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Opioid based versus opioid free general anaesthesia in laparoscopic surgeries: A Randomised double blinded clinical study

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ABSTRACT

Background: To mitigate the adverse effects associated with opioid use, opioid-free multimodal analgesic approaches are being investigated. Opioid-free anaesthesia may improve postoperative recovery by minimising opioid-related complications

AIM: To compare the effects and postoperative outcome for participants receiving opioid-based versus opioid-free general anaesthesia in laparoscopic surgeries.

Methodology: This randomised double-blinded clinical trial included 82 patients scheduled for laparoscopic surgery, allocated into two equal groups (n = 41 each).

Group A: (opioid-free) received a combination of Dexmedetomidine (0.3 mcg/kg), lignocaine (1 mg/kg), ketamine (0.2 mg/kg).

Group B :(opioid-based) received fentanyl 10mcg/ml during induction.

Depth of anaesthesia and hemodynamic parameters were monitored intra and post operatively. Postoperative pain was assessed using VAS scores and the time to first rescue analgesia along with incidence of postoperative side effects was recorded.

Results: Group A had significantly lower MAC of Sevoflurane (0.92 ± 0.12) compared to Group B (1.34 ± 0.15) ($p < 0.001$). Postoperative VAS scores at all time points (1h to 12h) were significantly lower in Group A. Time to first analgesic request was delayed in Group A, with fewer rescue analgesics required.Opioid-free anaesthesia group also had fewer side effects like nausea and vomiting.

Conclusion: Opioid-free anaesthesia using a multimodal regimen is a safe and effective alternative to opioid-based anaesthesia in laparoscopic surgeries. It offers comparable intra operative stability and postoperative pain control, with fewer postoperative side effects.

Keywords: *Opioid-free anaesthesia, laparoscopic surgery, fentanyl, sevoflurane, postoperative pain.*

1. INTRODUCTION

Laparoscopic surgeries have become the preferred modality across various surgical specialties due to their minimally invasive nature, faster recovery, and reduced postoperative morbidity. Despite these advantages, patients frequently experience significant postoperative pain, particularly in the first 24 hours. Adequate anaesthetic technique is essential not only for intraoperative hemodynamic stability but also for enhancing postoperative recovery and minimizing complications.

Opioid-based general anaesthesia (OBA) has traditionally been the standard approach for intraoperative analgesia. Opioids such as fentanyl effectively blunt the nociceptive response to surgical stimuli. However, their use is increasingly scrutinized due to a wide range of adverse effects, including respiratory depression, postoperative nausea and vomiting (PONV), ileus, urinary retention, sedation, tolerance, and opioid-induced hyperalgesia. These complications can delay recovery, prolonged hospital stays, and contribute to opioid dependence, especially in high-risk populations.

In recent years, opioid-free anaesthesia (OFA) has emerged as a promising alternative. This approach utilizes a combination of non-opioid drugs—such as dexmedetomidine, ketamine, and lignocaine—that act synergistically at multiple levels of the pain pathway. OFA aims to provide adequate analgesia and stress response attenuation while avoiding opioid-related adverse effects. Preliminary studies have shown that OFA may reduce anaesthetic requirements, improve postoperative pain control, and decrease the incidence of PONV.

However, evidence comparing OFA and OBA in laparoscopic surgeries remains limited and inconsistent. Given the potential benefits of opioid-free approaches, this study was designed to compare opioid-based and opioid-free general anaesthesia in elective laparoscopic surgeries. We focused on intraoperative sevoflurane requirements (MAC), postoperative pain scores, time to first rescue analgesia, hemodynamic stability, and adverse effects.

2. MATERIALS AND METHODS

Study Design and Setting: Prospective, randomized, double-blind clinical study conducted at Krishna Hospital over 18 months after IEC approval.

Sample Size: 82 patients (41 in each group), calculated for 80% power and 5% significance.

Inclusion Criteria: ASA I–II patients aged 18–60 years undergoing elective laparoscopic surgery.

Exclusion Criteria: Patients with allergy to study drugs, ASA III/IV, BMI >30, emergency surgeries, significant systemic illness, Chronic alcoholic and substance abuse patients.

Randomization and Blinding: Block randomization (size = 41), double-blinded approach with coded drug syringes.

Intervention:

Group A- Opioid free group-Unlabelled 50cc syringe contains- Inj.Dexmed

200mcg (4 mcg/ ml);Inj.lignocaine 665mg(13.3mg/ml);Inj.Ketamine 130mg (2.6mg/ml)

[This dosage/dilution is got by taking 1 Amp of 200 mcg Dexmedetomidine 33 ml of

lignocaine+2.7 ml of ketamine+NS] and Unlabelled 10cc syringe contains -10cc of NS.

The patient are induced with bolus of 12 ml of opioid free mixture which covers(Dexmed

0.3mcg/kg;Lignocaine 1 mg/kg;Ketamine 0.2 mg/kg) over 10 mins along with propofol

1.5mg/kg ,Inj Cisatra 0.2mg/kg andSevoflurane.

Group B- Opioid based group-Unlabelled 50cc syringe containing NS and unlabelled

10cc of fentanyl (10mcg/ml).

The patients are induced with bolus of 12 ml of NS in an unlabelled 50 cc syringe over

10 mins along with propofol 1.5mg/kg ,Inj Cisatra 0.2mg/kg andSevoflurane.

Both groups received standardized general anaesthesia with sevoflurane and monitored for hemodynamic changes, depth of anaesthesia (BIS 40–60), postoperative pain and postoperative analgesia.

Statistical Analysis

Data was entered into Microsoft Excel version 17 and analysed utilizing Statistical Package for Social Sciences (SPSS). Descriptive format & a diagrammatic presentation was done using bar diagram or pie chart as required.

For descriptive analysis we used mean, standard deviation, ratio and proportion

with percentage. The quantitative data, if required, was analysed using

independent student's t test, $p<0.05$ was considered as a level of statistically

significant.

3. RESULTS

Demographics: Age, gender, BMI, ASA status, and surgery duration were comparable ($p > 0.05$).

Comparison of MAC of Sevoflurane Between Group A (OFA) and Group B (OBA):

Parameter	Group A(n=41) (OFA)	Group B(n=41) (OBA)	p value
MAC of sevoflurane (Mean±SD)	0.92±0.12	1.34±0.15	<0.001***

The mean MAC value of sevoflurane was significantly lower in Group A (0.92 ± 0.12) compared to Group B (1.34 ± 0.15), with a p value of < 0.001, indicating a statistically significant difference.

This result suggests that patients who received opioid-free anaesthesia required less sevoflurane to maintain adequate depth of anaesthesia compared to those who received opioid-based general anaesthesia

Distribution According To Postoperative VAS Score In Both Groups:

VAS (Postoperative)	**Group A (N=41)(OFA)**	**Group B (N=41)(OBA)**	**p Value**
	Mean ± SD	**Mean ± SD**	
1 Hour	1.55 ± 0.50	1.91 ± 0.64	0.025
2 Hour	2.91 ± 0.79	3.42 ± 0.73	0.003
4 Hour	4.12 ± 0.88	4.54 ± 0.96	0.042
6 Hour	4.91 ± 0.61	5.35 ± 0.70	0.018
12 Hour	5.02 ± 0.65	5.53 ± 0.49	0.025

At all observed time points (1h, 2h, 4h, 6h, 12h), Group A reported significantly lower VAS scores than Group B.

These findings suggest that opioid-free anesthesia provided consistently superior postoperative pain control during the first 12 hours after surgery.

Comparison Of Number Of Patients Requiring First Rescue Analgesia At Different Time Intervals:

Time To First Rescue Analgesia (Hrs)	**Group A (N=41)(OFA)**	**Group B (N=41)(OBA)**
	No Of Cases (%)	**No Of Cases (%)**
0-3	0	0
3-6	5 (12.19%)	16 (39.02%)
6-9	32 (78.06%)	22 (53.66%)
9-12	4 (9.75%)	3 (7.32%)
Total	41	41
Chi-square, p-value	Chi-square=7.76, p-value= 0.02	

Group A required most of their first rescue analgesia between 6-9 hours (78.06%), while Group B needed it earlier, mainly between 3-6 hours (39.02%). The difference between the groups was statistically significant (p = 0.02).

Indicate that Group A had longer post op analgesia than Group B.

Comparison Of Mean Time To First Rescue Analgesia Dose Requirement:

Group	Time Of First Rescue Analgesia In Hrs	T-Test	p-Value
Group A	6.45 ± 1.12	-5.49	<0.0001
Group B	5.19 ± 0.95		

Group A required the first rescue analgesia at a significantly later time (6.45 ± 1.12 hours) compared to Group B (5.19 ± 0.95 hours), with a highly significant difference (p< 0.0001).

GroupA had longer postoperative analgesia than groupB.

Distribution according to side effects:

Side Effect	N (Group A)(OFA)	Percentage	N (Group B)(OBA)	Percentage
Vomiting	2	40%	10	33%
Nausea	1	20%	5	17%
Bradycardia	1	20%	12	40%
Hypotension	1	20%	3	10%
Total	5	100%	30	100%
Chi-square, p-value	Chi-square=0.91, p-value= 0.82			

Group B experienced an overall higher incidence of postoperative side effects (30 cases) compared to Group A (5 cases).

The most common side effect in Group B was bradycardia (40%), while vomiting was most common in Group A (40%).

However, the Chi-square value of 0.91 and p -value of 0.82 indicate no statistically significant difference between the groups in terms of side effect distribution.

Discussion : The present randomized double-blinded clinical trial compared the efficacy and safety of opioid-free anaesthesia (OFA) with conventional opioid-based anaesthesia (OBA) in patients undergoing elective laparoscopic surgeries. Our findings demonstrate that OFA, using a multimodal combination of dexmedetomidine, ketamine, and lignocaine, resulted in significantly improved postoperative analgesia, lower anaesthetic requirements, and more stable hemodynamic profiles compared to OBA.

The significant reduction in the minimum alveolar concentration (MAC) of sevoflurane in the OFA group (0.92 ± 0.12 vs. 1.34 ± 0.15; p < 0.001) highlights the anaesthetic-sparing effects of the OFA regimen. This is clinically important as lower volatile anaesthetic requirements are associated with faster emergence, less respiratory depression, and reduced postoperative cognitive dysfunction. Dexmedetomidine, a selective α2-adrenergic agonist, reduces sympathetic tone and provides sedation and analgesia without causing significant respiratory depression. Its synergistic action with lignocaine and ketamine likely accounts for the reduced need for sevoflurane observed in our study. These findings are consistent with those reported by Bakan et al. and Yu et al., who observed reduced volatile anaesthetic consumption in OFA groups using similar multimodal regimens【Bakan M, 2015】【Yu JM, 2023】.

Pain control was consistently superior in the OFA group, as evidenced by significantly lower VAS scores at all measured postoperative intervals (1 to 12 hours). Moreover, the time to first rescue analgesic was significantly longer in Group A, and fewer patients required early postoperative analgesia. This supports the view that OFA, by targeting multiple pain pathways,

can offer effective and sustained analgesia in the immediate postoperative period. Similar observations have been reported by Vishnuraj et al. and Mahdy et al., who showed delayed analgesic requirements and lower cumulative opioid use in OFA patients【Vishnuraj KR, 2024】【Mahdy EW, 2024】.

Hemodynamic stability is another critical concern in anaesthetic practice. In our study, Group A patients had consistently lower postoperative heart rate and blood pressure values. This can be attributed to the sympatholytic properties of dexmedetomidine, which attenuates stress-induced autonomic responses. While bradycardia and hypotension are known side effects of dexmedetomidine, no significant adverse events were observed in our study, likely due to the careful titration of doses. Other studies, including those by Regis et al. and An G et al., have reported similar trends of intraoperative stability in OFA patients【Regis MJ, 2024】【An G, 2022】.

Adverse effects such as nausea, vomiting, pruritus, and respiratory depression are hallmark complications of perioperative opioid use. While the incidence of side effects in our study was not statistically significant, Group B patients experienced a higher frequency of nausea and vomiting. Opioids like fentanyl are known to stimulate the chemoreceptor trigger zone and reduce gastrointestinal motility, contributing to PONV. OFA regimens, by avoiding opioids, inherently reduce these risks. This is particularly beneficial in ambulatory surgeries where early discharge is prioritized.

From a mechanistic perspective, the multimodal approach of OFA provides a broader blockade of nociceptive pathways. Ketamine, as an NMDA receptor antagonist, not only attenuates central sensitization but also prevents opioid-induced hyperalgesia. Lignocaine, through its sodium channel blockade, reduces peripheral and spinal nociception. When combined with α2 agonists like dexmedetomidine, which modulate both central and peripheral adrenergic activity, the resultant analgesia is comprehensive and opioid-sparing.

Despite these advantages, the adoption of OFA has not been universal. One of the concerns raised in the literature pertains to the complexity of drug preparation and potential for adverse effects such as bradycardia, delayed emergence, and hallucinations with ketamine. However, our study found that these events were rare and manageable, emphasizing the safety of well-monitored OFA protocols.

Furthermore, opioid-sparing techniques have broader implications beyond immediate postoperative outcomes. There is growing evidence that perioperative opioid use may be linked to immunosuppression and potentially increased cancer recurrence in oncological surgeries. While our study did not focus on long-term outcomes, the role of OFA in enhancing recovery and reducing chronic opioid dependence warrants further investigation.

Limitations: This study was conducted in a single tertiary care center, and the sample size, though statistically adequate, may limit generalizability.

4. CONCLUSION

Opioid-free anaesthesia provided better perioperative hemodynamic stability and longer duration of postoperative pain relief and lower incidence of adverse effects such as nausea, vomiting, and bradycardia compared to opioid-based anesthesia.

Thus, this study demonstrates that opioid-free general anesthesia is a safe and effective alternative to opioid-based anesthesia, offering improved clinical outcomes in laparoscopic surgeries.

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