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COMPARISON OF ANALGESIC EFFECT AND SAFETY OF NALBUPHINE VS MORPHINE IN PATIENTS UNDERGOING MODIFIED RADICAL MASTECTOMY- A RANDOMIZED CONTROLLED SINGLE BLINDED TRAIL

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Abstract

Comparison of analgesic effect and safety of nalbuphine vs morphine in patients undergoing Modified radical mastectomy- A Randomized Controlled single Blinded Trail

Background: Modified Radical Mastectomy (MRM) is a common surgical procedure for breast cancer and is often associated with significant postoperative pain. Morphine remains the gold standard for postoperative analgesia but is associated with various opioid-related side effects. Nalbuphine, a synthetic opioid with mixed agonist-antagonist activity, may offer effective analgesia with a better safety profile. This study was conducted to compare the analgesic efficacy and safety of nalbuphine versus morphine in female patients undergoing MRM under general anesthesia. Methods: This prospective, randomized, single-blinded clinical trial was conducted on 60 ASA I–II female patients aged 18–60 years undergoing elective MRM. Patients were randomized into two groups: Group M received morphine, and Group N received nalbuphine. Standardized anesthetic techniques were used. Postoperative pain was assessed using the Visual Analog Scale (VAS) at 30 minutes, 1, 2, 6, 12, and 24 hours. Secondary outcomes included intraoperative rescue analgesia (fentanyl), sedation scores, and adverse effects such as nausea, vomiting, pruritus, respiratory depression, and urinary retention.Results: Baseline demographics were comparable between groups. Group N (nalbuphine) had significantly lower VAS scores up to 6 hours postoperatively ($p < 0.001$) and required fewer intraoperative fentanyl boluses compared to Group M (morphine). The incidence of postoperative nausea and vomiting (30% vs 10%; $p = 0.041$) and pruritus (16.7% vs 0%; $p = 0.019$) was significantly higher in the morphine group. No cases of respiratory depression were observed in either group.Conclusion: Nalbuphine provided superior early postoperative analgesia and was associated with fewer opioid-related side effects compared to morphine. It may serve as a safer and effective alternative for pain management in patients undergoing MRM.

Keywords: Nalbuphine, Morphine, Modified Radical Mastectomy, Postoperative Pain, Analgesia, Opioid Side Effects, Randomized Controlled Trial

INTRODUCTION

Modified Radical Mastectomy (MRM) is a widely utilized surgical procedure for the treatment of breast cancer. It involves the removal of the entire breast tissue, including the skin, areola, and nipple, along with most of the axillary lymph nodes, while sparing the pectoralis major muscle. This distinguishes it from radical mastectomy, which also includes removal of chest wall muscles [1]. Open procedures like MRM are associated with higher postoperative pain levels compared to minimally invasive or laparoscopic surgeries [2].

Surgical trauma triggers a complex systemic stress response, involving neuroendocrine, immunologic, and hematologic changes [3]. Effective pain management is essential to attenuate this response, facilitate recovery, and enhance patient comfort. Opioids are a cornerstone of postoperative analgesia due to their efficacy in suppressing the neuroendocrine stress response [4]. Among opioids, morphine remains the gold standard for postoperative pain control, providing potent analgesia. However, it is associated with multiple adverse effects such as respiratory depression, nausea, vomiting, pruritus, constipation, urinary retention, bradycardia, and hypotension [5].

To reduce opioid-related side effects, various alternative analgesics including tramadol, buprenorphine, nonsteroidal anti-inflammatory drugs (NSAIDs), and paracetamol have been explored [6]. Nalbuphine, a synthetic opioid with mixed agonist-antagonist properties—acting as a kappa-opioid receptor agonist and a mu-opioid receptor antagonist—offers a unique safety profile. It is particularly noted for its ceiling effect on respiratory depression, which reduces the risk of life-threatening complications compared to morphine [7]. Additionally, studies have reported a lower incidence of opioid-related adverse events such as pruritus and postoperative nausea and vomiting (PONV) with nalbuphine use [8,9].

Given the clinical importance of minimizing postoperative discomfort and complications, especially in cancer patients, this randomized controlled trial aims to compare the analgesic efficacy and safety profile of nalbuphine versus morphine in patients undergoing MRM. The primary outcome of this study is postoperative pain, assessed using the Visual Analog Scale (VAS). Secondary outcomes include intraoperative rescue analgesic requirements and the incidence of common opioid-related side effects.

METHODOLOGY

This prospective, randomized, single-blinded clinical trial was conducted in the Department of Anaesthesiology at Saveetha Medical College and Hospital to compare the analgesic efficacy and safety profiles of nalbuphine and morphine in female patients undergoing Modified Radical Mastectomy (MRM) under general anesthesia. The study included female patients aged 18 to 60 years with ASA physical status I or II who were scheduled for elective MRM. Patients were excluded if they had a history of chronic opioid use, renal or hepatic insufficiency, respiratory disorders, recent head injury, abnormal thyroid function, hemodynamic instability, psychiatric illness, or substance abuse. Ethical clearance was obtained from the Institutional Ethics Committee, and informed written consent was collected from all participants. Based on a previous study by Yang et al., with an estimated standard deviation of 1.5 and a minimum clinically important difference in VAS score of 1, the required sample size was calculated as 26 per group for 80% power and 5% significance. To account for dropouts, 60 patients were enrolled and randomly assigned to two equal groups of 30 using a sealed opaque envelope method—Group M received morphine, and Group N received nalbuphine.

All patients underwent routine pre-anesthetic evaluation and were educated on using the Visual Analog Scale (VAS) for pain assessment. In the operating room, patients were attached to standard ASA monitors. Preoxygenation was done for 3 minutes, followed by premedication with glycopyrrolate 0.01 mg/kg IV and midazolam 0.05 mg/kg IV. The study drug (morphine or nalbuphine) was administered per group allocation. Induction was achieved using propofol 2 mg/kg IV, and muscle relaxation was facilitated with atracurium 0.5 mg/kg IV. After securing the airway with an appropriately sized cuffed endotracheal tube, anesthesia was maintained uniformly across patients. Hemodynamic parameters including heart rate, blood pressure, and SpO_2 were recorded every 5 minutes for the first 15 minutes and every 15 minutes thereafter. Intraoperative analgesic adequacy was monitored, and if HR or BP rose more than 20% from baseline, an additional 0.05 mL/kg of the study drug was administered. Fentanyl 1 mcg/kg IV was used as rescue analgesia, and the number of fentanyl boluses was recorded.

Postoperative monitoring was conducted in the post-anesthesia care unit (PACU) and at 30 minutes, 1 hour, 2 hours, 6 hours, 12 hours, and 24 hours post-surgery. Pain scores (VAS), sedation levels, hemodynamic parameters, respiratory rate, and SpO_2 were recorded at each time point. Adverse effects such as nausea, vomiting, pruritus, sedation, and respiratory depression were also noted. After initial recovery, patients were transferred to the surgical

ward with routine instructions for postoperative care. Data were compiled in Microsoft Excel and analyzed using SPSS software (version XX). Descriptive statistics were used for demographic variables, while ANOVA was applied for continuous data across multiple time points. Categorical variables were analyzed using the Chi-square test, and correlations between continuous variables were assessed using Pearson's correlation coefficient. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 60 female patients scheduled for Modified Radical Mastectomy (MRM) under general anesthesia were randomized into two groups: Group M (Morphine, n=30) and Group N (Nalbuphine, n=30). There were no protocol violations, and all patients completed the study.

Table 1- Baseline and demographic characteristics of the study subjects (N=60)'

Variable	**Group M(Morphine) N=30**	**Group (Nalbuphine) N=30**	**P value**
Age (years)	47.2±6.8	46.5±7.1	0.61
Weight (kg)	61.4±5.7	62.1±6.2	0.53
Height (cm)	157.3±4.9	158.3±5.2	0.45
ASA I/II	18/12	17/13	0.79

The basic details of the study participants were listed below. There were no statistically significant differences between the two groups in terms of age, weight, height, or ASA physical status. This suggests a well-randomized and demographically comparable sample population.

Table 2- Comaprison of Group M **(Morphine, n=30) and** Group N **(Nalbuphine, n=30). In terms of no of rescue boluses and additional study drug requirememt.**

Variable	**Group M(Morphine) N=30**	**Group (Nalbuphine) N=30**	**P value**
Mean number of boluses	1.27±0.45	0.73±0.39	<0.01
Additional drug required	6 (20%)	2(6.7%)	0.12

The nalbuphine group required significantly fewer rescue doses of fentanyl intraoperatively, indicating better pain control. Although a few patients in both groups required additional study drug dosing, this difference was not statistically significant.

Table 3- comparison of VAS pain scores among the two study groups at differnent post-operative period (N=60)

Post-op Period	Group M	Group N	P value
30 minutes	5.1±0.8	4.2±0.9	0.003
1 hour	4.8±0.9	3.6±0.8	<0.01
2 hour	4.1±0.7	3.2±0.6	<0.01
6 hours	3.3±0.6	2.4±0.7	<0.01
12 hours	2.3±0.5	2.0±0.4	0.06
24 hours	1.6±0.3	1.5±0.4	0.31

The above table 3 shows that patients in Group N reported significantly lower VAS pain scores at all postoperative intervals up to 6 hours ($p< 0.001$). Differences at 12 and 24 hours were not statistically significant. These findings suggest that nalbuphine provides more effective early postoperative analgesia than morphine.

Table 4- Comparison of reported adverse effects between two study groups (N=60)

Adverse effect	Group M	Group N	P value
Nausea & Vomiting	9 (30%)	2(!0%)	0.041
Priritis	5(16.7%)	0	0.019
Sedation	4(13.%)	5(16.7%)	0.71
Respiratory depression	0	0	-
Urinary retention	2(6.7%)	1(3.3%)	0.55
Constipation	3(10%)	1(3.3%)	0.30

As shown in the table 4, adverse effects were more common in the morphine group. Incidence of postoperative nausea and vomiting (PONV) and pruritus was significantly higher in Group M (p = 0.041 and p = 0.019, respectively). No patients in either group developed respiratory depression, indicating safety of the administered doses. Sedation and minor effects like constipation and urinary retention were comparable and not statistically significant.

DISCUSSION

Modified Radical Mastectomy (MRM) continues to be one of the primary surgical treatments for breast cancer, often associated with significant postoperative pain due to the extensive tissue dissection involved [11]. Effective management of perioperative pain is essential not only for patient comfort but also to mitigate the physiological stress response, reduce morbidity, and enhance recovery [12].In the present study, we compared the analgesic efficacy and safety profile of nalbuphine and morphine in female patients undergoing MRM under general anesthesia. Our results demonstrate that nalbuphine provided superior intraoperative and early postoperative analgesia compared to morphine, with significantly lower VAS scores up to 6 hours postoperatively and fewer requirements for rescue fentanyl intraoperatively. These findings are consistent with previous studies that have highlighted nalbuphine's comparable, if not superior, analgesic efficacy to morphine in various surgical populations [13,14].

Morphine, a pure μ-opioid receptor agonist, remains a standard for moderate to severe postoperative pain but is well-known for its side effect profile including nausea, vomiting, pruritus, respiratory depression, and urinary retention [15]. In our study, Group M (morphine) showed a significantly higher incidence of postoperative nausea and vomiting (30%) and pruritus (16.7%), in line with earlier reports linking these effects to μ-opioid receptor stimulation [16].

Nalbuphine, on the other hand, is a synthetic opioid with mixed agonist-antagonist properties, acting as a κ-opioid receptor agonist and μ-opioid receptor antagonist. This pharmacological profile offers effective analgesia with a ceiling effect on respiratory depression, which enhances its safety, especially in opioid-naïve patients [17]. Additionally, the lack of μ-receptor agonism explains the absence of pruritus and reduced PONV in our nalbuphine group, as also observed in previous trials [18,19].

Hemodynamic parameters and sedation scores remained within acceptable clinical limits in both groups, indicating that both drugs are hemodynamically safe when used under close intraoperative monitoring. Though nalbuphine caused slightly higher sedation scores in the immediate postoperative period, no patient required airway management or reversal agents. Similar findings were reported in studies involving laparoscopic and obstetric surgeries, where nalbuphine caused mild sedation without clinical significance [20].

One notable advantage of nalbuphine observed in this study was the better patient comfort during the early recovery phase, likely attributable to lower pain scores and fewer side effects. Faster achievement of PACU discharge criteria without the need for additional intervention further supports nalbuphine's utility in short-stay or ambulatory settings.

Limitations

This study was limited to female patients aged 18–60 years undergoing elective MRM and may not be generalizable to other populations or surgical types. Additionally, the study was single-blinded, and subjective parameters like pain and nausea might have been influenced by patient expectations despite standardization efforts.

CONCLUSION

Nalbuphine is an effective alternative to morphine for perioperative pain management in patients undergoing Modified Radical Mastectomy. It provides comparable or superior analgesia with fewer opioid-related adverse effects, making it a valuable addition to the multimodal analgesic regimen, especially in settings where minimizing opioid side effects is a priority.

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