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Original Research Article

Comparative Evaluation of Intrathecal Magnesium Sulphate *vs.* Clonidine as Adjuvants to Hyperbaric Bupivacaine in Spinal Anaesthesia

Pushkal Yadav[1], Santosh Priya[2], Ritu Kumari[3], Rajesh Verma[4]

[1]Senior Resident, Department of Anaesthesia, Patna Medical College & Hospital, Patna, Bihar, India
[2]Senior Resident, Department of Anaesthesia, Patna Medical College & Hospital, Patna, Bihar, India
[3]Senior Resident, Department of Anaesthesia, Patna Medical College & Hospital, Patna, Bihar, India
[4]Professor, Department of Anaesthesia, Patna Medical College & Hospital, Patna, Bihar, India

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Corresponding author: Santosh Priya
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Abstract:

Background: Spinal anaesthesia is the favored approach for lower abdomen and lower limb procedures because it is simple and effective. However, due to the short duration of analgesia provided by local anaesthetics alone, adjuvants are frequently used in conjunction.

Objective: The major goal of this study was to assess and compare the onset and duration of sensory and motor block, hemodynamic stability, and duration of postoperative analgesia between Magnesium Sulphate and Clonidine when used as intrathecal adjuvant.

Methods: The Department of Anaesthesia at Patna Medical College and Hospital (PMCH) carried out a prospective, cross-sectional comparative study between February and September. 99 adult patients with ASA physical status I or II, ages 18 to 60, who were scheduled for elective lower abdominal or lower limb procedures made up the study population. To assess various anesthetic regimens, these individuals were divided into three equal groups of thirty-three at random. While the intervention groups got adjuvants, Group B received 0.5% hyperbaric Bupivacaine mixed with normal saline; Group M received Bupivacaine with 50 mg of magnesium sulphate; and Group C received Bupivacaine plus 30 µg of Clonidine.

Results: According to the study, Group C experienced sensory and motor block far more quickly than both Group M and Group B ($p < 0.05$). Group C had the longest duration of postoperative analgesia (330.7 ± 47.7 min), followed by Group M (246.3 ± 55.9 min), and Group B had the smallest length (134.4 ± 17.9 min). Group M showed a more favorable profile in terms of hemodynamic stability, while Group C was associated with a higher incidence of bradycardia and hypotension despite its stronger analgesic efficacy.

Conclusion: Magnesium Sulfate and Clonidine are both excellent adjuvants for intrathecal bupivacaine. Clonidine has a longer duration of analgesia and a speedier onset, although it requires close hemodynamic monitoring. Magnesium Sulphate is a valuable option that provides extended analgesia while also having a higher safety profile in terms of hemodynamic stability.

Introduction

Spinal anesthesia, also known as subarachnoid block, is still the gold standard for lower abdominal, pelvic, and lower limb procedures. It has several specific advantages, including a quick onset of action, extensive neuraxial blocking, less intraoperative blood loss, and considerable protection against the neuroendocrine stress response induced by surgery [1]. Due to its consistent distribution and efficacy, hyperbaric bupivacaine is the most commonly used local anesthetic for these procedures. However, when taken alone, bupivacaine has a severe restriction in that its duration of action is rather brief. This frequently causes the block to resolve before complex surgeries are completed, or it needs the early administration of systemic rescue analgesics in the immediate postoperative period, which can result in undesired opioid-related adverse effects [2].

Anesthesiologists have thoroughly studied a number of pharmacological adjuvants intended to improve the quality of the spinal block in order to get around these problems. An intrathecal adjuvant should ideally increase the analgesic effect, prolong the duration of both sensory and motor blockage, and enable a decrease in the necessary local anesthetic dosage. In order to minimize systemic toxicity and lower the risk of hemodynamic instability, this dose-sparing capacity is essential. Alpha-2 adrenergic agonists like clonidine and dexmedetomidine, opioids like fentanyl and morphine, vasoconstrictors like epinephrine, and N-methyl-D-aspartate (NMDA) receptor antagonists like magnesium sulphate have all been used over time with differing degrees of success [3-5].

Clonidine as an Adjuvant

Clonidine selectively activates the alpha-2 adrenergic receptor. Its application in neuraxial anesthesia has been thoroughly documented throughout the last few decades. The mechanism of action involves the stimulation of alpha-2 receptors in the spinal cord's dorsal horn, which decreases the production of nociceptive neurotransmitters including Substance P and Calcitonin Gene-Related Peptide (CGRP) [5]. It also causes hyperpolarization of afferent neurons, which inhibits nerve impulse transmission. Clonidine has been shown to extend both sensory and motor blockage while also providing drowsiness, however its usage is occasionally limited by side effects such as hypotension and bradycardia [6].

Magnesium Sulphate as an Adjuvant

Magnesium is the body's fourth most prevalent cation and works as a non-competitive antagonist to the NMDA receptor. The activation of NMDA receptors is an important mechanism in the development of central sensitization and wind-up phenomena in the spinal cord in response to nociceptive stimuli. Magnesium inhibits calcium ion influx and consequent central sensitization by inhibiting these channels [7]. Intrathecal magnesium sulphate has been shown in animal and human trials to enhance opioid analgesia and extend the duration of spinal anesthesia while maintaining a favorable safety profile, particularly in terms of hemodynamic stability [8].

Rationale for the Study

While both medications have been investigated individually, there is limited comparison data on their efficacy and safety profile in the unique population of eastern India. This prospective study, undertaken at PMCH in Patna, intends to directly assess the therapeutic effects of Magnesium Sulphate and Clonidine as adjuvants to hyperbaric bupivacaine, with an emphasis on block features, hemodynamic factors, and postoperative analgesia duration.

Materials and Methods

Study Design and Setting

This study was planned as a prospective, randomized, double-blind, cross-sectional comparison. It was carried out in the Department of Anaesthesiology at Patna Medical College and Hospital (PMCH) in Patna. The data collection process lasted eight months, beginning in February 2025 and ending in September 2025.

Study Population and Sample Size

99 patients were enrolled in order to attain an 80% study power and a 95% confidence interval after a statistical power analysis based on prior research on analgesic duration was carried out to identify the suitable sample size. Adults between the ages of 18 and 60 who were between 150 and 180 cm tall and classed as American Society of Anesthesiologists (ASA) Physical Status I or II made up the study population. Patients slated for elective lower abdominal, gynecological, or orthopaedic lower limb procedures were the subjects. Strict exclusion criteria were used to guarantee patient safety and data accuracy. Patients who declined the operation or showed signs of spinal anesthesia contraindications, such as coagulopathy, elevated intracranial pressure, or injection site infection, were not included. Pregnant patients were also excluded, as were those with a history of chronic pain and long-term opioid use, substantial cardiac, renal, or hepatic dysfunction, or known allergies to the study medicines.

Randomization and Blinding

A computer-generated random number table was used to divide the 99 research participants into three equal groups of 33 in order to assure fair distribution. To avoid bias, the study followed a rigorous double-blind methodology; the study medications were prepared by a designated anesthesiologist who was not involved in intraoperative monitoring or data collecting. This made sure the observer documenting the clinical parameters didn't know the patients' particular group assignments. A standardized total intrathecal volume of 3.5 mL was administered to each of the three groups. In particular, 3.0 mL of 0.5% Hyperbaric Bupivacaine (15 mg) combined with 0.5 mL of Normal Saline was given to Group B (control). Group C received the same amount of bupivacaine along with 30 µg of Clonidine, likewise diluted to 0.5 mL, whereas Group M received 3.0 mL of 0.5% Hyperbaric Bupivacaine along with 50 mg of preservative-free magnesium sulphate (diluted to 0.5 mL).

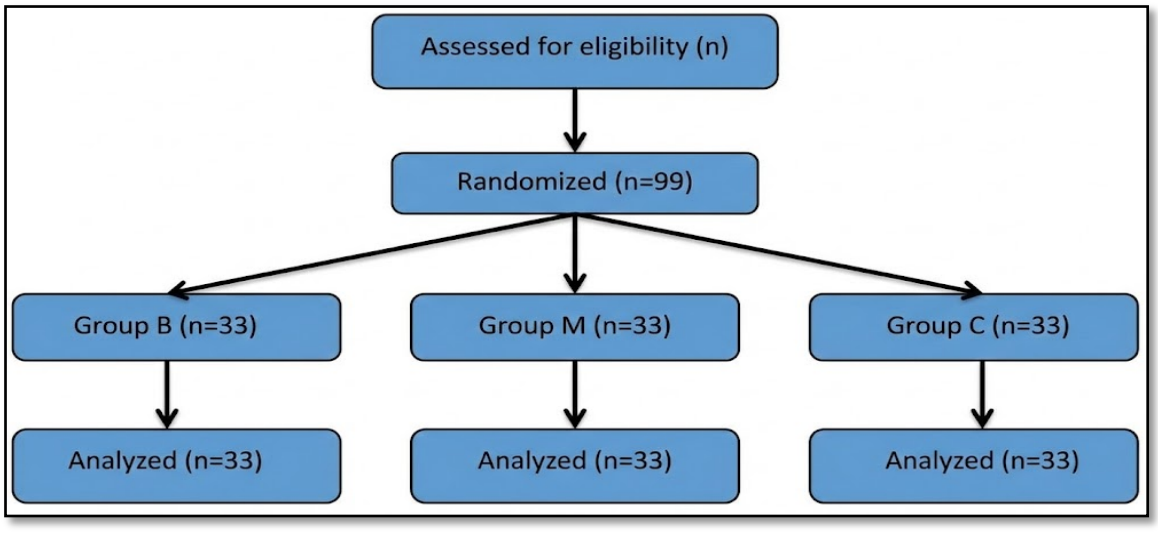

Figure 1 Patient enrollment and group allocation.

Anaesthetic Procedure

Standard ASA monitoring, such as electrocardiogram (ECG), non-invasive blood pressure (NIBP), and pulse oximetry, was set up to capture baseline vital signs as soon as the patient entered the operating room. Each patient received fluid preloading with Ringer's Lactate solution at a dose of 10–15 mL/kg in order to prevent any hypotension brought on by spinal anesthesia. The patient was placed in either a sitting or lateral decubitus position, and a 25G Quincke spinal needle was used to execute the subarachnoid block in the L3–L4 or L4–L5 interspace under strict aseptic circumstances. The chosen study medication was given over a period of 10 to 15 seconds once the free flow of cerebrospinal fluid (CSF) verified proper needle placement. The patient was then promptly put back in a supine posture.

Monitoring and Assessment

Starting with a sensory examination utilizing a pinprick test with a 23G hypodermic needle along the mid-clavicular line, the nerve block assessment was carried out methodically. The Modified Bromage Scale, which ranges from 0 (no block) to 3 (full block), was used to concurrently rate motor blockage. Key time milestones, such as the beginning of motor block and the onset of sensory block at the T10 dermatome, were meticulously documented. The maximum sensory level attained, the total length of sensory block measured from the point of maximal block till regression to S1, and the time required for full motor recovery were also recorded. The time between the intrathecal injection and the patient's initial need for rescue pain treatment was the primary outcome, or duration of analgesia. Heart rate (HR), systolic and diastolic blood pressure (SBP, DBP), and mean arterial pressure (MAP) were recorded at baseline, 2, 5, 10, 15, 30, 45, and 60 minutes, and then every 30 minutes after that to monitor hemodynamic stability. Additionally, we kept an eye out for side effects such nausea, vomiting, hypotension, bradycardia, shivering, or respiratory depression, and we handled any issues in accordance with recognized guidelines.

Statistical Analysis

SPSS software (version 22.0) was used to examine the data after it had first been produced in Microsoft Excel. Using Analysis of Variance (ANOVA) and post-hoc Tukey testing for group comparisons, we reported continuous variables as Mean ± Standard Deviation (SD). Chi-square tests were used to assess categorical data, and a p-value of less than 0.05 was deemed statistically significant.

Results

Demographic Profile

The randomization technique was successful since the three groups were comparable in terms of demographic factors. There were no statistically significant variations in age, weight, height, ASA status, or surgery length between the three groups ($p > 0.05$). The average age in Group B was 38.5 ± 10.2 years, in Group M it was 39.1 ± 9.8 years, and in Group C it was 37.8 ± 10.5 years.

Table 1 Demographic Data (Mean ± SD)

Parameter	Group B (n=33)	Group M (n=33)	Group C (n=33)	p-value
Age (years)	38.5 ± 10.2	39.1 ± 9.8	37.8 ± 10.5	0.82
Weight (kg)	62.4 ± 8.1	63.1 ± 7.5	61.9 ± 8.3	0.76
Duration of Surgery (min)	95.5 ± 20.4	98.2 ± 18.5	96.1 ± 19.2	0.88

Block Characteristics

Adjuvant addition had a substantial effect on block properties when compared to the control group. Group C (Clonidine) had the fastest onset of sensory block, with an average of 2.4 ± 0.6 minutes, much faster than Group B (3.5 ± 0.8 minutes). In contrast, Group M (Magnesium) had a significantly delayed onset of 4.8 ± 0.9 minutes. A similar pattern was found in the start of motor blockage. In terms of efficacy duration, both adjuvants considerably increased sensory and motor blockage. Group C had the longest duration of analgesia (330.7 ± 47.7 minutes), which was statistically better to Groups M (246.3 ± 55.9 minutes) and B (134.4 ± 17.9 minutes).

Table 2 Comparison of Block Characteristics and Analgesia Duration

Parameter	Group B (Control)	Group M (Magnesium)	Group C (Clonidine)	p-value
Onset of Sensory Block (min)	3.5 ± 0.8	4.8 ± 0.9	2.4 ± 0.6	<0.05
Onset of Motor Block (min)	4.2 ± 1.1	5.5 ± 1.2	3.1 ± 0.7	<0.05
Duration of Motor Block (min)	110.5 ± 15.2	190.4 ± 30.1	245.2 ± 28.5	<0.001
Duration of Analgesia (min)	**134.4 ± 17.9**	**246.3 ± 55.9**	**330.7 ± 47.7**	**<0.001**

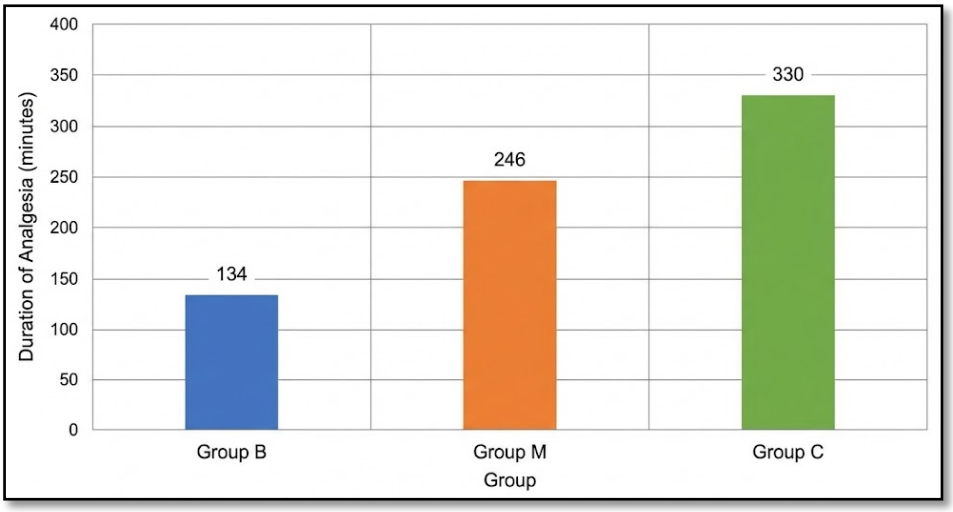

Figure 2 Comparison of mean duration of postoperative analgesia

Hemodynamic Parameters and Side Effects

Hemodynamic evaluations showed different patterns in each batch. Group B needed little remedial action and followed typical hemodynamic patterns. Patients in Group C showed a statistically significant decrease in mean heart rate and mean arterial pressure (MAP) between the 15th and 45th minutes following operation, in contrast to the other groups. Group C showed a significant rise in the incidence of bradycardia and hypotension, but Group M maintained a steady hemodynamic profile similar to the control. In terms of secondary outcomes, Group C's sedation scores were noticeably higher than the control, while both adjuvant groups' rates of shivering were significantly decreased.

Table 3 Incidence of Intraoperative Side Effects

Side Effect	Group B (n=33)	Group M (n=33)	Group C (n=33)	p-value
Hypotension	3 (9.0%)	2 (6.0%)	6 (18.1%)	<0.05
Bradycardia	0 (0%)	0 (0%)	4 (12.1%)	<0.05
Sedation > Grade 2	0 (0%)	1 (3.0%)	9 (27.2%)	<0.001
Shivering	8 (24.2%)	2 (6.0%)	1 (3.0%)	<0.05
Nausea/Vomiting	2 (6.0%)	1 (3.0%)	2 (6.0%)	>0.05

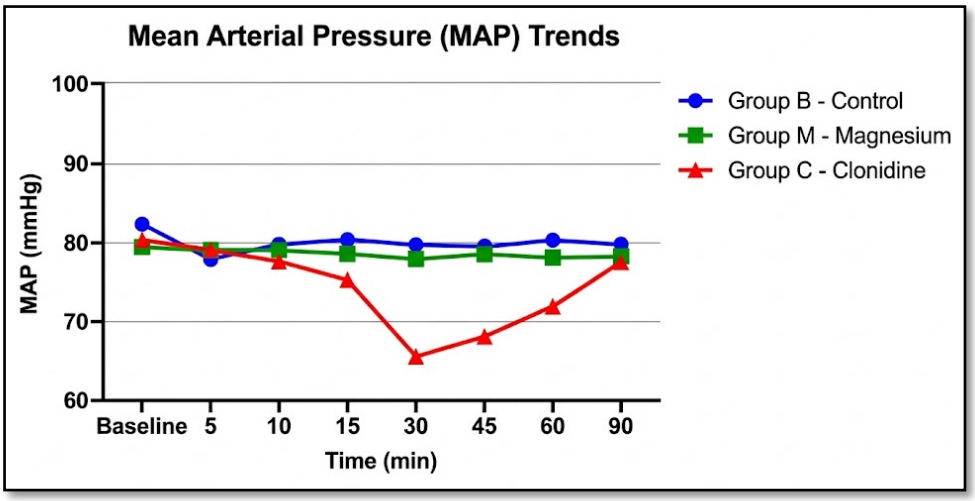

Figure 3 Intraoperative trends of Mean Arterial Pressure (MAP) over time

Discussion

The current study, done at PMCH, Patna, aimed to assess the efficacy of Magnesium Sulphate and Clonidine as intrathecal adjuvants. The results confirm that both medications enhance the quality of the block, although they have differing clinical characteristics.

Onset and Duration

The data shows that Clonidine (30 µg) is more efficient than Magnesium Sulphate (50 mg) in causing sensory block and prolonging analgesia. This is consistent with the results of comparison studies in similar demographics, which found that alpha-2 agonists such as Clonidine have potent local anaesthetic-sparing effects [9, 10]. The process is ascribed to a synergistic effect on conduction block in A-delta and C fibers, as well as suppression of neurotransmitter release in the dorsal horn. In our investigation, magnesium sulphate considerably increased the duration of the block compared to the control, but it also somewhat delayed its onset. Other researches have confirmed this delay in onset [8], which is probably caused by the solution's different pH and osmolality or the particular mechanism of NMDA antagonism, which would need a longer latency period to effectively influence calcium influx.

Hemodynamic Stability

The better hemodynamic stability seen in the magnesium group is a crucial conclusion of this investigation. Patients in Group C (Clonidine) were more likely to have bradycardia and hypotension. This is a well-known systemic action of clonidine that results in a decrease in sympathetic outflow via activating presynaptic alpha-2 receptors in the brainstem's vasomotor center and peripheral sympathetic nerve terminals [11]. Magnesium sulphate, on the other hand, kept hemodynamic values near baseline. This lends credence to the idea that magnesium does not produce widespread sympathetic blockage to the same degree as alpha-2 agonists, while preventing central sensitization. Because hemodynamic fluctuations must be avoided, magnesium may be a safer option

for elderly patients or those with little cardiac reserve.

Side Effect Profile

Sedation was a common adverse effect in the Clonidine group, affecting over 27% of patients, according to the review of side events. Clonidine's action on the brainstem's locus coeruleus, which controls alertness, is principally responsible for this sedative effect. Excessive sedation may impede recovery or make it difficult to measure cerebral perfusion in critical situations, even while perioperative sedation may be helpful for patient anxiolysis during regional anesthesia. Magnesium, on the other hand, did not significantly induce sedation, which is beneficial in ambulatory situations. Additionally, when compared to the control group, both adjuvants successfully decreased the frequency of shivering. Their central activities on the hypothalamic thermoregulatory center, which lessen the body's reaction to heat redistribution brought on by vasodilation, are probably responsible for this anti-shivering effect [12, 13].

Comparison with Global Literature

The study's findings are consistent with a meta-analysis conducted by Pascual-Ramírez et al. [7], which found that intrathecal magnesium lengthens the duration of spinal anesthesia. In a similar vein, our data on clonidine confirms its potency while highlighting the danger of autonomic depression, matching the profile reported by Sethi et al. [6]. Our Magnesium group experienced analgesia for about 246 minutes, which is similar to the results of Buvanendran et al. [14], who initially clarified the function of intrathecal magnesium. Additionally, while clonidine offers a longer duration of block, magnesium offers a clear advantage in terms of hemodynamic stability, according to comparative studies by Jabalameli et al. [15] and Shukla et al. [16], a conclusion that our study at PMCH strongly supports. The dose-dependent nature of the hypotension seen in our Clonidine group is supported by recent research on alpha-2 agonists by Elia et al. [17].

Limitations

There are some limitations to the study that should be discussed. First off, a complete dose-response study may produce multiple ideal dosages that enhance analgesia while avoiding side effects. The fixed doses (50 mg magnesium and 30 µg clonidine) were chosen based on standard procedure and prior research. Second, although toxicity from 50 mg intrathecal magnesium is extremely unlikely given the tiny dose in comparison to systemic magnesium therapy, the study did not test serum magnesium levels [18]. Furthermore, although the Visual Analog Scale (VAS) is a validated technique, individual differences in pain threshold may affect the reported duration of analgesia because pain evaluation is essentially subjective. Lastly, even though the sample size was statistically determined, it was somewhat little; a bigger multicentric trial would yield more reliable information about uncommon adverse events [19].

Conclusion

We can make a number of firm conclusions about the usage of intrathecal adjuvants based on the thorough examination of the data gathered from this prospective comparative study carried out at PMCH, Patna. Clonidine (30 µg) is the medication of choice for lengthy surgeries when maximizing the pain-free interval is the main objective because it clearly outperforms other medications in terms of the duration of postoperative analgesia and the speed of block onset. But this greater strength comes at the expense of hemodynamic changes, particularly bradycardia and hypotension, which call for close observation. However, compared to bupivacaine alone, magnesium sulphate (50 mg) is a useful adjuvant that considerably prolongs analgesia, albeit not as much as

clonidine. Its outstanding safety profile, which is marked by greater hemodynamic stability and minimal sedation, is its clear advantage. As a result, clinical choices ought to be customized: For younger, hemodynamically stable patients having lengthy procedures, clonidine is advised; for older patients or those with impaired cardiac reserve, where hemodynamic stability is critical, magnesium sulphate is the better option.

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