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COMPARATIVE STUDY OF OPIOID-FREE VERSUS OPIOID-SPARING ANAESTHESIA ON POSTOPERATIVE RECOVERY AND ANALGESIC REQUIREMENT

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ABSTRACT

Background: Opioids are commonly used during general anaesthesia for perioperative analgesia; however, their use may be associated with postoperative nausea, vomiting, sedation, respiratory depression, delayed recovery, and increased postoperative opioid requirement. Opioid-free anaesthesia uses multimodal non-opioid agents to provide adequate antinociception while minimizing opioid-related adverse effects. The aim is to compare opioid-free anaesthesia with opioid-sparing anaesthesia in terms of postoperative recovery, pain scores, analgesic requirement, perioperative hemodynamic parameters, and adverse events.

Materials and Methods: This prospective comparative study included 92 adult patients undergoing elective surgery under general anaesthesia at a tertiary care hospital. Patients were divided into Group OFA (n=46), receiving opioid-free anaesthesia, and Group OSA (n=46), receiving opioid-sparing anaesthesia. Postoperative pain was assessed using the Numeric Rating Scale at predefined intervals up to 24 hours. Time to first rescue analgesia, total 24-hour opioid-equivalent requirement, recovery characteristics, Modified Aldrete Score, hemodynamic parameters, and postoperative adverse events were recorded. Data were analysed using IBM SPSS version 27.0, with $p<0.05$ considered statistically significant.

Results: Baseline demographic and perioperative characteristics were comparable between the groups. Post-intubation heart rate and mean arterial pressure were significantly lower in Group OFA ($p=0.012$ and $p=0.008$, respectively). NRS pain scores were significantly lower in Group OFA from 0 to 6 hours postoperatively, while 12- and 24-hour scores were comparable. Time to first rescue analgesia was longer in Group OFA (365.40 ± 94.20 vs 286.70 ± 82.60 minutes; $p<0.001$), and rescue analgesia was required in 52.17% versus 76.09% of patients ($p=0.017$). The 24-hour opioid-equivalent requirement was lower in Group OFA (3.20 ± 2.10 vs 5.90 ± 2.80 mg; $p<0.001$). Time to eye opening, extubation, PACU stay, oral intake, and mobilization were significantly shorter with OFA. Postoperative nausea occurred in 8.70% versus 28.26% of patients ($p=0.030$).

Conclusion: Opioid-free anaesthesia provided better early postoperative analgesia, reduced opioid requirement, faster recovery, and lower postoperative nausea compared with opioid-sparing anaesthesia, while maintaining acceptable perioperative safety.

Keywords: Opioid-free anaesthesia; Opioid-sparing anaesthesia; Postoperative analgesia; Multimodal analgesia; Postoperative recovery.

INTRODUCTION

Effective perioperative pain management is an essential component of modern anaesthetic practice and has a major influence on postoperative comfort, physiological stability, mobilization, functional recovery, and overall quality of surgical care. Opioids have traditionally occupied a central position in

balanced general anaesthesia because of their potent analgesic properties and their ability to suppress nociceptive responses to surgical stimulation. They are commonly administered during induction, maintenance of anaesthesia, emergence, and the early postoperative period. However, increasing awareness of opioid-related adverse effects has led to reconsideration of routine or excessive perioperative opioid administration. These adverse effects may include respiratory depression, postoperative nausea and vomiting, sedation, ileus, urinary retention, pruritus, impaired gastrointestinal recovery, opioid-induced hyperalgesia, tolerance, and the possibility of persistent opioid use after surgery. Consequently, contemporary perioperative practice increasingly emphasizes rational opioid administration rather than unrestricted reliance on these drugs.[1] The concept of opioid stewardship has therefore gained importance in perioperative medicine. Opioid stewardship does not imply complete avoidance of opioids in every patient; instead, it focuses on appropriate patient selection, individualized prescribing, use of the lowest effective opioid dose, and incorporation of non-opioid analgesic techniques whenever clinically suitable. Optimal perioperative analgesia requires a balance between avoiding unnecessary opioid exposure and preventing inadequately treated surgical pain. Failure to control postoperative pain may delay mobilization, interfere with respiratory exercises, impair sleep, increase physiological stress, and contribute to prolonged recovery. At the same time, excessive opioid exposure may adversely affect recovery through sedation, gastrointestinal dysfunction, respiratory complications, and other opioid-related adverse events. A structured multimodal approach has therefore become an important element of perioperative pain management and enhanced recovery pathways.[2] Multimodal analgesia is based on the simultaneous use of agents and techniques acting through different mechanisms within the nociceptive pathway. Common components include paracetamol, non-steroidal anti-inflammatory drugs, N-methyl-D-aspartate receptor antagonists such as ketamine, alpha-2 adrenergic agonists such as dexmedetomidine, intravenous lignocaine, glucocorticoids, and local or regional anaesthetic techniques. By combining drugs with complementary mechanisms, adequate antinociception may be obtained while limiting reliance on a single pharmacological class. This approach forms the basis of both opioid-sparing and opioid-free anaesthetic strategies. Selection of individual drugs must nevertheless consider the surgical procedure, expected intensity of postoperative pain, patient comorbidities, contraindications, and potential adverse effects of the alternative agents themselves.[3] Opioid-sparing anaesthesia represents a pragmatic approach in which opioids are not completely eliminated but their intraoperative and postoperative doses are substantially reduced by integrating non-opioid analgesics and regional techniques. This strategy maintains the option of opioid administration when required for intense nociceptive stimulation while attempting to minimize dose-related complications. In contrast, opioid-free anaesthesia is generally defined as an anaesthetic technique in which systemic opioids are completely avoided during the intraoperative period, with antinociception provided through combinations of non-opioid agents. The growing interest in these techniques has been supported by the broader movement toward multimodal anaesthesia, enhanced recovery, early mobilization, reduced postoperative sedation, and more conservative opioid prescribing.[4] The development of opioid-free anaesthesia has expanded the traditional concept of balanced anaesthesia by separating unconsciousness, immobility, autonomic control, and antinociception into components that can be targeted with different pharmacological agents. Dexmedetomidine may provide sympatholysis, sedation, and analgesic-sparing activity; ketamine contributes through N-methyl-D-aspartate receptor antagonism and antihyperalgesic properties; lignocaine may provide analgesic and anti-inflammatory effects; and paracetamol and non-steroidal anti-inflammatory drugs act through peripheral and central analgesic pathways. Regional and local anaesthetic techniques may further reduce nociceptive input from the surgical site. Such combinations provide a theoretical framework for avoiding intraoperative opioids without necessarily compromising postoperative analgesia. Nevertheless, opioid-free anaesthesia should not be considered a single standardized technique because drug combinations, doses, monitoring requirements, and clinical applicability vary considerably among surgical procedures and patient populations.[5] Despite increasing clinical interest, complete opioid avoidance remains an evolving concept. Non-opioid agents are not without adverse effects; alpha-2 agonists may produce bradycardia or hypotension, ketamine may cause psychomimetic effects or excessive sympathetic stimulation in susceptible individuals, and systemic local anaesthetics require careful dosing because of potential toxicity. Therefore, the objective of perioperative analgesic optimization should not simply be the elimination of opioids but the achievement of effective analgesia, hemodynamic stability, rapid recovery, minimal adverse events, and reduced exposure to unnecessary medications. Current evidence emphasizes that the clinical value of opioid-free anaesthesia depends considerably on the alternative drugs selected and on the manner in which the multimodal regimen is implemented.[6]

MATERIALS AND METHODS

This prospective comparative study was conducted in the Department of Anaesthesiology at a tertiary care hospital. A total of 92 adult patients scheduled to undergo elective surgery under general anaesthesia

were included in the study after obtaining approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants before enrolment. Patients were divided into two groups of 46 patients each according to the anaesthetic technique employed: Group OFA (n=46) received an opioid-free anaesthesia protocol, whereas Group OSA (n=46) received an opioid-sparing anaesthesia protocol. Adult patients aged 18–65 years, belonging to the American Society of Anesthesiologists (ASA) physical status I–III, and scheduled for elective surgical procedures under general anaesthesia were considered eligible. Patients with known allergy or contraindication to any study medication, chronic opioid use or opioid dependence, significant hepatic or renal dysfunction, uncontrolled cardiovascular disease, severe respiratory disease, pregnancy, psychiatric illness affecting pain assessment, inability to understand the pain scoring system, or requirement for postoperative mechanical ventilation were excluded from the study.

Methodology: All patients underwent a detailed pre-anaesthetic evaluation, including medical and surgical history, history of previous anaesthesia, medication use, substance or opioid consumption, relevant comorbidities, airway assessment, and general and systemic examination. Baseline demographic and clinical parameters including age, sex, body mass index, ASA physical status, type of surgery, baseline heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, and peripheral oxygen saturation were recorded. Routine laboratory investigations were performed according to institutional protocol.

Anaesthetic Technique: Standard monitoring comprising electrocardiography, non-invasive blood pressure, pulse oximetry, end-tidal carbon dioxide, temperature, and neuromuscular monitoring, wherever indicated, was instituted in all patients. Anaesthesia was induced and maintained according to standardized institutional protocols to minimize intergroup variations.

Patients in the opioid-free anaesthesia group (Group OFA) received a multimodal opioid-free regimen using non-opioid analgesic and anaesthetic adjuncts such as intravenous paracetamol, non-steroidal anti-inflammatory drugs when not contraindicated, dexmedetomidine, lignocaine and/or ketamine in appropriate clinically accepted doses. Regional or local anaesthetic infiltration was used when considered appropriate for the surgical procedure. No intraoperative opioid was administered in this group.

Patients in the opioid-sparing anaesthesia group (Group OSA) received multimodal non-opioid analgesic agents similar to routine institutional practice, with a reduced dose of an opioid such as fentanyl administered during induction and/or intraoperatively whenever clinically indicated. The total intraoperative opioid dose was documented for each patient.

Anaesthesia was maintained with an inhalational or intravenous anaesthetic agent with an oxygen-air mixture, and muscle relaxation was provided when required. Ventilation was adjusted to maintain end-tidal carbon dioxide within the physiological range. At the end of surgery, neuromuscular blockade was reversed and patients were extubated after fulfilling standard extubation criteria.

Intraoperative Assessment: Hemodynamic parameters including heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, and oxygen saturation were recorded at baseline, after induction, after intubation, at predefined intraoperative intervals, and before extubation. Episodes of hypotension, hypertension, bradycardia, or tachycardia requiring treatment were documented. The total amount of intravenous fluids, blood loss, duration of anaesthesia, duration of surgery, requirement for vasoactive medications, and intraoperative rescue analgesia were also recorded.

Postoperative Pain and Analgesic Assessment: Postoperative pain was assessed using an 11-point Numeric Rating Scale (NRS) ranging from 0, indicating no pain, to 10, indicating the worst imaginable pain. Pain scores were recorded at rest at 0, 1, 2, 4, 6, 12, and 24 hours following surgery. Rescue analgesia was administered according to the institutional postoperative analgesic protocol when the NRS score reached the predetermined intervention threshold. The time to first rescue analgesic, total postoperative rescue analgesic consumption during the first 24 hours, and proportion of patients requiring rescue analgesia were recorded. Where opioids were required postoperatively, total consumption was converted to an equivalent opioid dose for comparison.

Postoperative Recovery Assessment: The quality of early postoperative recovery was evaluated using clinically relevant parameters including time to eye opening, time to extubation, time to achieve discharge criteria from the post-anaesthesia care unit (PACU), postoperative sedation, time to first oral intake, and time to mobilization. The Modified Aldrete Score was used to assess recovery in the PACU. Length of postoperative hospital stay was also documented wherever applicable.

Postoperative Adverse Events: Patients were monitored for postoperative complications including nausea, vomiting, respiratory depression, excessive sedation, dizziness, pruritus, shivering, urinary retention, hypotension, bradycardia, and postoperative hypoxemia. Postoperative nausea and vomiting and requirement for rescue antiemetic therapy were specifically documented during the first 24 postoperative hours.

Outcome Measures: The primary outcome measures were postoperative pain scores and total rescue analgesic requirement during the first 24 hours after surgery. Secondary outcome measures included time to first rescue analgesia, intraoperative hemodynamic stability, recovery characteristics, Modified Aldrete Score, postoperative nausea and vomiting, opioid-related adverse effects, time to oral intake, time to mobilization, and postoperative length of stay.

Statistical Analysis: Data were entered into Microsoft Excel and analysed using IBM SPSS Statistics for Windows, version 27.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation or median with interquartile range according to data distribution, whereas categorical variables were presented as frequencies and percentages. Normality of continuous data was assessed using the Shapiro–Wilk test. Normally distributed continuous variables were compared using the independent-samples Student's t-test, while non-normally distributed variables were analysed using the Mann–Whitney U test. Serial pain and hemodynamic measurements were analysed using repeated-measures analysis of variance or an appropriate non-parametric equivalent. Categorical variables were compared using the Chi-square test or Fisher's exact test, as appropriate. A p-value <0.05 was considered statistically significant.

RESULTS

[Table 1] Comparison of baseline demographic and perioperative characteristics between the two groups

A total of 92 patients were included in the study, with 46 patients in Group OFA and 46 patients in Group OSA. The mean age of patients was 42.15 ± 11.26 years in Group OFA and 43.04 ± 10.94 years in Group OSA. The difference in mean age between the two groups was not statistically significant (p=0.702). The mean body mass index was 24.86 ± 3.18 kg/m² in Group OFA and 25.21 ± 3.34 kg/m² in Group OSA, with no statistically significant difference between the groups (p=0.608). In Group OFA, 25 (54.35%) patients were male and 21 (45.65%) were female, whereas in Group OSA, 27 (58.70%) patients were male and 19 (41.30%) were female. The sex distribution was comparable between the two groups (p=0.674). With regard to ASA physical status, 20 (43.48%) patients in Group OFA and 18 (39.13%) patients in Group OSA belonged to ASA I. ASA II status was observed in 21 (45.65%) and 23 (50.00%) patients, respectively, while ASA III status was present in 5 (10.87%) patients in each group. The distribution of ASA physical status did not differ significantly between the groups (p=0.906). The mean duration of surgery was 92.41 ± 20.63 minutes in Group OFA and 95.13 ± 21.48 minutes in Group OSA (p=0.537). Similarly, the mean duration of anaesthesia was 111.28 ± 22.64 minutes in Group OFA and 114.67 ± 23.11 minutes in Group OSA, and this difference was also statistically non-significant (p=0.479).

[Table 2] Comparison of intraoperative hemodynamic and clinical parameters between the two groups

The mean baseline heart rate was 78.30 ± 8.50 beats/minute in Group OFA and 79.10 ± 8.10 beats/minute in Group OSA, with no statistically significant difference between the groups (p=0.645). Following intubation, the mean heart rate increased to 82.20 ± 9.00 beats/minute in Group OFA and 87.10 ± 9.40 beats/minute in Group OSA. The difference in heart rate after intubation was statistically significant (p=0.012). The mean baseline mean arterial pressure was 91.40 ± 7.20 mmHg in Group OFA and 92.00 ± 7.40 mmHg in Group OSA, showing no significant difference (p=0.694). After intubation, the mean arterial pressure was 88.50 ± 7.00 mmHg in Group OFA and 92.60 ± 7.50 mmHg in Group OSA, and the difference was statistically significant (p=0.008). The mean volume of intraoperative fluid administered was 1045.00 ± 275.00 mL in Group OFA compared with 1090.00 ± 290.00 mL in Group OSA (p=0.447). Mean estimated blood loss was 145.00 ± 82.00 mL and 152.00 ± 88.00 mL, respectively, with no statistically significant difference (p=0.694). Intraoperative hypotension occurred in 5 (10.87%) patients in Group OFA and 7 (15.22%) patients in Group OSA (p=0.536). Bradycardia was observed in 6 (13.04%) patients in Group OFA and 3 (6.52%) patients in Group OSA (p=0.292). Vasopressor support was required in 5 (10.87%) patients in Group OFA compared with 8 (17.39%) patients in Group OSA; however, this difference was not statistically significant (p=0.369).

[Table 3] Comparison of postoperative NRS pain scores and analgesic requirements

The postoperative Numeric Rating Scale pain score at 0 hour was 2.78 ± 0.81 in Group OFA and 3.26 ± 0.88 in Group OSA, with a statistically significant difference between the groups (p=0.008). At 1 hour, the mean NRS score was 2.54 ± 0.75 in Group OFA compared with 3.09 ± 0.83 in Group OSA, and the difference was statistically significant (p=0.001). At 2 hours, the mean NRS score was 2.31 ± 0.72 in Group OFA and 2.87 ± 0.79 in Group OSA, showing a highly statistically significant difference (p<0.001). At 4 hours, the mean NRS score was 2.48 ± 0.76 in Group OFA and 2.93 ± 0.82 in Group OSA (p=0.008). At 6 hours, mean pain scores were 2.63 ± 0.78 and 2.98 ± 0.84, respectively, with a statistically significant difference (p=0.041). At 12 hours, the mean NRS score was 2.41 ± 0.69 in Group OFA and 2.59 ± 0.74 in Group OSA, with no statistically significant difference (p=0.231). Similarly, at 24 hours, the mean NRS values were 2.18 ± 0.61 and 2.27 ± 0.64, respectively, and the difference was not statistically significant (p=0.492).

The mean time to first rescue analgesia was 365.40 ± 94.20 minutes in Group OFA compared with 286.70 ± 82.60 minutes in Group OSA, and the difference was statistically significant (p<0.001). Rescue analgesia was required by 24 (52.17%) patients in Group OFA and 35 (76.09%) patients in Group OSA, representing a statistically significant difference between the groups (p=0.017). The mean 24-hour opioid-equivalent requirement was 3.20 ± 2.10 mg in Group OFA and 5.90 ± 2.80 mg in Group OSA. This difference was highly statistically significant (p<0.001).

[Table 4] Comparison of postoperative recovery characteristics between the two groups

The mean time to eye opening was 7.86 ± 2.03 minutes in Group OFA and 9.21 ± 2.18 minutes in Group OSA, and this difference was statistically significant (p=0.003). The mean time to extubation was 10.54 ± 2.45 minutes in Group OFA compared with 12.11 ± 2.61 minutes in Group OSA, with a statistically significant difference between the groups (p=0.004). The mean duration of stay in the post-anaesthesia care unit was 58.70 ± 11.30 minutes in Group OFA and 67.90 ± 13.20 minutes in Group OSA, and the difference was highly statistically significant (p<0.001). A Modified Aldrete score of ≥9 at 15 minutes was achieved by 37 (80.43%) patients in Group OFA and 29 (63.04%) patients in Group OSA. Although a greater proportion of patients in Group OFA achieved this recovery score, the difference did not reach statistical significance (p=0.064).

The mean time to first oral intake was 5.31 ± 1.42 hours in Group OFA and 6.18 ± 1.67 hours in Group OSA, with a statistically significant difference (p=0.009). The mean time to mobilization was 9.46 ± 2.15 hours in Group OFA compared with 10.83 ± 2.54 hours in Group OSA, and this difference was also statistically significant (p=0.006). The mean postoperative hospital stay was 2.11 ± 0.62 days in Group OFA and 2.37 ± 0.74 days in Group OSA. The difference in postoperative hospital stay was not statistically significant (p=0.071).

[Table 5] Comparison of postoperative adverse events between the two groups

Postoperative nausea was observed in 4 (8.70%) patients in Group OFA and 13 (28.26%) patients in Group OSA. The difference in the occurrence of nausea between the two groups was statistically significant (p=0.030). Vomiting occurred in 2 (4.35%) patients in Group OFA compared with 8 (17.39%) patients in Group OSA; however, the difference did not reach statistical significance (p=0.090). Excessive sedation was recorded in 3 (6.52%) patients in Group OFA and 10 (21.74%) patients in Group OSA, with a p-value of 0.069. Dizziness was reported in 4 (8.70%) patients in Group OFA and 9 (19.57%) patients in Group OSA, without a statistically significant difference (p=0.231).

Pruritus was not observed in any patient in Group OFA, whereas it occurred in 4 (8.70%) patients in Group OSA; the difference was statistically non-significant (p=0.117). Shivering occurred in 3 (6.52%) patients in Group OFA and 5 (10.87%) patients in Group OSA (p=0.714). Postoperative hypotension was recorded in 4 (8.70%) patients in Group OFA compared with 7 (15.22%) patients in Group OSA, with no statistically significant difference (p=0.522). Postoperative hypoxemia was observed in 1 (2.17%) patient in Group OFA and 4 (8.70%) patients in Group OSA, and the difference was statistically non-significant (p=0.361).

Table 1: Comparison of baseline demographic and perioperative characteristics between the two groups (n=92)

Parameter	Group OFA (n=46)	Group OSA (n=46)	p-value
Age (years), Mean ± SD	42.15 ± 11.26	43.04 ± 10.94	0.702
BMI (kg/m²), Mean ± SD	24.86 ± 3.18	25.21 ± 3.34	0.608
Male, n (%)	25 (54.35%)	27 (58.70%)	0.674
Female, n (%)	21 (45.65%)	19 (41.30%)	
ASA I, n (%)	20 (43.48%)	18 (39.13%)	0.906
ASA II, n (%)	21 (45.65%)	23 (50.00%)	
ASA III, n (%)	5 (10.87%)	5 (10.87%)	
Duration of surgery (min), Mean ± SD	92.41 ± 20.63	95.13 ± 21.48	0.537
Duration of anaesthesia (min), Mean ± SD	111.28 ± 22.64	114.67 ± 23.11	0.479

Table 2: Comparison of intraoperative hemodynamic and clinical parameters between the two groups

Parameter	Group OFA (n=46)	Group OSA (n=46)	p-value
Baseline heart rate (beats/min), Mean ± SD	78.30 ± 8.50	79.10 ± 8.10	0.645
Heart rate after intubation (beats/min), Mean ± SD	82.20 ± 9.00	87.10 ± 9.40	0.012*
Baseline MAP (mmHg), Mean ± SD	91.40 ± 7.20	92.00 ± 7.40	0.694
MAP after intubation (mmHg), Mean ± SD	88.50 ± 7.00	92.60 ± 7.50	0.008*
Intraoperative fluid (mL), Mean ± SD	1045.00 ± 275.00	1090.00 ± 290.00	0.447
Estimated blood loss (mL), Mean ± SD	145.00 ± 82.00	152.00 ± 88.00	0.694
Hypotension, n (%)	5 (10.87%)	7 (15.22%)	0.536
Bradycardia, n (%)	6 (13.04%)	3 (6.52%)	0.292
Vasopressor requirement, n (%)	5 (10.87%)	8 (17.39%)	0.369

*Statistically significant.

Table 3: Comparison of postoperative NRS pain scores and analgesic requirements

Parameter	Group OFA (n=46)	Group OSA (n=46)	p-value
NRS at 0 hour, Mean ± SD	2.78 ± 0.81	3.26 ± 0.88	0.008*
NRS at 1 hour, Mean ± SD	2.54 ± 0.75	3.09 ± 0.83	0.001*
NRS at 2 hours, Mean ± SD	2.31 ± 0.72	2.87 ± 0.79	<0.001*
NRS at 4 hours, Mean ± SD	2.48 ± 0.76	2.93 ± 0.82	0.008*
NRS at 6 hours, Mean ± SD	2.63 ± 0.78	2.98 ± 0.84	0.041*
NRS at 12 hours, Mean ± SD	2.41 ± 0.69	2.59 ± 0.74	0.231
NRS at 24 hours, Mean ± SD	2.18 ± 0.61	2.27 ± 0.64	0.492
Time to first rescue analgesia (min), Mean ± SD	365.40 ± 94.20	286.70 ± 82.60	<0.001*

Patients requiring rescue analgesia, n (%)	24 (52.17%)	35 (76.09%)	0.017*
24-hour opioid equivalent requirement (mg), Mean ± SD	3.20 ± 2.10	5.90 ± 2.80	<0.001*

*Statistically significant.

Table 4: Comparison of postoperative recovery characteristics between the two groups

Recovery parameter	Group OFA (n=46)	Group OSA (n=46)	p-value
Time to eye opening (min), Mean ± SD	7.86 ± 2.03	9.21 ± 2.18	0.003*
Time to extubation (min), Mean ± SD	10.54 ± 2.45	12.11 ± 2.61	0.004*
PACU stay (min), Mean ± SD	58.70 ± 11.30	67.90 ± 13.20	<0.001*
Modified Aldrete score ≥9 at 15 min, n (%)	37 (80.43%)	29 (63.04%)	0.064
Time to first oral intake (hours), Mean ± SD	5.31 ± 1.42	6.18 ± 1.67	0.009*
Time to mobilization (hours), Mean ± SD	9.46 ± 2.15	10.83 ± 2.54	0.006*
Postoperative hospital stay (days), Mean ± SD	2.11 ± 0.62	2.37 ± 0.74	0.071

*Statistically significant.

Table 5: Comparison of postoperative adverse events between the two groups

Adverse event	Group OFA (n=46), n (%)	Group OSA (n=46), n (%)	p-value
Nausea	4 (8.70%)	13 (28.26%)	0.030*
Vomiting	2 (4.35%)	8 (17.39%)	0.090
Excessive sedation	3 (6.52%)	10 (21.74%)	0.069
Dizziness	4 (8.70%)	9 (19.57%)	0.231
Pruritus	0 (0.00%)	4 (8.70%)	0.117
Shivering	3 (6.52%)	5 (10.87%)	0.714
Postoperative hypotension	4 (8.70%)	7 (15.22%)	0.522
Postoperative hypoxemia	1 (2.17%)	4 (8.70%)	0.361

DISCUSSION

The present study included 92 patients, equally distributed between the opioid-free anaesthesia (OFA) and opioid-sparing anaesthesia (OSA) groups. Both groups were comparable for baseline characteristics, with mean ages of 42.15 ± 11.26 and 43.04 ± 10.94 years (p=0.702), mean BMI of 24.86 ± 3.18 and 25.21 ± 3.34 kg/m² (p=0.608), and no significant differences in sex, ASA status, duration of surgery, or duration of anaesthesia. Baseline heart rate and MAP were also comparable. However, after intubation, heart rate was significantly lower in the OFA group than in the OSA group (82.20 ± 9.00 vs 87.10 ± 9.40 beats/min; p=0.012), as was MAP (88.50 ± 7.00 vs 92.60 ± 7.50 mmHg; p=0.008). Hypotension, bradycardia, and vasopressor requirements did not differ significantly. Bao et al. (2024), in a randomized trial involving patients undergoing video-assisted thoracoscopic surgery, similarly reported comparable baseline characteristics between groups but found a different hemodynamic pattern after intubation: heart rate was higher with OFA (89 ± 17 vs 77 ± 15 beats/min; p<0.001) and diastolic blood pressure was also higher (87 ± 17 vs 80 ± 13 mmHg; p=0.003). Nevertheless, hypotensive episodes were less frequent with OFA, averaging 0.5 ± 0.8 versus 1.0 ± 2.0 episodes per patient (p=0.02). These differences indicate that the hemodynamic response to OFA may vary with the combination and doses of non-opioid agents used.[7] Postoperative pain assessment in the present study demonstrated significantly lower NRS scores in the OFA group during the early postoperative period. NRS scores at 0, 1, 2, 4, and 6 hours were 2.78 ± 0.81, 2.54 ± 0.75, 2.31 ± 0.72, 2.48 ± 0.76, and 2.63 ± 0.78 in the OFA group compared with 3.26 ± 0.88, 3.09 ± 0.83, 2.87 ± 0.79, 2.93 ± 0.82, and 2.98 ± 0.84 in the OSA group, respectively, with all differences statistically significant. By 12 and 24 hours, however, the difference was no longer significant. Ding et al. (2025), in a randomized controlled trial of radical mastectomy, also found significantly lower postoperative NRS scores with OFA. Their NRS scores were 1.89 ± 0.80 versus 2.36 ± 1.20 at 30 minutes (p=0.010), 1.21 ± 0.60 versus 1.66 ± 0.80 at 24 hours (p<0.01), and 1.03 ± 0.40 versus 1.28 ± 0.60 at 48 hours (p=0.011) for OFA and opioid-based anaesthesia, respectively. In contrast to the present study, their significant analgesic advantage persisted to 48 hours, possibly reflecting differences in surgery and the use of interpectoral and pectoralis-serratus plane blocks as part of the OFA regimen.[8] The reduction in postoperative analgesic requirement was another important finding of the present study. Time to first rescue analgesia was significantly longer with OFA (365.40 ± 94.20 vs 286.70 ± 82.60 minutes; p<0.001), while rescue analgesia was required in 24/46 (52.17%) OFA patients compared with 35/46 (76.09%) OSA patients (p=0.017). The mean 24-hour opioid-equivalent requirement was also significantly lower with OFA (3.20 ± 2.10 vs 5.90 ± 2.80 mg; p<0.001). Bakan et al. (2015) reported comparable opioid-sparing effects in 80 patients undergoing laparoscopic cholecystectomy. At two postoperative hours, fentanyl consumption was 75 ± 59 µg with opioid-free dexmedetomidine-lidocaine-propofol anaesthesia compared with 120 ± 94 µg with remifentanil-propofol anaesthesia, representing a statistically significant reduction. They also reported significantly lower rescue analgesic requirements in the OFA group, although fentanyl consumption became comparable between groups at six hours. Thus, both studies demonstrated the most evident analgesic-sparing benefit during the early postoperative period.[9] The reduced opioid

requirement observed in the present study is also consistent with findings reported after major abdominal surgery, although the magnitude of benefit varies considerably according to the operative procedure. Hublet et al. (2022) compared OFA with opioid-based anaesthesia in 77 patients undergoing pancreatic resection. At 24 hours, cumulative morphine consumption was only 4 mg [IQR 0–12] in the OFA group compared with 24 mg [18.5–33] in the opioid-based group (p=0.0007); by 48 hours, consumption was 10 mg [2–24] versus 36 mg [24–52] (p=0.005). They also reported markedly lower NRS scores at 24 hours (0 [0–2] vs 5 [4–6]; p=0.005). In the present study, the OFA group similarly required substantially less opioid during the first 24 hours, although NRS scores at 24 hours were comparable (2.18 ± 0.61 vs 2.27 ± 0.64; p=0.492). Hublet et al. additionally reported a shorter median hospital stay with OFA (10 [6–16] vs 14 [7–46] days; p<0.001), whereas the reduction in hospital stay in the present study did not reach statistical significance.[10] Early postoperative recovery was significantly faster in the OFA group in the present study. Mean time to eye opening was 7.86 ± 2.03 versus 9.21 ± 2.18 minutes (p=0.003), and time to extubation was 10.54 ± 2.45 versus 12.11 ± 2.61 minutes (p=0.004). PACU stay was also significantly shorter with OFA (58.70 ± 11.30 vs 67.90 ± 13.20 minutes; p<0.001). A Modified Aldrete score ≥9 at 15 minutes was achieved in 80.43% of OFA patients compared with 63.04% of OSA patients, although the difference was not statistically significant (p=0.064). Xue et al. (2024), in a randomized controlled trial of 60 patients undergoing shoulder arthroscopy, similarly demonstrated a significantly shorter PACU stay with OFA using esketamine and dexmedetomidine: 39.4 ± 6.76 minutes compared with 48.7 ± 7.90 minutes with propofol-remifentanil anaesthesia (p<0.001). Their groups remained comparable for the Modified Aldrete score, supporting the finding that reduced PACU duration did not compromise attainment of standard recovery criteria.[11] Functional recovery parameters also favoured OFA in the present study. Time to first oral intake was significantly shorter in the OFA group (5.31 ± 1.42 vs 6.18 ± 1.67 hours; p=0.009), while mobilization occurred at 9.46 ± 2.15 hours compared with 10.83 ± 2.54 hours in the OSA group (p=0.006). Postoperative hospital stay was numerically shorter with OFA (2.11 ± 0.62 vs 2.37 ± 0.74 days), but this difference was not statistically significant (p=0.071). Accurso et al. (2025), in a randomized controlled trial of laparoscopic abdominal surgery, also demonstrated earlier mobilization with their blended OFA protocol. Median mobilization time was 36.00 [18.00–48.00] hours in the OFA group compared with 48.00 [24.00–72.00] hours in the opioid-treated group (p<0.001). Their median hospital stay was also significantly shorter, at 4.00 [2.00–6.00] versus 6.00 [4.00–9.00] days (p<0.001). Thus, the direction of the mobilization findings was similar, although the present study did not demonstrate a statistically significant reduction in overall hospital stay.[12] Postoperative nausea showed one of the clearest differences in adverse effects in the present study. Nausea occurred in only 4/46 (8.70%) patients receiving OFA compared with 13/46 (28.26%) receiving OSA (p=0.030). Vomiting was also less frequent with OFA, occurring in 2/46 (4.35%) versus 8/46 (17.39%) patients, although this did not reach statistical significance (p=0.090). Ziemann-Gimmel et al. (2014) reported a similar reduction in PONV in their prospective randomized bariatric surgery trial. Despite triple antiemetic prophylaxis, PONV occurred in 12/60 (20.00%) patients receiving opioid-free TIVA with propofol, ketamine, and dexmedetomidine compared with 22/59 (37.30%) receiving conventional volatile-opioid anaesthesia (p=0.04). The absolute risk reduction was 17.30%, with a number needed to treat of six. Their postoperative opioid consumption was similar between groups, suggesting that avoidance of intraoperative opioids itself contributed importantly to the observed difference in PONV.[13] Other opioid-related adverse events in the present study were generally less frequent with OFA, although the differences were not statistically significant. Excessive sedation occurred in 6.52% versus 21.74%, dizziness in 8.70% versus 19.57%, pruritus in 0.00% versus 8.70%, postoperative hypotension in 8.70% versus 15.22%, and postoperative hypoxemia in 2.17% versus 8.70% in the OFA and OSA groups, respectively. Bradycardia occurred intraoperatively in 13.04% and 6.52%, respectively (p=0.292). These safety findings should be interpreted alongside the multicentre POFA trial reported by Beloeil et al. (2021), which was stopped prematurely after five cases of severe bradycardia occurred in the dexmedetomidine-based OFA group. Hypoxemia occurred in 72% of dexmedetomidine-treated patients compared with 61% receiving remifentanil (p=0.030), and the composite opioid-related adverse outcome occurred in 78% versus 67% (p=0.031). Nevertheless, postoperative morphine consumption was lower with OFA (median 6 mg [0–17] vs 11 mg [5–21]), and PONV was also reduced (24% vs 37%). These findings contrast with the relatively low rates of bradycardia and hypoxemia recorded in the present study and emphasize that the safety profile of OFA depends considerably on the agents selected, particularly the dose and administration of dexmedetomidine.[14]

CONCLUSION

Opioid-free anaesthesia was associated with lower early postoperative pain scores, reduced rescue analgesic and opioid requirements, and faster postoperative recovery compared with opioid-sparing anaesthesia. It also showed a lower incidence of postoperative nausea with comparable overall perioperative safety. These findings suggest that a well-planned multimodal opioid-free technique can

be an effective alternative for selected surgical patients. Appropriate patient selection and careful use of non-opioid adjuncts remain essential for maintaining hemodynamic stability and safety.

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