Original Article

Opioid Free Anesthesia in Laparoscopic Surgery: A New Emerging Technique

Carolin Smita Kerketta[1], Heena Sunil Chhanwal[1], Divya Kheskani[1], Vidhyasagar Sharma[2], Palak Sitapara[3], Vasu Girdhar Rathod[4]

Abstract

Background: Opioid-free anesthesia (OFA) is a new anesthesiological technique where opioid is avoided intra and post-operative due to side effects. Hence, this study compared opioid-free with opioid-based anesthesia for postoperative analgesia in laparoscopic surgeries. The primary objective was to assess pain scores in the postoperative period with the Numerical rating scale (NRS) for 24 hours, and the secondary objective was to compare intraoperative vitals, postoperative analgesia period, and utilization of total analgesics in the first 24 hours.

Materials and Methods: Prospective randomized control trial, 100 patients aged 20-70 years, American Society of Anaesthesiologists physical class I and II posted for elective upper and lower abdominal laparoscopic surgeries. Patients were divided into two groups (n=50 in each group): opioid-free (Group A) and opioid (Group B). Group A received anesthetic doses of lidocaine, magnesium, and paracetamol in combination with Erector spinae plane block for post-operative pain relief, while group B received intermittent doses of fentanyl. Postoperatively, NRS was observed at 0, 2, 4, and 6 hours during rest and at 0, 2, 4, 6, and 24 hours during movement. Data were analyzed by independent t-test.

Results: Group A showed a significant decrease in NRS score at rest at 0, 2, 4, and 6 hours, whereas there was a significant decrease in NRS score at movement in group A at 0, 2, 6, and 24 hours compared to group B ($P< 0.05$). Total duration of analgesia (hour) was significantly more in group A (17.86 ± 7.85) as compared to group B (7.76 ± 3.98) ($P<0.001$). Intraoperative vitals were comparable. The total rescue analgesia (milligram) requirement was significantly low in group A (0.92 ± 0.8) as compared to group B (2.02 ± 0.38).

Conclusion: For patients undergoing elective upper and lower abdominal laparoscopic surgeries, multimodal analgesia was safe in unwanted opioid side-effects cases and unavailability of opioids.

Keywords: Laparoscopic surgeries, Block, Magnesium, Opioid-free anesthesia, Pain

1. GCS Medical College, Hospital and Research Centre, Ahmedabad, Gujarat, India
2. Department of Surgery, GCSMCH & RC, Ahmedabad
3. Department of Anaesthesia, GCSMCH & RC, Ahmedabad
4. Department of Community Medicine, GCSMCH & RC, Ahmedabad

Corresponding Author: Heena Sunil Chhanwal, Professor and Head, Department of Anaesthesiology, GCS Medical College, Hospital and Research Centre, Ahmedabad, Gujarat, India; **Email:** drmrshc@gmail.com

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Introduction

Since the inception of anesthesia 50 years ago, the triad of balanced anesthesia has been achieved by hypnotic or inhalational agents. Therefore, high doses were required to achieve a satisfactory anesthesia level. However, it led to hemodynamic instability (1). Later, opioids significantly optimized the triad with many adverse effects (2). Hence, currently, the opioid-free anesthesia concept is gaining popularity globally. It is a newly emerging technique based on multimodal analgesia, where several analgesic drugs are administered to improve pain control, decrease over-dependence on opioids for analgesia, and reduce side effects (3). The primary objective was to assess pain scores in the postoperative period with a numerical rating scale (NRS) for 24 hours, and the secondary objective was to compare intraoperative vitals, the postoperative analgesia period, and the utilization of total analgesics in the first 24 hours. Thus, multimodal analgesia is a proven technique for achieving tasks. The primary objective of the study was to assess pain scores in the postoperative period with the Numerical rating scale (NRS) for 24 hours, and the secondary objective was to compare intraoperative vitals, postoperative analgesia period, and utilization of total analgesics in the first 24 hours.

Methods

This prospective randomized controlled study was conducted at a tertiary care hospital from July to November 2022. After obtaining Institutional Ethics Committee approval and CTRI (Central Trial Registry of India) registration, written informed consent was taken from patients with a convenient sampling technique. A total of 100 patient sample sizes were taken, and grouping was done per Consort Statement 2010; each group consists of 50 patients, as in Figure 1. The power of the study was taken at 80%, and the confidence interval at 95% for the statistical analysis. A computer-generated system does randomization. Double blinding by the sealed cover, done at the patient and anesthesiologist levels, collects the data for analysis. Patients included in the study were aged between 20 to 70 years, either gender, ASA grade I and II posted for elective upper and lower abdominal laparoscopic surgeries. Patients excluded from the study were refused consent, communication problems, allergy to study drugs, uncontrolled comorbid conditions, altered coagulation profile, BMI>35 kg/m2, and spinal deformities. Those surgeries converted from laparoscopic to open technique for various reasons were considered dropouts. Group A was an opioid-free group (ESPB Block), and group B was an opioid-based group (without ESPB Block). All patients were explained about the NRS scale. The primary objective was to assess the pain scores in the pre-, intra, and post-operative period with a Numerical rating scale (NRS) for 24 hours, and the secondary objective was to compare intraoperative hemodynamic parameters, time of the block, demand for the first rescue analgesia, duration of postoperative analgesia and total analgesics consumed in the first 24 h.

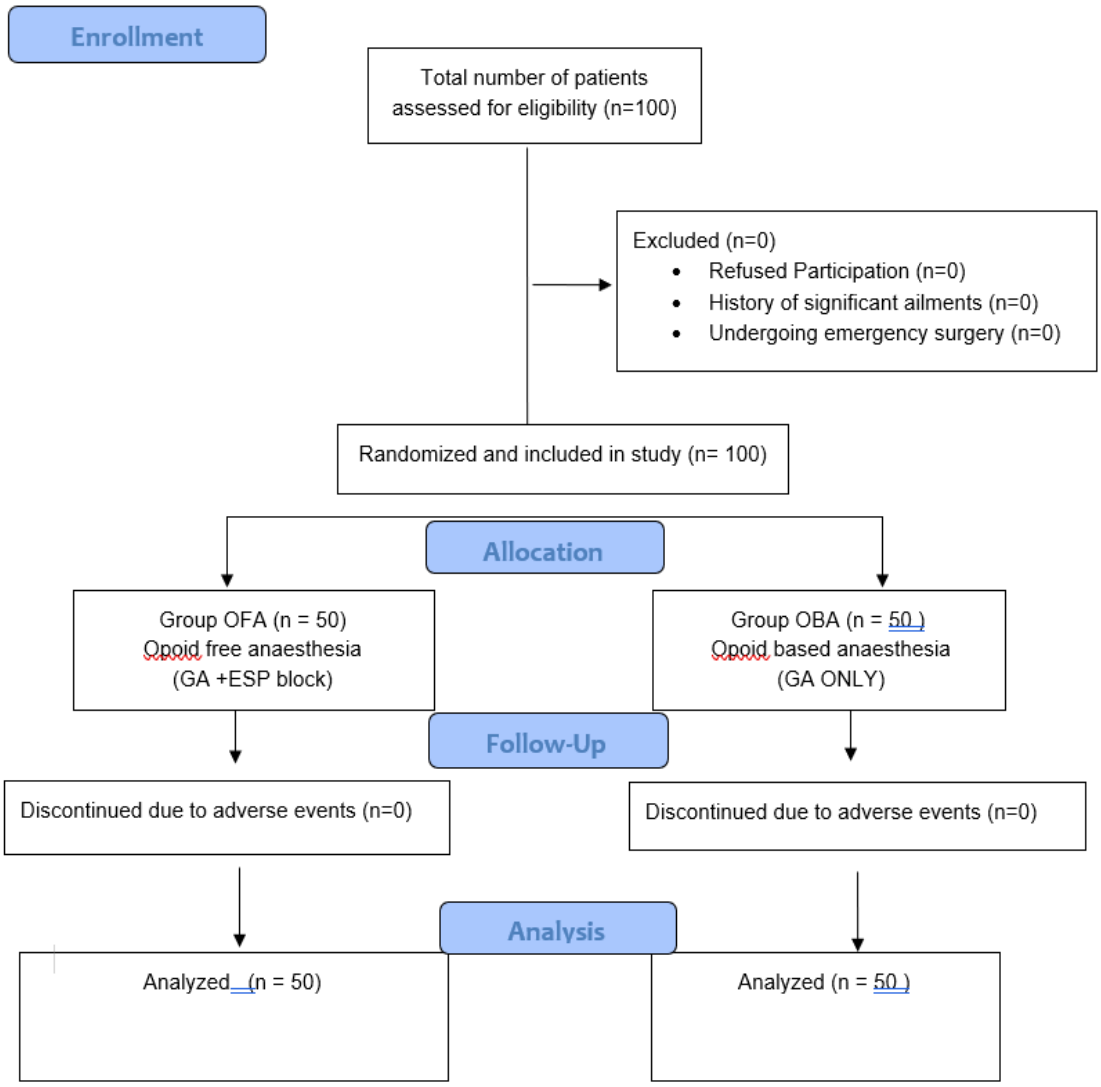
The pre-anesthetic check-up was done for all the patients posted for elective laparoscopic surgeries. On the day of surgery, nil by mouth (NBM) status was confirmed, and a large bore intravenous cannula was taken, followed by preloading with crystalloid 10ml/kg.

In the operation theatre, a multipara monitor was attached. Baseline parameters such as pulse rate (PR), systolic blood pressure (SBP), Diastolic blood pressure (DBP), SpO2, and end-tidal CO2 (EtCO2) were recorded.

In both groups, pre-emptive analgesia was achieved with IV Dexamethasone 0.1 mg/kg stat, IV Paracetamol 15mg/kg, and after 15 minutes, IV Magnesium sulfate 2 gm bolus slowly, IV Xylocard 1.5mg/kg. General Anesthesia induction was done with IV Propofol 2mg/kg and IV Succinylcholine 2mg/kg, followed by the trachea being intubated with an appropriate-size cuffed endotracheal tube (ET). Placement of ET was verified clinically and with EtCO2 graph plus values. Immediately, a bolus dose of IV Atracurium 0.5 mg/kg was administered. Anesthesia was maintained with air 50%, oxygen 50%, sevoflurane 1-2 MAC, and with IV Atracurium infusion (0.1 mg/kg/hr)

During the maintenance period, in group A, Xylocard 1.5 mg/kg IV infusion started, and USG guided Erector Spinae plane block with Ropivacaine 0.2% 30ml on each side (Total volume 60ml) was given before surgical incision and immediately after ET. In group B, Fentanyl 1 mcg/kg IV is given

Figure 1 : Consort Diagram



intermittently if SBP and HR are more than 20% of baseline. Intraoperatively, the vitals such as PR, SBP, DBP, MA, SpO2and EtCO2 were recorded at 0, 5, 10, 15, 30, 60, 90, and 120 minutes. At the end of the surgery, IV Ondansetron 4mg was given in both groups. Reversal of the patient and achieving satisfactory extubation criteria were done. The patient was shifted to the post-op recovery room. Duration of surgery, duration of anesthesia, NRS score at rest, and movement for 24 h, at 0, 2, 4, 6, 12, and 24 hours were recorded. The total duration of postoperative analgesia (from extubation to first rescue analgesic required) and total analgesics consumed in the first 24 hours were also recorded. The first rescue analgesia dose was given to those with an NRS score of over three postoperatively in IV Tramadol 50 mg.

Results

The data was analyzed using SPSS version 2.0, and the data was tested for normality. The mean standard

Table 1: Demographic characteristics.

Demographic data	Group A		Group B		t-test (P value)
	Mean	SD	Mean	SD	
Age	46.56	12.24	48.72	12.25	0.88 (0.380)
BMI	23.68	3.40	21.40	5.56	2.46 (0.015)
Duration of surgery	113.50	19.90	123	32.02	1.78 (0.078)
Duration of Anesthesia (min.)	134.50	20.63	134.60	32.65	0.018 (0.985)

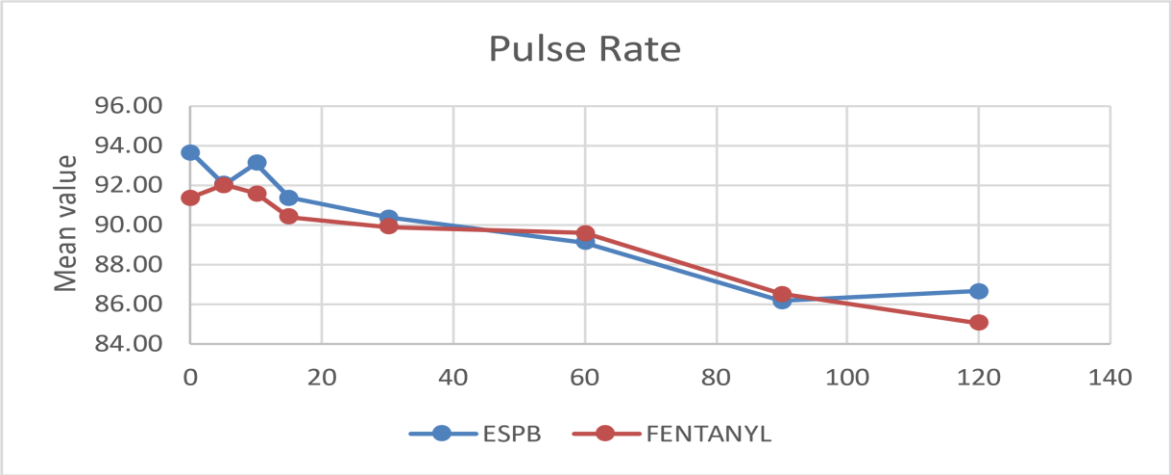


Figure 2. Comparison of intraoperative pulse rate among groups A and B.

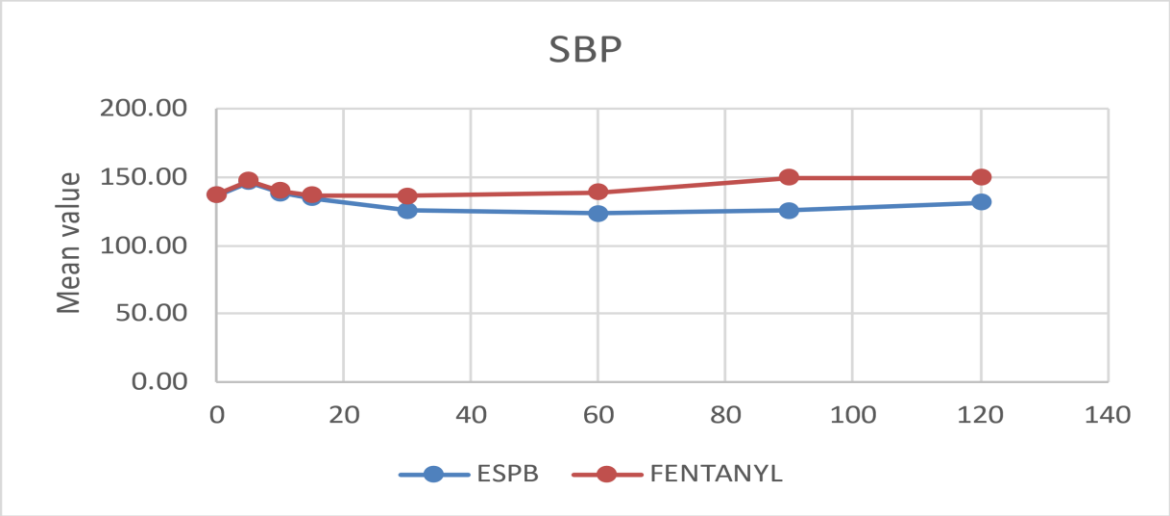


Figure 3. Comparison of intraoperative systolic blood pressure among groups A and B.

deviation (SD) was used to express quantitative data. For independent samples, a t-test was used while comparing quantitative data. A hundred patients were enrolled in the study and were divided into two groups of 50 each. The two groups, A and B, showed no significant difference in demographic data (age, sex, body mass index (BMI), and duration of surgery. (*P* value>0.05) as shown in Table 1.

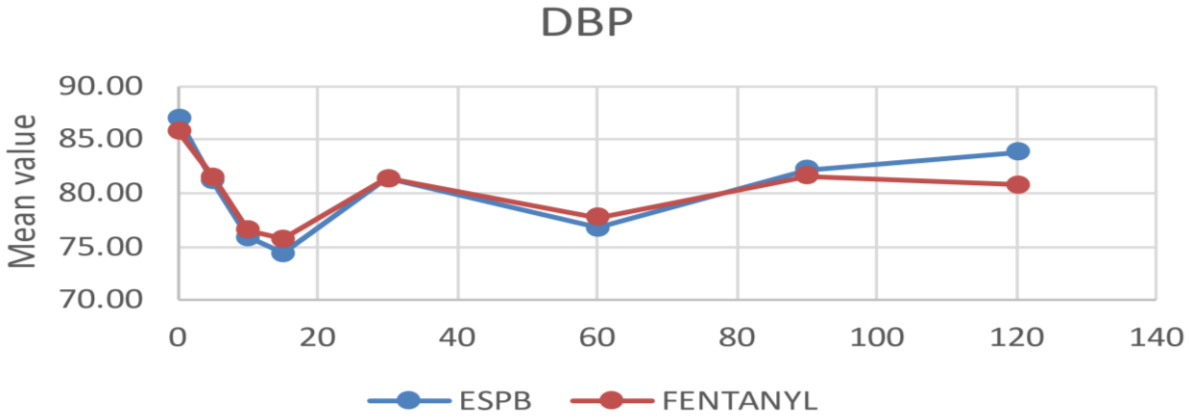


Figure 4. Comparison of intraoperative diastolic blood pressure among groups A and B.

Table 2: Postoperative NRS score at rest between groups A and B.

Hours	Group A		Group B		t-test (P value)
	Mean	SD	Mean	SD	
0	1.76	1.20	4.12	1.00	10.64 (<0.0001)
2	1.58	0.54	4.70	0.68	25.49 (<0.0001)
4	2.42	1.49	3.84	0.71	6.09 (<0.0001)
6	2.52	0.71	4.00	0.88	9.26 (<0.0001)
12	1.32	0.47	1.68	0.62	3.26 (0.002)
24	1.52	0.50	1.64	0.66	1.01 (0.311)

Table 3: Postoperative NRS score at movement between groups A and B.

Hours	Group A		Group B		t-test (P value)
	Mean	SD	Mean	SD	
0	4.16	0.93	5.54	0.54	9.03 (<0.0001)
2	3.52	0.71	5.16	0.74	11.34 (<0.0001)
4	4.00	0.81	4.20	0.67	1.34 (0.181)
6	3.80	0.73	5.34	0.66	11.09 (<0.0001)
12	2.48	0.50	2.64	0.48	1.61 (0.109)
24	1.68	0.68	3.64	0.63	14.89 (<0.0001)

Intraoperative vital data such as pulse rate (PR) per minute, systolic blood pressure (SBP) in mmHg, Diastolic blood pressure (DBP) in mmHg, Mean arterial pressure (MAP) in mmHg, end-tidal CO2 (EtCO2) in mmHg were compared in both the groups, shown in Figure 2, 3 and 4. In group A, SPB at 60 min. (123.52±9.42). Moreover, 90 mins (125.24±3.127) after induction were significantly stable, with not more than a 20% increase in SBP from baseline (132.8±10.44) as compared to group B at 60 min. (138.6±20.76) and 90 min. (145.6±5.75). MAP at 60 min. (92.36±6.25), 90 min. (96.57±6.54), and 120 min. (98.67±9.89) after induction, there was a significantly stable, not more than 20% increase in MAP from baseline (103.60±8.91) compared to group B at 60 min. (98.04±7.8), 90 min. (104.29±6.56) and 120 min. (101.53±12.65). Other parameters, such as PR, DBP, and EtCO2, showed no difference in the groups.

The two groups were compared for post-operative pain relief. A numeric rating scale (NRS) was used to assess pain postoperatively and was used at regular intervals at 0, 2, 4, 6, 12, and 24 hours at rest and movement, as shown in Tables 2 and 3. Group A showed a significant decrease in NRS score at rest at 0, 2, 4, and 6 hours and movement at 0, 2, 6, and 24 hours compared to group B ($P< 0.05$).

Table 4: Postoperative analgesic requirement between groups A and B.

Analgesic Requirements	Group A		Group B		t-test (P value)
	Mean	SD	Mean	SD	
Total duration of analgesia (hr)	17.86	7.85	7.76	3.94	8.13 (<0.0001)
Total analgesic requirement in 24 hrs	0.92	0.80	2.02	0.38	8.75 (<0.0001)

Total duration of analgesia (hours) was significantly longer in group A (17.86 ± 7.85) as compared to group B (7.76 ± 3.98) P-value <0.05, as shown in Table 4. The total rescue analgesia requirement (number of doses requirement) was significantly low in Group A (0.92 ± 0.8) as compared to Group B (2.02 ± 0.38), as shown in Table 4. Thirty-two patients did not require rescue analgesia.

Discussion

The triad of anesthesia was completed by hypnotic agents, either with intravenous or inhalational agents, before the invention of opioids. Therefore, the requirement for hypnotic agents was very high, leading to severe hemodynamic instability (1).

After introducing synthetic opioids, balanced anesthesia was maintained by opioid-induced blocking of the ascending nociceptive stimuli. Simultaneously, we achieved the goal of hemodynamic stability without compromising coronary perfusion and spontaneous breathing. Moreover, it facilitates the reduction of hypnotic agents. Thus, opioids became popular as they improved outcomes after anesthesia and surgery (1). However, opioids are often associated with well-recognized side effects like sedation, dysphoria, delirium, constipation, urinary retention, postoperative nausea and vomiting. Sometimes, life-threatening

respiratory depression and airway obstruction may happen. All these side effects are based on their effect on mu, delta, and kappa receptor activation and their effect on the immune system (4). Side effects prolong the hospital's length of stay and affect the economy of the hospital (5). In the United States, 2 million opioid-dependent users and 12 million opioid misusers were found in 2015, resulting in significant morbidity and mortality (1). Postoperative hyperalgesia and tolerance due to neuroadaptation increase the requirement for longer-acting opioids (6). Opioid anesthesia inhibits cellular and humoral immunity, leading to early cancer recurrence (4).

Pain is the unpleasant perception of noxious stimulus, and nociception is the stimulus of noxious receptors. Under general anesthesia, there is a pain-free nociception because anesthesia blocks the noxious receptor activity (7). The adequate control of hemodynamic responses during anesthesia addresses nociceptive pathways and the autonomic system (1). Anti-nociception suppresses the consequences of the stimulus of noxious receptors (8). Heleni Beloeil remarks that OFA is multimodal analgesia; here, one drug will not replace opioids. The association of drugs and /or techniques allows good-quality anesthesia without opioids. It is a new, emerging, exciting anesthesia technique for enthusiastic researchers (3).

The primary rationale is to avoid the usage of opioid during the intraoperative period and promotes rapid recovery by ensuring effective analgesia. Current ERAS protocol supports the same (3).

Opioid administration during surgery (during tissue injury) aggravates acute pain in the postoperative period, while in contrast, Opioid administration after surgery (after tissue injury) offers better postoperative analgesia. Here, the OFA concept fits well (3).

High-dose use of opioids has its limitations: less efficacy on pain during movement, dose-dependent side effects, delayed post-operative rehabilitation, dose-dependent hyperalgesia, and immunomodulation, which impress negatively infectious or cancerous pathologies and possible neurotoxicity. (9,10,11) Nociception potentially induces CNS changes during sensitization. It is the rationale for using a multimodal antinociceptive approach during OFA(1,12). Hemodynamic stability with opioid analgesia is achieved by blocking enkephalins within pain pathways. Other transmitters like glutamate, noradrenaline, Gamma-aminobutyric acid, and serotonin play important roles in heart rate and blood pressure regulation. It opens the usage of other pharmacological agents that act on ascending and descending pathways (1).

Our study showed no changes in Pulse rate, DBP, and EtCO2, but there is a significant change in SBP and MAP at 15, 30, and 45 min, after starting laparoscopic surgery.

Sympathetic attenuation can be achieved by the direct action of alfa two agonists or beta blockers and indirectly with MgSO4 and lignocaine (1).

One analgesia mode is insufficient to cover all triggers of nociception because perioperative pain is different in character, individual sensitivity, and possible site of modification on pain pathways. Therefore, a multimodal approach with two or more nonopioid adjuvants should give additive or synergistic effects, allowing a reduction in the side effects of each while maintaining hemodynamic stability (1). Multimodal nonopioid analgesic adjuvants used in our study OFA include lignocaine, MgSO4, Paracetamol, and dexamethasone. Many worldwide studies mention nonopioid analgesics like alfa two agonists, beta-blockers, ketamine, and gabapentinoids as a part of the OFA regimen (1, 13).

Lignocaine (Lidocaine) has analgesic, anti-inflammatory, opioid-sparing effects and co-anesthesia properties. The primary mechanism is the downregulation of neutrophil degranulation as an antinociceptive effect, and the secondary mechanism is the sodium channel-blocking property. Many research studies on large databases established that perioperative infusion of intravenous lignocaine significantly decreased the anesthetic and opioid requirement, reduced postoperative nausea and vomiting with a faster return of bowel function, and improved quality of recovery (14). Chu R et al. used a loading dose of IV Lidocaine 1-2 mg/kg, maintenance infusion Lidocaine 1-2 mg/kg/h (15). Our study used IV lidocaine 1.5 mg/kg in GA induction and IV lignocaine 1.5 mg/kg/h for maintenance infusion.

Magnesium is also an N-methyl-D-aspartate receptor antagonist in addition to its effects on calcium influx. The anti-inflammatory and opioid-sparing

effects make it a popular component of OFA. It is extensively used for perioperative analgesia in a 30 to 50 mg/kg intravascular bolus dose followed by a 10- to 15-mg/kg/h infusion. (16) It has some adverse effects, including potentiating neuromuscular blockers and hypnotics. It can also cause hypotension secondary to vasodilatation, which should be borne in min.d when combined with a2 agonists and propofol. Mohamed EH and Essam M did a comparative study between Group ketamine and Group ketamine with the MgSO4 combination. They concluded that Adding Mg to ketamine infusion can safely improve intraoperative and postoperative analgesia with opioid-sparing effect in cancer breast surgery. (17) Pia di Benedetto et al. used MgSO4 (1 gm) slowly bolus during induction and 8-10 mg/kg/hr during maintenance infusion and concluded that OFA is better than Opioid inclusive anesthesia (18). Our study used MgSO4 (2 gm) slow bolus during G induction.

Dexamethasone - C. Mitchell et al. used IV dexona 0.1 mg/kg (8 mg) in the beginning only and concluded that the single dose administered at the beginning of the procedure (0.1 mg/Kg) thus allows both a prevention of PONV and an analgesic benefit (19). We have used IV Dexamethasone 0.1 mg/kg in beginning means in pre-emptive analgesia in laparoscopic surgeries. Kasper Smidt et al. used two doses of dexona compared in Orthopaedic arthroscopy surgeries and concluded that the two doses of dexamethasone reduced morphine consumption during 48 hours after total knee arthroplasty and reduced postoperative pain (20). Mitchell et al. systemic review and meta-analysis in elective abdominal surgeries, pain score at rest, and movement in 5728 patients concluded that the total duration of analgesia is prolonged with reduced requirements of rescue analgesics (19). Our findings are similar to this study; pain score at rest and movement decreased significantly in Group A as compared to Group B. P value<0.05 Total duration of analgesia was significantly more in Group A (17.86 ± 7.85) as compared to Group B (7.76 ± 3.98) P value<0.001. The total rescue analgesia requirement was significantly lower in Group A (0.92 ± 0.8) compared to Group B (2.02 ± 0.38).

PCM is a centrally acting inhibitor of cyclooxygenases, and the active metabolite of paracetamol is phenacetin; a raised pain threshold is administered with all routes, and IV Paracetamol crosses the blood-brain barrier easily. Khyati et al. A comparative study of intravenous febrile vial (150mg/ml) vs intravenous paracetamol (1gm/100 ml) pint formulation for postoperative analgesia (21). We have used IV PCM 1 gm pint slowly in pre-emptive analgesia in laparoscopic surgeries 15 minutes before GA induction. It has central analgesic action with an onset of 15 min., peak of 1 h, and duration of 4 to 6 hrs.

Regional analgesic techniques, including peripheral nerve blocks, facial plane blocks, paravertebral and paravertebral variant blocks, and neuraxial blocks, have been incorporated with multimodal analgesic protocols to decrease postoperative opioid requirements and hospital stay after abdominal surgery (5). Peripheral nerve blocks or superficial wound site infiltration with local anesthetics are also highly effective for perioperative analgesia. We used a USG-guided erector spinae block immediately after endotracheal intubation using an injection of Ropivacaine 0.2 % 30 ml on each side.

Indications of OFA are opioid addiction, OSA, Obesity, cancer surgeries, colorectal ERAS, and Chronic pain syndrome. The benefits of OFA are better recovery, better comfort, and reduced postoperative pain while consuming less postoperative morphine, reduced PONV, less postoperative oxygen desaturation, and postoperative complications. A retrospective study reported on 9246 patients who underwent bariatric surgery.

Disadvantages/ Limitations of OFA

Limitations were in Bariatric laparoscopic surgery, patients having malignancy, uncontrolled co-morbid conditions, psychiatric illness, and small study size population with shorter duration. Therefore, studies with longer duration and larger population sizes can be considered.

Multimodal analgesia is based on patient characteristics, Individual familiarity, and availability.

Relative Contraindications are Critical coronary stenosis, Acute coronary syndrome, Uncorrected Hypovolemic shock, and autonomic dysfunction.

Future needs of Agenda OFA

- Analgesia -nociception Index based on Cardiac vagal activity monitor based on heart rate variability.

- Surgical pleth Index derived from

photoplethysmography waveform and R-R interval changes.

- Pupillary measurement, which is more sensitive in monitoring nociceptive stimulus, is based on parasympathetic stimulus.

- Monitor for intraoperative nociception and Procedure-specific studies and protocols are needed.

Conclusion

Opioid-free anesthesia, along with erector spinae plane block, compared to conventional opioid anesthesia, provides better post-operative pain relief and is a safe and feasible alternative method. Still, future studies will be required to reach a concrete conclusion.

Acknowledgment

GCS medical college management plus GCS laparoscopic surgery patients.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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