Original Article

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# Comparison between Epidural Bupivacaine with and without Magnesium Sulphate in Patients undergoing Elective Total Abdominal Hysterectomy: A Double-blinded Randomised Clinical Trial

Anaesthesia Section

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## ABSTRACT

**Introduction:** The effectiveness of a local anaesthetics increased by the addition of an adjuvant. Magnesium sulphate along with bupivacaine is effective in reducing the pain and extending the analgesia period.

**Aim:** To compare the duration of analgesia among subjects receiving plain bupivacaine and bupivacaine with magnesium sulphate among patients undergoing total abdominal hysterectomy.

**Materials and Methods:** This double-blinded randomised clinical trial was conducted in Department of Anaesthesiology at Shri Sathya Sai Medical College and Research Institute, Ammapettai, Tamil Nadu, India, (tertiary care center) between November 2019 to October 2021. The study was done among 50 subjects undergoing elective total abdominal hysterectomy. The subjects were divided into two groups: one group received only bupivacaine while the other group received bupivacaine with 500 mg magnesium sulphate. Onset and duration of blocks were observed. Haemodynamic parameters were monitored intraoperatively and postoperatively. Data was analysed using Chi-square test and Fischer's-exact test.

**Results:** Demographic variables like age (p-value=0.17), height (p-value=0.62), weight (p-value=0.14) and Body Mass Index (BMI) (p-value=0.24) were comparable between the two groups. The mean duration of analgesia was significantly more among the bupivacaine with magnesium sulphate group (416.72±93.6) in comparison to the bupivacaine alone group (204.96±71.25). The bupivacaine with magnesium sulphate group required two doses of rescue analgesia in 24 hours, while the other group required four doses of analgesia. Significantly more side-effects were noted among the bupivacaine alone group (12 vs 6) (p-value=0.04).

**Conclusion:** The study showed that bupivacaine with magnesium sulphate group showed less intraoperative side effects, reduced postoperative Visual Analogue Scale (VAS) score, increased duration of analgesia, decreased requirement of analgesia required in 24 hours and reduced postoperative side-effects.

**Keywords:** Epidural anaesthesia, Perioperative management, Postoperative analgesic requirement, Rescue analgesia

## INTRODUCTION

Perioperative management, which includes effective intraoperative monitoring and relief of postoperative pain, is an essential objective for anaesthesiologists. Effective perioperative pain management can have analgesic benefits, patients are less probable to suffer cardiac, respiratory, or gastrointestinal side effects during or immediately after the intervention. Ineffective perioperative pain is related with deep vein thrombosis and formation of an embolus in the lung, it may decrease life's quality and delayed recovery [1,2]. Effective postoperative pain management delivers enhanced patient comfort, earlier mobilisation, and speedy recovery [3,4].

Total Abdominal Hysterectomy (TAH) is a surgical technique which is related to significant postoperative pain and morbidity and is regarded to be a major surgery [5]. A variety of anaesthetic methods containing general anaesthesia or different modalities of regional anaesthesiahas been utilised to perform TAH [6]. Epidural analgesia has been extensively utilised in patients requiring TAH. Epidural anaesthesia technique is an efficient approach, with the advantage of safety, effectiveness, and sustained postoperative pain alleviation [1,6].

The selection of local anaesthetic is based on potency of the agent, onset and period of anaesthesia, and adverse reactions to the drug [7]. Bupivacaine amide group of local anaesthetic, enters nerve fibres as a neutral free base, stops transmission by their interaction on the inner surface of the sodium ion (Na+) channel. The blockade causes reduction in conduction of vascular smooth muscle, leading to relaxation [8-10].

The addition of adjuvant extends and reinforces the sensory blockade formed by local anaesthetics with decrease in dose of the latter, thus dipping the side-effects. Adjuvants are drugs that augment the efficacy of other drugs when given simultaneously [11]. Magnesium is a physiological blocker of calcium channel and non competitive antagonist of N-methyl-D Aspartate (NMDA) receptor. It has been utilised with a local anaesthetic solution in diverse regional/local anaesthesia method [12,13].

The effectiveness of a local anaesthetic would be increased by addition of an adjuvant with the use of magnesium sulphate along with bupivacaine is effective in reducing the pain and extending the analgesia period. There are few studies on magnesium as adjuvant, but none compared the intraoperative and postoperative effectiveness and also the rescue analgesia in addition to the adjuvant. This study aimed to assess the duration of analgesia of epidural block with plain bupivacaine and bupivacaine with magnesium sulphate in patients undergoing total abdominal hysterectomy. The primary measure of the study aimed to see the onset and intraoperative requirement of analgesia. The secondary outcome was the side-effects for the same.

## MATERIALS AND METHODS

This double-blinded randomised clinical trial was conducted in Department of Anaesthesiology at Shri Sathya Sai Medical College

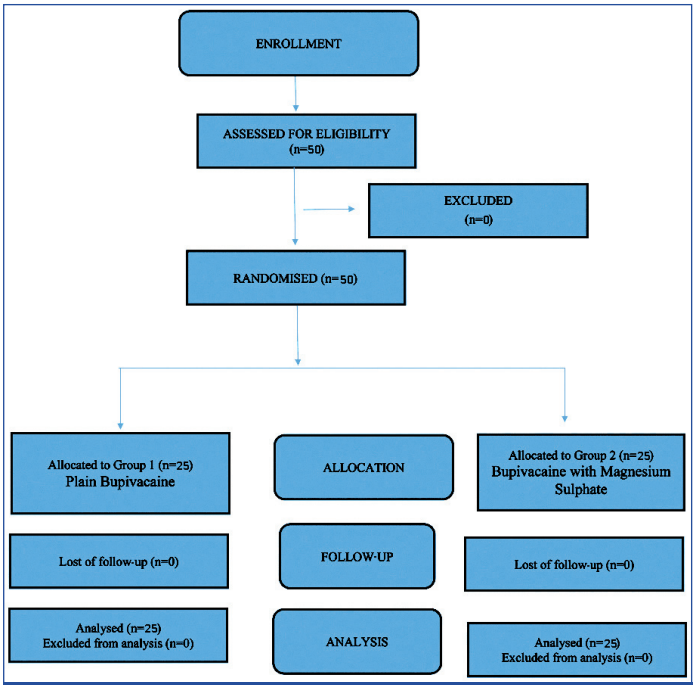
and Research Institute, Ammapettai, Tamil Nadu, India, (tertiary care center) between November 2019 to October 2021. The ethical clearance was obtained from Institutional Ethical Committee (IEC 2019/560) and Clinical Trials Registry India (CTRI) registration (CTRI No.:CTRI/2020/02/023169). An informed consent was obtained from each patient.

**Sample size calculation:** Sample size was calculated based on previous study [14] and 95% confidence interval with 80% power, the sample size required for each group was 25 with the total sample size of 50.

**Inclusion criteria:** Female patients undergoing elective total abdominal hysterectomy, in the age group 40 to 60 years, and American Society of Anesthesiologists (ASA) grade I and II were included in the study.

**Exclusion criteria:** Patient refusing for epidural, allergy to local anesthetics/magnesium sulphate, patients having coagulation disorders, local site infection, Body Mass Index (BMI) >30 kg/$m^2$ were excluded.

The patients and respective anaesthesiologist were blinded with the study drug [Table/Fig-1].




**[Table/Fig-1]:** Consolidated Standards of Reporting Trials (CONSORT) flowchart.

The subjects were randomly divided into two groups, by computer generated list of random number.

- **Control group:** Patient received 0.5% 20 mL of bupivacaine through epidural catheter.
- **Study group:** Patient received 0.5% 20 mL of bupivacaine with 500 mg magnesium sulphate through epidural catheter.

### Procedure

The patients fulfilling the inclusion criteria were kept nil per oral 8 hours before surgery. After shifting the patients to the operation theatre, standard ASA monitors were connected and their baseline values was recorded. Intravenous (i.v.) access was secured using an 18 gauge cannula. Under all aseptic precautions, epidural block was performed by using 18G Tuohy needle, advanced at L1-L2 or L2-L3 intervertebral space. Space was identified using loss of resistance technique, then a 22 gauge multiorifice catheter was advanced, 5 cm of the catheter was kept in-situ through which a test dose of 3 mL solution of 1.5% lidocaine with 5 µg/mL adrenaline was given to rule out intravascular placement of the catheter. The epidural catheter was safely secured with plaster.

The duration of analgesia was assessed using Visual Analogue Scale (VAS) - 0 to 10 score from no pain to worst pain - at 15, 30, 60 minutes and thereafter at 4 hour interval for 24 hour postoperative period. Patients above score 4 received rescue analgesia in the form of inj. tramadol 50 mg i.v. in the postoperative period. Patient haemodynamics were monitored for any postoperative complications like bradycardia and hypotension. Total amount of rescue analgesic given was monitored along with haemodynamic vitals of the patient.

## STATISTICAL ANALYSIS

Data was entered in Microsoft Excel sheet and analysed using Statistical Package for Social Sciences (SPSS) software version 16.0. For test of significance, Chi-square test was used. Fisher's exact test was used when more than 20% of the cell values have expected cell value less than 5. A p-value <0.05 was considered statistically significant.

## RESULTS

Demographic variables were comparable between two groups [Table/Fig-2].

| Variables | Bupivacaine alone group | Bupivacaine with magnesium sulphate | p-value |
|---|---|---|---|
| Age (Mean±SD) (years) | 53.52±4.72 | 51.60±5.07 | 0.17 |
| **American Society of Anesthesiologists (ASA)** | | | |
| Grade I | 12 (48%) | 10 (40%) | 0.33 |
| Grade II | 13 (52%) | 15 (60%) | 0.33 |
| Mean height (cm) | 157.76±5.28 | 158.52±5.43 | 0.62 |
| Mean weight (kg) | 60.00±5.84 | 62.76±7.11 | 0.14 |
| Mean BMI (kg/$m^2$) | 23.80±1.98 | 24.56±2.50 | 0.24 |

**[Table/Fig-2]:** Demographic variables.

The association of postoperative pulse rate and oxygen saturation ($SpO_2$) among the groups showed nil significant association between the groups. The association of postoperative Systolic Blood Pressure (SBP) among the groups showed nil significant association between the groups in terms of SBP at 15 minutes, 30 minutes, 60 minutes, 8$^{th}$ hour, 16$^{th}$ hour, 20$^{th}$ hour and 24$^{th}$ hour. At 4$^{th}$ hour there was significant difference between the groups where bupivacaine with magnesium sulphate showed increased systolic blood pressure in comparison to Bupivacaine alone group (112.96±9.24 mmHg vs 107.88±6.82 mmHg). At 12$^{th}$ hour there was significant difference between the groups where bupivacaine with magnesium sulphate group showed decreased systolic blood pressure in comparison to bupivacaine alone group (107.20±7.92 mmHg vs 113.68±9.20 mmHg).

The association of postoperative Diastolic Blood Pressure (SBP) among the groups showed nil significant association between the groups in terms of DBP at 15 minutes, 30 minutes, 60 minutes, 4$^{th}$ hour, 16$^{th}$ hour, 20$^{th}$ hour and 24$^{th}$ hour. At 8$^{th}$ hour there was significant difference between the groups where bupivacaine with magnesium sulphate showed decreased diastolic blood pressure in comparison to bupivacaine alone group (71.76±6.91 vs 68.04±6.15 mmHg). At 12$^{th}$ hour there was significant difference between the groups where bupivacaine with magnesium sulphate group showed decreased diastolic blood pressure in comparison to bupivacaine alone group (71.60±8.78 vs 66.56±5.58 mmHg).

The association of postoperative MAP among the groups showed nil significant association between the groups in terms of MAP at 15 minutes, 30 minutes, 60 minutes, 4$^{th}$ hour, 8$^{th}$ hour, 16$^{th}$ hour, 20$^{th}$ hour and 24$^{th}$ hour. At 12$^{th}$ hour there was significant difference between the groups where bupivacaine with magnesium sulphate group showed decreased mean arterial blood pressure in comparison to bupivacaine alone group (85.64±8.53 vs 80.12±5.66 mmHg).

At 15 minutes, 30 minutes, 60 minutes, 4$^{th}$ hour, 12$^{th}$ hour, 16$^{th}$ hour, and 24$^{th}$ hour VAS score was significantly more among bupivacaine alone group in comparison to bupivacaine with magnesium sulphate group (1.64±0.64 vs 1.12±0.33), (1.60±0.50 vs 1.00±0), (2.56±0.92

vs 1.08±0.28), (3.44±0.92 vs 1.52±0.51), (3.04±1.34 vs 2.12±0.73), (2.36±1.25 vs 3.00±0), (2.60±1.41 vs 1.36±0.49), respectively. At 8th hour the VAS score was significantly more among bupivacaine with magnesium sulphate group in comparison to bupivacaine alone group (4.08±0.28 vs 3.16±0.85) [Table/Fig-3].

| VAS score at | Bupivacaine alone (Mean±SD) | Bupivacaine with magnesium sulphate (Mean±SD) | p-value |
|---|---|---|---|
| 15 minutes | 1.64±0.64 | 1.12±0.33 | 0.001 |
| 30 minutes | 1.60±0.50 | 1.00±0 | <0.001 |
| 60 minutes | 2.56±0.92 | 1.08±0.28 | <0.001 |
| 4th hour | 3.44±0.92 | 1.52±0.51 | <0.001 |
| 8th hour | 3.16±0.85 | 4.08±0.28 | <0.001 |
| 12th hour | 3.04±1.34 | 2.12±0.73 | 0.004 |
| 16th hour | 2.36±1.25 | 3.00±0 | 0.02 |
| 20th hour | 3.68±1.28 | 4.00±0 | 0.22 |
| 24th hour | 2.60±1.41 | 1.36±0.49 | <0.001 |

**[Table/Fig-3]:** VAS score association among the population between the groups based on postoperative period.
p-values <0.05 were considered statistically significant

Number of analgesia required in 24 hours among the groups showed that 23 (92%) of bupivacaine with magnesium sulphate group required 2 doses and 15 (60%) of bupivacaine alone group required 4 doses [Table/Fig-4].

| Number of doses of analgesia given | Bupivacaine alone n (%) | Bupivacaine with magnesium sulphate n (%) | p-value |
|---|---|---|---|
| 2 doses | 0 | 23 (92%) | - |
| 3 doses | 0 | 2 (8%) | - |
| 4 doses | 15 (60%) | 0 | <0.001 |
| 5 doses | 10 (40%) | 0 | - |
| Duration of analgesia for 24 hours (minutes), (Mean±SD) | 204.96±71.25 | 416.72±93.86 | <0.001 |

**[Table/Fig-4]:** Number of analgesia required in 24 hours among the groups.
p-values <0.05 were considered statistically significant

The mean duration of analgesia was significantly more among bupivacaine with magnesium sulphate in comparison to bupivacaine alone group (416.72±93.86 vs 204.96±71.25). The result shows the association of intraoperative side-effects among the groups. Intraoperatively, more side-effects were noted among bupivacaine alone group in comparison to bupivacaine with magnesium sulphate {12 (48%) vs 6 (24%)} [Table/Fig-5].

| Side-effects noted (hypotension and shivering) | Bupivacaine alone n (%) | Bupivacaine with magnesium sulphate n (%) | p-value |
|---|---|---|---|
| No | 13 (52%) | 19 (76%) | 0.04 |
| Yes | 12 (48%) | 6 (24%) | |

**[Table/Fig-5]:** Side-effects.
p-values <0.05 were considered statistically significant

## DISCUSSION

The main objective was to compare the duration of analgesia among subjects receiving plain bupivacaine and bupivacaine with magnesium sulphate in patients undergoing total abdominal hysterectomy. The association of intraoperative pulse rate, SBP, DBP, mean arterial pressure, $SpO_2$ and intraoperative analgesia requirement among the groups showed nil significant association between the groups in terms of these variables.

The present study has shown that the duration of analgesia among subjects receiving Plain Bupivacaine (PB) was less, when compared with subjects receiving Bupivacaine with Magnesium Sulphate (BM). Tramer MR et al., showed that subjects who were administered magnesium sulphate, utilised lesser morphine during the first 48 hour (65 mg vs 90 mg), which was more during the initial six hours, and they suffered less discomfort in the course of the first and second postoperative days [15]. In the present study too, the mean duration of analgesia was more in the BM group, and the patients had a reduced postoperative hospital stay.

Similar findings were reported by Arcioni R et al., They concluded that adding intra-thecal magnesium sulphate to bupivacaine showed extended the period of anaesthesia and devoid of side-effects [16]. Ghatak T et al., studied The impact of magnesium or clonidine, as accessory, to epidural bupivacaine in abdominal and limb surgeries. Beginning of anaesthesia was fast in the magnesium group. In the clonidine category there was a longer period of anaesthesia and sedation with reduced pain score, but there was an elevated incidence of shivering [17]. In contrast, the present study found a prolonged pain score in the BM group.

Malleeswaran S et al., showed that the duration of spinal anaesthesia was considerably longer in the magnesium category in comparison to saline group. Both groups had additional bupivacaine and fentanyl. Diclofenac needs for one day subsequent to surgery was considerably lower in the magnesium category (147.5 versus 182.5 mg) [18]. The present study did not record the duration of spinal anaesthesia, but the intraoperative and postoperative rescue analgesia were recorded. In the BM group, lesser subjects had single dose requirement of analgesia during intraoperative period.

Abd-Elsalam KA et al., also showed that the mean postoperative AS score was significantly decreased in bupivacaine with magnesium group, compared to the bupivacaine alone group. The mean value of time of the first call for rescue analgesia was considerably lengthened in bupivacaine with magnesium category (15.67 hours) compared to the other (7.33 hours) [19]. In the present study, it was noted that the number of analgesic required in 24 hours among the group was two doses against four doses in the PB group.

Thus, it was found that the BM group had less intraoperative and postoperative side-effects, reduced postoperative VAS score, increased duration of analgesia, and decreased requirement of analgesia required in 24 hours.

### Limitation(s)

The non inclusion of patient satisfaction score and surgeon satisfaction measures like volume of bleeding. Varied dosages of magnesium sulphate were not studied. The blood level of magnesium and its influence on the effects were also not studied.

## CONCLUSION(S)

Patients that were administered bupivacaine along with magnesium sulphate had less intraoperative and postoperative side-effects, reduced postoperative VAS score, decreased requirement of analgesia required in 24 hours, and also showed an increased duration of analgesia. Thus, magnesium sulphate is indeed efficacious for epidural use. In future, multiple age groups and surgical techniques need to be compared, to assess disparity in efficiency. Different doses of magnesium sulphate, blood level of magnesium, and its influence on the effects also need to be studied.

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## REFERENCES

[1] Nimmo SM, harrington LS. What is the role of epidural analgesia in bdominal surgery? Continuing Education in Anaesthesia Critical Care & Pain. 20141;14(5):224-29. Available from:https://academic.oup.com/bjaed/article/14/5/224/286776.
[2] Pietri L de, Montalti R, Begliomini B. Anaesthetic perioperative management of patients with pancreatic cancer. World Journal of Gastroenterology: WJG 2014;20(9):2304. Available from:/pmc/articles/PMC3942834/.
[3] Gan TJ. Poorly controlled postoperative pain: prevalence, consequences, and prevention. Journal of Pain Research. 2017;10:2287-98.

[4] Joshi GP, Ogunnaike BO. Consequences of inadequate postoperative pain relief and chronic persisten tpostoperative pain. Anesthesiology Clinics of North America. 2005;23(1):21-36.
[5] Azari L, Santoso JT, Osborne SE. Optimal pain management in total abdominal hysterectomy. Obstetrical & Gynecological Survey. 2013;68(3):215-27.
[6] Morosan M, Popham P. Anaesthesia for gynaecological oncological surgery. Continuing Education in Anaesthesia Critical Care & Pain. 20141;14(2):63-68. Available from: https://doi.org/10.1093/bjaceaccp/mkt035.
[7] Spinal Anesthesia -NYSORA. Available from: https://www.nysora.com/techniques/neuraxial-and-perineuraxial-techniques/spinal-anesthesia/.
[8] Iskander A, Gan TJ. Novel analgesics in ambulatory surgical patients. Current opinion in anaesthesiology. 2018;31(6):685-92.
[9] Shah J, Votta-Velis EG, Borgeat A. New local anesthetics. Bestpractice & research Clinical Anaesthesiology. 2018;32(2):179-85.
[10] Shafiei FT, McAllister RK, Lopez J. Bupivacaine. The Essence of Analgesia and Analgesics. 2021 1;274-76. Available from: https://www.ncbi.nlm.nih.gov/books/NBK532883/.
[11] Adjuvant agents in neuraxial blockade anaesthesia tutorial of the week 230: WFSA-Resources. Available from: https://resources.wfsahq.org/atotw/adjuvant-agents-in-neuraxial-blockade/.
[12] Do SH. Magnesium: A versatile drug for anesthesiologists. Korean J Anesthesiol. 2013;65(1):04-08.
[13] Gunduz A, Bilir A, Gulec S.Magnesium added to prilocaine prolongs the duration of axillary plexus block. Reg Anesth Pain Med. 2006;31(3):233-36.
[14] Elsharkawy RA, Farahat TE, Abdelhafez MS. Analgesic effect of adding magnesium sulfate to epidural levobupivacaine in patiebts with pre-eclampsia undergoing elective caesarean section. Journal of Anaesthesiology, Clinical Pharmacology. 2018;34(3):328-34.
[15] Tramer MR, schneider J, Marti RA , Rifat K. Role of magnesium sulfate in post operative. Anaesthesiology. 1996;84(2):340-47.
[16] Arcioni R, Palmisani S, Tigano S, Santorsola C, Sauli V, Romanò S, et al. Combined intrathecal and epidural magnesium sulfate supplementation of spinal anesthesia to reduce post-operative analgesic requirements: A prospective, randomised, double-blind, controlled trial in patients undergoing major orthopedic surgery. Acta anaesthesiological Scandinavica. 2007;51(4):482-99.
[17] Ghatak T, Chandra G, Malik A, Singh D, Bhatia VK. Evaluation of theeffect of magnesium sulphate vs. clonidine as adjunct to epidural bupivacaine. Indian Journal of Anaesthesia. 2010;54(4):308-13.
[18] Malleeswaran S, Panda N, Mathew P, Bagga R. A randomised study of magnesium sulphate as an adjuvant to intrathecal bupivacaine in patients with mild preeclampsia undergoing caesarean section. International Journal of Obstetric Anesthesia. 2010;19(2):161-66.
[19] Abd-Elsalam KA, Fares KM, Mohamed MA, Mohamed MF, El-Rahman AMA, Tohamy MM, et al. Efficacy of magnesium sulfate added to local anesthetic in a transversus abdominis plane block for analgesia following total abdominal hysterectomy: A randomised trial. Pain Physician. 2017;20(7):641-47.

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