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Comparison of Intravenous Acetaminophen and Ketorolac for Postoperative Pain Relief After Elective Midline Laparotomy: A Prospective Non-randomized Comparative Study

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Abstract

Background

Postoperative pain is a common concern following elective midline laparotomy and may impair coughing, deep breathing, early mobilization, and postoperative recovery. Effective analgesia is essential to improve patient comfort and facilitate recovery while minimizing adverse effects. Intravenous acetaminophen and ketorolac are non-opioid analgesics with different mechanisms of action and safety profiles. Comparing these medications may help inform analgesic selection in patients undergoing elective open abdominal surgery.

Objective

The aim of this study is to compare the analgesic effectiveness and safety of intravenous acetaminophen and intravenous ketorolac in adult patients undergoing elective open abdominal surgery through a midline incision, with the primary outcome being the numerical rating scale (NRS) pain score at two hours postoperatively.

Methods

A prospective, non-randomized comparative study was conducted among 114 adults undergoing elective open abdominal surgery through a midline incision at the Department of Anesthesia, Bangladesh Medical University (BMU), Dhaka, Bangladesh. Patients were allocated according to the analgesic regimen selected by the treating anesthesiologist to receive either intravenous acetaminophen (Group A, n = 57) or intravenous ketorolac (Group K, n = 57). The primary outcome was the NRS pain score at two hours postoperatively. Secondary outcomes included pain scores at other postoperative time points, rescue analgesia requirements, time to first rescue analgesia, and adverse events during the first 24 postoperative hours. Between-group differences were analyzed using appropriate statistical tests, with a two-sided p-value of less than 0.05 considered statistically significant.

Results

The mean NRS pain score at two hours postoperatively was significantly lower in Group K than in Group A (3.6 ± 1.6 vs. 4.6 ± 1.6; mean difference, 1.0 point; 95% confidence interval, 0.43-1.57; p = 0.001). Pain scores were also significantly lower in Group K at one, four, and six hours postoperatively, whereas no significant differences were observed at 12 or 24 hours. Rescue analgesia was required by fewer patients in Group K than in Group A (27/57 (47.4%) vs. 39/57 (68.4%); p = 0.023). The median time to first rescue analgesia was longer in Group K (180 minutes (interquartile range (IQR), 90-360)) than in Group A (120 minutes (IQR, 60-240); p = 0.040). The mean number of rescue analgesic doses was also lower in Group K (0.9 ± 0.8 vs. 1.3 ± 0.9; p = 0.015). Nausea and/or vomiting occurred in 15.8% of patients in Group K and 19.3% in Group A (p = 0.622). No clinically significant bleeding, acute kidney injury, or serious adverse events were recorded in either group during the 24-hour observation period. The findings suggest better early postoperative analgesia with ketorolac; however, the non-randomized design and short follow-up limit causal interpretation and conclusions regarding comparative safety.

Conclusion

This prospective comparative study evaluated intravenous acetaminophen and ketorolac for postoperative pain management after elective midline laparotomy. The results favor ketorolac for early pain control, but comparative effectiveness must be established using observed patient data and appropriate adjustment for confounding.

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Introduction

Postoperative pain is a common concern following open abdominal surgery. Midline laparotomy can produce substantial somatic and visceral pain, potentially impairing deep breathing, coughing, early mobilization, and participation in postoperative rehabilitation [1]. Effective postoperative analgesia is therefore an essential component of perioperative care, supporting patient comfort and functional recovery [2].

Although opioids provide effective analgesia, their use may be associated with nausea, vomiting, sedation, respiratory depression, constipation, and delayed recovery. Multimodal analgesia combines medications with different mechanisms of action to improve pain control while potentially reducing opioid requirements. Non-opioid analgesics are consequently important components of contemporary postoperative pain management [1,2].

Intravenous acetaminophen is widely used for mild-to-moderate postoperative pain and as part of multimodal analgesic regimens. Evidence suggests that it can provide postoperative pain relief, although its opioid-sparing effects vary across surgical populations and comparators [2,3]. It generally has minimal effects on platelet function at therapeutic doses, although excessive cumulative exposure may cause hepatic injury. Ketorolac, a nonsteroidal anti-inflammatory drug (NSAID), provides analgesia by inhibiting cyclooxygenase-mediated prostaglandin synthesis. However, its administration requires careful assessment of renal function, gastrointestinal risk, bleeding risk, intravascular volume status, and concomitant medications [4].

The comparative effectiveness of intravenous acetaminophen and ketorolac may vary according to the surgical population and perioperative analgesic practices. Factors such as incision type, operative duration, tissue injury, intraoperative opioid exposure, and background analgesia may influence postoperative pain intensity and rescue analgesic requirements [5]. Evaluating these medications in a relatively consistent surgical population undergoing elective open abdominal surgery through a midline incision may help clarify their comparative analgesic performance in this clinical setting [6].

Surgical procedures induce a physiological stress response that may contribute to postoperative pain, nausea, vomiting, impaired pulmonary function, increased cardiac demand, and delayed recovery. Effective postoperative analgesia is therefore an essential component of perioperative care, not only for improving patient comfort but also for facilitating restoration of physiological function, early mobilization, and recovery. Multimodal analgesic strategies, incorporating different pharmacological and regional techniques, may improve pain control while reducing the adverse effects associated with reliance on individual analgesic agents [7].

Therefore, this study aimed to compare the postoperative analgesic effectiveness of intravenous acetaminophen and intravenous ketorolac in adults undergoing elective open abdominal surgery through a midline incision. The primary outcome was the numerical rating scale (NRS) pain score at two hours postoperatively. Secondary outcomes included postoperative pain scores at other time points, rescue analgesia requirements, time to first rescue analgesia, and adverse events during the first 24 postoperative hours.

Materials And Methods

Study design and setting

This prospective, non-randomized, two-group comparative study was conducted in the Department of Anesthesia, Bangladesh Medical University (BMU), Dhaka, Bangladesh, from January 2025 to December 2025. The study compared the postoperative analgesic effectiveness and short-term adverse events associated with intravenous acetaminophen and intravenous ketorolac in patients undergoing elective open abdominal surgery through a midline incision.

Treatment allocation was determined by the treating anesthesiologist according to clinical assessment and the selected analgesic regimen. Patients were not randomly assigned, and no allocation concealment was performed. Consecutive eligible patients were considered for enrollment. The study was reported with reference to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations [8].

Ethical approval

The study protocol was approved by the Institutional Ethical Review Committee (ERC) of Bangladesh Medical University, Dhaka, Bangladesh, under Memo No. ERC-BMU/ECC/165/2024, dated October 2, 2024. The study was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from participants before enrollment, and patient confidentiality was maintained

throughout data collection and analysis.

Study population

The study population comprised adult patients undergoing elective open abdominal surgery through a midline incision under general anesthesia. Eligible procedures included open colectomy, small bowel resection, open gastric surgery, and other elective gastrointestinal operations performed through a midline laparotomy.

Inclusion criteria

Patients aged 18-65 years with an American Society of Anesthesiologists (ASA) physical status [9] of I-II were eligible if they were scheduled for elective open abdominal surgery through a midline incision under general anesthesia. Participants were required to be able to understand and use the 0-10 NRS for pain assessment [10], complete postoperative assessments, and provide written informed consent.

Exclusion criteria

Patients with known hypersensitivity to acetaminophen, ketorolac, aspirin, or other NSAIDs were excluded. Other exclusion criteria included active peptic ulcer disease, previous gastrointestinal bleeding, recent gastrointestinal perforation, clinically significant renal impairment, perioperative hypovolemia, significant hepatic dysfunction, coagulopathy, active bleeding, incomplete surgical hemostasis, unacceptable bleeding risk, therapeutic anticoagulation or concomitant medication making ketorolac inappropriate, chronic opioid therapy likely to substantially alter postoperative analgesic requirements, and inability to provide informed consent or reliably report pain. Patients were not exposed to a study medication when it was clinically contraindicated.

Sample size calculation

The sample size was calculated based on the primary outcome and the NRS pain score at two hours after surgery. The calculation assumed a between-group difference of one NRS point, a common standard deviation (SD) of 1.8, a two-sided significance level of 0.05, and 80% statistical power [11].

The sample size for comparing two independent means was estimated using the following formula:

$$n = \frac{2(Z_{\alpha/2} + Z_{\beta})^2 \sigma^2}{\Delta^2}$$

Where (n) represents the required sample size per group, $(Z_{\alpha/2} = 1.96)$, $(Z_{\beta} = 0.84)$, $(\sigma = 1.8)$, and $(\Delta = 1.0)$.

Substituting these values gives:

$$n = \frac{2(1.96 + 0.84)^2 (1.8)^2}{1.0^2}$$
$$= 50.80 \approx 51$$

After allowing for 10% attrition, the adjusted sample size was calculated as (51/0.90=56.67), rounded to 57 patients per group. The total target sample size was therefore 114 patients. This calculation did not account for potential confounding associated with non-randomized treatment allocation.

Group allocation

Eligible patients were assigned to one of two groups according to the analgesic regimen selected by the treating anesthesiologist. Group A comprised patients receiving intravenous acetaminophen, whereas Group K comprised patients receiving intravenous ketorolac. The treating anesthesiologist selected the medication according to clinical assessment, contraindications, and the institution-approved treatment protocol. No randomization was performed. Clinical considerations relevant to treatment selection included renal function, bleeding risk, hepatic status, concomitant medications, and clinician preference. The allocation process was therefore clinician-directed rather than randomized.

Analgesic regimen

Group A received intravenous acetaminophen 1,000 mg infused over 15 minutes near the end of surgery, provided that further acetaminophen administration was clinically appropriate. Group K received

intravenous ketorolac 30 mg according to the institution-approved protocol near the end of surgery, following assessment of renal function, volume status, surgical hemostasis, and bleeding risk. Drug administration followed institutional policies, applicable prescribing guidance, and patient-specific contraindications.

Subsequent analgesia followed the same background and rescue protocol in both groups. Additional acetaminophen, NSAIDs, opioids, and other analgesics were recorded. Total acetaminophen exposure from all routes and combination preparations was monitored to avoid exceeding the applicable daily limit.

Standardization of anesthesia and background analgesia

All patients received general anesthesia. Induction was performed using propofol at the standard induction dose. Anesthesia was maintained with an inhalational volatile anesthetic, either isoflurane or sevoflurane, according to the treating anesthesiologist's preference and clinical judgment. Intraoperative opioid analgesia was administered according to the anesthesiologist's decision and individual patient requirements.

No regional anesthetic technique, epidural analgesia, or local anesthetic wound infiltration was administered. The assigned study medication was given near the end of surgery according to the respective group protocol.

Patients received routine postoperative monitoring in the post-anesthesia care unit (PACU). Pain assessment began when patients were awake and able to communicate reliably.

Study outcomes

Primary Outcome

The primary outcome was the postoperative pain score measured using the 11-point NRS at two hours after surgery. The NRS ranged from 0, indicating no pain, to 10, indicating the worst imaginable pain. The primary comparison was the difference in the mean two-hour NRS score between patients receiving intravenous acetaminophen and those receiving intravenous ketorolac.

Secondary Outcomes

Secondary outcomes included NRS pain scores at the initial PACU assessment and at 1, 4, 6, 12, and 24 hours after surgery; the proportion of patients requiring rescue analgesia during the first 24 postoperative hours; time from study drug administration to the first rescue analgesic dose; the number of rescue analgesic doses and total rescue analgesic consumption during the first 24 hours; and the incidence of adverse events during the same period. Adverse events included postoperative nausea and vomiting, dizziness, dyspepsia, allergic reactions, clinically significant bleeding, and suspected acute kidney injury when sufficient clinical data were available.

Postoperative pain assessment

Postoperative pain intensity was assessed using the 11-point NRS, ranging from 0 (no pain) to 10 (worst imaginable pain). The initial postoperative assessment was performed in the PACU. Subsequent assessments were conducted at 1, 2, 4, 6, 12, and 24 hours after the end of surgery.

The primary outcome was the NRS pain score at two hours after the end of surgery. Secondary pain outcomes included NRS scores at the initial PACU assessment and at 1, 4, 6, 12, and 24 hours postoperatively. Pain scores were recorded before administration of rescue analgesia at the respective assessment time points. The PACU measurement represented the initial postoperative pain assessment and was not a pretreatment baseline measurement because the study medication had already been administered.

Rescue analgesia

Rescue analgesia was administered whenever clinically indicated and was not delayed for scheduled research assessments. Intramuscular pethidine at a dose of 1 mg/kg was administered when the NRS pain score was 4 or greater than 4. The same rescue medication and threshold were applied in both groups. Pain scores were documented before rescue medication administration whenever assessment was possible without delaying treatment. The proportion of patients requiring rescue analgesia, the number of rescue doses administered during the first 24 postoperative hours, and the time to first rescue administration were recorded. Time to first rescue analgesia was measured from administration of the study medication.

Safety assessment

Patients were monitored for adverse events during the first 24 postoperative hours. Clinical records were reviewed for postoperative nausea and/or vomiting, dizziness, dyspepsia, clinically significant bleeding,

suspected renal complications, suspected hepatic complications, and other serious adverse events. Renal and hepatic function tests were performed when clinically indicated rather than routinely in all participants. Therefore, the assessment of renal and hepatic adverse events was based on available clinical findings, indicated investigations, and medical records. The 24-hour observation period was intended to capture short-term adverse events and was not designed to establish the comparative long-term safety of either medication.

Operational definitions

The primary outcome was the NRS pain score at two hours after surgery. Moderate-to-severe postoperative pain was defined as an NRS score of 4 or higher. Rescue analgesia requirement was defined as receipt of additional analgesia according to the predefined rescue protocol. Time to first rescue analgesia was measured in minutes from administration of the study medication to the first rescue dose. Postoperative nausea and vomiting referred to patient-reported nausea and/or observed vomiting within 24 hours. Suspected acute kidney injury was assessed using a prespecified clinical definition, such as the Kidney Disease: Improving Global Outcomes (KDIGO) creatinine and urine-output criteria [12], when sufficient measurements were available.

Statistical analysis

Data were analyzed using IBM SPSS Statistics for Windows, version 31.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± SD or median with interquartile range (IQR), as appropriate. Categorical variables were presented as frequencies and percentages.

The primary outcome, the NRS pain score at two hours after surgery, was compared between groups using an independent-samples t-test. The mean between-group difference and corresponding 95% confidence interval (CI) were calculated. Categorical variables were compared using the Pearson chi-square test or Fisher's exact test, as appropriate. Continuous secondary outcomes were compared using independent samples tests appropriate to their distributions.

The comparisons were unadjusted. No multivariable adjusted analysis or repeated measures/mixed effects longitudinal analysis was performed. Secondary outcome comparisons were interpreted cautiously, considering the potential for multiple comparisons.

A two-sided p-value of less than 0.05 was considered statistically significant.

Results

A total of 126 patients were assessed for eligibility. Of these, 12 were not enrolled: seven did not meet the inclusion criteria, three declined participation, and two met other exclusion criteria. The remaining 114 patients were included in the analysis, with 57 patients in Group A, who received intravenous acetaminophen, and 57 patients in Group K, who received intravenous ketorolac.

The mean age was 47.8 ± 10.6 years in Group A and 48.5 ± 9.9 years in Group K. Male patients accounted for 32 (56.1%) participants in Group A and 30 (52.6%) in Group K. The mean body mass index was 24.1 ± 3.2 kg/m² in Group A and 23.8 ± 3.4 kg/m² in Group K. Regarding ASA physical status, 22 (38.6%) patients in Group A and 24 (42.1%) in Group K were classified as ASA I, while 35 (61.4%) and 33 (57.9%), respectively, were classified as ASA II. Open colectomy was performed in 25 (43.9%) patients in Group A and 24 (42.1%) in Group K. Small bowel resection was performed in 17 (29.8%) and 18 (31.6%) patients, respectively, while open gastric surgery was performed in 15 (26.3%) patients in each group. The mean operative duration was 158 ± 42 minutes in Group A and 162 ± 45 minutes in Group K (Table *1*).

Characteristic	Group A (n = 57)	Group K (n = 57)	Test statistic	p-value
Age, years, mean ± SD	47.8 ± 10.6	48.5 ± 9.9	t(112) = −0.36	0.716
Male sex, n (%)	32 (56.1)	30 (52.6)	$\chi^2(1) = 0.14$	0.707
BMI, kg/m², mean ± SD	24.1 ± 3.2	23.8 ± 3.4	t(112) = 0.49	0.629
ASA physical status I, n (%)	22 (38.6)	24 (42.1)	$\chi^2(1) = 0.15$	0.703
ASA physical status II, n (%)	35 (61.4)	33 (57.9)	—	—
Open colectomy, n (%)	25 (43.9)	24 (42.1)	$\chi^2(1) = 0.04$	0.850
Open small bowel resection, n (%)	17 (29.8)	18 (31.6)	$\chi^2(1) = 0.04$	0.839
Open gastric surgery, n (%)	15 (26.3)	15 (26.3)	$\chi^2(1) = 0.00$	1.000
Operative duration, minutes, mean ± SD	158 ± 42	162 ± 45	t(112) = −0.49	0.625

TABLE 1: Baseline demographic and clinical characteristics of study population

Values are presented as mean ± standard deviation (SD) or number (percentage). The continuous variable statistics are approximate calculations from the supplied summary data. The categorical tests compare the listed category with all remaining categories. ASA I and II are complementary categories, so a separate test for ASA II is unnecessary.

ASA: American Society of Anesthesiologists; BMI: body mass index.

The mean NRS pain score at the primary assessment point of two hours after surgery was 4.6 ± 1.6 in Group A and 3.6 ± 1.6 in Group K. The unadjusted mean difference (Group A minus Group K) was 1.0 point (95% CI, 0.43-1.57; p = 0.001). At one hour, the mean NRS scores were 4.9 ± 1.6 in Group A and 4.2 ± 1.6 in Group K (p = 0.021). At four hours, the corresponding scores were 4.2 ± 1.5 and 3.4 ± 1.5 (p = 0.005). At six hours, the scores were 3.8 ± 1.5 and 3.2 ± 1.4, respectively (p = 0.029). At 12 hours, the mean scores were 3.2 ± 1.3 in Group A and 2.9 ± 1.3 in Group K (p = 0.22). At 24 hours, the corresponding scores were 2.6 ± 1.2 and 2.5 ± 1.2 (p = 0.65) (Table *2*).

Assessment time	Group A, mean ± SD	Group K, mean ± SD	Mean difference (A − K)	t statistic	p-value
PACU baseline	5.0 ± 1.5	4.8 ± 1.5	0.2	t(112) = 0.71	0.479
1 hour	4.9 ± 1.6	4.2 ± 1.6	0.7	t(112) = 2.34	0.021
2 hours (primary outcome)	4.6 ± 1.6	3.6 ± 1.6	1.0	t(112) = 3.34	0.001
4 hours	4.2 ± 1.5	3.4 ± 1.5	0.8	t(112) = 2.85	0.005
6 hours	3.8 ± 1.5	3.2 ± 1.4	0.6	Welch's t ≈ 2.21	0.029
12 hours	3.2 ± 1.3	2.9 ± 1.3	0.3	t(112) = 1.23	0.221
24 hours	2.6 ± 1.2	2.5 ± 1.2	0.1	t(112) = 0.44	0.657

TABLE 2: Comparison of postoperative numerical rating scale (NRS) pain scores

Values are expressed as mean ± standard deviation (SD). The mean difference was calculated as Group A minus Group K. NRS scores range from 0 (no pain) to 10 (worst imaginable pain). Group A: intravenous acetaminophen; Group K: intravenous ketorolac; PACU: post-anesthesia care unit.

During the first 24 postoperative hours, rescue analgesia was required by 39 (68.4%) patients in Group A and 27 (47.4%) patients in Group K (p = 0.023). The mean number of rescue analgesic doses per patient, calculated across all participants in each group, was 1.3 ± 0.9 in Group A and 0.9 ± 0.8 in Group K (p = 0.015). Among patients who received rescue analgesia, the median time to the first rescue dose was 120 minutes (IQR, 60-240) in Group A and 180 minutes (IQR, 90-360) in Group K. These median times are descriptive comparisons among rescue recipients and were not interpreted as time-to-event estimates for the entire study population.

Nausea and/or vomiting occurred in 11 (19.3%) patients in Group A and nine (15.8%) patients in Group K (p = 0.62). Dizziness was reported in five (8.8%) patients in Group A and six (10.5%) patients in Group K (p = 0.75). Dyspepsia occurred in two (3.5%) patients in Group A and five (8.8%) patients in Group K (p = 0.44). No clinically significant bleeding, acute kidney injury, suspected hepatic adverse events, or serious adverse events were recorded in either group during the 24-hour observation period (Table *3*). The absence of these events during short-term follow-up does not establish equivalent safety between the two medications.

Adverse event	Group A (n = 57), n (%)	Group K (n = 57), n (%)	Test statistic	p-value
Nausea and/or vomiting	11 (19.3)	9 (15.8)	$\chi^2(1) = 0.24$	0.622
Dizziness	5 (8.8)	6 (10.5)	$\chi^2(1) = 0.10$	0.751
Dyspepsia	2 (3.5)	5 (8.8)	Fisher's exact test; OR = 0.38	0.438
Clinically significant bleeding	0 (0.0)	0 (0.0)	Not estimable	Not estimable
Acute kidney injury	0 (0.0)	0 (0.0)	Not estimable	Not estimable
Suspected hepatic adverse event	0 (0.0)	0 (0.0)	Not estimable	Not estimable
Serious adverse event	0 (0.0)	0 (0.0)	Not estimable	Not estimable

TABLE 3: Adverse events during the first 24 postoperative hours

Pearson chi-square tests were used for nausea/vomiting and dizziness. Fisher's exact test was used for dyspepsia because of small expected cell frequencies. The OR for dyspepsia compares Group A with Group K. When no events occur in either group, a comparative test statistic cannot be estimated. These calculations are based on the supplied counts.

OR: odds ratio.

The observed values indicate lower mean NRS pain scores at two hours and fewer rescue analgesic requirements in Group K than in Group A. The between-group differences in pain scores were smaller at 12 and 24 hours. Nausea and/or vomiting occurred at similar frequencies in the two groups, while no major safety events were recorded during the observation period. Because treatment allocation was non-randomized, the findings should be interpreted as unadjusted associations. Differences in clinical selection, surgical characteristics, anesthetic management, and other measured or unmeasured confounders may have influenced the results.

Discussion

This study compared the analgesic effectiveness and short-term safety of intravenous acetaminophen and ketorolac in patients undergoing elective midline laparotomy. Patients receiving ketorolac had lower early postoperative NRS pain scores and required less rescue analgesia. At two hours, the mean NRS score was 3.6 ± 1.6 in the ketorolac group compared with 4.6 ± 1.6 in the acetaminophen group, representing an unadjusted mean difference of 1.0 point (95% CI, 0.43-1.57; p = 0.001). Rescue analgesia was required by 47.4% of patients receiving ketorolac and 68.4% receiving acetaminophen (p = 0.023). However, these associations should not be interpreted as definitive evidence of causal superiority because treatment allocation was non-randomized.

Postoperative pain following midline laparotomy arises from tissue injury, inflammation, and activation of peripheral nociceptive pathways. Effective analgesia is important because pain can interfere with coughing, deep breathing, mobilization, sleep, and participation in postoperative recovery. A large prospective randomized study evaluating pain intensity after abdominal surgical procedures demonstrated substantial variation in postoperative pain, highlighting the importance of evaluating analgesic outcomes within a clearly defined surgical population [13].

In the present study, the difference in pain scores was most apparent during the first six postoperative hours. The mean NRS score at one hour was 4.2 ± 1.6 in the ketorolac group and 4.9 ± 1.6 in the acetaminophen group. At four hours, the corresponding scores were 3.4 ± 1.5 and 4.2 ± 1.5, respectively. By 12 and 24 hours, the between-group differences were smaller and were not statistically significant. This pattern suggests that the observed association favoring ketorolac was concentrated in the early postoperative period rather than persisting throughout the first 24 hours.

Evidence supports multimodal postoperative analgesia using agents with complementary mechanisms to improve pain control and reduce opioid requirements. The 2024 PROSPECT recommendations for open colorectal surgery recommend paracetamol and, for eligible patients undergoing colonic surgery, an NSAID

or a cyclooxygenase-2-selective inhibitor as part of a procedure-specific analgesic regimen [14]. A prospective randomized trial comparing intravenous ketorolac with intravenous acetaminophen in patients undergoing gynecological laparotomy found similar visual analog scale pain scores and morphine consumption, although ketorolac was associated with lower hydromorphone use [15]. These findings provide relevant comparative evidence but also demonstrate that the relative benefits may vary according to the surgical population, dosing regimen, and accompanying analgesia.

A meta-analysis of intravenous acetaminophen after abdominal surgery found no significant overall differences in pain scores at 12 or 24 hours or in 24-hour narcotic consumption compared with other analgesic interventions, although subgroup analyses suggested potential benefits in open surgery [6]. A systematic review of intravenous acetaminophen for post-caesarean pain also reported limited and inconsistent evidence of improved pain control and reduced opioid use [16]. In addition, a broader systematic review found that the opioid-sparing effect of intravenous acetaminophen was inconsistent when it was compared with active analgesic treatments [17]. Therefore, neither acetaminophen nor ketorolac should be considered universally superior across all surgical procedures.

Rescue analgesia was required by 68.4% of patients in the acetaminophen group and 47.4% in the ketorolac group. Median time to the first rescue dose was 120 versus 180 minutes, respectively, while mean rescue doses were 1.3 ± 0.9 versus 0.9 ± 0.8. Collectively, these findings are consistent with better early analgesic control among patients receiving ketorolac in this cohort. However, rescue requirements depend on standardized administration thresholds, clinician practice, and background analgesia.

The study has several strengths, including a defined surgical population, prospective outcome collection, a prespecified primary endpoint, standardized pain assessment times, and a common rescue analgesia protocol. These features support a structured comparison of analgesic effectiveness and short-term tolerability in patients undergoing elective midline laparotomy.

Several limitations should be considered when interpreting these findings. First, treatment allocation was non-randomized and determined by the attending anesthesiologist, potentially introducing confounding by indication and selection bias. Second, the absence of blinding may have influenced pain assessment and decisions regarding rescue analgesia. Although the same predefined rescue protocol was applied to both groups, intraoperative opioid administration and additional postoperative analgesia were determined by clinical judgment and may have influenced postoperative pain outcomes. Third, no multivariable adjusted analysis or formal longitudinal analysis was performed; therefore, the reported between-group differences represent unadjusted comparisons. The PACU pain assessment was performed after study drug administration and did not represent a pretreatment baseline measurement. Furthermore, the study did not separately evaluate pain during coughing or mobilization. Finally, the relatively small sample size and 24-hour safety observation period limited the assessment of uncommon or delayed adverse events. Renal and hepatic investigations were performed when clinically indicated rather than systematically in all participants. Accordingly, the absence of recorded major adverse events should not be interpreted as evidence of equivalent safety. These limitations should be considered when interpreting the observed associations between the analgesic regimens and postoperative outcomes.

Future studies should standardize drug doses, administration schedules, background analgesia, and rescue treatment criteria. Randomized controlled trials would provide stronger evidence of comparative efficacy. Non-randomized studies should use prespecified confounder adjustment and sensitivity analyses. Future research should also assess pain during movement, opioid consumption, mobilization, patient satisfaction, and length of hospital stay, with longer follow-up to evaluate renal, gastrointestinal, hepatic, and bleeding complications.

Conclusions

Intravenous ketorolac was associated with lower early postoperative pain scores and reduced rescue analgesia requirements compared to intravenous acetaminophen following elective midline laparotomy. The differences in pain scores became smaller at later assessment times. These findings suggest that ketorolac may provide an early analgesic advantage in appropriately selected patients, but they do not establish causal superiority or comparative safety. Treatment selection should account for renal function, volume status, gastrointestinal risk, hemostasis, hepatic considerations, and the broader multimodal analgesic regimen. Randomized studies with standardized treatment protocols and longer safety follow-up are needed to clarify the comparative effectiveness of these agents.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Md. Kamrul Hasan, Md. Ashraful Islam, Md. Zahin Arefin, Sadia Rahman

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Drafting of the manuscript: Md. Kamrul Hasan, Md. Zahin Arefin, Sadia Rahman

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Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. Ethical Review Committee of Bangladesh Medical University issued approval ERC-BMU/ECC/165/2024. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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