RESEARCH PAPER

Comparative Evaluation of Opioid-Free Versus Opioid-Based Anaesthesia in Patients Undergoing Spine Surgery: A Prospective Observational Study

Dr Sneha Sheelvanth[1], Dr Akshata Aravind Kulkarni[2], Dr Shruti Sagar[3], Dr Asha Beegum[4]

[1]Assistant Professor, Department of Anaesthesiology, KLES JGMMMC Hubballi, India.
[2]Assistant Professor, Department of Anaesthesiology, KLES JGMMMC Hubballi, India.
[3]Senior Resident, Department of Anaesthesiology, KLES JGMMMC Hubballi, India.
[4]Consultant, Department of Anaesthesiology, Apollo Hospital, BG road, Bangalore, India.
Currently working at Rajagiri Hospital, Ernakulam, Kerala, India.

Corresponding author addresses: E-mail id/ Social Media Link
Dr. Asha Beegum, Consultant, Department of Anaesthesiology, Apollo Hospital, BG road, Bangalore, India.
(Currently working at Rajagiri Hospital, Ernakulam, Kerala, India.)
Email: sneha.sheelvanth@gmail.com

Received Date: 10/10/2025; **Accepted:** 22/01/2026; **Published Date:** 31/03/2026

ABSTRACT

Background: Opioid-based anaesthesia (OBA) has traditionally been used for perioperative pain management; however, it is associated with adverse effects such as respiratory depression, postoperative nausea and vomiting (PONV), and delayed recovery. Opioid-free anaesthesia (OFA), based on multimodal analgesia, has emerged as a promising alternative, particularly in spine surgeries where optimal hemodynamic stability and early recovery are essential. **Aim:** To comparatively evaluate the efficacy and safety of opioid-free anaesthesia versus opioid-based anaesthesia in patients undergoing spine surgery. **Objectives:** To compare intraoperative hemodynamic parameters between OFA and OBA groups. To assess postoperative pain scores and analgesic requirements. To evaluate postoperative recovery outcomes including PONV, sedation, and duration of hospital stay. **Materials and Methods:** This prospective observational study included 94 patients undergoing spine surgery, divided into OFA (n=47) and OBA (n=47) groups. Baseline demographic data were recorded. Intraoperative hemodynamic parameters (HR, SBP, DBP, MAP) were monitored. Postoperative pain was assessed using the Visual Analog Scale (VAS) at multiple time intervals. Analgesic consumption, PONV, sedation scores, extubation time, PACU stay, and hospital stay were recorded. Statistical analysis was performed using appropriate tests, with $p < 0.05$ considered significant. **Results:** Baseline characteristics were comparable between groups ($p > 0.05$). The OFA group demonstrated significantly lower intraoperative HR, SBP, DBP, and MAP ($p < 0.01$), indicating better hemodynamic stability. Postoperative VAS scores were significantly lower in the OFA group at all time intervals ($p < 0.001$), with reduced rescue analgesia requirement and total analgesic consumption. The incidence of PONV was significantly lower in the OFA group (17.0% vs 46.8%, $p = 0.002$). Additionally, OFA was associated with lower sedation scores, shorter extubation time, reduced PACU stay, and shorter hospital stay ($p < 0.001$). **Conclusion:** Opioid-free anaesthesia is a safe and effective alternative to opioid-based anaesthesia in spine surgery, providing superior hemodynamic stability, improved postoperative analgesia, reduced complications, and enhanced recovery.

KEYWORDS: Opioid-free anaesthesia. Spine surgery. Multimodal analgesia

How to cite this article: Sheelvanth S, Kulkarni AA, Sagar S, Beegum A. Comparative Evaluation of Opioid-Free Versus Opioid-Based Anaesthesia in Patients Undergoing Spine Surgery: A Prospective Observational Study. Int J Drug Deliv Technol. 2026;16(61s): 24-30. DOI: 10.25258/ijddt.16.61s.4

Source of support: Nil.

Conflict of interest: None.

INTRODUCTION

Spine surgeries are increasingly performed worldwide for degenerative, traumatic, and neoplastic conditions, and they are often associated with significant

intraoperative and postoperative pain. Traditionally, opioid-based anaesthesia (OBA) has been the cornerstone of perioperative pain management due to its potent analgesic effects. However, the use of opioids is associated with several adverse effects such as respiratory depression, postoperative nausea and vomiting (PONV), ileus, sedation, opioid-induced hyperalgesia (OIH), and risk of long-term dependence. These complications can delay recovery, prolong hospital stay, and negatively impact patient outcomes.[1]

In recent years, there has been a paradigm shift toward opioid-sparing and opioid-free anaesthesia (OFA) techniques. OFA involves the use of multimodal analgesia using non-opioid agents such as dexmedetomidine, ketamine, lidocaine, magnesium sulphate, NSAIDs, and regional anaesthesia techniques to achieve adequate analgesia without opioids. This approach aligns with Enhanced Recovery After Surgery (ERAS) protocols, which emphasize minimizing opioid use to improve recovery profiles and reduce perioperative complications.[2][3]

Spine surgeries present unique challenges for anaesthesiologists, including the need for stable hemodynamics, optimal surgical conditions, neuromonitoring compatibility, and effective postoperative pain control. Opioids, while effective, may interfere with intraoperative neurophysiological monitoring and contribute to delayed awakening. Conversely, OFA techniques have been shown to provide stable hemodynamics, reduce stress response, and improve recovery characteristics without compromising analgesia.[4]

AIM

To comparatively evaluate the efficacy and safety of opioid-free anaesthesia versus opioid-based anaesthesia in patients undergoing spine surgery.

OBJECTIVES

1. To compare intraoperative hemodynamic parameters between opioid-free and opioid-based anaesthesia groups.
2. To assess postoperative pain scores and analgesic requirements in both groups.
3. To evaluate postoperative recovery outcomes including PONV, sedation, and duration of hospital stay.

MATERIALS AND METHODOLOGY

Source of Data

The data were collected from patients undergoing elective spine surgery under general anaesthesia at a tertiary care hospital. Patients were recruited from the Department of Anaesthesiology in collaboration with the Department of Neurosurgery.

Study Design

The study was a prospective observational comparative study.

Study Location

The study was conducted at a tertiary care teaching hospital equipped with advanced neurosurgical and anaesthesia facilities.

Study Duration

The study was conducted over a period of 18-24 months after obtaining ethical committee approval.

Sample Size

A total of **94 patients** were included in the study and were divided into two groups:

- Group OFA (Opioid-Free Anaesthesia): 47 patients
- Group OBA (Opioid-Based Anaesthesia): 47 patients

Inclusion Criteria

- Patients aged 18-65 years
- ASA physical status I-III
- Patients scheduled for elective spine surgery under general anaesthesia
- Patients providing informed written consent

Exclusion Criteria

- Patients with ASA grade IV or above
- Known allergy to study drugs
- Chronic opioid use or opioid dependence
- Severe hepatic, renal, or cardiac dysfunction
- Pregnant or lactating women
- Patients with psychiatric illness or inability to assess pain scores

Procedure and Methodology

After obtaining informed consent, patients were randomly allocated into OFA and OBA groups. All patients underwent a detailed pre-anaesthetic evaluation. Standard fasting guidelines were followed. On arrival in the operating room, baseline parameters including heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and oxygen saturation (SpO_2) were recorded. Standard monitoring including ECG, NIBP, pulse oximetry, and $EtCO_2$ was instituted.

Anaesthesia induction in both groups was performed using standard agents such as propofol and muscle relaxants.

- **OFA Group:** Received dexmedetomidine infusion, ketamine, lignocaine, magnesium sulphate, and NSAIDs without opioid administration.

- **OBA Group:** Received opioids such as fentanyl or morphine along with standard anaesthetic agents.

Maintenance of anaesthesia was achieved using inhalational agents or total intravenous anaesthesia (TIVA) as per institutional protocol. Hemodynamic parameters were recorded at regular intervals intraoperatively.

Postoperatively, pain was assessed using Visual Analog Scale (VAS) or Numerical Rating Scale (NRS) at predefined intervals (15 min, 2 hr, 6 hr, 12 hr, and 24 hr). Rescue analgesia was administered as required. Incidence of PONV, sedation scores, and other complications were recorded.

Sample Processing

All clinical and hemodynamic data were recorded in a structured proforma. Pain scores, drug dosages, and recovery parameters were documented systematically. Data were checked for completeness and accuracy before analysis.

Statistical Methods

Data were analysed using SPSS version 22.0.

- Quantitative variables were expressed as mean ± standard deviation (SD)
- Qualitative variables were expressed as frequency and percentage (%)
- Student's t-test was used for comparison of continuous variables
- Chi-square test (χ^2) was used for categorical variables
- A p-value <0.05 was considered statistically significant
- Confidence intervals (95% CI) were calculated where applicable

Data Collection

Data were collected prospectively using a predesigned and pretested proforma. Demographic details, intraoperative parameters, drug usage, postoperative pain scores, complications, and recovery outcomes were recorded for each patient. Follow-up was done up to 24 hours postoperatively.

OBSERVATION AND RESULTS

Table 1: Baseline Demographic and Clinical Profile (OFA vs OBA) (N = 94)

Variable	OFA (n=47)	OBA (n=47)	Test of Significance	95% CI (Mean diff)	p value
Age (years)	44.8 ± 10.2	46.1 ± 11.0	t = 0.58	-3.1 to 5.7	0.56
Gender (Male)	28 (59.6%)	30 (63.8%)	$\chi^2 = 0.18$		0.67
Gender (Female)	19 (40.4%)	17 (36.2%)			
BMI (kg/m²)	25.4 ± 3.2	25.9 ± 3.5	t = 0.74	-1.8 to 0.9	0.46
ASA I	18 (38.3%)	16 (34.0%)	$\chi^2 = 0.39$		0.82
ASA II	21 (44.7%)	23 (48.9%)			
ASA III	8 (17.0%)	8 (17.0%)			
Duration of surgery (min)	138.5 ± 32.4	141.2 ± 34.1	t = 0.39	-10.6 to 15.9	0.69

The baseline demographic and clinical characteristics of patients in both the opioid-free anaesthesia (OFA) group and opioid-based anaesthesia (OBA) group were comparable. The mean age in the OFA group was 44.8 ± 10.2 years, while in the OBA group it was 46.1 ± 11.0 years, with no statistically significant difference (t = 0.58, p = 0.56; 95% CI: -3.1 to 5.7). Gender distribution was also similar between the two groups, with males constituting 59.6% in the OFA group and 63.8% in the OBA group ($\chi^2 = 0.18$, p = 0.67). The mean body mass index (BMI) was comparable between groups (25.4 ± 3.2 kg/m² in OFA vs 25.9 ± 3.5 kg/m² in OBA; p = 0.46).

Regarding ASA physical status, the majority of patients in both groups belonged to ASA II category (44.7% in OFA vs 48.9% in OBA), followed by ASA I and ASA III, with no statistically significant difference ($\chi^2 = 0.39$, p = 0.82). The mean duration of surgery was also similar between the groups (138.5 ± 32.4 minutes in OFA vs 141.2 ± 34.1 minutes in OBA; p = 0.69; 95% CI: -10.6 to 15.9).

Table 2: Intraoperative Hemodynamic Parameters (OFA vs OBA)

Parameter	OFA (Mea	OBA (Mea	Test	95% CI	p value

	n ± SD)	**n ± SD)**			
HR (beats/min)	72.6 ± 8.4	78.9 ± 9.2	t = 3.39	-10.1 to -2.5	0.001*
SBP (mmHg)	118.2 ± 10.6	125.7 ± 12.3	t = 3.09	-12.2 to -2.8	0.003*
DBP (mmHg)	72.5 ± 7.8	77.1 ± 8.4	t = 2.70	-8.1 to -1.1	0.008*
MAP (mmHg)	87.7 ± 8.3	93.5 ± 9.1	t = 3.18	-9.4 to -2.1	0.002*
$EtCO_2$ (mmHg)	35.2 ± 3.1	36.1 ± 3.4	t = 1.31	-2.2 to 0.5	0.19

The intraoperative hemodynamic parameters showed significant differences between the two groups. The mean heart rate (HR) was significantly lower in the OFA group (72.6 ± 8.4 beats/min) compared to the OBA group (78.9 ± 9.2 beats/min), which was statistically significant ($t = 3.39$, $p = 0.001$; 95% CI: -10.1 to -2.5).

Similarly, systolic blood pressure (SBP) was significantly lower in the OFA group (118.2 ± 10.6 mmHg) compared to the OBA group (125.7 ± 12.3 mmHg) ($p = 0.003$; 95% CI: -12.2 to -2.8). Diastolic blood pressure (DBP) and mean arterial pressure (MAP) were also significantly lower in the OFA group ($p = 0.008$ and $p = 0.002$ respectively), indicating better hemodynamic stability.

However, there was no statistically significant difference in end-tidal CO_2 ($EtCO_2$) levels between the two groups (35.2 ± 3.1 mmHg in OFA vs 36.1 ± 3.4 mmHg in OBA; $p = 0.19$).

Table 3: Postoperative Pain Scores and Analgesic Requirement

Parameter	**OFA**	**OBA**	**Test**	**95% CI**	**p value**
VAS (15 min)	3.1 ± 1.2	4.6 ± 1.4	t = 5.54	-2.1 to -0.9	<0.001*
VAS (2 hr)	2.8 ± 1.1	4.2 ± 1.3	t = 5.49	-1.9 to -0.8	<0.001*
VAS (6 hr)	2.5 ± 1.0	3.8 ± 1.2	t = 5.42	-1.7 to -0.7	<0.001*
VAS (12 hr)	2.3 ± 0.9	3.5 ± 1.1	t = 5.49	-1.6 to -0.7	<0.001*
VAS (24 hr)	2.1 ± 0.8	3.2 ± 1.0	t = 5.69	-1.5 to -0.7	<0.001*
Rescue analgesia required	14 (29.8%)	28 (59.6%)	$\chi^2 = 8.27$		0.004*
Total analgesic dose (mg)	78.5 ± 18.6	112.4 ± 24.3	t = 7.42	-42.1 to -25.6	<0.001*

Postoperative pain scores assessed using the Visual Analog Scale (VAS) were significantly lower in the OFA group at all time intervals. At 15 minutes postoperatively, the mean VAS score was 3.1 ± 1.2 in the OFA group compared to 4.6 ± 1.4 in the OBA group ($p < 0.001$; 95% CI: -2.1 to -0.9). Similar statistically significant reductions in pain scores were observed at 2 hours, 6 hours, 12 hours, and 24 hours postoperatively (all $p < 0.001$).

The requirement of rescue analgesia was significantly lower in the OFA group, with only 29.8% of patients requiring additional analgesia compared to 59.6% in the OBA group ($\chi^2 = 8.27$, $p = 0.004$). Furthermore, the total postoperative analgesic consumption was significantly lower in the OFA group (78.5 ± 18.6 mg) compared to the OBA group (112.4 ± 24.3 mg), which was highly significant ($p < 0.001$; 95% CI: -42.1 to -25.6).

Table 4: Postoperative Recovery Outcomes

Parameter	**OFA**	**OBA**	**Test**	**95% CI**	**p value**
PONV present	8 (17.0%)	22 (46.8%)	$\chi^2 = 9.52$		0.002*
Sedation score (Ramsay)	2.1 ± 0.6	3.4 ± 0.8	t = 8.52	-1.6 to -1.0	<0.001*
Time to extubation (min)	9.8 ± 2.4	14.2 ± 3.1	t = 7.68	-5.5 to -3.2	<0.001*
PACU stay (min)	42.6 ± 10.5	58.3 ± 12.7	t = 6.49	-20.3 to	<0.001*

				-10.7	
Hospital stay (days)	4.2 ± 1.1	5.6 ± 1.4	t = 5.27	-2.0 to -0.8	<0.001*

Postoperative recovery outcomes were significantly better in the OFA group compared to the OBA group. The incidence of postoperative nausea and vomiting (PONV) was significantly lower in the OFA group (17.0%) compared to the OBA group (46.8%) (χ^2 = 9.52, p = 0.002).

The mean sedation score was also significantly lower in the OFA group (2.1 ± 0.6) compared to the OBA group (3.4 ± 0.8), indicating less postoperative sedation (p < 0.001; 95% CI: -1.6 to -1.0). Time to extubation was significantly shorter in the OFA group (9.8 ± 2.4 minutes) compared to the OBA group (14.2 ± 3.1 minutes) (p < 0.001).

Additionally, the duration of stay in the post-anaesthesia care unit (PACU) was significantly reduced in the OFA group (42.6 ± 10.5 minutes vs 58.3 ± 12.7 minutes; p < 0.001). The overall hospital stay was also significantly shorter in the OFA group (4.2 ± 1.1 days) compared to the OBA group (5.6 ± 1.4 days) (p < 0.001; 95% CI: -2.0 to -0.8).

DISCUSSION

Table 1: Baseline Demographic and Clinical Profile

In the present study, both the OFA and OBA groups were comparable in terms of baseline demographic and clinical characteristics, including age, gender distribution, BMI, ASA grading, and duration of surgery (p > 0.05). The mean age in our study was 44.8 ± 10.2 years in the OFA group and 46.1 ± 11.0 years in the OBA group, which is consistent with findings reported by Barakat *et al.* (2024)[1], who observed similar age distribution in patients undergoing opioid-free anaesthesia protocols.

The gender distribution in our study showed a slight male predominance, comparable to the findings of Tripodi *et al.* (2025)[2], where males constituted the majority of spine surgery patients. Similarly, BMI and ASA classification were comparable between groups, which aligns with the observations of Chattopadhyay *et al.* (2025)[3], who emphasized the importance of comparable baseline characteristics to ensure unbiased comparison of anaesthetic techniques.

The absence of statistically significant differences in baseline parameters in our study confirms appropriate matching between groups and minimizes confounding bias. This is in agreement with Taylor *et al.* (2023)[4], who highlighted that comparable baseline profiles are essential for evaluating perioperative interventions effectively.

Table 2: Intraoperative Hemodynamic Parameters

In the present study, intraoperative hemodynamic parameters such as HR, SBP, DBP, and MAP were significantly lower in the OFA group compared to the OBA group (p < 0.01), indicating better hemodynamic stability. These findings are consistent with Barakat *et al.* (2024)[1], who reported that opioid-free anaesthesia using dexmedetomidine and multimodal agents results in reduced sympathetic response and improved cardiovascular stability.

Similarly, Tripodi *et al.* (2025)[2] demonstrated that OFA significantly reduces intraoperative heart rate and blood pressure fluctuations due to its sympatholytic effects. The lower MAP observed in our study further supports the role of non-opioid agents like dexmedetomidine in attenuating stress response during surgery.

However, there was no significant difference in $EtCO_2$ levels between the two groups (p = 0.19), suggesting that both anaesthetic techniques maintained adequate ventilation. This finding is comparable to the results of Mathew *et al.* (2023)[5], who also reported no significant differences in respiratory parameters between OFA and OBA groups.

Thus, our study supports existing evidence that OFA provides superior hemodynamic stability without compromising respiratory function, as also supported by systematic reviews such as Feenstra *et al.* (2023)[9].

Table 3: Postoperative Pain Scores and Analgesic Requirement

The present study demonstrated significantly lower postoperative pain scores (VAS) in the OFA group at all time intervals (p < 0.001), along with reduced need for rescue analgesia and lower total analgesic consumption. These findings are in strong agreement with Barakat *et al.* (2024)[1], who reported that multimodal analgesia in OFA reduces postoperative pain and opioid requirements.

Similarly, Sangadala *et al.* (2024)[6] observed that opioid-free techniques significantly decrease postoperative analgesic consumption due to the synergistic action of non-opioid agents. The reduced requirement of rescue analgesia in our study (29.8% vs 59.6%) further supports the analgesic efficacy of OFA.

In addition, Tripodi *et al.* (2025)[2] emphasized that multimodal analgesia improves postoperative pain control and reduces opioid-related adverse effects. Our findings are also consistent with Mathew *et al.* (2023)[5], who reported significantly lower VAS scores and analgesic requirements in patients receiving opioid-sparing anaesthesia. Comparable findings have

also been highlighted in spine-specific analyses such as Ambreen *et al.* (2025)[8].

Table 4: Postoperative Recovery Outcomes

In the present study, postoperative recovery parameters were significantly improved in the OFA group. The incidence of PONV was significantly lower in the OFA group (17.0%) compared to the OBA group (46.8%) (p = 0.002). This finding is consistent with Tripodi *et al.* (2025)[2], who reported a marked reduction in PONV with opioid-free techniques due to avoidance of opioid-related emetogenic effects.

The sedation score was significantly lower in the OFA group, indicating faster recovery and better alertness. Similar findings were reported by Rani *et al.* (2024)[7], who observed reduced sedation and faster awakening with OFA.

Time to extubation and PACU stay were significantly shorter in the OFA group in our study, which is in agreement with Ambreen *et al.* (2025)[8], who demonstrated that opioid-sparing strategies enhance recovery and reduce postoperative care duration. These findings are further supported by broader systematic evidence from Feenstra *et al.* (2023)[9], emphasizing enhanced recovery profiles with OFA.

Furthermore, the hospital stay was significantly shorter in the OFA group (4.2 ± 1.1 days vs 5.6 ± 1.4 days), which aligns with findings of Hublet *et al.* (2022)[10], who reported improved recovery profiles and early discharge with opioid-free anaesthesia.

CONCLUSION

The present prospective observational study aimed to comparatively evaluate the efficacy and safety of opioid-free anaesthesia (OFA) versus opioid-based anaesthesia (OBA) in patients undergoing spine surgery. Based on the findings of this study, it can be concluded that opioid-free anaesthesia is a safe, effective, and advantageous alternative to conventional opioid-based techniques in the perioperative management of spine surgery patients.

The baseline demographic and clinical characteristics of both groups were comparable, ensuring that the observed outcomes were attributable to the anaesthetic technique rather than confounding factors. Intraoperatively, patients in the OFA group demonstrated significantly better hemodynamic stability, evidenced by lower heart rate, systolic and diastolic blood pressures, and mean arterial pressure. This can be attributed to the sympatholytic and analgesic properties of non-opioid agents such as dexmedetomidine, ketamine, and lignocaine, which effectively attenuate the surgical stress response.

Postoperative pain control was significantly superior in the OFA group, with consistently lower VAS scores at all measured time intervals. Additionally, the requirement for rescue analgesia and total analgesic consumption were markedly reduced in the OFA group. These findings highlight the effectiveness of multimodal analgesia in achieving adequate pain relief without reliance on opioids, thereby minimizing opioid-related adverse effects.

Furthermore, postoperative recovery outcomes were significantly improved in the OFA group. The incidence of postoperative nausea and vomiting (PONV) was considerably lower, and patients exhibited lower sedation scores, indicating faster recovery and improved alertness. The time to extubation and duration of stay in the post-anaesthesia care unit (PACU) were also significantly reduced, contributing to enhanced recovery profiles. Importantly, the overall hospital stay was shorter in the OFA group, suggesting potential benefits in terms of healthcare resource utilization and cost-effectiveness.

LIMITATIONS OF THE STUDY

1. The study was conducted at a single tertiary care center, which may limit the generalizability of the results.
2. The sample size, although adequate, was relatively small for detecting rare complications.
3. Being an observational study, there was no randomization, which may introduce selection bias.
4. Variability in surgical techniques and duration could have influenced intraoperative and postoperative outcomes.
5. The study evaluated short-term outcomes only; long-term follow-up was not included.
6. Pain assessment using VAS is subjective and may vary between patients.
7. Different combinations of non-opioid drugs in OFA protocols may affect reproducibility.
8. Blinding was not possible, which could introduce observer bias.

REFERENCES

1. Barakat H, Al Nawwar R, Abou Nader J, Aouad M, Yazbeck Karam V, Gholmieh L. Opioid-free versus opioid-based anesthesia in major spine surgery: a prospective, randomized, controlled clinical trial. Minerva Anestesiol. 2024 Jun 1;90(6):482-90.
2. Tripodi VF, Sardo S, Ippolito M, Cortegiani A. Effectiveness and safety of opioid-free anesthesia compared to opioid-based anesthesia: a systematic review and network

meta-analysis. Journal of Anesthesia, Analgesia and Critical Care. 2025 Aug 13;5(1):53.
3. Chattopadhyay S, Bhattacharyya T, Kumari K, Prasad CM. Comparative study of enhanced recovery (eras) between opioid free anaesthesia and opioid based anaesthesia in lumbar fixation surgery. Int J Acad Med Pharm. 2025;7(1):1117-23.
4. Taylor C, Metcalf A, Morales A, Lam J, Wilson R, Baribeault T. Multimodal analgesia and opioid-free anesthesia in spinal surgery: a literature review. Journal of PeriAnesthesia Nursing. 2023 Dec 1;38(6):938-42.
5. Mathew DM, Fusco PJ, Varghese KS, Awad AK, Vega E, Mathew SM, Polizzi M, George J, Mathew CS, Thomas JJ, Calixte R. Opioid-free anesthesia versus opioid-based anesthesia in patients undergoing cardiovascular and thoracic surgery: a meta-analysis and systematic review. InSeminars in Cardiothoracic and Vascular Anesthesia 2023 Sep (Vol. 27, No. 3, pp. 162-170). Sage CA: Los Angeles, CA: SAGE Publications.
6. Sangadala P, Talawar P, Tripathy DK, Kaushal A, Gupta A, Raj N. Comparison of block characteristics and outcomes in opioid-free and opioid-based thoracic continuous spinal anaesthesia in patients undergoing major abdominal surgery: A double-blinded randomised controlled trial. Indian Journal of Anaesthesia. 2024 Mar 1;68(3):280-6.
7. Rani US, Panda NB, Chauhan R, Mahajan S, Kaloria N, Tripathi M. Comparison of the effects of opioid-free anesthesia (OFA) and opioid-based anesthesia (OBA) on postoperative analgesia and intraoperative hemodynamics in patients undergoing spine surgery: A prospective randomized double-blind controlled trial. Saudi Journal of Anaesthesia. 2024 Apr 1;18(2):173-80.
8. Ambreen Y, Veliky C, Ibrahim MT, Humeidan M, Yu E. P49. Opioid-free anesthesia versus opioid-based anesthesia in spine surgery: a systematic review and meta-analysis of randomized controlled trials. The Spine Journal. 2025 Nov 1;25(11):S97.
9. Feenstra ML, Jansen S, Eshuis WJ, van Berge Henegouwen MI, Hollmann MW, Hermanides J. Opioid-free anesthesia: a systematic review and meta-analysis. Journal of clinical anesthesia. 2023 Nov 1;90:111215.
10. Hublet S, Galland M, Navez J, Loi P, Closset J, Forget P, Lafère P. Opioid-free versus opioid-based anesthesia in pancreatic surgery. BMC anesthesiology. 2022 Jan 4;22(1):9.