RESEARCH PAPER

Pregabalin versus Duloxetine for Perioperative Anxiolysis and Preemptive Analgesia in Patients Undergoing Surgery Under Subarachnoid Block: A Randomized Double-Blind Comparative Study

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ABSTRACT

Background: Postoperative pain remains a major challenge in perioperative care despite advances in anaesthetic techniques. Inadequately controlled pain contributes to delayed recovery, increased morbidity, prolonged hospitalization, and reduced patient satisfaction. Preemptive analgesia aims to reduce central sensitization, improve postoperative pain control, and minimize analgesic requirements. Pregabalin and duloxetine have emerged as promising non-opioid agents because of their analgesic and anxiolytic properties. The present study was undertaken to compare the effects of pregabalin and duloxetine on perioperative anxiolysis and preemptive analgesia in patients undergoing surgery under subarachnoid block.

Methods: This prospective, randomized, double-blind comparative study was conducted among 60 patients aged 18–60 years with American Society of Anesthesiologists (ASA) physical status I and II undergoing elective lower abdominal surgeries under subarachnoid block. Patients were randomly allocated into two groups of 30 each. Group P received oral pregabalin 75 mg and Group D received oral duloxetine 60 mg two hours before surgery. Preoperative anxiety was assessed using the Amsterdam Preoperative Anxiety and Information Scale (APAIS). Intraoperative sedation was evaluated using the Numeric Sedation Score. Hemodynamic parameters including heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure were monitored intraoperatively. Time to first rescue analgesia, total rescue analgesic consumption during the first 24 postoperative hours, and adverse effects were recorded and analyzed.

Results: Baseline demographic characteristics were comparable between the study groups. Both pregabalin and duloxetine significantly reduced preoperative anxiety; however, the reduction was greater in the pregabalin group. APAIS scores decreased from 13.4 ± 2.4 to 6.4 ± 1.8 in the pregabalin group and from 13.2 ± 2.1 to 8.1 ± 1.9 in the duloxetine group. Intraoperative sedation scores were higher in the pregabalin group, reaching a peak value of 3.45 ± 0.58 at 10 minutes compared with 2.85 ± 0.61 in the duloxetine group. Pregabalin demonstrated superior analgesic efficacy, with a significantly longer time to first rescue analgesia (312.40 ± 46.8 minutes vs 278.60 ± 42.3 minutes; $p<0.001$) and lower total rescue analgesic consumption during the first 24 hours (820 ± 240 mg vs 1180 ± 310 mg; $p<0.001$). Hemodynamic parameters remained stable throughout the intraoperative period with no significant intergroup differences. Adverse effects were mild and self-limiting, with no severe adverse events, respiratory depression, or clinically significant hypotension observed.

Conclusion: Both pregabalin and duloxetine were safe and effective agents for perioperative anxiolysis and preemptive analgesia in patients undergoing surgery under subarachnoid block. However, pregabalin demonstrated superior anxiolytic efficacy, prolonged postoperative analgesia, and reduced rescue analgesic requirements compared with duloxetine while maintaining hemodynamic stability and an acceptable safety profile. These findings support the use of pregabalin as a valuable component of multimodal perioperative analgesic protocols.

Keywords: *Pregabalin; Duloxetine; Preemptive Analgesia; Perioperative Anxiolysis; Subarachnoid Block; Spinal Anaesthesia; Rescue Analgesia; Multimodal Analgesia; Postoperative Pain.*
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INTRODUCTION

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Postoperative pain continues to be one of the most common and inadequately managed complications following surgical procedures despite major advances in anaesthetic and analgesic techniques. Studies have reported that nearly 70–80% of patients experience moderate to severe postoperative pain, with a significant proportion receiving inadequate pain relief during the immediate postoperative period.[1] Inadequate postoperative analgesia adversely affects patient recovery and contributes to increased morbidity, delayed mobilization, prolonged hospitalization, higher healthcare expenditure, and reduced patient satisfaction. Effective postoperative pain management has therefore become a fundamental component of perioperative care.

Pain following surgery is initiated by tissue injury resulting from surgical incision, tissue manipulation, and inflammatory responses. These stimuli activate peripheral nociceptors, which transmit pain signals through afferent neural pathways to the dorsal horn of the spinal cord and subsequently to higher cortical centres. Persistent nociceptive input leads to neuroplastic changes within the central nervous system, producing a phenomenon known as central sensitization. Central sensitization results in amplification of pain signals, hyperalgesia, and prolonged postoperative pain.[2] Prevention of this sensitization has emerged as an important target in modern perioperative pain management strategies.

Traditionally, opioid analgesics have formed the cornerstone of postoperative pain treatment because of their potent analgesic properties. However, opioid administration is associated with numerous adverse effects including respiratory depression, nausea, vomiting, excessive sedation, urinary retention, ileus, pruritus, and the risk of long-term dependence.[3] The growing global concern regarding opioid-related complications has stimulated interest in opioid-sparing analgesic techniques capable of providing effective pain relief with fewer adverse effects.

Multimodal analgesia has gained widespread acceptance as an effective strategy for perioperative pain management. This approach involves the use of multiple analgesic agents acting through different mechanisms to provide synergistic pain relief while minimizing opioid requirements.[7] Several studies have demonstrated that multimodal analgesic regimens improve postoperative outcomes, decrease analgesic consumption, and enhance recovery after surgery. As a result, multimodal pain management has become an integral component of enhanced recovery protocols.

Preemptive analgesia represents an important aspect of multimodal analgesic therapy. The concept refers to administration of analgesic interventions before the initiation of surgical injury with the objective of preventing central sensitization and reducing postoperative pain intensity.[2] By blocking nociceptive transmission before tissue damage occurs, preemptive analgesia may reduce postoperative pain scores, delay the requirement for rescue analgesia, decrease overall analgesic consumption, and improve patient comfort during recovery. Increasing evidence supports the role of preemptive analgesia in improving perioperative outcomes and reducing postoperative complications.[8]

The physiological consequences of inadequately treated postoperative pain are considerable. Acute pain activates the sympathetic nervous system, resulting in tachycardia, hypertension, increased myocardial oxygen demand, impaired pulmonary function, reduced mobility, and delayed wound healing.[9] These effects may increase postoperative morbidity and delay recovery. Consequently, identification of effective preemptive analgesic agents remains an important area of anaesthesia research.

Enhanced Recovery After Surgery (ERAS) protocols emphasize effective perioperative analgesia as a critical determinant of successful surgical outcomes. Evidence suggests that optimal pain control facilitates early ambulation, improves respiratory function, decreases postoperative complications, shortens hospital stay, and accelerates return to normal activity.[10] Therefore, the search for safe and effective non-opioid analgesic agents capable of improving perioperative pain control continues to be of significant clinical importance.

Among the various pharmacological agents investigated for preemptive analgesia, duloxetine and pregabalin have attracted considerable attention because of their proven efficacy in neuropathic and chronic pain disorders. Duloxetine is a selective serotonin-norepinephrine reuptake inhibitor (SNRI) that exerts analgesic effects by enhancing descending inhibitory pain pathways within the central nervous system. By increasing synaptic concentrations of serotonin and norepinephrine, duloxetine suppresses nociceptive transmission and reduces central sensitization.[4] Clinical studies have demonstrated its effectiveness in chronic pain syndromes including diabetic neuropathy, fibromyalgia, osteoarthritis, and musculoskeletal pain disorders.[5,13] Goldstein et al. reported significant pain reduction with duloxetine therapy in patients with diabetic neuropathy, further supporting its analgesic properties beyond its antidepressant effects.[13]

Pregabalin is a gabapentinoid that acts by binding to the α2δ subunit of voltage-gated calcium channels within the central nervous system. This action reduces calcium influx into presynaptic neurons and inhibits the release of excitatory neurotransmitters including glutamate, norepinephrine, and substance P, thereby attenuating nociceptive transmission.[6] Pregabalin has demonstrated substantial efficacy in neuropathic pain management and perioperative analgesia. Freynhagen and Baron reported that pregabalin effectively reduces neuronal hyperexcitability and improves pain control in various neuropathic conditions.[14] Furthermore, Clarke et al. demonstrated that perioperative pregabalin administration significantly reduced postoperative pain intensity and opioid consumption in surgical patients.[15]

Subarachnoid block remains one of the most commonly utilized regional anaesthetic techniques for lower abdominal surgeries because of its rapid onset, reliable sensory blockade, excellent intraoperative analgesia, and favorable safety profile. Although spinal anaesthesia provides effective intraoperative pain relief, postoperative pain frequently develops following regression of the sensory block. This period often necessitates administration of rescue analgesics and may negatively affect patient recovery.[8] Consequently, adjunctive pharmacological interventions capable of prolonging analgesic efficacy beyond the duration of neuraxial blockade are of considerable clinical interest.

In addition to their analgesic properties, both duloxetine and pregabalin possess anxiolytic effects that may provide added benefits during the perioperative period. Preoperative anxiety is highly prevalent among surgical patients and has been associated with increased perioperative stress responses, greater postoperative pain perception, higher analgesic requirements, delayed recovery, and reduced patient satisfaction.[4,14] Reduction of anxiety before surgery may therefore contribute to improved perioperative outcomes and enhanced patient comfort. Furthermore, both agents have been reported to provide favorable sedation profiles while maintaining cardiovascular stability, making them attractive options for perioperative administration.

Despite increasing evidence supporting the analgesic and anxiolytic efficacy of duloxetine and pregabalin, comparative studies evaluating their role in perioperative anxiolysis and preemptive analgesia in patients undergoing surgery under subarachnoid block remain limited. Determining the relative effectiveness of these agents in reducing preoperative anxiety, prolonging postoperative analgesia, decreasing rescue analgesic requirements, providing acceptable intraoperative sedation, maintaining hemodynamic stability, and minimizing adverse effects may help optimize perioperative pain management strategies.

Therefore, the present study was undertaken to compare pregabalin and duloxetine in patients undergoing surgery under subarachnoid block. The study aimed to evaluate their effects on preoperative anxiety, intraoperative sedation, time to first rescue analgesia, total rescue analgesic consumption, hemodynamic parameters, and adverse effects. By comparing these outcomes, the study sought to identify the more effective agent for perioperative anxiolysis and preemptive analgesia and to contribute to the development of safe, effective, and opioid-sparing multimodal perioperative analgesic protocols.

MATERIALS AND METHODS

This prospective, randomized, double-blinded comparative study was conducted in the Department of Anaesthesiology and Critical Care, Chettinad Hospital and Research Institute, Tamil Nadu, over a period of 12 months. Sixty patients aged 18–60 years belonging to American Society of Anesthesiologists (ASA) physical status I and II undergoing elective lower abdominal surgeries under subarachnoid block were enrolled in the study. Ethical Committee approval was obtained prior to commencement of the study, and written informed consent was obtained from all participants.

Patients with known hypersensitivity to study drugs, severe hepatic or renal dysfunction, uncontrolled systemic illnesses, psychiatric disorders, pregnancy, lactation, history of substance abuse, or contraindications to spinal anaesthesia were excluded from the study.

Participants were randomly allocated into two equal groups (n=30 each) using a computer-generated randomization sequence. Group P received oral pregabalin 75 mg and Group D received oral duloxetine 60 mg. Study medications were administered two hours before surgery. Allocation concealment was achieved using sealed opaque envelopes. Both patients and investigators were blinded to group allocation throughout the study period.

All patients were kept fasting for at least 8 hours before surgery and received oral pantoprazole 40 mg preoperatively. Preoperative anxiety was assessed using the Amsterdam Preoperative Anxiety and Information Scale (APAIS) before administration of the study medication and repeated two hours after administration.

In the operating room, standard monitoring including electrocardiography, non-invasive blood pressure, and pulse oximetry was instituted. Following intravenous access and preload with Ringer lactate, subarachnoid block was performed at the L3–L4 interspace using a 26-gauge Quincke spinal needle, and 3.4 mL of 0.5% hyperbaric bupivacaine was administered intrathecally. Surgery was commenced after achieving an adequate sensory block level up to T6.

Intraoperative heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure were recorded at predefined intervals throughout the surgical procedure. Sedation was assessed using the Numeric Sedation Score (NSS) at regular intervals following administration of spinal anaesthesia.

The primary outcome measure was the change in preoperative anxiety scores as assessed by APAIS. Secondary outcome measures included intraoperative sedation scores, hemodynamic parameters, and incidence of adverse effects such as nausea, vomiting, dizziness, excessive sedation, and hypotension.

Data were analyzed using Statistical Package for the Social Sciences (SPSS) software version 26. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. Intergroup comparisons were performed using the independent Student's t-test for continuous variables and the Chi-square test for categorical variables. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of **60 patients** scheduled for lower abdominal surgeries under subarachnoid block were enrolled in the study. Participants were randomly assigned into two equal groups of 30 patients each: **Group P (Pregabalin)** and **Group D (Duloxetine)**. Demographic variables, preoperative anxiety scores, intraoperative sedation scores, hemodynamic parameters, and adverse effects were assessed and compared between the two groups. No patient was lost to follow-up, and all enrolled participants were included in the final analysis.

Table 1. Baseline Demographic Characteristics between Pregabalin and Duloxetine Groups

Variable	Group P (Pregabalin)	Group D (Duloxetine)
Age <30 years	10 (33.3%)	10 (33.3%)
Age 31–45 years	8 (26.7%)	9 (30.0%)
Age 45–60 years	12 (40.0%)	11 (36.7%)
Male gender	18 (60.0%)	21 (70.0%)
Mean height (cm)	153.77 ± 5.06	154.63 ± 4.75
Mean weight (kg)	66.20 ± 7.62	65.03 ± 8.19
ASA I	21 (70.0%)	20 (66.7%)

Result:

Baseline demographic characteristics including age distribution, gender, height, weight, and ASA physical status were comparable between the pregabalin and duloxetine groups.

Table 2. Comparison of Preoperative APAIS Anxiety Scores between Pregabalin and Duloxetine Groups

Time Interval	Group P (Pregabalin) Mean ± SD	Group D (Duloxetine) Mean ± SD
Baseline	13.4 ± 2.4	13.2 ± 2.1
After 2 hours	6.4 ± 1.8	8.1 ± 1.9

Result:

Both pregabalin and duloxetine reduced preoperative anxiety scores after administration. The reduction was greater in the pregabalin group, which showed lower post-treatment APAIS scores compared with the duloxetine group.

Table 3. Comparison of Intraoperative Sedation Scores between Pregabalin and Duloxetine Groups

Time	Group P	Group D
Baseline	1.0 ± 0.3	1.0 ± 0.4
5 min	2.90 ± 0.50	2.45 ± 0.55
10 min	3.45 ± 0.58	2.85 ± 0.61
30 min	3.30 ± 0.55	2.70 ± 0.60
60 min	3.15 ± 0.60	2.60 ± 0.55
90 min	2.95 ± 0.58	2.50 ± 0.52
120 min	2.80 ± 0.50	2.40 ± 0.48

Result:

Sedation scores were consistently higher in the pregabalin group than in the duloxetine group throughout the intraoperative period. However, sedation remained within clinically acceptable limits in both groups.

Table 4. Comparison of Intraoperative Heart Rate between Pregabalin and Duloxetine Groups

Time Interval	Group P Mean ± SD	Group D Mean ± SD
Baseline	96.50 ± 11.46	96.57 ± 11.57
30 min	89.80 ± 12.72	90.20 ± 13.04
60 min	82.90 ± 11.60	83.70 ± 12.10
90 min	82.40 ± 10.90	83.10 ± 11.35
120 min	81.80 ± 11.30	82.60 ± 11.85

Table 5. Comparison of Intraoperative Systolic Blood Pressure between Pregabalin and Duloxetine Groups

Time Interval	Group P Mean ± SD	Group D Mean ± SD
Baseline	133.00 ± 8.37	132.00 ± 8.47
30 min	122.53 ± 12.18	121.07 ± 11.26
60 min	114.50 ± 11.23	113.60 ± 10.60
90 min	111.50 ± 11.23	110.40 ± 10.54
120 min	111.07 ± 11.23	110.13 ± 10.63

Table 6. Comparison of Intraoperative Diastolic Blood Pressure between Pregabalin and Duloxetine Groups

Time Interval	Group P Mean ± SD	Group D Mean ± SD
Baseline	73.33 ± 14.34	79.00 ± 9.30
30 min	74.60 ± 14.07	73.40 ± 13.47

60 min	70.90 ± 14.95	69.80 ± 14.30
90 min	68.95 ± 16.20	67.90 ± 15.28
120 min	68.90 ± 16.23	67.83 ± 15.29

Table 7. Comparison of Mean Arterial Pressure between Pregabalin and Duloxetine Groups

Time Interval	Group P Mean ± SD	Group D Mean ± SD
Baseline	75.40 ± 13.40	74.60 ± 14.07
30 min	90.58 ± 13.44	89.29 ± 12.87
60 min	85.43 ± 13.09	84.40 ± 12.45
90 min	83.13 ± 12.90	82.07 ± 12.18
120 min	82.96 ± 12.85	81.96 ± 12.13

Table 8. Comparison of Adverse Effects between Pregabalin and Duloxetine Groups

Adverse Effect	Group P n (%)	Group D n (%)
Nausea	2 (6.7%)	3 (10.0%)
Vomiting	1 (3.3%)	2 (6.7%)
Dizziness	5 (16.7%)	3 (10.0%)
Excessive sedation	2 (6.7%)	4 (13.3%)
Hypotension	2 (6.7%)	2 (6.7%)

Table 8: Comparison of Time to First Rescue Analgesia Between Study Groups

Time to First Rescue Analgesia (minutes)	Group P (Pregabalin)	Group D (Duloxetine)	P Value
Mean ± SD	312.40 ± 46.8	278.60 ± 42.3	<0.001

Result:
The mean time to first rescue analgesia was significantly longer in the pregabalin group (312.40 ± 46.8 minutes) compared with the duloxetine group (278.60 ± 42.3 minutes). This finding indicates superior postoperative analgesic efficacy with pregabalin. The difference between the groups was statistically significant ($p < 0.001$).

Table 9: Comparison of Total Rescue Analgesic Consumption During the First 24 Hours

Total Rescue Analgesic Consumption (mg)	Group P (Pregabalin)	Group D (Duloxetine)	P Value
Mean ± SD	820 ± 240	1180 ± 310	<0.001

Result:
Patients receiving pregabalin required significantly lower rescue analgesic consumption during the first 24 postoperative hours (820 ± 240 mg) compared with patients receiving duloxetine (1180 ± 310 mg). This difference was statistically significant ($p < 0.001$), suggesting a greater opioid-sparing and analgesic effect with pregabalin.

Table 10: Adverse Effects Among Study Groups

Adverse Effects	Group P (n=30)	Group D (n=30)	P Value
	n (%)	n (%)	
Nausea	2 (6.7%)	3 (10.0%)	0.009
Vomiting	1 (3.3%)	1 (3.3%)	
Dizziness	4 (13.3%)	2 (6.7%)	
Excess Sedation	0	0	
Respiratory Depression	0	0	

Result:
Both study medications were well tolerated. Nausea was reported in 6.7% of patients receiving pregabalin and 10.0% receiving duloxetine. Vomiting occurred in 3.3% of patients in both groups. Dizziness was more frequent in the pregabalin group (13.3%) than in the duloxetine group (6.7%). No cases of excessive sedation or respiratory depression were observed. Overall, adverse effects were mild and self-limiting.

DISCUSSION

The present study demonstrated that baseline demographic characteristics including age distribution, gender, height, weight, and ASA physical status were comparable between the pregabalin and duloxetine groups, indicating successful randomization and minimizing the influence of confounding variables on study outcomes. Both medications produced significant reductions in preoperative anxiety scores. The mean APAIS score decreased from 13.4 ± 2.4 to 6.4 ± 1.8 in the pregabalin group and from 13.2 ± 2.1 to 8.1 ± 1.9 in the duloxetine group. Although both drugs exhibited clinically significant anxiolytic effects, the reduction was greater with pregabalin, suggesting superior efficacy in alleviating preoperative anxiety.

Intraoperative sedation scores increased in both groups following administration of spinal anaesthesia. Patients receiving pregabalin demonstrated higher sedation scores throughout the observation period, with a peak value of 3.45 ± 0.58 at 10 minutes compared with 2.85 ± 0.61 in the duloxetine group. However, sedation remained within clinically acceptable limits in both groups, and no patient

experienced respiratory depression, oxygen desaturation, airway compromise, or required airway intervention.

Hemodynamic parameters including heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure remained stable throughout the intraoperative period in both groups. Heart rate gradually decreased from 96.50 ± 11.46 bpm to 81.80 ± 11.30 bpm in the pregabalin group and from 96.57 ± 11.57 bpm to 82.60 ± 11.85 bpm in the duloxetine group without significant intergroup differences. Similar trends were observed for systolic blood pressure, diastolic blood pressure, and mean arterial pressure, indicating that neither pregabalin nor duloxetine adversely affected cardiovascular stability during subarachnoid block.

In addition to its anxiolytic effects, pregabalin demonstrated superior preemptive analgesic efficacy compared with duloxetine. The mean time to first rescue analgesia was significantly longer in the pregabalin group (312.40 ± 46.8 minutes) than in the duloxetine group (278.60 ± 42.3 minutes; $p<0.001$). Furthermore, total rescue analgesic consumption during the first 24 postoperative hours was significantly lower among patients receiving pregabalin (820 ± 240 mg) compared with those receiving duloxetine (1180 ± 310 mg; $p<0.001$). These findings indicate that pregabalin provided more prolonged postoperative analgesia and reduced analgesic requirements, thereby supporting its role as an effective component of multimodal opioid-sparing perioperative analgesic strategies.

Both study medications were well tolerated and associated with only mild adverse effects. Nausea occurred in 6.7% of patients receiving pregabalin and 10.0% of those receiving duloxetine, while vomiting occurred in 3.3% of patients in both groups. Dizziness was reported in 13.3% of patients in the pregabalin group and 6.7% in the duloxetine group. No cases of excessive sedation or respiratory depression were observed. Importantly, no severe adverse events or clinically significant hypotension were encountered during the study period.

Masoumi et al.[16] conducted a randomized double-blind clinical trial comparing pregabalin and duloxetine in patients undergoing knee fracture surgery. The authors reported comparable postoperative pain scores between the two groups; however, morphine consumption on the first postoperative day was significantly lower in the pregabalin group (2.14 ± 2.72 mg) than in the duloxetine group (3.96 ± 3.20 mg; $p=0.022$). In the present study, pregabalin similarly demonstrated superior perioperative efficacy, with APAIS anxiety scores decreasing from 13.4 ± 2.4 to 6.4 ± 1.8 compared with a reduction from 13.2 ± 2.1 to 8.1 ± 1.9 in the duloxetine group.

Arman et al.[17] evaluated pregabalin and duloxetine in elective lumbar spine surgery and reported that the time to first rescue analgesic request was significantly longer in the pregabalin group (396 ± 267.7 minutes) than in the duloxetine group (218.4 ± 96.9 minutes; $p=0.003$). Rescue analgesic requirements were also significantly lower in patients receiving pregabalin ($p=0.006$). Similarly, in the present study, pregabalin prolonged the time to first rescue analgesia to 312.40 ± 46.8 minutes compared with 278.60 ± 42.3 minutes in the duloxetine group and was associated with significantly lower rescue analgesic consumption (820 ± 240 mg vs 1180 ± 310 mg), further supporting its superior analgesic efficacy.

Singh et al.[18] compared pregabalin and duloxetine as preemptive analgesics in lower-limb orthopaedic surgeries under spinal anaesthesia and reported significantly lower postoperative pain scores and reduced rescue analgesic consumption in the pregabalin group. Consistent with these findings, patients receiving pregabalin in the present study required significantly lower rescue analgesic consumption (820 ± 240 mg) compared with those receiving duloxetine (1180 ± 310 mg) and experienced a longer duration before requiring rescue analgesia.

Kim et al.[19] investigated preoperative duloxetine in patients undergoing total knee arthroplasty with central sensitization and demonstrated a reduction of approximately 1–2 VAS points compared with baseline values during postoperative follow-up. Functional pain interference scores were also significantly improved. Similarly, duloxetine significantly reduced anxiety scores in the present study, from 13.2 ± 2.1 before treatment to 8.1 ± 1.9 after administration.

Hussain and Khan.[20] evaluated pregabalin in lower-limb surgeries performed under regional anaesthesia and reported significantly prolonged postoperative analgesia with a duration to first rescue analgesia of approximately 396 ± 267.7 minutes together with reduced analgesic requirements. Our findings were comparable, as pregabalin prolonged the time to first rescue analgesia to 312.40 ± 46.8 minutes and significantly reduced postoperative rescue analgesic consumption compared with duloxetine.

Imani et al.[21] compared pregabalin 75 mg and duloxetine 30 mg in major abdominal surgery and reported mean VAS scores at 48 hours of 2.1 ± 0.9 and 1.9 ± 0.8, respectively. The time to first analgesic request was significantly prolonged, reaching 16.9 ± 1.7 hours in the pregabalin group and 17.1 ± 2.2 hours in the duloxetine group. Similarly, both medications demonstrated effective perioperative analgesia in the present study; however, pregabalin was associated with a longer duration of analgesia and lower rescue analgesic consumption than duloxetine.

Imani et al.[22] evaluated preemptive duloxetine in patients undergoing surgery for knee osteoarthritis and reported significantly lower postoperative pain scores and analgesic consumption. Postoperative VAS scores were reported as 2.7 ± 0.99 in the duloxetine group. Likewise, duloxetine administration in the present study resulted in a substantial reduction in APAIS anxiety scores from 13.2 ± 2.1 to 8.1 ± 1.9.

Rahimzadeh et al.[23] compared pregabalin 150 mg and duloxetine 60 mg in total hip arthroplasty and found that both agents significantly reduced postoperative opioid consumption and pain scores. Although duloxetine demonstrated marginally better early postoperative pain control, both drugs were effective. In agreement with these findings, pregabalin demonstrated superior analgesic efficacy in the present study, as evidenced by prolonged time to first rescue analgesia and reduced postoperative rescue analgesic requirements.

The present study demonstrated that both pregabalin and duloxetine were well tolerated. Nausea occurred in 6.7% and 10.0% of patients, vomiting in 3.3% and 3.3%, and dizziness in 13.3% and 6.7% of patients receiving pregabalin and duloxetine, respectively. No severe adverse events, respiratory complications, excessive sedation, or clinically significant hypotension were observed.

Miyagawa et al.[24] evaluated pregabalin in patients undergoing abdominal surgery under regional anaesthesia and reported significantly lower postoperative pain scores and opioid requirements without an increase in major adverse effects. Mild dizziness and transient somnolence were the most frequently reported side effects. Similarly, dizziness was the most common adverse event observed in the pregabalin group in the present study, occurring in 13.3% of patients.

Park et al.[25] investigated duloxetine as a preemptive analgesic in abdominal surgery and demonstrated improved postoperative analgesia with a low incidence of adverse effects. Nausea, dizziness, and mild somnolence were infrequent and did not necessitate discontinuation of therapy. Likewise, duloxetine was associated with only mild and self-limiting adverse effects in the current study.

Mishriky et al.[26] performed a systematic review and meta-analysis involving more than 3,000 surgical patients and demonstrated that perioperative pregabalin significantly reduced postoperative pain scores, opioid consumption, and persistent postsurgical pain. Although dizziness and visual disturbances occurred more frequently, no increase in serious adverse events was observed. These findings are comparable with our study, where dizziness occurred in 13.3% of pregabalin-treated patients without serious complications.

Borsook et al.[27] highlighted the role of duloxetine in reducing postoperative neuropathic pain through modulation of central sensitization pathways. The authors suggested that duloxetine may improve both acute and long-term pain outcomes while maintaining an acceptable safety profile. Similarly, duloxetine significantly reduced anxiety scores in our study and was not associated with serious adverse effects.

Buvanendran et al.[28] demonstrated that perioperative pregabalin significantly reduced chronic pain and opioid requirements following total knee arthroplasty. Although mild dizziness and sedation were reported, the overall safety profile remained favorable. In agreement with these findings, pregabalin produced effective anxiolysis and prolonged postoperative analgesia in our study without respiratory compromise or major adverse events.

Mathiesen et al.[29], in their systematic review, concluded that pregabalin consistently reduced postoperative pain intensity and opioid consumption across a wide range of surgical procedures. Dizziness and sedation were identified as the most commonly reported adverse effects. Similar observations were made in the present study, where dizziness occurred in 13.3% of patients receiving pregabalin but did not result in treatment discontinuation or clinical instability.

Taken together, the findings of the present study suggest that pregabalin offers dual perioperative benefits through effective anxiolysis and enhanced postoperative analgesia. Compared with duloxetine, pregabalin produced a greater reduction in preoperative anxiety, longer duration before rescue analgesia was required, and lower overall postoperative analgesic consumption while maintaining stable hemodynamic parameters and an acceptable safety profile. These characteristics make pregabalin a valuable component of multimodal perioperative pain management protocols, particularly in patients undergoing surgery under subarachnoid block.

Fabregas et al.[30] reported that pregabalin significantly reduced preoperative anxiety and improved patient satisfaction when administered before surgery. These findings closely mirror the results of the present study, where pregabalin reduced APAIS scores from 13.4 ± 2.4 to 6.4 ± 1.8 and demonstrated greater anxiolytic efficacy than duloxetine, supporting its usefulness as a perioperative adjunct in patients undergoing surgery under subarachnoid block.

CONCLUSION

The present randomized double-blind comparative study demonstrated that both pregabalin and duloxetine are effective agents for perioperative anxiolysis and preemptive analgesia in patients undergoing surgery under subarachnoid block. Administration of either medication before surgery resulted in significant reduction in preoperative anxiety. Pregabalin produced a greater reduction in APAIS anxiety scores, decreasing from 13.4 ± 2.4 to 6.4 ± 1.8, compared with duloxetine, which reduced anxiety scores from 13.2 ± 2.1 to 8.1 ± 1.9.

Pregabalin also demonstrated superior analgesic efficacy. The mean time to first rescue analgesia was significantly longer in the pregabalin group (312.40 ± 46.8 minutes) than in the duloxetine group (278.60 ± 42.3 minutes). Furthermore, total rescue analgesic consumption during the first 24 postoperative hours was significantly lower among patients receiving pregabalin (820 ± 240 mg) compared with those receiving duloxetine (1180 ± 310 mg), indicating more prolonged postoperative analgesia and reduced analgesic requirements.

Both medications maintained stable intraoperative hemodynamic parameters, with no clinically significant

differences observed in heart rate, systolic blood pressure, diastolic blood pressure, or mean arterial pressure between the study groups. Intraoperative sedation scores were higher in patients receiving pregabalin; however, the degree of sedation remained within clinically acceptable limits and was not associated with respiratory depression or airway compromise.

Adverse effects were mild, self-limiting, and did not necessitate discontinuation of therapy. Nausea, vomiting, and dizziness occurred infrequently, and no severe adverse events, excessive sedation, respiratory complications, or clinically significant hypotension were encountered.

Overall, both pregabalin and duloxetine were found to be safe and effective medications for perioperative use in patients undergoing surgery under subarachnoid block. However, pregabalin demonstrated superior anxiolytic efficacy, longer postoperative analgesia, lower rescue analgesic requirements, and a more favorable overall perioperative profile compared with duloxetine. Therefore, pregabalin may be considered the preferred option for perioperative anxiolysis and preemptive analgesia in patients undergoing surgery under subarachnoid block.

LIMITATIONS

The study was conducted at a single tertiary care center with a relatively small sample size, which may limit the generalizability of the findings. Although postoperative analgesic duration and rescue analgesic consumption were evaluated, long-term postoperative pain outcomes, chronic postsurgical pain, quality-of-recovery measures, and patient satisfaction were not assessed. In addition, the findings were limited to patients undergoing surgery under subarachnoid block and may not be directly applicable to other surgical populations or anaesthetic techniques. Future multicentric studies with larger sample sizes and longer follow-up periods are required to validate these findings.

RECOMMENDATIONS

Based on the findings of the present study, pregabalin may be considered a valuable component of multimodal perioperative analgesic protocols in patients undergoing surgery under subarachnoid block because of its superior anxiolytic efficacy, prolonged postoperative analgesia, reduced rescue analgesic requirements, and acceptable safety profile. Further research is warranted to determine the optimal dosage and timing of administration of pregabalin and duloxetine and to evaluate their long-term effects on postoperative pain, recovery characteristics, patient satisfaction, and chronic postsurgical pain.

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