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Evaluation of two different doses of gabapentin given as preemptive analgesia for Lumbar Laminectomy - A randomized double-blind study

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Abstract
Background and Aims: Postoperative pain after lumbar laminectomy benefits from pre-emptive analgesia as part of Enhanced Recovery After Surgery (ERAS) protocols. Gabapentin has shown promise as a pre-emptive analgesic, but the optimal dose remains unclear. This study compares the efficacy of 300 mg and 600 mg doses of gabapentin administered preoperatively for postoperative pain management in lumbar laminectomy patients.
Methods: In this prospective, double-blinded randomized controlled study, after approval from the Institutional Ethics Committee (IEC) and registering with the Clinical Trials Registry of India (CTRI), 64 patients were randomly assigned to two groups to receive either 300 mg or 600 mg of gabapentin preoperatively. Postoperative pain was assessed using the Visual Analog Scale (VAS) at various intervals up to 24 hours along with requirements for rescue analgesics and duration of analgesia. Secondary outcomes included sedation scores, and the incidence of nausea and vomiting. Statistical analysis was carried out using SPSS version 20, with significance defined as $p < 0.05$.
Results: There were no significant differences in VAS scores, total rescue analgesic doses ($p=0.953$), and duration of analgesia ($p=0.124$) between the 300 mg and 600 mg gabapentin groups. Sedation scores and the incidence of postoperative nausea and vomiting were comparable across the groups.
Conclusions: The study concludes that 300 mg of gabapentin is as effective as 600 mg for pre-emptive analgesia in lumbar laminectomy, without significant differences in pain relief, rescue analgesic requirements, or side effects. We suggest that 300 mg of gabapentin is a sufficient dose for managing postoperative pain.

Keywords: Gabapentin, Lumbar laminectomy, Pre-emptive analgesia, Postoperative pain

Introduction

Lumbar laminectomy is one of the most common spine surgeries, involving the removal of the lamina to relieve pressure on the spinal cord or nerves, thus reducing pain radiation. Patients often experience intense postoperative pain of inflammatory and neuropathic origins. [1] Persistent pain can lead to conditions like allodynia, hyperalgesia, hyperpathia, and chronic pain. [2] Multimodal analgesic approaches help manage this postoperative pain, with opioids being a mainstay. However, opioid-sparing analgesics are preferred to minimize opioid-related adverse effects. [3]

Pre-emptive analgesia, as a part of Enhanced Recovery After Surgery (ERAS) protocols, aims to reduce postoperative pain, opioid consumption, nausea, and vomiting while delaying the need for rescue analgesia. [4, 5] Gabapentin, as a pre-emptive analgesic in spine surgeries, has shown promise in lowering opioid consumption and improving postoperative pain scores. [6, 7] Gabapentin is associated with dose-related gastrointestinal side effects such as nausea and vomiting, and while it can reduce these symptoms, the exact dose-response relationship remains unclear. [8] While the optimal pre-emptive dose of gabapentin for acute postoperative pain remains unclear, a lower dose may reduce potential side effects while still providing effective analgesia. This study evaluates the efficacy of two gabapentin doses, 300 mg and 600 mg, administered orally for postoperative analgesia for patients undergoing lumbar laminectomy.

The primary objective of the study was to assess the Visual Analogue Scale (VAS) scores and consumption of rescue analgesics and duration of analgesia in the first 24 hours postoperatively in patients receiving pre-emptive gabapentin. The secondary objectives were to evaluate postoperative sedation scores using the Modified Ramsay Sedation Score (MRSS) and to determine the incidence of postoperative nausea and vomiting.

Materials and methods

This prospective, unicentric, double-blinded randomized controlled study was conducted in a tertiary care hospital over one year. After obtaining approval from the institutional ethics committee and scientific committee, and securing informed consent, 64 patients over the age of 20 years, classified as American Society of Anaesthesiologists (ASA) grade 1 and 2, who were slated for elective lumbar laminectomy under general anaesthesia, were enrolled in the study. The exclusion criteria for this study included ASA grades 3 and 4, pregnancy and lactation, maintenance use of gabapentin for any indication, emergency cases, a history of allergies to gabapentin or common anesthetic drugs, surgeries lasting more than 4 hours, a body mass index of 30 kg/m² or more, a history of previous spine surgery, and undergoing multilevel lumbar laminectomy. Eligible patients were randomized using computer-generated randomization tables into two groups: GL (receiving 300 mg of gabapentin orally) and GH (receiving 600 mg of gabapentin orally), to receive their respective interventions. Allocation concealment was performed using sequentially numbered, coded, sealed envelopes.

Patients were visited the day before surgery, and detailed medical histories were taken along with general and

systemic examinations. Patients were educated about the study, the anaesthesia plan, and the use of the VAS for postoperative pain assessment. Routine investigations included complete hemogram, random blood sugar, bleeding time, clotting time, international normalized ratio, blood urea, serum creatinine, chest X-ray (PA view), and electrocardiogram (ECG). Drug administration, anesthetized patient management, postoperative pain assessment, and monitoring of the need for rescue analgesics were performed by clinicians not involved in the study. Data collection continued for the first 24 hours postoperatively, with both patients and data collectors blinded to group allocation.

Premedication was done with Ondansetron 4 mg, Pantoprazole 40 mg, and Alprazolam 0.25 mg PO the night before surgery. Patients were required to fast for six hours before undergoing surgery. On the morning of surgery, intravenous infusion of Ringer Lactate at 2ml/kg/hr was initiated after securing an 18G cannula. Ondansetron 4 mg and Pantoprazole 40 mg were given orally. Preoperative sedation scores were assessed, followed by administration of either Gabapentin 300 mg or 600 mg PO according to group assignment.

Upon arrival in the operating room, monitoring included oxygen saturation (SpO2), blood pressure, and ECG. Baseline vital parameters—heart rate (HR), non-invasive blood pressure (NIBP), respiratory rate (RR), and SpO2—were recorded and continuously monitored. Premedication was done with Glycopyrrolate 0.2 mg IV and Midazolam 1 mg IV. Anaesthesia was induced with Morphine (0.1 mg/kg), Propofol (2 mg/kg), and Vecuronium (0.1 mg/kg) IV and maintained with sevoflurane, nitrous oxide, oxygen, and Vecuronium (0.01 mg/kg) IV. A Foley's catheter was placed to monitor urine output. Patients were positioned prone with proper padding to avoid pressure points and abdominal compression. Intraoperative fluid management with crystalloids was maintained at 2ml/kg/hr, adjusted according to urine output and blood loss.

After surgery, patients were repositioned supine and anaesthesia was reversed with Neostigmine (0.05 mg/kg) and Glycopyrrolate (0.01 mg/kg) IV, followed by extubation. Postoperatively, Diclofenac 75 mg IV was administered, and patients were transferred to the postoperative unit, receiving supplemental oxygen via Hudson's face mask at 5L/min. Diclofenac 75 mg IV was continued every 12 hours, and Pantoprazole 40 mg IV was given once daily for gastroprotection. Postoperative monitoring included HR, NIBP, and SpO2.

Demographic factors, including age, sex, weight, and height, were recorded, along with the duration of surgery. Pain was assessed using VAS scores at 0,1,2,4,6,8,12, and 24 hours postoperatively. The duration from arrival at the postoperative care unit to the first rescue analgesic requirement was considered as the duration of analgesia. Rescue analgesia with Tramadol 2 mg/kg IV was administered when VAS was three or higher, with the duration of analgesia recorded. The total dose of rescue analgesic in milligrams was also noted. Sedation scores, and nausea and vomiting scores were recorded at 0,1,2,4,6,8,12, and 24 hours postoperatively. Sedation was evaluated using the Modified Ramsay Sedation Scale (MRSS) with the following scores: 0= paralyzed or unable to evaluate, 1= awake, 2= lightly sedated, 3= moderately sedated, follows simple commands, 4= deeply sedated, responding to non-painful stimuli, 5= deeply sedated, responding to painful stimuli, and 6= deeply sedated, unresponsive to painful stimuli. Nausea and vomiting were rated on a scale of 0 to 3, where 0 meant none, 1 indicated mild, 2 was moderate, and 3 was severe. Ondansetron (0.1 mg/kg) IV was administered if nausea and vomiting score exceeded one.

Data were processed using the Statistical Package for the Social Sciences (SPSS) version 20. Keeping the precision of estimates of outcome statistics as 95% confidence limits with a power of 80% and based on previously published study, sample size was calculated as 32 per group. Qualitative variables were represented by frequency and percentage, while quantitative variables were represented by mean and standard deviation. Independent sample t-tests and Mann-Whitney tests were used to compare quantitative variables between groups. Chi-square tests were employed for qualitative variable comparisons. A p-value below 0.05 was considered significant.

Results

The primary objective of this study was to assess the Visual Analogue Scale (VAS) scores and the consumption of rescue analgesics within the first 24 hours postoperatively in patients receiving pre-emptive gabapentin. The demographic data (age, sex, weight, height), ASA status, and length of operation are presented in Table 1 and show no statistically significant differences between the two groups, GH (receiving 600 mg of gabapentin) and GL (receiving 300 mg of gabapentin). This confirms that the two groups are comparable at baseline.

Table 1: Comparison of demographic data, ASA Grades and duration of surgery between groups GH and GL

		Group GL n=32	Group GH n=32	p - value
Mean Age in years (SD)		55.34±11.92	51.38±13.29	
Sex	Male	20	18	0.611
	Female	12	14	
Mean Weight in Kg (SD)		68.34± 7.92	71.19± 6.72	0.127
Mean Height in cm (SD)		163.8± 8.80	163± 7.93	0.711
Mean BMI in kg/m^2 (SD)		25.72± 4.16	26.98± 3.62	0.198
ASA	Grade 1	14 (43.8%)	12 (37.5%)	0.611
	Grade 2	18 (56.3%)	20 (62.5%)	
Mean duration of surgery in minutes (SD)		152.2± 13.13	147.5±10.78	0.124

Independent sample t-test was performed.GL= Gabapentin 300 mg. GH= Gabapentin 600 mg

The VAS scores at all measured time intervals (0,1, 2, 4, 6, 8, 12, 24 hours postoperatively) are presented in Table 2 and Fig 1. The mean duration of analgesia and the total dose of rescue analgesics are presented in Table 3. The total dose of rescue analgesics used was lower in Group GH compared to Group GL, though the difference was not statistically significant (p-value = 0.953). The mean duration of analgesia showed no statistically significant difference between the two groups (p-value = 0.124).

Table 2: Comparison of visual analogue scale score between groups GH and GL

VAS Score	Group GL (n = 32)		Group GH (n = 32)		p - value
	Mean ± SD	Median (Range)	Mean ± SD	Median (Range)	
0 Hours	0.81 ± 0.69	1 (0 - 2)	1.06 ± 0.80	1 (0 - 2)	0.195
1 Hour	1.03 ± 0.65	1 (0 - 2)	1.41 ± 0.84	1 (0 - 3)	0.063
2 Hours	1.25 ± 0.76	1 (0 - 3)	1.59 ± 0.76	1 (1 - 4)	0.085
4 Hours	1.38 ± 0.83	1 (0 - 3)	1.41 ± 0.56	1 (1 - 3)	0.674
6 Hours	1.25 ± 0.67	1 (0 - 3)	1.03 ± 0.59	1 (0 - 3)	0.124
8 Hours	0.78 ± 0.66	1 (0 - 2)	0.84 ± 0.57	1 (0 - 3)	0.674
12 Hours	0.78 ± 0.66	1 (0 - 3)	0.59 ± 0.50	1 (0 - 1)	0.292
24 Hours	0.38 ± 0.49	0 (0 - 1)	0.50 ± 0.51	0.5 (0 - 1)	0.317

Mann-Whitney test was performed. VAS= Visual analogue scale GL= Gabapentin 300 mg GH= Gabapentin 600 mg

Original Fig

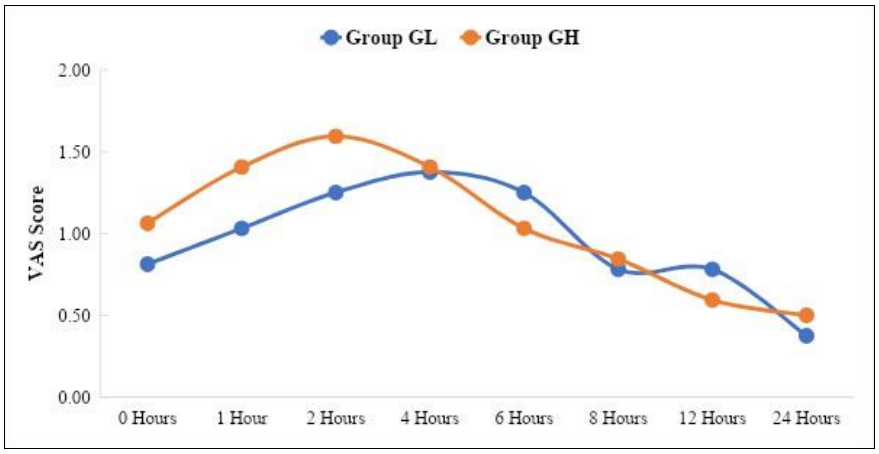

Fig 1: Line diagram comparing VAS score between groups

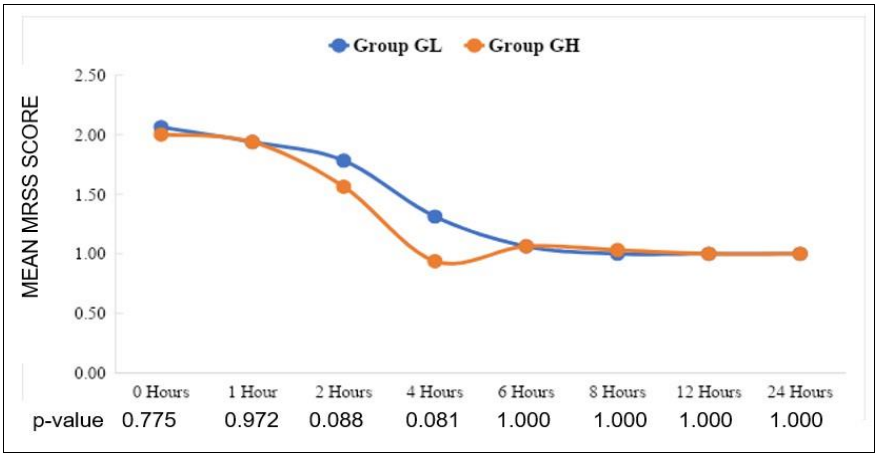

Fig 2: Line diagram comparing Modified Ramsay Sedation Score between groups

Table 3: Comparison of mean duration of analgesia and total dose of rescue analgesic between groups GH and GL

	Group GL (n = 32)	Group GH (n = 32)	p - value
Mean duration of analgesia in minutes (SD)	1592(13.13)	1588(10.78)	0.124
Total dose of rescue analgesic (SD)	0.219 (0.491)	0.188(0.397)	0.953

Independent sample t-test for comparison of mean duration of analgesia between groups. Mann-Whitney test for comparison of total dose of rescue analgesic between groups.GL= Gabapentin 300 mg. GH= Gabapentin 600 mg

Regarding the secondary objectives, the sedation scores (Fig 2) were comparable between the two groups. Although the incidence of postoperative nausea and vomiting (Fig 3) was lower at 1 and 2 hours postoperatively in Group GH, these differences were not statistically significant, with p-values of 0.071 and 0.447, respectively.

Discussion

Effective pain management enhances patient comfort and reduces complications. In the present study, 64 patients posted for elective lumbar laminectomy were selected according to the inclusion and exclusion criteria and randomized into two groups of 32 each by computer generated randomisation table and received either 300 mg (Group GL) or 600 mg (Group GH) of gabapentin preoperatively as a preemptive analgesic. The primary objectives were to assess the visual analogue scale (VAS)

scores, the consumption of rescue analgesics, and the duration of analgesia. Our analysis revealed no statistically significant differences in these measures between Group GH and Group GL, suggesting that both dosages provide similar pain relief. While the effectiveness of gabapentin as a preemptive analgesic is well established, there is variability in the optimal dosage of gabapentin. Pandey CK *et al*. [9] observed that the optimal dose of gabapentin for postoperative pain relief was 600 mg, as it significantly reduced pain scores and fentanyl consumption compared with the 300 mg dose. However higher doses were associated with an increase in side effects such as respiratory depression, nausea, vomiting, and light-headedness. Although these side effects were not clinically significant, they raised concerns regarding patient comfort and safety. Khan ZH *et al*. [10] reported lower pain scores with 900 or 1200 mg doses compared to 600 mg or placebo. A meta-analysis by Peng C *et al*. [11] indicated that while gabapentin 600 mg was effective for pain control, there was a ceiling effect for analgesia at a dose of 900 mg. The frequency and severity of side effects like nausea, vomiting, drowsiness, and dizziness, appear to escalate with increasing doses. [10] [11] In contrast, Radhakrishnan M *et al*. found no significant difference in pain scores with 800 mg of gabapentin compared with placebo. [12] Overall, these studies suggest that, while gabapentin can be effective for pain management, there can be variability in patient responses to gabapentin, and careful consideration of dosage is crucial to minimize adverse effects.

The efficacy of gabapentin in reducing postoperative opioid requirements in a dose dependent manner has been well-documented. In the present study, the total dose of rescue analgesics was lower in Group GH compared to Group GL, though the difference was not statistically significant. Turan A *et al*. demonstrated significantly lower morphine use with 1200 mg gabapentin post-spinal surgery. [13] Khan ZH *et al*. noted lower morphine use in the first 12 hours post-lumbar laminectomy with 900 or 1200 mg doses compared to 600 mg or placebo. [10] Pandey CK *et al*. reported reduced fentanyl use with 600 mg of gabapentin compared with 300 mg. [9] Arumugam S *et al*. [14] in a meta-analysis observed a dose-dependent response in reducing postoperative opioid consumption and pain scores when preoperative gabapentin was administered.

Our results revealed no significant differences in sedation scores or the incidence of postoperative nausea and vomiting between the study groups, consistent with the findings of Liu B *et al*. [15] Therefore, In the present study gabapentin 300 mg dose was equally effective for postoperative analgesia compared with 600 mg dose while the side effect profile was similar.

We conclude that a 300 mg dose of gabapentin is as effective as 600 mg for preemptive analgesia in lumbar laminectomy. Gabapentin is a potent analgesic adjuvant and should be considered an essential component of the multimodal analgesic protocol. This study is limited by its unicentric design and the absence of a control group. We recommend future multicentric studies with larger sample sizes and to assess outcomes over longer durations to validate these findings.

Acknowledgments: Nil
Conflicts of Interest: Nil

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