

Original Research Article

Comparative evaluation of perioperative multimodal analgesia and single-bolus epidural analgesia in lower abdominal surgery: a randomized controlled study

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ABSTRACT

Background: Effective postoperative pain management is essential for enhanced recovery after lower abdominal surgeries. While epidural analgesia has been widely used, multimodal analgesia offers a less invasive, opioid-sparing alternative. This study aimed to compare perioperative multimodal analgesia using pregabalin, nefopam, and paracetamol with epidural analgesia in terms of analgesic efficacy and recovery outcomes.

Methods: This prospective, randomized, single-blind study included 70 female patients (ASA I-II) undergoing lower abdominal surgeries under general anesthesia. Patients were allocated into two groups: Group A (multimodal analgesia) and group B (epidural analgesia). Postoperative pain (VAS score), hemodynamic parameters, time to first rescue analgesia, total rescue analgesic requirement, adverse effects, and time to ambulation were recorded over 24 hours. Statistical analysis was performed using independent t test and Fisher's exact test.

Results: Baseline characteristics were comparable between groups. The multimodal group demonstrated significantly lower early postoperative pain scores and prolonged time to first rescue analgesia (147±94 vs 107±72 minutes, $p=0.049$). Fewer patients required ≥ 3 rescue doses (17.1% vs 40.0%). Hemodynamic parameters were largely comparable, although episodic elevations were observed in the epidural group. Time to ambulation was significantly shorter in the multimodal group (34.83±5.10 vs 37.94±5.25 hours, $p=0.014$). Adverse effects such as nausea, headache, and shivering were more frequent in the epidural group, though not statistically significant.

Conclusions: Perioperative multimodal analgesia provides effective pain control, reduces analgesic requirements, and facilitates earlier ambulation compared to epidural analgesia. It represents a safe, practical, and effective alternative for postoperative pain management in lower abdominal surgeries.

Keywords: Multimodal analgesia, Epidural analgesia, Postoperative pain, Lower abdominal surgery, Visual analogue scale, Analgesic consumption, Early ambulation, Perioperative care

INTRODUCTION

Effective perioperative pain management remains a central goal of contemporary anaesthetic practice, particularly in patients undergoing lower abdominal surgery, in whom inadequately controlled pain can delay

recovery and contribute to adverse postoperative outcomes. Surgical injury triggers nociceptive, neuroendocrine, and inflammatory responses that may lead to impaired pulmonary function, thromboembolic risk, delayed mobilization, prolonged convalescence, and increased healthcare utilization. Despite advances in

perioperative care, postoperative pain continues to be undertreated in a substantial proportion of patients; in a landmark survey, approximately 80% of patients reported postoperative pain, and most described it as moderate to extreme in intensity.^{1,2}

Epidural analgesia has long been considered a highly effective technique for perioperative and postoperative analgesia in abdominal surgery because it provides superior segmental pain relief and can attenuate the surgical stress response. Meta-analytic evidence has shown that postoperative epidural analgesia offers better pain control than parenteral opioid-based regimens, and additional studies have suggested benefits for selected postoperative outcomes, including pulmonary complications and recovery-related parameters.^{3,4} However, epidural analgesia is not without limitations. Catheter placement is technically demanding, hemodynamic instability such as hypotension may occur, and its use can be constrained by contraindications, resource availability, and the need for close monitoring.^{5,6}

In parallel, multimodal analgesia has become a major principle of perioperative pain management. By combining agents with different mechanisms of action, multimodal regimens aim to improve analgesia while reducing opioid exposure and opioid-related adverse effects. Contemporary guidelines continue to recommend multimodal analgesia as a core perioperative strategy, and recent reviews reaffirm its role in enhancing recovery pathways and supporting opioid-sparing postoperative care.⁵⁻⁷ Within such regimens, pregabalin has been associated with reduced postoperative analgesic requirements and opioid consumption, paracetamol has demonstrated opioid-sparing effects, and nefopam has shown value as a non-opioid adjuvant with early postoperative analgesic benefit.⁸⁻¹²

Although both epidural and multimodal strategies are widely used, the comparative evidence base remains incomplete for many common surgical settings. Recent work illustrates this uncertainty rather than resolving it. In a 2024 randomized trial after laparoscopic gastrectomy, epidural analgesia provided better early pain relief than patient-controlled intravenous analgesia, but postoperative recovery parameters were broadly similar and epidural-related hypotension was more frequent.⁶ Likewise, a 2025 systematic review and meta-analysis in major abdominal surgery found that epidural analgesia was associated with better pain relief during the first 24 hours than intravenous lidocaine, while emphasizing heterogeneity across studies and the need for further standardized trials.¹³ These findings suggest that while epidural analgesia remains effective, the optimal balance between analgesic efficacy, hemodynamic stability, adverse effects, and functional recovery is still uncertain.

This knowledge gap is especially relevant in lower abdominal surgery, where early ambulation, stable postoperative physiology, and reduction in rescue

analgesic requirement are clinically meaningful endpoints. Moreover, in high-volume and resource-constrained settings, a non-neuraxial multimodal regimen that is easier to administer and less invasive than epidural analgesia could offer practical advantages if comparable or superior perioperative outcomes are achieved. However, data directly comparing pregabalin-nefopam-paracetamol-based perioperative multimodal regimen with epidural analgesia in this context remain limited.

Against this background, the present study was undertaken to compare perioperative multimodal analgesia using pregabalin, nefopam hydrochloride, and paracetamol with epidural analgesia in women undergoing lower abdominal surgeries under general anaesthesia. The primary objective was to evaluate postoperative analgesic efficacy, including perioperative antinociception, postoperative pain intensity, and rescue analgesic requirement. The secondary objective was to compare early postoperative ambulation and related recovery outcomes between the two groups.

METHODS

Study design and setting

This prospective, randomized, controlled, parallel-group, single-blind study was conducted in the Department of Anaesthesiology, at tertiary care hospital, over a period of one year (02 January 2021 to 01 January 2022), after obtaining approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants prior to enrolment. Patient confidentiality was strictly maintained, and all data were used solely for research purposes. The study flow including patient enrolment, randomization, allocation, follow-up, and analysis is illustrated in Figure 1.

Study participants

Adult female patients aged 20-70 years, belonging to the American Society of Anesthesiologists (ASA) physical status I or II, and scheduled to undergo elective lower abdominal surgeries under general anaesthesia were included in the study. Patients who refused consent, were pregnant, had a history of drug abuse/ seizures, belonged to ASA physical status III/ IV, had significant cardiovascular, hepatic, pulmonary, renal, haematological, neurological/ psychiatric illness, had known hypersensitivity to any of the study drugs, had a history of drug/ alcohol abuse within the preceding year, had pre-existing acute/ chronic pain/ had undergone abdominal or any other surgery within the preceding 3 months were excluded.

Sample size calculation

The sample size was calculated based on expected difference in visual analog scale (VAS) pain scores between the two groups. Assuming a standard deviation

of 3.76, a minimum clinically significant difference of 0.75, type I error (α) of 5%, and power of 90% ($\beta=10\%$), the required sample size was calculated to be 32 patients

per group. Considering a potential dropout rate of 10%, a total of 35 patients were included in each group.

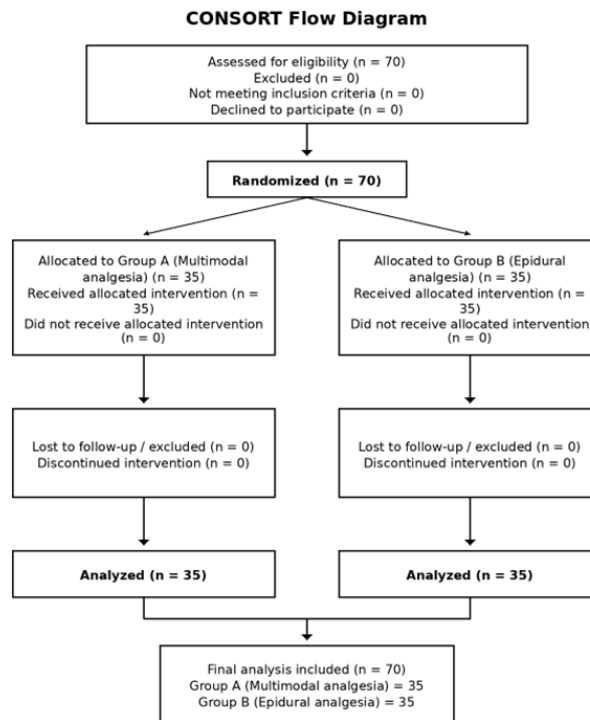


Figure 1: CONSORT flow diagram of participant enrolment, allocation, follow-up and analysis.

Randomization and blinding

Participants were randomly allocated in a 1:1 ratio to either the multimodal analgesia group (Group A) or the epidural analgesia group (Group B) using a computer-generated random sequence. The randomization sequence was generated by an independent investigator not involved in patient enrolment or outcome assessment. Allocation concealment was ensured using sequentially numbered, opaque, sealed envelopes, which were opened only after patient enrolment. The study was conducted in a single-blind manner. Patients were blinded to group allocation. Due to the nature of the interventions, the anesthesiologists performing the procedure could not be blinded. However, postoperative outcome assessments were carried out by an investigator who was blinded to group allocation to minimize assessment bias.

Study groups and interventions

Patients were divided into two groups:

Group A (Multimodal analgesia group)

Patients received oral pregabalin 75 mg with sips of water 2 hours prior to surgery. In the operating room, intravenous access was secured and 500 mL of 0.9% normal saline containing nefopam hydrochloride 20 mg was infused. Additionally, intravenous paracetamol 1 g

was administered. Standard monitoring including electrocardiography, non-invasive blood pressure, pulse oximetry, and end-tidal CO₂ monitoring was instituted.

Group B (Epidural analgesia group)

In the operating room, intravenous access was secured and 500 mL of 0.9% normal saline was infused. Epidural catheterization was performed under strict aseptic precautions at the lumbar interspace using the loss-of-resistance technique. After confirming correct placement with a test dose of lignocaine with adrenaline, a bolus of 10 mL of 0.125% bupivacaine was administered. Standard monitoring was instituted as in group A.

Anaesthetic technique

In both groups, general anaesthesia was administered using a standardized protocol. Anaesthesia was induced with fentanyl (1-2 µg/kg), propofol (2-3 mg/kg), and vecuronium bromide (0.1 mg/kg), followed by endotracheal intubation. Anaesthesia was maintained with nitrous oxide in 40% oxygen, sevoflurane, and intermittent vecuronium. Ondansetron (0.1 mg/kg) was administered 20 minutes prior to completion of surgery. At the end of surgery, neuromuscular blockade was reversed and patients were extubated and shifted to the postoperative ward.

Postoperative monitoring and pain assessment

Postoperatively, patients were monitored for haemodynamic stability and analgesia for 24 hours. Pain was assessed using the VAS, where 0 indicated no pain and 10 indicated the worst imaginable pain. Pain assessments were performed every 5 minutes during the first hour, every 2 hours for the next 12 hours, and every 4 hours thereafter up to 24 hours. Rescue analgesia was administered when the VAS score exceeded 4, in the form of intramuscular diclofenac 75 mg. The time to first rescue analgesia and total number of rescue doses administered within 24 hours were recorded.

Outcome measures

The primary outcome was postoperative analgesic efficacy, assessed by VAS pain scores and time to first rescue analgesia. Secondary outcomes included total rescue analgesic requirement within 24 hours, time to ambulation, and postoperative haemodynamic parameters (heart rate, systolic and diastolic blood pressure, and mean arterial pressure). The incidence of postoperative adverse effects, including nausea/vomiting, headache, shivering, respiratory difficulty, and itching, was also recorded. Outcome assessment was performed by an investigator blinded to group allocation.

Statistical analysis

Statistical analysis was performed using SPSS version 21.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean $\pm$ standard deviation (SD), and categorical variables as number (percentage). Between-group comparisons for continuous variables were performed using the independent-samples Student's t-test. Categorical variables were analyzed using Fisher's exact test where appropriate. All statistical tests were two-tailed, and a p value of less than 0.05 was considered statistically significant.

RESULTS

Baseline characteristics

A total of 70 patients were enrolled and equally allocated into group A (multimodal analgesia) and group B (epidural analgesia), with 35 patients in each group. Baseline demographic and anthropometric characteristics were assessed to ensure comparability between the two groups. The mean age of patients in group A and group B was 46.03 $\pm$ 8.81 years and 49.17 $\pm$ 8.70 years, respectively, with no statistically significant difference between the groups ($p=0.138$). The age range was comparable (30-70 years in group A vs 32-70 years in group B). With respect to body mass index (BMI), the majority of patients in both groups belonged to the normal BMI category (68.6% in group A vs 54.3% in group B), while the remaining patients were overweight. The distribution of

BMI categories did not differ significantly between the groups ($p=0.326$) (Table 1).

Hemodynamic parameters and pain scores

Hemodynamic parameters were largely comparable between 2 groups; however, at certain postoperative time points, statistically significant differences were observed (Table 2). Heart rate was significantly higher in group B compared to group A at 2 hours ($p=0.031$) and 3 hours ($p=0.045$). Systolic blood pressure was significantly higher in group B at 60 minutes ($p<0.001$), 3 hours ($p=0.003$), and 10 hours ($p=0.022$). Diastolic blood pressure showed significant differences at multiple postoperative time points, including 60 minutes, 2, 4, 6, 8, 10, 12, 16, and 20 hours, with values generally higher in group B ($p<0.05$ for all). Similarly, mean arterial pressure was significantly higher in group B at 60 minutes and at 2, 3, 4, 6, 10, 12, 16, and 20 hours postoperatively ($p<0.05$ for all). Pain assessment using VAS scores revealed significantly higher pain scores in group B during early postoperative period at 40 minutes ($p=0.002$), 45 minutes ($p<0.001$), and 50 minutes ($p=0.018$). At 20 hours, however, VAS scores were slightly higher in group A ($p=0.040$). The temporal trend of postoperative pain scores in both groups (Figure 2).

Primary and secondary outcomes

Primary and secondary perioperative outcomes is depicted in table 3. The mean time to first rescue analgesia was significantly longer in group A compared to group B (147 $\pm$ 94 minutes vs 107 $\pm$ 72 minutes; $p=0.049$), indicating prolonged analgesic effect in the multimodal analgesia group. A higher proportion of patients in group A required ≤ 2 rescue analgesic doses within 24 hours (82.9% vs 60.0%), whereas a greater proportion of patients in group B required ≥ 3 doses (40.0% vs 17.1%); however, this difference did not reach statistical significance on exact testing ($p=0.063$). The mean time to ambulation was significantly shorter in group A compared to group B (34.83 $\pm$ 5.10 hours vs 37.94 $\pm$ 5.25 hours; $p=0.014$), indicating earlier postoperative recovery in the multimodal analgesia group.

Postoperative adverse effects

Postoperative adverse effects for the study groups are summarized in table 4. Postoperative adverse effects were more frequently observed in group B compared to group A. Nausea/vomiting was reported in 60.0% of patients in group B compared to 37.1% in group A ($p=0.093$), while headache was observed in 42.9% and 25.7% of patients, respectively ($p=0.208$). Shivering occurred only in group B (11.4%) and was not observed in group A; however, this difference was not statistically significant ($p=0.114$). No cases of respiratory difficulty or itching were reported in either group. Adverse effects were higher in Group B, none of the differences reached statistical significance.

Effect size analysis of key outcomes

The key perioperative outcomes with effect estimates are presented in Table 5. Effect size analysis demonstrated clinically meaningful differences between 2 groups. Time to first rescue analgesia was prolonged by 40 min in group A compared to group B (95% CI: 0.2 to 79.8; $p=0.049$). Risk of requiring ≥ 3 rescue analgesic doses

was reduced by 22.9% in group A compared to B (95% CI: -44.8% to -1.0%; $p=0.063$). Time to ambulation was reduced by 3.11 hrs in group A (95% CI: -5.55 to -0.67; $p=0.014$). Additionally, incidence of nausea/ vomiting, headache, and shivering was lower in group A, although these differences were not statistically significant, as reflected by confidence intervals crossing zero.

Table 1: Baseline characteristics of the study groups.

Variables	Group A, (n=35)	Group B, (n=35)	Statistical test	P value
Age (in years)	46.03 $\pm$ 8.81	49.17 $\pm$ 8.70	T=1.502	0.138
Age (in years) range,	30-70	32-70	-	-
BMI 18.5-24.9 kg/m ² , (%)	24 (68.6)	19 (54.3)	Fisher's exact test	0.326
BMI 25.0-29.9 kg/m ² , (%)	11 (31.4)	16 (45.7)		

*Group A: Multimodal analgesia group; Group B: Epidural analgesia group. BMI: Body mass index. Independent t-test was used for comparison of continuous variables and Fisher's exact test for categorical variables

Table 2: Comparison of hemodynamic parameters and VAS pain scores at time points.

Parameters	Time point	Group A (n=35)	Group B (n=35)	T value	P value
Heart rate (beats/min)	2 h	84.80 $\pm$ 8.03	88.80 $\pm$ 7.12	-2.205	0.031
	3 h	82.26 $\pm$ 7.48	88.14 $\pm$ 15.29	-2.045	0.045
Systolic blood pressure (mmHg)	60 min	122.77 $\pm$ 5.86	129.34 $\pm$ 6.30	-4.519	<0.001
	3 h	126.57 $\pm$ 6.07	130.69 $\pm$ 5.22	-3.040	0.003
	10 h	123.26 $\pm$ 6.26	126.63 $\pm$ 5.73	-2.349	0.022
Diastolic blood pressure (mmHg)	60 min	79.14 $\pm$ 2.71	85.51 $\pm$ 6.34	-5.466	<0.001
	2 h	89.09 $\pm$ 2.72	97.77 $\pm$ 2.03	-15.154	<0.001
	4 h	91.11 $\pm$ 3.22	98.54 $\pm$ 2.50	-10.788	<0.001
	6 h	76.54 $\pm$ 3.48	88.37 $\pm$ 2.51	-16.298	<0.001
	8 h	79.80 $\pm$ 4.87	75.91 $\pm$ 4.33	3.525	0.001
	10 h	77.54 $\pm$ 2.49	86.89 $\pm$ 2.51	-15.648	<0.001
	12 h	89.17 $\pm$ 2.76	96.60 $\pm$ 2.89	-10.993	<0.001
	16 h	77.29 $\pm$ 5.41	83.34 $\pm$ 3.61	-5.508	<0.001
	20 h	88.34 $\pm$ 2.68	98.14 $\pm$ 2.66	-15.364	<0.001
	60 min	93.63 $\pm$ 2.61	100.11 $\pm$ 4.74	-7.090	<0.001
Mean arterial pressure (mmHg)	2 h	101.57 $\pm$ 2.50	108.26 $\pm$ 2.47	-11.264	<0.001
	3 h	94.77 $\pm$ 4.85	98.11 $\pm$ 5.09	-2.815	0.006
	4 h	101.60 $\pm$ 3.11	107.31 $\pm$ 2.60	-8.345	<0.001
	6 h	90.71 $\pm$ 2.95	99.34 $\pm$ 2.63	-12.917	<0.001
	10 h	92.74 $\pm$ 2.72	100.17 $\pm$ 2.37	-12.194	<0.001
	12 h	100 $\pm$ 2.84	105.34 $\pm$ 2.58	-8.244	<0.001
	16 h	92.37 $\pm$ 4.56	96.23 $\pm$ 3.15	-4.113	<0.001
	20 h	97.77 $\pm$ 3.35	105.46 $\pm$ 3.09	-9.972	<0.001
VAS pain score	40 min	1.26 $\pm$ 1.09	2.20 $\pm$ 1.37	-3.185	0.002
	45 min	1.89 $\pm$ 0.58	2.66 $\pm$ 0.68	-5.081	<0.001
	50 min	2.14 $\pm$ 0.77	2.60 $\pm$ 0.81	-2.414	0.018
	20 h	1.23 $\pm$ 0.55	1.00 $\pm$ 0.34	2.095	0.040

*Values are presented as mean $\pm$ standard deviation. Group A: Multimodal analgesia group; Group B: Epidural analgesia group. VAS: Visual analogue scale; HR: Heart rate; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; MAP: Mean arterial pressure. Independent t-test was used for comparison between groups.

Table 3: Summary of primary and secondary perioperative outcomes.

Outcome	Group A (n=35)	Group B (n=35)	Statistical test	P value
Time to first rescue analgesia (min)	147 $\pm$ 94	107 $\pm$ 72	T=2.003	0.049
Patients requiring ≤ 2 rescue doses in 24 h, (%)	29 (82.9)	21 (60.0)	Fisher's exact test	0.063
Patients requiring ≥ 3 rescue doses in 24 h, (%)	6 (17.1)	14 (40.0)		
Time to ambulation (hr)	34.83 $\pm$ 5.10	37.94 $\pm$ 5.25	T=2.518	0.014

*Values are presented as mean $\pm$ standard deviation or number (%). Group A: Multimodal analgesia group; Group B: Epidural analgesia group. Independent t-test was used for comparison of continuous variables and Fisher's exact test for categorical variables.

Table 4: Postoperative adverse effects in the two study groups.

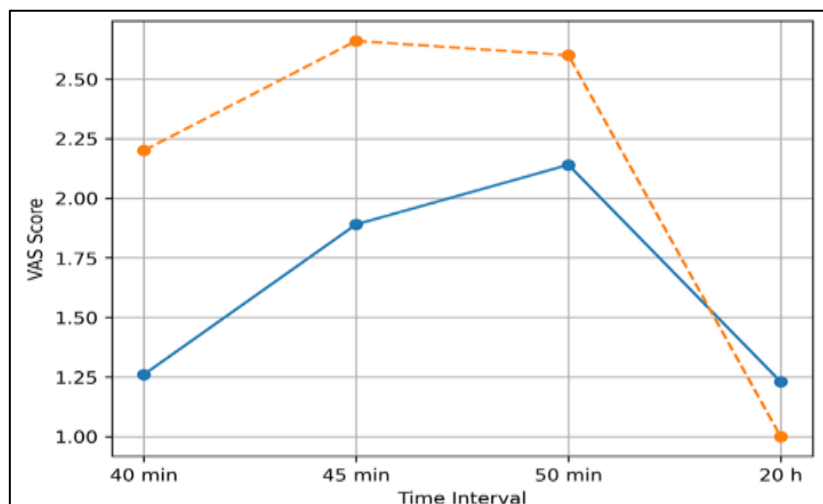
Adverse effect	Group A, (n=35) (%)	Group B, (n=35) (%)	Statistical test	P value
Nausea/vomiting	13 (37.1)	21 (60.0)	Fisher's exact test	0.093
Headache	9 (25.7)	15 (42.9)	Fisher's exact test	0.208
Shivering	0 (0.0)	4 (11.4)	Fisher's exact test	0.114
Respiratory difficulty	0 (0.0)	0 (0.0)	Not tested	-
Itching	0 (0.0)	0 (0.0)	Not tested	-

*Values are presented as number (%). Group A: Multimodal analgesia group; Group B: Epidural analgesia group. Fisher's exact test was used for comparison of categorical variables. Statistical analysis was not performed for outcomes with zero events in both groups.

Table 5: Summary of key perioperative outcomes with effect estimates.

Outcomes	Group A, (n=35)	Group B, (n=35)	Effect estimate, (A vs B)	95% CI	P value
Time to first rescue analgesia (min)	147±94	107±72	+40.0 min	0.2 to 79.8	0.049
Patients requiring ≥3 rescue doses	6 (17.1%)	14 (40.0%)	-22.9% (risk difference)	-44.8% to -1.0%	0.063
Time to ambulation (hours)	34.83±5.10	37.94±5.25	-3.11 h	-5.55 to -0.67	0.014
Nausea/vomiting	13 (37.1%)	21 (60.0%)	-22.9% (risk difference)	-45.5% to -0.3%	0.093
Headache	9 (25.7%)	15 (42.9%)	-17.2% (risk difference)	-39.2% to +4.8%	0.208
Shivering	0 (0.0%)	4 (11.4%)	-11.4% (risk difference)	-22.9% to +0.1%	0.114

*Values are presented as mean±SD or number (%). Group A: Multimodal analgesia group; Group B: Epidural analgesia group. Effect estimates are expressed as mean difference for continuous variables and risk difference for categorical variables. Independent t test was used for continuous variables and Fisher's exact test for categorical variables.

**Figure 2: Comparison of postoperative VAS pain scores between group A and Group B.**

*Line graph depicting mean VAS pain scores in Group A (multimodal analgesia) and Group B (epidural analgesia) at different postoperative time intervals. Group B demonstrated higher VAS scores during the early postoperative period (40-50 minutes), while scores were comparable at later time points.

DISCUSSION

The present study suggests that perioperative multimodal analgesia with pregabalin, nefopam, and paracetamol provided clinically meaningful advantages over the

epidural regimen used here, particularly in terms of early postoperative pain control, longer time to first rescue analgesia, reduced rescue analgesic requirement, and earlier ambulation, while maintaining acceptable safety. Baseline comparability between groups strengthens the

internal validity of these findings, and the overall pattern indicates that the multimodal strategy achieved effective perioperative antinociception without procedural burden of neuraxial catheterization. These findings are clinically relevant because poorly controlled postoperative pain is known to delay recovery, impair pulmonary function, increase thromboembolic risk, and prolong convalescence after surgery.¹

The comparable age and BMI distributions between groups are important because both variables can influence perioperative analgesic response, hemodynamics, and postoperative mobilization. A well-balanced baseline profile reduces the likelihood that differences in pain scores, rescue analgesic use, or ambulation were driven by confounding rather than by the analgesic strategy itself. This is particularly relevant in perioperative trials, where patient factors, procedure type, and analgesic technique can all modify postoperative recovery trajectories.⁵

The hemodynamic findings are also noteworthy. Although most perioperative values remained within clinically acceptable ranges, heart rate and blood pressure tended to be lower and more stable in the multimodal group at several postoperative time points. A plausible explanation is that better early pain control attenuated postoperative sympathetic activation. Surgical pain increases catecholamine release and cardiovascular stress, whereas effective antinociception blunts this response. Kehlet and Dahl emphasized that inadequately controlled postoperative pain contributes to physiologic stress and delayed recovery, and guideline-based multimodal analgesia aims precisely to reduce this stress response.¹ In the present setting, the multimodal approach may have provided more sustained non-opioid analgesic coverage during the early postoperative window, whereas the single-bolus epidural regimen may have been less durable over time.

The early postoperative VAS findings support the primary analgesic benefit of the multimodal regimen. Pain scores were lower during the early postoperative period in the multimodal group, which is consistent with the mechanistic rationale of combining agents acting at different levels of the pain pathway. Pregabalin reduces central sensitization and excitatory neurotransmitter release, paracetamol contributes central analgesic and opioid-sparing effects, and nefopam provides additional non-opioid antinociception through monoaminergic and glutamatergic modulation. This pharmacologic complementarity is one of the core principles underlying multimodal analgesia. Meta-analyses have shown that pregabalin can reduce postoperative opioid consumption and opioid-related adverse effects, while acetaminophen/paracetamol has demonstrated a significant morphine-sparing effect after major surgery.^{8,9,11} Nefopam has also been shown to provide effective non-opioid analgesia and improve early postoperative pain outcomes.^{10,12} Furthermore,

contemporary clinical guidelines and recent reviews strongly support multimodal opioid-sparing protocols as a central element of perioperative pain management.^{5,7,14}

The finding of prolonged time to first rescue analgesia in the multimodal group is clinically important because this outcome reflects both early analgesic durability and patient comfort. This result is directionally consistent with prior literature supporting multimodal non-opioid regimens. Mathiesen et al reported improved postoperative pain control with pregabalin-containing combinations after abdominal hysterectomy, and recent contemporary evidence also supports the role of multimodal approaches in reducing breakthrough pain and rescue medication use.¹⁵ In a randomized study after laparoscopic colon surgery, Kitagawa et al found that multimodal analgesia combined with TAP block reduced additional analgesic use compared with epidural analgesia, even though overall VAS scores were similar between groups.¹⁶ These studies support the concept that multimodal strategies may offer practical analgesic advantages even when absolute pain scores are not dramatically different at all time points.

The lower rescue analgesic requirement observed with multimodal analgesia further reinforces this interpretation. Reduced breakthrough analgesic need usually indicates more consistent control of nociceptive input across the early postoperative period. This aligns with the broader literature on perioperative multimodal regimens, which has repeatedly shown opioid-sparing and rescue-sparing benefits when analgesic agents with different mechanisms are combined. Chou et al recommended routine use of multimodal analgesia for postoperative pain management, and more recent reviews continue to endorse this strategy as a foundation of adult postoperative pain care.^{5,7,14}

Earlier ambulation in the multimodal group is one of the most clinically meaningful findings because functional recovery is a major perioperative endpoint, especially in abdominal surgery. Early mobilization reduces the risk of pulmonary complications, venous thromboembolism, and overall postoperative deconditioning. The advantage seen here may reflect the combined effect of better analgesia, absence of neuraxial instrumentation, and avoidance of some epidural-related limitations such as lower-limb heaviness, monitoring burden, or delayed mobilization. This interpretation is consistent with Rawal, who argued that the benefits of epidural analgesia in modern practice may be offset in some settings by adverse effects and potential interference with enhanced recovery pathways.¹⁷

The present findings both agree with and diverge from the existing literature on epidural analgesia. Landmark meta-analyses by Block et al and Pöpping et al established that epidural analgesia can provide superior pain relief and reduce some postoperative pulmonary complications, particularly in major thoracic and

abdominal procedures.^{3,4} These data explain why epidural analgesia has historically been regarded as a reference technique. However, more recent work has questioned whether epidural analgesia remains the best routine option in all surgical settings, particularly when less invasive multimodal strategies are available. Rawal highlighted the declining role of epidural analgesia in some enhanced recovery pathways, while Kikuchi et al reported that although epidural analgesia produced better early pain relief than intravenous analgesia after laparoscopic gastrectomy.^{17,4} Overall recovery outcomes were broadly similar and epidural-associated hypotension remained a concern. Thus, the present findings do not invalidate epidural analgesia as a technique; rather, they suggest that in specific regimen studied here, perioperative multimodal approach may offer a more favorable balance between analgesic efficacy and recovery.

The adverse-effect profile in this study also deserves attention. Nausea/vomiting, headache, and shivering were numerically more frequent in the epidural group, although statistical testing did not demonstrate significant between-group differences. This directional trend remains clinically relevant. Reduced rescue analgesic use in the multimodal group may have contributed indirectly to fewer postoperative symptoms, particularly nausea and vomiting, as opioid-sparing strategies are known to reduce emetogenic burden.^{2,5} Prior meta-analytic evidence has shown that pregabalin-containing regimens can reduce postoperative opioid consumption and associated adverse effects.^{8,9} Similarly, paracetamol-based multimodal analgesia has demonstrated significant opioid-sparing effects and a reduction in opioid-related side effects, including nausea and vomiting.¹¹ Furthermore, nefopam, as a non-opioid analgesic, has been shown to provide effective analgesia without respiratory depression and with a favorable side-effect profile.^{10,12} At the same time, the absence of statistically significant differences for most adverse events in the present study should be interpreted cautiously and not overemphasized, given the modest sample size and relatively low event rates, which may limit the statistical power to detect differences.

The pattern of results is also biologically plausible in relation to the individual agents used. Pregabalin is known to reduce dorsal horn hyperexcitability and central sensitization; paracetamol contributes central analgesia and opioid-sparing benefit; and nefopam may add early postoperative analgesic support without respiratory depression. In a randomized double-blind study, Chalermkitpanit et al found that perioperative intravenous nefopam improved early postoperative pain outcomes and shortened hospital stay, supporting its role as a component of enhanced recovery-oriented multimodal regimens.¹² Recent broader analyses of non-opioid analgesics and adjuvants also support the value of such agents as part of multimodal perioperative analgesia.¹²

From a practical perspective, these findings have important implications for routine perioperative care, particularly in resource-constrained/high-volume settings. A pregabalin-nefopam-paracetamol regimen is easier to administer than epidural catheter placement, avoids neuraxial procedure-related logistics, and may be especially attractive where technical expertise, monitoring resources, or patient acceptance limit routine epidural use. In such settings, non-neuraxial multimodal protocol that achieves good analgesia and facilitates earlier ambulation could improve workflow and postoperative recovery without increasing complications. The present findings therefore support consideration of multimodal analgesia not merely as an adjunct, but as a practical primary strategy in selected lower abdominal procedures.

This study used a prospective randomized controlled design, included clearly defined perioperative protocols, evaluated clinically meaningful patient-centered outcomes, and compared two strategies that are directly relevant to routine anaesthesia practice. The inclusion of serial hemodynamic assessment, pain scores, rescue analgesia, ambulation, and adverse effects provide a clinically integrated picture rather than a single-endpoint comparison. The study also contributes locally relevant evidence in an area where direct head-to-head data on this exact multimodal combination remain limited.

The study was conducted at a single center with a modest sample size, which limits generalizability and reduces power for less frequent adverse events. Only women undergoing lower abdominal surgery were included, so the findings may not apply to men, to other surgical categories, or to major open upper abdominal procedures. In addition, repeated hemodynamic and pain measurements were compared at individual time points rather than with a mixed-effects or repeated-measures model, which may not fully capture temporal treatment effects. The epidural regimen evaluated was also protocol-specific; therefore, the findings should not be generalized to all epidural analgesic techniques, especially continuous optimized thoracic epidural protocols used in enhanced recovery pathways. These limitations, however, do not negate the internal consistency of the observed analgesic and recovery advantages of the multimodal regimen studied here.

Future studies should include larger multicenter randomized trials comparing standardized multimodal regimens with contemporary optimized epidural protocols, ideally using repeated-measures modeling and broader recovery outcomes such as patient satisfaction, bowel recovery, length of stay, and chronic postsurgical pain. It would also be valuable to evaluate cost-effectiveness and procedure-specific applicability across different abdominal operations. Recent systematic reviews continue to call for more standardized head-to-head trials in this space, which supports the relevance of further work building on the present findings.

CONCLUSION

Overall, the findings suggest that perioperative multimodal analgesia with pregabalin, nefopam, and paracetamol is a feasible and effective alternative to the epidural protocol studied here for lower abdominal surgery. The observed combination of better early pain control, longer analgesia before rescue medication, fewer rescue doses, and earlier ambulation supports its use as a pragmatic recovery-oriented strategy. In contemporary perioperative care, where simplicity, safety, and functional recovery are increasingly emphasized, such multimodal regimens may offer substantial clinical value.

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REFERENCES

- Kehlet H, Dahl JB. Anaesthesia, surgery, and challenges in postoperative recovery. *Lancet*. 2003;362(9399):1921-8.
- Apfelbaum JL, Chen C, Mehta SS, Gan TJ. Postoperative pain experience: results from a national survey suggest postoperative pain continues to be undermanaged. *Anesth Analg*. 2003;97:534-40.
- Block BM, Liu SS, Rowlingson AJ, Cowan AR, Cowan JA Jr, Wu CL. Efficacy of postoperative epidural analgesia: a meta-analysis. *JAMA*. 2003;290(18):2455-63.
- Pöpping DM, Elia N, Marret E, Remy C, Tramèr MR. Protective effects of epidural analgesia on pulmonary complications after abdominal and thoracic surgery: a meta-analysis. *Arch Surg*. 2008;143(10):990-9.
- Chou R, Gordon DB, de Leon-Casasola OA, Rosenberg JM, Bickler S, Brennan T, et al. Management of postoperative pain: a clinical practice guideline from the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists. *J Pain*. 2016;17(2):131-57.
- Kikuchi S, Matsusaki T, Mitsunashi T, Kuroda S, Kashima H, Takata N, et al. Epidural versus patient-controlled intravenous analgesia on pain relief and recovery after laparoscopic gastrectomy for gastric cancer: randomized clinical trial. *BJS Open*. 2024;8(1):zrad161.
- Chen X, Chu Q, Peng Y, Chen Y, Kaye AD, Liu H, et al. Clinical practice guidelines for postoperative pain management in adults (2024 edition). *J Anesth Transl Med*. 2025;4(3):161-85.
- Peng PW, Wijesundera DN, Li CC. Use of gabapentin for perioperative pain control: a meta-analysis. *Pain Res Manag*. 2007;12(2):85-92.
- Zhang J, Ho KY, Wang Y. Efficacy of pregabalin in acute postoperative pain: a meta-analysis. *Br J Anaesth*. 2011;106(4):454-62.
- Evans MS, Lysakowski C, Tramèr MR. Nefopam for the prevention of postoperative pain: quantitative systematic review. *Br J Anaesth*. 2008;101(5):610-7.
- Remy C, Marret E, Bonnet F. Effects of acetaminophen on morphine side-effects and consumption after major surgery: meta-analysis of randomized controlled trials. *Br J Anaesth*. 2005;94(4):505-13.
- Chalermkitpanit P, Yingsakmongkol W, Limthongkul W, Tanasansomboon T, Pannangpetch P, Tangchitcharoen N, et al. Perioperative intravenous nefopam on pain management and ambulation after open spine surgery: a randomized double-blind controlled study. *Asian Spine J*. 2023;17(4):632-8.
- Jawwad M, Dar DNA, Khan RFU, Chaudhry A, Arkam F, Rao AG, et al. Comparative effectiveness of epidural analgesia and intravenous lidocaine for postoperative pain in major abdominal surgery: a systematic review and meta-analysis. *Anesthesiol Res Pract*. 2025;2025:9822744.
- Kianian S, Bansal J, Lee C, Zhang K, Bergese SD. Perioperative multimodal analgesia: a review of efficacy and safety of the treatment options. *Anesthesiol Perioper Sci*. 2024;2:9.
- Mathiesen O, Rasmussen ML, Dierking G, Lech K, Hilsted KL, Fomsgaard JS, et al. Pregabalin and dexamethasone in combination with paracetamol for postoperative pain control after abdominal hysterectomy: a randomized clinical trial. *Acta Anaesthesiol Scand*. 2009;53(2):227-35.
- Kitagawa H, Manabe T, Yamada Y, Sato H, Takesue S, Hiraki M, et al. A prospective randomized study of multimodal analgesia combined with single injection transversus abdominis plane block versus epidural analgesia after laparoscopic colon cancer surgery. *Int J Colorectal Dis*. 2024;39(1):12.
- Rawal N. Epidural analgesia for postoperative pain: improving outcomes or adding risks? *Best Pract Res Clin Anaesthesiol*. 2021;35(1):53-65.

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