Preoperative Pregabalin Dosage for Postoperative Pain Management Following Spinal Surgery: A Randomized Controlled Trial

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ABSTRACT:

INTRODUCTION:

In the field of spinal surgery, managing postoperative pain effectively is a critical concern. These surgeries are often invasive and entail extended recovery periods. Thus, finding the right approach to pain control a crucial area of research. Pregabalin, a medication in the gabapentinoid class, is emerging as a promising alternative to traditional opioid-based pain relief. However, the optimal preoperative pregabalin

dosage for maximum pain relief in spinal surgery patients remains a topic of ongoing research. This study aims to investigate the effectiveness of different preoperative pregabalin doses in alleviating postoperative pain following spinal surgery, potentially offering insights to improve the postoperative experience for these patients.

METHODOLOGY:

This trial was conducted at Fauji Foundation Hospital Rawalpindi and included 80 patients aged 20-65 undergoing elective spinal surgery. Patients were divided into two groups: Group A received 75mg of oral pregabalin, while Group B received 150mg, one hour before surgery. Various parameters, including age, weight, height, BMI, surgery duration, gender, and ASA status, were recorded. Postoperative pain was assessed using the Visual Analog Scale (VAS) at 4 hours.

RESULTS:

Patients receiving 150mg of pregabalin had significantly lower postoperative pain scores (mean VAS 3.23) compared to those receiving 75mg (mean VAS 7.45). Stratification showed this difference was significant for both shorter and longer surgeries.

CONCLUSION:

Preoperative pregabalin 150 mg is more effective in reducing postoperative pain after spinal surgery compared to 75mg.

KEY WORDS:

Pregabalin, spinal surgery, postoperative pain, gabapentinoids, Enhanced Recovery After Surgery (ERAS)

INTRODUCTION:

Despite significant advancements in medicine, acute postoperative pain remains a considerable challenge, impacting approximately 66.6% of hospitalized patients globally.(1) Acute pain occurs following tissue injury associated with surgery and is expected to resolve within three months; if it persists beyond this period, it becomes chronic.(2) Post-surgical complications, including postoperative pain, contribute to higher mortality, longer hospital stays, and increased economic burdens. In low-middle-income countries (LMICs), the economic consequences of inadequate postoperative pain management are poorly documented, exacerbating healthcare challenges.(3)(4)

The prevalence of postoperative pain varies among countries, with higher reports from women, older individuals, and rural residents, averaging at 27.5%.(5)
Spine surgery, in particular, is associated with significant postoperative pain, and effective pain control can influence both early postoperative rehabilitation and long-term outcomes. (6)

The use of opioid-based pain relief can lead to undesirable side effects such as nausea and vomiting, potentially hindering rehabilitation efforts. Therefore, it is crucial to establish precise dosing and combinations of non-opioid alternatives, known as "multimodal anesthesia," to effectively replace opioid-based analgesia10/8/2025 6:50:00 AM Opioid tolerance, which necessitates higher doses for pain relief, and opioid-induced hyperalgesia, where opioids paradoxically increase pain, can further complicate pain management.(7) In recent years, gabapentinoids including gabapentin and pregabalin, have emerged as relatively safe alternatives, especially for patients with renal or cardiac risk factors. They do not hinder fusion after spinal surgery, show opioid-sparing effects, and decrease the adverse effects of intravenous patient-controlled analgesia (IV PCA). Due to these advantages and their efficacy, gabapentinoids are widely used for the management of postoperative pain after various surgeries.(8) Preoperative administration of analgesic drugs, such as Pregabalin and Gabapentin, has shown effectiveness in minimizing postoperative pain and analgesic needs, improving patient satisfaction.(9) Unlike gabapentin, pregabalin has a linear pharmacokinetic profile and less variable bioavailability, thus making it a superior option for most patients.(10)
The efficacy of Pregabalin in controlling post operative pain has only been observed for limited procedures. The primary objective of this study is to assess the effectiveness and determine the standard dosage of pre-operative pregabalin for the reduction of postoperative pain following spinal surgery. Additionally, this research aims to compare the average postoperative pain levels between patients receiving two distinct preoperative doses of pregabalin (75mg and 150mg) during spinal surgery.

METHODOLOGY:

This research was conducted in the Department of Anesthesia at Fauji Foundation Hospital Rawalpindi. The sample size calculation was carried out using the WHO calculator, with parameters including a 95% confidence level, 5% level of significance, 90% power of the test, a population mean of 3 ± 0.75, and a test value of the population mean of 2.5 ± 0.625. This calculation determined a sample size of approximately 40 participants in each group (Group A and Group B), totaling 80 participants. The non-probability consecutive technique was used to select participants, and the study extended over six months after research synopsis approval.
Inclusion criteria encompassed patients aged 20-65 years, of any gender, scheduled for elective spinal surgery and classified as ASA1 and ASA2. Exclusion criteria included patients with ASA classification 3 or higher, a history of cardiovascular or respiratory disease, dizziness, frequent headaches, active alcoholism or drug abuse, recent analgesic use within 24 hours before surgery, impaired renal or hepatic functions, and a BMI exceeding 35.
After obtaining ethical approval and written informed consent, 80 patients were enrolled. Standard pre-operative assessments, including anesthesia fitness evaluations,

were conducted a day before surgery. Patients fasted overnight and were randomly assigned to either Group A or Group B by an independent anesthesiology nurse using a lottery method. Group A received 75mg of oral pregabalin with water, while Group B received a 150mg dose of pregabalin with water one hour before surgery. An independent anesthesiology nurse provided follow-up care.
In the pre-operative room, intravascular access with two 18G cannulas was established. In the operating theater, electrocardiography, pulse oximetry, and noninvasive blood pressure monitoring were initiated, and vital signs were closely monitored. Both groups received a crystalloid preload of 10ml/kg. Patients were pre-oxygenated for 3 minutes via a face mask, and general anesthesia was induced with 10 mg of Nalbuphine, followed by 2 mg/kg of Propofol and 0.5 mg/kg of Atracurium for induction and intubation, respectively. After intubation, anesthesia was maintained with 60% Nitrous oxide, 40% Oxygen, and 0.8 - 1% Isoflurane. Injection Atracurium, at 1/5th of the induction dose, was repeated every 25-30 minutes to maintain muscle relaxation. Vital signs were monitored, and appropriate interventions were administered at 3-minute intervals. Patients were reversed with injection Neostigmine (0.05 mg/kg) and Atropine (0.02 mg/kg) after surgery completion, with all anesthesia administration performed by a registrar-level anesthetist who was blinded to the drug to eliminate bias.
Upon surgery completion, patients were extubated and transferred to the post-anesthesia care unit (PACU) for 24-hour monitoring, where post-operative pain control was closely monitored by an independent anesthesiology nurse. Pain scores were assessed at 4 hours postoperatively using the Visual Analog Scale (VAS), graded from no pain (0 cm) to worst unbearable pain (10 cm).
Data were analyzed using SPSS 15 version. Continuous variables, including pain scores, age, weight, height, BMI, and duration of surgery (in minutes), were presented as mean ± standard deviation (S.D.), while categorical variables, such as ASA status, type of surgery, and gender, were expressed as frequencies and percentages. An independent sample T-test was applied to compare mean pain scores between the two groups, with statistical significance defined as $p < 0.05$. Effect modifiers and confounders, such as age, gender, duration of surgery, type of surgery, and ASA status, were controlled through stratification and post-stratification, with a significance level of $p < 0.05$.

RESULTS:

A total of 80 patients were included in the study. Patients were randomly divided into two equal groups: Group A received 75mg of oral Pregabalin with water whereas Group B was given 150mg Pregabalin with water one hour before surgery.
Descriptive statistics revealed a mean age of patients in the study to be 43.21+11.57 years, with an average pain score of 5.34+2.36. Mean height and weight in the study was 162.20+14.63 cm and 68.34+10.35 kg respectively, with a resulting mean body mass index (BMI) of 24.07+2.98. Mean surgery duration was 88.50+9.85 minutes.
Frequency and percentage of gender distribution showed 52 (65%) male and 28 (35%) female patients respectively. Similarly, ASA grades included 28 (35%) ASA grade-I and 52 (65%) ASA grade-II patients.
A comparison between post-operative pain with two different preoperative doses of Pregabalin (75 mg vs 150 mg) in patients undergoing spinal surgery with use of

independent sample t-test revealed statistically significant differences (p-value 0.000) with mean post-operative pain scores of 7.45+1.26 in group A and 3.23+0.76 in group B. Table 1.
Stratification with respect to gender, age, duration of surgery, type of surgery, and ASA grade showed no significant differences between the two groups, except for surgery duration. In patients having duration of surgery less than 90 mins in both the groups, mean post-operative pain score was 8.10+1.17 and 2.72+0.16, respectively, which was statistically significant (p-value 0.000). Similarly, in patients having duration of surgery equal or greater than 90 min in both the groups the score was 8.11+0.25 and 2.36+0.72, respectively, which was also statistically significant (p-value 0.000).

Table. No. 01 Comparison of Mean Pain Score in both the groups

	Two Groups	n	Mean	Std. Deviation	P-value
Pain Score	Group A (Pregabalin 75 mg)	40	7.45	1.26	0.000
	Group B (Pregabalin 150 mg)	40	3.23	0.76	

Table. No. 2 Effect modifier like Duration (mins) of Surgery stratification with Mean Pain Score in both the groups

Duration (mins) of Surgery	**Groups**	n	Mean Pain Score	P-value
< 90 mins	Pregabalin 75 mg	28	8.10±1.17	0.000
	Pregabalin 150 mg	12	2.72±0.16	
≥ 90 mins	Pregabalin 75 mg	24	8.11±0.25	0.000
	Pregabalin 150 mg	16	2.36±0.72	

DISCUSSION:

Our study employed a randomized controlled trial design with the aim of providing evidence regarding the efficacy of varying doses of pregabalin for the management of post-operative pain after spinal surgery. These findings offer promising implications for optimizing pain management strategies and improving postoperative outcomes in patient populations.
Spinal surgery is traditionally a highly invasive intervention with a prolonged recovery phase, often requiring intensive postoperative pain management.(11)

In recent years, Enhanced Recovery After Surgery (ERAS) protocols have become an important focus of operative management, with the aim improving surgical outcomes, reducing complications, improving patient experience, and reducing the length of stay.(12)

Oral multimodal analgesia is now integral to enhanced recovery protocols, designed not only for early postoperative pain relief and discharge but also to mitigate undesirable side effects associated with opioid use, including postoperative nausea and vomiting (PONV), pruritus, and urinary retention. Preemptive forms of MMA have also traditionally been performed by using acetaminophen and NSAIDs, but NSAIDs have limited use in elderly patients or in patients having renal insufficiency and have also been reported to increase the rate of non-union after spinal fusion.(13)

Pregabalin is a gabapentinoid that acts by binding to presynaptic voltage-gated calcium channels at the alpha-2-delta subunit in central and peripheral nervous tissues. This binding decreases the depolarization-induced influx of calcium into neurons and reduces the calcium dependent release of excitatory neurotransmitters. This action may account for the anticonvulsant and analgesic effects of gabapentinoids. (14) Pregabalin however has a superior pharmacological profile compared to gabapentin due to its higher bioavailability, rapid rate of absorption and linear increase in plasma concentration with an increase in dosage. As lower doses of pregabalin are required for its analgesic effects, this results in better tolerance of the drug, with fewer side effects. (15)

A comparison of post-operative pain among both groups in our study revealed lower VAS scores in patients who received a higher pre-operative dose of pregabalin (150 mg) compared to those who received a lower dose (75 mg), highlighting the potential benefits of a higher dosage regimen. Beyond its statistical significance, this result carries practical implications, signifying an enhancement in patient comfort and pain control.

Various studies have shown similar results to our findings. Tsai SHL et al. conducted a systemic review and meta analysis on different gabapentin and pregabalin dosages for perioperative pain control in patients undergoing spine surgery. Compared with placebo, the VAS pain score was lowest with gabapentin followed by pregabalin. (16)

Peene et al. observed that while gabapentinoids have demonstrated their effectiveness in pain management for patients undergoing lumbar laminectomy, they are not the recommended initial choice of treatment due to the significant risk of noteworthy adverse effects, such as sedation, dizziness, and blurred vision. Carefully weighing the potential benefits against the risks associated with gabapentin is crucial when

considering their prescription. (17) Our study further contributes to existing literature by specifically investigating and comparing effectiveness of various pregabalin dosage levels within the context of spine surgery.

A study in France reported an interesting finding by comparing post- operative opioid requirements between chronic users of PGB (who had been prescribed PGB for management of chronic lower back pain) to naïve users who were administered PGB only prior to spinal surgery. Chronic users experienced less opioid consumption when compared with naive patients receiving PGB during to the first 2 PODs.(18)

Jiang et al. conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) to evaluate the efficacy and safety of pregabalin for pain management following spine surgery. The metaanalysis results indicated that pregabalin can decrease VAS score **with rest** at 24hours and at 48hours but there were no significant differences between PGB group and control group in VAS scores **with mobilization** at 24hrs and 48hrs. The pooled results indicated that a high dose of pregabalin (≥300mg/d) can reduce the VAS score with rest at 12hours, 24hours, and 48hours with a significant difference compared to a lower dose of pregabalin (<300mg/d). Additionally, both low doses and high doses of pregabalin can reduce the cumulative morphine consumption at 24hours and 48hours ($P<0.05$). (19)

Another study in Egypt reported significantly lower VAS scores at different times of postoperative assessment among the pregabalin group in comparison to the placebo group, and the time to patients' request for rescue analgesia for the first time was also significantly longer in the pregabalin group than in the placebo group. A single dose of 150 mg of pregabalin preoperatively may have the ability to reduce the acute postoperative pain and opioids consumption after spinal fusion surgeries.(20)

Atul Sharma et.al. studied the effect of oral gabapentin vs. pregabalin as preemptive analgesic for postoperative pain in patients undergoing lumbar spine surgeries and concluded that Pregabalin along with IV Paracetamol has a better analgesic profile and delays the time for requirement of first dose of rescue analgesic compared to Gabapentin along with IV Paracetamol following lumbar spinal surgery.(21)

Baloch et al. reported that the use of pregabalin in addition to the routine analgesia has better control of postoperative neuropathic pain in patients with single-level microdiscectomy compared to the patients who are receiving only routine analgesia through a randomised control trial. They also found that preoperative pregabalin decreased usage of postoperative opioid use for pain management significantly. Our study further adds to this by comparing the effectiveness of two different doses in a similar patient population. (24)

CONCLUSION:

Preoperative pregabalin 150 mg is more effective in reducing postoperative pain after spinal surgery compared to 75mg.

LIMITATIONS:

These include a limited sample size and single center study.

SUGGESTIONS AND RECOMMENDATIONS:

Future research that focuses on particular spinal surgery procedures could provide more tailored insights into the efficacy of pregabalin dosing for various interventions.

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