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Efficacy and Safety of Nalbuphine Hydrochloride and Ketorolac in Pain Control of Post Operative Patients

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ABSTRACT

Introduction: *Effective postoperative pain management is essential for recovery. Nalbuphine hydrochloride and ketorolac are widely used analgesics with different safety profiles. This study aimed to compare their efficacy and safety in controlling postoperative pain.* ***Methods:*** *This descriptive study was conducted from July, 2023 to June, 2024 in the Department of Anaesthesia at North Bengal Medical College, Sirajganj. A total of 160 patients scheduled for elective surgery under general anesthesia were randomized into two groups: ketorolac (n-80) and nalbuphine hydrochloride (n-80) for postoperative analgesia. Pain intensity was assessed using the Visual Analog Scale (VAS) at multiple time points, and adverse effects were recorded. Standardized anesthesia protocols and continuous intraoperative monitoring were maintained. Data were analyzed using SPSS version 22.0.* ***Results:*** *Among 160 patients mean age was 40.35 ± 11.1 years and male were predominant in both groups. Ketorolac showed slightly better pain control than nalbuphine at 1, 6, 24, and 32 hours postoperatively. Pain scores were similar at 12 and 48 hours. Vomiting, dizziness, constipation and sedation were more common adverse effects in nalbuphine.* ***Conclusion:*** *Ketorolac provided slightly better pain relief with fewer adverse effects, making it a preferable option over nalbuphine for postoperative pain control.*

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INTRODUCTION

Postoperative pain management is essential after any surgical procedures. This pain can exacerbate various physiological responses, such as endocrine and metabolic disturbances, autonomic reflexes, ileus, and muscle spasms, leading to increased postoperative morbidity and mortality.[1] Effective pain management is crucial for promoting early ambulation, accelerating recovery and reducing the risk of associated complications. Despite continuous improvements in anesthesia techniques and postoperative pain strategies, many patients still experience moderate to severe pain following surgery, indicating a substantial gap in effective pain control.[2-4] Furthermore, the risk of prolonged

analgesic uses post-surgery presents additional concerns, including higher medical costs, delayed recovery and the potential for long-term complications.[5,6]

Nalbuphine hydrochloride, a synthetic κ-opioid receptor agonist and μ-opioid receptor antagonist, has been introduced as a safer alternative to traditional opioids in postoperative pain management.[7] Its dual action provides effective analgesia with reduced risk of adverse effects like respiratory depression, sedation, nausea, and vomiting.[8] Compared with pure opioid agonists, nalbuphine demonstrates favorable outcomes in terms of sedation and reduced opioid-related complications, especially in moderate to severe pain contexts.[9,10] Moreover, nalbuphine has shown promise in minimizing postoperative shivering and enhancing overall comfort by activating κ receptors in the central nervous system.[11]

Meanwhile, nonsteroidal anti-inflammatory drugs (NSAIDs), particularly ketorolac, have gained increasing attention for their role in multimodal pain management. Ketorolac possesses potent analgesic properties, comparable to opioids in certain settings, and has demonstrated a significant reduction in postoperative opioid consumption, particularly following orthopedic and abdominal surgeries.[12-15] Early administration of ketorolac has been shown to decrease opioid use and improve recovery outcomes such as shorter hospital stays and reduced complications.[16,17] Despite these advantages, NSAIDs carry risks such as gastrointestinal bleeding and renal impairment, necessitating careful selection in vulnerable populations.[18]

Both nalbuphine hydrochloride and ketorolac play important roles in modern multimodal pain management strategies aimed at reducing reliance on traditional opioids. Nalbuphine, through its central κ-receptor activity and μ-antagonism, offers effective systemic analgesia with a lower incidence of opioid-related side effects.[19,20] Ketorolac, a potent NSAID, provides peripheral analgesia by inhibiting prostaglandin synthesis and is effective in reducing postoperative opioid requirements. Incorporating these agents into individualized pain control protocols may enhance patient outcomes by balancing efficacy with safety.

Therefore, this study was aimed to compare the efficacy and safety of nalbuphine hydrochloride and ketorolac in controlling postoperative pain and minimizing adverse outcomes.

METHODS

This descriptive study was conducted in the Department of Anaesthesia at North Bengal Medical College and Hospital, Sirajganj from July, 2023 to June, 2024. A total of 160 surgical patients were enrolled and randomly assigned into two groups: nalbuphine hydrochloride group (n-80) and ketorolac group (n-80), to compare postoperative pain control and associated adverse effects. All the patients recruited from North Bengal Medical College and Hospital, Khwaja Yunus Ali Medical College and Hospital and Said M. Monsur Ali Medical College and Hospital, Sirajganj, Bangladesh. Inclusion Criteria were 1) Patients scheduled for elective orthopedic, general, gynecological, or obstetric surgery under general anesthesia. 2) Patients who provided written informed consent for participation in the study. Exclusion Criteria were 1) Known allergy or contraindication to nalbuphine or ketorolac. 2) Individuals with pre-existing gastrointestinal disorders, renal impairment, or coagulation abnormalities. 3) Patients with chronic opioid use or dependency. 4) Patients who had incomplete medical records.

Informed written consent was obtained from all participants. Preoperative evaluations included clinical history, physical examination and baseline vital signs. Pain was measured using the Visual Analog Scale (VAS) at 1, 6, 12, 24, 32, and 48 hours postoperatively. Adverse effects such as nausea, vomiting, dizziness, headache, constipation, sedation, and gastrointestinal bleeding—were monitored. Standard anesthesia protocols were followed for all cases, with continuous monitoring of Heart Rate, SpO_2 and respiratory rate. Pain management was adjusted according to pain scores and patient response. Data analysis was performed using SPSS version 22.0, applying descriptive statistics for categorical variables and independent t-tests for continuous variables. A p-value <0.05 was considered statistically significant.

RESULTS

The study included 160 participants divided equally between the ketorolac group (n-80) and the nalbuphine group (n-80). The overall mean age was 40.35 ± 11.1 years, with the ketorolac group 39.6 ± 11.8 years and the nalbuphine group 41.0 ± 11.7 years. Maximum patients were within 40-49 years group. (Table I).

Table I: Age Distribution of patients (N-160)

Age (In years)	Ketorolac Group (n-80)	Nalbuphine Group (n-80)	Total (N-160)
18–29	17 (21.25%)	14 (17.5%)	31 (19.4%)
30–39	23 (28.75%)	20 (25.0%)	43 (26.9%)
40–49	25 (31.25%)	28 (35.0%)	53 (33.1%)
50–59	12 (15.0%)	15 (18.75%)	27 (16.9%)
≥60	3 (3.75%)	3 (3.75%)	6 (3.7%)
Mean ± SD	39.6 ± 11.8	41.0 ± 11.7	40.35 ± 11.1

Males constituted 58.7% in the ketorolac group and 86.2% in the nalbuphine group (Figure 1).

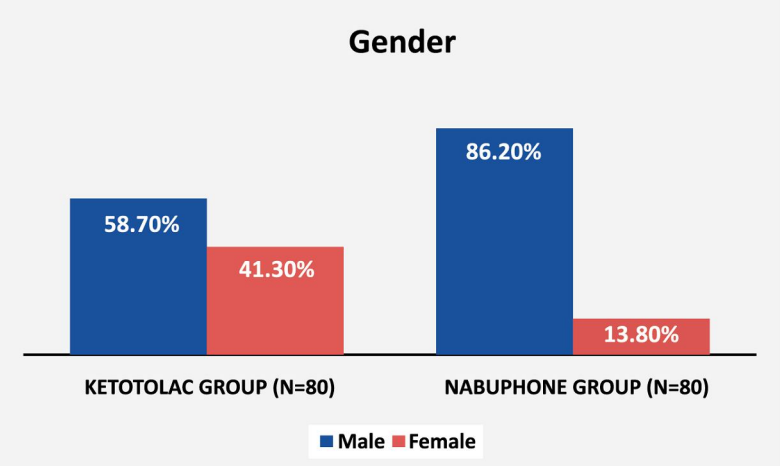

Figure 1: Gender Distribution of the patients

Orthopedic surgeries were the most common procedures, performed in 30 patients (37.5%) in the ketorolac group and 34 patients (42.5%) in the nalbuphine group, making a combined total of 64 cases (40.0%). (Figure 2)

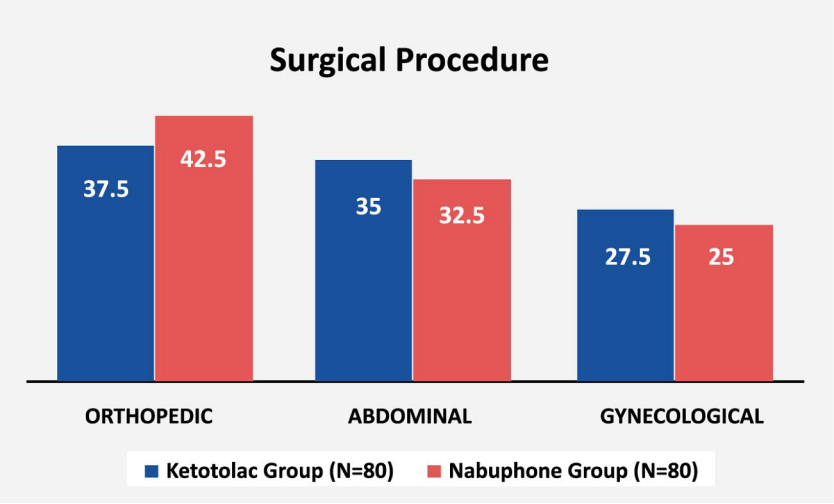

Figure 2: Surgical procedure of the patients

Table II shows the Visual Analog Scale (VAS) scores assessing postoperative pain at various time points. Both groups experienced progressive pain reduction over time. Postoperative pain reduction by Ketorolac was more than nalbuphine at all intervals. Statistically significant differences favoring ketorolac were observed at 1 hour (p = 0.016), 6 hours (p = 0.023), 24 hours (p = 0.041), and 32 hours (p = 0.028), indicating better analgesia during early to mid-postoperative periods. Differences at 12 hours (p = 0.092) and 48 hours (p = 0.083) were not statistically significant, suggesting comparable efficacy between the two drugs in these phases.

Table II: Percentage reduction of Postoperative Pain by VAS Score

Time Period	Time Post-Surgery	Nalbuphine Group (%)	Ketorolac Group (%)	*p*-value
Early Postoperative	1 hour	43.0	45.5	0.016[s]
	6 hours	34.2	36.7	0.023[s]
Mid Postoperative	12 hours	31.0	32.8	0.092[ns]
	24 hours	27.5	29.8	0.041[s]
Late Postoperative	32 hours	23.0	25.3	0.028[s]
	48 hours	11.7	13.1	0.083[ns]

s:significant; ns:not significant

Table III presents the incidence of adverse effects. Nausea, vomiting, dizziness, constipation, and sedation were more frequently reported in the nalbuphine group. Headache and gastrointestinal bleeding incidences were comparable and did not differ significantly between groups.

Table III: Incidence of Adverse Effects in Opioid and Ketorolac Groups

Adverse Effect	Ketorolac Group (n, %)	Nalbuphine Group (n, %)	p-value
Nausea	2 (2.5%)	8 (10.0%)	0.051[s]
Vomiting	2 (2.5%)	10 (12.5%)	0.016[s]
Dizziness	4 (5.0%)	16 (20.0%)	0.004[s]
Headache	6 (7.5%)	12 (15.0%)	0.130[ns]
GI Bleeding	2 (2.5%)	3 (3.8%)	0.650[ns]
Constipation	1 (1.3%)	9 (11.3%)	0.009[s]
Sedation	3 (3.8%)	14 (17.5%)	0.005[s]

s: significant; ns: not significant

DISCUSSION

This study assesses the efficacy and safety of nalbuphine, an opioid, versus ketorolac, a nonsteroidal anti-inflammatory drug, for postoperative pain management in patients undergoing elective orthopedic, abdominal, and gynecological surgeries. Effective postoperative pain control is vital for patient recovery, yet analgesic agents differ in both their pain-relief potency and risk profiles. By comparing these two commonly used analgesics, this study aims to highlight their relative benefits and adverse effects, providing valuable guidance for optimizing postoperative care and enhancing patient outcomes.

In this study, the 160 participants had a mean age of 40.35 ± 11.1 years, with the ketorolac group 39.6 ± 11.8 years and the nalbuphine group 41.0 ± 11.7 years. The age distribution was similar between groups, with most patients aged 40–49 years (33.1%), followed by 30–39 years (26.9%). This aligns with previous studies by Naji et al.[21] and Uddin et al.[22], which reported comparable age ranges among patients undergoing postoperative pain management with nalbuphine and ketorolac. The similar age profiles in both groups help reduce age-related bias, ensuring a fair comparison of analgesic efficacy and safety.

The male predominance observed in this study, with males comprising 72.5% (n = 116) of participants, is consistent with findings from similar research by Behman et al.[23] and Niazi et al.[24], which report higher rates of surgical interventions among male. This gender disparity

may reflect differences in pain perception, healthcare-seeking behaviors, and the prevalence of conditions necessitating surgery.

The surgical procedures were predominantly orthopedic (40.0%), followed by abdominal (33.8%) and gynecological (26.2%) surgeries. Orthopedic surgeries were the most frequent, with 30 patients (37.5%) in the ketorolac group and 34 patients (42.5%) in the nalbuphine group. Abdominal surgeries accounted for 28 cases (35.0%) and 26 cases (32.5%) in the ketorolac and nalbuphine groups, respectively, while gynecological surgeries involved 22 patients (27.5%) in the ketorolac group and 20 patients (25.0%) in the nalbuphine group. This balanced distribution across surgical types ensures a comprehensive assessment of pain management efficacy and safety for both analgesics across diverse clinical settings.

In this study, postoperative pain scores measured by the Visual Analog Scale (VAS) showed a gradual decrease over time in both ketorolac and nalbuphine groups. Postoperative pain reduction by Ketorolac was more than nalbuphine at all intervals. Ketorolac demonstrated significantly lower VAS scores than nalbuphine during the early postoperative period indicating superior immediate analgesic efficacy. This advantage persisted at 24 hours and 32 hours reflecting better mid-postoperative pain control. However, at 12 hours and 48 hours, pain relief was comparable between the groups, suggesting similar effectiveness in the later postoperative phase. These findings align with Uddin et al.[22] who reported effective early ketorolac analgesia with comparable long-term outcomes. Overall, both drugs provide effective postoperative analgesia, with ketorolac offering a modest benefit in early pain relief.

Adverse effects were more frequently observed in the nalbuphine group compared to the ketorolac group. The most common side effects among nalbuphine group were dizziness , vomiting, and sedation, whereas the ketorolac group reported lower incidences of these effects. Nausea occurred in 10% (n-8) of patients receiving nalbuphine versus 2.5% (n-2) in the ketorolac group. Gastrointestinal (GI) bleeding was rare and comparable between groups (3.8% vs. 2.5%). Statistically significant differences were found for vomiting (p-0.016), dizziness (p-0.004), constipation (p-0.009), and sedation (p = 0.005), all higher in the nalbuphine group. These findings are consistent with Solomon et al.[25] that highlighted the favorable safety profile of ketorolac, and Avouac et al.[26], that reported increased adverse effects with nalbuphine use. This supports the consideration of ketorolac as a safer alternative for postoperative pain management, particularly in reducing nausea, vomiting, dizziness and sedation.

Limitations of the study include a small sample size, purposive sampling technique and limited study area.

CONCLUSION

Both ketorolac and nalbuphine hydrochloride were effective in reducing postoperative pain, with ketorolac demonstrating slightly better pain control in the early to mid-postoperative period. Nalbuphine was associated with more adverse effects. Based on these findings, and in line with clinical preference, ketorolac may be considered the more favorable option due to its consistent analgesic efficacy and better safety profile.

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Conflict of interest: None

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