

# Comparison of bupivacaine and bupivacaine plus magnesium sulphate infiltration for postoperative analgesia in patients undergoing lumbar laminectomy: A prospective randomised double-blinded controlled study

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## Abstract

**Background:** Laminectomy is associated with considerable postoperative pain. Providing analgesia locally in the area of surgical trauma, with minimal systemic side effects, is an attractive option and has become an integral part of multimodal analgesia. The objective of this study was to assess and compare the effectiveness and safety of local infiltration of bupivacaine and bupivacaine plus magnesium sulphate for postoperative analgesia in patients undergoing lumbar laminectomy. **Materials and Methods:** Sixty adult patients of the American Society of Anaesthesiologists (ASA) class 1 and 2 were randomly allocated into two groups, comprising 30 patients in each group. After the completion of lumbar laminectomy, the study drug was locally infiltrated into the paravertebral muscles on either side. Group bupivacaine with magnesium (BM) was given 20 ml of 0.25% bupivacaine with 500 mg of magnesium sulphate (constituted with normal saline); and Group bupivacaine (B) was given 20 ml of 0.25% bupivacaine constituted with normal saline. Postoperative visual analogue scale (VAS) pain scores at 1, 2, 4, 6, 8, 12 and 24 hours; rescue analgesia, the time to first analgesic consumption, degree of overall patient satisfaction and side effects were recorded. Comparison of continuous data between groups was done using independent T-test. Comparison of nominal data was done using Chi-square analysis and ordinal data using Mann-Whitney test. A *P* value less than 0.05 was considered significant. **Results:** Time to first analgesic consumption was significantly longer in BM group ( $7.78 \pm 1.350$  hours) compared to B group ( $4.62 \pm 0.997$  hours) ( $P < 0.0001$ ). The consumption of Tramadol was significantly higher in B group ( $202.5 \pm 76.9$  mg) compared to BM ( $117.5 \pm 63.4$  mg) ( $P < 0.0001$ ). The degree of overall satisfaction with postoperative pain management on a 4-point satisfaction scale was better in BM group ( $2.77 \pm 0.626$ ) compared to B group ( $2.0 \pm 0.587$ ) ( $P < 0.001$ ). **Conclusion:** Wound infiltration with bupivacaine and magnesium sulphate provided better pain control and analgesic effect was more significant, providing effective and safe postoperative analgesia in patients undergoing laminectomy surgeries.

**Keywords:** Anesthesia, bupivacaine, laminectomy, local, magnesium sulfate, postoperative pain

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## INTRODUCTION

Laminectomy is associated with considerable postoperative pain.<sup>[1-3]</sup> Good and optimal pain relief is important for postoperative laminectomy, and it may influence the overall outcome.<sup>[4,5]</sup> Different modalities and drugs for pain management following lumbar laminectomy have evolved over time. This

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includes intravenous, intramuscular, epidural, spinal, instillation and infiltration routes of analgesia.<sup>[6]</sup> Addition of adjuvants like clonidine, magnesium and dexmedetomidine has shown promising results.<sup>[7-9]</sup> Providing infiltration analgesia locally in the area of surgical trauma, with minimal systemic side effects, is an attractive option.<sup>[8,10]</sup>

There are very few recent studies reporting the usage of infiltration anaesthesia with local anaesthetics for relief of postoperative pain following lumbar laminectomy procedures.<sup>[11-13]</sup> Magnesium is widely used in perioperative settings and has shown to decrease the anaesthesia and analgesia requirements effectively.<sup>[9,14,15]</sup> And there are no studies revealing the use of magnesium as an adjuvant to infiltration anaesthesia following lumbar laminectomy.

The objective of this study was to assess and compare the effectiveness and safety of local infiltration of bupivacaine and bupivacaine plus magnesium sulphate for postoperative analgesia in patients undergoing lumbar laminectomy.

## MATERIAL AND METHODS

Following institutional ethics committee approval, informed and written consent was obtained from 60 patients of American Society of Anaesthesiologists (ASA) class 1 and 2, scheduled to undergo lumbar laminectomy of ages 18-65 years and body mass index <30. The exclusion criteria included patients with severe systemic disease, ASA class 3 and 4, allergy or intolerance to study drugs, psychiatric illness, seizure disorder, regular narcotic use and refusal by the patient. All patients were familiarised with a 10 cm visual analogue scale (VAS) preoperatively with 0: No pain, 1-3: Mild pain, 4-6: Moderate pain, 7-9: Severe pain and 10: The worst imaginable pain.

Preoperative VAS scores were obtained from all patients by asking the average intensity of pain at the preanaesthetic checkup. Premedication consisted of tab Ranitidine 150 mg and tab Alprazolam 0.25 mg 2 hours prior to surgery. Patients were assigned into two groups by computer randomisation. As per the randomisation number allocated, the drug was prepared by an anaesthesia technician. The contents of the study drug were blinded to the surgeon and the anaesthesiologist. The study drugs for both the groups were prepared accordingly. Group BM: 50 mg of bupivacaine (10 ml), 500 mg of magnesium sulphate (1 ml) made up to 20 ml solution with normal saline (NS), 10 ml given on either side.

### Group B

50 mg of bupivacaine (10 ml) made up to 20 ml solution with NS, 10 ml given on either side.

In both groups, general anaesthesia technique was used. All the patients were induced with standard dose of thiopentone sodium 4-7 mg/kg, fentanyl 2 µg/kg and injection glycopyrrolate 0.2 mg intravenously. Muscle relaxation for tracheal intubation was facilitated with loading dose of vecuronium 0.08 mg/kg. Intraoperative anaesthesia and muscle relaxation was maintained with isoflurane 0.6-1% and atracurium infusion dose of 0.3 to 0.6 mg/kg/hour. Intraoperative analgesia was maintained with continuous infusion of fentanyl at a dosage of 1-5 µg/kg/hour. Standard monitoring techniques like electrocardiography (ECG), blood pressure, pulse oximetry, capnography and heart rate were used. Both atracurium and fentanyl infusions were stopped 15 minutes before expected time for completion of the procedure. After the completion of the surgical procedure, local infiltration with the study drug was given into the paravertebral muscles on either side by the operating surgeon. After application of the plasters, the patient was made supine and neuromuscular blockade was reversed with neostigmine and glycopyrrolate. All the patients were extubated on the table. Once completely awake, all the patients were assessed for pain. Patients who remained drowsy after 1 hour were excluded from the study.

After the operation, patients were transferred to postoperative ward where VAS pain scores was obtained from all patients at 1, 2, 4, 6, 8, 12 and 24 hours. Rescue analgesia was carried out with tramadol 100 mg (intramuscular, IM) to a maximum dose of 150 mg once the VAS recorded was > 5. The repeat second dose was given atleast after 30 minutes of the initial dose. The time to first analgesic consumption was recorded. Analgesic duration was defined as the time from completion of surgery till the time for first request for tramadol.

Patients were asked to indicate the degree of overall satisfaction with postoperative pain management on a 5-point satisfaction scale after 24 hours of surgery: 0 = unsatisfactory/poor, 1 = somewhat satisfactory/adequate, 2 = satisfactory/adequate, 3 = very good and 4 = excellent.

Blood pressure, heart rate, respiratory rate and oxygen saturation and the presence of side effects such as nausea, vomiting, sedation, hypotension, dizziness, headache, dry mouth, allergic reaction, respiratory depression and urinary retention were recorded postoperatively for each patient at the same time as pain assessment over 24 hours.

### Statistical analysis

Data were expressed as mean and 95% confidence interval of mean for continuous variables (height, weight, duration, age). Data was analysed using Statistical

Package for the Social Sciences (SPSS) version 15 (SPSS Inc, Chicago, IL). Normality and variance of the data was assessed by Anderson Darling test and Modified Leven's test, respectively. Comparison of continuous data between groups was done using independent T-test (ANOVA of means). Comparison of nominal data was done using Chi-square analysis and ordinal data using Mann-Whitney test. *P* value less than 0.05 was considered statistically significant between groups.

Sample size for the study was estimated by taking into consideration the results of two studies reported by Tauzin-Fin *et al.* (Acta Anaesthesiol Scand, 2009)<sup>[16]</sup> and Milligan *et al.* (J Bone Joint Surg (Br), 1993).<sup>[17]</sup> The study results by Tauzin *et al.* was as follows: Tramadol consumption in Group intravenous magnesium was  $221 \pm 64.1$  mg and was  $134 \pm 74.9$  mg in Group local magnesium. In another study by Milligan *et al.* morphine consumption was  $37 \pm 17.19$  mg in Group bupivacaine and was  $50.9 \pm 19.14$  mg in Group control. The effect size calculated from the results of these two studies was found to be 1. In the power analysis by G power, the sample size required was found to be 50 with  $\alpha = 0.05$ , power of  $(1-\beta) = 0.95$  and effect size = 1.0. As dropout cases would be expected due to extended duration of surgery, a sample size of 60 was selected for the study.

## RESULTS

All the groups were comparable with respect to demographic variables (age, gender, weight) [Table 1]. The data were found to be normally distributed and homoscedasticity of the data was maintained with

**Table 1: Demographic data**

Parameters	Gr B	Gr BM	<i>P</i> value
Age (yrs)	41.33±3.96 (1.2)	40.4±4.2 (1.8)	0.35
Weight (kgs)	61.4±8.15 (1.82)	62.15±8.44 (1.88)	0.73
Gender	20/10	19/11	0.5

B = Bupivacaine, BM = Bupivacaine with Magnesium, yrs = years, kgs = kilograms; Gr = Group

**Table 2: VAS score at 1, 2, 4, 6, 8, 12 and 24 hour after completion of surgery**

Groups	Preoperation pain (%)	Pain (hr) (%)						
		1	2	3	6	8	12	24
B mild	15 (50)	21 (70)	23 (76.7)	2 (6.7)	12 (40)	9 (30)	13 (43.3)	7 (23.3)
Moderate	15 (50)	9 (30)	7 (23.3)	28 (93.3)	16 (53.3)	21 (70)	17 (56.7)	22 (73.3)
Severe	0				2 (6.7)			1 (3.3)
BM mild	8 (26.7)	14 (46.7)	16 (53.3)	13 (43.3)	7 (23.3)	1 (3.3)	9 (30)	13 (43.3)
Moderate	21 (70)	16 (53.3)	14 (46.7)	17 (56.7)	23 (76.7)	29 (96.7)	21 (70)	7 (56.7)
Severe	1 (3.3)							
<i>P</i> value	0.13	0.058	0.052	0.001	0.1	0.006	0.21	0.18

VAS = Visual analogue scale, B = Bupivacaine, BM = Bupivacaine with magnesium, hr=hour

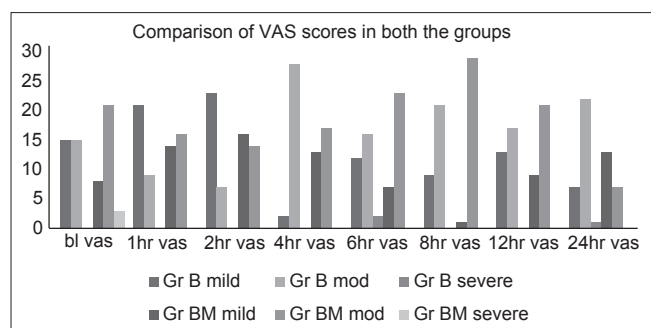
respect to the demographic data and baseline VAS score. The changes in the VAS score at 1, 2, 4, 6, 8, 12 and 24 hour after completion of surgery were depicted in Table 2. VAS scores were significantly less in B group when compared to BM group in the first 4 hours and was considered significant (*P* value < 0.05). At 2 hours, number of patients with mild VAS was less in group BM and number of patients with moderate VAS was less in group B compared with the other group. At 4 hours, patients with moderate VAS was significantly less in group BM; but again at 6, 8 and 12 hours postoperatively, patients with moderate VAS scores were on a rise in group BM. VAS scores were statistically insignificant at 1 hour and at 12 and 24 hour postoperatively [Figure 1].

The time to first analgesic consumption, tramadol consumption and the degree of overall satisfaction with postoperative pain management on a 5-point satisfaction scale was highly significant in group BM compared to group B (*P* < 0.001) [Figure 2].

There were no side effects like nausea, vomiting, allergic reaction, dry mouth, respiratory depression and urinary retention in both the groups.

## DISCUSSION

The results of our study showed that local infiltration of magnesium sulphate added to bupivacaine provided better pain control without any added side effects compared to bupivacaine alone. This was evident by reduction in the total analgesic consumption and decrease in the number of patients requiring supplementary analgesics. The origin of back pain sensation is mediated by nociceptors and mechanoreceptors from the vertebrae, intervertebral disc, dura and nerve root sleeves, facet joint capsules, muscles, ligaments and fascia. Innervation is by the posterior rami of the spinal nerve roots, which are linked to the sympathetic and parasympathetic nerves. Inflammation of these structures or mechanical compression of the nerves in this area results in pain.<sup>[18,19]</sup>



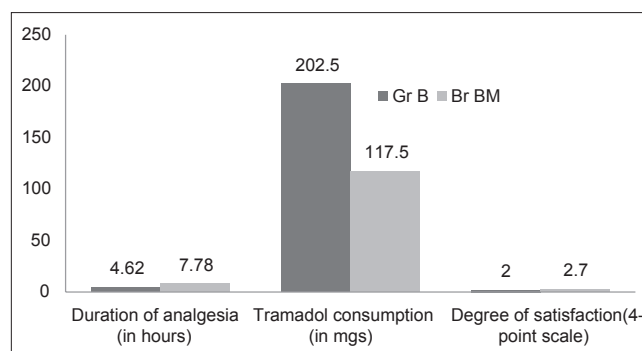
**Figure 1:** Mean VAS scores at 1, 2, 4, 6, 8, 12 and 24 hour for two groups. Abbreviations: VAS = Visual Analogue Scale; B = Bupivacaine; BM = Bupivacaine with magnesium; mod = moderate

All surgical procedures initially stir up an array of nociceptive signals followed by a secondary inflammatory response contributing considerably to postoperative pain. This is called peripheral sensitisation. These signals further cause sustained alterations in both the peripheral and the central nervous system called central sensitisation that eventually leads to exaggeration and protraction of postoperative pain.<sup>[19]</sup>

After laminectomy, poorly managed pain may inhibit the early ability to mobilise the patient. Good pain relief is important for patients undergoing laminectomy, and it may considerably influence the overall outcome.<sup>[20,21]</sup>

In an attempt to improve fast rehabilitation after laminectomy, research has been directed towards new techniques for postoperative analgesia. Different modalities of pain therapy like intramuscular, intravenous, infiltration, epidural, spinal and instillation are in use. Recent literature has focused on multimodal approach for postoperative pain relief following lumbar decompression procedures. This included both the use of opioids and non-opioid drugs parenterally. But parenteral use of such drugs has limitations like respiratory depression, gastrointestinal irritation, renal dysfunction, bleeding problems and bowel and bladder disturbances. Regional analgesia in the form of spinal and epidural instillation of medications has shown to have delayed neurological recovery.<sup>[22]</sup>

Infiltration analgesia nowadays has shown a significant steep rising curve for immediate postoperative pain management. Infiltration with local anaesthetics acts directly on the pain-producing mechanisms with lesser incidence of side effects. Therefore, infiltration mode of analgesia was considered for this study. Literature has shown effective use of bupivacaine, levo-bupivacaine and ropivacaine for infiltration analgesia.<sup>[12]</sup> Bupivacaine was regularly used for the same in our institute but not reported. Addition of magnesium to local anaesthetic has shown to have beneficial effect in prolonging the duration of analgesia.<sup>[23,24]</sup> Addition of adjuvants to local



**Figure 2:** Comparison of duration of analgesia, tramadol consumption and degree of satisfaction in both the groups

anaesthetics for postoperative analgesia in patients undergoing lumbar laminectomy was rarely reported.

N-methyl-D-aspartate (NMDA) receptors play an important role in central nociceptive transmission, modulation and sensitisation of acute pain states.<sup>[4,3,25]</sup> In addition to their central location, recent studies identified NMDA receptors peripherally in the skin and muscles, and found that they play a role in sensory transmission of noxious signals.<sup>[25]</sup> In its inactive state, the NMDA receptor is blocked by the presence of a centrally positioned magnesium ion. Afferent activity in nociceptor fibres dislodges the central magnesium ion from the NMDA receptor, therefore allowing calcium influx into the cell. Magnesium can be considered as a physiological blocker of NMDA receptors.

Use of magnesium in the perioperative setting was reported widely in the literature.<sup>[14]</sup> Both intrathecal and systemic administration of magnesium has shown to enhance postoperative analgesia through its voltage-dependent blockade of NMDA receptors.<sup>[9]</sup> This current study was done to determine whether magnesium might provide analgesia when administered at surgical site, especially with the evidence of NMDA receptor existence in the peripheral nerve fibres and immune cells in which their activation was found to play a potential role in nociception.<sup>[19]</sup>

In the literature, it was reported that total analgesic consumption was a better parameter than time to first analgesic request.<sup>[26]</sup> Magnesium has been demonstrated to reduce postoperative analgesic requirements significantly. At the same time, the infiltration of magnesium with local anaesthetics has shown effective pain relief following other procedures like radical prostatectomy and tonsillectomy.<sup>[16,25]</sup>

In this current study, patients receiving bupivacaine and magnesium had a significantly longer time to first analgesic request with reduced overall analgesic consumption and an overall higher degree of satisfaction. The proposed mechanism of magnesium infiltration may



be due to the reduction of NMDA-induced current thus promoting analgesia. This was strongly evident by a significant reduction in the total analgesic requirements in the first 24 hours after surgery.

In conclusion, magnesium sulphate seems justified to its use as a safe adjuvant to local anaesthetics like bupivacaine in amplifying their effect for infiltration analgesia in patients undergoing laminectomy surgeries.

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