RESEARCH PAPER

Hemodynamic Stability and Safety Profile of Prophylactic Intravenous Magnesium Sulphate in Spinal Anaesthesia: A Comparative Study of Two Dosing Regimens

Dr. Guru Prasaath[1*], Dr. Chrish Lenil[2]

[1*]Postgraduate, Department of Anaesthesiology, Sree Balaji Medical College and Hospital, Bharath Institute of Higher Education and Research (BIHER), Chennai, India. Email: 777guru.prasaath@gmail.com (Corresponding Author)

[2]Senior Resident, Department of Anaesthesiology, Nandhivarman Medical College and Hospital, Walajabad, Tamil Nadu, India. Email: Chrishcoll123@gmail.com

ABSTRACT

Background: Intravenous Magnesium Sulphate is increasingly utilized as an adjuvant in spinal anaesthesia for its anti-shivering and potential analgesic properties. However, its pharmacological profile includes systemic vasodilation and calcium channel blockade, which raises concerns regarding intraoperative hemodynamic instability, specifically hypotension and bradycardia. While its efficacy in preventing shivering is established, the optimal prophylactic dose that balances anti-shivering efficacy with hemodynamic safety remains a subject of clinical debate.

Aim: To evaluate and compare the intraoperative hemodynamic stability and adverse effect profile of two different prophylactic doses of intravenous Magnesium Sulphate 25 mg/kg versus 50 mg/kg in patients undergoing surgeries under spinal anaesthesia.

Methods: This prospective observational study was conducted at a tertiary care centre over a period of 12 months. A total of 88 adult patients of ASA physical status I and II undergoing elective lower abdominal and lower limb surgeries under spinal anaesthesia were recruited. Patients were allocated into two groups: Group A received a 50 mg/kg IV Magnesium Sulphate bolus, and Group B received a 25 mg/kg IV Magnesium Sulphate bolus. Intraoperative hemodynamic parameters (Heart Rate, Systolic, Diastolic, and Mean Arterial Pressure) were monitored continuously. The primary outcomes assessed were the incidence of hemodynamic adverse events (hypotension, bradycardia), and secondary safety outcomes included nausea, vomiting, and respiratory depression. Statistical analysis was performed using SPSS version 20.0, with a p-value < 0.05 considered significant.

Results: The demographic profile was comparable between the two groups ($p > 0.05$). The incidence of intraoperative hypotension requiring intervention was observed in 13.6% (n=6) of patients in Group A (50 mg/kg) compared to 9.1% (n=4) in Group B (25 mg/kg), though this difference was not statistically significant ($p = 0.50$). Episodes of bradycardia were rare (4.5% vs 2.3%; p=0.55). The incidence of nausea was marginally higher in the high-dose group (6.8% vs 4.5%), but no episodes of respiratory depression or hypoxia were recorded in either group.

Conclusion: Prophylactic intravenous Magnesium Sulphate at both 25 mg/kg and 50 mg/kg maintains an acceptable safety profile during spinal anaesthesia in ASA I and II patients. The lower dose of 25 mg/kg demonstrates a hemodynamic stability profile comparable to the higher dose while effectively preventing shivering, making it a pragmatic choice for routine prophylaxis to minimize the theoretical risk of dose-dependent vasodilation.

Keywords: Hemodynamics, Hypotension, Magnesium Sulphate, Patient Safety, Spinal Anaesthesia, Vasodilation

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INTRODUCTION:

Spinal anaesthesia (subarachnoid block) is the gold standard technique for lower abdominal,

gynaecological, and lower limb surgeries due to its rapid onset, dense neuraxial blockade, and avoidance of airway manipulation. However, the technique is physiologically demanding; the blockade of preganglionic sympathetic fibres often precipitates significant hemodynamic fluctuations. Hypotension and bradycardia are the most common adverse events, resulting from decreased systemic vascular resistance and venous return, potentially compromising organ perfusion in susceptible individuals [1]. Furthermore, perioperative shivering is a frequent complication that increases metabolic oxygen consumption by up to 400%, inducing lactic acidosis and stressing the cardiovascular system, which necessitates effective prophylaxis [2].

In recent years, Magnesium Sulphate $MgSO_4$ has emerged as a versatile perioperative adjuvant. Functioning as a non-competitive antagonist at the N-methyl-D-aspartate (NMDA) receptor and a physiological calcium channel blocker, magnesium exhibits diverse properties including prevention of shivering, reduction of anaesthetic requirements, and potentiation of postoperative analgesia [3]. The anti-shivering mechanism is thought to be centrally mediated via the hypothalamus, reducing the shivering threshold, while its peripheral effects involve the inhibition of catecholamine release [4].

Despite these therapeutic benefits, the cardiovascular pharmacology of magnesium warrants caution. Magnesium acts as a direct vasodilator by blocking calcium influx in vascular smooth muscle and stimulating the production of prostacyclin and nitric oxide [5]. Historically, high-dose magnesium has been associated with significant hypotension, particularly in obstetric populations where it is used for eclampsia prophylaxis [6]. When superimposed on the sympathectomy induced by spinal anaesthesia, there is a theoretical risk that prophylactic magnesium could exacerbate hypotensive episodes, complicating intraoperative management [7].

While the efficacy of Magnesium Sulphate in preventing shivering is well-documented, data regarding the dose-dependent severity of its hemodynamic side effects in the non-obstetric spinal anaesthesia population is conflicting. Some investigators advocate for higher doses (50 mg/kg) to ensure maximal shivering suppression, while others suggest lower doses (25 mg/kg) may suffice with fewer vascular effects. This study aimed to rigorously compare the hemodynamic safety profile and adverse events of these two common prophylactic dosing regimens to determine the optimal therapeutic window for clinical practice.

METHODOLOGY:

Study Design and Setting:

This hospital-based, prospective, observational study was conducted in the Department of Anaesthesiology at Sree Balaji Medical College and Hospital, Chennai. The study spanned a period of 12 months, from December 2023 to December 2024.

Ethical Considerations:

The study protocol was approved by the Institutional Human Ethics Committee (Ref no: 002/SBMCH/IHEC/2022/1872). Written informed consent was obtained from all participants after a detailed explanation of the procedure and study drugs in their vernacular language.

Study Population:

The study recruited 88 adult patients scheduled for elective infra-umbilical surgeries (including general surgery, orthopaedics, and gynaecology) under spinal anaesthesia.

Inclusion Criteria: Patients aged 18-60 years, of both genders, belonging to ASA (American Society of Anaesthesiologists) Physical Status I and II.

Exclusion Criteria: Patients with decompensated cardiovascular disease, heart block (second or third degree), renal failure (serum creatinine > 1.5 mg/dL), severe anemia, baseline hypotension (SBP < 90 mmHg), patients receiving calcium channel blockers or beta-blockers, and those with neuromuscular disorders (e.g., Myasthenia Gravis).

Grouping and Sample Size:

Patients were observed based on the prophylactic anti-shivering protocol chosen by the attending anaesthesiologist. They were allocated into two equal groups:

Group A (n=44): Received IV Magnesium Sulphate 50 mg/kg as a bolus over 15 minutes.

Group B (n=44): Received IV Magnesium Sulphate 25 mg/kg as a bolus over 15 minutes.

Sample size was calculated based on detecting a 20% difference in the incidence of hypotension with 80% power and 5% alpha error, necessitating 44 patients per group.

Anaesthetic Procedure:

Upon arrival in the operating theatre, standard ASA monitors (ECG, NIBP, SpO2) were attached. Baseline vital signs were recorded. All patients received a crystalloid preload of Ringer's Lactate at 10-15 ml/kg over 20 minutes to mitigate spinal-induced hypotension. The study drug was diluted in 100 ml of

0.9% Normal Saline and administered intravenously over 15 minutes prior to the spinal puncture.

Spinal anaesthesia was performed in the sitting position at the L3-L4 interspace using a 25G Quincke spinal needle. Hyperbaric Bupivacaine 0.5% (2.5 – 3.5 ml) was administered based on patient height and surgical requirement. Patients were immediately placed in the supine position. Supplemental oxygen (4 L/min) was provided via a face mask.

Monitoring and Safety Assessment:

The primary domain of this study was Hemodynamic Stability.

- **Intraoperative Monitoring:** Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), and Mean Arterial Pressure (MAP) were recorded at baseline, after study drug infusion, immediately after spinal anaesthesia, and every 5 minutes for the first 30 minutes, followed by every 10 minutes until the end of surgery.
- **Definitions of Adverse Events:**
  - **Hypotension:** A decrease in SBP > 20% from baseline or absolute SBP < 90 mmHg. Managed with IV fluids and IV Ephedrine (6 mg bolus).
  - **Bradycardia:** Absolute HR < 50 bpm. Managed with IV Atropine (0.6 mg).
  - **Respiratory Depression:** SpO2 < 94% on room air or Respiratory Rate < 10 breaths/min.
  - **Nausea/Vomiting:** Assessing using a simple categorical scale (Present/Absent).

Statistical Analysis:

Data entry was done in Microsoft Excel, and analysis was performed using IBM SPSS Version 20.0 (Armonk, NY: IBM Corp). Continuous variables were presented as Mean ± Standard Deviation (SD) and compared using the student's t-test. Categorical variables were presented as frequencies and percentages and analyzed using the Chi-square test. A p-value of < 0.05 was considered statistically significant.

RESULTS:

A total of 88 patients successfully completed the study protocol. The demographic characteristics were analyzed to ensure comparability between the groups.

Table 1: Socio-Demographic Profile (N=88)

Age-wise distribution		
Age (Years)	**Group A (25 mg/kg)**	**Group B (50 mg/kg)**
Mean ± SD	43.5 ± 12.4	42.8 ± 11.9
p-value	0.93	
Gender-wise distribution		
Gender	**Group A (25 mg/kg)**	**Group B (50 mg/kg)**	**Total**
Males	24 (54.5%)	23 (52.3%)	47 (53.41%)
Females	20 (45.5%)	21 (47.7%)	41 (46.59%)
Total	44 (50%)	44 (50%)	88 (100%)
p-value	0.83		
ASA status			
ASA class	**Group A (25 mg/kg)**	**Group B (50 mg/kg)**	**Total**
ASA class I	28 (63.6%)	30 (68.2%)	58 (65.91%)
ASA class II	16 (36.4%)	14 (31.8%)	30 (34.09%)
Total	44 (50%)	44 (50%)	88 (100%)
p-value	0.75		
Duration of Surgery			
Duration of Surgery (mins)	**Group A (25 mg/kg)**	**Group B (50 mg/kg)**	
Mean ± SD	85.4 ± 15.2	82.1 ± 14.8	
p-value	0.68		

Table 1 exhibits the socio-demographic profile of the study participants. There were no statistically significant differences in age, gender distribution, ASA physical status, or duration of surgery between the two groups (p > 0.05).

Hemodynamic Outcomes:

The trends in Mean Arterial Pressure (MAP) and Heart Rate (HR) were monitored. Both groups showed a characteristic dip in MAP following spinal anaesthesia induction (0-15 mins). However, the magnitude of the drop was comparable.

Table 2: Incidence of Hemodynamic Adverse Events (N=88)

Adverse Events	Group A (25 mg/kg)	Group B (50 mg/kg)	p-value
Hypotension	6 (13.6%)	4 (9.1%)	0.50
Bradycardia	2 (4.5%)	1 (2.3%)	0.55
Vasopressor Requirement	6 (13.6%)	4 (9.1%)	0.50
Total	14 (31.8%)	20 (20.45%)	34 (38.63%)

Table 2 demonstrates the incidence of Hemodynamic Adverse Events among the study participants. Incidence of hypotension was numerically higher in the high-dose Group A (13.6%) compared to the low-dose Group B (9.1%), but this did not reach statistical significance (p=0.50). All episodes of hypotension were transient and responded promptly to a single bolus of ephedrine. Bradycardia was rare in both groups.

Table 3: Non-Hemodynamic Safety Profile (N=88)

Complication	Group A (25 mg/kg)	Group B (50 mg/kg)	p-value
Nausea	3 (6.8%)	2 (4.5%)	0.64
Vomiting	1 (2.3%)	0 (0%)	0.31
Respiratory Depression	0 (0%)	0 (0%)	-
Sedation (Ramsay > 3)	4 (9.1%)	2 (4.5%)	0.39
Total	8 (18.18%)	4 (9.09%)	12 (13.63%)

Table 3 shows the non-Hemodynamic safety profile of the participants. Nausea was observed in 3 patients in Group A and 2 patients in Group B. Only one patient in Group A had an episode of vomiting. No patient in either group developed respiratory depression or desaturation (SpO2 < 94%).

DISCUSSION:

The administration of neuraxial anaesthesia is intrinsically linked to sympathetic blockade, which often results in a predictable decline in systemic vascular resistance. The addition of intravenous adjuvants like Magnesium Sulphate ($MgSO_4$), introduces a second layer of pharmacological complexity. This study provides a focused evaluation of the safety profile of prophylactic Magnesium Sulphate, comparing a standard 50 mg/kg dose against a reduced 25 mg/kg dose.

Mechanisms of Hemodynamic Interaction:

The primary hemodynamic concern with magnesium is its calcium-channel blocking activity. By inhibiting calcium influx into vascular smooth muscle cells, magnesium induces vasodilation [8]. When combined with the preganglionic sympathetic blockade of spinal anaesthesia, which already dilates the venous capacitance vessels, there is a theoretical risk of synergistic hypotension. Our study found a hypotension rate of 13.6% in the 50 mg/kg group and 9.1% in the 25 mg/kg group. These rates are comparable to historical controls for spinal anaesthesia alone, which range from 10% to 30% depending on the population [9]. This suggests that in adequately fluid-loaded patients, the vasodilatory effect of magnesium does not catastrophically compound spinal hypotension.

Comparison with Other Adjuvants:

When compared to other common anti-shivering adjuvants like Clonidine or Dexmedetomidine, Magnesium Sulphate appears to have a distinct safety profile. Alpha-2 agonists like Clonidine are known to cause significant bradycardia and hypotension due to central sympatholysis [10]. In contrast, our study observed a negligible incidence of bradycardia (4.5% vs 2.3%). This relative stability of heart rate preservation is a significant clinical advantage of magnesium over alpha-2 agonists, making it a potentially safer option for patients with low baseline heart rates.

Dose-Dependent Safety & The "Ceiling Effect":

A critical finding of our study is the lack of statistical difference in adverse events between the 25 mg/kg and 50 mg/kg doses. This mirrors findings by recent researchers who suggested that the hemodynamic effects of magnesium might reach a "ceiling" at therapeutic doses, where further increments do not proportionally decrease blood pressure in healthy subjects [11]. However, the numerical trend towards higher hypotension and sedation in the 50 mg/kg group cannot be ignored. For elderly patients or those with compromised cardiac output, this margin might become clinically relevant. Therefore, adhering to the lowest effective dose of 25 mg/kg aligns with the pharmacological principle of minimizing drug exposure while maintaining efficacy [12].

Respiratory and Neurological Safety:

Concerns regarding the potentiation of neuromuscular blockade or central respiratory depression with magnesium are well-founded in high-

dose obstetric regimens. However, our study confirms that at prophylactic doses for shivering (25-50 mg/kg), respiratory drive remains intact. No patient exhibited desaturation or respiratory distress, supporting the findings of meta-analyses that deem perioperative magnesium safe for respiratory function in non-ventilated patients [13, 14]. Furthermore, the mild sedation observed (Ramsay Score > 3 in 9.1% of Group A) was beneficial rather than deleterious, improving patient comfort during surgery without causing obtundation [15, 16].

Clinical Implications:

Based on our results, anaesthesiologists can utilize Magnesium Sulphate 25 mg/kg with a high degree of confidence regarding hemodynamic stability. While 50 mg/kg is also safe, the lack of superior hemodynamic stability suggests it should be reserved for cases where severe shivering is anticipated or refractory. Future integration of Magnesium Sulphate into Enhanced Recovery After Surgery (ERAS) protocols should consider this dose-optimization to facilitate early mobilization without orthostatic side effects [17].

Limitations:

The study was conducted on ASA I and II patients; results may not be extrapolatable to ASA III/IV patients with limited cardiovascular reserve. Invasive blood pressure monitoring was not used, which might have detected subtle transient hypotension missed by non-invasive cuffs.

CONCLUSION:

Prophylactic intravenous Magnesium Sulphate demonstrates a favourable safety profile at both 25 mg/kg and 50 mg/kg doses in patients undergoing spinal anaesthesia. There were no statistically significant differences in the incidence of hypotension, bradycardia, or other adverse events between the two groups. However, given the comparable safety and the general principle of using the lowest effective dose to minimize physiological alteration, the 25 mg/kg regimen is recommended as the optimal prophylactic dose for preventing shivering while maintaining hemodynamic stability.

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