group, a 100-ml saline solution was infused over half an hour, followed by a continuous saline infusion at 0.15 ml · kg^{-1} · h^{-1} (in a 50-ml syringe) and stopped when the tumor was fully resected.

In the operating room, an intra-arterial catheter was inserted to monitor beat-to-beat hemodynamics, starting before the induction of anesthesia. Other intraoperative monitoring included electrocardiogram, pulse oxygen saturation, capnogram, inhalational anesthetic concentration, Bispectral Index, nasopharyngeal temperature, and urine output. Central venous lines were established after endotracheal intubation. General anesthesia was performed for all subjects. Propofol and/or etomidate were administered for anesthesia induction; propofol infusion and/or sevoflurane inhalation was used for anesthesia maintenance. Sufentanil and/or remifentanil were administered for analgesia.

A standardized protocol was pre-established to manage intraoperative hemodynamic fluctuations. Target hemodynamic parameters were defined as systolic arterial pressure (SAP) less than 160 mmHg, mean arterial pressure (MAP) greater than 60 mmHg, and heart rate less than 100 beats/min. Vasoactive drug administration was restricted to episodes in which parameters exceeded these thresholds. For hypertension, phentolamine (1 to 2 mg) served as the primary vasodilator, with nicardipine (0.2 to 0.4 mg) as adjunctive therapy. Hypotension was managed primarily with norepinephrine (4 to 20 μg or 0.05 to 0.1 μg · kg^{-1} · min^{-1}), while epinephrine and, in specific cases, dopamine were used based on the tumor's predominant catecholamine secretion pattern. Tachycardia was treated with esmolol (20 to 100 mg). Our center employed a routine fluid infusion protocol for PPGL management. Generally, after anesthesia induction, 1,000 to 1,500 ml of fluids were rapidly administered to achieve a mild hypervolemic state, thereby mitigating relative hypovolemia and hypotension after tumor vessel ligation. After tumor removal, fluid infusion rates were adjusted in accordance with the patient's hemodynamic status and urine output.

At the end of the surgery, the decision to extubate the subject was contingent upon recovery of muscle relaxation and their overall clinical and hemodynamic status. Patients were then transferred to the intensive care unit (ICU), where blood pressure was continuously monitored *via* the intra-arterial catheter until ICU discharge. The thresholds for hemodynamic management in the ICU were consistent with those during their surgery. Upon transfer to the urology ward, vital signs were monitored for 12 h, with noninvasive blood pressure measured every 15 min.

Data Collection and Outcomes

Baseline data comprised demographic characteristics, clinical diagnosis, preoperative comorbidities, American Society of Anesthesiologists classification, PPGL features (symptoms, tumor location/diameter, and biochemical profiles), PPGL pretreatment details (medication type and duration), and hemodynamic parameters before α-blockade and before surgery. Intraoperative data included surgical approach, type of anesthesia, anesthesia duration, surgical duration, vasoactive drug usage, fluid infusion rates, and hemodynamic parameters. Postoperative data encompassed the proportion of patients admitted to the ICU, the length of ICU stay, postoperative mechanical ventilation duration, vasopressor use duration, incidence of postoperative prolonged hypotension, hospital length of stay, and complications within 30 days after surgery.

Hemodynamic data were retrieved from the anesthesia information system, which captured and stored variables in real-time at 10-s intervals. For each participant, collected

Copyright © 2025 American Society of Anesthesiologists. All Rights Reserved. Unauthorized reproduction of this article is prohibited.

hemodynamic data were saved in individual Excel files. Hemodynamic data were analyzed by Python 3.7.0 (Python Software Foundation, USA). The principles for processing hemodynamic data are reported in supplemental material 1 (https://links.lww.com/ALN/E256).

Blood samples were collected to monitor magnesium ion concentration at three specific time points: at the conclusion of the loading dose (when magnesium ion levels reached their peak), at surgery completion, and on the first postoperative morning. Catecholamine levels were also monitored during surgery. Specifically, three time points were selected during tumor manipulation by the surgeon, with 1 ml of blood withdrawn at each time point (cumulative total, 3 ml) to measure average catecholamine levels.

The primary endpoint was a composite reflecting intraoperative hemodynamic instability, defined as the cumulative time outside blood pressure and heart rate target ranges (SAP greater than 160 mmHg, MAP less than 60 mmHg, and heart rate greater than 100 beats/min), expressed as a percentage of total anesthesia duration (from anesthesia induction to operating room discharge; supplemental material 2, https://links.lww.com/ALN/E256). The secondary endpoints were (1) the three components of the primary composite endpoint: cumulative time of SAP greater than 160 mmHg, cumulative time of MAP < 60 mmHg, and cumulative time of heart rate greater than 100 beats/min; (2) intraoperative maximum SAP, minimum MAP, and maximum heart rate; (3) proportions and cumulative dosages of intraoperatively administered vasoactive drugs; and (4) serum catecholamine levels during tumor manipulation. The safety endpoints included (1) magnesium ion concentrations measured at three predefined time points; (2) proportion of patients requiring postoperative mechanical ventilation (*i.e.*, not extubated in the operating room) and duration of postoperative mechanical ventilation; (3) incidence of postoperative prolonged hypotension, defined as MAP less than 60 mmHg for greater than 30 min or continuous catecholamine infusion for blood pressure support greater than 30 min; and (4) postoperative complications occurring within 30 days after surgery. The classification and definition of postoperative complications are provided in supplemental material 3 (https://links.lww.com/ALN/E256).

Statistical Analysis

Sample Size Calculation. Based on retrospective data from 74 pheochromocytoma patients who did not receive magnesium sulfate between 2019 and 2020 in our center, the cumulative time during which blood pressure and heart rate were outside the target ranges (*i.e.*, SAP greater than 160 mmHg, MAP less than 60 mmHg, and heart rate greater than 100 beats/min) accounted for 9.0 ± 4.7% of the total anesthesia duration. Assuming a potential one-third reduction (from 9.0 to 6.0%) with 80% statistical power and a two-sided α of 0.05, 40 participants were required per group. Given the non-normal distribution of the primary outcome, a nonparametric test was selected for analysis. The power efficiency of the Wilcoxon rank sum test is expected to be about 95% compared with a *t* test, and therefore, the sample size needed for a Wilcoxon test would be 1.053-fold that of a *t* test. After applying this multiplier and accounting for a 10% follow-up loss, the target sample size was set at 46 per group (92 total). Sample size calculations were performed *a priori* using PASS (NCSS, LLC, USA) software version 11.

Outcome Analysis. The safety analysis was conducted on all patients who received the allocated treatment. Efficacy and exploratory analyses were performed in a modified intention-to-treat population, defined as excluding individuals whose pathologic examination of the resected tumor was inconsistent with PPGL, as they were deemed not to be at risk for catecholamine-induced hemodynamic instability.

For continuous variables, the Kolmogorov–Smirnov test was used to evaluate their distribution. Variables with a normal distribution were presented as means ± SD, and those with a non-normal distribution were presented as medians (interquartile range [IQR]). Categorical variables were presented as absolute numbers (%).

The balance of baseline variables between the two groups was assessed using absolute standardized differences, defined as absolute differences in means, mean ranks, or proportions divided by the pooled SD. Based on the cutoff point $(1.96 \times \sqrt{[n1 + n2]/[n1 \times n2]})$ recommended by Austin,[17] baseline variables with an absolute standardized difference greater than 0.409 were considered imbalanced.

For the primary endpoint, the cumulative time of SAP greater than 160 mmHg, MAP less than 60 mmHg, and heart rate greater than 100 beats/min was compared using the Mann–Whitney *U* test. For the three individual components of this composite outcome, Bonferroni correction was applied to mitigate type I error inflation associated with multiple comparisons: the nominal significance level (α = 0.05) was adjusted to $\alpha = 0.05/3 \approx 0.017$ for statistical inference. Additionally, the 98.3% CI for between-group median differences of these components were calculated using the Hodges–Lehmann estimator.

For secondary endpoints and safety endpoints, continuous variables with normal distribution were compared with the *t* test; between-group differences are expressed as mean difference and 95% CI. Continuous variables with non-normal distribution or ordinal variables were analyzed with the Mann–Whitney *U* test; differences between two medians and 95% CI were calculated using the Hodges–Lehmann estimators. Categorical variables were analyzed with chi-square tests or Fisher's exact tests; the relative differences are expressed as odds ratios and 95% CI, and the absolute differences between groups are expressed as risk differences and 95% CI. The risk difference was calculated

Copyright © 2025 American Society of Anesthesiologists. All Rights Reserved. Unauthorized reproduction of this article is prohibited.

as the absolute difference in event rates (magnesium sulfate group rate − placebo group rate). The 95% CI for the risk difference was estimated using the normal approximation method or exact methods. Missing data were not imputed.

As exploratory analyses, we calculated the time-weighted averages (TWAs) of values outside the specified ranges of SAP, MAP, and heart rate and modified hemodynamic instability score (supplemental material 4, https://links.lww.com/ALN/E256) to further assess hemodynamic fluctuation. TWA was calculated as the summation of SAP, MAP, or heart rate excursions outside a predefined threshold multiplied by the recording interval (10 s) and divided by the anesthesia duration, in units of mmHg or beats/min (supplemental material 5, https://links.lww.com/ALN/E256). The modified hemodynamic instability score, which consists of three intraoperative components (hemodynamic variables, cumulative dosage of vasoactive drugs, and fluid therapy), was first introduced by Buitenwerf *et al.*[18] for hemodynamic analysis in PPGL, and we also compared this score between the two groups. In addition, we divided the anesthetic duration for PPGL into seven phases (anesthesia induction and tracheal intubation, surgical preparation, skin incision and/or pneumoperitoneum establishment, tumor manipulation, immediate postresection, early postresection, and emergence) to explore the efficacy of magnesium sulfate on hemodynamics at each phase. All of the above exploratory endpoints were compared by Mann–Whitney *U* tests, with median difference and 95% CI calculated using the Hodges–Lehmann estimators.

Sensitivity analyses were performed to assess the robustness of the findings. First, given the relatively small sample size and potential for random baseline imbalances, multiple linear regression was used to adjust for baseline characteristics with between-group absolute standardized difference exceeding 0.20. Due to substantial right-skewness in the primary endpoint, log-transformation and Box–Cox transformation were applied, and an inverse Gaussian distribution with a log link function was fitted to the untransformed primary endpoint in statistical models. Second, different thresholds were used to define hypertension (SAP greater than 160 mmHg, greater than 180 mmHg, and greater than 200 mmHg), hypotension (MAP less than 65 mmHg, less than 60 mmHg, and less than 55 mmHg), and tachycardia (heart rate greater than 90 beats/min, greater than 100 beats/min, and greater than 110 beats/min). Hemodynamic instability was redefined as three composite endpoints: (1) cumulative time of SAP greater than 160 mmHg, MAP less than 65 mmHg, and heart rate greater than 90 beats/min; (2) cumulative time of SAP greater than 180 mmHg, MAP less than 60 mmHg, and heart rate greater than 100 beats/min; and (3) cumulative time of SAP greater than 200 mmHg, MAP less than 55 mmHg, and heart rate greater than 110 beats/min. The Mann–Whitney *U* test was used to compare these three composites between groups.

Statistical analyses were performed using SPSS version 29.0 for Windows (IBM Corp., USA) and RStudio version 2024.12.0 (RStudio, USA). The scatter plot was generated with GraphPad Prism version 10.1.2 (GraphPad Software, USA).

Results

Participants

Between May 27, 2021, and June 30, 2023, 138 patients were assessed for eligibility. Of the 105 eligible patients, 92 were enrolled and randomized to the magnesium sulfate group (n = 46) or placebo group (n = 46). During the study period, one patient in the magnesium sulfate group withdrew consent before intervention; one patient in the magnesium sulfate group and two in the placebo group were diagnosed with non-PPGL on postoperative pathology. Consequently, 91 subjects were included in the safety analysis, with 88 in the modified intention-to-treat analysis (fig. 1).

Baseline and Preoperative Data

The baseline characteristics were well balanced between the two groups (all absolute standardized differences less than 0.409; table 1). Preoperative data, including demographics, comorbidities, American Society of Anesthesiologists class, the features of PPGLs, pretreatments, and baseline hemodynamic parameters, showed no significant differences. Surgical approach, type of anesthesia, surgical duration, anesthesia duration, and anesthetic use were also comparable between groups (table 1; supplemental table 1, https://links.lww.com/ALN/E256).

Efficacy Endpoints of the Study

The primary composite endpoint of intraoperative hemodynamic instability was 4.3% (IQR: 2.4 to 9.6%) in the magnesium sulfate group compared to 8.3% (5.2 to 14.8%) in the placebo group ($P = 0.003$; table 2; fig. 2A). This difference in the primary composite endpoint was primarily driven by a reduction in the cumulative time of SAP greater than 160 mmHg, whereas the cumulative time of MAP less than 60 mmHg and heart rate greater than 100 beats/min were comparable between the two groups (fig. 2B).

Compared with the placebo group, intraoperative maximum SAP, proportion of patients requiring phentolamine, and phentolamine dose were all lower in the magnesium sulfate group. No significant differences were observed between the two groups in minimum MAP, maximum heart rate, vasoconstrictors or esmolol use, or fluid infusion rate (table 2). Intraoperative cardiac index and stroke volume variability monitored by the FloTrac/Vigileo system (Edwards Lifesciences LLC, USA) are presented in supplemental table 2 (https://links.lww.com/ALN/E256). There were no significant differences in serum norepinephrine (median, 40.9 pmol/ml [IQR, 7.4 to 141.9 pmol/ml] *vs.* 93.6 pmol/ml [22.9 to 222.5 pmol/ml];

Copyright © 2025 American Society of Anesthesiologists. All Rights Reserved. Unauthorized reproduction of this article is prohibited.

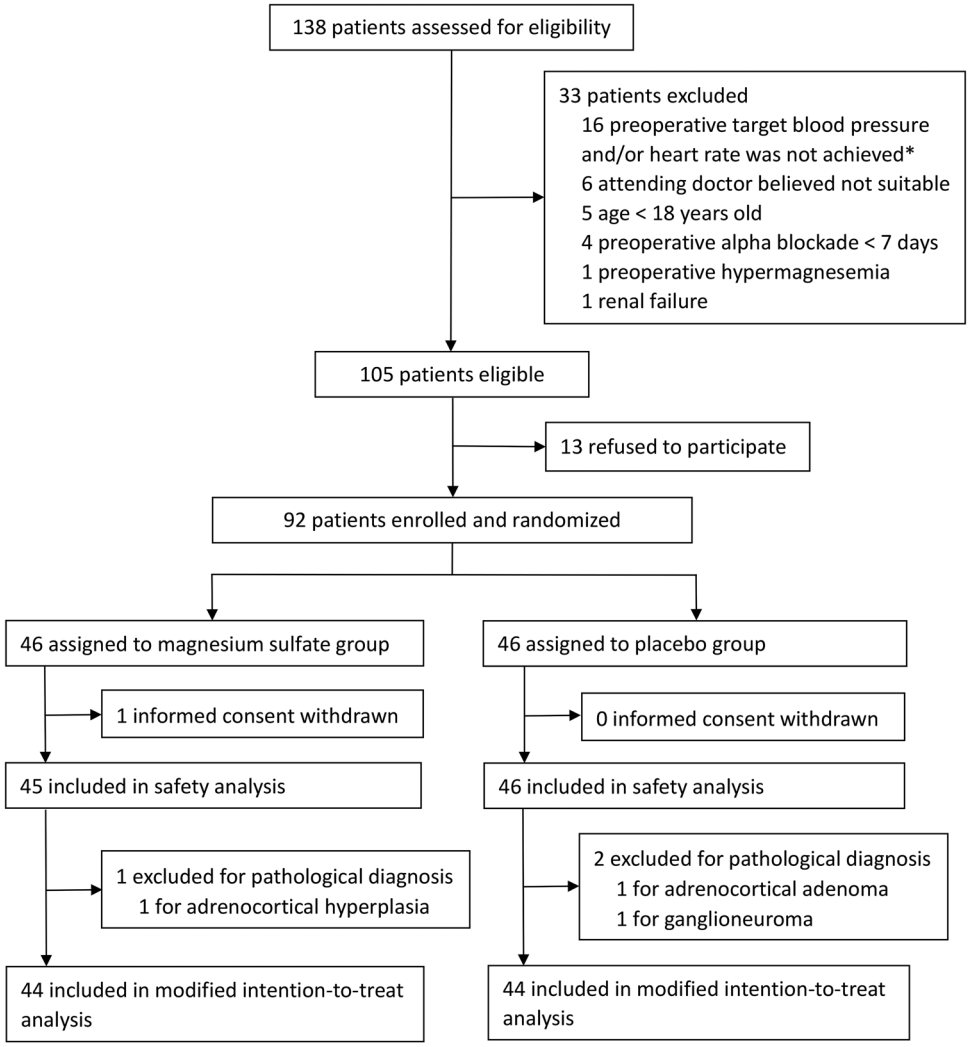


Fig. 1. Recruitment outline. *Preoperative blood pressure greater than 140/90 mmHg and/or heart rate greater than 90 beats/min.

P = 0.075) or epinephrine (2.6 pmol/ml [0.2 to 28.3 pmol/ml] *vs.* 6.1 pmol/ml [0.9 to 46.1 pmol/ml]; P = 0.509) concentrations during tumor manipulation between the two groups (supplemental fig. 1, https://links.lww.com/ALN/E256).

Safety Endpoints of the Study

For patients in the magnesium sulfate group, the median magnesium sulfate dose was 4.6 g (IQR, 4.0 to 5.2 g). The serum magnesium ion concentrations of the two groups are presented in table 3. Between-group comparisons showed similarity in postoperative mechanical ventilation rate and duration, incidence of postoperative hypotension, vasoconstrictor use, in-hospital mortality, ICU admission rate and duration, postoperative length of stay, and total hospital length of stay. The incidence of complications within 30 days after surgery did not differ between groups (table 3).

Exploratory Endpoints of the Study

For the exploratory endpoints, the TWA of SAP greater than 160 mmHg, MAP less than 60 mmHg, and heart rate greater than 100 beats/min was significantly lower in the magnesium sulfate group. The median modified hemodynamic instability score was also lower in the magnesium sulfate group compared with the placebo group (table 2).

We further explored the efficacy of magnesium sulfate on hemodynamics during seven anesthetic/surgical phases, respectively. During anesthesia induction and tracheal intubation, the magnesium sulfate group showed a significantly lower primary composite endpoint. During tumor manipulation, this group also had a shorter primary composite endpoint, alongside decreased cumulative times of SAP greater than 160 mmHg and heart rate greater than 100 beats/min. Additionally, during the immediate postresection period, the magnesium sulfate group presented

Copyright © 2025 American Society of Anesthesiologists. All Rights Reserved. Unauthorized reproduction of this article is prohibited.

Table 1. Baseline Data

Characteristics	Magnesium Sulfate (n = 44)	Placebo (n = 44)	Absolute Standardized Difference*
Demographics			
Age, yr	50 ± 13	51 ± 15	0.027
Sex			0.181
Male, No. (%)	19 (43)	23 (52)	
Female, No. (%)	25 (57)	21 (48)	
Height, cm	165 ± 8	167 ± 8	0.175
Weight, kg	67 ± 11	66 ± 14	0.122
Preoperative comorbidities			
Diabetes mellitus, No. (%)	11 (25)	10 (23)	0.052
Coronary artery disease, No. (%)	1 (2)	2 (5)	0.151
Stroke, No. (%)	2 (5)	2 (5)	0.000
Chronic kidney disease, No. (%)	1 (2)	2 (5)	0.151
ASA class, No. (%)			0.053
II	34 (77)	33 (75)	
III	10 (23)	11 (25)	
Features of PPGL			
Symptoms, No. (%)			
With hypertension	36 (82)	36 (82)	0.000
With typical "triad" symptoms†	5 (11)	6 (14)	0.071
With partial "triad" symptoms‡	23 (52)	19 (43)	0.180
Maximal tumor diameter, cm	4.3 (3.4–5.3)	4.4 (3.1–6.2)	0.116
Origin of tumor, No. (%)			0.065
Adrenal gland	38 (86)	37 (84)	
Paraganglioma	6 (14)	7 (16)	
Biochemical profile, nmol/l			
Plasm-free metanephrine	403 (152–1,941)	358 (147–1,305)	0.292
Plasm-free normetanephrine	3,569 (1,341–7,631)	3,127 (1,352–8,863)	0.041
Peak SBP before α-blockade, mmHg	178 (150–198)	170 (145–189)	0.108
Pretreatments			
α-Blockade			0.078
Phenoxybenzamine, No. (%)	40 (91)	39 (87)	
Doxazosin, No. (%)	4 (9)	5 (11)	
Duration, day	30 (21–50)	30 (21–49)	0.059
β-Blockade, No. (%)	17 (39)	14 (32)	0.183
Hemodynamic parameters before surgery§			
SBP, mmHg	130 (118–137)	128 (117–138)	0.063
DBP, mmHg	80 (74–86)	77 (70–83)	0.150
Heart rate, beats/min	78 (74–79)	77 (72–80)	0.270
Surgical approach			0.299
Laparoscopic, No. (%)	27 (61)	25 (57)	
Robotic, No. (%)	10 (23)	7 (16)	
Open, No. (%)	7 (16)	12 (27)	
Type of anesthesia, No. (%)			0.131
Total intravenous anesthesia	4 (9)	6 (14)	
Balanced inhalation	40 (91)	38 (86)	
Anesthesia duration, min	180 (146–239)	184 (147–223)	0.124
Surgical duration, min	103 (77–164)	100 (77–137)	0.148

*An absolute standardized difference of 0.409 or greater was considered unbalanced. †With the "triad" symptoms (headaches, palpitations, and sweating) at the first clinic visit. ‡With one or two of the "triad" symptoms (headaches, palpitations, and sweating) at the first clinic visit. §Measured on the day before the surgery day in the ward.

ASA, American Society of Anesthesiologists; DBP, diastolic blood pressure; PPGL, pheochromocytoma and paraganglioma; SBP, systolic blood pressure.

a decreased primary composite endpoint and a shorter cumulative time of MAP less than 60 mmHg (fig. 3; supplemental table 3, https://links.lww.com/ALN/E256).

Sensitivity Analysis

We analyzed the primary endpoint with adjustment for imbalanced baseline characteristics. Plasma-free metanephrine, heart rate before surgery, and surgical approach were adjusted given absolute standardized differences greater than 0.20. Multiple linear regression models were used, along with log-transformation and Box–Cox transformation for the primary endpoint, and an inverse Gaussian distribution with a log link function was applied to the untransformed primary endpoint. All models consistently showed that magnesium sulfate was independently

Copyright © 2025 American Society of Anesthesiologists. All Rights Reserved. Unauthorized reproduction of this article is prohibited.

Table 2. Efficacy Endpoints

Endpoint	Magnesium Sulfate (n = 44)	Placebo (n = 44)	MD, OR, and/or RD (95% CI)	*P* Value
Primary endpoint				
Accumulative time of SAP > 160 mmHg + MAP < 60 mmHg + heart rate > 100 beats/min*, %	4.3 (2.4 to 9.6)	8.3 (5.2 to 14.8)	MD = −3.7 (−6.0 to −1.2)	0.003
Secondary endpoints				
Hemodynamic parameters				
Hypertension				
Maximum SAP, mmHg	185 (170 to 197)	196 (185 to 215)	MD = −13 (−22 to −4)	0.004
Accumulative time of SAP > 160 mmHg*, %	2.0 (0.8 to 4.3)	5.2 (2.4 to 9.9)	MD = −2.6 (98.3% CI, −4.9 to −0.7)	< 0.001†
Hypotension				
Minimum MAP, mmHg	55 (49 to 59)	52 (48 to 58)	MD = 2 (−2 to 5)	0.314
Accumulative time of MAP < 60 mmHg*, %	1.0 (0.1 to 2.4)	2.1 (0.1 to 2.9)	MD = −0.4 (98.3% CI, −1.5 to 0.2)	0.146†
Tachycardia				
Maximum heart rate, beats/min	106 (100 to 112)	109 (98 to 118)	MD = −3 (−8 to 2)	0.258
Accumulative time of heart rate > 100 beats/min*, %	0.8 (0.0 to 2.3)	1.3 (0.0 to 3.1)	MD = −0.1 (98.3% CI, −1.1 to 0.4)	0.459†
Accumulative time of heart rate > 100 beats/min combined with SAP > 160 mmHg*, %	0.0 (0.0 to 0.2)	0.0 (0.0 to 0.5)	MD = 0.0 (−0.2 to 0)	0.018
Accumulative time of heart rate > 100 beats/min combined with MAP < 60 mmHg*, %	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	0.487
Vasoactive drugs				
Vasodilators				
Phentolamine, No. (%)	29 (66)	39 (89)	OR = 0.248 (0.081 to 0.760) RD = −23% (−40 to −6%)	0.011
Phentolamine dose, mg	3 (0 to 7)	9 (2 to 15)	MD = −3 (−7 to 0)	0.011
Nicardipine, No. (%)	9 (21)	10 (23)	OR = 0.874 (0.316 to 2.417) RD = −2% (−20 to 15%)	0.796
Nicardipine dose‡, mg	0.4 (0.2 to 2.6)	1.0 (0.4 to 1.0)	MD = −0.2 (−0.8 to 0.6)	0.356
Esmolol, No. (%)	30 (68)	34 (77)	OR = 0.630 (0.244 to 1.627) RD = −9% (−28 to 9%)	0.338
Esmolol dose, mg	80 (0 to 210)	140 (23 to 310)	MD = −20 (−100 to 20)	0.294
Vasoconstrictors				
Epinephrine, No. (%)	3 (7)	3 (7)	OR = 1.000 (0.191 to 5.248) RD = 0% (−17 to 17%)	> 0.999
Norepinephrine, No. (%)	25 (57)	31 (71)	OR = 0.552 (0.229 to 1.331) RD = −14% (−34 to 6%)	0.184
Dopamine, No. (%)	0 (0)	1 (2)	RD = −2% (−17 to 17%)	> 0.999
Equivalent dose of vasoconstrictors§, mg	5.1 (0.0 to 33.2)	7.5 (0.0 to 47.9)	MD = −0.8 (−7.5 to 0.0)	0.279
Continuous delivery duration, min	20 (0 to 45)	30 (0 to 50)	MD = 0 (−18 to 0)	0.314
Infusion rate of fluids, ml/h	1,086 (889 to 1,272)	1,067 (840 to 1,318)	MD = 3 (−124 to 132)	0.822
Exploratory endpoints				
TWA-SAP > 160 mmHg + TWA-MAP < 60 mmHg + TWA–heart rate > 100 beats/min	0.350 (0.112 to 0.925)	0.747 (0.415 to 1.692)	MD = −0.370 (−0.635 to −0.108)	0.004
TWA-SAP > 160 mmHg	0.212 (0.048 to 0.670)	0.618 (0.221 to 1.423)	MD = −0.310 (−0.587 to −0.109)	0.002
TWA-MAP < 60 mmHg	0.026 (0.004 to 0.066)	0.085 (0.001 to 0.145)	MD = −0.030 (−0.073 to 0.000)	0.055
TWA–heart rate> 100 beats/min	0.036 (0.000 to 0.148)	0.066 (0.000 to 0.210)	MD = −0.007 (−0.060 to 0.009)	0.363
Modified hemodynamic instability score	36 (29 to 52)	49 (37 to 59)	MD = −9 (−16 to −2)	0.012

*Expressed as a percentage of total anesthesia duration. ‡Only patients who received nicardipine were compared. §Equivalent dose = (dopamine dose) + (epinephrine dose × 100) + (norepinephrine dose × 100). †Due to the application of Bonferroni correction, a $P < 0.05/3 = 0.017$ was considered statistically significant. The between-group median differences and CI are presented as 98.3% CIs, corresponding to the corrected α level.

MAP, mean arterial pressure; MD, median difference; OR, odds ratio; RD, risk difference; SAP, systolic arterial pressure; TWA, time-weighted average.

associated with reducing intraoperative hemodynamic instability (all $P < 0.05$; supplemental table 4, https://links.lww.com/ALN/E256).

Hemodynamic instability was redefined as three distinct composite endpoints. Compared with the placebo group, all three composite endpoints were significantly lower in

Copyright © 2025 American Society of Anesthesiologists. All Rights Reserved. Unauthorized reproduction of this article is prohibited.

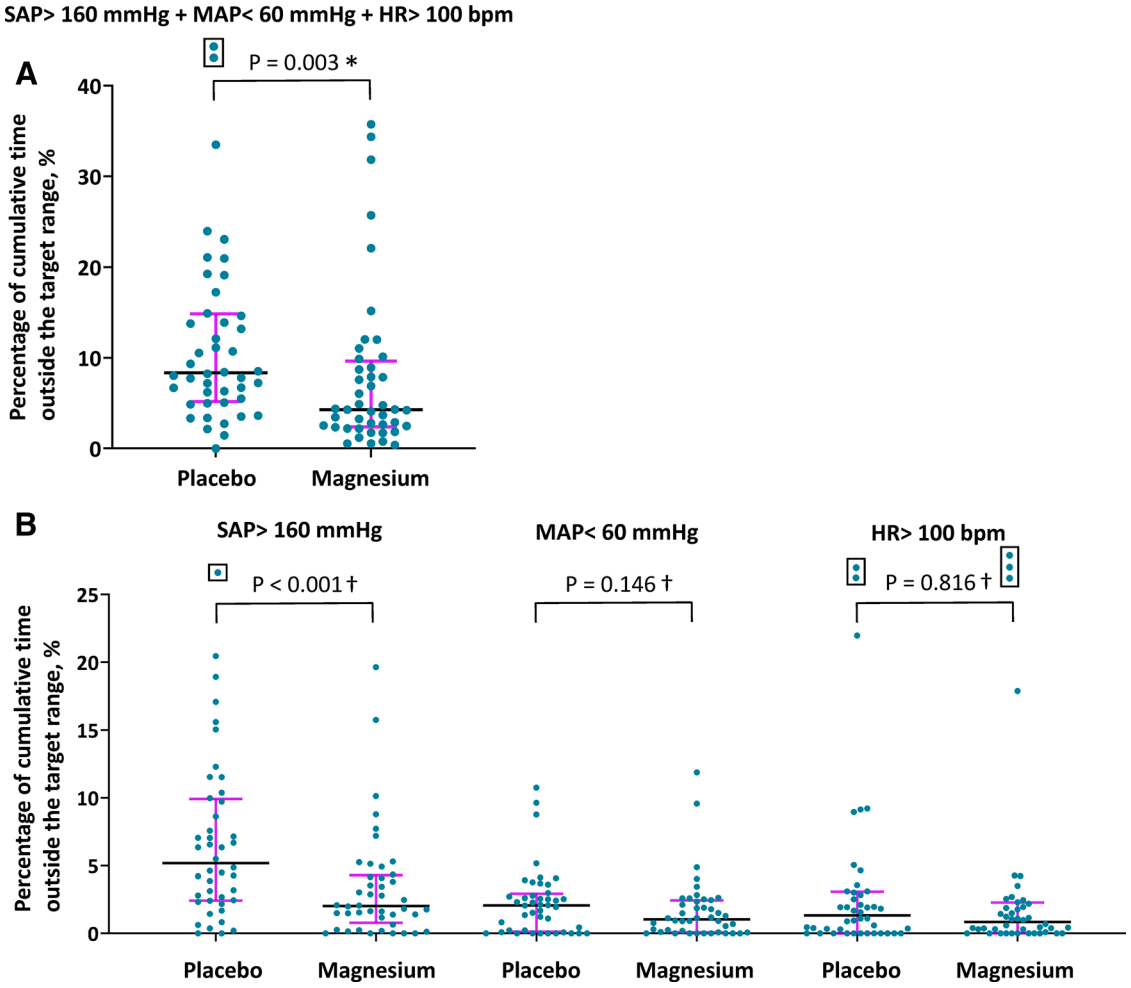


Fig. 2. Comparison of the cumulative time outside the blood pressure and heart rate target ranges between the two groups. (*A*) Primary composite endpoint. (*B*) Three components of the composite. The *green dots* represent each patient. The *dots* within the *black boxes* indicate values that are out of range. The *black horizontal line* represents the median, and the *purple horizontal lines* represents the interquartile range. **P* < 0.05 indicates a statistically significant difference; †*P* < 0.017 indicates a statistically significant difference. bpm, beats/min; HR, heart rate; MAP, mean arterial pressure; SAP, systolic arterial pressure.

the magnesium sulfate group (supplemental table 5, https://links.lww.com/ALN/E256).

Discussion

In this randomized controlled trial of patients undergoing PPGL resection, the magnesium sulfate regimen reduced the cumulative duration of hemodynamic instability (as defined) by approximately 50%, with *post hoc* analysis indicating that the effect of magnesium sulfate predominantly occurred during three phases: anesthesia induction and tracheal intubation, tumor manipulation, and immediate post-resection periods.

The difference in hemodynamic instability between the two groups was primarily driven by a reduction in the cumulative time of hypertension, whereas the cumulative time of hypotension and tachycardia was comparable between the two groups. In our trial, the magnesium sulfate group had significantly shorter cumulative time of intraoperative systolic hypertension, consistent with previous research.[5,13,14] A potential mechanism for magnesium-mediated blood pressure reduction in PPGLs involves its effects on the catecholamine system, specifically through the inhibition of catecholamine release from both the adrenal medulla and peripheral adrenergic nerve terminals.[4] While the laparoscopic cholecystectomy study showed higher peak norepinephrine levels in placebo *versus* magnesium groups (1.25 ± 0.22 *vs.* 0.82 ± 0.11 pmol · ml^{-1}; $P < 0.05$),[19] our trial found no significant difference in intraoperative catecholamine levels between groups, likely because massive catecholamine release during PPGL tumor manipulation blunted magnesium's direct inhibitory effect on such release. Indeed, our patients had far higher norepinephrine (median, 40.9 [IQR, 7.4 to 141.9]

Copyright © 2025 American Society of Anesthesiologists. All Rights Reserved. Unauthorized reproduction of this article is prohibited.

Table 3. Safety Endpoints

Endpoint	Magnesium Sulfate (n = 45)	Placebo (n = 46)	MD, OR, and/or RD (95% CI)	*P* Value
Dose of magnesium sulfate, mg	4.6 (4.0 to 5.2)			
Magnesium ion concentrations, mmol/l				
Preoperative concentration	0.85 (0.80 to 0.90)	0.86 (0.81 to 0.88)		
Measured after loading dose	1.82 (1.47 to 2.14)	0.78 (0.74 to 0.83)		
Measured at the end of surgery	1.26 (1.12 to 1.36)	0.73 (0.67 to 0.80)		
Measured on the morning of the first postoperative day	0.95 (0.87 to 1.04)	0.83 (0.80 to 0.87)		
Intraoperative urine output, ml	700 (500 to 1,000)	700 (300 to 1,000)	100 (–100 to 300)	0.296
Mechanical ventilation				
Extubation at the end of surgery, No. (%)	12 (27)	16 (35)	OR = 0.714 (0.281 to 1.813) RD = –8% (–27 to 11%)	0.402
Duration of postoperative mechanical ventilation, h	2 (0 to 4)	2 (0 to 6)	0 (–2 to 1)	0.719
Postoperative prolonged hypotension, No. (%)	8 (18)	8 (17)	OR = 1.027 (0.349 to 3.023) RD = 0% (–15 to 16%)	0.961
Use of vasoconstrictors, No. (%)	8 (18)	8 (17)	OR = 1.027 (0.349 to 3.023) RD = 0% (–15 to 16%)	0.961
Duration of vasoconstrictors*, h	5 (1 to 31)	8 (2 to 16)	0 (–8 to 29)	0.959
Postoperative arrhythmia†, No. (%)	1 (2)	1 (2)	OR = 1.023 (0.062 to 16.865) RD = 0% (–12 to 12%)	> 0.999
Postoperative hypoglycemia, No. (%)	3 (7)	7 (15)	OR = 0.398 (0.096–1.648) RD = –9% (–28 to 12%)	0.315
In-hospital death, No. (%)	0 (0)	0 (0)	NA	NA
ICU admission after surgery, No. (%)	45 (100)	45 (98)	RD = 2% (–8 to 12%)	> 0.999
LOS in ICU, h	19 (17 to 27)	19 (17 to 23)	0 (–2 to 2)	0.949
LOS after surgery, days	5 (4 to 6)	5 (4 to 7)	0 (–1 to 1)	0.961
Length of hospital stay, days	7 (6 to 10)	7 (6 to 10)	0 (–1 to 1)	0.926
Complications within 30 days after surgery‡, No. (%)				
Acute kidney injury	2 (4)	4 (9)	OR = 0.488 (0.085 to 2.810) RD = –4% (–20 to 13%)	0.677
Myocardial injury	7 (16)	6 (13)	OR = 1.228 (0.378 to 3.986) RD = 3% (–12 to 17%)	0.732
Chyle fistula	2 (4)	0 (0)	RD = 4% (–7 to 15%)	0.494
Pleural effusion	1 (2)	1 (2)	OR = 1.023 (0.062 to 16.865) RD = 0% (–12 to 12%)	> 0.999
Venous thrombosis	1 (2)	0 (0)	RD = 2% (–8 to 12%)	> 0.999
Pancreatitis	0 (0)	1 (2)	RD = –2% (–12 to 8%)	> 0.999
Aspiration	0 (0)	0 (0)	NA	NA

*Only patients who received vasoconstrictors were compared. †One patient experienced atrial premature contractions in bigeminy in the magnesium sulfate group, and one developed supraventricular tachycardia in the placebo group. ‡The diagnostic criteria for complications are detailed in supplemental material 3 (https://links.lww.com/ALN/E256).

ICU, intensive care unit; LOS, length of stay; MD, median difference; OR, odd ratio; RD, rate difference.

versus mean ± SD, 0.82 ± 0.11 pmol · ml^{-1}) and epinephrine (median, 2.6 [IQR, 0.2 to 28.3] *versus* mean ± SD, 0.21 ± 0.05 pmol · ml^{-1}) levels during tumor manipulation than reported in cholecystectomy.[19] Another blood pressure-lowering mechanism of magnesium sulfate involves direct vasodilation of vessel walls, mediated by enhancing endothelial production of nitric oxide and prostacyclin while inhibiting N-type calcium channels.[4] A randomized controlled trial showed that magnesium sulfate administration reduced systemic vascular resistance and stabilized cardiac output during pneumoperitoneum establishment.[20] Thus, magnesium's combined vasodilatory and catecholamine-inhibiting effects collectively contribute to the reduction in intraoperative hypertension among PPGL patients.

In our trial, hypotensive episodes did not differ significantly between the magnesium sulfate and placebo groups. However, *post hoc* analysis revealed that within 10 min after complete tumor resection, the cumulative time of hypotension was significantly lower in the magnesium sulfate group. This finding may relate to residual effects of excessive vasodilator use after tumor extirpation in the placebo group. Sivrikoz *et al.*[14] showed that combining magnesium sulfate with dexmedetomidine reduced intraoperative hypotensive episodes, likely by decreasing sodium nitroprusside requirements in the treatment group. Similarly, Siddiqi *et al.*[15] noted that during pheochromocytoma resection, the magnesium sulfate group had less frequent vasoconstrictor use (24% *vs.* 45%) and a higher intraoperative minimum MAP (66 [56 to 69] mmHg *vs.* 60 [55 to 71] mmHg). In

Copyright © 2025 American Society of Anesthesiologists. All Rights Reserved. Unauthorized reproduction of this article is prohibited.

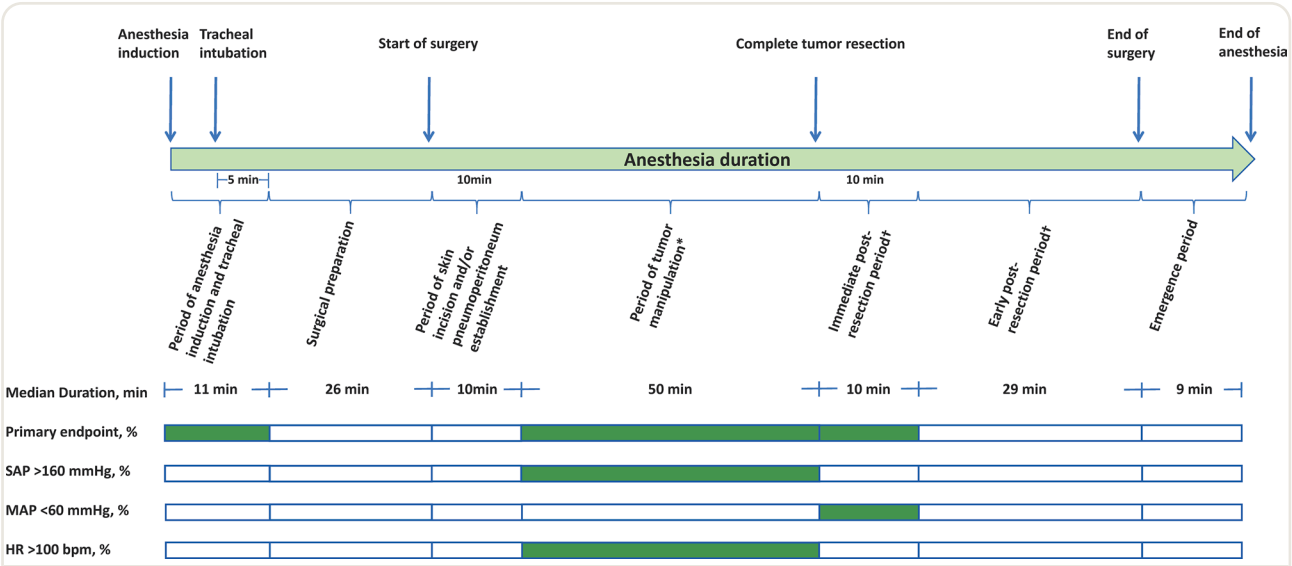


Fig. 3. Definition of the seven anesthetic/surgical phases and magnesium sulfate's efficacy on hemodynamics during these phases. *Since we did not record the exact start time of tumor manipulation, we defined the tumor manipulation period as starting 10 min after the initiation of surgery and ending when the tumor was completely resected. †The post–tumor resection period is divided into two phases: the first 10 min, a high-risk window for hypotension, during which anesthesiologists prioritize hypotension management; and the period beyond 10 min, by which time circulation is typically stabilized *via* continuous catecholamine infusion. The *dark green section* indicates that during this period, magnesium sulfate, compared with placebo, improved the intraoperative hemodynamic parameter, with a statistically significant difference between the two groups (for the composite endpoint, $P < 0.05$ was considered statistically significant; for its individual components, $P < 0.017$ applied). HR, heart rate; MAP, mean arterial pressure; SAP, systolic arterial pressure.

our study, both the proportion of patients requiring phentolamine and total phentolamine dosage were significantly lower in the magnesium sulfate group, findings that may explain the reduced hypotension observed in the immediate postresection period.

Regarding heart rate, no significant differences emerged in intraoperative maximum heart rate or cumulative time of heart rate greater than 100 beats/min in our study. Our exploratory analysis also revealed that magnesium sulfate did reduce the cumulative time of tachycardia during the tumor manipulation period; however, no significant differences were observed in other surgical/anesthesia phases. Although magnesium sulfate is widely used in clinical practice for preventing or treating tachyarrhythmias,[21,22] previous studies have reported inconsistent findings regarding its antitachycardia efficacy.[19,20] While magnesium sulfate is recognized for its antiarrhythmic properties and has reduced arrhythmia incidence in cardiac[23] and noncardiac surgeries,[24] no such differences were detected in our trial, potentially due to the overall low occurrence of arrhythmias in our subjects.

The major toxic effect of magnesium is neuromuscular paralysis.[25] Notably, in our study, magnesium administration did not increase the incidence or duration of postoperative respiratory support. Toxic manifestations, such as loss of deep tendon reflexes, typically emerge when plasma magnesium concentrations reach 4 to 5 mmol · l^{-1}, a threshold our study's mean peak concentration remained well below. Additionally, postoperative prolonged hypotension, another potential concern, was not observed significant increase due to magnesium sulfate infusion in our trial.

Intraoperative magnesium sulfate regimens typically involve an initial 30 to 50 mg · kg^{-1} loading dose followed by 6 to 20 mg · kg^{-1} · h^{-1} continuous infusion until surgery completion.[25] Tan *et al.*[20] confirmed the safety and efficacy of 50 mg · kg^{-1} loading plus 30 mg · kg^{-1} · h^{-1} maintenance for mitigating pneumoperitoneum-related hemodynamic instability in gastrointestinal laparoscopy. However, optimal dosing for PPGL resection remains undefined; existing reports mostly use 40 to 60 mg · kg^{-1} bolus followed by 15 mg · kg^{-1} · h^{-1} maintenance,[8,9,11,14,26,27] consistent with our regimen.

The optimal serum magnesium concentration for effective hemodynamic control remains unclear. Tan *et al.*[20] found efficacy above 2 mM for pneumoperitoneum-related instability, while James[8] and Minami *et al.*[9] recommended 2 to 4 mM for maximal efficacy in PPGL surgery. However, Latendresse *et al.*[10] (1.75 to 2.20 mM), Bryskin and Weldon[27] (as low as 1.4 mM), and an animal study[28] (1.66 mM) showed effectiveness at lower levels in PPGL patients. Our study's mean peak of 1.83 mM supports hemodynamic stability without excessively high magnesium concentrations.

The key strengths of this study include its randomized placebo-controlled design and the implementation

Copyright © 2025 American Society of Anesthesiologists. All Rights Reserved. Unauthorized reproduction of this article is prohibited.

of a well established perioperative management protocol. However, several limitations warrant acknowledgment. First, we evaluated only a fixed magnesium sulfate regimen, leaving the optimal dosage and potential benefits of higher doses for hemodynamic stability undetermined. Second, our trial consisted solely of adult patients, so the efficacy and safety of magnesium sulfate in pediatric populations remain unclear. Third, we observed substantial interpatient variability, underscoring the need for further efforts to refine and individualize hemodynamic management in high-risk patients. Fourth, we lacked accurate real-time monitoring tools for cardiac output and volume status, such as transesophageal echocardiography. Although most patients were monitored using the FloTrac/Vigileo system, its accuracy may be impaired during pneumoperitoneum and in the lateral decubitus position. Fifth, our study showed a modest primary composite endpoint difference (around 7.3 min), and due to limited sample size, no difference was detected in complication rates. Further research with larger cohorts is required to verify its impact on complications, but this low-cost, simple, and safe intervention merits promotion, even with its currently observed effect size.

In summary, the findings of this study highlight that magnesium sulfate is an effective and safe adjunct for hemodynamic control in patients undergoing PPGL resection. This economical and simple intervention with magnesium sulfate infusion should be recommended as a therapeutic measure for stabilizing intraoperative hemodynamic instability in PPGL surgery.

Acknowledgments

The authors gratefully acknowledge Dan-Dan Ma, M.D. (Department of Anesthesiology, Yidu Central Hospital, Qingzhou, China), for help in patient recruitment and Xue-Ying Li, M.S. (Department of Statistics, Peking University First Hospital, Beijing, China), for help in study design and statistical analysis.

Research Support

Supported by grant No. 2023IR22 from the National High-Level Hospital Clinical Research Funding, Interdepartmental Research Project of Peking University First Hospital (Beijing, China) and grant No. 2021CR19 from the Youth Clinical Research Project of Peking University First Hospital.

Competing Interests

The authors declare no competing interests.

Reproducible Science

Full protocol available at: konghao2438@126.com. Raw data available at: konghao2438@126.com.

Correspondence

Address correspondence to Dr. Kong: Peking University First Hospital, No. 8 Xishiku Street, Xicheng District, Beijing 100034, China. konghao2438@126.com or konghao@bjmu.edu.cn

Supplemental Digital Content

Supplemental file, https://links.lww.com/ALN/E256
Supplemental Material 1. Artifact removing algorithm.
Supplemental Material 2. Calculation of the primary endpoint.
Supplemental Material 3. The classification and definition of postoperative complications.
Supplemental Material 4. Modified hemodynamic instability score.
Supplemental Material 5. Calculation of time-weighted averages.
Supplemental Table 1. Intraoperative anesthetic medications.
Supplemental Table 2. Intraoperative CI and SVV.
Supplemental Table 3. Hemodynamics during the seven anesthetic/surgical phases.
Supplemental Table 4. Multivariate analysis.
Supplemental Table 5. Sensitivity analysis.
Supplemental Fig. 1. Intraoperative catecholamine concentrations.

References

1. Neumann HPH, Young WF Jr, Eng C: Pheochromocytoma and paraganglioma. N Engl J Med 2019; 381:552–65. doi:10.1056/NEJMra1806651
2. Herroeder S, Schönherr ME, De Hert SG, Hollmann MW: Magnesium—Essentials for anesthesiologists. Anesthesiology 2011; 114:971–93. doi:10.1097/ALN.0b013e318210483d
3. Lord MS, Augoustides JG: Perioperative management of pheochromocytoma: Focus on magnesium, clevidipine, and vasopressin. J Cardiothorac Vasc Anesth 2012; 26:526–31. doi:10.1053/j.jvca.2012.01.002
4. Schutten JC, Joosten MM, de Borst MH, Bakker SJL: Magnesium and blood pressure: A physiology-based approach. Adv Chronic Kidney Dis 2018; 25:244–50. doi:10.1053/j.ackd.2017.12.003
5. Greenwood J, Nygard B, Brickey D: Effectiveness of intravenous magnesium sulfate to attenuate hemodynamic changes in laparoscopic surgery: A systematic review and meta-analysis. JBI Evid Synth 2021; 19:578–603. doi:10.11124/JBISRIR-D-19-00414
6. Mendonça FT, de Queiroz LM, Guimarães CC, Xavier AC: Effects of lidocaine and magnesium sulfate in attenuating hemodynamic response to tracheal intubation: Single-center, prospective, double-blind, randomized study. Braz J Anesthesiol 2017; 67:50–6. doi:10.1016/j.bjane.2015.08.004

Copyright © 2025 American Society of Anesthesiologists. All Rights Reserved. Unauthorized reproduction of this article is prohibited.

7. James MF: The use of magnesium sulfate in the anesthetic management of pheochromocytoma. Anesthesiology 1985; 62:188–90. doi:10.1097/00000542-198502000-00020
8. James MF: Use of magnesium sulphate in the anaesthetic management of phaeochromocytoma: A review of 17 anaesthetics. Br J Anaesth 1989; 62:616–23. doi:10.1093/bja/62.6.616
9. Minami T, Adachi T, Fukuda K: An effective use of magnesium sulfate for intraoperative management of laparoscopic adrenalectomy for pheochromocytoma in a pediatric patient. Anesth Analg 2002; 95:1243–4. doi:10.1097/00000539-200211000-00024
10. Latendresse TR, Goldin AB, Jonmarker C: Anesthesia for pheochromocytoma resection in a child with Fontan circulation. Can J Anaesth 2011; 58:642. doi:10.1007/s12630-011-9507-5
11. Jayatilaka G, Abayadeera A, Wijayaratna C, Senanayake H, Wijayaratna M: Phaeochromocytoma during pregnancy: Anaesthetic management for a caesarean section combined with bilateral adrenalectomy. Ceylon Med J 2013; 58:173–4. doi:10.4038/cmj.v58i4.6310
12. Morton A, Poad D, Harms P, Lambley J: Phaeochromocytoma in pregnancy: Timing of surgery, mode of delivery and magnesium. Obstet Med 2010; 3:164–5. doi:10.1258/om.2010.100033
13. Livingstone M, Duttchen K, Thompson J, et al.: Hemodynamic stability during pheochromocytoma resection: Lessons learned over the last two decades. Ann Surg Oncol 2015; 22:4175–80. doi:10.1245/s10434-015-4519-y
14. Sivrikoz N, Turhan O, Yavru HA, et al.: Magnesium and dexmedetomidine combination reduces sodium nitroprusside requirement in laparoscopic pheochromocytoma. Ulus Travma Acil Cerrahi Derg 2022; 28:1563–9. doi:10.14744/tjtes.2022.92672
15. Siddiqi HK, Yang HY, Laird AM, et al.: Utility of oral nicardipine and magnesium sulfate infusion during preparation and resection of pheochromocytomas. Surgery 2012; 152:1027–36. doi:10.1016/j.surg.2012.08.023
16. Zhang JY, Yan LX, Tang JL, et al.: Estimating daily salt intake based on 24 h urinary sodium excretion in adults aged 18–69 years in Shandong, China. BMJ Open 2014; 4:e005089. doi:10.1136/bmjopen-2014-005089
17. Austin PC: Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. Stat Med 2009; 28:3083–107. doi:10.1002/sim.3697
18. Buitenwerf E, Osinga TE, Timmers HJLM, et al.: Efficacy of α-blockers on hemodynamic control during pheochromocytoma resection: A randomized controlled trial. J Clin Endocrinol Metab 2020; 105:2381–91. doi:10.1210/clinem/dgz188
19. Jee D, Lee D, Yun S, Lee C: Magnesium sulphate attenuates arterial pressure increase during laparoscopic cholecystectomy. Br J Anaesth 2009; 103:484–9. doi:10.1093/bja/aep196
20. Tan W, Qian DC, Zheng MM, Lu X, Han Y, Qi DY: Effects of different doses of magnesium sulfate on pneumoperitoneum-related hemodynamic changes in patients undergoing gastrointestinal laparoscopy: A randomized, double-blind, controlled trial. BMC Anesthesiol 2019; 19:237. doi:10.1186/s12871-019-0886-4
21. Piotrowski AA, Kalus JS: Magnesium for the treatment and prevention of atrial tachyarrhythmias. Pharmacotherapy 2004; 24:879–95. doi:10.1592/phco.24.9.879.36092
22. Hoffer M, Tran QK, Hodgson R, Atwater M, Pourmand A: Utility of magnesium sulfate in the treatment of rapid atrial fibrillation in the emergency department: A systematic review and meta-analysis. Eur J Emerg Med 2022; 29:253–61. doi:10.1097/MEJ.0000000000000941
23. Naghipour B, Faridaalaee G, Shadvar K, Bilehjani E, Khabaz AH, Fakhari S: Effect of prophylaxis of magnesium sulfate for reduction of postcardiac surgery arrhythmia: Randomized clinical trial. Ann Card Anaesth 2016; 19:662–7. doi:10.4103/0971-9784.191577
24. Khalil MA, Al-Agaty AE, Ali WG, Abdel Azeem MS: A comparative study between amiodarone and magnesium sulfate as antiarrhythmic agents for prophylaxis against atrial fibrillation following lobectomy. J Anesth 2013; 27:56–61. doi:10.1007/s00540-012-1478-3
25. Do SH: Magnesium: A versatile drug for anesthesiologists. Korean J Anesthesiol 2013; 65:4–8. doi:10.4097/kjae.2013.65.1.4
26. Sanath Kumar SB, Date R, Woodhouse N, El-Shafie O, Nollain K: Successful management of phaeochromocytoma using preoperative oral labetalol and intraoperative magnesium sulphate: Report of four cases. Sultan Qaboos Univ Med J 2014; 14:e236–40. doi:10.1016/j.tacc.2011.01.009
27. Bryskin R, Weldon BC: Dexmedetomidine and magnesium sulfate in the perioperative management of a child undergoing laparoscopic resection of bilateral pheochromocytomas. J Clin Anesth 2010; 22:126–9. doi:10.1016/j.jclinane.2009.01.017
28. Maidanskaia EG, Spadavecchia C, Vincenti S, Mirra A: Anaesthetic management of a labrador retriever undergoing adrenalectomy for phaeochromocytoma excision: A case report. Front Vet Sci 2022; 9:789101. doi:10.3389/fvets.2022.789101

Copyright © 2025 American Society of Anesthesiologists. All Rights Reserved. Unauthorized reproduction of this article is prohibited.