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# Comparison of Effect of Preservative Free Ketamine and Magnesium Sulphate used as an Adjuvant to 0.5 % Hyperbaric Bupivacaine in Orthopaedic Lower Limb Surgeries under Spinal Anaesthesia - A Prospective Double Blind Randomised Control Study

**Pratheev E[1], Arpita Bhargava[2], Ritushree Sharma[3]**

[1]Post Graduate (3rd year resident), Department of Anaesthesiology, Jhalawar Medical College, Jhalawar, Rajasthan, India
E mail ID: *pratheev26[at]gmail.com*

[2]Post Graduate (3rd year resident), Department of Anaesthesiology, Jhalawar Medical College, Jhalawar, Rajasthan
E mail ID: *arpita.bhargava20[at]gmail.com*

[3]Post Graduate (3rd year resident), Department of Anaesthesiology, Jhalawar Medical College, Jhalawar, Rajasthan
E mail ID: *sharmaritushree[at]gmail.com*

**Abstract:** ***Background and aim: Spinal anaesthesia is preferred because of its simplicity and reliability in lower limb surgery. It has become a common practice to use adjuvants with local anaesthetics for spinal anaesthesia for treatment of intra and postoperative pain. The aim of the study was to assess the effects of ketamine and magnesium sulphate added to 0.5 % hyperbaric bupivacaine, for spinal anaesthesia in patients undergoing lower limb surgeries. Methodology: This study included 90 patients, who were divided into 3 groups of 30 each. Group Magnesium received 50% magnesium sulphate 50 mg plus 0.5 % hyperbaric bupivacaine 12.5 mg (2.5 ml). Group Ketamine received preservative free ketamine 25 mgplus 0.5 % hyperbaric bupivacaine 12.5 mg. Group Control received plain 0.5% hyperbaric bupivacaine 12.5 mg plus 0.5 ml normal saline. Parameters like sensory and motor block characteristics, visual analog scores (VAS) were recorded. Result: The mean duration of analgesia was 164, 170 and 224 minutes in group C, group K and group M respectively. These differences were statistically significant. Conclusion: This study shows that intrathecal magnesium sulphate, as an adjuvant to 0.5 % hyperbaric bupivacaine prolongs the duration of analgesia, sensory and motor blockade without any major side effects.***

**Keywords:** Ketamine, Magnesium Sulphate, Spinal Anaesthesia.

## 1. Introduction

Spinal anaesthesia is preferred because of its simplicity and reliability in lower limb surgery. Plain hyperbaric bupivacaine when used alone intrathecallywill produce analgesia for 2.5–3 hours, thus it is unsuitable for longer duration surgeries (1). Spinal anesthesia is a simple procedure and isused widely as compared with general anesthesia because it has benefits like reduction of stress responses, reduced amount of blood loss, low cost and decreased morbidity and mortality rates (2). As an alternative to general anesthesia, regional anaesthesia is preferredto reduce the risk of general anesthetic exposure (3) and infrequent complications such as shivering (4, 5). The drawbacks associated with spinal anaesthesia is its shortened duration of action and lack of postoperative analgesia. Larger dose of analgesic is required to provide pain relief with high incidence of side effects when local anaesthetic is used alone for spinal anaesthesia.

It has become a common practice to use adjuvants with local anaesthetics for spinal anaesthesia for treatment of intra and postoperative pain. Intrathecal adjuncts, such as ketamine, magnesium sulphate, opioids, vasoconstrictors, alpha 2 agonists, and neostigmine are often added to enhance spinal anaesthesia (6 - 10). Even though these adjuncts are effective in improving the efficacy of low - dose spinal anaesthesia, their use is limited because of side - effects. Neuraxial opioids though effective have worrisome respiratory depression, nausea, vomiting, urinary retention, and pruritus that limit their use in the ward. Recent research has focused on nonopioid spinal receptors that inhibit transmission of pain signals.

In experimental studies, spinally administered NMDA receptor antagonists such as ketamine or magnesium have been shown to inhibit nociception and produce motor dysfunction (11 - 12). These affect likely results from antagonism of NMDA receptors on dorsal horn sensory neurons as well as motor neurons in the ventral horn of the spinal cord.

Epidurally, ketamine can be given to human beings for pain relief with no side - effects, such as respiratory depression, urinary retention, or pruritus which is usually noticed after epidural opioids (13). Although, the addition of opioids to spinal local anaesthetics has been reported to potentiate the

effect of local anaesthetics, it is known that the addition of ketamine to spinal bupivacaine could result in similar potentiation. Several in vitro and in vivo studies have demonstrated the potential of ketamine for producing neuroprotective effects (14 - 16). This ability is indicated by the observations that ketamine blocks NMDA - receptor activation, mediates beneficial changes in apoptosis - regulating proteins and interferes with the inflammatory response to injury when administered in typical sedative or anesthetic doses.

Magnesium sulphate is found to have analgesic effects, mediated through antagonism of NMDA receptors in the CNS (17) and also related to regulation of calcium influx into the cells (18). It has the property to prevent central sensitization from peripheral nociceptive stimulation. The antinociceptive property of magnesium sulphate appears to be relevant not only to chronic pain (19, 20) but it also determines intensity of duration, postoperative pain (21, 22). Intrathecal and epidural administration of magnesium sulphate also increase the mean duration of analgesia (23).

**Aim**

The aim of this study is to compare the effects of preservative free ketamine and magnesium sulphate used as adjuvants to 0.5 % hyperbaric bupivacaine in the orthopaedic patients under spinal anaesthesia.

**Objectives**

**Primary Objective**:

To determine the difference in the duration of analgesia in patients receiving magnesium sulphate and preservative free ketamine as adjuvant to 0.5 % hyperbaric bupivacaine in lower limb surgeries under spinal anaesthesia.

**Secondary Objectives:**

1) To compare the time of onset of sensory and motor blockade in patients receiving magnesium sulphate and preservative free ketamine as spinal adjuvants for lower limb surgeries.
2) To determine the duration of motor blockade and sensory blockade in these groups of patients.
3) To determine any complications and side effects in these patients.

## 2. Review of Literature

**Raghavan R K et al** (2017) (24) conducted a randomised control study to evaluate the effects of magnesium sulphate and preservative free ketamine used as adjuvants to epidural bupivacaine in cases posted for abdominal hysterectomy. After obtaining informed consent, the patients were divided into 3 groups of 40 each to receive 20 mL 0.5% isobaric bupivacaine (group B), 19 mL 0.5% isobaric bupivacaine + 50 mg magnesium sulphate (group BM), 19 mL 0.5% isobaric bupivacaine + 50 mg preservative - free ketamine (group BK). Epidural catheter was inserted at L1 - L2 space using standard technique. Correct placement was confirmed by a test dose of 2% lignocaine + adrenaline 1 in 2 lakhs. Postoperative analgesia was assessed by VAS score and 0.125% bupivacaine infusion and 1 g paracetamol IV infusion was given as rescue analgesics when VAS ≥4. Mean time of duration of onset in group B, BM, BK were 20, 14, 18 minutes, respectively. Mean time for rescue analgesia were 180, 240 and 480 minutes in group B, BM, BK respectively. These differences were statistically significant (P<0.001). The side effects noticed in each group were not statistically significant. They concluded that the onset of effect is faster when magnesium sulphate was added as an adjunct to bupivacaine as compared to preservative - free ketamine.

**El - Morabaa et al** (2018) (25) conducted a randomised control study to compare 3 different doses of Magnesium Sulfate as a spinal adjuvant to Bupivacaine - Fentanyl combination in spinal anesthesia on the spread, duration, regression of spinal block, and postoperative analgesia in patients undergoing lower limb orthopedic surgeries. One hundred and twenty patients aged between 18 - 60 years, 30 in each group (ASA I or II) scheduled for lower limb orthopedic surgeries were included in our study. The patients were randomly divided into four equal groups of 30 each: Group 1 (control group) patients received intrathecal injection hyperbaric bupivacaine (0.5%) 2.5ml with fentanyl (25 µ g) 0.5ml and normal saline 1ml. Group 2 patients received intrathecal injection hyperbaric bupivacaine (0.5%) 2.5ml with fentanyl (25µg) 0.5ml, MgSO4 (50mg) 0.5ml and normal saline 0.5ml. Group3 patients received intrathecal injection hyperbaric bupivacaine (0.5%) 2.5ml with fentanyl (25µg) 0.5ml, MgSO4 (75mg) 0.75ml and normal saline 0.25ml. Group 4 patients received intrathecal injection hyperbaric bupivacaine (0.5%) 2.5ml with fentanyl (25 µg) 0.5ml and MgSO4 (100mg) 1ml. The onset of sensory block was significantly delayed in groups2, 3, 4 (3.53 ± 0.86 minutes, 4.63± 0.93 minutes, 5.8 ±1.06 minutes) compared to group 1 (1.7 ±0.79 minutes) with p<0.001. The mean onset time for motor blockade was 3.23 ±0.97 minutes in group 1, 5.83± 1.6 minutes in group 2, 6.63 ±1.47 minutes in group 3, 7.67 ±1.47 minutes in group 4. The onset of motor blockade was significantly earlier in group 1 comparing other three groups (p<0.001). The mean duration of sensory block was 176.33 ±24.03 minutes (group1), 222 ±36.62 minutes in group 2, 271.67 ± 48.73 minutes in group 3, 293.67 ±56.06 minutes in group 4, with no statistical difference among the groups (p=0.11). The mean duration of motor block was 209.17 ± 22.93 minutes in group 1, 267 ±31.67 minutes in group 2, 308.17 ±48.65 minutes in group 3, 334.33 ±58.56 minutes in group 4. Group 4 had more duration of motor block comparing the other groups, but it was not statistically significant (p>0.05). The total duration of analgesia were 323 ±52.45 minutes in group 1, 397.83 ±76.2 minutes in group 2, 448.17 ± 81.9 minutes in group 3, 493 ±92.26 minutes in group 4. The total duration of analgesia was significantly prolonged in group 4 (p<0.001) compared to the other three groups. They concluded that the addition of magnesium sulfate to intrathecally bupivacaine - fentanyl in patients undergoing lower limb orthopedic surgery receiving spinal anesthesia prolongs the duration and quality of analgesia better than bupivacaine - fentanyl only.

**Peyyety JS et al** (2021) (26) conducted a prospective, randomised, double - blind and placebo - controlled study to compare the analgesic effects of ketamine, fentanyl and saline added to hyperbaric bupivacaine for central neuraxial

blockade in total knee replacement surgery. Ninety patients were randomly allocated into three groups of 30 each. Standardised anaesthetic technique and monitoring for subarachnoid block (and epidural catheter placement) with 3 mL of 0.5% hyperbaric bupivacaine was followed. In addition, Group K (*n* = 30) received 0.3 mg/kg of preservative - free ketamine, Group F (*n* = 30) received 25 µg (0.5 mL) of fentanyl and Group C (control group, placebo, *n* = 30) received 0.5 mL normal saline. The mean time to onset of sensory block was 118.5 ± 40.2 Sec in Group K, 94 ± 37.8 Sec in Group F and 116 ± 45 Sec in Group C. This difference was statistically significant (P = 0.045). With regard to the mean time to regression of block below L1 level (i. e., mean duration of sensory block), Group K took 96.7 ± 41.9 min, Group F took 237.7 ± 48.7 min and Group C took 219.4 ± 43.4 min. The difference was statistically significant between the three groups (P = 0.003). The mean time to onset of motor block was 163.4 ± 7.8 sec in Group K, 127.9 ± 42.5 sec in Group F and 158.1 ± 49.8 sec in Group C, and this difference was a statistically significant with a P value of 0.029. The mean duration of motor block was 212.2 ± 48.9 min in Group K, 253 ± 51.3 min in Group F and 231.8 ± 50.6 min in Group C and this was a statistically significant difference among the three groups with a P = 0.009. The mean duration of analgesia was 226.3 ± 37.1 min in Group K, 260.6±54.9 min in Group F and 239.1±48.6 min in Group C. There was a statistically significant difference with regard to duration of analgesia among the three groups, with a P = 0.022. All three groups were comparable with regard to the incidence of adverse effects. They concluded that fentanyl (25 µg) was superior to 0.3 mg/kg of ketamine and placebo as an intrathecal adjuvant with minimal side effects.

## 3. Methodology

This is a prospective interventional study done in the department of Anaesthesiology and Critical Care. Jhalawar (Rajasthan). This included patients undergoing elective lower limb orthopaedic surgery, who were more than 18 years and less than 60 years of age, in ASA GRADE 1, 2.

**Exclusion Criteria:**
Patients who had localised skin infection at the spinal site, patients refusing for subarachnoid block, patients who are on anticoagulation therapy or with bleeding disorders, patients with cardiopulmonary dysfunction, neurological, psychological, hepatic, renal disorders, pregnant and lactating women, patients with BMI >35 and patients who have history of hypersensitivity to the study drugs were excluded from the study.

They were divided into three groups. First group (group Magnesium sulphate) (n=30) received 50% magnesium sulphate 50 mg (0.5 ml) plus 0.5 % hyperbaric bupivacaine 12.5 mg (2.5 ml) for spinal anaesthesia in lower limb surgeries. Second group (group Ketamine) (n=30) received preservative free ketamine 25 mg (0.5 ml) plus 0.5 % hyperbaric bupivacaine 12.5 mg (2.5 ml) for spinal anaesthesia in lower limb surgeries. Third group (group Control) (n=30) received plain 0.5% hyperbaric bupivacaine 12.5 mg (2.5 ml) plus 0.5 ml normal saline for spinal anaesthesia in lower limb surgeries. The anaesthesiologist administering the drug and the patient were not aware of which group they were allotted to.

## 4. Procedure

Each patient after pre anaesthetic check - up were kept overnight fasting after midnight for surgery. Patient's written informed consent and PAC were checked. All patients were pre - medicated with Tab. Ranitidine 150mg and Tab. Ondansetron 8mg orally on the night before surgery. Intravenous access with 18 - gauge i. v cannula were secured at forearm level. Baseline vital parameter like BP, pulse rate, $SpO_2$, respiratory rate were documented preoperatively. Patient was preloaded with lactated Ringer's solution as a bolus of 10 ml/kg before subarachnoid block. Spinal anaesthesia was performed at L3 - L4 interspace with the patient in left lateral position by using a 25 Gauge Quincke needle under strict aseptic conditions. Free flow of cerebrospinal fluid was verified before injection of the anaesthetic solution 3.0 ml volume, which was administered at 0.2 ml/ second. The direction of the needle aperture was cranial during the injection. All patients were immediately placed in a supine position. Monitoring was done perioperatively using continuous electrocardiography, heart rate, non - invasive blood pressure and continuous pulse oximetry and patients were given 5.0 L/min of oxygen by hudson - mask. Vitals were checked every 5 minutes for first 30 minutes then every 10 minutes till surgery and then every 30 minutes for 6 hours postoperatively. Arterial pressure was maintained within 20% of the baseline by the infusion of crystalline. If the systolic BP dropped below 90 mm of hg, patients were supported with iv mephentermine in small doses. When adequate spinal block was achieved, the time from the end of intrathecal injection to readiness for surgery was recorded. Then the patients were positioned for planned surgery. Patients were monitored at different time intervals (intraoperatively every 5min for 30 minutes, then every 15 minutes till 90 minutes and postoperatively – hourly till $5^{th}$ hour and then $2^{nd}$ hourly till 12 hours then at 24 hours) to calculate the onset and duration of sensory and motor blockade. After completion of surgery patients were shifted to post - operative ward and duration of analgesia was noted. Monitoring of vital parameters like pulse, BP (SBP, DBP & MAP) and oxygen saturation ($SpO_2$) were done throughout procedure and were noted at following point -

1) Preoperative before subarachnoid block.
2) Intraoperative after subarachnoid block.
3) Postoperatively (hourly till $5^{th}$ hour and then $2^{nd}$ hourly till 12 hours then at 24 hours)

Sensory blockade will be assessed bilaterally by analgesia to pinprick with short hypodermic needle in the midclavicular line. Onset time defined as the time interval between the end of LA administration and loss of sensation of pinprick (score 1). Duration of sensory block defined as the time interval between loss of sensation of pinprick (onset time) and feeling of pain sensation on pinprick. Motor blockade will be assessed by modified Bromage scale (0 - no motor lock, 1 - inability to raise extended leg, able to move knee and feet; 2 - inability to raise extended leg and move knee, able to move feet; 3 - complete block of motor limb). Motor block onset time: Defined as the time interval between the end of LA administration and not able to lift leg but can flex the leg

(MBS score 1). Duration of motor block: Defined as the time interval from the onset (MBS score 1) to the recovery of complete motor function (MBS score 0). Postoperatively, pain will be assessed by visual analogue score (VAS). Score ≥3 is considered painful. Duration of analgesia will be considered from loss of pinprick sensation to complain of pain or demand for rescue analgesia or VAS>3. The occurrence of any adverse effect if any will be recorded.

**Statistical Tests**

To determine the significance in the difference in the mean of the three groups with respect to, onset of sensory blockade, onset of motor blockade, duration of sensory blockade, duration of motor blockade, duration of analgesia were done by ANOVA test. Determination the significance in the difference of side effects in the three groups was done by chi square test. Determination of the significance in the difference in the hemodynamic parameters was done by ANOVA test.

## 5. Result

In this prospective randomized controlled trial, 90 patients were studied in this trial, divided into 3 groups of 30 each. The focus of this study was on the onset of sensory and motor blockade, duration of sensory and motor blockade duration of analgesia and on the complications associated with the study drugs. The results of this study are described in the below tables and graphs.

**Table 1:** Demographic data and preoperative parameters

| Characteristics | Ketamine Group (N=30) | Magnesium Group (N=30) | Control Group (N=30) | p Value |
|---|---|---|---|---|
| Age (years) | 47.03 ± 11.82 | 42.13 ± 10.97 | 45.33 ± 10.2 | 0.22 |
| ASA (I/II) | 27/3 | 28/3 | 27/3 | 0.87 |
| Weight (kg) | 76.06 ± 7.52 | 75.9 ± 6.99 | 73.9 ± 8.97 | 0.49 |
| SEX (M/F) | 17/13 | 17/13 | 20/10 | 0.65 |
| Preoperative Heart Rate (bpm) | 81.4 ± 8.45 | 82.93 ± 8.11 | 79.66 ± 9.74 | 0.35 |
| Preoperative Mean Blood Pressure (mm of Hg) | 86.63 ± 5.59 | 84.50 ± 4.84 | 84.06 ± 6.59 | 0.18 |
| Duration Of Surgery (minutes) | 120.43 ± 5.76 | 118.76 ± 5.33 | 121.23 ± 4.98 | 0.19 |

**Demographic data and preoperative parameters:**

The patient baseline characteristics variables of patients are show in the above table. There were no significant differences between groups in patient characteristics and the duration of surgery between the groups.

**Hemodynamic Parameters:**

A decrease in the heart rate is noted in the ketamine group following spinal anaesthesia at the 15, 20 and 25 minutes which was significantly lower compared to the magnesium sulphate group and control group. (p<0.001). There is no variation among the three groups regarding the intraoperative mean blood pressure. There is no statistical significance (p>0.05). There is significant difference in the intraoperative respiratory rate and spo2 among the three groups.

**Table 2:** Intraoperative heart rate (beats/minute)

| *Time* | *Ketamine* | *Magnesium* | *Control* | p Value |
|---|---|---|---|---|
| 0 MIN | 82.93± 8.11 | 84.4 ±8.45 | 82.75 ±9.90 | 0.23 |
| 5MIN | 84.97± 8.34 | 84.4± 8.67 | 85.80 ±9.02 | 0.828 |
| 10 MIN | 82.96± 8.24 | 90.4 ±9.04 | 87.90 ±9.92 | 0.035 |
| 15 MIN | 82.90± 8.65 | 93.70 ±8.65 | 91.90 ±9.87 | <0.001 |
| 20 MIN | 80.93± 8.12 | 91.46 ±8.89 | 94.90 ±9.56 | <0.001 |
| 25 MIN | 77.93 ±9.12 | 92.00 ±9.78 | 91.90 ±9.76 | <0.001 |
| 30 MIN | 76.89 ±8.34 | 88.40 ±8.63 | 90.90 ±9.57 | <0.05 |
| 45 MIN | 78.93 ±8.56 | 80.60 ±7.98 | 81.90 ±9.84 | >0.05 |
| 60 MIN | 79.89 ±9.67 | 80.50 ±9.89 | 79.90 ±9.56 | >0.05 |
| 90 MIN | 80.78 ±7.56 | 78.53 ±6.90 | 78.90 ±9.67 | >0.05 |

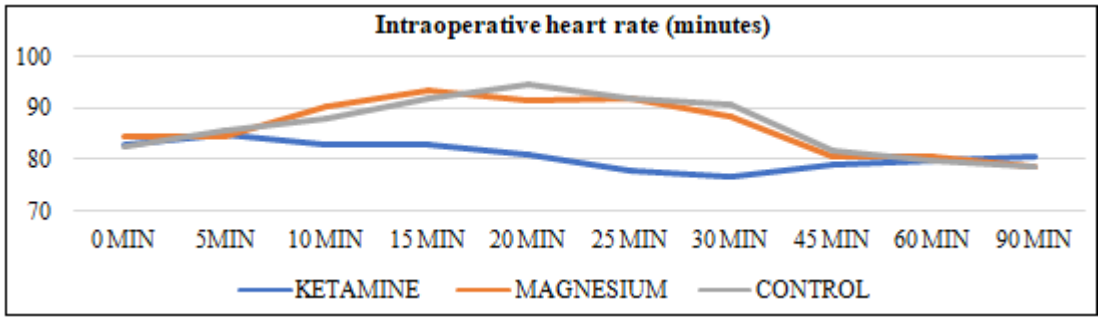


**Figure 1:** Intraoperative heart rate

**Sensory, motor blockade and duration of analgesia:**

The onset of sensory block was earliest in the ketamine group (2.7 ± 0.83 minutes) compared to the magnesium group (5± 0.98 minutes) and the control group (4.33 ± 0.66 minutes) and this difference was statistically significant (P<0.05). The onset of the motor blockade was also earlier in the ketamine group (4.53 ± 0.73 minutes) compared to the magnesium group (6.50 ± 0.62 minutes) and the control group (5.83 ± 0.69) and this difference was statistically significant (p<0.001). The duration of sensory blockade with addition of magnesium sulphate as an adjuvant to 0.5 % hyperbaric bupivacaine helps in prolonging the duration with 196.76 ± 8.62 minutes in the magnesium group and 159.36 ± 5.04 minutes in the ketamine group and 155.26 ± 5.45 minutes in the control group and this difference was statistically significant (p<0.05). The duration of sensory

blockade was longest in the magnesium sulphate group compared to ketamine group and control group and this difference was statistically significant ($p<0.05$). The duration of motor blockade was 181.90 ± 8.21 minutes in the magnesium group, compared to 120.26 ± 6.73 minutes in the ketamine group and 138.50 ± 6.53 minutes in the control group and the difference was statistically significant ($p<0.05$). The duration of motor blockade was longest in the magnesium sulphate group compared to ketamine group and control group and was statistically significant ($p<0.05$). In this study the total duration of analgesia was longer in the magnesium group with 224.76 ± 4.62 minutes in it, while it was 170.50 ± 13.11 minutes in the ketamine group and 164.17 ± 4.56 minutes in the control group and this difference was statistically significant ($p <0.05$). Regarding the VAS score, the score in the postoperative period was significantly lower in the magnesium sulphate group till the 7th hour compared to the ketamine group and the control group.

**Side effects:**

Nystagmus and sedation were observed exclusively in the ketamine group. No major complications occurred, but minor complications like nausea, vomiting, bradycardia and hypotension were present in all the three groups with no statistical difference among the groups ($p>0.05$).

**Table 3:** Sensory and motor blockade

| *Parameter* | *Ketamine* | *Magnesium* | *Control* | *p Value* |
|---|---|---|---|---|
| Onset of Sensory Block (minutes) | 2.7 ± 0.83 | 5.0 ±0.98 | 4.33±0.66 | <0.05 |
| Onset of Motor Blockade (minutes) | 4.53 ± 0.73 | 6.50 ± 0.62 | 5.83± 0.69 | <0.05 |
| Duration of Sensory Blockade (minutes) | 159.36 ± 5.04 | 196.76 ± 8.62 | 155.26 ± 5.45 | <0.05 |
| Duration of Motor Blockade (minutes) | 120.26 ± 6.73 | 181.90 ± 8.21 | 138.50 ± 6.53 | <0.05 |
| Duration of Analgesia (minutes) | 170.50 ±13.11 | 224.76 ± 4.62 | 164.17 ± 4.56 | <0.05 |

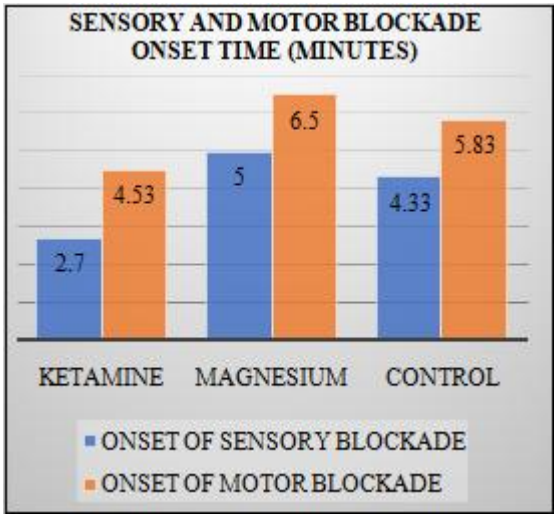


**Figure 2:** Onset of sensory and motor blockade was earlier in the ketamine group compared to the magnesium sulphate group and control group and were statistically significant ($p<0.05$).

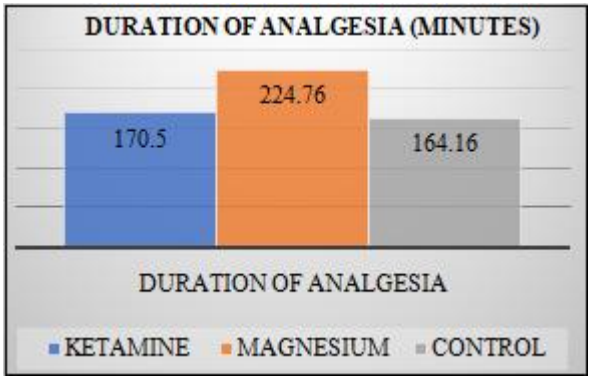


**Figure 3:** Duration of analgesia was significantly prolonged in the magnesium group compared to the ketamine group and the control group ($p<0.05$)

**Table 4:** Post operative VAS score

| Post OP Time | Ketamine | Magnesium | Control | p Value |
|---|---|---|---|---|
| O Hour | 0.0 ± 0 | 0.0 0 | 0.0 ± 0 | - |
| 1 Hour | 0.0 ± 0 | 0.0 ± 0 | 0.0 ± 0 | - |
| 2 Hour | 0.2 ± 0.2 | 0.0 ± 0 | 0.3 ± 0.7 | <0.001 |
| 3 Hour | 2.5 ± 0.6 | 0.0 ± 0 | 3.3 ± 1 | <0.001 |
| 4 Hour | 2.8 ± 0.7 | 0.0 ± 0 | 3.4 ± 0.4 | <0.001 |
| 5 Hour | 3.4 ± 0.7 | 0.3 ± 0.6 | 3.5 ± 0.6 | <0.001 |
| 7 Hour | 3.6 ± 0.7 | 2.1 ± 0.4 | 3.8 ± 0.9 | <0.001 |
| 9 Hour | 3.7 ± 0.6 | 3.4 ± 0.7 | 3.9 ± 0.7 | 0.060 |
| 12 Hour | 3.9 ± 0.5 | 3.9 ± 0.8 | 4.2 ± 0.7 | >0.05 |
| 24 Hour | 3.7 ± 0.6 | 3.6 ± 0.4 | 3.6 ± 0.8 | >0.05 |

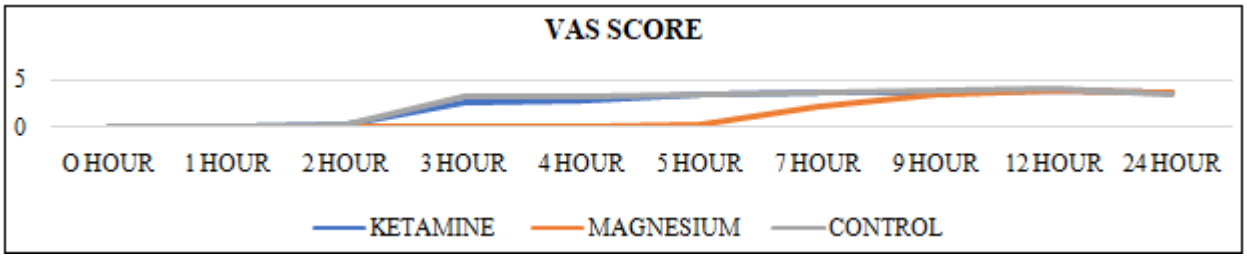


**Figure 4:** This graph shows the longer duration of analgesia in the magnesium group (reduced VAS score) compared to the ketamine group and the control group from the 2nd hour to the 7th hour post operatively which was statistically significant ($p<0.001$)

**Table 5:** Side Effects

| Complications | Ketamine Group (n=30) | Magnesium Group (n=30) | Control Group (n=30) | p value |
|---|---|---|---|---|
| HYPOTENSION (n) | 4 | 3 | 5 | >0.05 |
| BRADYCARDIA (n) | 1 | 1 | 1 | >0.05 |
| SEIZURES (n) | 0 | 0 | 0 | - |
| NAUSEA/VOMITING (n) | 3 | 4 | 5 | >0.05 |
| NYSTAGMUS (n) | 5 | 0 | 0 | < 0.05 |
| SEDATION SCORE (2/3) | 4 | 0 | 0 | <0.05 |
| PRURITIS (n) | 0 | 0 | 0 | - |

## 6. Discussion

Local anesthetics and spinal analgesics are commonly co - administered to improve analgesia or reduce local anesthetic requirements. Effective treatment of pain represents an important component of postoperative recovery. It serves to blunt autonomic, somatic, and endocrine reflexes with a resultant potential decrease in perioperative morbidity. Despite advances in treatment of postoperative pain, many patients still suffer from pain after surgery, probably due to difficulties in balancing postoperative analgesia with acceptable side effects.

**Demographic and baseline parameters:**
In this prospective randomized controlled trial, 90 patients were studied in this trial. In this study the baseline parameters like age, weight sex, ASA grading and preoperative vitals were comparable between the three groups and were not statistically significant (p>0.05).

The result of our study was comparable with the studies done by **Kathirvel S et al (**27), **Yektas AK** (28) and **Unlugenc H et al** (6) where they found that the demographic data, preoperative vitals and duration of surgery were comparable and statistically insignificant (p>0.05).

**Hemodynamic parameters:**
In this study, the intra operative mean blood pressure, spo2 and respiratory rate were comparable between the groups. The intra operative heart rate were comparable between the magnesium group and the control group, but the patients in the ketamine group showed a decrease in the heart rate compared to the other two groups which was statistically significant (p<0.05).

Our result regarding intraoperative heart rate decrease in the ketamine group is also consistent with the studies done by **Togal T et al (**29) **and Sunil BV et al (**30) which also showed a decrease in the heart rate in the intraoperative period compared to the magnesium sulphate group and control group and this difference was also statistically significant in both the studies (p<0.05), with no variations in the intraoperative mean blood pressure, respiratory rate and spo2.

Our result showed no variations in the intra operative heart rate and mean blood pressure, spo2 and respiratory rate in the magnesium sulphate group compared to the control group and our results were consistent with the studies done by **Chaudhary S K et al (**31) and **El - Morabaa et al** (25).

**Onset of sensory and motor blockade:**
This study showed that the onset of sensory block was earliest in the ketamine group (2.7 ± 0.83 minutes) compared to the magnesium group (5± 0.98 minutes) and the control group (4.33 ± 0.66 minutes) and this difference was statistically significant (P<0.05). The onset of the motor blockade was also earlier in the ketamine group (4.53 ± 0.73 minutes) compared to the magnesium group (6.50 ± 0.62 minutes) and the control group (5.83 ± 0.69) and this difference was statistically significant (p<0.001). Thus, this shows that addition of ketamine as an adjuvant to hyperbaric bupivacaine will help in fastening the onset time of sensory and motor blockade. This was consistent with the previous studies.

This result in our study is consistent and comparable with the studies done by **Hawskworth C et al (**32), **Kathirvel S et al (**27) and **Peyyety JS et al** (26) which also showed an earlier onset time of sensory and motor blockade in the ketamine group compared to the magnesium group and control group which was statistically significant (p<0.05) in all the three studies.

**Duration of sensory and motor blockade:**
In our study, regarding the duration of sensory blockade, addition of magnesium sulphate as an adjuvant to 0.5 % hyperbaric bupivacaine helps in prolonging the duration with 196.76 ± 8.62 minutes in the magnesium group and 159.36 ± 5.04 minutes in the ketamine group and 155.26 ± 5.45 minutes in the control group and this difference was statistically significant (p<0.05). The duration of sensory blockade was longest in the magnesium sulphate group compared to ketamine group and control group and this difference was statistically significant (p<0.05). The duration of motor blockade was 181.90 ± 8.21 minutes in the magnesium group, compared to 120.26 ± 6.73 minutes in the ketamine group and 138.50 ± 6.53 minutes in the control group and the difference was statistically significant (p<0.05). The duration of motor blockade was longest in the magnesium sulphate group compared to ketamine group and control group and was statistically significant (p<0.05).

Our result regarding the duration of sensory and motor blockade is consistent with the studies done by **Unlugenc H et al (**6), **Chaudhary S K et al (**31) **a**nd **El - Morabaa et al** (25) which also shows a longer duration of sensory and motor blockade in the magnesium sulphate group compared to the ketamine group and the control group which was statistically significant (p<0.05) in both the studies.

**Duration of analgesia:**
In this study the total duration of analgesia was longer in the magnesium group with 224.76 ± 4.62 minutes in it, while it

was 170.50 ± 13.11 minutes in the ketamine group and 164.17 ± 4.56 minutes in the control group and this difference was statistically significant (p <0.05). We observed that the addition of magnesium sulphate as an adjuvant to 0.5 % hyperbaric bupivacaine helps in prolonging the duration of analgesia and reducing the dose of rescue analgesia required in the post operative period.

This result in our study is consistent with the study done by **Raghavan R K et al** (24), **Unlugenc H et al (**6) and **El - Morabaa et al** (25) which also shown that the duration of analgesia was prolonged in the magnesium sulphate group compared to the ketamine and control group which was statistically significant (p<0.05) in both the studies.

**Side effects:**

Four patients in the ketamine group had a Ramsay sedation score of 2/3 and none had any sedation in the magnesium and the control group. Nystagmus was present in 05 patients in the ketamine group, whereas none had nystagmus in the control and the magnesium group which was statistically significant (p<0.05). The incidence of nausea and vomiting were comparable between the groups and were not statistically significant. The incidence of hypotension was also comparable between the groups and were not statistically significant (p>0.05).

This finding was consistent with the studies done by **Kathirvel S et al (**27), **Shrestha SK et al (**33) and **Peyyety JS et al** (26) which also shown that nystagmus was common in the ketamine group compared to the magnesium sulphate group and control group, which was statistically significant in all the three studies (p<0.05).

## 7. Summary

The simplicity of spinal anaesthesia and its reliability has made it one of the preferred techniques in lower limb surgery. Hyperbaric bupivacaine 0.5% is commonly used for spinal anaesthesia. The present study was to assess the effects of the adjuvants like ketamine and magnesium added to 0.5 % hyperbaric bupivacaine, for spinal anaesthesia in patients undergoing orthopaedic lower limb surgeries.

This study included patients admitted from the department of orthopaedics posted for elective lower limb surgeries who were above 18 years of age. The patients were divided into 3 groups of 30 each. First group (group Magnesium sulphate) (n=30) received 50% magnesium sulphate 50 mg (0.5 ml) plus 0.5 % hyperbaric bupivacaine 12.5 mg (2.5 ml) for spinal anaesthesia. Second group (group Ketamine) (n=30) received preservative free ketamine 25 mg (0.5 ml) plus 0.5 % hyperbaric bupivacaine 12.5 mg (2.5 ml). Third group (group Control) (n=30) received plain 0.5% hyperbaric bupivacaine 12.5 mg (2.5 ml) plus 0.5 ml normal saline. Monitoring of vital parameters like pulse, BP (SBP, DBP & MAP) and oxygen saturation ($SpO_2$) were done throughout procedure and post operatively. Other parameters like sensory and motor block characteristics, pain - free period, side - effects including: hypotension, bradycardia, nausea, vomiting, sedation, pruritus, respiratory depression and dissociative manifestations, and patients' satisfaction visual analog scores (VAS) were recorded.

Our study showed a decrease in the heart rate is noted in the ketamine group following spinal anaesthesia at the 15, 20 and 25 minutes (p<0.001), earlier onset of sensory and motor blockade in the ketamine group compared to the magnesium sulphate group and control group and this difference was statistically significant (p<0.05), a longer duration of analgesia in the magnesium group (reduced VAS score) compared to the ketamine group and the control group from the 2$^{nd}$ hour till 7$^{th}$ hour post operatively and this difference was statistically significant (p<0.001). Nystagmus and sedation were observed exclusively in the ketamine group. No major complications occurred, but minor complications like nausea, vomiting, bradycardia and hypotension were present in all the three groups with no statistical difference among the groups (p>0.05).

## 8. Conclusion

We conclude by this study that intrathecal magnesium sulphate as an adjuvant to 0.5 % hyperbaric bupivacaine prolongs the duration of analgesia, without producing any major side effects. Ketamine used as an intrathecal adjuvant helps in fastening the onset time of sensory and motor blockade. Intrathecal magnesium sulphate, as an adjuvant helps in prolonging the duration of both sensory and motor blockade without increasing any side effects.

## 9. Future Scope

Spinal anaesthesia with plain bupivacaine has a major drawback of shorter duration of action. Hence adjuvants are used with bupivacaine which help by either earlier onset of action or longer duration of action of the block. Combination of multiple adjuvants with different mechanisms of action (earlier onset, longer duration, less side effects) with hyperbaric bupivacaine can help in better regional anaesthesia.

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## Author Profile

**Dr. Pratheev E**, I am 33 years old from Pondicherry, I am doing my third year residentship in the department of Anaesthesiology, Jhalawar medical college, Rajasthan. I completed my U. G. in Sri ManakulaVinayagar Medical College, Pondicherry. I

have a passion for critical care and I would work to get the D. M. Critical Care as early as possible. E mail ID: pratheev26[at]gmail.com

**Dr. Arpita Bhargava** is 29 years old from Jodhpur, Rajasthan, doing her third year residentship in the department of Anaesthesiology, Jhalawar medical college, Rajasthan. She completed her U. G. in Jhalawar medical college, Rajasthan. She is passionate about teaching in MARROW online coaching class for NEET PG. E mail ID: arpita.bhargava20[at]gmail.com

**Dr. Ritushree Sharma** is 27 years old from Jaipur, Rajasthan, doing her third year residentship in the department of Anaesthesiology, Jhalawar medical college, Rajasthan. She completed her U. G. in Mahatma Gandhi medical college, Jaipur, Rajasthan. She is passionate about joining obstetric anaesthesia. E mail ID: sharmaritushree[at]gmail.com