

## Effects of adding Magnesium Sulphate to Ropivacaine and Fentanyl for spinal anaesthesia

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### Abstract:

**Objective:** To compare the block characteristics and haemodynamic stability of intrathecal Ropivacaine and Fentanyl; with and without Magnesium as adjuvant for lower limb surgeries. **Method:** Sixty patients of ASA grade I and II coming for elective lower limb surgeries under spinal anaesthesia were randomly allocated into two groups with 30 patients in each group. Group F received Isobaric Ropivacaine 0.75% -2.4ml + Fentanyl 20 $\mu$  + 0.2ml NS and Group M received Isobaric ropivacaine - 2.4ml + Fentanyl 20 $\mu$  + 25% Magnesium Sulphate 0.2ml. Sensory and motor block characteristics were assessed by pin prick and modified Bromage scale respectively and haemodynamics were recorded. **Results:** Time to reach T10 dermatome was delayed in group M (4.23 $\pm$ 0.94min) compared to group F (2.92 $\pm$ 0.81mins). The onset of motor block was also significantly delayed in group M (4.63 $\pm$ 0.85mins) than group F (3.30 $\pm$ 0.79mins). Duration of analgesia was higher in group M and time for motor recovery was also delayed in group M (p<0.001). **Conclusion:** Time for onset and recovery of sensory and motor block was delayed with intrathecal ropivacaine in combination with Fentanyl and Magnesium Sulphate as adjuvants than intrathecal Ropivacaine and fentanyl alone.

**Key words:** intrathecal injection, Ropivacaine, Fentanyl, Magnesium Sulphate.

### I. Introduction

Spinal anaesthesia is a widely used technique, providing a fast onset and dense sensory and motor blockade. Various intrathecal adjuvants have been used to improve the quality and the duration of spinal anaesthesia. Ropivacaine is a newer local anaesthetic with lower risk of neurotoxicity and cardiotoxicity compared with bupivacaine and Lidocaine. <sup>(1, 2, 3)</sup> Ropivacaine has been advocated as a drug with a shorter duration of motor block and prolonged sensory analgesia than bupivacaine. Prolongation of spinal anaesthesia is desirable both for long procedures and postoperative pain relief. Highly lipid soluble opioids have higher affinity for opioid receptors and improve the quality of intraoperative anaesthesia and permit lower doses of local anaesthetics when used intrathecally. They provide faster onset and prolonged duration analgesia <sup>(16,17,18)</sup>. Intrathecal opioids can cause pruritis, urinary retention, respiratory depression, nausea and vomiting as adverse effects. Thus addition of intrathecal magnesium sulphate has been used to study the effect of potentiation of opioids at lower doses on local anaesthetics <sup>(20,21,22)</sup>. Anti-nociceptive effect of Magnesium appears to be relevant not only for chronic pain, but also in postoperative pain based on regulation of calcium influx into the cell. Magnesium blocks calcium influx and noncompetitively antagonizes NMDA channels <sup>(23,24,25,26,27)</sup> and addition of magnesium sulphate improves postoperative analgesia.

### II. Methods

A prospective randomised study was conducted at Adichunchunagiri Institute of Medical Sciences, B.G. Nagara, after obtaining written informed consent from 60 patients in the age group of 18 to 60 years. Patients of ASA grade 1 and 2 posted for elective lower limb surgeries were randomly selected and allocated into two groups. Group F received Isobaric Ropivacaine - 2.4ml + Fentanyl 20 $\mu$  + 0.2ml NS and Group M received Isobaric Ropivacaine - 2.4ml + Fentanyl 20 $\mu$  + 0.2ml of 25% Magnesium Sulphate (50mg). All patients were preloaded with 500ml RL. With the patient in lateral position, subarachnoid block was performed at L3-L4 space with 23G spinal needle. After injection of drug, patients were placed supine.

Heart rate and blood pressure were recorded before intrathecal injection and 5 minutes after the intrathecal drug administration up to first half an hour and thereafter every 10 minutes till the end of the operation and at hourly interval after the end of the surgery. MAP lower than 60 mm of Hg or systolic BP less than 30% from base line and HR less than 50 beats / min were treated with Inj. Ephedrine 6mg and Inj. Atropine 0.6 mg respectively. The time for onset for two segment regression of sensory block and duration of sensory and motor block were recorded. The onset of sensory block was defined as the time between injection and loss of response to pinprick at T10 dermatome. The maximum level of sensory block was determined by pinprick every

2 minutes. The duration of analgesia was taken as the time from intrathecal injection to first request of analgesics. The onset of motor block was assessed by Modified Bromage score. Patients were discharged from the recovery room when the motor block was completely resolved and when stable. Patients were also assessed for the occurrence of any adverse events like nausea, vomiting and pruritis.

### III. Results

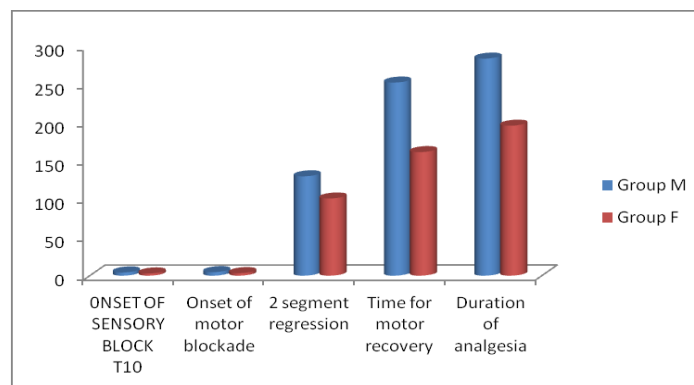
Demographic data such as: age, sex, age, height, weight and BMI and the block characteristics events were statistically analyzed. The p value of <0.05 was considered to be statistically significant. The Demographic Variables of the patients are shown in the Table-1.

	Group F	Group M	P value
Age in years	40.77±12.19	40.55±8.05	0.921
Weight(kg)	61.90±8.05	64.73±9.49	0.217
Height(cm)	161.57±8.23	165.57±7.49	0.100
Duration of surgery (min)	72.83±14.78	75.17±11.93	0.504
BMI	23.62 ±1.76	23.49±2.17	0.818

There was no significant difference among the groups with respect to age, height, weight and duration of surgery. Maximum sensory level attained was comparable in both the groups and was between T6 and T8.

Comparison of block characteristics in the two groups:

	Group M	Group F	P value
Onset of sensory block ( in min)	4.23±0.94	2.92±0.81	<0.001**
Onset of motor block (in min)	4.63±0.85	3.30±0.79	<0.001**
2 segment regression (in min)	129.83±18.36	100.83±12.18	<0.001**
Time for motor recovery (in min)	252.33±27.03	161.50±23.60	<0.001**
Duration of analgesia(in min)	283.67±30.57	196.00±23.21	<0.001**



Onset and recovery of sensory and motor block was significantly shorter in group F than Group M. Duration of analgesia was also longer in group M (283.67±30.57 min) than with group F (196±23.21 min) (P<0.001). There was no significant difference in frequency of side effects in both the groups. No neurological deficit or other complication was observed in any patient. Haemodynamic parameters in the intra and post operative period were similar in both our study groups.

### IV. Discussion

Bupivacaine is an amide type local anesthetic, a racemic (50:50) mixture of S and R enantiomers. Since its introduction in 1956, it has been used as the drug of choice for spinal anesthesia due to its longer duration of action (3-7 hours), limited placental transfer, and minimal neonatal effects compared to other local anesthetics. In 1979, attention was drawn towards the cardiotoxic and neurotoxic effects of bupivacaine, linked to its R-enantiomer. Another amide type local anesthetic, ropivacaine, the s-enantiomer of propyl derivative of pipercoloxylidide was first introduced in 1996 and approved for spinal anesthesia in the European union in 2004<sup>(1,2)</sup>. Ropivacaine, being a pure s-enantiomer, has low lipid solubility and blocks nerve fibres involved in pain transmission to a greater degree than those involved in motor function and is less cardiotoxic<sup>(3,4,5)</sup>

Central sensitization is an activity-dependent increase in the excitability of spinal neurons and is considered to be one of the mechanisms implicated in the persistence of postoperative pain. Magnesium sulfate acts by blocking the N Methyl D Aspartate channels in a voltage-dependent way to be improve the quality and

duration of spinal anaesthesia. The magnesium sulfate safety profile has been documented by histopathological analysis in experimental studies<sup>(19)</sup>. The addition of intrathecal magnesium to intrathecal lipophilic opioid along with local anaesthetics led to delay in the onset of both sensory and motor blockade, along with an increase in the duration of spinal anaesthesia. The duration of spinal anaesthesia was found to be increased when magnesium was added to opioid with intrathecal local anaesthetics compared with a combination of local anaesthetic and opioid mixture ( $p < 0.001$ )<sup>(26)</sup>. The incidence of adverse events (hypotension, pruritis) was not increased by adding intrathecal magnesium. But it seemed that this drug was enough to provide effective anaesthesia.

Magnesium exerts its analgesic action as a non-competitive NMDA receptor antagonist, blocking ion channels in a voltage dependent manner<sup>(20,21,22)</sup>. This drug is both analgesic and anti-nociceptive additive drug. When used with local anaesthetic, it resulted in prolongation of analgesia without significant complication<sup>(23,24)</sup>. This prolongation of anaesthesia is consistent with the experimental synergistic action between spinal local anaesthetic and NMDA antagonists like magnesium sulphate, which use anti-nociceptive effects via different mechanisms;<sup>(25,26,27)</sup> hence the rationale for combining the two. There are no selective NMDA receptor antagonists available for pain management; hence, drugs with other clinical uses, such as magnesium sulphate and ketamine, shown promises as analgesics, have been used. Magnesium sulphate is also known as nature's physiological calcium channel blocker. In animals, calcium channel blockers have demonstrated an anti-nociceptive effect and in chronic pain patients, they potentiate the effects of morphine. In the presence of intrathecal opioid, there is a beneficial effect, which may suggest that magnesium potentiates the effect of opioid. These findings correlate that with those of Kroin and colleagues<sup>(25)</sup>, who demonstrated that the addition of intrathecal mg increased the peak effect. Potentiating of opioid anti-nociception occurs by blocking the spinally mediated facilitatory component evoked by C fibre stimulation. This effect would be expected to continue in the postoperative period. The binding and dissociation of non competitive NMDA receptor antagonists is relatively slow, which may explain the continuation of anaesthesia into the postoperative period and the requirement of reduction in the postoperative analgesics. It is possible that the solution to which magnesium sulfate added had a different PH, which might be the cause for delay in the onset of sensory and motor blockade. Fentanyl added to local anaesthetic agent seems to be the most frequently used combination to enhance and increase the duration of sensory analgesia without intensifying the motor blockade or delaying recovery from spinal anaesthesia. The dose of magnesium used in this study was based on data from Buvendraan et al, where 50 mg of spinal magnesium sulfate potentiated fentanyl anti-nociception. In 1985, Lejuste, described the inadvertent intrathecal injection of 1000mg of mg so4, producing a dense motor block followed by complete resolution within 90 mts, with no neurological deficit at long term follow up.<sup>(29)</sup> A recent human study found no harmful effects of IT magnesium on spinal opioid analgesia in labour. Thus intrathecal MgSO4 seems to have a good safety profile.<sup>(20)</sup>

Thus an attempt was done to study the effects of addition of magnesium to the newer local anaesthetic ropivacaine with adjuvant fentanyl.

This analysis demonstrates that the addition of intrathecal magnesium to intrathecal lipophilic opioid fentanyl along with local anaesthetic. Ropivacaine leads to delay in the onset of both sensory and motor blockade but significantly prolongs the duration of sensory and motor block following spinal anaesthesia. The duration of analgesia was also found to be increased with magnesium as adjuvant. The incidence of adverse events (hypotension, pruritis) were insignificant with intrathecal magnesium. This was consistent with the results of other studies<sup>(20,21,22,23)</sup>

Mitrajabalameli and Seyed Hamid Pakzadmoghadam et al compared effects of adding different doses of intrathecal magnesium sulfate for spinal anaesthesia in the cesarean section and showed that all doses studied provide safe and effective anaesthesia, but 75 mg of this drug increases duration of postoperative analgesia and prolong than sensory and motor block without significant increase in maternal and neonatal side effects<sup>(20)</sup>.

Dayioğlu et al studied the effects of adding intrathecal magnesium sulfate 50 mg to low-dose bupivacaine - fentanyl on the spread, duration, regression of spinal block, and postoperative analgesia in patients undergoing knee arthroscopy. They found that the addition of intrathecal magnesium (50 mg) to spinal anaesthesia prolonged the time for regression of two segments in the maximum block height and time to L2 regression, but did not affect maximum sensory level or the time to reach the highest level of sensory block. Even though the mean times to complete recovery of motor function were similar in the two groups, time to ambulation was significantly longer in the magnesium group than in the saline group. Total analgesic consumption in the first 24 h was not decreased significantly with the addition of magnesium to spinal anaesthesia, but the time to first analgesic requirement was prolonged significantly<sup>(21)</sup>.

Khalili G et al evaluated the effect of additional magnesium sulfate 100 mg to intrathecal isobaric 0.5% bupivacaine 3 ml on spinal anaesthesia in patients undergoing lower extremity orthopedic surgery and concluded that addition of 100 mg intrathecal magnesium to 15 mg bupivacaine without opioid supplement, prolonged the duration of the sensory block, decreased postoperative analgesic consumption, and significantly prolonged the onset of spinal anaesthesia.<sup>(22)</sup>

Arcioni.R et al investigated whether supplementation of spinal anesthesia with combined intrathecally and epidurally infused MgSO<sub>4</sub>. reduced patients' post-operative analgesia requirements. They found that supplementation of spinal anesthesia with combined intrathecal and epidural magnesium sulphate significantly reduces patients' post-operative analgesia requirement<sup>(23)</sup>

In conclusion we found that isobaric 0.75% ropivacaine (2.5ml) with fentanyl 20 microgm along with 50mg Magnesium sulphate provided effective anesthesia for lower limb surgeries compared to ropivacaine with fentanyl alone.

## V. Conclusion

The present study shows that addition of 50 mg magnesium sulphate to 2.4 ml of 0.75% isobaric ropivacaine with 20 µ fentanyl delays the onset of sensory and motor blockade compared to only ropivacaine and fentanyl alone and shows that addition of intrathecal magnesium sulphate potentiates the action of opioid with local anesthetics when added intrathecally and prolongs the duration of block both sensory and motor.

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