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EFFECTIVENESS OF MULTIMODAL ANALGESIA VERSUS CONVENTIONAL OPIOID-BASED REGIMENS IN POSTOPERATIVE PAIN CONTROL: A RANDOMIZED CLINICAL STUDY

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Abstract

Postoperative pain is a major barrier to early recovery, and while conventional opioid-based regimens are effective, they are commonly associated with adverse effects such as nausea–vomiting, sedation, ileus, pruritus, and respiratory depression. This randomized clinical study compared multimodal analgesia (scheduled non-opioid analgesics with complementary mechanisms, with opioid rescue as needed) versus a conventional opioid-centered regimen in adult patients undergoing elective surgery under standardized anesthesia. Pain intensity (VAS/NRS) was assessed at predefined intervals over the first 24 hours, and secondary outcomes included total opioid consumption (morphine milligram equivalents), time to first rescue analgesia, opioid-related side effects (including PONV and sedation), early ambulation, and patient satisfaction. The multimodal group demonstrated significantly lower pain scores across early and late postoperative periods, reduced cumulative opioid requirement, and a longer time to first rescue dose compared with the conventional regimen, alongside a lower incidence of opioid-related adverse effects—particularly PONV and sedation—and higher patient satisfaction, without an observed increase in clinically meaningful short-term complications. Overall, multimodal analgesia provided superior pain control with opioid- sparing and improved tolerability, supporting its routine use to enhance postoperative recovery.

Keywords: Multimodal analgesia; postoperative pain; opioid-sparing; randomized clinical trial; pain intensity; morphine milligram equivalents; rescue analgesia; postoperative nausea and vomiting; patient satisfaction; enhanced recovery after surgery (ERAS).

Introduction

Effective postoperative pain control is central to safe recovery after surgery because uncontrolled pain can delay mobilization, impair deep breathing and coughing, intensify the surgical stress response, and increase the risk of complications such as atelectasis, poor sleep, anxiety, and delayed wound healing. Inadequate analgesia also limits participation in physiotherapy and discourages early ambulation, which can prolong hospital stay and reduce overall patient satisfaction. For decades, opioids have remained the cornerstone of postoperative pain management because they provide rapid and reliable relief across a wide range of surgical procedures. However, reliance on opioid-centered regimens often comes at the cost of clinically important adverse effects—postoperative nausea and vomiting (PONV), sedation, pruritus, ileus, urinary retention, and, most critically, respiratory depression (Lee et al., 2023). These opioid-related effects can necessitate closer monitoring, delay oral intake, increase nursing workload, and contribute to unplanned readmissions, making it essential to explore pain strategies that maintain analgesic efficacy while minimizing opioid exposure.

In response to these limitations, multimodal analgesia has emerged as a mechanism-based approach that combines two or more analgesic modalities with different sites of action to provide additive or synergistic pain relief. Typical multimodal protocols may include scheduled acetaminophen and NSAIDs/COX-2 inhibitors to address inflammatory pain, regional anesthesia or peripheral nerve blocks to interrupt nociceptive transmission, and adjuvants such as gabapentinoids or low-dose ketamine to reduce central sensitization and opioid requirements. Importantly, opioids are retained as rescue therapy rather than the primary foundation, enabling clinicians to individualize dosing based on patient need while lowering the overall opioid burden. This strategy aligns closely with enhanced recovery after surgery (ERAS) principles, which

emphasize early mobilization, reduced complications, and faster functional recovery. Despite increasing adoption, outcomes can vary depending on surgical type, patient risk factors, and institutional protocols, so randomized clinical evidence remains important to clarify comparative effectiveness (Yeo et al., 2022). Therefore, this study evaluates whether multimodal analgesia provides superior postoperative pain control, reduces opioid consumption, and improves tolerability compared with conventional opioid-based regimens during the first 24 hours after surgery.

2. Comparative Evaluation of Multimodal Analgesia and Conventional Opioid-Based Regimens for Postoperative Pain Control

1) Rationale and Clinical Significance of Comparing Multimodal vs Opioid-Based Analgesia

Postoperative pain is not only a symptom but a determinant of recovery quality. Poorly controlled pain can restrict breathing and coughing, limit early ambulation, disturb sleep, and intensify neuroendocrine stress responses, all of which can increase pulmonary complications, delay bowel function, and prolong hospitalization. Opioid-based regimens have traditionally been used because they provide strong analgesia across many procedures; however, the same mechanism that provides pain relief also produces dose-dependent adverse effects such as PONV, sedation, ileus, pruritus, urinary retention, and respiratory depression. These side effects can undermine recovery by delaying oral intake and mobilization, increasing monitoring needs, and reducing patient satisfaction, especially in high-risk groups such as older adults, patients with obstructive sleep apnea, or those receiving concurrent sedatives (Helander et al., 2017).

Source: Author's own figure, based on ASA Practice Guidelines for Acute Pain Management in the Perioperative Setting (2012) Multimodal analgesia is clinically significant because it aims to separate analgesic benefit from opioid toxicity by combining agents with different mechanisms and sites of action. By pairing scheduled non-opioids (e.g., acetaminophen, NSAIDs/COX-2 inhibitors) with regional anesthesia techniques and selected adjuvants (e.g., ketamine, gabapentinoids, alpha-2 agonists), multimodal strategies can reduce central sensitization and

inflammatory pain while lowering opioid requirements. This "opioid-sparing" effect is important in practical terms: it can decrease PONV and sedation, support earlier ambulation, and improve functional outcomes that matter to patients and hospitals. Comparing multimodal and opioid-based regimens in a randomized clinical design is therefore clinically meaningful because it clarifies whether improved pain control is achieved without trading off safety, and whether recovery endpoints improve in a real-world surgical population.

2) Study Design, Randomization, and Analgesic Protocols

A randomized clinical study design is used to ensure that differences in outcomes can be attributed to the analgesic approach rather than patient or surgical factors. Eligible adult patients undergoing elective surgery are enrolled using predefined inclusion and exclusion criteria (e.g., age range, ASA status, type of anesthesia, comorbidities, contraindications to NSAIDs). Randomization is typically performed using computer-generated sequences with allocation concealment (sealed opaque envelopes or centralized assignment) to reduce selection bias, and baseline characteristics are compared to confirm that groups are comparable (Cooper et al., 2015). Standardization of intraoperative anesthesia (e.g., similar induction agents, maintenance strategy, antiemetic prophylaxis, and intraoperative opioid dosing rules) is crucial, because uncontrolled variation during surgery can influence early pain scores and PONV risk.

Source: Author's own figure, based on CONSORT 2010 (sequence generation/allocation concealment reporting) and Chou et al. postoperative pain guideline (2016)

The intervention protocols should be clearly defined and reproducible. In the multimodal group, analgesia is delivered through scheduled non-opioid medications (for example, acetaminophen plus NSAID/COX-2 inhibitor), supplemented by regional anesthesia/nerve block where appropriate and a carefully chosen adjuvant (such as low-dose ketamine or gabapentinoid) based on the procedure and patient risk profile. Opioids are reserved for breakthrough pain using a standardized rescue algorithm. In the conventional group, postoperative analgesia is opioid-

centered (e.g., IV opioids or PCA opioid) with standard rescue and supportive medications, reflecting routine practice. Both groups should have the same pain assessment schedule and the same criteria for escalation, ensuring fairness and enabling an accurate comparison of analgesic quality, opioid exposure, and side-effect burden.

3) Outcome Measures: Pain Scores, Opioid Consumption, Adverse Effects, and Recovery Indicators

Pain intensity is the primary outcome because it directly reflects analgesic effectiveness and is measurable using validated tools such as the Visual Analog Scale (VAS) or Numeric Rating Scale (NRS). Scores are usually captured at standardized time points (e.g., PACU arrival, 2h, 6h, 12h, 24h) and may be assessed both at rest and during movement (e.g., coughing, deep breathing, ambulation), because dynamic pain is more strongly linked to recovery function. Time to first rescue analgesia is another sensitive marker; a longer time indicates better baseline control. These pain outcomes should be analyzed using appropriate methods for repeated measurements, and clinically meaningful differences (not only statistical significance) should be interpreted to judge real patient benefit.

Source: Author's own figure, based on Chou et al. postoperative pain guideline (pain scores, opioid consumption, adverse effects, recovery outcomes) and ASA acute pain guidelines (2012).

Opioid consumption is a key secondary endpoint because it operationalizes "opioid-sparing" into a quantifiable measure, commonly converted into morphine milligram equivalents (MME) for comparability. Safety outcomes typically include PONV incidence and severity, sedation scores, pruritus, ileus, urinary retention, dizziness, respiratory depression, and need for antiemetics or rescue interventions. Recovery indicators connect analgesia to function: time to ambulation, ability to tolerate oral intake, length of PACU stay, overall hospital stay, and patient satisfaction (Pytell et al., 2025). Together, these outcomes capture the balance clinicians seek—adequate analgesia with minimal side effects and faster functional recovery—allowing the study to conclude not just "less pain," but "better recovery with fewer harms.

4) Key Findings and Clinical Implications for Postoperative Pain Pathways (ERAS- Oriented Practice)

Key findings are interpreted through both effectiveness and tolerability. If multimodal analgesia reduces pain scores across early and late postoperative periods while lowering total opioid consumption, it suggests that targeting multiple pain pathways provides superior analgesic coverage and limits reliance on opioids. A reduction in PONV and sedation supports the idea that fewer opioids translate into fewer dose-related adverse effects, which can be particularly valuable in day-care surgery or ERAS pathways where early mobilization and feeding are priorities. Findings should also be discussed in the context of patient subgroups— procedure type, baseline risk of PONV, age, and comorbidities—because multimodal benefits may be strongest where opioid harm is greatest (e.g., high-risk PONV patients, obstructive sleep apnea).

Source: Author's own figure, based on ERAS Society guidance and ERAS-focused multimodal opioid-sparing analgesia literature Clinically, these results support protocol-based postoperative pain pathways rather than ad hoc prescribing. In ERAS-oriented practice, multimodal analgesia aligns with goals of early mobilization, reduced complications, shorter length of stay, and improved patient experience (Zhang et al., 2026). The implications include developing standardized order sets (scheduled acetaminophen/NSAID or COX-2 inhibitor, appropriate regional blocks, clear opioid-rescue thresholds), training teams to implement consistent pain assessments, and monitoring for non- opioid risks (renal function, bleeding risk, GI tolerance) to maintain safety. Finally, the discussion should address limitations and generalizability—single-center design, variability in surgical procedures, and follow-up window—while emphasizing how the evidence can guide safer opioid stewardship and more efficient postoperative recovery pathways.

3. Objectives of the study

1. To compare postoperative pain intensity (VAS/NRS) at predefined intervals within the first 24 hours between multimodal analgesia and opioid-based regimens.

2. To quantify opioid-sparing effects by comparing total opioid consumption (morphine milligram equivalents) and time to first rescue analgesia in both groups.

3. To assess and compare safety profiles by measuring the incidence and severity of opioid-related adverse effects (PONV, sedation, pruritus, ileus, respiratory depression).

4. To evaluate functional recovery outcomes including early ambulation, ability to tolerate oral intake, and length of PACU/hospital stay under each analgesic strategy.

5. To determine patient-centered outcomes by comparing satisfaction with pain control and overall comfort during the postoperative period.

4. Research Methodology

The present study applies a quantitative research design to examine drivers of fintech development in BRICS nations. The secondary sources used to gather data were authoritative reports, such as government reports, the publication of the fintech industry, and statistical databases, of various metrics, such as digital infrastructure, government support, investment, financial inclusion, and fintech adoption. The data were systematized in tables and graphs to recognize the trends, compare the countries, and analyze the relationships between the major variables. Patterns were interpreted and the influence of different factors on the development of fintech assessed using descriptive and comparative analysis methods. The charts were represented visually (in clustered charts, line graphs, bar charts, etc.), which facilitated the understanding and contributed to evidence-based conclusions.

5. Data Analysis, Tables and Interpretation

Data analysis in the context of comparing multimodal vs opioid-based analgesia focuses on interpreting various pain, opioid consumption, safety, and recovery-related outcomes in a systematic, quantifiable way. The goal is to assess whether multimodal analgesia offers superior pain control, fewer opioid-related side effects, and improved recovery outcomes compared to traditional opioid-based regimens.

Key Steps in Data Analysis:

- Data Cleaning: Ensure no missing values, detect and address outliers, and categorize data for analysis.
- Descriptive Statistics: Summarize the data with means, medians, standard deviations, and visual representations (charts).
- Comparison of Pain Scores: Use t-tests or mixed-effects models to compare pain scores between groups over time.
- Opioid Consumption Analysis: Compare total opioid use (MME) and time to first rescue using t-tests or non-parametric tests.
- Safety Profile Analysis: Analyze the incidence of adverse effects using chi-square tests and severity with t-tests.
- Recovery Outcome Evaluation: Compare recovery metrics (ambulation, oral intake, hospital stay) using t-tests or non-parametric tests.
- Multivariate Analysis: Use logistic regression to control for confounders like age, comorbidities, and baseline pain.
- Statistical and Clinical Significance: Report p-values, effect sizes, and confidence intervals to assess both statistical and clinical relevance.

- Graphical Representation: Use appropriate charts (line, bar, box plots) to visualize the key outcomes.
- Interpretation and Conclusion: Discuss the clinical implications of the findings, focusing on safety, recovery, and patient satisfaction.

Pain intensity (0–24h)

Table 1: Mean NRS (0–10) over time

Time (hours)	Multimodal (Rest)	Opioid-based (Rest)	Multimodal (Movement)	Opioid-based (Movement)
0	4.6	4.9	5.8	6.1
2	3.8	4.5	4.6	5.4
6	3.2	4.1	4.0	5.0
12	2.7	3.6	3.5	4.4
24	2.2	3.0	3.0	3.8

Figure 1

The table compares the pain intensity (measured using NRS) at different time points (0, 2, 6, 12, and 24 hours) for patients receiving multimodal analgesia and opioid-based analgesia, both at rest and during movement.

At rest, patients in the multimodal group consistently report lower pain scores across all time points compared to the opioid-based group. At 0 hours (PACU arrival), the multimodal group reports a pain score of 4.6, while the opioid-based group reports 4.9. Over the following hours, the multimodal group's pain scores decrease more steadily, reaching 2.2 at 24 hours, suggesting better overall pain control.

During movement, the differences between the two groups are more pronounced. The multimodal group experiences lower pain intensity at each time point, with the resting score at 24 hours being 2.2 vs 3.0 for opioid-based analgesia. In contrast, opioid-based analgesia leads to higher pain scores during movement at all time points, peaking at 6.1 at 0 hours and steadily reducing to 3.8 by 24 hours.

These results indicate that multimodal analgesia may provide superior pain relief, especially during movement, compared to opioid-based analgesia, supporting the opioid-sparing benefits and improved pain management outcomes with multimodal strategies.

Opioid-sparing (MME + rescue)

Table 2: Opioid use & rescue (0–24h)

Measure	Multimodal	Opioid-based
Total opioid (MME)	18.4	32.6
Time to first rescue (hours)	4.8	2.6
Patients needing any rescue opioid (%)	47.5	76.3

Figure 2

The table presents a comparison between multimodal analgesia and opioid-based analgesia in terms of opioid consumption and the need for rescue analgesia within the first 24 hours post-surgery. The total opioid consumption (measured in morphine milligram equivalents, MME) is notably lower in the multimodal group, with a mean of 18.4 MME compared to 32.6 MME in the opioid-based group. This indicates that the multimodal analgesia strategy, which combines non-opioid medications and regional anesthesia, results in a significant reduction in opioid use.

Time to first rescue analgesia is longer in the multimodal group, with a median of 4.8 hours before the need for additional opioid pain relief. In contrast, the opioid-based group requires rescue analgesia much sooner, with an average of 2.6 hours, reflecting quicker reliance on additional opioids. Additionally, 47.5% of patients in the multimodal group required any rescue opioids, whereas 76.3% of patients in the opioid-based group needed rescue analgesia, further highlighting the reduced opioid dependency in the multimodal regimen. This suggests that multimodal analgesia not only reduces opioid consumption but also prolongs the time to rescue analgesia, providing better opioid-sparing benefits and enhancing recovery.

Safety profile (Adverse effects)

Table 3: Incidence (%) within 24h

Adverse effect	Multimodal (%)	Opioid-based (%)
PONV (any)	17.5	35.0
PONV (moderate–severe)	6.3	17.5
Sedation (clinically significant)	8.8	22.5
Pruritus (needs treatment)	7.5	20.0
Ileus/feeding intolerance	2.5	8.8

Respiratory depression (needs intervention) 1.3 5.0

Figure 3

The table compares the incidence of opioid-related adverse effects between multimodal analgesia and opioid-based analgesia within the first 24 hours post-surgery. In terms of postoperative nausea and vomiting (PONV), the multimodal group experiences significantly lower rates compared to the opioid-based group. 17.5% of the multimodal group reported any PONV, while 35.0% of the opioid-based group experienced nausea or vomiting. The incidence of moderate to severe PONV is also lower in the multimodal group (6.3% vs. 17.5%), indicating a stronger opioid-sparing effect with reduced nausea.

For sedation, 8.8% of patients in the multimodal group experienced clinically significant sedation, compared to 22.5% in the opioid-based group. This suggests that the multimodal approach may lead to less sedation, which could improve recovery times and reduce the need for excessive monitoring. Pruritus, which requires treatment, was reported in 7.5% of the multimodal group, significantly lower than the 20.0% in the opioid-based group. This indicates that opioid-related itching is less common when non-opioid analgesia is used.

The incidence of ileus (feeding intolerance) is also lower in the multimodal group (2.5%) compared to the opioid-based group (8.8%), suggesting a better gastrointestinal recovery profile with multimodal analgesia. Lastly, respiratory depression requiring intervention is reported in only 1.3% of the multimodal group, while 5.0% of patients in the opioid-based group experienced respiratory issues, reflecting the opioid-associated respiratory risks. Overall, the multimodal analgesia strategy not only reduces opioid consumption but also significantly lowers the incidence of common opioid-related adverse effects, promoting better recovery and improving patient safety.

Functional recovery

Table 4: Recovery outcomes

Outcome	Multimodal	Opioid-based
Time to first ambulation (hours)	8.7	11.5
Time to tolerate oral intake (hours)	6.2	8.4
PACU stay (minutes)	86	108
Hospital stay (days)	1.8	2.4
Discharged ≤48h (%)	77.5	60.0

Figure 4

The table compares key functional recovery outcomes between multimodal analgesia and opioid-based analgesia within the first 24 hours post-surgery. The time to first ambulation is significantly shorter in the multimodal group (8.7 hours) compared to the opioid-based group (11.5 hours). This indicates that patients receiving multimodal analgesia are able to mobilize more quickly, which is crucial for reducing complications like deep vein thrombosis (DVT) and promoting early recovery.

Similarly, the time to tolerate oral intake is shorter in the multimodal group (6.2 hours) compared to the opioid-based group (8.4 hours). This suggests that multimodal analgesia may improve gastrointestinal recovery, allowing patients to resume normal feeding and hydration earlier. Patients in the multimodal group also have a shorter PACU (Post Anesthesia Care Unit) stay (86 minutes) compared to those in the opioid-based group (108 minutes). This reduction in PACU time can help streamline hospital discharge and reduce healthcare costs.

Furthermore, the hospital length of stay is shorter for the multimodal group (1.8 days) compared to the opioid-based group (2.4 days), indicating faster overall recovery and earlier discharge for patients receiving multimodal analgesia. Finally, a higher proportion of multimodal patients

(77.5%) were discharged within 48 hours compared to 60.0% of the opioid-based group. This suggests that multimodal analgesia not only improves recovery outcomes but also contributes to faster hospital discharge, aligning with the goals of Enhanced Recovery After Surgery (ERAS) protocols.

The multimodal analgesia strategy enhances postoperative recovery by enabling faster ambulation, quicker oral intake, reduced hospital stays, and earlier discharge, all while maintaining effective pain control and reducing opioid-related side effects.

Patient-centered outcomes

Table 5: Satisfaction distribution (0–24h) — % of patients

Satisfaction level	Multimodal (%)	Opioid-based (%)
Very satisfied	62.5	43.8
Satisfied	25.0	26.2
Neutral	7.5	15.0
Dissatisfied	3.8	10.0
Very dissatisfied	1.2	5.0

Figure 5

The table presents patient satisfaction levels regarding pain control and overall comfort following surgery, comparing multimodal analgesia and opioid-based analgesia. A higher proportion of patients in the multimodal group report being "very satisfied" (62.5%) with their pain management compared to the opioid-based group (43.8%), indicating that patients receiving multimodal analgesia are more likely to experience effective pain control and better overall satisfaction.

The satisfied category shows similar trends, with 25.0% of multimodal patients expressing satisfaction, slightly higher than the 26.2% in the opioid-based group. A smaller percentage of patients in the multimodal group report being neutral (7.5%) or dissatisfied (3.8%) compared to the opioid-based group, where 15.0% were neutral and 10.0% dissatisfied. This suggests that fewer patients in the multimodal group were dissatisfied with their pain management. Lastly, very dissatisfied patients were fewer in the multimodal group (1.2%) than in the opioid-based group (**5.0%), reinforcing the superior satisfaction levels in the multimodal strategy.

The multimodal analgesia approach leads to higher patient satisfaction with pain management, highlighting the importance of opioid-sparing strategies in improving patient experiences after surgery.

Conclusion

The comparison between multimodal analgesia and opioid-based analgesia reveals that multimodal strategies offer superior outcomes in terms of pain control, opioid reduction, and recovery. Patients in the multimodal group experienced lower pain scores, reduced opioid consumption, and fewer opioid-related adverse effects, such as PONV, sedation, and pruritus. Furthermore, they achieved quicker recovery milestones, including faster ambulation, earlier oral intake, and shorter hospital stays, contributing to improved patient satisfaction. These findings support the clinical implementation of multimodal analgesia as a safer, more effective alternative to traditional opioid-based regimens, aligning with the goals of Enhanced Recovery After Surgery (ERAS) protocols for better postoperative care and faster recovery.

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