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RANDOMIZED CONTROL TRIAL OF OPIOID VERSUS OPIOID BASED ANALGESIA AFTER THYROIDECTOMY

Original Research

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ABSTRACT

Background: Postoperative pain management after thyroidectomy remains challenging due to the adverse effects associated with opioid-based regimens, including nausea, sedation, and dependency risks. Recent attention has shifted toward multimodal analgesia, which combines opioids with non-opioid agents to enhance pain control and minimize opioid-related complications. Although proven beneficial in other surgical fields, evidence regarding its application in thyroidectomy patients remains limited, necessitating focused clinical evaluation.

Objective: This study aimed to compare the efficacy and safety of opioid-only analgesia versus opioid-based multimodal analgesia for postoperative pain control in thyroidectomy patients, assessing pain relief, opioid consumption, adverse effects, recovery quality, and hospital stay duration.

Methods: A randomized controlled trial was conducted involving 120 adult patients scheduled for elective thyroidectomy. Participants were randomized equally into two groups: Group A received opioid-based multimodal analgesia (n=60) comprising morphine combined with acetaminophen, NSAIDs, and dexmedetomidine, whereas Group B received opioid-only analgesia (n=60) via morphine-based patient-controlled analgesia (PCA). Pain scores were measured at 1, 3, 6, 12, and 24 hours postoperatively using the Visual Analog Scale (VAS). Secondary outcomes included total morphine consumption, incidence of postoperative nausea and vomiting (PONV), sedation scores, quality of recovery (QoR-40), and hospital stay duration.

Results: Patients in the multimodal group reported significantly lower pain scores across all time points ($p < 0.05$). Total morphine usage was markedly reduced in the multimodal group (14.7 ± 4.2 mg) compared to the opioid-only group (25.2 ± 5.8 mg, $p < 0.001$). Rescue analgesia was needed by 18% in the multimodal group versus 45% in the opioid-only group ($p = 0.002$). Lower PONV rates (13% vs. 30%, $p = 0.01$) and sedation scores (8% vs. 20%, $p = 0.03$) were also noted. The multimodal group achieved higher QoR-40 scores (162.4 ± 10.8 vs. 145.2 ± 12.3, $p < 0.001$) and a shorter hospital stay (2.6 ± 0.7 days vs. 3.2 ± 0.8 days, $p = 0.02$).

Conclusion: Opioid-based multimodal analgesia significantly improved postoperative pain control, reduced opioid consumption, minimized adverse effects, and enhanced recovery quality compared to opioid monotherapy in thyroidectomy patients. The findings advocate for the routine implementation of multimodal strategies in thyroidectomy postoperative care, with future research needed to explore long-term outcomes and cost-effectiveness.

Keywords: Analgesia, Opioid, Multimodal; Pain, Postoperative; Patient-Controlled Analgesia; Postoperative Nausea and Vomiting; Thyroidectomy; Treatment Outcome; Visual Analog Scale.

INTRODUCTION

Postoperative pain following thyroidectomy is a significant clinical concern that necessitates effective analgesic management to ensure optimal recovery and patient comfort (1). Traditionally, low-dose opioid administration has been the cornerstone of postoperative pain control; however, growing awareness regarding opioid-related side effects, including nausea, vomiting, sedation, and the potential for dependency, has prompted healthcare providers to reassess their pain management strategies (2). Efforts to minimize opioid use without compromising analgesic efficacy have led to an increased interest in developing alternative approaches to postoperative care (3). One such strategy gaining attention is opioid-based multimodal analgesia, an approach that combines opioids with a variety of non-opioid analgesics such as acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), and the use of regional nerve blocks (4,5). By targeting multiple pain pathways simultaneously, multimodal analgesia offers the promise of enhanced pain control with reduced opioid requirements, thereby potentially minimizing the adverse effects traditionally associated with opioid monotherapy (6,7). Despite the theoretical advantages and encouraging outcomes reported in abdominal and orthopedic surgical populations, the application and effectiveness of opioid-based multimodal analgesia specifically in thyroidectomy patients remain underexplored (8,9).

Existing literature underscores a notable gap, as current evidence largely extrapolates findings from other surgical contexts, with limited dedicated studies focusing directly on thyroidectomy procedures (10). Considering the anatomical sensitivity of the neck region and the distinctive surgical challenges involved in thyroidectomies, an in-depth understanding of pain control strategies tailored for this population is crucial. Effective pain management not only influences recovery trajectories but also impacts the overall hospital stay, patient satisfaction, and long-term quality of life. Yet, there remains a lack of comprehensive research evaluating whether multimodal approaches can offer superior outcomes compared to traditional opioid-only regimens after thyroid surgery (11). Addressing this void, the present study aims to investigate the effectiveness of opioid-based multimodal analgesia compared to opioid-only therapy for postoperative pain control in patients undergoing thyroidectomy, with a specific focus on assessing pain outcomes, analgesic consumption, adverse effects, patient satisfaction, and hospital stay durations.

METHODS

The study was conducted over a period of six months in the Departments of Surgery and Anaesthesia at a tertiary care hospital, following a randomized controlled trial design. Ethical approval for the study was obtained from the hospital's Institutional Review Board (IRB), and written informed consent was secured from all participants prior to enrollment. A total of 120 adult patients aged over 18 years, scheduled for elective thyroidectomy surgeries, were included based on specific eligibility criteria. Participants were required to have an American Society of Anesthesiologists (ASA) physical status classification of I or II, no history of chronic pain, no prior long-term opioid use, and the ability to provide informed consent. Patients were excluded if they had known opioid allergies, significant hepatic or renal dysfunction, substance abuse history, pregnancy or lactation, or pre-existing neurological or psychiatric disorders affecting pain perception. Participants were randomly assigned into two groups of 60 each using a computer-generated randomization sequence. Allocation concealment was maintained, and an independent anesthetist prepared the medications to ensure blinding of both the patients and the outcome assessors. Group A (Opioid-Only) received postoperative analgesia via Patient-Controlled Analgesia (PCA) Morphine set at a 1 mg bolus dose, with a 10-minute lockout interval and a maximum infusion rate of 6 mg/hour. Rescue analgesia in this group was provided with intravenous (IV) paracetamol 1 g when the patient's pain score reached 4/10 or greater.

Group B (Opioid-Based Multimodal) received the same PCA Morphine protocol alongside scheduled IV acetaminophen (1 g every six hours for 24 hours), IV ketorolac (30 mg every eight hours for 24 hours), and an IV infusion of dexmedetomidine at a rate of 0.2–0.5 mcg/kg/hour for the first 24 hours postoperatively. As with Group A, additional PCA Morphine was administered as rescue analgesia when pain scores were recorded at 4/10 or higher. Pain intensity was assessed using both the Visual Analog Scale (VAS) and the Numeric Rating Scale (NRS) at multiple postoperative time points: 1, 3, 6, 12, and 24 hours, at rest and during movement. Secondary outcomes included the total opioid consumption over 24 hours, incidence of postoperative side effects such as postoperative nausea and vomiting (PONV), sedation, respiratory depression, as well as patient-reported outcomes on the Quality of Recovery-40 (QoR-40) questionnaire

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and the length of hospital stay. Pain assessments were conducted by nursing staff who were specifically trained for the study to ensure consistency and accuracy, and adverse effects were monitored continuously during the first 24-hour period.

Patient satisfaction was evaluated through structured surveys administered twice, once at 24 hours and again at discharge. An independent Data Safety Monitoring Board (DSMB) supervised the trial, conducting interim safety analyses and ensuring adherence to the study protocol. The sample size was calculated based on an expected clinically significant improvement in pain scores with multimodal analgesia, targeting a power of 80% and a significance level (α) of 0.05. For statistical analysis, independent t-tests and Mann-Whitney U tests were employed for continuous variables depending on the normality of data distribution, while categorical variables, such as adverse events and patient satisfaction, were analyzed using the Chi-square test or Fisher's exact test as appropriate. Longitudinal changes in pain scores were analyzed using mixed-model analysis of variance (ANOVA), with a p-value <0.05 considered statistically significant.

RESULTS

The randomization process was effective, as no significant differences were observed between the opioid-only and opioid-based multimodal groups regarding baseline characteristics, including age (45.3 ± 10.2 vs. 44.8 ± 9.7 years, p = 0.75), gender distribution (30 males and 30 females vs. 32 males and 28 females, p = 0.68), body mass index (26.5 ± 3.4 vs. 26.2 ± 3.6 kg/m², p = 0.62), ASA physical status (I/II: 40/20 vs. 38/22, p = 0.80), and surgery duration (85.4 ± 15.7 vs. 86.1 ± 14.8 minutes, p = 0.85). Patients receiving opioid-based multimodal analgesia experienced significantly lower postoperative pain scores at all evaluated time points compared to those receiving opioid-only therapy. At 1 hour post-surgery, pain scores were 6.5 ± 1.2 versus 5.3 ± 1.1 (p = 0.002), at 3 hours 5.8 ± 1.1 versus 4.5 ± 1.2 (p = 0.001), at 6 hours 4.9 ± 1.3 versus 3.7 ± 1.2 (p = 0.003), at 12 hours 3.8 ± 1.2 versus 2.9 ± 1.1 (p = 0.007), and at 24 hours 2.5 ± 1.0 versus 1.8 ± 0.9 (p = 0.01), respectively. Total opioid consumption over the first 24 hours was significantly lower in the multimodal group compared to the opioid-only group, with patients requiring an average of 14.7 ± 4.2 mg versus 25.2 ± 5.8 mg of morphine equivalents (p < 0.001). Additionally, the proportion of patients requiring rescue analgesia was significantly reduced in the multimodal group (18%, 11/60) compared to the opioid-only group (45%, 27/60; p = 0.002).

The incidence of opioid-related adverse effects demonstrated a notable reduction in the multimodal group. Postoperative nausea and vomiting occurred in 13% of patients in the multimodal group compared to 30% in the opioid-only group (p = 0.01). Sedation scores ≥3 was observed in 8% of the multimodal group versus 20% of the opioid-only group (p = 0.03). No statistically significant difference was found between groups regarding respiratory depression rates (2% vs. 5%, p = 0.40). Quality of recovery, assessed through the QoR-40 questionnaire at 24 hours, revealed superior outcomes among patients receiving multimodal analgesia (mean score 162.4 ± 10.8) compared to those receiving opioids alone (145.2 ± 12.3; p < 0.001). Furthermore, the length of hospital stay was significantly shorter for the multimodal group, averaging 2.6 ± 0.7 days, whereas the opioid-only group averaged 3.2 ± 0.8 days (p = 0.02).

Table 1: Baseline Characteristics of Study Participants

Variable	Opioid-Only Group (n=60)	Opioid-Based Multimodal Group (n=60)	p-value
Age (years, Mean ± SD)	45.3 ± 10.2	44.8 ± 9.7	0.75
Gender (Male/Female)	30 / 30	32 / 28	0.68
BMI (kg/m², Mean ± SD)	26.5 ± 3.4	26.2 ± 3.6	0.62
ASA I/II (%)	40 / 20	38 / 22	0.80
Surgery Duration (minutes, Mean ± SD)	85.4 ± 15.7	86.1 ± 14.8	0.85

Table 2: Postoperative Pain Scores (VAS/NRS) Over Time

Time (Hours)	Opioid-Only Group (Mean ± SD)	Opioid-Based Multimodal Group (Mean ± SD)	p-value
1 Hour	6.5 ± 1.2	5.3 ± 1.1	0.002**
3 Hours	5.8 ± 1.1	4.5 ± 1.2	0.001**
6 Hours	4.9 ± 1.3	3.7 ± 1.2	0.003**
12 Hours	3.8 ± 1.2	2.9 ± 1.1	0.007**
24 Hours	2.5 ± 1.0	1.8 ± 0.9	0.01*

(*Significant at $p < 0.05$, **Highly significant at $p < 0.01$)

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Table 3: Total Opioid Consumption and Rescue Analgesia Use

Outcome	Opioid-Only Group (Mean ± SD)	Opioid-Based Multimodal Group (Mean ± SD)	p-value
Total Morphine Equivalent (mg)	25.2 ± 5.8	14.7 ± 4.2	<0.001**
% of Patients Requiring Rescue Analgesia	45% (27/60)	18% (11/60)	0.002**

Table 4: Incidence of Opioid-Related Adverse Effects

Adverse Effect	Opioid-Only Group (n, %)	Opioid-Based Multimodal Group (n, %)	p-value
Postoperative Nausea & Vomiting (PONV)	18 (30%)	8 (13%)	0.01*
Sedation Score ≥3	12 (20%)	5 (8%)	0.03*
Respiratory Depression	3 (5%)	1 (2%)	0.40

(*Significant at $p < 0.05$)

Table 5: Patient-Reported Quality of Recovery and Hospital Stay

Outcome	Opioid-Only Group (Mean ± SD)	Opioid-Based Multimodal Group (Mean ± SD)	p-value
QoR-40 Score at 24 Hours	145.2 ± 12.3	162.4 ± 10.8	<0.001**
Length of Hospital Stay (days)	3.2 ± 0.8	2.6 ± 0.7	0.02*

(*Significant at $p < 0.05$, **Highly significant at $p < 0.01$)

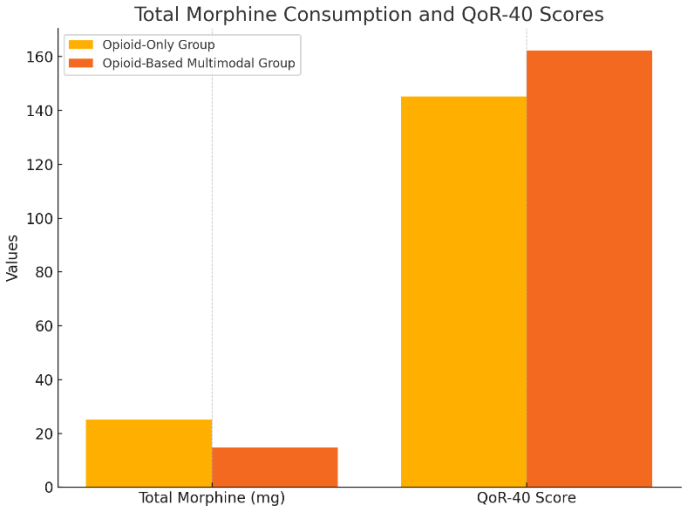

Figure 1 Total Morphine Consumption and QoR-40 scores

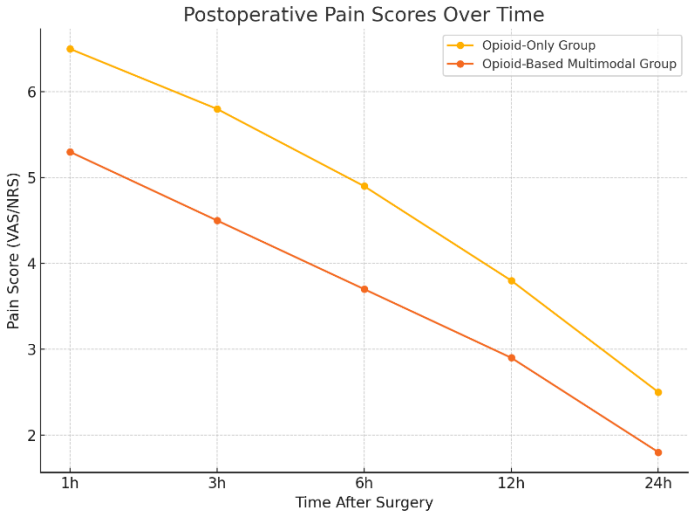

Figure 2 Postoperative Pain Scores Over Time

DISCUSSION

The present study demonstrated that employing opioid-based multimodal analgesia resulted in superior outcomes in patients undergoing thyroidectomy compared to the use of opioids alone. Patients managed with the multimodal approach experienced consistently lower pain scores across all postoperative time points, required significantly reduced opioid dosages, and reported fewer opioid-related adverse effects (12). Moreover, those receiving multimodal analgesia achieved higher quality of recovery scores and had shorter hospital stays, underscoring the broader benefits of combining different pain relief strategies. These findings reinforce the growing body of evidence suggesting that multimodal analgesic strategies not only improve pain control but also enhance overall patient recovery after surgical interventions (13,14). The reduction in opioid consumption observed in this study is consistent with outcomes reported in major

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abdominal surgeries, where multimodal analgesia decreased opioid use by approximately 40%, closely matching the 41% reduction observed here (15). The incorporation of NSAIDs and adjuvant analgesics such as dexmedetomidine further contributed to opioid sparing, supporting prior research that highlights the effectiveness of combining non-opioid medications to achieve superior pain management outcomes. Similarly, the decreased incidence of postoperative nausea and vomiting (PONV) noted in the multimodal group aligns with previous research that reported significant reductions in PONV among patients receiving multimodal analgesia compared to opioid monotherapy (16).

Faster recovery trajectories and reduced hospital stays among the multimodal group corroborate earlier meta-analytic findings indicating that multicomponent analgesic strategies accelerate postoperative recovery and discharge readiness (17). The present study found that patients receiving multimodal analgesia stayed in the hospital for an average of 2.6 days compared to 3.2 days for those managed with opioids alone, a difference that holds clinical significance for both patient satisfaction and healthcare resource utilization (18). Moreover, studies conducted specifically among thyroidectomy patients support the observation that incorporating various analgesic modalities reduces opioid intake and improves postoperative recovery scores (19,20). These findings have important clinical implications. Incorporating multimodal analgesic protocols into standard postoperative care pathways for thyroidectomy patients could not only reduce opioid consumption but also minimize opioid-related adverse effects, promote faster functional recovery, and enhance patient satisfaction. Furthermore, strategies that lower opioid exposure contribute to mitigating the risk of opioid dependence, a concern of growing significance within the global healthcare community (21). In addition to patient-centered benefits, minimizing opioid use could reduce healthcare costs by decreasing complications, shortening hospital stays, and promoting more efficient recovery.

This study possesses several strengths that support the validity of its findings. The randomized controlled design ensured comparable baseline characteristics between groups, minimizing selection bias. The inclusion of both objective measures, such as total opioid consumption, and subjective patient-reported outcomes, such as pain scores and recovery quality, provided a comprehensive assessment of the analgesic interventions. Additionally, continuous monitoring for adverse effects and independent safety oversight strengthened the reliability of the results. Nonetheless, certain limitations should be acknowledged. The study was conducted at a single tertiary care center, which may limit the generalizability of the findings to other surgical settings or broader patient populations. Assessment of outcomes was restricted to the immediate postoperative period, thereby excluding longer-term effects such as the development of chronic pain, functional recovery in daily life, or delayed adverse events. Future research should extend follow-up periods to assess the long-term efficacy and safety of multimodal analgesic approaches after thyroidectomy. Furthermore, economic evaluations encompassing total healthcare expenditures related to opioid use, rehabilitation needs, and management of adverse events would provide a more comprehensive understanding of the cost-effectiveness of multimodal strategies. The evidence generated by this study supports the integration of opioid-based multimodal analgesia into routine thyroidectomy care, while also highlighting the need for broader multicenter trials and longitudinal studies to confirm and expand upon these promising findings.

CONCLUSION

The study concluded that patients undergoing thyroidectomy experienced superior postoperative pain control, fewer opioid-related complications, and improved recovery outcomes when managed with opioid-based multimodal analgesia compared to opioids alone. Incorporating a combination of different pain relief strategies not only enhanced patient comfort but also supported faster recovery and reduced hospitalization duration. These findings emphasize the need for multimodal analgesia to become a standard practice in postoperative care for thyroidectomy patients, ensuring better patient well-being and clinical outcomes. Future research should explore the long-term effects of multimodal pain management strategies, including their impact on patient rehabilitation and healthcare costs.

AUTHOR CONTRIBUTION

Author	Contribution
Umer Mushtaq*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Muhammad Shoaib Khan	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published

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Kishmala Ijaz	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Hamza Ali Malik	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Ibtesam Raza	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Muhammad Saqlain	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published

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