

Opioid-free anaesthesia for laparoscopic surgeries - A prospective non-randomised study in a tertiary care hospital

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ABSTRACT

Background and Aims: Opioids have nowadays become superfluous because of their adverse effects involving post-operative recovery of the patients. So, we aimed at comparing opioid-free anaesthesia with opioid-based technique for post-operative pain relief in laparoscopic surgeries. The primary objective was to assess the pain scores in the post-operative period using visual analogue scale (VAS) for 24 h, and the secondary objective was to compare intraoperative haemodynamic parameters, duration of postoperative analgesia and total analgesics consumed in the first 24 h. **Methods:** This study was conducted in 60 patients aged between 20 and 70 years, belonging to the American Society of Anesthesiologists physical class I and II posted for laparoscopic surgeries. Anaesthetic doses of lidocaine, magnesium and paracetamol in combination with fascial plane block for post-operative pain relief were given for 30 patients, and the other 30 patients received the conventional opioid-based anaesthesia. Mann–Whitney test was used for VAS scores, and Friedman test was used for repeated measures comparison. **Results:** VAS scores were higher in the conventional group as compared to the opioid-free group at 0, 2, 4, and 6 h during rest and at 0, 2, 4, 6, 24 h during movement and were statistically significant (P -value < 0.05). The duration of analgesia for the conventional group was $13.8 + 6.7$ h, and for opioid-free anaesthesia was $6.7 + 2.2$ hours. Intraoperative haemodynamic parameters did not show a statistically significant difference except for systolic blood pressure which was higher in the opioid-free group but was clinically insignificant. (P -value 0.013). **Conclusion:** Opioid-free anaesthesia along with erector spinae plane block provides better post-operative pain relief when compared to conventional opioid anaesthesia.

Key words: Block, magnesium, opioid, postoperative pain

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INTRODUCTION

Though laparoscopic surgeries are considered relatively painless and are associated with early recovery and lesser duration of hospital stay, they can cause severe pain, especially in the first 4 h of the immediate post-operative period.^[1] This may be attributed to the peritoneal irritation caused by the carbon dioxide insufflation pressures, bowel handling by the surgeons or irritation caused by the residual or retained blood. Opioids have been the main mode of analgesia in the perioperative period and are associated with significant side effects such as dizziness, sedation, nausea, constipation, vomiting,

physical dependence, muscle rigidity, tolerance, respiratory depression and addiction.^[2] The prevalence of opioid use in India is around 0.7%, and it has twice the global prevalence of illicit consumption from drug abuse and dependence.^[3] Acute surgical pain in

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the immediate post-operative period is a significant risk factor for the development of chronic pain and controlling it is a key factor for reducing the risk of chronic post-operative pain.^[4] Anaesthesiologists play an important role in identifying at-risk patients for long-term opioid use and thereby reducing perioperative opioid administration and decreasing related side effects.^[5] Though opioid-free regimens have been studied earlier, there is sparsity of literature incorporating regional anaesthesia and avoiding ketamine use in such regimens.^[6] This study was planned to provide multimodal analgesia with drugs other than opioids such as lignocaine, magnesium along with fascial plane blocks for post-operative analgesia with an aim to reduce opioid requirement and its associated adverse effects. The main objective was to compare the post-operative pain scores using visual analogue scale (VAS) between the opioid-free anaesthesia and opioid-based technique.

METHODS

This prospective non-randomised study was conducted in a tertiary care hospital from September 2020 to April 2021 for a period of 8 months after getting Institutional Ethics Committee approval in accordance with the declaration of Helsinki. Each patient was given a form explaining the drugs used, fascial plane blocks performed and their postoperative analgesic effects, and informed consent was obtained. Patients aged between 20 and 70 years, with the American Society of Anesthesiologists physical status I and II posted for laparoscopic surgeries were included in the study. Participants having body mass index >35 kg/m², known allergy to local anaesthetic agents, or having liver and renal insufficiency were excluded. Conversion to open technique and continuation of post-operative ventilation were considered as dropouts. Laparoscopic surgeries performed were cholecystectomy, appendicectomy, and totally extraperitoneal inguinal hernia repair. A group size of 30 was calculated using power analysis based on a previous study report.^[7] Convenience sampling was done, and the study included 60 patients out of which 30 patients were given opioid-sparing anaesthesia, and the rest 30 patients received the conventional opioid-based anaesthesia. The primary objective was to compare the pain scores in the post-operative period using VAS for 24 h, and the secondary objective was to compare intra-operative haemodynamic parameters, duration of postoperative analgesia (defined as the time from completion of erector spinae plane block (ESPB)

post-induction till the first analgesic requirement as indicated by VAS >5) and total analgesics consumed in the first 24 h.

A routine pre-operative evaluation was done and on the arrival of the patients to the theatre complex, the intravenous (IV) cannula was checked for the flow and patency. Pre-loading was done using IV crystalloids 10 mL/kg. Pre-emptive analgesia was given using IV dexamethasone 8 mg and IV paracetamol 15 mg/kg. Baseline parameters such as heart rate, systolic and diastolic blood pressure, mean arterial pressure (MAP), oxygen saturation, respiratory rate and end-tidal carbon dioxide monitoring were noted. After pre-oxygenation with 100% oxygen, anaesthesia was induced with IV propofol mg/kg, lignocaine 1.5 mg/kg (bolus dose) and succinylcholine 1.5 mg/kg. Endotracheal intubation was done, and cisatracurium 0.2 mg/kg was administered. Anaesthesia was maintained using nitrous oxide 0.5 L/min, oxygen 0.5 L/min, sevoflurane 1%, and cisatracurium was administered in incremental doses as needed.

During the maintenance phase, opioid-free anaesthesia group received lidocaine 1.5 mg/kg as infusion along with magnesium 2 g (bolus dose) as a slow intravenous injection. Analgesia was supplemented with ESPB post-induction under ultrasound guidance with the patient in lateral position. High-frequency linear probe “(sonosite - Fujifilm)” was used and positioned longitudinally at the level of the T6 vertebra in a parasagittal orientation, with the end of rhomboid muscle as the landmark.^[8] Tip of the transverse process of the corresponding vertebra along with the underlying pleura was visualised, and the target was to open up the plane between the erector spinae muscle and the transverse process [Figure 1]. The



Figure 1: Image showing erector spinae plane with transducer placed in a parasagittal orientation and local anaesthetic is seen deposited underneath the erector spinae muscle. [ESM = Erector spinae muscle, LA = Local anaesthetic, TP = Transverse process]

tip of the stimuplex (B Braun) needle was advanced using in-plane technique in a craniocaudal direction to contact the transverse process. Hydro dissection was done to visualise needle position deep to erector spinae muscle. After confirmation, 30 mL of 0.25% bupivacaine was injected deep into the muscle bilaterally (total volume 60 mL).

Haemodynamic parameters such as heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure were monitored just before induction and at 5, 10, 15, 30, 60 min after induction for all patients. Non-opioid analgesic, injection paracetamol 1 g, was given by the end of surgery intravenously.

In the conventional opioid-based anaesthesia group, a similar induction protocol was followed. Intraoperative rise in blood pressure was maintained with fentanyl boluses of 0.5 µg/kg. At the end of the surgery, all the patients received paracetamol 1 g and ondansetron 4 mg intravenously.

In both the groups, intra-abdominal pressure during pneumoperitoneum was maintained within 12–15 mm Hg. End-tidal carbon dioxide was maintained at less than 35 mmHg. Conventionally, four ports were made for all the laparoscopic surgeries with a 10 mm port at the level of the xiphoid process and the lowermost port at the level of the umbilicus (T6–T10).

After extubation, pain scores, vital signs and any adverse effects in the post-anaesthesia care unit were assessed in all patients. Follow up scores and monitoring were done at 0, 2, 4, 6, 12, 24 hours postoperatively and rescue non-opioid analgesic paracetamol 1 g was given if VAS score was >5 and for those complaining of persistent severe pain [VAS 8–10] limiting movement, opioid analgesic was given in the form of injection tramadol 50 mg. During the follow up period, the time for the first analgesic request and the total analgesic consumption was documented in the data collection proforma.

Data analysis was done using R programming 3.6.1 version (GNU GPL v2) and entered in Microsoft excel sheet. Descriptive statistics were calculated for all variables in which categorical variables were expressed as frequency, and numerical variables were expressed as mean ± standard deviation. Mann–Whitney test was used to compare the VAS score between both the groups. Friedman test was used for repeated measures

comparison. A confidence interval of 95% was used in all statistical tests, and *P* value <0.05 was considered significant.

RESULTS

Sixty-eight patients were assessed for eligibility, and sixty patients were recruited. All of them completed the study and were included in the analysis. VAS score for pain comparison both during rest and movement was significantly higher in the conventional group at 0, 2, 4, 6, 12, 24 h postoperatively than in the opioid-free anaesthesia group [as shown in Tables 1 and 2]. The total duration of analgesia differed significantly among both the groups. Duration of analgesia achieved with opioid-free anaesthesia group was 13.8 ± 6.7 h which is significantly higher as compared to the conventional group (6.7 ± 2.2) h. There was no significant difference in the duration of surgery between the groups [Table 3]. In the opioid-free anaesthesia group, about 23% (n = 7) did not require any analgesics in the post-operative period for the first 24 h. The total postoperative consumption of analgesics differed between both the groups. About

Table 1: VAS score comparison at rest

Variables	Opioid-free anaesthesia (Median)	Conventional group (Median)	<i>P</i>
VAS 0 hour	2	4	0.000
VAS 2	2	4	0.000
VAS 4 h	2	4	0.000
VAS 6 h	2	4	0.000
VAS 12 h	1	2	0.177
VAS 24 h	0	1	0.606

**P* (< 0.05) = statistically significant. VAS=Visual Analogue Scale

Table 2: VAS score comparison during movement

Variables	Opioid-free anaesthesia (Median)	Conventional group (Median)	<i>P</i>
VAS 0 h	3	5	0.001
VAS 2 h	3	5	0.002
VAS 4 h	3	5	0.000
VAS 6	2	3	0.077
VAS 12 h	2	2	0.744
VAS 24 h	2	2	0.036

**P* (<0.05) = statistically significant. VAS=Visual Analogue Scale

Table 3: Duration of analgesia and surgery using descriptive statistics

Variable	Opioid-free anaesthesia Mean±SD	Conventional group Mean±SD
Age (years)	43.87±10.51	42.26±12.56
Duration of surgery (h)	1.61±0.35	1.43±0.53
Duration of analgesia (h)	13.80±6.73	6.71±2.20

SD- standard deviation

67% (n = 20) required one dose of paracetamol (1 g) and 32% (n = 10) required one dose of paracetamol along with opioid (tramadol 50 mg) in view of severe pain as assessed by VAS (score > 5) in the conventional group, whereas 63% (n = 19) required one dose of paracetamol (1 g) and 13% (n = 4) required two doses of paracetamol (total 2 g) at an interval of 8 to 12 h in the opioid-free anaesthesia group [Table 4]. Clinically, haemodynamic parameters were comparable among the opioid-free anaesthesia group and the conventional group. Inferential statistics was applied, and the results showed that both groups did not show any significant difference in heart rate (0.72 bpm; 95% CI [-3.92 to 5.63], $P = 0.72$) and diastolic blood pressure (0.064 mmHg; 95% CI [-0.26 to 8.96], $P = 0.06$) but had a statistically significant decrease in systolic blood pressure in the conventional group (0.01 mmHg; 95% CI [1.41 to 11.31], $P = 0.013$). However, the difference was clinically insignificant. Similarly, the difference in mean arterial pressure (MAP) ($P = 0.01$) was statistically significant [Table 5].

DISCUSSION

In the current study, lesser VAS scores were seen postoperatively in the opioid-free group. This can be attributed to the use of fascial plane block which is part of our routine care for laparoscopic surgeries and our opioid-sparing regimen which included lignocaine and magnesium. A randomised controlled trial (RCT) on 40 patients to evaluate the efficacy of ESPB on cholecystectomy, where both the groups received IV patient-controlled analgesia containing morphine showed that pain scores were 0 at 12 and

24 h compared to pain scores (0–1) at 12 and 24 h of the control group, and the difference was statistically significant.^[8]

Additionally, in the current study, the greater difference in duration of analgesia (7 hours) among both the groups is ascribed to the ESPB and the volume used (60 mL) which emphasises its efficacy in post-operative pain relief. Also, ESPB was combined with systemic non-opioid analgesics such as lignocaine and magnesium infusions for desired results, and ketamine was avoided due to its adverse effects and impact on recovery such as emergence reactions, hallucinations, dissociative states, apnoea, and vivid dreams. This makes our study interesting and different from previous studies on opioid-free analgesia.

In the opioid-free anaesthesia group, total analgesic consumption was less, and none required opioid as rescue analgesia, whereas in the conventional opioid group, 10 patients required tramadol 50 mg secondary to paracetamol as they had a higher VAS score which limited movement. This proves to us that a multimodal analgesic approach will eliminate the need for opioids in the perioperative period.

ESPB is a recently described technique, by Forero *et al.*^[9] for treating chronic thoracic neuropathic pain. Local anaesthetic injected in EPSB, diffuses along the thoracolumbar fascia and exerts its effects on the ventral and dorsal rami of the spinal nerve providing visceral and somatic analgesia.^[10] A study conducted on open cardiac surgeries showed that continuous ESPB produced a significant decrease in morphine consumption, rapid patient mobilisation and reduced pain.^[11] As this procedure is safe and easy to perform, several authors have expressed their opinion that it could be part of the multimodal analgesia for the ‘enhanced recovery after surgery’ programmes.^[11]

A meta-analysis in 2014 evaluated the clinical consequences of intraoperative doses of opioid and revealed that high doses of opioids during surgery cause higher acute postoperative pain, leading to increased postoperative analgesic consumption and long-term analgesic use.^[12] The capacity of opioids to increase the area of secondary hyperalgesia around the surgical wound has been highlighted in a few clinical studies. This is associated with two inter-related phenomena called as ‘tolerance’ and ‘opioid-induced hyperalgesia’ which are mostly observed with remifentanyl infusions.^[13]

Table 4: Consumption of analgesics using frequency table

Variables	Opioid-free anaesthesia n (%)	Conventional group n (%)
No dose of analgesics	7 (23)	-
1 dose of paracetamol	19 (63)	20 (67)
2 doses of paracetamol	4 (13)	-
1 dose of paracetamol + tramadol	-	10 (32)

n- number

Table 5: Comparison of intraoperative haemodynamics

Variables	Opioid-free anaesthesia Mean±SD	Conventional group Mean±SD	P
SBP (mmHg)	117.33±9.89	110.97±9.44	0.013
DBP (mmHg)	79.83±8.75	75.48±9.25	0.064
HR (bpm)	73.47±8.00	72.61±10.43	0.722
MAP (mmHg)	92.53±8.10	87.22±7.76	0.011

* $P < 0.05$ =statistically significant); SBP=systolic blood pressure; DBP=Diastolic blood pressure; HR=Heart rate MAP=Mean arterial pressure, SD=standard deviation

Lidocaine, a prototype of amino-amides, is a weak base and short-acting local anaesthetic. At higher levels, side effects such as confusion, agitation, metallic taste, perioral numbness, dizziness, slurred speech, diplopia, tinnitus, muscular spasms, and seizures are being reported. Perioperative advantages of intravenous lignocaine include reduction in pain, nausea, opioid consumption, inflammation and early bowel function after surgery.^[14] Analgesic effects of lignocaine are noted with levels lower than 5 µg/mL.

Additionally, it has anti-hyperalgesic and anticonvulsant properties.^[15] Intraoperative lidocaine infusion reduces the requirement of inhalational agents, muscle relaxants, and reduces post-operative ileus. In the current study, repeat doses of muscle relaxants were not required throughout the surgery which provided an added advantage with respect to cost-effectiveness. A Cochrane review study which included 68 RCTs showed that continuous infusion of lidocaine did not show a significant difference in pain scores at 24 h versus the placebo group.^[16] Also, the effects of IV lignocaine on anaesthetic requirement and intraoperative haemodynamics have been evaluated in numerous clinical trials. A double-blinded RCT showed no significant differences in MAP and heart rate before induction, during surgery and in the recovery but showed that mean end-tidal sevoflurane concentration was 48% lower in the lignocaine group.^[17] In the current study, haemodynamic parameters remained almost stable in 80% of the patients in both the groups and in those who had intraoperative rises in blood pressure, diltiazem 5 mg was given as needed.

Also, magnesium, an N-methyl-aspartate receptor antagonist, exerts its analgesic effects by regulating calcium entry into the cells. It prevents central sensitisation and abolishes hypersensitivity in post-injury states.^[18] Data have been published regarding the role of magnesium in reducing anaesthetic requirements and achieving controlled hypotension.^[19]

In the current study, intraoperative use of magnesium sulphate (MgSO₄) was associated with better intraoperative haemodynamics and good post-operative analgesia with no obvious side effects. A meta-analysis of four RCTs on the analgesic effect of magnesium after laparoscopic cholecystectomy reported a substantial decrease in pain scores at an early stage (at 2 and 8 h) and reduction in analgesic consumption post-operatively.^[20] Also, a systematic

review of 11 RCTs showed that perioperative administration of MgSO₄ intravenously could reduce adverse effects such as vomiting, nausea, shivering and post-operative analgesic consumption.^[21]

Several studies have been published regarding various regimens for opioid-free anaesthesia. An RCT showed that using propofol, dexmedetomidine and lignocaine infusions for laparoscopic cholecystectomy was associated with lower pain scores, reduced rescue analgesia consumption and was also described as an alternative to opioid, especially for patients at high risk for post-operative nausea and vomiting.^[22] In the current study, none of the patients experienced significant adverse effects of opioids in the post-operative period like nausea, vomiting, respiratory depression and ileus. One-third of the patients had right shoulder tip pain in the recovery room post-surgery which is attributed to the effects of residual carbon dioxide.

There are a few limitations in this study. This study is limited by biases as randomisation was not done. Secondly, VAS >5 was taken as cut-off for pain management because higher VAS scores limit movement and cough thereby delaying ambulation and recovery. Hence, results with other studies may be dissimilar.

CONCLUSION

Integration of ESPB into intravenous opioid-free analgesic regimen using lignocaine and magnesium provides better postoperative pain relief with lower VAS scores, increased duration of analgesia and reduced opioid consumption as compared to the routine conventional opioid anaesthesia. Opioid-free anaesthesia can serve as an alternative for selected patients with unwanted side-effects due to opioids.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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