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Original Research Article

# Comparison of the Effect of Intrathecal Dexmedetomidine-Magnesium Sulfate Combination and Intrathecal Dexmedetomidine Alone on Subarachnoid Blockade with 0.75% Isobaric Ropivacaine in Knee Arthroplasty: A Prospective Randomised Double Blind Study

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**Conflict of interest: Nil**

**Abstract:**

**Background, Aims & Objectives:** Intrathecal local anesthetic alone is associated with relatively short duration of action and early analgesic intervention is needed in post-operative period. The addition of adjuvants provides a dose sparing effect of local anesthetics and accelerates the onset of sensory blockade as well as prolongs the duration of spinal block for long procedures and also provides postoperative pain relief. The aim of this study was to study the adjuvant effect of magnesium sulfate on ropivacaine and dexmedetomidine combination when used intrathecally with 0.75% isobaric Ropivacaine in lower limb surgeries. Block characteristics (onset, level and duration of sensory block and onset, level and duration of motor block), postoperative analgesia, hemodynamic parameters and adverse effects were noted.

**Material & Methods:** In this observational study, 100 adult patients (18-65 years) ASA-PS I & II undergoing total knee replacement surgeries under spinal anesthesia were included and randomized into two groups of 50 patients each. In Group D patients received 2ml of 0.75% isobaric Ropivacaine plus 10 micrograms Dexmedetomidine (in 1.0 ml) Total volume= 3ml. In Group DM patients received 2ml of 0.75 % isobaric Ropivacaine and 10 mcg dexmedetomidine (in 0.5ml) and 50 mg of preservative-free magnesium sulfate 50% diluted in 0.5ml. Total volume=3ml. The sensory block was assessed by loss of temperature discrimination to ice packs and pain sensation to needle-prick. The peak sensory level was noted. Motor blockade was assessed by Modified Bromage Scale. Adverse effects -hypotension (>30% decrease in SBP or SBP< 90 mmHg), bradycardia (heart rate <50bpm), nausea, vomiting, pruritus were noted.

**Results:** It was observed that the mean time to onset of sensory block was 4.45+0.38 minutes and mean time to onset of motor block was 6.12+0.5 minutes in Group DM compared to 2.15+0.63 minutes and 2.72+0.46 minutes in Group D respectively. Duration of sensory and motor blockade observed was 297.2+30.9 minutes and 202.3+0.6 minutes in Group DM and 191.6+0.71 minutes and 152.5+4.77 minutes in Group D respectively. Duration of postoperative analgesia was 441.2+0.83 minutes in Group DM and 302.47+0.21 minutes in Group D.

**Conclusions:** Though addition of Magnesium sulfate to Ropivacaine and Dexmedetomidine combination delayed the onset of subarachnoid blockade but it prolonged the duration of sensory and motor blockade and the duration of postoperative analgesia significantly.

**Keywords:** Dexmedetomidine, Ropivacaine, isobaric, magnesium sulfate, intrathecal.



## Introduction

Subarachnoid injection of a small dose of local anesthetic can rapidly produce dense surgical anesthesia and can provide excellent operating conditions for lower abdominal, pelvic and lower extremity surgeries. [1] The first case of spinal anesthesia in humans was performed by August Bier in 1898 and since then the technique has been widely used to provide anesthesia in lower abdominal and lower limb surgeries. [2] Ropivacaine is a long acting amide local anesthetic, S (-) enantiomer of bupivacaine with propyl tail on piperidine ring. In addition to a more favorable interaction with cardi-

ac sodium channels, it has more propensity to produce vasoconstriction, which may contribute to its reduced cardiotoxicity. [3] It has a high pK and low lipid solubility and is less likely to penetrate large myelinated motor fibres. It blocks nerve fibres involved in pain transmission (Aδ and C fibres) to a greater degree than those controlling motor function (Aβ fibres).[4] Ropivacaine causes reversible inhibition of sodium ion influx, and thereby blocks impulse conduction in nerve fibres. This action is potentiated by dose-dependent inhibition of potassium channels. [5, 6]

**Dexmedetomidine** is a relatively new drug approved at the end of 1999 by FDA and a useful sedative agent with analgesic properties, hemodynamic stability and facilitates early weaning in mechanically ventilated ICU patients. [7] Alpha 2-adrenergic receptor agonists have been successfully used in several clinical settings in view of diverse actions which include sedation, analgesia, anxiolysis, perioperative sympatholysis, cardiovascular stabilizing effects, reduced anaesthetic requirements, and preservation of respiratory function. [7] Locus ceruleus of the brainstem is the principal site for the sedative action and spinal cord is the principal site for the analgesic action of dexmedetomidine.

**Magnesium sulfate [8]** is an N-Methyl-d-aspartate (NMDA) antagonist that mediates the entry of calcium into neurons and has demonstrated efficacy in prolonging intravenous and intrathecal analgesia. Magnesium sulfate has been shown to enhance the effect of lidocaine in Aβ fibers but not in C fibers. Because of its synergistic effect with local anesthetics, magnesium has been administered primarily as an adjuvant to peripheral nerve blocks and neuraxial anesthesia to prolong analgesia. Normal serum magnesium levels range from 1.3 to 2.1 mEq/liter.

Because magnesium is removed from the body solely by the kidneys, the drug should be used with caution in patients with renal impairment. Urine output should be maintained at a level of 100 mL every four hours.

Monitoring serum magnesium levels and the patient's clinical status is essential to avoid the consequences of overdosage. Clinical indications of a safe dosage regimen include the presence of the patellar reflex (knee jerk) and absence of respiratory depression.

The strength of the deep tendon reflexes begins to diminish when serum magnesium levels exceed 4 mEq/liter. Reflexes may be absent at 10 mEq/liter, where respiratory paralysis is a potential hazard. Heart block also may occur at this or lower serum levels. The central and peripheral effects of Mg2+ poisoning are antagonized to some extent by intravenous administration of calcium. An injectable calcium salt should be immediately available to counteract the potential hazards of magnesium intoxication.

Spinal anaesthesia has the advantage of being relatively inexpensive with quicker onset of action as compared to epidural block and is technically easier. Neuraxial blocks not only reduce the incidence of deep venous thrombosis, pulmonary embolism, cardiac complications, bleeding, transfusion requirements, and respiratory depression but also provide effective post-operative analgesia. [9, 10] Disadvantages of spinal anaesthesia include shorter duration of the block in the absence of intrathecal additives, lack of top-up facilities unless a catheter is in, and post-dural puncture headache. [4] Moreover, geriatric patients have a particularly high incidence of hypotension during spinal anaesthesia. [11, 12, 13]

The inability to extend the duration of intraoperative block and postoperative analgesia with single shot spinal anesthesia is a major drawback and prompted us to conduct this study wherein magnesium sulfate was used as an intrathecal additive in addition to intrathecal dexmedetomidine to prolong block duration.

**Aim of the Study**

To study effect of intrathecal dexmedetomidine and dexmedetomidine and magnesium sulfate combination as adjuvants to Ropivacaine on block characteristics (onset, level and duration of sensory and motor blockade), hemodynamic parameters and postoperative analgesia.

**Material and Methods**

This prospective, randomized, double-blind observational study was conducted in Department of Anesthesiology, Sher-I-Kashmir Institute of Medical Sciences, Soura, and Srinagar, Jammu and Kashmir for a period of 2 years from August 2019 to August 2021.

**Inclusion Criteria:** After obtaining institutional ethical committee approval (and written informed consent from study subject, 100 adult patients of age group 18 to 65 years of either sex belonging to American Society of Anesthesiologists Physical status (ASA-PS) I & II undergoing knee arthroplasty under spinal anesthesia were included in the study.

Patients were randomized into two groups of 50 each:

**Group DM** (n=50) comprised of 50 patients and received 2ml of 0.75%isobaric ropivacaine plus 10 micrograms dexmedetomidine (in 0.5ml) and 50mg of $MgSO_4$ (in 0.5ml) intrathecally to a total volume of 3ml.

**Group D**(n=50) comprised of 50 patients and received 2ml of 0.75%isobaric ropivacaine plus 10 mcg of dexmedetomidine diluted in 1ml intrathecally to a total volume of 3ml.

**Exclusion Criteria:**Following patients were excluded from the study: Patient refusal/uncooperative patients

- Pregnant females
- Age below 18 years and above 65 years
- Allergy/hypersensitivity to drugs used
- Coagulopathy
- Local site infection
- Severe cardiopulmonary and renal ailments
- Hypovolemia
- Raised intracranial pressures
- Recent use of alpha 2 receptor antagonists

A detailed medical history was obtained from all patients, general and systemic examinations were carried out and appropriate investigations were done. All patients were pre-medicated with tablet alprazolam 0.5mg at 10pm and absolute fasting 8 hours was ensured. All the study drugs were prepared and coded by an anaesthetist who was not part of the study and the anaesthetist conducting the study was unaware of the drug being injected. The patient was blind to the drug injected as well. On arrival in the operation theatre, each patient was connected to standard monitors to record baseline blood pressure, heart rate and oxygen saturation. Intravenous line was secured with 18 G IV cannula and patients were preloaded with lactated ringer's solution at 15ml/kg. The patients were supported in sitting posture on a horizontal table, by an assistant. The lumbar area was prepared aseptically and draped. The intervertebral space at L3-L4 was identified and reached using 26G or 27G quincke's spinal needle by midline approach and the study drug was deposited intrathecally at a rate of 0.2ml/sec. After withdrawal of needle antiseptic seal was applied at the site of lumbar puncture and patient placed in supine position immediately. Patients were oxygenated via face mask oxygen if pulse oximetry reading was <90%.

The sensory block was assessed by loss of temperature discrimination to ice packs and loss of pain sensation to needle-prick in each dermatomal level. The peak sensory dermatomal level was noted. Time to achieve peak sensory level and the duration of sensory block was noted. Motor block of lower limbs was assessed by using Modified Bromage Scale (Grade 0- no motor block, Grade 1- inability to raise extended leg, able to move knees and ankle. Grade 2- inability to flex hip and knee but is able to flex his ankle. Grade 3- inability to flex hip, knee and ankle). Time to achieve the maximum level of motor block and duration was noted. Pain was assessed by Visual Analogue Score (VAS) with values ranging from 0 (No Pain) to 10 (Worst Pain). Patients feeling uncomfortable and interfering with the surgical procedure were excluded from the study and were given general anaesthesia. Vitals including heart rate (beats/min), blood pressure (mmHg) and oxygen saturation were monitored and recorded initially at 0,5,10,15,20,25,30 minutes after injection and subsequently at 10-minute intervals till end of surgery. In the postoperative period vitals were noted every 15 minutes for the first 2 hours and then at 30 minute interval for 24 hours. Also, any side effects like hypotension, bradycardia, nausea, vomiting were noted. Hypotension was defined as a >30% decrease in mean arterial blood pressure (MAP) compared to pre-anesthetic pressure or systolic blood pressure <90 mm Hg and was treated with Inj. Ephedrine 6 mg intravenously and iv fluids. Bradycardia was defined as heart rate HR<50 beats per min and was treated with inj. Atropine 0.6 mg intravenously. In the postoperative period, the time to first rescue analgesia was noted with VAS ≥ 4 and intravenous Paracetamol 1 gram 8 hourly was given for pain relief.

## Results

### Statistical Analysis

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as Mean ± SD and categorical variables were summarized as frequencies and percentages.

Graphically the data was presented by bar and pie diagrams. Student's independent t-test or Mann-Whitney U-test, whichever feasible, was employed for comparing continuous variables. Chi square test or Fisher's exact test, whichever appropriate, was applied for comparing categorical variables. A P-value of less than 0.05 was considered statistically significant. All P-values were two tailed. In our study, 118 patients were screened, of which 18 were excluded because of violation of the inclusion criteria or lack of confidence in understanding and handling the VAS pain scoring. 4 patients in the D group required conversion to general anesthesia as operating time got prolonged and patients became restless. 100 patients were randomized to receive the study drugs and thereafter completed the study without any exclusion or dropout [Figure 1].

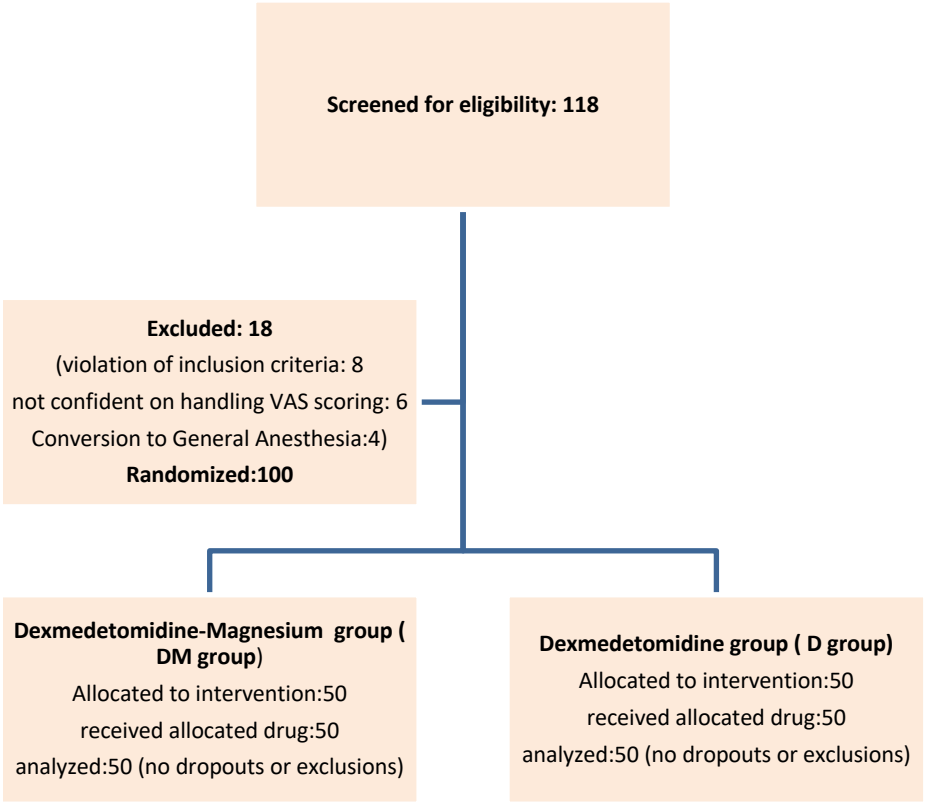


**Figure 1: Flowchart showing patient disposal in the study**

A total of 100 patients who underwent total knee arthroplasty were randomized into two groups of 50 each. In both groups, Demographic parameters such as age, weight, sex and ASA-PS were comparable (Table 1). Duration of surgery was comparable in both groups.

**Block characteristics:**

**Sensory block** (Table 2)

The mean onset of sensory block at L1 dermatome was earlier in D group (2.15+0.63 minutes) compared to DM group (4.45+0.38 minutes).However, the duration of sensory blockade was prolonged in DM group. Highest level of sensory block observed was T6 in DM group and T7 in D group.

**Motor block**

The mean onset of motor block was earlier in D group. However, duration of motor blockade was prolonged in DM group compared to D group. (Table 3)

**Postoperative analgesia**

Time to first rescue analgesia was significantly delayed in DM group. (Table 4)

**Side effect profile**

Overall 8 patients developed hypotension and bradycardia (5 in DM group and 3 in D group) which was managed with IV fluids and inj. Ephedrine 6mg IV boluses. (Table 5)

**Table 1: Demographic profile of patients**

| Variables | Group DM | Group D | p-value |
|---|---|---|---|
| Age (in years) | 41.2+10.8 | 40.6+11.79 | 0.813 |
| Sex (Female/Male) | 18/22 | 17/23 | 0.822 |
| Weight (in kg) | 62.73+4.2 | 64.10+4.76 | 0.176 |
| ASA I/II | 36/4 | 34/6 | 0.5017 |
| Height (in cm) | 166.2+2.8 | 166.13+2.9 | 0.912 |
| Duration of surgery | 64.5+13.4 | 66.9+3.75 | 0.278 |

**Table 2: Sensory Block**

| Block parameter | Group DM (Mean + SD) | Group D (Mean + SD) | p-value |
|---|---|---|---|
| Time of onset at L1 (in minutes) | 4.45+0.38 | 2.15+0.63 | <0.0001* |
| Maximum level of sensory block | $T_6$($T_4$-$T_9$)(85%) | $T_7$ ($T_5$-$T_{11}$)(80%) | 0.558 |
| Duration of sensory block (in minutes) | 297.2+30.9 | 191.6+0.71 | <0.0001* |

**Table 3: Motor Block**

| **Block parameter** | **Group DM** (Mean+ SD) | **Group D** (Mean+ SD) | **p-value** |
|---|---|---|---|
| Mean onset of motor block (in minutes) | 6.12+ 0.5 | 2.72+0.46 | <0.0001* |
| Duration of motor block (in minutes) | 202.3+0.6 | 152.5+4.77 | <0.0001* |
| Maximum motor block(MBS grade III) | 47/50 | 44/50 | 0.296 |

**Table 4: Postoperative analgesia**

| **Time of requirement of rescue analgesia** | **Group DM (Mean + SD)** | **Group D (Mean + SD)** | **p-value** |
|---|---|---|---|
| Time of requirement of first dose of rescue analgesia (in minutes) | 441.2+ 0.83 | 302.47+0.21 | <0.0001* |

**Table 5: Complications in both groups**

| **Complication** | **Group DM (n / %)** | **Group D (n / %)** | **p-value** |
|---|---|---|---|
| Bradycardia | 5/ 10% | 3/ 6% | 0.463 |
| Hypotension | 5/ 10% | 3/ 6% | 0.463 |
| Nausea | 1/ 2% | 1/ 2% | 1.0 |
| Shivering | 0/ 0 | 0/ 0% | - |

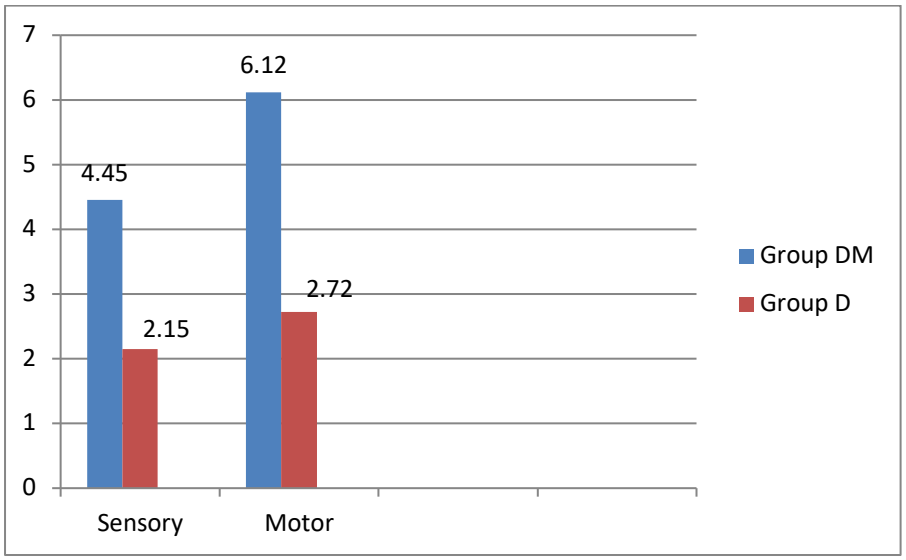


**Figure 2: Onset of Block (in minutes):**

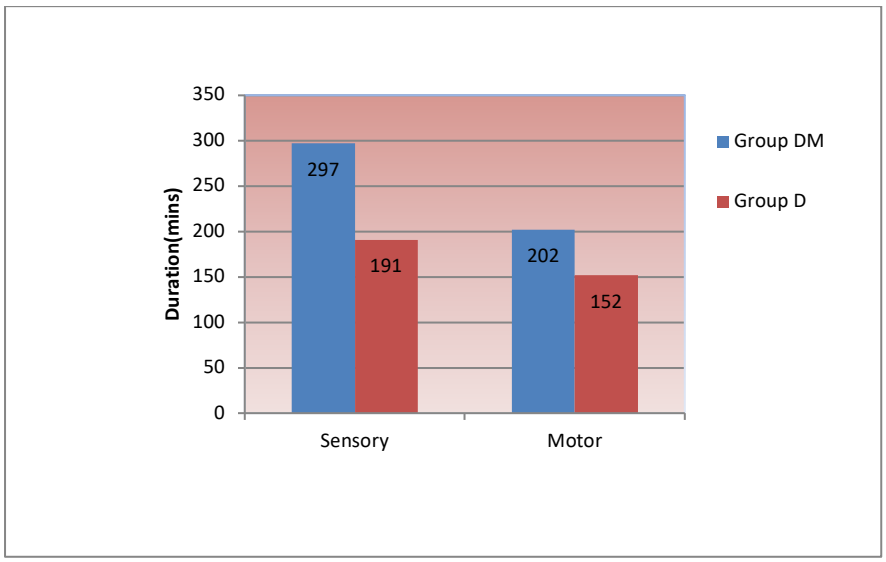


**Figure 3: Duration of Block (in minutes):**

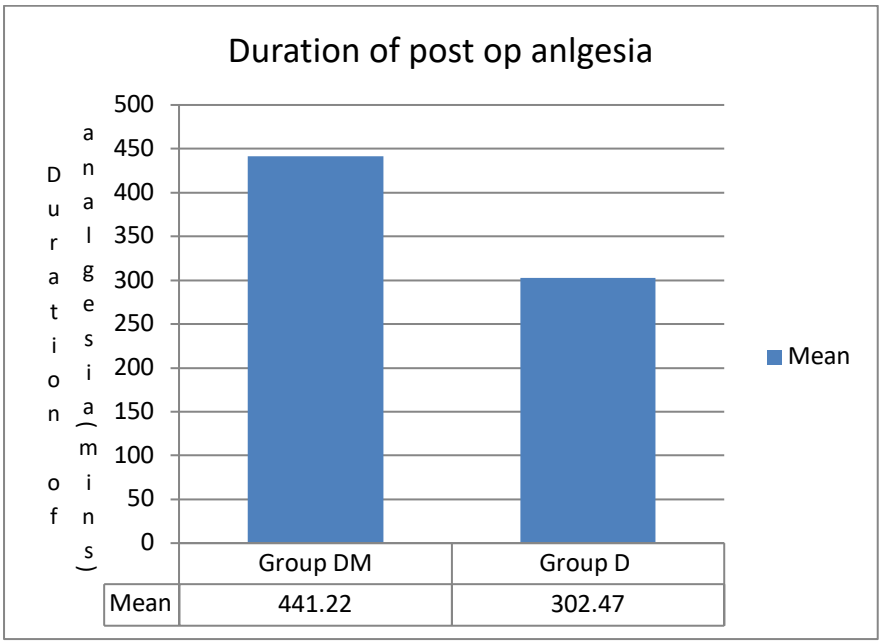


**Figure 4: Postoperative analgesia (in minutes):**

## Discussion

Contemporary anaesthesia demands airway manipulation sparing techniques, use of regional anesthesia over general anesthesia, early post-operative mobilization and rehabilitation with minimal pain.[14, 15] Dexmedetomidine, a new highly selective α2-agonist, when used as a neuraxial adjuvant has shown to provide stable hemodynamic conditions, good quality of intraoperative and prolonged postoperative analgesia with minimal side effects.[16, 17]Magnesium blocks NMDA channels in a voltage-dependent way, and the addition of magnesium produces a reduction of NMDA-induced currents. Magnesium sulfate has been used systemically, and has shown antinociceptive effects. Intrathecal magnesium has been found to prolong the duration of analgesia in various surgical procedures[18]. However the combined effect of both these intrathecal adjuvants when used simultaneously has not been studied yet.

In our study demographic parameters were comparable in both groups.Delayed onset of sensory block and motor block was observed with the use of magnesium. This finding is in concordance with the studies conducted by Nath et al (2012) [19] and Makhni et al (2017)[20] All these studies demonstrated an earlier onset of sensory and motor block in the dexmedetomidine group and the results were clinically and statistically significant ($p<0.0001$).

Dexmedetomidine-Magnesium sulfate group showed significant prolongation in sensory and motor block duration similar to studies conducted by Yadav et al (2015)[21] and Nath et al (2012) [19] ($p<0.0001$). Time to first recue analgesic need in the postoperative period was significantly prolonged with use of dexmedetomidine-magnesium combination compared to dexmedetomidine alone. Bradycardia and hypotension was observed in 5 patients in DM group and 3 patients in D group, however the finding was statistically insignificant and was managed well with inj. Ephedrine IV bolus along withIV fluids without any complications. One patient in each group complained of nausea which was attributed to hypotension and managed with i.v. fluids and inj. Ondansetron.

None of the patients developed shivering preoperatively which could be explained by possible roles of dexmedetomidine[22, 23] and magnesium sulfate[24] in ameliorating shivering.

## Conclusion

Combined use of magnesium sulfate and dexmedetomidine as intrathecal adjuvants to Isobaric Ropivacaine 0.75% delayed the onset of blockade but provided a longer duration of sensory and motor block as well as prolonged the duration of post-operative analgesia. Magnesium and dexmedetomidine combination can be safely used as intrathecal adjuvants to spinal drug on a routine basis to extend the duration of intraoperative blockade especially in the absence of indwelling catheters.

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