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Original Research Article

Post-operative wound infiltration with dexmedetomidine and magnesium sulphate as adjuvant to levobupivacaine for lumbar laminectomy: a prospective, double blinded, randomized controlled study

Neelesh Bhatnagar, Vikram S. Rathore*, Malavsinh Jadeja, Alka Chhabra, Seema Partani, Tarun Singh

Department of Anaesthesiology and Critical Care, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India

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***Correspondence:**
Dr. Vikram S. Rathore,
E-mail: vikram2021.mmc@gmail.com

ABSTRACT

Background: Wound infiltration with local anaesthetic is safe and effective technique for providing postoperative analgesia following lumbar laminectomy. The objective of this study was to compare the efficacy of local wound infiltration on postoperative analgesia with levobupivacaine, levobupivacaine plus magnesium sulphate and levobupivacaine plus dexmedetomidine in patient undergoing lumbar laminectomy.
Methods: Ninety adult patients were randomly allocated into three groups. After the completion of lumbar laminectomy, the drug was locally infiltrated into the paravertebral muscles on either side. Group L received 10 ml of 0.5% levobupivacaine plus 10 ml normal saline, group LM received 10 ml of 0.5% levobupivacaine plus 500 mg magnesium sulphate (1 ml) plus 9 ml normal saline, group LD received 10 ml of 0.5% levobupivacaine plus 50 µg dexmedetomidine (0.5 ml) plus 9.5 ml normal saline. Postoperative visual analogue scale (VAS) pain score at 0, 1, 2, 4, 6, 8, 12 and 24 hours, time to first rescue analgesic drug and its total dose, quality of recovery score (QoR) and side effects were noted.
Results: Postoperative VAS was significantly higher in group L as compared to group LM and LD ($p<0.05$). The time to first rescue analgesic drug was significantly longer in group LD (11.07±7.20 hr) than group LM (6.20±2.64 hr) and group L (3.93±2.70 hr) ($p<0.001$). The QoR score was significantly better in group LD as compared to group LM and L postoperatively (<0.01).
Conclusions: Addition of magnesium sulphate or dexmedetomidine to levobupivacaine for local wound infiltration demonstrated enhanced postoperative analgesia.

Keywords: Lumbar laminectomy, Postoperative pain, Levobupivacaine, Dexmedetomidine, Magnesium sulphate

INTRODUCTION

Lumbar laminectomy, nowadays, a very common procedure. Pain in these patients is mainly due to iatrogenic retraction with mechanical damage to neuronal and soft tissue during surgery along with devascularization of musculoskeletal structures.[1] Effective analgesia is an important component of patient care. Post-operative pain control helps in early start of physiotherapy, better mobilization thus reducing the morbidity and mortality.[2]

The infiltration of local anaesthetic at surgical site is accepted to be an effective technique for analgesia, as

surgical pain originates locally.[3] Levobupivacaine is the pure S (-) enantiomer of racemic bupivacaine. Similar to other local anaesthetic agents, it causes reversible blockade of neuronal sodium channels.[4,5] Magnesium sulfate (N-methyl-D-aspartate (NMDA) receptor antagonist) and dexmedetomidine (selective α-2 adrenoreceptor agonist) effectively decrease the anesthetic and analgesic requirements in the postoperative period. Addition of these two agents in local infiltrate as an adjuvant has resulted in better outcomes.[6]

The objective of the study was to compare the efficacy of local wound infiltration on postoperative analgesia with levobupivacaine, levobupivacaine plus magnesium sulphate and levobupivacaine plus dexmedetomidine in patient undergoing lumbar laminectomy.

METHODS

Following approval from institutional research ethical board and written informed patient consent, this prospective double blinded randomized controlled study was conducted at Geetanjali medical college and hospital (GMCH) Udaipur, Rajasthan, India from February 2019 to June 2020.

Allocated groups

A total 90 patients undergoing lumbar laminectomy were enrolled and randomized into three groups of 30 each by computer generated random number.

Group L: 10 ml of 0.5% levobupivacaine and 10 ml 0.9% NS.

Group LM: 10 ml of 0.5% levobupivacaine with 500 mg magnesium sulfate (1 ml) and 9 ml 0.9% NS.

Group LD: 10 ml of 0.5% levobupivacaine with 50 µg dexmedetomidine (0.5 ml) and 9.5 ml 0.9% NS.

To keep it double blinded, the study drugs were prepared by an anaesthesia resident not taking part in study. Both the surgeon as well as the anaesthetist participating in the procedure were blinded to the study drug.

Inclusion criteria

Patients of ASA physical status I and II, aged 18 to 65 years with of BMI <30 scheduled for single/multiple level lumbar laminectomy were included.

Exclusion criteria

It Included patient with instrumentation due to spondylolisthesis or spinal stenosis, and are planned to have multiple distance or double site laminectomy, patient who underwent prior lumbar disc surgery, have ASA III-IV status, prior neurological deficits, preoperative opioid use or any history of substance abuse or on steroids, infection, have known history of local anesthetics allergy.

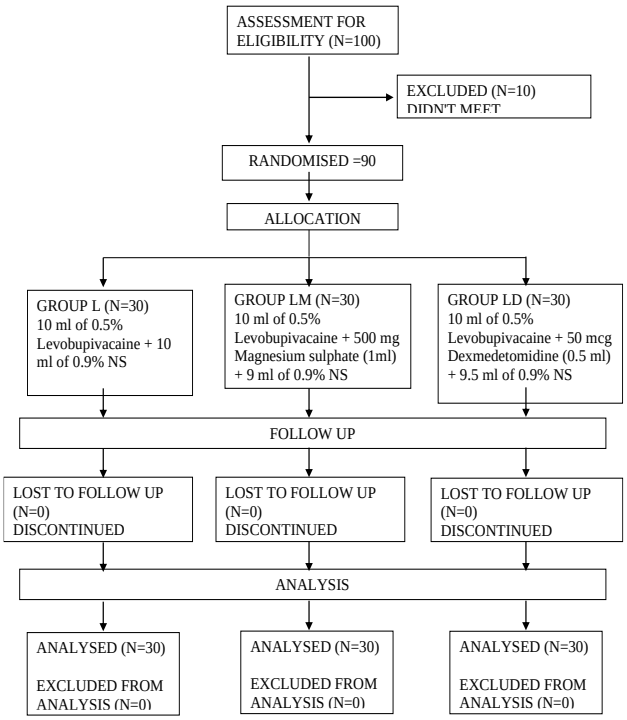

Figure 1: Consort flow diagram.

The anaesthesiologist explained the visual analogue pain scale (VAS) score to the patient preoperatively and obtained preoperative VAS by asking the average intensity of pain at the pre-anaesthetic check-up, with score 0: No pain, 1-3: Mild pain, 4-6: Moderate pain, 7-9 Severe pain and 10: The worst imaginable pain.[7]

In the operating room, standard ASA monitors were attached, and baseline vitals were recorded. All the patients were premedicated with injection fentanyl 2 µg/kg intravenously (IV) followed by induction with IV propofol 2 mg/kg. Muscle relaxation was achieved with injection rocuronium 1.0 mg/kg IV for tracheal intubation. Patients were adequately positioned and ventilated using volume-controlled mode with a tidal volume of 6-8 ml/kg. Patients were maintained with oxygen, nitrous oxide, and sevoflurane at 1-1.2 MAC with a flow of 2 l/min with target $EtCO_2$ of 35±2 mmHg and divided doses of rocuronium 0.2 mg/kg was used for muscle relaxation. Incremental doses of fentanyl as 0.5 µg/kg was given if the heart rate or blood pressure increased by more than 20% of the baseline value. Fall in blood pressure was managed with 250 ml of fluid bolus and incremental dose of inj. Ephedrine 6 mg. Intraoperative monitoring included electrocardiogram, non-invasive blood pressure, oxygen saturation, capnography.

Before skin closure local infiltration with the study drug according to the designated drug was done by the surgeon into the paravertebral muscles 10 ml volume on either side. Simultaneously, paracetamol 1 gm (100 ml) IV. was given over 10-15 min. After completion, patient was made supine, and neuromuscular blockade was reversed adequately with neostigmine and glycopyrrolate. All the patients were extubated when awake and following commands. Patients who remained sedated up to 1 hour post extubation was excluded from our study group. After operation, patient was transferred to postoperative ward.

The patients demographic characteristic like age, sex, weigh and ASA classification were noted. Hemodynamic parameters like blood pressure and heart rate were recorded at induction of anesthesia, before and immediate after local infiltration of drug. Total duration of surgery, duration of anaesthesia, the size of incision and fentanyl used intraoperatively was also noted. Postoperatively VAS pain score was obtained from all patient at 0, 1, 2, 4, 6, 8, 12 and 24 hours, both at rest and on active coughing. Rescue analgesia included injection tramadol 100 mg in 100 ml NS over 15 minutes IV till the VAS recorded was ≥4 or patient demands for analgesia with lockout period of 6 hrs and maximum dose of 400 mg/day.

The time to first rescue analgesic and total number of doses required was recorded. Analgesic duration was defined as the time from completion of surgery till the time for first request for rescue analgesic. Hemodynamic parameters like blood pressure, heart rate, and the presence of side effect such as nausea, vomiting, sedation, hypotension, 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.

Patients was assessed for sedation after extubation using Ramsay sedation score (Grade 1-Patient appears anxious, agitated, or restless, grade 2-Patient is cooperative, tranquil, and oriented, grade 3-Patient responds to verbal command, grade 4-Patient is asleep and shows response only to light, glabellar tap, or loud auditory stimuli, grade 5-Patient is asleep and sluggish response to above, and grade 6-Patient is asleep and shows no response to above.[3]

Patients were also assessed for the degree of overall satisfaction using quality of recovery score (QoR score) which is a 15-point questionnaire. QoR was assessed preoperatively and at 24 hours after surgery.

Statistical analysis

Statistical analysis was done using SPSS software (version 17, SPSS, Chicago, IL). Data was presented as mean, standard deviation, median (range), or percentage, as appropriate. Analysis of variance (ANOVA) was used to find the significance between three groups of patients for continuous variables and paired t-test was used for intergroup comparison. Chi-square test was used to find the significance of study parameters on categorical scale. P values less than 0.05 were considered significant.

RESULTS

Demographic data regarding mean value of age, weight, sex, ASA grade, and preoperative VAS in different groups and surgical data including duration of surgery, incision size and duration of anaesthesia were comparable among different groups (Table 1). There was no significant difference in baseline haemodynamic variables and haemodynamic variables immediately before and after local infiltration of study drug and in the postoperative period. We also found no significant difference in intraoperative requirement of fentanyl in different groups.

In our study, group L patients experienced more post-operative pain with significantly higher VAS score as compared to group LM and LD at 2-hour, 12-hour, 24 hours ($p<0.05$) while there was no significant difference among group LM and group LD ($p>0.05$) (Table 2). The time to first request of rescue analgesic drug postoperatively was found to be significantly longer in group LD (11.07±7.20 hr) than group LM (6.20±2.64 hr) and group L (3.93±2.70 hr) and longer in group LM as compared to group L ($p<0.001$) (Figure 2). The total rescue analgesic consumption in 24 hours postoperatively was significantly lower in group LD (150±90.02 mg) as compared to group LM (220±66.44 mg, $p<0.01$) which was lower than L group (270±79.44 mg, $p<0.01$). Frequency of rescue analgesics varies in different groups (Table 3).

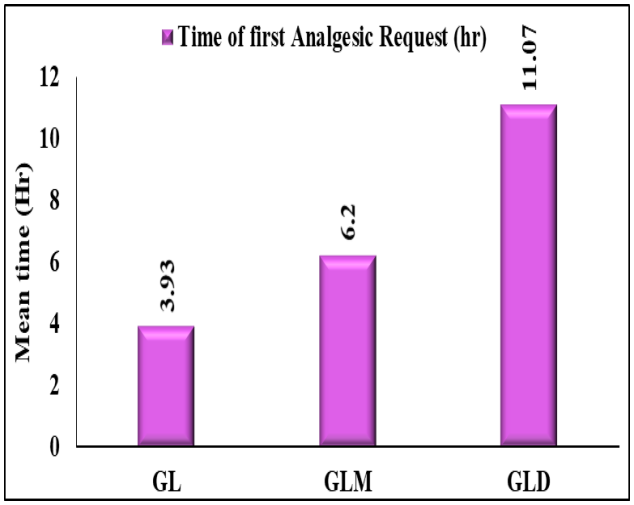

Figure 2: Comparison of time to first analgesic request (hours) in different groups.

Figure 1 shows the time to the first analgesic (hour) which was prolonged in LD group (11.07±7.20) compared to LM group (6.20±2.64) and L group (3.93±2.70) and was highly statistically significant ($p<0.001$).

There was no significant difference in preoperative QoR in all the three group (p>0.05). The QoR score was significantly better in group LD as compared to group LM and L postoperatively (p<0.01) (Table 4). Nausea/vomiting and urinary retention were the only postoperative side effects (Table 5). There was no difference in sedation score among three groups in the postoperative period.

Table 1: Comparison of demographic data

Variable		G_L (n=30)	G_{LM} (n=30)	G_{LD} (n=30)	ANOVA, p value
Age (years)		43.93±10.71	40.17±9.58	40.20±11.32	>0.05
Weight (kg)		57.80±9.90	62.80±10.16	57.17±10.40	>0.05
Sex	M	18	13	17	>0.05
	F	12	17	13	
Duration of anaesthesia (min)		148.50±33.17	141.00±26.31	149.50±41.30	>0.05
Duration of surgery (min)		103.17±6.90	102.50±6.83	102.00±6.53	>0.05
Size of incision (cm)		6.90±1.71	6.83±1.26	6.77±1.25	>0.05
ASA	I	23	22	22	>0.05
	II	7	8	10	
Preoperative VAS		4.80±1.65	4.97±1.47	4.53±2.01	>0.05

Data represented as Mean ± Standard Deviation.

Table 2: Comparison of VAS score in first 24 hr after surgery.

Time (hrs)	G_L (n=30)		G_{LM} (n=30)		G_{LD} (n=30)		ANOVA P value	
	Rest	**Coughing**	**Rest**	**Coughing**	**Rest**	**Coughing**	**Rest**	**Coughing**
0	2.50±1.17	2.73±1.05	2.07±1.01	2.27±0.83	1.70±1.18	1.97±1.13	>0.05	>0.05
2	3.57±1.45	3.67±1.42	2.47±1.22	2.63±1.16	2.40±1.04	2.60±1.04	<0.001**	<0.001**
4	3.63±1.47	3.70±1.47	3.17±1.39	3.30±1.21	2.67±0.84	3.03±0.81	>0.05	>0.05
6	3.77±1.48	3.83±1.49	3.57±1.33	3.73±1.39	2.97±1.16	3.23±1.01	>0.05	>0.05
8	3.90±1.49	4.10±1.60	3.63±1.33	3.77±1.38	3.07±1.07	3.47±1.14	>0.05	>0.05
12	4.17±1.52	4.47±1.53	3.70±1.24	3.90±1.30	3.17±1.17	3.40±1.09	<0.05*	<0.05*
24	4.37±1.25	4.53±1.21	3.77±1.12	3.91±1.25	3.23±1.42	3.50±1.28	<0.01*	<0.01*

** P value <0.001(highly significant), *p value <0.05(significant)

Table 3: Comparison of number of patients requiring one or multiple doses of rescue analgesic in 24 hours in various group.

Frequency of rescue analgesic (n)	Group L (n=30) (%)	Group LM (n=30) (%)	Group LD (n=30) (%)	ANOVA P value
0 dose	0	0	2 (6.66)	0.129
1 dose	2 (6.66)	4 (13.33)	13 (43.33)	0.001
2 doses	9 (30)	16 (53.33)	11 (36.66)	0.164
3 doses	13 (43.33)	10 (33.33)	4 (13.33)	0.036
4 doses	6 (20)	0	0	0.002

Table 3 shows maximum number of patients (n=13) required only one dose in group LD as compared to group L (n=2) and group LM (n=4). In group L, maximum patient (n=19) required either three (n=13) or four doses (n=6) while in group LM & LD no patients required four doses.

Table 4: Comparison of QoR score.

Variable	G_L	G_{LM}	G_{LD}	P value
Pre-operative QoR score	129.63± 5.39	130.67± 7.37	130.0± 7.93	>0.05
Post-operative QoR score	110.57± 11.49	115.33± 9.08	120.2± 9.11	<0.01*

*p value<0.05 (significant)

Table 5: Comparison of post-operative side effect in different group.

Side effects	G_L (n=30) (%)	G_{LM} (n=30) (%)	G_{LD} (n=30) (%)	ANOVA, p value
Nausea/ vomiting	7 (23.33)	6 (20)	4 (13.33)	0.52
Urinary retention	4 (13.33)	5 (16.66)	4 (13.33)	0.45

DISCUSSION

This study shows that addition of either magnesium or dexmedetomidine as an adjuvant to levobupivacaine provided better postoperative analgesia and decrease requirement of rescue analgesic without any increase in side effects. In lumbar laminectomy effective postoperative pain control is an important factor in reducing the incidence of morbidity and in promoting early mobilization and discharge from hospital. Different modalities and drugs for pain management following lumbar laminectomy have evolved over time. This includes intravenous, intramuscular, epidural, spinal, instillation and infiltration routes of analgesia. Infiltration with local anaesthetic acts directly on the pain producing mechanism with lesser incidence of side effects.[6] Therefore, infiltration mode of analgesia was considered for this study. Magnesium sulfate, an N-methyl-D-aspartate (NMDA) receptor antagonist, effectively decrease the anesthetic and analgesic requirements in the postoperative period. As NMDA receptors are present in both the central nervous system and in the peripheral tissues such as the skin and the muscles, magnesium sulphate with its NMDA receptor antagonistic property, effectively reduces the central and peripheral mechanism of pain transmission, modulation, sensitization.[6,7] Dexmedetomidine is a selective α-2 adrenoreceptor agonist used as sedative as well as adjuvant anesthetic.[3] Several mechanisms have been postulated for its analgesic action which include reduction in conduction of impulses in afferent pain fibers, anti-inflammatory effects by decreasing the production of inflammatory cytokines, α2-adrenergic receptor mediated vasoconstriction leading to prolonged analgesic effect and central analgesic due to its systemic absorption.[8]

In our study, group L patients experienced more post-operative pain with significantly higher VAS score as compared to group LM and LD. Similar to our study, Ahmed et al and Eldaba et al used magnesium as an adjuvant and Deshwal et al, Mitra et al and Li et al used dexmedetomidine as an adjuvant.[3,9-12] They also found higher VAS in the control group as compared to adjuvant group. In contrast, Khorasanizadeh et al and Rajavi et al compared local wound infiltration with local anaesthetic agent (0.5% ropivacaine and 0.5% bupivacaine respectively) and magnesium sulphate 20%. They found lower VAS in local anaesthetic group as compared to magnesium sulphate.[13,14] This could be attributed to the fact that they used magnesium alone for infiltration, whereas in present study, magnesium was used as an adjuvant to levobupivacaine, which contributed to longer duration of analgesia than control group. In contrast to our study, Abdelnaim et al compared dexmedetomidine and magnesium sulphate as an adjuvant to bupivacaine in hernia repair and found lower VAS in dexmedetomidine group as compared to magnesium group postoperatively for first 6 hrs.[15] Higher sedation score in the patients receiving dexmedetomidine could be attributed to lower VAS in the patients in the dexmedetomidine group in this study whereas in the present study, sedation score was similar in all the groups.

In our study, the time to first request of rescue analgesic drug postoperatively was found to be significantly longer and its total dose was significantly lower in group LD and group LM as compared to group L. This result was similar to other studies.[3,6,9-12]

Similar to our study, Abdelnaim et al also found time of first rescue analgesia was maximum in dexmedetomidine group (2 hr 45 min) as compared to magnesium group (1 hr 15 min) and control group (30 min) ($p<0.05$), however, the duration was less in all the three group as compared to present study.[15] This could be attributed to the fact that they have used low dose of fentanyl at induction (1 v/s 2 µg/kg), no additional analgesic at the completion of surgery along with different dose of magnesium (1 v/s 500 mg) and dexmedetomidine (1 µg/kg v/s 50 mg). In our study, the QoR score was significantly better in group LD as compared to group LM and L postoperatively which was similar to studies of Donadi et al and Bhardhwaj et al.[6,8]

There are some limitations in this study. This study has analysed patients for 24 hours only. However, long term follow up could have given better results to evaluate chronic neuropathic pain which results from spinal cord or nerve root injury. Secondly, only a single bolus dose of local infiltration was used while continuous or intermittent postoperative doses of drugs in local wound infiltration with catheter technique could have resulted in better pain control.

CONCLUSION

Local infiltration of surgical wound with magnesium sulphate or dexmedetomidine as an adjuvant to levobupivacaine after lumbar laminectomy demonstrated enhanced postoperative analgesia by reducing the postoperative pain score, total rescue analgesic consumption in the first 24 hour and increasing the time of first request for rescue analgesia. There was also better degree of quality of recovery score among the two study groups.

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