Original Article

Effect of epidural levobupivacaine with or without dexamethasone soaked in gelfoam for postoperative analgesia after lumbar laminectomy: A double blind, randomised, controlled trial

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ABSTRACT

Background and Aims: Postoperative pain results in prolonged hospital stay and delayed return to normal activity. This study was conducted with the aim of evaluating the analgesic efficacy of gelfoam soaked in levobupivacaine with or without dexamethasone placed in the epidural space in patients undergoing lumbar laminectomy. **Methods:** Ninety adult patients were randomised into three groups. Gelfoam was soaked in 12 mL of 0.9% sodium chloride in Group P, 10 mL of 0.25% levobupivacaine + 2 mL of 0.9% sodium chloride in Group L, and 10 mL of 0.25% levobupivacaine + 2 mL of dexamethasone in group LD. The primary outcome was time to first request for rescue analgesia. Total 24-h tramadol consumption, and postoperative visual analog scale (VAS) scores were recorded. Chi-square test and analysis of variance test were used, and $P < 0.05$ was considered significant. **Results:** 75 patients completed the study. Time to first rescue analgesia was longer in group LD [10.11 ± 3.10 h] compared with group L [6.48 ± 2.36 h] and group P [1.76 ± 1.13 h]. Total 24-h tramadol consumption was lower in group LD (88 ± 66.58 mg) and group L (120 ± 70.7 mg) compared with group P (280 ± 64.5 mg). Postoperative VAS scores were lower in group LD and group L compared with group P, both at rest and on movement. **Conclusion:** Epidural gelfoam soaked in levobupivacaine and dexamethasone prolongs the duration of analgesia and decreases rescue analgesic consumption and VAS score postoperatively, in patients undergoing lumbar laminectomy.

Key words: Analgesia, dexamethasone, epidural, laminectomy, levobupivacaine, postoperative

INTRODUCTION

Lumbar laminectomy surgeries are done with the main goal to relieve pain, but the surgery itself results in substantial postoperative pain and discomfort resulting in prolonged hospital stays and delayed return to normal activity. Parenteral nonsteroidal anti-inflammatory drugs (NSAIDs) and/or opioids are commonly used postoperatively for lumbar laminectomy patients, but are associated with side effects and wide fluctuations in clinical effect.[1,2] To minimize these unwanted side effects, epidural analgesia is an effective and safe method in abdominal, thoracic, and spine surgeries.[3] Bupivacaine with or without methylprednisolone has been reported to provide good postoperative analgesia after spine surgery.[4] When compared with direct

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administration of opioids, use of gelfoam soaked in opioids in epidural space prolongs the effect of epidural opioid.[5] Dexamethasone as an adjuvant to local anaesthetic in brachial plexus block results in prolonged duration of analgesia,[6] but search of the available literature revealed no study comparing the analgesic efficacy of dexamethasone as an adjuvant to epidural levobupivacaine in laminectomy surgery.

This study was conducted with the aim of evaluating the analgesic efficacy of gelfoam soaked in levobupivacaine placed in epidural space and the effect of dexamethasone on the duration of postoperative analgesia when added to epidural levobupivacaine in patients undergoing single-level lumbar laminectomy.

METHODS

After Institutional Ethics Committee approval and written informed consent, this prospective, randomised, double-blind, placebo-controlled study was carried over a period of 1 year (Nov 2016 to Nov 2017). Ninety patients, 18–60 years old, American Society of Anesthesiologists (ASA) physical status I/II, of either sex, scheduled to undergo single-level lumbar laminectomy under general anaesthesia were enrolled in the study. Exclusion criteria were body mass index ≥30 kg/m^2, moderate to severe heart or lung disease, history of previous lumbar spinal surgery, prior neurological deficits, prior neuromuscular disease or psychological disease, history of preoperative opioid or steroid use, history of substance abuse, or history of allergic reactions to local anaesthetics. Patients with excessive bleeding requiring placement of drain or cerebrospinal fluid leak were excluded after initial recruitment.

All patients underwent preoperative anaesthetic evaluation and were explained about visual analog scale (VAS) (0–10, where 0 = no pain and 10 = worst imaginable pain).[7] On the day of surgery, all patients were premedicated with midazolam 2 mg, metoclopramide 10 mg, and glycopyrolate 0.2 mg intravenously half an hour before induction in preoperative area. After shifting to operation theater, monitoring with electrocardiogram, pulse oximetry (SPO_2), noninvasive blood pressure (NIBP), end-tidal carbon dioxide ($EtCO_2$), and body temperature, was started and baseline vital parameters were recorded and monitoring was continued at 5-min intervals till extubation. General anaesthesia was induced with fentanyl 2 μg/kg and propofol 2–3 mg/kg till loss of verbal response and tracheal intubation was facilitated by atracurium 0.5 mg/kg, intravenously. Subsequently, anaesthesia was maintained using isoflurane achieving end-tidal concentration of 0.9%–1.2% in a mixture of 60% N_2O in O_2. Neuromuscular blockade was maintained with intermittent atracurium bolus (0.15 mg/kg every 20 min). Ventilation was adjusted to maintain $EtCO_2$ between 30 and 35 mm Hg. Intraoperative supplemental analgesia was provided by intravenous (i.v.) fentanyl 0.5–1 μg/kg boluses as judged by an increase in heart rate (HR) or systolic blood pressure by more than 20% of the baseline.

Patients were randomised into three groups [placebo group (group P), levobupivacaine group (group L), and levobupivacaine + dexamethasone group (group LD)] of 30 each using computer-generated random table numbers, and the allotment was done using coded sealed opaque envelopes. At the end of surgery, after securing hemostasis and before final closure, two pieces of absorbable gelatin sponge, each piece measuring 5 × 2 × 1 cm, soaked in study drug were placed in epidural space over paraspinal region, above the nerve roots by the surgeon. In group P, gelfoam was soaked in 12 mL of 0.9% sodium chloride; in group L, gelfoam was soaked in 10 mL of 0.25% levobupivacaine + 2 mL of 0.9% sodium chloride; and in group LD, gelfoam was soaked in 10 mL of 0.25% levobupivacaine + 2 mL of dexamethasone. After placing the gelfoam, the wound was closed in layers without mopping or suctioning.

At the end of surgery, patients were turned supine and residual neuromuscular blockade was reversed with i.v. neostigmine 50 μg/kg and glycopyrrolate 10 μg/kg and the trachea was extubated when the patient was fully awake and breathing adequately and was shifted to postanaesthesia care unit.

In the postoperative period, pain at rest and on movement was measured by 0–10 VAS, at intervals of 0, 1, 2, 4, 8, 12, 18, and 24 h by an anaesthesiologist blinded to the drugs administered. Effective pain control was defined as VAS scores <3. HR, NIBP, and respiratory rate (RR) were also noted during this time period. Tramadol 100 mg i.v. slowly was given as rescue analgesic in case patient's VAS score was ≥4 on movement. A minimum period of 4 h was specified before tramadol could be repeated and on demand of repeat tramadol before 4 h, alternative analgesics were given and such patients were excluded from the study. The total 24-h tramadol consumption and time to first

request for rescue analgesic were recorded. Side effects such as nausea, vomiting, and urinary retention and any other adverse effects with the use of study drugs in all three groups were also noted. Nausea or vomiting was managed with injection ondansetron 0.15 mg/kg i.v. as necessary. Urinary retention was managed by insertion of Foley's catheter if required. At the end of 24 h, patients were asked about their overall opinion of the quality of pain relief they had received using the following – excellent, very good, good, and poor.

Statistical analysis was carried out using Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA; version 15.0 for Windows). Normality of data was checked by measures of Kolmogorov–Smirnov tests of normality. Normally distributed data are presented as mean and standard deviation. Nonparametric data are expressed as median and interquartile range. Age, weight, and duration of surgery are expressed by analysis of variance (ANOVA), whereas sex distribution and ASA grades were compared by Chi-square test. Intergroup comparisons of time to first rescue analgesic, total postoperative tramadol use, postoperative pain scores, and postoperative haemodynamic parameters at different time intervals were done by ANOVA with appropriate *post hoc* testing with Bonferroni correction. Side effects and quality of pain relief were evaluated by Chi-square test. All tests were evaluated for 95% confidence limits. *P* value <0.05 was considered as significant.

The primary outcome measures were duration of analgesia (time to first rescue analgesia after administration of study drug) and 24-h rescue analgesic (tramadol) consumption. The secondary outcome measures were pain scores, haemodynamic parameters, and adverse effects (nausea, vomiting, urinary retention).

The sample size was calculated on the basis of *a* pilot study. A 40% difference in 24-h analgesic consumption, was considered a clinically relevant difference. For a significance level of 0.05 and power of 0.8, we required 25 patients in each group. We included 30 patients in each group to compensate for drop outs.

RESULTS

The CONSORT flow diagram is presented in Figure 1, which shows that 100 patients were assessed for eligibility, 90 patients were randomised (30 in each group). In group P, 27 patients received allocated intervention (one patient due to dural tear and two patients due to placement of drain were not received allocated intervention) and during follow up two patients discontinued intervention due to excessive vomiting, side effect of tramadol. In group L, 25 patients received allocated intervention (one patient due to dural tear and four patients due to placement of drain did not receive allocated intervention). In group LD, 26 patients received allocated intervention (four patients did not receive intervention) and one patient was lost to follow up due to shift to another ward. 75 patients were involved for final analysis.

The demographic characteristics of the patients were comparable between all the three groups. Preoperative VAS scores and duration of surgery were also similar between the three groups [Table 1].

The time for demand of first rescue analgesia (tramadol) was significantly longer in group LD patients [10.11 ± 3.10 h] when compared with group L [6.48 ± 2.36 h] and group P [1.76 ± 1.13 h] patients. The difference was found to be statistically significant ($P < 0.001$) across the groups and also on intergroup comparison [Table 2]. The mean total tramadol consumption up to 24 h was significantly less in group LD (88 ± 66.58 mg) and group L (120 ± 70.7 mg) when compared with group P (280 ± 64.5 mg) ($P < 0.001$). The difference was statistically not significant between group LD and group L ($P = 0.29$) [Table 2].

Table 1: Demographic characteristics of patients

	Group P (*n*=25)	Group L (*n*=25)	Group LD (*n*=25)	*P*
Age (years)	46.44±10.52	45.56±10.04	47.76±9.11	0.733
Weight (kg)	64.88±7.51	63.12±7.94	68.96±10.02	0.763
Sex (M/F)	15/10	15/10	14/11	0.946
ASA (I/II)	20/5	20/5	19/6	0.924
Preoperative VAS score	5.52±1.29	5.40±1.47	5.72±1.40	0.72
Duration of surgery (min)	85.76±14.39	85.00±15.86	86.96±15.29	0.90

ASA, American Society of Anaesthesiologists; VAS, visual analog scale; SD, standard deviation. Values are mean±SD or number

Table 2: Rescue analgesia parameters

	Group P (*n*=25)	Group L (*n*=25)	Group LD (*n*=25)	*P*
Time to request for first rescue (tramadol) analgesia (h)	1.76±1.13	6.48±2.36	10.11±3.10	<0.001
Total tramadol consumption in 24 h (mg)	280±64.55	120±70.71	88±66.58	<0.001

SD, standard deviation. Values are mean±SD

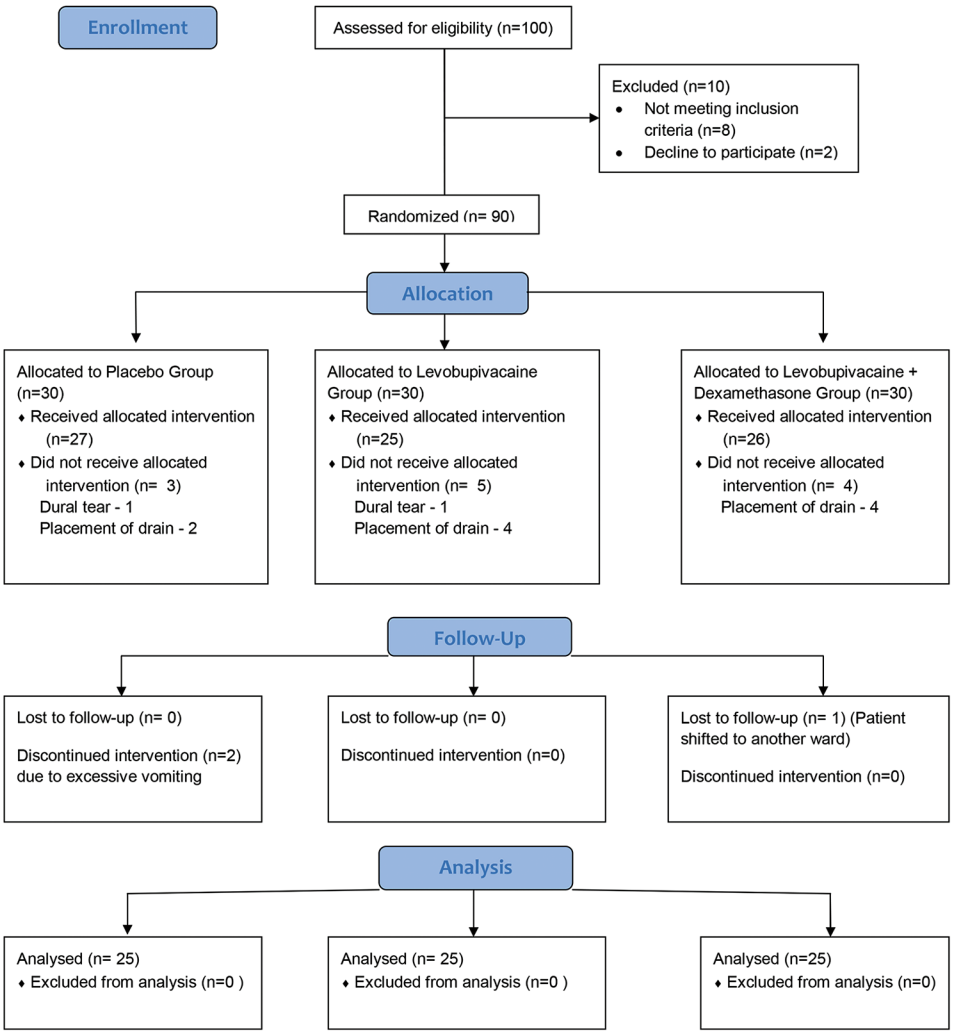

Figure 1: CONSORT flow diagram of the patients included in the study

VAS pain score at rest and on movement in the three groups from 0 to 24 h postoperatively is depicted in Tables 3a and b, respectively. At all time intervals, the mean VAS pain scores were minimum in group LD and maximum in group P both at rest and on movement. The mean VAS pain scores in group L were less compared with group P but more than that of group LD. Both at rest and on movement, postoperative VAS pain score was significantly lower in group LD and group L patients, at almost all time intervals (except at 12 h postoperatively) compared to that of group P patients ($P < 0.05$)

Postoperative haemodynamic parameters (HR, NIBP, RR) were similar between all three groups and no significant haemodynamic deterioration was seen in any group. Quality of pain relief as assessed by patients was best in group LD, followed by that of group L and poor in group P. The difference in quality of pain relief among patients was statistically significant among the three groups ($P = 0.00$) [Table 4].

The incidence of side effects, postoperative nausea (36% vs 16% vs 8%), and vomiting (28% vs 12% vs 4%) was higher in group P when compared with group L and group LD, respectively. The difference was statistically significant for nausea ($P = 0.04$) but not for vomiting ($P > 0.05$). Urinary retention was seen in only one patient in group LD which was statistically not significant ($P > 0.05$) compared with other two groups [Table 5].

DISCUSSION

This study demonstrated that in patients undergoing single-level laminectomy, gelfoam soaked in levobupivacaine placed in epidural space resulted in better postoperative analgesia in terms of lower

Table 3a: Post-operative VAS scores at rest. Values are mean±SD

Post-operative VAS scores	Group P (*n*=25)	Group L (*n*=25)	Group LD (*n*=25)	*P*
At 0 h	0.6±0.87	0±0	0±0	0.00
At 1 h	2.24±1.76	0.04±0.2	0±0	0.00
At 2 h	2.2±1.38	0.76±0.72	0.44±0.65	0.00
At 4 h	2.24±1.2	2.36±1.08	1.36±0.7	0.00
At 8 h	3.04±0.98	2.48±1.26	2.2±1.12	0.03
At 12 h	2.56±0.77	2.2±0.71	2.28±0.68	0.18
At 18 h	2.8±0.76	2.04±0.89	1.8±0.58	0.00
At 24 h	1.8±0.58	0.84±0.62	0.76±0.72	0.00

Table 3b: Post-operative VAS scores on movement. Values are mean±SD

Post-operative VAS scores	Group P (*n*=25)	Group L (*n*=25)	Group LD (*n*=25)	*P*
At 0 h	1.08±1.32	0±0	0±0	0.00
At 1 h	4.24±2.49	0.12±0.44	0±0	0.00
At 2 h	3.52±2.14	1.72±0.98	1.08±0.86	0.00
At 4 h	3.28±1.31	3.68±1.55	2.28±1.02	0.00
At 8 h	4.52±1.23	3.96±1.49	3.4±1.22	0.01
At 12 h	3.8±1.04	3.08±1.22	3.36±0.95	0.06
At 18 h	3.8±0.76	3.08±0.95	2.76±0.78	0.00
At 24 h	2.64±0.57	2.04±0.54	2.04±0.53	0.00

Table 4: Quality of pain relief among patients

Quality of pain relief	Group P (*n*=25)	Group L (*n*=25)	Group LD (*n*=25)	*P*
Excellent	0 (0%)	2 (8%)	7 (28%)	0.00
Very good	0 (0%)	9 (36%)	11 (44%)	0.00
Good	10 (40%)	10 (40%)	6 (24%)	0.00
Poor	15 (60%)	4 (16%)	1 (4%)	0.00

Values are No. (%)

Table 5: Side effects

Side effects	Group P (*n*=25)	Group L (*n*=25)	Group LD (*n*=25)	*P*
Nausea	9 (36%)	4 (16%)	2 (8%)	0.04
Vomiting	7 (28%)	3 (12%)	1 (4%)	0.051
Urinary retention	0 (0%)	0 (0%)	1 (4%)	0.36

Values are No. (%)

requirement of rescue analgesia and less postoperative pain score when compared with control group. Addition of dexamethasone to epidural levobupivacaine prolonged the duration of postoperative analgesia and further reduced the requirement of rescue analgesia and postoperative pain score compared with levobupivacaine alone.

Multimodal approach like parenteral analgesics in form of NSAIDs and/or opioids or local wound infiltration is a commonly used postoperative analgesic strategy for lumbar laminectomy patients. Despite their efficacy, all parenteral medications are associated with adverse effects (sedation, nausea, vomiting, respiratory depression) and wide fluctuations in clinical effect.[1,2] Various studies have reported good postoperative analgesia with such multimodal approach in laminectomy patients,[4] but search of the available literature revealed no study comparing the analgesic efficacy of epidural levobupivacaine with or without dexamethasone after laminectomy surgery. This study was conducted to fill this gap in literature with the aim to evaluate the analgesic efficacy of gelfoam soaked in levobupivacaine placed in epidural space and to study the effect of dexamethasone on duration of postoperative analgesia when added to epidural levobupivacaine in patients undergoing single-level lumbar laminectomy.

In this study, the time to first demand of rescue analgesia was prolonged in group LD [10.11 ± 3.10 h (607 min)] and group L [6.48 ± 2.36 h (389 min)] when compared with group P [1.76 ± 1.13 h (106 min)]. Cumulative rescue analgesic consumption in the first 24 h was significantly lower in group LD (88 ± 66.58 mg) and group L (120 ± 70.7 mg) compared with group P (280 ± 64.5 mg). Postoperative mean VAS pain score was less in group LD and group L when compared with group P both at rest and on movement, implying that epidural levobupivacaine resulted in better postoperative analgesia. Our results are in agreement with previous studies which have reported good postoperative analgesia with use of bupivacaine with or without adjuvant drugs in spine surgeries. A study reported significant postoperative analgesia by wound infiltration with 30 mL of 0.375% bupivacaine after lumbar laminectomy, compared with placebo group. All 21 placebo recipients required analgesics in the first 9 h postoperatively, compared with only 11 of 24 patients who received bupivacaine ($P < 0.001$).[8] In another study injection of 10 mL of 0.5% bupivacaine into the wound resulted in less pain scores and longer duration of analgesia following lumbar discectomy.[9] Another study compared wound infusion of 0.25% bupivacaine and 0.25% ropivacaine into the paraspinal muscle and skin before closure of wound following lumbar laminectomy and found that compared with ropivacaine or control group, the mean time to first demand for rescue analgesia was significantly longer in bupivacaine group.[10] In study of continuous wound instillation of ropivacaine in patients undergoing lumbar arthrodesis, ropivacaine was associated with decrease in pain scores and analgesic

requirement compared with placebo.[11] Similar study of wound instillation with 20 mL of 0.25% bupivacaine also provided better postoperative analgesia when compared with placebo in lumbar laminectomy.[12]

Most of the above-quoted studies have used a minimum of 20 mL of bupivacaine/ropivacaine for wound infiltration or instillation or infusion. However, in this study, we used only 10 mL of 0.25% of levobupivacaine with good success in our subset of population because gelfoam soaked with study drug was directly placed over the nerve roots in epidural space. Gelfoam has the capability to absorb drug several times its weight and prevents dilution of drug by blood and tissue fluids and systemic absorption thus increasing duration of action and providing good results even with 10 mL of 0.25% of levobupivacaine. Previous studies have reported that when compared with direct administration of opioids, use of gelfoam soaked in opioids in epidural space prolongs the effect of epidural opioid.[5,13,14] In laminectomy, surgical gelfoam is commonly used at the completion of surgery, and gelfoam soaked in study drug can be easily placed over nerve root due to easy access to epidural space during laminectomy.

Dexamethasone is a very potent and highly selective glucocorticoid with powerful anti-inflammatory and analgesic property by inhibiting inflammatory mediators that play role in pain formation. Use of dexamethasone as an adjuvant to local anaesthetics in brachial plexus block has been reported to prolong duration of analgesia.[6,15] A recent systematic review has shown that dexamethasone when used along with local anaesthetic significantly reduces the VAS score and analgesic consumption. However, the duration of significant relief is variable.[16] Epidural steroids reduce inflammation at nerve roots and thus help in decreasing the postoperative pain and prolonging the analgesic effect of local anaesthetic. Many randomised studies have demonstrated the benefit of locally applied epidural methylprednisolone in perioperative lumbar spine surgery,[17-20] but analgesic efficacy of dexamethasone as an adjuvant to epidural levobupivacaine in laminectomy surgery has not been studied earlier.

In this study, we used dexamethasone 8 mg as an adjuvant to levobupivacaine, and the results of our study showed that addition of dexamethasone to epidural levobupivacaine prolonged the duration of postoperative analgesia by increasing the time to demand for first rescue analgesia and further reduced the requirement of rescue analgesia and postoperative pain score compared with levobupivacaine alone. Our results are in agreement to previous studies using epidural methylprednisolone with bupivacaine. In a study, patients undergoing lumbar microdiscectomy receieved bupivacaine and methylprednisolone and reported complete relief of back and radicular pain on postoperative day one, required less postoperative narcotic analgesia, and had a statistically significantly shorter hospital stay compared with the control group and group receiving bupivacaine alone.[17] Similar results were reported in a study where methylprednisolone and bupivacaine was infiltrated at surgical site in open discectomy.[18] A study comparing the bupivacaine alone and bupivacaine with methylprednisolone-soaked piece of autogenous fat over nerve root at the end of the surgery was found that bupivacaine alone was not effective in controlling postoperative pain after lumbar decompression.[19] A study that compared perioperatively corticosteroids in form of 250 mg of solumedrol i.v., 160 mg of depomedrol intramuscularly, and free fat transplant soaked in 80 mg of depomedrol placed on dural sac improved the outcome of microscopic disc surgery in terms of length of hospital stay and time taken to return to full work.[20]

In this study, no statistically significant difference was found with regard to adverse effects among the three study groups. The incidence of postoperative nausea and vomiting was higher in group P when compared with group L and group LD, which may be due to more tramadol consumption as rescue analgesia, in Group P. Patients were not followed up for long term to see any adverse effects such as pressure symptoms or infections, which is one of the limitations of this study.

The strengths of our study include its randomised, double-blind design, the uniformity of population, and procedure. But our study also has several limitations. First, the number of patients included in the study is small, thus masking potential complications with the use of epidural gelfoam. Second, patients could have been followed up for long term for any pressure symptoms due to epidural gelfoam, any infections, and to evaluate for chronic pain. The lack of patient-controlled analgesia (PCA) pumps in postoperative wards in our institution was another drawback of the study as they are an excellent mode for rescue analgesia, and a comparison with PCA pumps delivering rescue analgesia is required for a

good comparison and complete study of the analgesic efficacy of levobupivacaine alone or levobupivacaine with dexamethasone.

CONCLUSION

In conclusion, we found that epidural administration of gelfoam soaked in levobupivacaine is a safe and effective method of postoperative analgesia in patients undergoing single-level lumbar laminectomy without complications. Addition of dexamethasone to epidural levobupivacaine further prolonged the duration of analgesia and decreased rescue analgesic (tramadol) consumption and postoperative pain score compared with levobupivacaine alone and was devoid of any side effects.

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Conflicts of interest
There are no conflicts of interest.

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