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Research Article

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"Comparison of Preemptive Intravenous Paracetamol, Paracetamol–Diclofenac, and Paracetamol–Ketorolac for Postoperative Analgesia Following Elective Abdominal Surgery under General Anaesthesia: A Prospective Randomized Double-Blind Study"

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Abstract

Background

Effective postoperative pain management is an essential component of perioperative care. Preemptive analgesia, as a part of multimodal analgesic strategies, aims to reduce central sensitization and postoperative pain while minimizing opioid requirements. Paracetamol, diclofenac, and ketorolac are commonly used non-opioid analgesics; however, comparative evidence regarding their preemptive combinations remains limited. This study evaluated the efficacy of intravenous paracetamol alone, paracetamol–diclofenac, and paracetamol–ketorolac combinations in patients undergoing elective abdominal surgery under general anaesthesia.

Methods

In this prospective, randomized, double-blind study, 99 patients aged 20–60 years with American Society of Anesthesiologists (ASA) physical status I–II undergoing elective abdominal surgery were enrolled and randomly allocated into three equal groups (n = 33 each). Group P received intravenous paracetamol 1 g, Group PD received intravenous paracetamol 1 g plus diclofenac 75 mg, and Group PK received intravenous paracetamol 1 g plus ketorolac 30 mg before surgical incision. The primary outcome was time to first rescue analgesia. Secondary outcomes included postoperative pain intensity assessed using the Visual Analogue Scale (VAS), haemodynamic parameters, and incidence of adverse effects. Rescue analgesia was administered with intravenous tramadol when VAS was ≥4.

Results

Ninety-nine patients were randomized equally into three groups (n = 33 each). The primary outcome, time to first rescue analgesic requirement, differed significantly among the groups and was longest in Group PK (148.76 ± 15.39 min), followed by Group PD (113.27 ± 9.59 min) and Group P (95.52 ± 6.82 min) ($F = 193.768$, $p < 0.001$). Postoperative pain scores also demonstrated significant intergroup differences. Group PK showed lower VAS scores during the immediate postoperative period (0 h, 30 min, and 1 h), whereas Group PD demonstrated lower pain scores at 2 and 4 hours postoperatively. At later assessment intervals, both combination therapy groups maintained lower pain scores

than paracetamol alone. Haemodynamic parameters remained stable and comparable among the groups. The incidence of postoperative adverse effects was low, with no statistically significant differences observed among the three groups.

Conclusions

Both paracetamol–ketorolac and paracetamol–diclofenac combinations provided superior postoperative analgesia compared with paracetamol alone in patients undergoing elective abdominal surgery under general anaesthesia. The paracetamol–ketorolac combination provided superior analgesia during the immediate postoperative period and significantly prolonged the time to first rescue analgesic requirement, whereas the paracetamol–diclofenac combination demonstrated superior analgesia during the intermediate postoperative period. Both multimodal analgesic regimens were associated with stable haemodynamic parameters and a favorable safety profile. These findings support the use of paracetamol–NSAID combinations as effective opioid-sparing strategies for postoperative pain management following elective abdominal surgery.

Keywords: Preemptive Analgesia, Paracetamol, Ketorolac, Diclofenac, Postoperative Pain, Multimodal Analgesia, Elective Abdominal Surgery, General Anaesthesia

1. Introduction

Postoperative pain remains one of the most common and challenging problems encountered in perioperative medicine. Despite advances in surgical and anaesthetic techniques, a substantial proportion of patients continue to experience moderate-to-severe pain following surgery, particularly after abdominal procedures. Inadequately treated postoperative pain is associated with adverse physiological and psychological consequences, including increased sympathetic activity, hypertension, tachycardia, myocardial ischemia, impaired pulmonary function, delayed ambulation, poor wound healing, prolonged hospital stay, and progression to chronic postsurgical pain. Effective pain management is therefore essential for enhanced recovery, patient satisfaction, and improved surgical outcomes.

Traditionally, opioid analgesics have served as the cornerstone of postoperative pain management. However, opioid administration is frequently associated with undesirable adverse effects such as nausea, vomiting, pruritus, sedation, respiratory depression, urinary retention, ileus, and the potential for dependence. These limitations have encouraged the development of opioid-sparing strategies and the widespread adoption of multimodal analgesia.

Multimodal analgesia refers to the use of analgesic agents with different mechanisms of action to achieve superior pain control while minimizing drug-related adverse effects. An important component of this strategy is preemptive analgesia, which involves the administration of analgesic medications before surgical incision and tissue injury. The rationale behind preemptive analgesia is to prevent or attenuate peripheral and central sensitization caused by surgical trauma, thereby reducing postoperative pain intensity and analgesic requirements.

Paracetamol (acetaminophen) is one of the most widely used analgesic and antipyretic agents worldwide. It exerts its analgesic effect primarily through inhibition of central prostaglandin synthesis and modulation of serotonergic pathways. Owing to its favorable safety profile, minimal gastrointestinal toxicity, and lack of significant effects on platelet function, paracetamol forms an important component of multimodal analgesic regimens.

Nonsteroidal anti-inflammatory drugs (NSAIDs) provide additional analgesic efficacy through inhibition of cyclooxygenase enzymes and suppression of prostaglandin-mediated inflammatory responses. Diclofenac, a phenylacetic acid derivative, possesses potent analgesic and anti-inflammatory properties and exhibits relative selectivity for cyclooxygenase-2 (COX-2). Ketorolac is a potent parenteral NSAID that has demonstrated analgesic efficacy comparable to moderate doses of opioids in acute postoperative pain. Its rapid onset of action and opioid-sparing effect make it an attractive option for perioperative analgesia.

Although paracetamol, diclofenac, and ketorolac are widely used in clinical practice, evidence comparing the efficacy of preemptive intravenous paracetamol alone with paracetamol–diclofenac and paracetamol–ketorolac combinations in abdominal surgery remains limited. Identifying the most effective non-opioid analgesic combination may improve postoperative pain control, reduce opioid consumption, and enhance patient recovery.

Therefore, the present study was undertaken to compare the analgesic efficacy of preemptive intravenous paracetamol alone, paracetamol–diclofenac, and paracetamol–ketorolac combinations in patients undergoing elective abdominal surgery under general anaesthesia. The primary objective was to compare the time to first rescue analgesic requirement, while secondary objectives included assessment of postoperative pain scores, haemodynamic parameters, and the incidence of adverse effects.

2. Materials and Methods

This prospective, randomized, double-blind, controlled study was conducted in the Department of Anaesthesiology, G.R. Medical College and J.A. Group of Hospitals, Gwalior, Madhya Pradesh, India, between April 2023 and March 2025 after obtaining approval from the Institutional Ethics Committee (IEC Approval No. 54/IEC-GRMC/2023). The study was performed in accordance with the ethical principles outlined in the Declaration of Helsinki, and written informed consent was obtained from all participants before enrollment. The trial was prospectively registered with the Clinical Trials Registry of India (CTRI/2024/05/066958).The study was designed, conducted, analyzed, and reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) 2010

Statement for randomized controlled trials.

A total of 99 patients aged between 20 and 60 years, belonging to American Society of Anesthesiologists (ASA) physical status I or II and scheduled for elective abdominal surgery under general anaesthesia, were enrolled in the study. Patients unwilling to participate, those belonging to ASA physical status III or IV, patients with known hypersensitivity to paracetamol, diclofenac, ketorolac, or tramadol, pregnant or lactating women, patients with significant cardiovascular, respiratory, hepatic, renal, neurological, psychiatric, or metabolic disorders, coagulation abnormalities, ongoing anticoagulant therapy, chronic pain syndromes, long-term analgesic use, or inability to comprehend the Visual Analogue Scale (VAS) were excluded.

The sample size was calculated based on previously published studies evaluating preemptive multimodal analgesia. Considering a significance level of 5%, a study power of 80%, and an anticipated difference in time to first rescue analgesic requirement among the study groups, the minimum required sample size was calculated to be 33 patients per group. Accordingly, 99 patients were recruited and randomly allocated into three equal groups using a computer-generated randomization sequence. Allocation concealment was ensured using sequentially numbered sealed opaque envelopes. The study followed a double-blind design wherein both the patients and the investigator responsible for postoperative assessment remained unaware of the treatment allocation. The anaesthesiologist preparing and administering the study medications was not involved in patient assessment, data collection, or statistical analysis.

Patients were allocated into one of three groups comprising 33 patients each. Group P received intravenous paracetamol 1 g administered before surgical incision. Group PD received intravenous paracetamol 1 g combined with diclofenac 75 mg diluted in 100 mL isotonic saline before surgical incision. Group PK received intravenous paracetamol 1 g combined with ketorolac 30 mg diluted in 100 mL isotonic saline before surgical incision. All study medications were administered approximately 30 minutes before surgical incision as part of a preemptive analgesic strategy.

All patients underwent a thorough pre-anaesthetic evaluation one day before surgery. Detailed history taking, physical examination, airway assessment, and routine laboratory investigations were performed. Patients were educated regarding the use of the 10-cm Visual Analogue Scale for postoperative pain assessment, where 0 represented no pain and 10 represented the worst imaginable pain.

Upon arrival in the operating room, standard ASA monitoring was instituted, including continuous electrocardiography, non-invasive blood pressure monitoring, pulse oximetry, and end-tidal carbon dioxide monitoring. Baseline heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, respiratory rate, and oxygen saturation were recorded before induction of anaesthesia. Intravenous access was secured using an 18-gauge cannula, and maintenance fluid therapy was initiated according to institutional protocol.

Premedication consisted of intravenous glycopyrrolate 0.2 mg and midazolam 1 mg. Following preoxygenation with 100% oxygen for three minutes, anaesthesia was induced using intravenous propofol 2 mg/kg and succinylcholine 2 mg/kg. Endotracheal intubation was performed using an appropriately sized cuffed endotracheal tube. Anaesthesia was maintained with a mixture of oxygen, nitrous oxide, and isoflurane (0.8–1%), while neuromuscular blockade was maintained using atracurium administered as a loading dose of 0.25 mg/kg followed by supplemental doses of 0.1 mg/kg as required. Controlled mechanical ventilation was adjusted to maintain end-tidal carbon dioxide between 35 and 45 mmHg. Intraoperative heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, oxygen saturation, and end-tidal carbon dioxide were monitored continuously and recorded at predefined intervals.

At the completion of surgery, residual neuromuscular blockade was reversed using intravenous neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg. Following return of adequate spontaneous ventilation and fulfillment of standard extubation criteria, patients were extubated and transferred to the post-anaesthesia care unit for postoperative observation.

Postoperative pain intensity was assessed using a 10-cm Visual Analogue Scale (VAS), where 0 represented “no pain” and 10 represented “the worst imaginable pain.” Patients were educated regarding the use of the VAS during the preoperative visit. Pain assessment was performed immediately after arrival in the post-anaesthesia care unit (0 hour) and subsequently at 30 minutes, 1 hour, 2 hours, 4 hours, 6 hours, 12 hours, and 24 hours postoperatively. Pain severity was categorized as mild (VAS 0–3), moderate (VAS 4–6), and severe (VAS 7–10). Rescue analgesia was administered in the form of intravenous tramadol 100 mg whenever the patient requested analgesia or when the VAS score was ≥4. The time from completion of surgery to administration of the first rescue analgesic dose was recorded and expressed in minutes.

Haemodynamic parameters including heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, and oxygen saturation were recorded at predetermined postoperative intervals. Patients were also monitored for adverse effects including nausea, vomiting, headache, shivering, sedation, bradycardia, tachycardia, hypotension, hypertension, and respiratory depression throughout the study period.

The primary outcome measure of the study was the time to first rescue analgesic requirement. Secondary outcome measures included postoperative VAS pain scores at various time intervals, haemodynamic responses, and the incidence of postoperative complications and adverse effects.

Data were entered into Microsoft Excel and analyzed using SPSS version 26.0. Continuous variables were expressed as mean ± standard deviation (SD), whereas categorical variables were expressed as frequency and percentage. Intergroup comparisons of continuous variables were performed using one-way analysis of variance (ANOVA), while categorical variables were analyzed using the Chi-square test or Fisher's exact test wherever appropriate. Post-hoc pairwise comparisons were performed using Tukey's honestly significant difference (HSD) test whenever a significant overall difference was identified. A p-value <0.05 was considered statistically significant.

3. Results

A total of 99 patients were enrolled and randomized equally into three groups, with 33 patients in each group. Baseline demographic and perioperative characteristics, including age, sex distribution, body weight, ASA physical status, duration of surgery, and duration of anaesthesia, were comparable among the groups, and no statistically significant differences were observed ($p > 0.05$) (Table 1).

Variable	Group PD (n=33)	Group PK (n=33)	Group P (n=33)	p value
Age (years), Mean ± SD	42.79 ± 5.37	43.03 ± 6.26	42.45 ± 5.67	0.921
Male/Female, n	15/18	17/16	16/17	0.886
ASA Grade I/II, n	20/13	19/14	21/12	0.881
Weight (kg), Mean ± SD	58.64 ± 5.80	57.82 ± 5.06	57.73 ± 2.48	0.685
Duration of Surgery (min), Mean ± SD	76.06 ± 12.45	79.39 ± 14.01	77.12 ± 13.54	0.509
Duration of Anaesthesia (min), Mean ± SD	92.42 ± 13.61	94.55 ± 15.07	93.03 ± 14.28	0.765

Table 1: Demographic and Perioperative Characteristics

Values are expressed as mean ± standard deviation (SD) or number of patients (n). No statistically significant differences were observed among the three groups ($p > 0.05$).

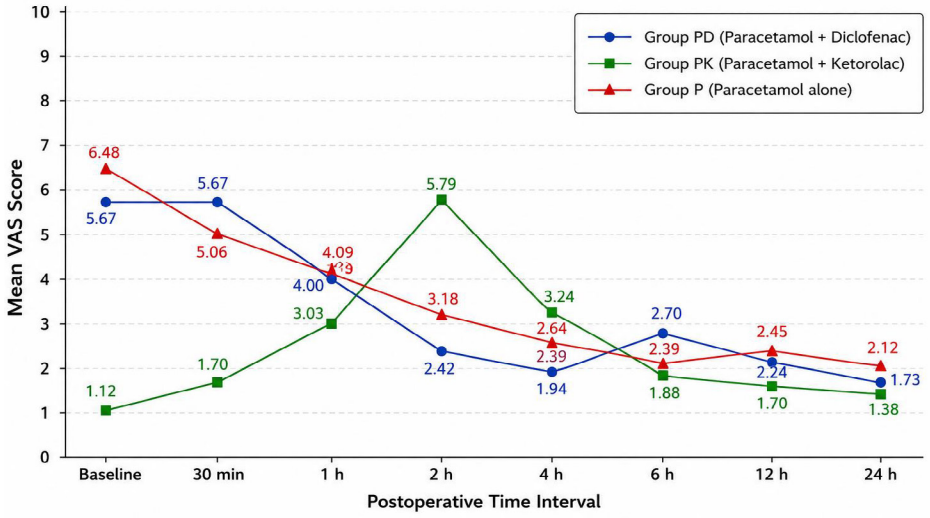
Postoperative pain intensity was assessed using the Visual Analogue Scale (VAS) at predefined intervals up to 24 hours after surgery. Significant intergroup differences were observed at multiple postoperative time points (Table 2, Figure 1). During the immediate postoperative period (0 h), Group PK demonstrated the lowest mean VAS score (1.12 ± 0.60), whereas Group P exhibited the highest score (6.48 ± 0.97) ($p < 0.001$). Similar findings were observed at 30 minutes and 1 hour postoperatively, where patients receiving the paracetamol–ketorolac combination experienced significantly lower pain scores than those in the other groups. At 2 and 4 hours postoperatively, Group PD demonstrated lower VAS scores compared with both Group PK and Group P, indicating superior analgesic efficacy during the intermediate postoperative period. At later assessment intervals (6, 12, and 24 hours), both combination therapy groups maintained lower pain scores than paracetamol alone, with Group PK again demonstrating the most favorable analgesic profile. Overall, both multimodal analgesic regimens provided superior postoperative pain control compared with paracetamol monotherapy, although their analgesic benefits differed according to the postoperative time interval.

Time Interval	Group PD (n=33) Mean ± SD	Group PK (n=33) Mean ± SD	Group P (n=33) Mean ± SD	p value
Immediate Postoperative (0 h)	5.67 ± 1.14	1.12 ± 0.60	6.48 ± 0.97	<0.001
30 Minutes	5.67 ± 1.14	1.70 ± 0.64	5.06 ± 0.75	<0.001
1 Hour	4.00 ± 1.75	3.03 ± 0.88	4.09 ± 0.84	0.001
2 Hours	2.42 ± 1.15	5.79 ± 1.17	3.18 ± 0.92	<0.001
4 Hours	1.94 ± 0.97	3.24 ± 1.06	2.64 ± 1.32	<0.001
6 Hours	2.70 ± 1.10	1.88 ± 0.82	2.39 ± 1.30	0.011
12 Hours	2.24 ± 0.97	1.70 ± 0.85	2.45 ± 1.06	0.006
24 Hours	1.73 ± 0.84	1.38 ± 0.61	2.12 ± 1.17	0.005

Table 2: Comparison of Postoperative Visual Analogue Scale (VAS) Scores Among the Study Groups

Values are expressed as mean ± standard deviation (SD). Lower VAS scores indicate better analgesia. Statistically significant differences were observed among the study groups at all postoperative assessment intervals.Abbreviations: VAS = Visual Analogue Scale; PD = Paracetamol + Diclofenac; PK = Paracetamol + Ketorolac; P = Paracetamol Alone.

Figure 1. Mean Postoperative VAS Scores at Different Time Intervals



VAS: Visual Analogue Scale; PD: Paracetamol + Diclofenac; PK: Paracetamol + Ketorolac; P: Paracetamol alone. Lower VAS scores indicate better analgesia.

The primary outcome measure, time to first rescue analgesic requirement, differed significantly among the study groups (Figure 2). Patients in Group PK experienced the longest duration before requiring rescue analgesia (148.76 ± 15.39 minutes), followed by Group PD (113.27 ± 9.59 minutes) and Group P (95.52 ± 6.82 minutes). One-way ANOVA demonstrated a highly significant difference among the groups ($F = 193.768$, $p < 0.001$), indicating that the paracetamol–ketorolac combination provided the most prolonged postoperative analgesic effect.

Haemodynamic parameters, including heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, and oxygen saturation, remained stable throughout the perioperative period and were comparable among the three groups. No clinically significant haemodynamic disturbances attributable to the study medications were observed.

Complication	Group PD (n=33) n (%)	Group PK (n=33) n (%)	Group P (n=33) n (%)	p value
Nausea and Vomiting	3 (9.1)	2 (6.1)	4 (12.1)	0.693
Headache	3 (9.1)	2 (6.1)	3 (9.1)	0.873
Hypotension	2 (6.1)	1 (3.0)	2 (6.1)	0.810
Hypertension	1 (3.0)	0 (0.0)	1 (3.0)	0.600
Shivering	3 (9.1)	3 (9.1)	2 (6.1)	0.873
Bradycardia	1 (3.0)	0 (0.0)	1 (3.0)	0.600
Tachycardia	2 (6.1)	1 (3.0)	3 (9.1)	0.587
Respiratory Depression	0 (0.0)	0 (0.0)	1 (3.0)	0.364

Table 3: Comparison of Postoperative Complications Among the Three Groups

Values are expressed as number of patients (n) and percentage (%). Chi-square test was applied for comparison among groups. A p value <0.05 was considered statistically significant. No statistically significant differences were observed among the three groups regarding postoperative complications.

Abbreviations: PD = Paracetamol + Diclofenac; PK = Paracetamol + Ketorolac; P = Paracetamol Alone.All adverse events were mild and self-limiting, and no serious drug-related complications were observed during the study period.

The incidence of postoperative complications and adverse effects was low and comparable among all groups (Table 3). Nausea and vomiting represented the most frequently observed adverse event, occurring in 12.1% of patients in Group P, 9.1% in Group PD, and 6.1% in Group PK. The incidences of headache, shivering, hypotension, hypertension, sedation, bradycardia, tachycardia, and respiratory depression were similarly low, and no statistically significant intergroup differences were identified ($p > 0.05$). No serious drug-related adverse events were observed during the study period, indicating that all three analgesic regimens were well tolerated.

Overall, both combination therapy groups demonstrated superior postoperative analgesia compared with paracetamol alone. The paracetamol–ketorolac combination provided more effective pain relief during the immediate postoperative period and maintained lower pain scores at later time points, whereas the paracetamol–diclofenac combination demonstrated superior analgesia during the intermediate postoperative period, particularly at 2 and 4 hours after surgery. Both multimodal analgesic regimens were associated with stable haemodynamic parameters and favorable safety profiles.

4. Discussion

Effective postoperative pain management remains an essential component of perioperative care and significantly influences postoperative recovery, patient satisfaction, early mobilization, and overall surgical outcomes. The present prospective randomized double-blind study compared the analgesic efficacy of preemptive intravenous paracetamol alone, paracetamol–diclofenac, and paracetamol–ketorolac combinations in patients undergoing elective abdominal surgery under general anaesthesia.

An important finding of the present study was the significant prolongation of the time to first rescue analgesic requirement in the ketorolac group. Patients receiving the paracetamol–ketorolac combination required rescue analgesia significantly later (148.76 ± 15.39 minutes) than those receiving paracetamol–diclofenac (113.27 ± 9.59 minutes) or paracetamol alone (95.52 ± 6.82 minutes). Since time to first rescue analgesia was the primary outcome measure of the study, this result strongly supports the superior analgesic efficacy of ketorolac when used as part of a preemptive multimodal analgesic regimen. Prolongation of analgesia is clinically important because it reduces the need for additional analgesic interventions and may contribute to improved patient comfort and recovery.

The principal finding of the present study was that both paracetamol–ketorolac and paracetamol–diclofenac combinations provided superior postoperative analgesia compared with paracetamol alone. However, differences were observed in the temporal analgesic profiles of the two combinations. The paracetamol–ketorolac combination produced significantly lower VAS scores during the immediate postoperative period (30 minutes and 1 hour), whereas the paracetamol–diclofenac combination demonstrated superior analgesia at 2 and 4 hours postoperatively. These findings suggest that ketorolac provides a more rapid onset of analgesia, while diclofenac offers a more sustained intermediate-duration analgesic effect. This observation has important clinical implications in tailoring postoperative pain management according to the expected pain trajectory following abdominal surgery.

The concept of preemptive analgesia is based on prevention of peripheral and central sensitization induced by surgical trauma. Administration of analgesics before the nociceptive stimulus reduces amplification of pain transmission and decreases postoperative pain intensity. Dahl and Møiniche reported that preemptive analgesia attenuates central sensitization and improves postoperative pain outcomes [1]. Similarly, Kissin emphasized that administration of analgesics before surgical injury can reduce postoperative hyperalgesia and analgesic requirements [2]. The findings of the present study support these observations and reinforce the role of preemptive multimodal analgesia in contemporary perioperative practice.

Paracetamol remains one of the most frequently used non-opioid analgesics because of its favorable safety profile and minimal gastrointestinal, renal, and platelet-related adverse effects. Graham and Scott described the central analgesic mechanisms of paracetamol, including inhibition of prostaglandin synthesis and modulation of serotonergic pathways [3]. Hinz and Brune further demonstrated the role of cyclooxygenase inhibition in the analgesic action of paracetamol [4]. Despite these advantages, paracetamol alone may be insufficient for procedures associated with moderate-to-severe postoperative pain. In the present study, patients receiving paracetamol alone consistently exhibited higher postoperative pain scores than those receiving combination therapy, suggesting that monotherapy may not provide adequate analgesia following elective abdominal surgery.

The addition of diclofenac to paracetamol significantly improved postoperative pain control compared with paracetamol alone. Diclofenac exerts its analgesic and anti-inflammatory effects through inhibition of cyclooxygenase-mediated prostaglandin synthesis and suppression of inflammatory responses associated with tissue injury. Todd and Sorkin reported that diclofenac possesses potent analgesic and anti-inflammatory properties with proven efficacy in acute postoperative pain management. Similarly, Altman et al. highlighted the effectiveness of diclofenac-containing multimodal analgesic regimens in improving postoperative pain outcomes [5,6]. In the present study, Group PD demonstrated

significantly lower VAS scores at 2 and 4 hours postoperatively, suggesting that diclofenac may provide prolonged analgesic coverage during the intermediate postoperative period.

Ketorolac demonstrated excellent analgesic efficacy during the early postoperative period. Patients receiving the paracetamol–ketorolac combination exhibited significantly lower VAS scores at 30 minutes and 1 hour postoperatively. Vadivelu et al. described ketorolac as one of the most effective non-opioid analgesics for acute postoperative pain, with analgesic efficacy approaching that of moderate-dose opioids [7]. Walton et al. reported superior postoperative pain control with ketorolac following oral surgical procedures, while Naidu et al. demonstrated effective postoperative analgesia with ketorolac-based regimens in surgical patients [8,9]. The rapid onset of action and potent inhibition of prostaglandin synthesis may explain the superior immediate postoperative analgesia observed in Group PK.

Our findings are broadly consistent with those reported by Aweke et al. (29), who compared preemptive paracetamol, paracetamol–diclofenac, and paracetamol-based multimodal analgesic combinations in abdominal surgery and demonstrated significantly lower postoperative pain scores and reduced rescue analgesic requirements in patients receiving combination therapy [10]. Likewise, Elia et al. reported that multimodal analgesia involving paracetamol and NSAIDs significantly reduces postoperative pain intensity and opioid consumption compared with single-agent therapy [11]. The present study further extends these observations by demonstrating distinct temporal analgesic patterns between ketorolac and diclofenac when used as part of a preemptive multimodal analgesic strategy.

haemodynamic parameters remained stable throughout the study period. Patients receiving ketorolac demonstrated lower postoperative pulse rates and systolic blood pressure values at several postoperative time points, which may reflect attenuation of sympathetic responses secondary to improved analgesia. Adequate pain control itself contributes to haemodynamic stability by reducing catecholamine release and minimizing physiological stress responses associated with surgery. Oxygen saturation remained comparable among all groups throughout the observation period, indicating that none of the study regimens adversely affected respiratory function.

The incidence of adverse effects was low and comparable among the three study groups. No serious drug-related complications were observed during the study period. These findings are consistent with previous studies demonstrating the safety of short-term perioperative use of paracetamol, diclofenac, and ketorolac in appropriately selected patients. Strom et al. and Vadivelu et al. reported that ketorolac is generally safe when administered for short durations in carefully selected surgical patients [7,12]. Similarly, the safety profile of diclofenac in acute postoperative pain management has been well documented by Todd and Sorkin [5]. The absence of significant differences in adverse effects among the groups suggests that improved analgesic efficacy achieved with combination therapy was not associated with an increased risk of complications.

The present study supports the growing body of evidence favoring multimodal analgesia as a standard approach to postoperative pain management. Kehlet emphasized that combining analgesics with different mechanisms of action enhances pain relief while minimizing opioid consumption and drug-related adverse effects [13]. Similarly, Kehlet and Wilmore highlighted the importance of effective multimodal analgesia within enhanced recovery pathways [14]. The combination of paracetamol with NSAIDs provides additive analgesic effects through complementary mechanisms while reducing reliance on opioid medications. Such strategies are particularly valuable in abdominal surgery, where optimal pain control is essential for early mobilization, improved pulmonary function, and enhanced postoperative recovery.

Nevertheless, certain limitations should be acknowledged. The study was conducted at a single tertiary care center and included a relatively modest sample size. Postoperative outcomes were assessed only during the first 24 hours after surgery, and long-term pain outcomes were not evaluated. Furthermore, opioid consumption beyond rescue tramadol administration and patient satisfaction scores were not analyzed. Additionally, Immediate Postoperative Period (0 h) VAS scores differed among the study groups before intervention, which may have influenced subsequent pain assessments and should be considered while interpreting the findings. Future multicenter studies involving larger populations and longer follow-up periods are warranted to further validate these findings and assess their impact on enhanced recovery pathways.

Overall, the findings of the present study demonstrate that preemptive multimodal analgesia using either paracetamol–ketorolac or paracetamol–diclofenac provides superior postoperative pain control compared with paracetamol alone in patients undergoing elective abdominal surgery under general anaesthesia. Both combination regimens resulted in lower postoperative pain scores, prolonged analgesic duration, and maintained favorable safety profiles. However, the analgesic effects of the two combinations exhibited distinct temporal patterns. The paracetamol–ketorolac combination demonstrated superior analgesia during the immediate postoperative period and significantly prolonged the time to first rescue analgesic requirement, whereas the paracetamol–diclofenac combination provided superior analgesia during the intermediate postoperative period, particularly at 2 and 4 hours after surgery. These findings suggest that both combinations are effective components of multimodal analgesia and may be selected according to the anticipated postoperative pain trajectory and clinical requirements of individual patients.

4.1. Clinical Practice Implications

The findings of the present study have important implications for perioperative pain management in patients undergoing elective abdominal surgery. Both paracetamol–ketorolac and paracetamol–diclofenac combinations provided superior postoperative analgesia compared with paracetamol alone and may serve as effective opioid-sparing components of multimodal analgesic protocols.

However, the choice between these combinations may be guided by the expected postoperative pain trajectory and recovery goals.

The paracetamol–ketorolac combination demonstrated superior analgesia during the immediate postoperative period and significantly prolonged the time to first rescue analgesic requirement. Therefore, this regimen may be particularly advantageous for minimally invasive and laparoscopic abdominal procedures, day-care surgeries, and enhanced recovery after surgery (ERAS) pathways where rapid pain relief, early ambulation, and early discharge are prioritized.

In contrast, the paracetamol–diclofenac combination demonstrated superior analgesic efficacy during the intermediate postoperative period, particularly at 2–4 hours after surgery. This regimen may be beneficial in patients undergoing open abdominal procedures or surgeries associated with sustained postoperative inflammatory pain, where continued analgesic coverage beyond the immediate recovery phase is desirable.

Both regimens were associated with stable haemodynamic parameters and a low incidence of adverse effects, supporting their safety and clinical applicability. Consequently, the selection of ketorolac- or diclofenac-based multimodal analgesia should be individualized according to the surgical procedure, anticipated postoperative pain pattern, patient comorbidities, and institutional analgesic protocols.

4.2. Strengths

The present study has several notable strengths. First, it employed a prospective, randomized, double-blind design, which minimized selection bias and observer bias while enhancing the internal validity and reliability of the findings. Second, equal allocation of participants among the three study groups ensured adequate comparability and reduced the risk of confounding. Baseline demographic and perioperative characteristics, including age, gender, ASA physical status, body weight, duration of surgery, and duration of anaesthesia, were comparable among the groups, confirming successful randomization and homogeneity of the study population.

Third, the study directly compared three clinically relevant preemptive analgesic regimens—intravenous paracetamol alone, paracetamol–diclofenac, and paracetamol–ketorolac—thereby providing practical evidence applicable to routine perioperative pain management. Fourth, postoperative pain was assessed at multiple predetermined intervals over a 24-hour period using the Visual Analogue Scale (VAS), allowing comprehensive evaluation of both immediate and sustained analgesic efficacy. This enabled identification of distinct temporal analgesic profiles, with ketorolac demonstrating superior early postoperative analgesia and diclofenac providing more sustained analgesic effects during the intermediate postoperative period.

Additionally, the study evaluated important secondary outcomes, including pulse rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, and oxygen saturation, providing a comprehensive assessment of haemodynamic stability and safety. The use of widely available, cost-effective, and commonly prescribed non-opioid analgesics further enhances the clinical applicability and external relevance of the findings, particularly in resource-constrained healthcare settings.

4.3. Limitations

Despite its strengths, the present study has certain limitations. The study was conducted at a single tertiary care teaching hospital, which may limit the generalizability of the findings to other institutions and patient populations. Although the sample size was adequate to detect significant differences in postoperative pain outcomes, it was relatively modest and may not have been sufficient to identify uncommon adverse events. The follow-up period was limited to the first 24 postoperative hours; therefore, the effects of the study interventions on long-term outcomes such as chronic postsurgical pain, quality of recovery, patient satisfaction, and prolonged analgesic requirements could not be evaluated. Furthermore, cumulative postoperative analgesic consumption beyond the first rescue analgesic dose was not assessed. An additional limitation was the presence of significant differences in immediate postoperative (0 h) VAS scores among the study groups despite randomization. Although baseline demographic and perioperative characteristics were comparable, variability in emergence from anaesthesia, individual pain perception, residual anaesthetic effects, and the timing of postoperative pain assessment may have contributed to this imbalance. Consequently, the observed difference in initial postoperative pain scores may have influenced subsequent pain assessments and should be considered when interpreting the study findings. Finally, inflammatory biomarkers, opioid consumption, and pharmacokinetic parameters were not evaluated, which may have provided additional insight into the mechanisms underlying the observed differences in analgesic efficacy between diclofenac and ketorolac. Future multicentre randomized controlled trials involving larger patient populations, longer follow-up periods, and broader outcome measures are warranted to validate these findings and further define the role of preemptive multimodal analgesia in elective abdominal surgery.

5. Conclusion

The present study demonstrates that both paracetamol–ketorolac and paracetamol–diclofenac combinations provide more effective postoperative analgesia than paracetamol alone in patients undergoing elective abdominal surgery under general anaesthesia. Both multimodal analgesic regimens were associated with significantly lower postoperative pain scores, prolonged analgesic duration, stable haemodynamic parameters, and a favorable safety profile.

The analgesic effects of the two combinations showed distinct temporal characteristics. The paracetamol–ketorolac combination provided superior analgesia during the immediate postoperative period and significantly prolonged the time to first rescue analgesic requirement. In contrast, the paracetamol–diclofenac combination demonstrated superior analgesic efficacy during the intermediate postoperative period, particularly at 2 and 4 hours after surgery.

These findings support the use of both paracetamol–ketorolac and paracetamol–diclofenac as effective opioid-sparing components of multimodal analgesic protocols. Ketorolac may be preferred when prolonged early postoperative analgesia is desired, whereas diclofenac may be advantageous when sustained intermediate postoperative pain control is required. Further multicenter studies with larger sample sizes and longer follow-up periods are warranted to validate these findings and establish procedure-specific analgesic recommendations [15-29].

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