

Magnesium Sulphate as an Adjuvant to Epidural Ropivacaine for Postoperative Analgesia in Patients Undergoing Vaginal Hysterectomy

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Abstract

Background: Effective postoperative analgesia following surgery is vital for early recovery and mobilization. This study aims to find out the analgesic efficacy of magnesium sulphate as an adjuvant to epidural ropivacaine for postoperative analgesia in patients undergoing vaginal hysterectomy under regional anaesthesia. **Subjects and Methods:** Forty consenting ASA I and II patients scheduled for vaginal hysterectomy under combined spinal epidural block were recruited. All patients received 2.5 ml hyperbaric bupivacaine intrathecally for the conduct of the procedure. Postoperatively, patients received ropivacaine with 50 mg magnesium sulphate (group RM) or ropivacaine with normal saline (group RS) through epidural catheter, when VAS ≥ 3 was achieved. Time to subsequent epidural top-up after study drug, VAS score, number of epidural top-ups, total dose of ropivacaine and diclofenac, haemodynamic parameters and sedation score were recorded. Data was analyzed using appropriate statistical tests. **Results:** Women who received magnesium with ropivacaine (group RM) had significantly longer mean time (214.15 \pm 91.03 min) to subsequent epidural top-up after the study drug as compared to group RS (203.41 \pm 129.11 min); $p=0.015$. The mean total dose of ropivacaine and diclofenac consumption in 24 hours was also less in group RM compared to group RS ($p<0.05$). The intraoperative and postoperative haemodynamics were comparable in both the groups. **Conclusion:** Epidural magnesium sulphate as an adjuvant to ropivacaine significantly prolonged the duration of postoperative analgesia, reduced the 24 hour ropivacaine and diclofenac requirements without any additional side effects.

Keywords: Epidural Magnesium, Postoperative Analgesia, Ropivacaine.

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Received: November 2019

Accepted: November 2019

Introduction

Pain is defined as an unpleasant sensory and emotional experience with actual or potential tissue damage or described in terms of such damage.^[1] Vaginal hysterectomy (VH) is a common gynaecological procedure which is associated with moderate to severe postoperative pain. Untreated pain induces stress, leading to multiple problems like myocardial ischemia, angina, dysrhythmias, infarction and hypercoagulability through activation of sympathetic nervous system.^[2-6] Thus, providing postoperative pain relief is one of the major responsibilities of an anaesthesiologist. Combined spinal-epidural anaesthesia (CSE) is preferred over spinal or epidural alone for conduct of lower abdominal and lower limb surgeries because of the advantage of early onset of action, the possibility of prolonging the duration of action and for provision of postoperative analgesia.^[7] Ropivacaine, with its property of sensory blockade comparable to and motor blockade less than bupivacaine, is a

good agent for postoperative analgesia.^[8] Adjuvants like midazolam, clonidine or fentanyl may be added to ropivacaine to potentiate and prolong postoperative analgesia. However, these drugs have significant side effects like sedation, pruritus, hypotension, shivering, nausea and vomiting. Recently magnesium has been reported to prolong the action of epidural bupivacaine.^[9] However, there are limited studies on the use of magnesium sulphate as an adjuvant to epidural ropivacaine for postoperative pain relief following VH.

Present study was planned to assess the efficacy of magnesium sulphate as an adjuvant to epidural ropivacaine for postoperative analgesia following VH for its analgesic effect, duration of analgesia and requirement of subsequent epidural top ups and other rescue analgesics in the first 24 hours.

Subjects and Methods

This randomized, double blind controlled study was

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conducted after clearance from the institutional ethical committee. Written, informed consent was obtained from all the participants. Forty female patients belonging to American Society of Anaesthesiologists grade I and II between 35-60 year of age and height between 140 and 170 cm scheduled for vaginal hysterectomy under CSE were included. Non-consenting patients or those with contraindications to CSE, allergies to drugs being used in the study, body weight >100 kg, significant pre-existing severe systemic illness like cardiovascular and hepatorenal disease were excluded from the study. Patients were familiarized with visual analogue scale (VAS) (where 0 represents no pain and 10 represents worst pain) a day before surgery. All patients were advised for overnight fasting and were pre medicated with oral 0.25 mg Alprazolam night before surgery.

In the operating theatre, routine monitoring including continuous electrocardiogram, non-invasive blood pressure and pulse oximetry was instituted. Baseline heart rate, blood pressure (systolic, diastolic and mean) and oxygen saturation were recorded. Intravenous access was established using 18-G intravenous cannula and 10ml/kg of lactated Ringer's infusion was started.

Under all aseptic precautions, patients received CSE anaesthesia using the needle through needle technique at L3-L4 interspinous space with 18-G Touhy's needle and 27-G Whitacre's needle. After identification of subarachnoid space, 2.5 ml of 0.5% hyperbaric bupivacaine was injected. Subsequently, epidural catheter was threaded 4 cm inside the epidural space and secured. At the end of surgery, patients were shifted to postoperative area where hemodynamic parameters and VAS score were monitored. When the VAS was ≥ 3 , patients were randomly allocated to one of the two groups, group RM or group RS, according to a computer generated random number table. Patients in group RM received 15 mg ropivacaine (0.25%, 6ml) with 50 mg of magnesium sulphate (1ml) and those in group RS received 15 mg of ropivacaine (0.25%, 6ml) with Normal Saline (1ml). All patients received the epidural drug after 3 ml lignocaine (2%) with adrenaline (1:200000) as test dose through the epidural catheter to rule out intrathecal and intravascular catheter placement. Subsequent epidural top-ups were given in the form of 6 ml ropivacaine (0.25%) when patient again complained of pain or when VAS score ≥ 3 . If any patient had a VAS score ≥ 3 after half an hour of the epidural drug injection, additional rescue analgesia was given with I.V. aqueous diclofenac sodium 1mg/kg. Sensory and motor block characteristics, time taken to achieve T10 sensory block and Bromage score 3 motor blockade were recorded in the intraoperative period. Heart rate, systolic, diastolic and mean blood pressure, oxygen saturation were recorded intraoperatively as well as postoperatively. Pain score was evaluated using a standard 10 cm linear Visual Analogue Scale (VAS) where 0 cm mark and 10 cm mark corresponds to "no pain" and "worst imaginable pain" respectively. All these parameters were recorded immediately on shifting the patient to postoperative area (baseline, 0 hour), then every hour for first 6 hour and at 9th, 12th and 24th postoperative hour. Patients were monitored for side effects like hypotension (defined as SBP <90 mmHg or a fall in SBP >20% of the baseline value), bradycardia

(defined as HR <50 beats/min or decrease in the HR by 20% of the baseline value), sedation, respiratory depression, nausea, vomiting, headache etc.

Considering a range of 3-5 hours of analgesia with ropivacaine and 5-11 hours with ropivacaine-magnesium combination, an estimated difference of 4 hours duration of analgesia in a study by Yousef GT et al in children undergoing inguinal hernia repair¹⁰, a sample of 5 cases was required in each group at $\alpha=5\%$ power=80%. Taking into consideration, the availability of time and patient, 20 patients were included in each group. Continuous variables were evaluated using unpaired student's t-test. Intra and inter-group comparisons for haemodynamic parameters and VAS were done using repeated measure ANOVA followed by Bonferroni correction. Chi-square/ Fisher's Exact Test was applied for comparing the proportion of side effects between the groups. A p value <0.05 was considered as significant. Statistical analysis was performed by SPSS program for windows, version 20.0.

Results

A total of 46 patients were assessed for eligibility. Six were excluded and a total of 40 patients were randomised to one of the two groups. [Figure 1] The demographic profile of the patients among the two groups was comparable with respect to age, weight, height and the duration of surgery [Table 1]. The sensory and motor block characteristics of subarachnoid block were comparable [Table 2]. The intraoperative and postoperative haemodynamics are depicted in [Figure 2 & 3] respectively.

The postoperative analgesic requirements are shown in [Table 3]. The mean time of injection of the epidural study drug was comparable in both the groups. The mean time to inject the subsequent epidural top-up after the study drug was significantly longer in group RM (214.15 \pm 91.03 min) compared to group RS (156.95 \pm 41.47 min); p=0.015. The mean total consumption of ropivacaine and diclofenac in 24 hour was less in group RM compared to group RS (Table 3). The mean time to administer first rescue analgesic drug was comparable among the two groups [Table 3].

The mean number of epidural top-ups and the number of diclofenac injections in 24 hour were significantly less in group RM compared to group RS. Figure 4 shows the VAS score of patients in the two groups in the postoperative period. The VAS score was comparable between the two groups at all the time points. There was no incidence of any side effects like sedation, respiratory depression, bradycardia, hypotension, nausea, vomiting, headache, sensory and motor block and any other complications after the study drug injection were noted in any of the group.

Table 1: Demographic profile

Parameters	Group RM (n=20)	Group RS (n=20)	p-value
Age (years)	45.15 \pm 7.47	46.45 \pm 7.65	0.590
Weight (kg)	55.85 \pm 9.43	56.41 \pm 8.59	0.845
Height (cm)	152.35 \pm 2.96	153.70 \pm 5.99	0.372
Duration of Surgery(min)	119.00 \pm 20.93	123.25 \pm 22.66	0.542

Values are expressed as mean \pm SD; p<0.05 is significant

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Table 2: Sensory and motor block characteristics of subarachnoid block

Parameters	Group RM (n=20)	Group RS (n=20)	p-value
Time to T10 level (min)	8.30±2.83	8.25±1.80	0.947
Time to achieve maximum level (min)	14.90±3.05	16.25±2.77	0.152
Time to two dermatomal regression (min)	103.00±8.01	108.00±8.7	0.065
Median sensory level	T6 [T6-T7]	T6 [T6-T7]	---
Time to Bromage 3 motor block (min)	7.95±2.16	8.05±1.84	0.876

Values are expressed as Mean ± SD or median [IQR]; p<0.05 is significant

Table 3: Postoperative analgesic requirement

Parameter	Group RM (n=20)	Group RS (n=20)	p-value
Time to epidural study drug (min)	177.60±28.96	187.10±29.20	0.308
Time to administer first rescue drug (min)	203.41±129.11	193.30±120.36	0.807
Time to subsequent epidural top-up requirement (min)	214.15±91.03	156.95±41.47	0.015
Total dose of ropivacaine in 24 hr (mg)	65.25±7.34	77.25±7.34	<0.001
Total dose of diclofenac in 24 hr (mg)	81.76±29.80	116.75±48.21	<0.001
No. of epidural top-up in 24 hr	4.35±0.48	5.10±0.55	0.014
No. of rescue drug injection in 24 hr	1.30±0.73	2.10±0.64	<0.001
Percentage of patients who required 1 dose of diclofenac	47.1%	15.0%	0.024
Percentage of patients who required 2 doses of diclofenac	52.9%	60.0%	
Percentage of patients who required 3 doses of diclofenac	0%	25%	

Values are expressed as Mean ± SD or percentage; p<0.05 is significant

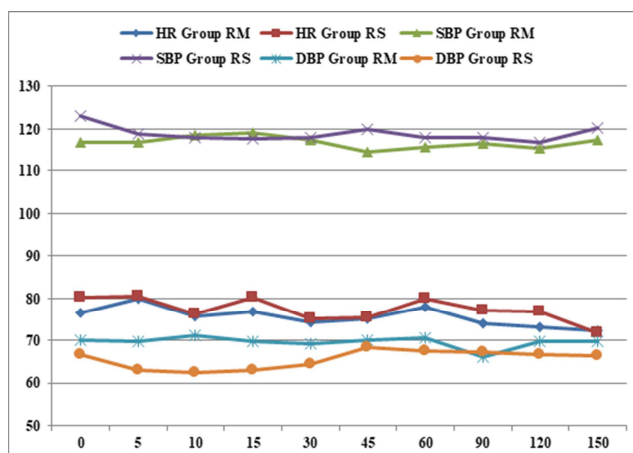


Figure 2: Postoperative haemodynamics at various time intervals

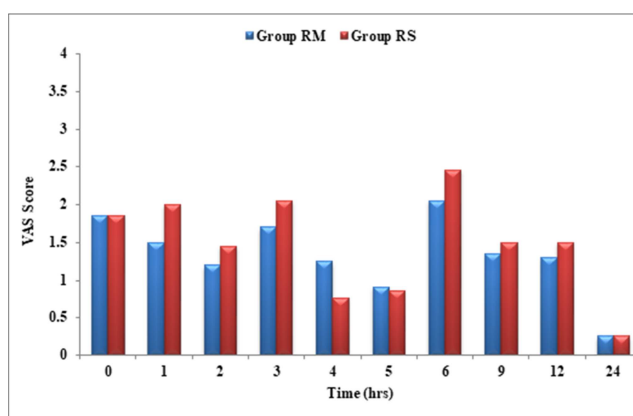


Figure 3: Postoperative VAS at various time intervals

Discussion

Magnesium sulphate, a non-competitive blocker of voltage gated N-methyl-D-aspartate (NMDA) receptor and inhibitor of calcium influx into the cells, decreases catecholamine release. It has recently been shown to prolong the action of epidural bupivacaine. It does not induce haemodynamic instability, respiratory depression, hyporeflexia, cardiac manifestations or sedation.^[11-14]

In the present study, we found that the addition of 50 mg magnesium sulphate as an adjuvant to epidural ropivacaine is safe and prolongs the duration of analgesia, reduces the total epidural ropivacaine and IV diclofenac requirement over 24 hour postoperative period. The total number of epidural top-ups as well as rescue analgesic requirement is also significantly reduced without any additional side effects.

The safety of magnesium sulphate for intrathecal as well as epidural use in doses as large as 100mg has been proven in previous study.^[15] Shahi et al have shown that 50mg magnesium sulphate single bolus as an adjuvant to epidural bupivacaine provides better postoperative analgesia compared to control group.^[16] We also used single bolus dose of 50mg magnesium sulphate as an adjuvant to epidural ropivacaine to find out its efficacy as a postoperative analgesic in patients undergoing VH.

We found that the addition of epidural magnesium sulphate as an adjuvant to ropivacaine significantly delayed the

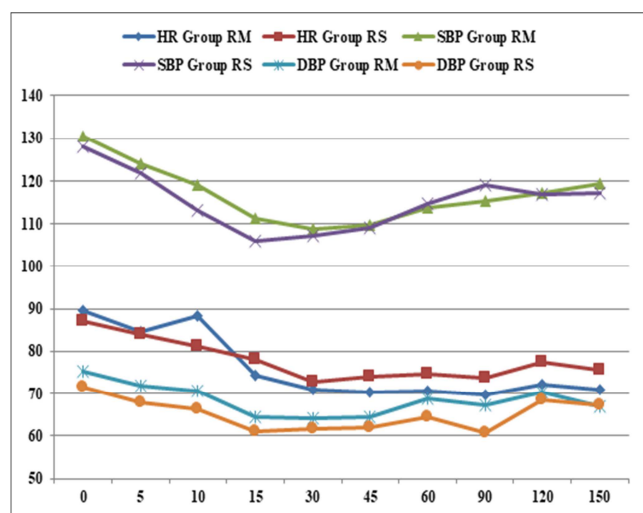


Figure 1: Intraoperative haemodynamics at various time intervals

0 requirement of next epidural ropivacaine top-up (214.15±91.03 min) as compared to ropivacaine alone (156.95±14.47 min). Similar results were found by Ghatak et al where 50mg magnesium sulphate was used as an adjuvant to epidural bupivacaine for lower abdominal and lower limb surgeries.^[9]

In our study, the mean time to inject first rescue dose of diclofenac was comparable in both the groups however, the total consumption of ropivacaine in 24hour was significantly less in the group which received a combination of ropivacaine and magnesium sulphate. Our results were similar to Mohamed et al who compared 50 mg magnesium sulphate with 0.5% bupivacaine for epidural anaesthesia in patients undergoing total knee replacement surgery and found that total fentanyl consumption in magnesium sulphate group was significantly less as compared to midazolam and control group.^[17] The mean total consumption of diclofenac (rescue analgesic) in our study was less in magnesium sulphate group compared to control group (P<0.001). These results are also in concurrence with the study by Mohamed et al.^[17] In the study done by Bilir et al, there was no requirement of rescue analgesia (tramadol) within the first 24 hour following epidural magnesium sulphate.^[18] In a recent study by Gupta et al ropivacaine with fentanyl and magnesium sulphate as adjuvants provided faster onset of analgesia and T10 sensory blockade and delayed the requirement of first epidural top up compared to ropivacaine with or without fentanyl.^[19]

In our study, the mean number of subsequent epidural top-ups of ropivacaine as well as the mean number of rescue drug (diclofenac) dose after the first top-up was also significantly less in magnesium sulphate group and findings were similar to studies by previous researchers.^[18,20,21]

In our study addition of epidural 50 mg magnesium sulphate to ropivacaine did not cause any significant incidence of hypotension, bradycardia or other adverse effects like sedation, respiratory depression, nausea, vomiting, headache, sensory block, motor block or any other complications postoperatively. These findings were comparable to previous studies.^[16-18,20]

Many authors have studied the role of magnesium for postoperative analgesia. Most of these studies showed that epidural administration of magnesium sulphate results in decreased analgesic requirement which can be explained by its possible mechanisms as a non-competitive NMDA blocker. It also inhibits calcium influx into the cells, inhibition of central sensitization and thus prolonging the action of local anaesthetics. Other possible mechanism is that analgesic effects of magnesium sulphate occurs at the supra-spinal level and might be related to its systemic absorption as well as the diffusion of magnesium sulphate from the dura.^[21-23]

However, there are certain limitations of our study. Different doses of magnesium with larger number of patients in different surgical settings were not studied. Also, magnesium sulphate was not compared to any other adjuvants.

Conclusion

The results of the present study indicate that epidural

magnesium sulphate in a dose of 50 mg significantly prolongs the duration of postoperative analgesia and also significantly reduced the subsequent analgesic requirement in 24 hour without any additional side effects.

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How to cite this article: Das N, Kaur M, Chaudhary S, Kumar M, Salhotra R, Chauhan J. Magnesium Sulphate as an Adjuvant to Epidural Ropivacaine for Postoperative Analgesia in Patients Undergoing Vaginal Hysterectomy. *Acad. Anesthesiol. Int.* 2019;4(2):276-80.

DOI: [dx.doi.org/10.21276/aan.2019.4.2.62](https://doi.org/10.21276/aan.2019.4.2.62)

Source of Support: Nil, **Conflict of Interest:** None declared.