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Comparative Evaluation of Oral Pregabalin as an Adjuvant to Spinal Anesthesia: Impact on Postoperative Analgesia, Sedation, and Hemodynamic Stability

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KEYWORDS

Pregabalin;
Spinal anesthesia;
Postoperative analgesia;
Sedation;
Hemodynamic stability.

ABSTRACT:

Background: Postoperative pain management remains a crucial component of perioperative care. Pregabalin, a gabapentinoid with analgesic and anxiolytic properties, has been increasingly explored as an adjuvant to spinal anesthesia to enhance postoperative analgesia while minimizing opioid consumption.

Objectives: To compare the effects of oral pregabalin 150 mg and 300 mg as adjuvants to spinal anesthesia on postoperative analgesia, sedation, and hemodynamic stability in patients undergoing elective lower abdominal surgeries.

Methods: This prospective, randomized, double-blinded study included 90 patients (ASA I-II) scheduled for elective lower abdominal surgery under spinal anesthesia. Patients were randomized into three groups: Group C (placebo), Group P150 (pregabalin 150 mg), and Group P300 (pregabalin 300 mg). All patients received intrathecal 0.5% hyperbaric bupivacaine. Parameters assessed included onset and duration of sensory and motor block, duration of postoperative analgesia, sedation score, hemodynamic variables, and adverse effects. Statistical analysis was performed using ANOVA and chi-square tests, with $p < 0.05$ considered significant.

Results: Both pregabalin groups demonstrated significantly prolonged postoperative analgesia compared to the control group, with the longest duration observed in the 300 mg group ($p < 0.001$). Time to first rescue analgesic and duration of motor blockade were significantly longer in the pregabalin groups. Sedation scores increased in a dose-dependent manner but remained within clinically acceptable limits. Hemodynamic parameters remained stable across all groups, with no significant adverse events observed.

Conclusion: Oral pregabalin is an effective and safe adjuvant to spinal anesthesia. A dose of 300 mg provides superior postoperative analgesia compared to 150 mg, with acceptable sedation and stable hemodynamics. Pregabalin can be considered a valuable component of multimodal analgesia for lower abdominal surgeries.

INTRODUCTION

Spinal anesthesia is one of the most commonly employed regional anesthetic techniques for lower abdominal and lower limb surgeries due to its rapid onset, ease of administration, cost-effectiveness, and ability to provide profound sensory and motor blockade. It also avoids airway manipulation and minimizes systemic drug exposure, thereby reducing perioperative morbidity. However, the relatively limited duration of postoperative analgesia associated with spinal anesthesia remains a significant clinical challenge. Inadequate postoperative pain control can lead to delayed mobilization, increased stress response, prolonged hospital stay, and reduced patient satisfaction.[1]

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Bupivacaine, particularly hyperbaric 0.5%, is the most widely used local anesthetic for subarachnoid block owing to its long duration of action and favorable sensory-motor block profile. Nevertheless, its analgesic duration is often insufficient for prolonged postoperative pain relief, necessitating additional analgesics. To overcome this limitation, various adjuvants such as opioids, α-2 agonists, ketamine, neostigmine, and benzodiazepines have been investigated. While effective, many of these agents are associated with undesirable adverse effects including respiratory depression, nausea, vomiting, hypotension, pruritus, urinary retention, and excessive sedation.[2][3]

Pregabalin, a structural analogue of γ-aminobutyric acid (GABA), exerts its analgesic effect by binding to the α2-δ subunit of voltage-gated calcium channels, thereby reducing the release of excitatory neurotransmitters such as glutamate, substance P, and noradrenaline. It possesses anxiolytic, anticonvulsant, and analgesic properties with minimal respiratory depression. Oral pregabalin has high bioavailability (>90%), predictable pharmacokinetics, and achieves peak plasma concentration within one hour, making it suitable for preoperative administration.[4]

AIM

To evaluate and compare the effect of oral pregabalin 150 mg and 300 mg as adjuvants to spinal anesthesia on postoperative analgesia, sedation, and hemodynamic stability.

OBJECTIVES

1. To compare the duration and quality of postoperative analgesia following administration of oral pregabalin 150 mg, 300 mg, and placebo.
2. To assess the effect of pregabalin on sensory and motor blockade characteristics and sedation levels.

MATERIALS AND METHODS

Source of Data

Patients scheduled for elective lower abdominal surgeries under spinal anesthesia at a tertiary care teaching hospital were enrolled for the study.

Study Design

A prospective, randomized, double-blind, placebo-controlled clinical study.

Study Location

Department of Anaesthesiology, tertiary care teaching hospital.

Study Duration

The study was conducted over a period of 12 months.

Sample Size

A total of 90 patients were included and randomly allocated into three equal groups:

- **Group C (Control):** Placebo (n = 30)
- **Group P150:** Oral pregabalin 150 mg (n = 30)
- **Group P300:** Oral pregabalin 300 mg (n = 30)

Inclusion Criteria

- Patients aged 20-60 years
- American Society of Anesthesiologists (ASA) physical status I and II
- Patients scheduled for elective lower abdominal surgeries under spinal anesthesia
- Patients providing informed written consent

Exclusion Criteria

- Refusal to participate
- ASA physical status III or IV
- Known allergy to pregabalin or local anesthetics
- Pregnancy and lactation
- Body mass index >28 kg/m²
- History of neurological disorders, renal or hepatic impairment
- Chronic opioid or sedative use

Procedure and Methodology

After institutional ethical committee approval, patients were randomly allocated using a closed-envelope technique. The study drugs were prepared and

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administered by an anesthesiologist not involved in data collection to maintain double blinding.

All patients received oral alprazolam 0.5 mg and ranitidine 150 mg the night before surgery. On the day of surgery, patients received either placebo, pregabalin 150 mg, or pregabalin 300 mg orally one hour before subarachnoid block.

Baseline vitals were recorded, and intravenous access was secured. Patients were preloaded with 10 mL/kg Ringer's lactate. Spinal anesthesia was performed at the L3-L4 interspace using a 25G Quincke needle, and 3 mL of 0.5% hyperbaric bupivacaine was administered.

Sensory block, motor block (modified Bromage scale), hemodynamic parameters, sedation (Ramsay Sedation Score), time to two-segment regression, duration of motor block, and duration of analgesia were recorded at predefined intervals. Rescue analgesia was administered when VAS ≥4.

Sample Processing

Clinical data were recorded on a structured proforma and entered into a standardized data collection sheet for analysis.

Statistical Methods

Data were analyzed using SPSS software version 17.0. Continuous variables were expressed as mean ± standard deviation and analyzed using ANOVA. Categorical variables were expressed as frequencies and percentages and analyzed using Chi-square test. A p-value <0.05 was considered statistically significant.

Data Collection

Parameters collected included demographic data, onset and duration of sensory and motor block, hemodynamic parameters, sedation scores, duration of postoperative analgesia, and adverse effects.

OBSERVATION AND RESULTS:

Table 1: Comparison of Baseline Characteristics and Hemodynamic Stability

Variable	Group C (n=30)	Group P150 (n=30)	Group P300 (n=30)	Test of Significance	Effect Size (95% CI)	P value
Age (years)	39.17 ± 10.00	36.60 ± 11.00	36.36 ± 10.76	One-way ANOVA	η^2 = 0.03 (-2.1 to 6.4)	0.421
Height (cm)	156.83 ± 7.95	158.77 ± 7.28	159.00 ± 6.71	One-way ANOVA	η^2 = 0.02 (-1.8 to 5.6)	0.462
Weight (kg)	57.70 ± 8.35	60.20 ± 5.96	58.27 ± 7.70	One-way ANOVA	η^2 = 0.04 (-1.9 to 6.3)	0.318
BMI (kg/m²)	23.69 ± 2.26	23.93 ± 2.32	22.78 ± 2.18	One-way ANOVA	η^2 = 0.05 (-0.6 to 1.8)	0.291

Table 1 presents the baseline demographic profile and hemodynamic parameters of patients across the three study groups—Group C (control), Group P150, and Group P300. The mean age of participants was comparable across the three groups (39.17 ± 10.00 years in Group C, 36.60 ± 11.00 years in Group P150, and 36.36 ± 10.76 years in Group P300), with no statistically significant difference (p = 0.421). Similarly, anthropometric parameters such as height, weight, and body mass index (BMI) were comparable among all groups, with p-values of 0.462, 0.318, and 0.291 respectively, indicating effective randomization and baseline homogeneity.

Hemodynamic parameters including mean heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure remained comparable across the three groups throughout the intraoperative period. Repeated-measures ANOVA demonstrated no statistically significant intergroup differences (p > 0.05 for all parameters).

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Table 2: Comparison of Postoperative Analgesia Parameters

Parameter	Group C (n=30)	Group P150 (n=30)	Group P300 (n=30)	Test of Significance	Effect Size (95% CI)	P value
Time to 2-segment regression (min)	67.83 ± 10.31	86.83 ± 12.69	121.53 ± 10.36	One-way ANOVA	η^2 = 0.71 (42.4-66.8)	<0.001
Total duration of analgesia (min)	183.66 ± 19.02	326.83 ± 29.49	669.00 ± 34.87	One-way ANOVA	η^2 = 0.89 (420-515)	<0.001
Time to first rescue analgesic (min)	183.66 ± 19.02	326.83 ± 29.49	669.00 ± 34.87	One-way ANOVA	η^2 = 0.89 (421-514)	<0.001

Table 2 demonstrates a statistically significant and dose-dependent improvement in postoperative analgesia with the use of oral pregabalin. The time to two-segment regression was significantly prolonged in Group P150 (86.83 ± 12.69 minutes) and further extended in Group P300 (121.53 ± 10.36 minutes) compared to the control group (67.83 ± 10.31 minutes), with a highly significant difference ($p < 0.001$).

Similarly, the total duration of analgesia showed a marked increase with escalating doses of pregabalin. Group C exhibited a mean analgesic duration of 183.66 ± 19.02 minutes, whereas Group P150 demonstrated a significantly prolonged duration of 326.83 ± 29.49 minutes. The longest duration was observed in Group P300 (669.00 ± 34.87 minutes), with a large effect size ($\eta^2 = 0.89$, $p < 0.001$).

The time to first rescue analgesic requirement mirrored this pattern, being significantly delayed in the pregabalin groups compared to the control group, again with maximum prolongation observed in the 300 mg group.

Table 3: Sensory-Motor Block Characteristics and Sedation Profile

Parameter	Group C (n=30)	Group P150 (n=30)	Group P300 (n=30)	Test of Significance	Effect Size (95% CI)	P value
Sensory onset (min)	2.56 ± 0.45	2.60 ± 0.63	2.60 ± 0.61	ANOVA	η^2 = 0.01	0.88
Motor onset (min)	3.08 ± 0.45	2.81 ± 0.43	2.78 ± 0.43	ANOVA	η^2 = 0.11	0.021*
Time to max sensory block (min)	5.01 ± 0.60	5.00 ± 0.50	5.10 ± 0.50	ANOVA	η^2 = 0.01	0.74
Time to max motor block (min)	6.46 ± 0.86	6.27 ± 0.69	6.33 ± 0.84	ANOVA	η^2 = 0.02	0.66
Total motor block duration (min)	148.0 ± 15.4	208.7 ± 27.4	380.0 ± 54.9	ANOVA	η^2 = 0.83	<0.001
Ramsay Sedation Score	1-2	2-3	3-4	Chi-square	Cramer's V = 0.71	<0.001

Table 3 illustrates the effects of pregabalin on sensory and motor blockade as well as sedation levels. The onset of sensory block was comparable among the three groups, with no statistically significant difference observed ($p = 0.88$). Similarly, the time to achieve maximum sensory block and maximum motor block did not differ significantly among the groups, indicating that pregabalin did not delay or hasten the establishment of spinal anesthesia.

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However, a statistically significant difference was observed in the onset of motor blockade, with faster onset in the pregabalin groups compared to control ($p = 0.021$). The total duration of motor blockade was markedly prolonged in the pregabalin groups, particularly in Group P300 (380.0 ± 54.9 minutes), followed by Group P150 (208.7 ± 27.4 minutes), compared to Group C (148.0 ± 15.4 minutes), with a highly significant difference ($p < 0.001$).

Sedation scores showed a clear dose-dependent increase. Group C predominantly had Ramsay scores of 1-2, indicating minimal sedation. Group P150 demonstrated moderate sedation (scores 2-3), while Group P300 showed deeper yet clinically acceptable sedation (scores 3-4). The difference in sedation levels across groups was statistically significant ($p < 0.001$), with no episodes of excessive sedation or respiratory compromise reported.

DISCUSSION

Baseline Characteristics and Hemodynamic Stability: As shown in Table 1, demographic variables such as age, height, weight, and BMI were comparable across the three study groups, confirming appropriate randomization. Hemodynamic parameters including heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure also remained comparable throughout the perioperative period. This indicates that oral pregabalin, even at a dose of 300 mg, does not adversely affect cardiovascular stability.

These findings are consistent with studies by Bhandari K *et al.* (2025)[5], who reported no significant hemodynamic fluctuations with preoperative pregabalin administration during spinal or general anesthesia. Similarly, Kohli *et al.* observed stable intraoperative hemodynamics with pregabalin 150 mg and 300 mg, supporting its cardiovascular safety profile. The absence of hypotension or bradycardia in the present study further strengthens the role of pregabalin as a safe oral adjuvant.

Postoperative Analgesia: As depicted in Table 2, the duration of postoperative analgesia increased significantly with escalating doses of pregabalin. The mean duration of analgesia was 183.66 ± 19.02 minutes in the control group, which increased to 326.83 ± 29.49 minutes with 150 mg pregabalin and further to 669.00 ± 34.87 minutes with 300 mg pregabalin ($p < 0.001$). The prolonged time to first rescue analgesic and delayed two-segment regression further reinforce the dose-dependent analgesic efficacy of pregabalin.

These findings are in strong agreement with the studies by Galal Eldin AM *et al.* (2025)[6], who demonstrated significantly prolonged analgesia with pregabalin 300 mg compared to placebo in spinal anesthesia. Similarly, Das R *et al.* (2022)[3] reported a significant extension in analgesic duration with pregabalin premedication, although the magnitude was less than that observed in the present study, possibly due to differences in dosing or timing of administration Lauretta MP *et al.* (2025)[7].

Studies by Kumari I *et al.* (2024)[8] also reported reduced postoperative analgesic requirements and delayed rescue analgesic consumption in patients receiving pregabalin, reinforcing its role as an effective analgesic adjunct. The dose-dependent effect observed in the present study supports the pharmacodynamic profile of pregabalin, where higher doses exert greater modulation of calcium channel-mediated neurotransmitter release.

Sensory and Motor Block Characteristics: As demonstrated in Table 3, the onset of sensory block and time to achieve maximum sensory block did not differ significantly among the three groups, indicating that pregabalin does not influence the onset kinetics of spinal anesthesia. These findings are consistent with reports by Alaasar NM *et al.* (2020)[2], who also observed no significant difference in sensory onset times with gabapentinoid premedication.

However, the onset of motor block was significantly faster in the pregabalin groups compared to the control group, suggesting enhanced facilitation of spinal anesthetic action. Furthermore, the total duration of motor block was significantly prolonged in the pregabalin groups, particularly in the 300 mg group (380.0 ± 54.9 minutes), demonstrating a clear dose-response relationship.

These findings correlate well with those of Shefa S *et al.* (2022)[9], who reported prolonged motor block durations with pregabalin premedication, although the magnitude of prolongation varied based on dosing and surgical population. The prolongation of motor block may be attributed to central modulation of neuronal excitability through calcium channel inhibition.

CONCLUSION

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The present study demonstrates that oral pregabalin, when administered as a premedication prior to spinal anesthesia, significantly enhances postoperative analgesia in a dose-dependent manner without causing hemodynamic instability. Both 150 mg and 300 mg doses of pregabalin were effective in prolonging the duration of analgesia and motor blockade compared to placebo. However, the 300 mg dose produced a significantly longer duration of analgesia and motor blockade than the 150 mg dose, along with a greater degree of sedation.

Importantly, despite the increased sedation observed with higher doses, no patient experienced excessive sedation, respiratory depression, or hemodynamic compromise. The onset of sensory and motor blockade remained comparable across all groups, indicating that pregabalin does not interfere with the establishment of spinal anesthesia. These findings suggest that oral pregabalin is a safe and effective adjuvant for enhancing postoperative analgesia following spinal anesthesia.

Overall, oral pregabalin—particularly at a dose of 300 mg—offers superior postoperative analgesia with acceptable sedation and stable hemodynamics, making it a valuable adjunct in patients undergoing lower abdominal surgeries under spinal anesthesia.

LIMITATIONS OF THE STUDY

1. The study was conducted at a single center with a relatively small sample size, which may limit the generalizability of the findings.
2. Only two doses of pregabalin (150 mg and 300 mg) were evaluated; intermediate or lower doses (e.g., 75 mg) were not assessed.
3. The study population included only ASA I and II patients; therefore, results may not be applicable to high-risk or elderly patients with significant comorbidities.
4. Postoperative pain assessment was limited to the immediate postoperative period and did not evaluate long-term analgesic outcomes.
5. Subjective assessment of sedation using the Ramsay Sedation Scale may introduce observer bias.
6. Plasma levels of pregabalin were not measured; hence, pharmacokinetic correlations could not be established.
7. The study did not evaluate patient satisfaction scores or quality-of-recovery indices, which could further support clinical applicability.

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