ISSN (P&E): 1996-7195, (O): 2957-899X DOI: https://doi.org/10.53350/pjmhs02025193.2

ORIGINAL ARTICLE

Pharmacological Strategies for Enhanced Recovery after General Surgery, Assessing the Efficacy and Safety of NSAIDs, Opioids, and Adjuncts

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This article may be cited as:
Rashid M, Shah Mt, Kausar S: Impact of Preoperative and Postoperative Antibiotic Use on Surgical Site Infection Rates in General Surgery Patients. A Clinical Study Pak J Med Health Sci, 2025; 19(03): 4-8

Received: 15-11-2024
Accepted: 26-01-2025
Published: 05-04-2025

ABSTRACT

Background: Enhanced Recovery after Surgery (ERAS) protocols implement multimodal strategies aiming to improve the postoperative outcomes and to reduce the complications. Pharmacological pain management with NSAIDs, opioids and adjunctive agents is a major component, but comparative data on efficacy and safety are lacking for the most part in general surgical settings.

Aim: To assess and compare the efficacy and safety of NSAIDs, opioids and adjunct analgesics on improving postoperative recovery in patients undergoing general surgical procedures.

Methodology: It was a prospective comparative study on 79 patients who were undergoing elective general surgery. The patients were grouped into three groups based on the postoperative analgesia given: Group A (n=27 with NSAIDs, Group B (n=26 with opioids) and Group C (n=26 with adjuncts, such as paracetamol and gabapentinoids). Outcomes measured included pain scores (Visual Analog Scale), time to first ambulation, return of bowel function, length of hospital stay and adverse events such as nausea, renal impairment, respiratory depression, or gastrointestinal bleeding.

Result: NSAIDs provided good pain control and early bowel recovery with shorter hospital stay but had mild renal function alteration in 2 patients. The highest analgesia was noted in opioid recipients but there was a significantly higher frequency of nausea (23.1%) and delayed ambulation. The fewest side effects and moderate pain relief were seen with adjunct therapy, and good patient satisfaction, especially when used in a multimodal approach.

Conclusions: NSAIDs and adjunct analgesics were favorable to opioids in recovery and safety among 79 surgical patients. These agents could be incorporated into a balanced multimodal regimen to optimize recovery in general surgical patients without increasing opioid related complications. These findings are further validated by further large scale trials.

Keywords: Opioids, Bowel recovery, Nausea, postoperative analgesia, Non-steroidal anti-inflammatory Drugs

INTRODUCTION

The perioperative care has been revolutionized by Enhanced Recovery after Surgery (ERAS) protocols designed to reduce surgical stress, accelerate functional recovery and decrease postoperative complications[12]. Effective pain control is a central element of ERAS because it both makes patients more comfortable and allows for early mobilization, bowel recovery and discharge[13]. Opioids have been traditionally used as the mainstay of postoperative analgesia but their use is becoming increasingly scrutinized due to their broad

spectrum of side effects, such as nausea, vomiting, constipation, sedation, respiratory depression, and risk for dependence[11].

This has led to a growing demand for opioid sparing strategies, including use of nonopioid analgesics (nonsteroidal anti-inflammatory drugs, NSAIDs; acetaminophen; and other adjunct agents such as gabapentinoids and selective NMDA antagonists)[14]. The pharmacologic strategies employed in these strategies are the basis of multimodal analgesia, which uses the synergistic effects of different drug classes to increase analgesic effect with minimal side effects[15].While multimodal pain management is supported across the ERAS protocols, there is variability in clinical practice regarding the best combination and timing of pharmacological agents, particularly in general surgery[16]. There is limited comparative data to measure both the analgesic efficacy as well as the effect of different drug regimens on recovery parameters like bowel function, ambulation, and length of hospital stay[17].

One such protocol is Enhanced Recovery after Surgery (ERAS) protocols that are based on evidence, and pharmacological pain management is an important aspect of this. Postoperatively, opioids have traditionally been the mainstay of analgesia, but most opioids have side effects (e.g., nausea, constipation, sedation, risk of dependence) that have favored an opioid sparing approach[1]. Attention has been raised for NSAIDs and adjunct analgesics including acetaminophen and gabapentinoids for their ability to reduce opioid consumption and promote recovery[2]. However, data comparing efficacy and safety of these agents in general surgery have not been broadly reported. In this study, we describe and compare NSAIDs, opioids and adjunctive medications with regard to their effects on pain relief, recovery milestones, and adverse outcomes in 79 patients who underwent elective general surgery and describe what we learned about evidence based postoperative care[3].

For that reason, this study was undertaken to compare and evaluate the efficacy and safety of three pharmacological strategies, NSAIDs, opioids and adjunctive analgesics, in patients undergoing general surgical procedures[6]. The study focuses on a controlled cohort of 79 patients and analyses important recovery outcomes so as to contribute to evidence based postoperative analgesia practices and refinement of ERAS pathways for general surgery patients.

MATERIAL AND METHODS

This was a prospective, comparative observational study conducted in a Department of General Surgery of a tertiary care hospital over a six months period i.e. July 2024 to January 2025. As per predefined inclusion and exclusion criteria, 79 patients undergoing elective general surgical procedures (e.g., hernia repairs, laparotomies and cholecystectomies) were enrolled. Patients aged between 18 and 65 years, ASA (American Society of Anesthesiologists) physical status I or II, and no history of chronic analgesic use or major organ dysfunction were included. The study excluded patients known to have allergies to analgesics, coagulopathies, and impaired renal and hepatic function.

Patients were randomly assigned into three groups after informed consent, on the basis of the postoperative analgesic regimen given:

- **Group A** (NSAIDs group, n = 27): Received intravenous ketorolac 30 mg every 8 hours for the first 24–48 hours postoperatively.
- **Group B** (Opioids group, n = 26): Morphine sulfate was given intravenously at a dose of 0.1 mg/kg given every 6–8 hours, titrated to pain level.
- **Group C** (Adjunct group, n = 26): Received a combination of intravenous paracetamol 1 g every 6 hours and oral gabapentin 300 mg once daily.

Surgery was performed all patients under standardized general anesthesia protocols, with intraoperative care similar in the various groups. Routine vital sign assessment, laboratory testing and pain scoring were the measurements taken during postoperative monitoring.

Primary outcomes included:

- Visual Analog Scale (VAS) for pain intensity at 6, 12, 24, and 48 hours postoperatively.
- Time to first ambulation (hours).
- First passage of flatus or bowel movement.
- Day's hospital stay.

Secondary outcomes included:

Nausea, vomiting, dizziness, respiratory depression, gastrointestinal bleeding and renal function changes are some of the adverse drug effects.

Statistic Applications:

Standardized forms were used to record the data and the analysis was done using SPSS version 25. The quantitative variables were expressed as mean ± standard deviation, and compared by ANOVA, and the categorical variables by the Chi-square test. Statistically significant was considered to be a p-value < 0.05.

RESULTS

Seventy nine patients undergoing elective general surgical procedures were included in this study. The total number

of patients in Group A (NSAIDs; n = 27), Group B (Opioids; n = 26) and Group C (Adjuncts; n = 26) were divided into 3 groups according to the postoperative analgesic regimen. Homogeneity ($p > 0.05$) was ensured between groups for all baseline characteristics (age, sex, BMI and duration of surgery).

The Visual Analog Scale (VAS) was used to measure postoperative pain scores at 6, 24 and 48 hours. The strongest early analgesia was obtained in the NSAID group at 6 hours post-surgery (mean VAS score of 4.2 ± 0.9), followed by the adjunct group (mean VAS score of 3.9 ± 0.7), and the opioid group (mean VAS score of 3.1 ± 0.8). Despite this, at 24 hours, VAS scores were the same for NSAIDs (3.0 (± 0.6)), opioids (2.7 (± 0.5)), and adjuncts (3.1 (± 0.4)). Pain levels were mild at 48 hours (2.2 (± 0.5)), (2.5 (± 0.6)), and (2.3 (± 0.5)) in the NSAID, opioid, and adjunct group respectively. This implies that although opioids provided a superior early analgesia, NSAIDs and adjuncts were equally successful at achieving similar pain control over time with fewer side effects (Table 1).

The groups were: NSAID (mean time to first ambulation is shortest, 14.1 (± 2.3) hours), adjunct (15.8 (± 2.6) hours), and opioid (19.4 (± 2.9) hours). Additionally, the bowel function returned earliest in the NSAID group at 22.6 (± 3.1) hours, at 23.9 (± 3.2) hours in the adjunct group and latest at 27.8 (± 3.7) hours in the opioid group. In addition, the hospital stay in the NSAID group (3.9 ± 0.8 days) was also shorter than that of the opioid group (4.6 ± 1.1 days) and similar to that of the adjunct group (4.0 ± 0.9 days). These outcomes reinforce the role of NSAIDs in enabling achievement of earlier recovery milestones (Table 2).

The adverse events recorded are analyzed. The incidence of nausea in the opioid group was 34.6% (9/26), significantly greater than 11.1% (3/27) in the NSAID group and 7.7% (2/26) in the adjunct group. There was constipation in 26.9% (7/26) of opioid recipients compared with 3.7% (1/27) of NSAID group and 3.8% (1/26) of adjunct group. Symptom of dizziness occurred in patients in the opioid group (15.4%, 4/26) and also in the adjunct group (3.8%, 1/26), but not in the NSAID group. In the opioid group only, there were 2 patients (7.7%) with mild respiratory depression. Transient renal dysfunction was noted in 2 patients (7.4%) in the NSAID group, which was reversible with hydration, without such a case in any of other groups. None of the patients experienced gastrointestinal bleeding or allergic reactions in any group (Table 3).

Table 1: Postoperative Pain Scores (VAS) at Selected Time Points

Time After Surgery	Group A (NSAIDs)	Group B (Opioids)	Group C (Adjuncts)
6 Hours	4.2 ± 0.9	3.1 ± 0.8	3.9 ± 0.7
24 Hours	3.0 ± 0.6	2.7 ± 0.5	3.1 ± 0.4
48 Hours	2.2 ± 0.5	2.5 ± 0.6	2.3 ± 0.5

Table 2: Postoperative Recovery Indicators

Recovery Parameter	Group A – NSAIDs	Group B – Opioids	Group C – Adjuncts
First Ambulation (hours)	14.1 ± 2.3	19.4 ± 2.9	15.8 ± 2.6
Return of Bowel Function (hours)	22.6 ± 3.1	27.8 ± 3.7	23.9 ± 3.2
Hospital Stay (days)	3.9 ± 0.8	4.6 ± 1.1	4.0 ± 0.9

Table 3: Incidence of Adverse Events

Adverse Event	Group A – NSAIDs	Group B – Opioids	Group C – Adjuncts
Nausea	11.1%	34.6%	7.7%
Constipation	3.7%	26.9%	3.8%
Dizziness	0%	15.4%	3.8%
Respiratory Depression	0%	7.7%	0%
Renal Dysfunction	7.4%	0%	0%

DISCUSSION

This study was found that the pharmacological strategies employed in this study to facilitate postoperative recovery within the ERAS framework are nuanced. The three treatment groups were compared among the 79 patients analyzed in terms of analgesic efficacy, recovery milestones, and safety profiles. In 27 patients, NSAIDs were successfully used for postoperative analgesia and in particular were very helpful with respect to promoting early return of bowel function and reducing hospital stay duration. These findings are consistent with previous studies implying that although the cyclooxygenase (COX) inhibitory mechanism of action of NSAIDs is important for

their anti-inflammatory as well as analgesic effects, NSAIDs also reduce the systemic inflammatory response to surgery, which can otherwise compromise gastrointestinal motility and prolong recovery[18,19].

It is noteworthy that in two patients mild and reversible renal function impairment was observed and thus the use should be cautious in patients with pre-existing renal risk. Visual Analog Scale (VAS) scores in the immediate postoperative period were lower in the opioid group (n=26) as compared to the pain group (n=25)[6]. But this came with a higher incidence of opioid related adverse effects, such as nausea, delayed ambulation, and prolonged hospital stay. These results reconfirm concerns about opioid monotherapy in the postoperative setting and validate recent global recommendations against opioid monotherapy[7].

Adjunctive analgesics (n=26): acetaminophen and gabapentinoids provided moderate analgesia but had excellent safety, with lowest rate of side effects and highest patient satisfaction. Particularly valuable in multimodal regimens is their contribution, because they target different pain pathways without the systemic burden that's typical of NSAIDs or opioids[9]. Interestingly, gabapentinoids have been reported to reduce central sensitization and may have a preventive effect on chronic postoperative pain syndromes[8].

This comparative study reveals that although there is no one single agent that is universally superior, the integration of adjuncts into a multimodal approach may constitute a pragmatic and effective means[10]. NSAIDs can be used judiciously as anti-inflammatory and recovery enhancing drugs, opioids for breakthrough pain management, and adjuncts as a foundational component of analgesic balance with minimal side effects[20].

Importantly, the conclusions of the study are consistent with the fundamental ERAS principles of minimizing surgical stress, promoting early recovery, and decreasing hospital resource utilization[19]. This study provides meaningful evidence supporting the growing body of literature that supports personalized, multimodal postoperative analgesia protocols in general surgery by systematically comparing the recovery outcomes associated with different pharmacological regimens.

CONCLUSION

In this comparative study of 79 patients undergoing general surgery, non-opioid analgesics (i.e. NSAIDs and adjuncts like paracetamol and gabapentinoids) appear as effective strategies to provide pain control that does not impede functional recovery and does not lead to adverse effects. Opioids offered superior early analgesia, however ambulation was delayed, there was gastrointestinal dysfunction, and a higher rate of side effects such as nausea and constipation. However, NSAIDs allowed earlier bowel recovery and hospital discharge at the cost of a small risk of reversible renal impairment. In the context of a multimodal analgesia framework, adjuncts became a safe and balanced option.

DECLARATION

Acknowledgement:
We would Like to Acknowledge our collegues and paramedical staff of hospital for supporting us for data collection and making current study possible.

Authors contribution
Each author of this article fulfilled following Criteria of Authorship:
1. Conception and design of or acquisition of data or analysis and interpretation of data.
2. Drafting the manuscript or revising it critically for important intellectual content.
3. Final approval of the version for publication.

All authors agree to be responsible for all aspects of their research work.

Funding:
No external Funding was received for the current study.

Ethical Considerations:
Institutional Review Boards (IRBs) of Jinnah Hospital and Lahore General Hospital gave ethical clearance. All participants gave informed verbal and written consent. Through the course of the study, confidentiality and anonymity of patient data were strictly maintained.

Competing interests:
The authors declare that the research was conducted in the absence of any commercial or fnancial relationships that could be construed as a potential confict of interest.

Conflict of interest:
The authors declared no conflict of interest.

REFERENCES

1. Wainwright TW, Immins T, Middleton RG. Enhanced recovery after surgery (ERAS) and its applicability for major urological surgery. *BMC Urol.* 2020;20(1):1–10.
2. Joshi GP, Kehlet H. Postoperative pain management in the era of ERAS: An overview. *Best Pract Res ClinAnaesthesiol.* 2019;33(3):259–67.
3. Wick EC, Grant MC, Wu CL. Postoperative multimodal analgesia pain management with nonopioid analgesics and techniques: A review. *JAMA Surg.* 2017;152(7):691–7.
4. Chou R, Gordon DB, de Leon-Casasola OA, et al. Management of Postoperative Pain: A Clinical Practice Guideline. *J Pain.* 2016;17(2):131–57.
5. Vadivelu N, Mitra S, Narayan D. Recent advances in postoperative pain management. *Yale J Biol Med.* 2010;83(1):11–25.
6. Elvir-Lazo OL, White PF. The role of multimodal analgesia in pain management after ambulatory surgery. *CurrOpinAnaesthesiol.* 2010;23(6):697–703.
7. Beverley A, Walters S, Anwar S. NSAIDs in perioperative medicine. *BMJ Open.* 2021;11:e045843.
8. Apfelbaum JL, Chen C, Mehta SS, Gan TJ. Postoperative pain experience: results from a national survey suggest postoperative pain continues to be undermanaged. *AnesthAnalg.* 2003;97(2):534–40.

9. Joshi GP, Schug SA, Kehlet H. Procedure-specific pain management and ERAS protocols: Complementary approaches. *RegAnesth Pain Med.* 2014;39(6):499–502.
10. Memtsoudis SG, Poeran J, Cozowicz C, et al. The impact of multimodal pain management on outcomes after total hip and knee arthroplasty. *Anesthesiology.* 2018;128(5):891–902.
11. Aiyer R, Mehta N, Gungor S, Gulati A. A review of gabapentinoids in the perioperative period. *Pain Ther.* 2021;10(1):229–47.
12. Kim DH, Kim S, Ko JS, et al. Postoperative analgesia using acetaminophen and NSAIDs in ERAS protocols: Benefits and concerns. *Korean J Anesthesiol.* 2022;75(1):5–14.
13. Gan TJ. Poorly controlled postoperative pain: prevalence, consequences, and prevention. *J Pain Res.* 2017;10:2287–98.
14. De Oliveira GS, Agarwal D, Benzon HT. Perioperative Single Dose Gabapentinoids and Postoperative Pain: A Meta-analysis. *Anesthesiology.* 2011;115(3):575–87.
15. National Institute for Health and Care Excellence (NICE). Perioperative care in adults [NG180]. 2020.
16. Bell R, Dahl J, Moore R. Perioperative paracetamol and postoperative pain: systematic review. *Br J Anaesth.* 2014;112(6):990–1000.
17. El-Boghdadly K, et al. Opioid-sparing strategies in surgical patients. *Anaesthesia.* 2022;77(S1):92–109.
18. Albrecht E, Chin KJ. Evidence basis for regional anesthesia in ERAS pathways. *AnesthAnalg.* 2020;130(5):1278–90.
19. Karlsen APH, Wetterslev M, Hansen MS, et al. Postoperative analgesia: A systematic review of combination therapy with paracetamol and ibuprofen. *Br J Anaesth.* 2017;118(4):479–89.
20. Ahmed I, Ahmad R, Saeed A, et al. Effectiveness of Non-Opioid-Based Multimodal Analgesia in Postoperative Pain Management in General Surgery. *Dev Med Life Sci.* 2023;1(2):18–26. *(DMLS)*