

## **Original Research Article**

### **COMPARISON BETWEEN OPIOID FREE ANAESTHESIA AND CONVENTIONAL OPIOID BASED ANAESTHESIA FOR PATIENTS UNDERGOING LAPROSCOPIC SURGERIES UNDER GENERAL ANESTHESIA**

#### **Abstract:**

Postoperative pain management plays a vital role in the recovery after surgery. All these days opioids were used to accomplish this but their use can be associated with adverse effects which can prolong the hospital stay. In the present era of opioid epidemic it is our responsibility to look for other alternatives, other drugs and modalities which can be safely be given to opioid naive surgical patients. The concept of multi-modal analgesia came as a paradigm shift lately by employing loco regional analgesia as well as drugs acting on different receptors of nociception. One of the pharmaceutical agents is Lignocaine which when given intravenously as continuous infusion produced analgesia in concentrations similar to epidural route. We conducted a study on continuous intra operative infusion of lignocaine in 1mg/kg/hr after a bolus dose. Lignocaine produced better hemodynamic stability, reduced consumption of volatile anesthetics, less postoperative nausea vomiting, sedation and facilitated early ambulation in patients after laparoscopic surgeries.

**Key words:** Opioid-free anaesthesia, Analgesia, Opioid, Peri operative period, Multi modal analgesia

#### **INTRODUCTION:**

For a long time Opioids play an important role in providing analgesia during surgeries as part of the three basic components of balanced anaesthesia<sup>1</sup>. Opioids used to be the ideal drug for providing analgesia while maintaining hemodynamic stability.<sup>2</sup> However it is associated with several undesirable side effects. Opioid free anaesthesia stands as a new paradigm,<sup>4</sup> has been recently developed to reduce the complications caused by opioids and its abuse. This is a multi model analgesia using several drugs as well as nerve blocks. Among the drugs used, Intravenous Lidocaine exerts analgesic, anti hyperalgesic and anti-inflammatory effects through its action on various receptors. It is found that the concentration of the neurotransmitter acetylcholine increases in the cerebrospinal fluid (CSF), which would exacerbate the inhibitory descending pain pathways resulting in analgesia<sup>7</sup>. Furthermore Lidocaine concentration reduces requirements of concomitant use of volatile anesthetics.<sup>3</sup> In the current era of day care and ERAS, early Postoperative ambulation and early recovery from anaesthesia are required. This can be accomplished with Opioid free anesthesia as it is found with opioids length of hospital stay is prolonged.

We hypothesize that Perioperative continuous infusion of Lignocaine provide good analgesia with intraoperative hemodynamic stability and extended postoperative analgesia in laparoscopic surgeries.<sup>5,6</sup>

### **AIM:**

This study aims to evaluate the efficacy of intravenous Lignocaine Infusion in terms of effective intraoperative pain management, with hemodynamic stability, and earlier postoperative rehabilitation when compared to Inj. Fentanyl.

### **PRIMARY OBJECTIVE:**

To compare the Hemodynamic stability intraoperatively with continuous Lidocaine infusion as opposed to conventional opioid based anaesthesia.

### **SECONDARY OBJECTIVE:**

Postoperative pain in first 24hrs and time to rescue analgesia is compared in both groups.

Postoperative nausea vomiting - PONV assessed in both groups

Sedation scoring in one hour after extubation was assessed in both groups using Ramsay sedation scoring

Acute rehabilitation, ambulation after surgery and total length of hospital stay were followed up in both groups.

### **MATERIALS AND METHODS:**

Institutional Ethical committee approval was obtained and written informed consent from each patient was taken.

#### **Inclusion criteria:**

- Age : 18 - 60 years
- ASA 1 and 2 patients
- Patients those who are undergoing laparoscopic surgeries under General Anesthesia
- Patients without local anesthetics allergy

#### **Exclusion criteria:**

- Patients with local anesthetics allergy
- ASA 3 and above
- Predicted Difficult Tracheal Intubation
- Body Mass Index More Than 30
- Patients with cardiac, renal or liver disease
- Chronic alcoholic and substance abuse patients
- Laparoscopic surgeries converting to open surgeries

This is a prospective head to head randomized comparative study with a total of 60 participants, who underwent laparoscopic surgeries under General Anesthesia were made into two groups with each having 30 participants were designated as GROUP O (opioid) and GROUP L(lignocaine)

### **Study Design:**

Prospective head to head randomized comparative double-blinded study.

Randomization: Computer generated.

Allocation concealment: SNOSE

Study area: Saveetha Medical College and Hospital

## **Methodology:**

All patients underwent regular preoperative screening for anesthetic fitness as in -patients and reviewed the night before surgery. Both the group patients were advised for NPO - 8 hours and Tab.Alprazolom 0.25 mg was given in the night prior to surgery.Intra dermal Lignocaine (preservative free) test dose was done in all patients in preoperative room.An anesthesia assistant not involved in the study prepared the drug solution after breaking the codes.

Patients received one of the two assigned study medications just before the induction of anesthesia.Routine monitors were connected and a 18 gauge cannula was secured and fluids connected at a rate of 5 ml/kg/hr.They were Premedicated with Inj. Midazolam 0.05 mg/kg , Inj. Glycopyrollate 0.01mg/kg and preoxygenated for 3 minutes.Both groups received Isoflurane maintained at MAC : 0.8 -1.0 , along with Nitrous oxide and oxygen and controlled ventilation with a tidal volume of 6–8 ml/kg, and the respiratory rate was adjusted to achieve normocapnia (EtCO<sub>2</sub> 30–35 mmHg).

Intra operative hemodynamics were monitored every 5mins from start of induction till laparoscopic port insertion and once in 15minutes thereafter.Injection Paracetamol 1gm Intravenously was given to both groups .At the end of the surgery the neuro muscular block was reversed with appropriate doses of Neostigmine and glycopyrolate and extubated.Patients were followed up till ambulation postoperatively.

## **GROUP O :**

After premedication Inj. Fentanyl 2mcg/kg bolus was given followed by infusion of N.Saline at the same rate as lignocaine. They were induced with Inj. Propofol 2mg/kg , after achieving good Bag mask Ventilation, Inj. Atracurium 0.5mg/kg was given. Intubation was done and position was confirmed with five point auscultation and a square waveform Etco<sub>2</sub> graph was ensured. Injection Paracetamol 1gm intravenously was given intra operatively.

## **GROUP L:**

After premedication Inj. Lidocaine 1.5mg/kg bolus given followed by infusion at 1mg/kg/hr.They were Induced with Inj. Propofol 2mg/kg , after achieving good Bag Mask Ventilation, Inj. Atracurium 0.5mg/kg was given. Intubation was done and position was confirmed with five point auscultation and a square waveform Etco<sub>2</sub> graph was ensured. Injection Paracetamol 1gm intravenously was given intra operatively. Injection Ketorolac 30mg Intramuscular prior to extubation.Intravenous Lidocaine infusion was continued till extubation and was discontinued in the recovery room

All patients received oxygen supplementation 3L/min.through mask. The patients were discharged from the PACU when their Aldrete score was higher than 9.

Patients were followed up post operatively till ambulation .

## **Statistical analysis:**

Sample size calculation : Statistical software EPI info 2000

Sample size of 30 patients in each group : Power of the test of 80%

Confidence interval of 95% and 5% alpha error.

Data was analyzed using SPSS version 16.0.

Comparison of Numerical variables between study group :ANOVA test

The comparison of categorical variables between study group : chi-square test with p value less than 0.05 were considered statistical significant

## RESULTS:

### **TABLE 1:**

Demographic data - There was equal distribution among participants in both groups with respect to Age, sex, height, weight and duration of anesthesia.

|                                  | Group O<br>n=30 | Group L<br>n=30 |
|----------------------------------|-----------------|-----------------|
| SEX M/F                          | 18/12           | 16/14           |
| Age in yrs                       | 38 +/- 13       | 42+/-10         |
| Height in cm                     | 158+/- 4        | 157+/-5         |
| Weight in kg                     | 67+/-5          | 70+/_6          |
| Duration of Anaesthesia in hours | 2.5 -3.5        | 2.5-3.0         |

### **INTRAOPERATIVE PARAMETERS:**

Comparison of Intra operative Heart rate trends between both groups were almost identical from induction to recovery.

### GROUP O and GROUP L

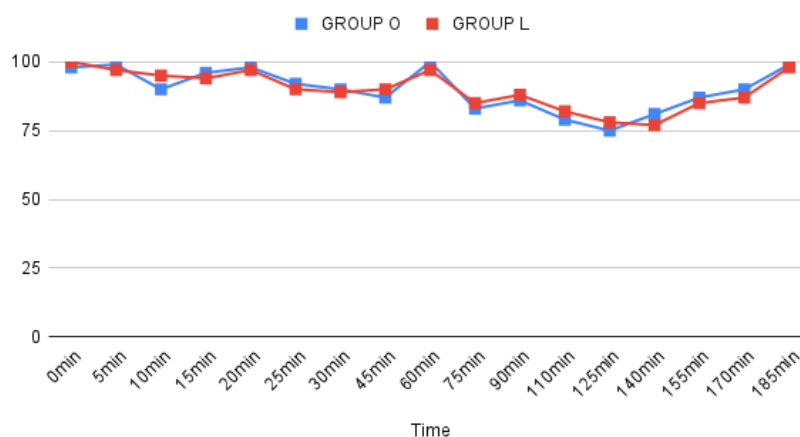


CHART 1 : Comparison Of Intra operative Heart rate trends between both groups.

Comparison Of Intraoperative variations in mean arterial pressure between both groups revealed no significant change.

### GROUP O and GROUP L

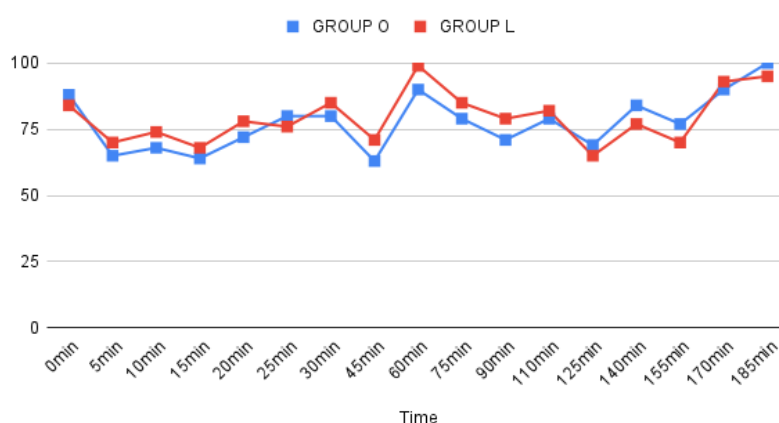
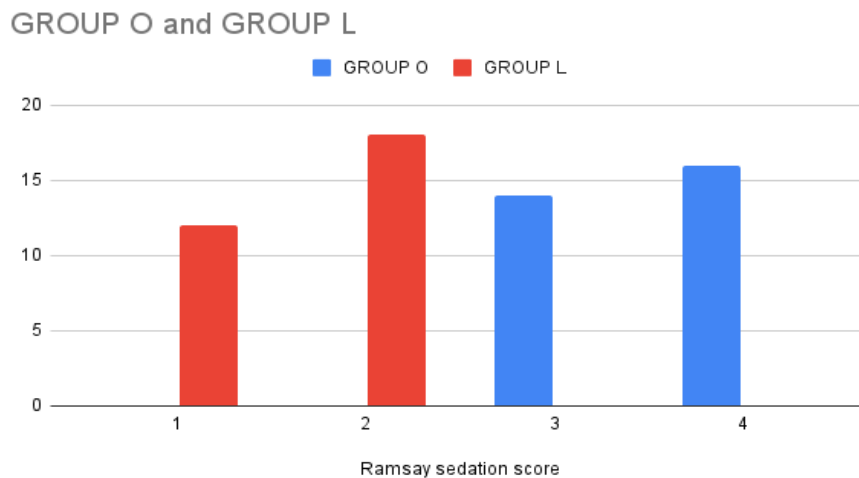


CHART 2: Comparison Of Intra operative variations in mean arterial pressure between both groups.

## POST OPERATIVE PARAMETERS

All patients in the study were observed for the level of sedation, occurrence of Post Operative Nausea Vomiting and magnitude of analgesia during the post operative period and the results are given below.

**CHART 3:** Ramsay sedation score was used to assess sedation one hour after extubation in both groups:



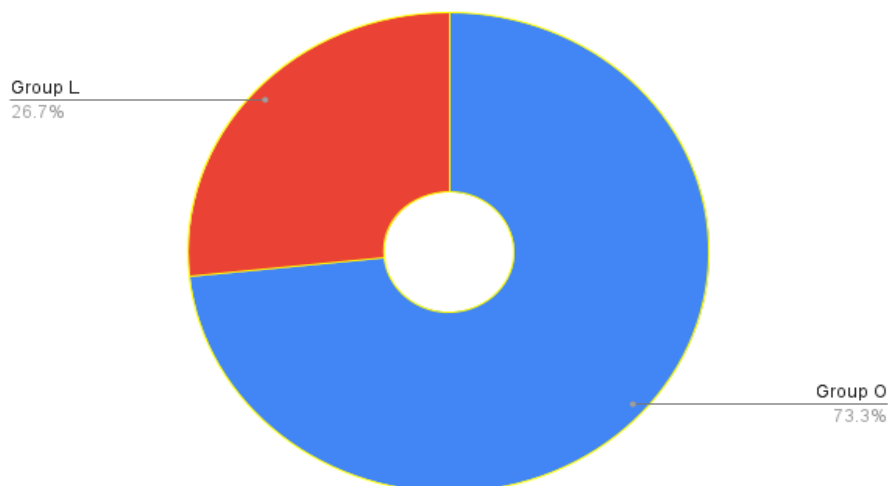
In Group L we found Ramsay scores of 1 in 12 out of 30 and Ramsay score 2 in 18 of 30 patients. In opioid group 14 out of 30 study subjects had Ramsay scores of 3 and 16 of 30 with Ramsay score of 4.

In Lidocaine group it was around : 1-2.  $p < 0.025$  and is statistically significant against the opioid group in which it was : 3-4.

None of the patients in opioid group showed any respiratory depression or hypoxia.

**CHART 4 :** Occurrence of PONV was assessed in both groups.

Occurrence of post operative nausea and vomiting were assessed in both groups and were found to be more common in opioid group. 22 of 30 patients in the group O and 8 of 30 in group L had post



operative nausea and vomiting which is significant.

**CHART 5:** Time to rescue analgesia was assessed Using the Visual Analogue scale in both groups and results are as given below.

Opioid group : 2.8 -4.5 hours.

Lidocaine group : 2.8 - 4.5 hours.

Post operative analgesia extended equally among both groups for almost comparable duration. Inj.Tramadol was used as rescue analgesic in both groups when the VAS score was 4 and above.

GROUP O and GROUP L

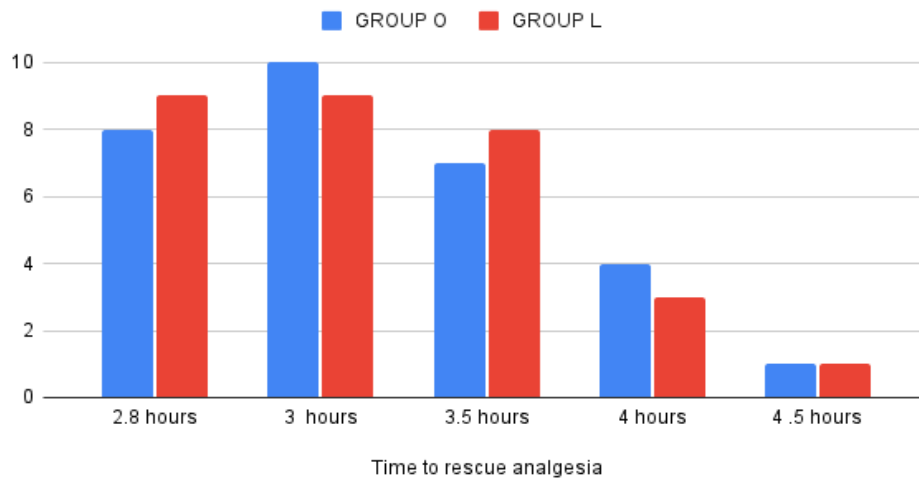
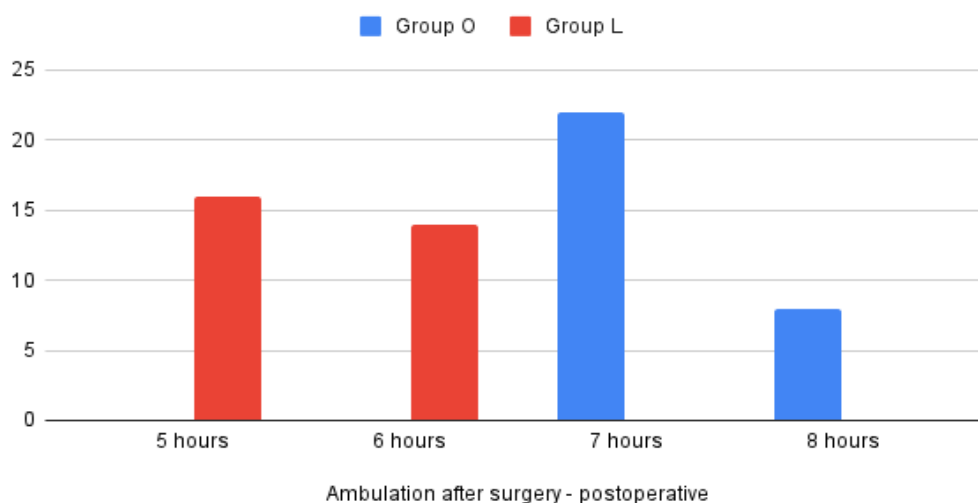


CHART 5: Postoperative Ambulation after surgery : Ambulation after surgery was achieved earlier in the lignocaine group.

Group O and Group L



This study proves the efficacy of Lidocaine is equivalent to Opioids in terms of intraoperative pain management, hemodynamic stability, and is superior to opioids in controlling PONV, postoperative pain and ambulation after surgery.

## DISCUSSION:

Opioids manage nociception as well as block the Autonomic nervous system, thereby maintaining the good intraoperative analgesia with hemodynamic stability.

There are some undesirable side effects of Opioids some of which can be of major concern like respiratory depression, anti-nociception, resistance and abuse. Egan et al<sup>8</sup> noted that persistent opioid use in the perioperative period can be a cause for the opioid epidemic. Studies are directed towards minimizing or completely avoiding opioids in the perioperative period for certain surgeries that require early ambulation, early bowel movement, surgeries where avoidance of PONV is required for the surgical grafts and surgeries which produce minimal pain post operatively not requiring strong analgesics. The concept of multi-model analgesia came to practice to manage such cases. This involves techniques like locoregional anaesthesia and many drugs. The common drugs used are non-opioid agents such as N-methyl-D-aspartate antagonists, local anesthetics, magnesium and  $\alpha_2$  agonists etc. They are called Postoperative and Opioid-free Anesthesia (POFA) trials<sup>9</sup>.

Chia et al<sup>10</sup> in their study found that anti-hyperalgesia therapies (e.g. ketamine, lidocaine, clonidine, and pregabalin) demonstrated decreases in pain scores, opioid analgesic consumption, and opioid side-effects. In addition to improving analgesia, perioperative lidocaine infusion, in doses ranging from 1.5 to  $3 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$  following a bolus of 1.5 mg/kg consistently improved postoperative pain scores in patients undergoing open or laparoscopic abdominal surgery. N Eipe, S Gupta, Penning et al<sup>11</sup> in their update on Intravenous lidocaine for acute pain reported plasma lignocaine levels varying from 1-3.8  $\mu\text{g/ml}$  for 6-24 hr infusion.

In another study by Carabalona JF, Delwarde B, Duclos A, et al.<sup>12</sup> Serum concentrations of lidocaine during bariatric surgery showed that serum concentrations of lidocaine never exceeded 5  $\mu\text{g/mL}$  and the median serum concentration was 1.45  $\mu\text{g/mL}$  (range, 0.98–1.88  $\mu\text{g/mL}$ ) during bariatric surgery. We did not do lignocaine drug assay as we restricted our infusion dose to 1 mg/kg/hr was fixed and the total duration was limited to 180 min to safeguard against its toxicity. Yet we made sure that lignocaine infusion wasn't more than toxic doses and patients were monitored for any LAST symptoms.

After abdominal surgeries pain relief can be provided by many techniques like thoracic epidural, Transversus Abdominis Plane (TAP) block, intra peritoneal instillation of Local Anesthetics, Intra Venous Lignocaine Infusion. In a systematic review by Vigneault L, Turgeon AF et al<sup>13</sup> it was found that Perioperative IVLI reduced postoperative pain and opioid requirement, as well as ileus recovery time, hospital length of stay, and nausea/vomiting.

Perioperative infusion of lidocaine may be non-inferior to epidural analgesia in the analgesic management of patients undergoing major abdominal surgery. Our study compares opioid with Lidocaine infusion for hemodynamic stability, intraoperative pain management, postoperative nausea vomiting, time to rescue analgesia, emergence from anaesthesia and early ambulation after surgery. As far as the intra operative analgesia and hemodynamic stability is concerned our study showed comparable effects in both groups in concordance with the study by TK K M, Kumar PV V et al<sup>14</sup>

Lidocaine, at target plasma concentrations of 1, 3, 5, 7, 9, and 11 mcg/mL, linearly decreased isoflurane MAC by -6% to 6%, 7% to 28%, 19% to 35%, 28% to



45%, 29% to 53%, and 44% to 59%, respectively in cats. Thus, Pypendop BH et al in their study concluded that lidocaine decreases the MAC of isoflurane.<sup>15</sup>

In our patients who had IV LI, it resulted in 35% reduction in Isoflurane end tidal concentration requirements intraoperatively. Statistical analysis could not be done as we did not monitor the depth of anesthesia which is a standard for assessment. But we found stable hemodynamics with lesser MAC of Isoflurane. Another study by Weinberg L, Jang J et al<sup>16</sup> on IVLI for radical Prostatectomy proved the ET-Sevo concentration to maintain a bispectral index of 40–60 was lower in the Lignocaine group compared to the Saline group [1.49% (SD: 0.32) vs. 1.89% (SD: 0.29).

Dunn LK, Durieux ME et al<sup>17</sup> found that laparoscopic surgeries cause low to medium grade visceral pain when compared to open surgeries and IV lignocaine reportedly alleviates this visceral abdominal pain. Intravenous lidocaine infusion in the perioperative period is safe and has clear advantages in patients undergoing abdominal surgery concluded Marret E, Rolin M et al in their study<sup>18</sup>

Immediate post operative period, patients experience nausea, vomiting after General anesthesia. Incidence is high with Opioid due to their action on CRZ in a dose related manner. Roberts GW, Bekker TB et al<sup>19</sup> reported that overall postoperative vomiting (POV) rate was 23.8%, whereas postoperative nausea (PON) was 51.3% due to Opioid use. In a study by Ziemann-Gimmel P et al<sup>20</sup> - a randomized control trial of opioid-free TIVA is associated with a large reduction in relative risk of PONV compared with balanced anaesthesia in patients undergoing bariatric surgery was reported. The advantage of PONV prevention was also noted in pediatric surgery by Nakajima D et al<sup>21</sup> and in laparoscopic gynecological surgeries by Wang T et al<sup>22</sup>

In our study we find Post operative nausea vomiting was significantly less in Lidocaine group ( $p < 0.001$  and is significant) when compared to opioid group. In the present study with initial IV bolus Fentanyl of 2mcg/kg body weight the incidence of POV was 73.3%.

In our study the time to rescue analgesia was comparable in both groups as our infusion dose was less than 2mg/kg/hr. The extended period of analgesia is dependent on the dose and duration of IV lignocaine infusion. Kranke P, Jokinen J, Pace NL et al<sup>23</sup> reviewed around 45 clinical trials on Continuous intravenous perioperative lidocaine infusion for postoperative pain and recovery, and found that perioperative lidocaine infusion at rates greater than or equal to 2mg/kg/hr was associated with decreased VAS pain scores and opioid consumption in the first 24h; however, there was no evidence of effect for rates less than 2mg/kg/hr. This study confirmed that patients receiving lidocaine had decreased analgesic requirements and pain scores that became more prominent 36 h after the lidocaine infusion had been terminated.

A review of 21 trials comparing systemic lidocaine with placebo by Sun Y, Li T, Wang N, Yun Y et al<sup>24</sup> it was reported that systemic lidocaine also significantly reduced postoperative pain intensity (VAS, 0-100 mm) for 6 hours after surgery at rest.

IV lidocaine administration during abdominal surgery was also found to have extended period of analgesia into the postoperative period, reduced postoperative

opioid requirement, accelerated postoperative recovery of the bowel function, and short the duration of hospitalization<sup>23,24,25,26</sup>

Marret E, Rolin M, Beaussier et al<sup>18</sup> in their meta analysis found that Continuous intravenous administration of lidocaine during and after abdominal surgery improved patient rehabilitation and shortened hospital stay. Early recovery is one of the relevant clinical outcomes after minimally invasive surgery. Early mobilization is considered an important element of postoperative care and forms the essential goal in ERAS protocol. ERAS guidelines for colorectal surgery also recommends the use of continuous infusion of intravenous lidocaine intraoperatively whenever thoracic epidural anesthesia is contraindicated. Under careful monitoring, it can be continued in the postoperative period also to provide analgesia<sup>27,28</sup>

Patient ambulation was prolonged in opioid group while Lidocaine group significantly showed early ambulation<sup>23,29,30</sup>. In our study we could find acute rehabilitation in 5-6 hrs in lidocaine group as opposed to 7-8 hrs in opioid group. Kaba et al<sup>31</sup> in their study on acute rehabilitation in colorectal surgery with IVLI found that lignocaine infusion patients had a hospital discharge 2-3 days earlier than the control group who were discharged after 3-4 days.

De Oliveira GS Jr, Fitzgerald P et al<sup>32</sup> found that patients undergoing ambulatory laparoscopic surgery who received lidocaine intraoperatively were discharged 26 min faster and required less opioid medication after discharge, which was correlated with better quality of recovery scores. Recovery score QoR40 was used in these studies while we followed Ramsay sedation score as a surrogate for the quality of recovery.

Opioids cause sedation extending to the immediate post extubation period, which may be of concern in patients with OSA<sup>33</sup>. OFA with lignocaine and dexmedetomidine showed better recovery profile with IV lignocaine, another study by Dogan SD, Ustun FE et al<sup>36</sup> comparing IV lignocaine and IV esmolol showed better recovery with esmolol when compared to lignocaine.

D. Fletcher, V. Martinez et al<sup>34</sup> in their meta analysis showed the adverse effects of opioid in that they can increase sensitivity to noxious stimuli and cause opioid-induced hyperalgesia, thus requiring higher requirement of opioids when high intraoperative doses of opioids were used. In our study we used only bolus dose and all patients received Inj. Paracetamol intraoperatively. The rescue analgesia used was Inj. Tramadol in both groups equally. Kopport et al<sup>35</sup> in their study concluded that intravenous lidocaine infusion during intra operative period reduces the requirement of analgesics as IV lidocaine may have a true preventive analgesic activity, most likely by preventing the induction of central hyperalgesia.

“Is it time to avoid Opioid totally, an opioid epidemic - a call to action” An article was published on November 9, 2016, at NEJM.org by Vivek H. Murthy, M.D., M.B.A. It was the first time in the 145-year history of the Office of the Surgeon

General that such a letter was issued specifically to medical professionals calling them to action<sup>37</sup>.

To conclude we are in a era of opioid epidemic and it is prudent to avoid opioid for surgeries which cause moderate pain

As Brown EN , Pavone KJ et al stated in their study of multimodal anaesthesia , Opioids can be replaced with multiple drugs with lesser concentration, which thereby will sensitize the receptors for pain management and autonomic system inhibitions.

Our study it proved that Intraoperative Intravenous infusion of nontoxic doses of Lidocaine improved accelerated ambulation postoperatively , maintained hemodynamic stability similar to opioid, reduced PONV and sedation postoperatively in patients under going laparoscopic surgeries under General Anesthesia.

Our results compliment with the results of Groudine et al and Koppert et al , that Lidocaine through its various actions on inhibiting G protein coupled receptor , sodium channel blockade and NMDA receptors blockade , which plays a major role in postoperative hyperalgesia.

## **CONCLUSION:**

Intraoperative Intravenous lidocaine infusion thus proved it is not only equivalent to Opioid but superior to it in terms of incidence of PONV, Post operative sedation and postoperative ambulation. It can be considered for ERAS protocol as it improves postoperative early recovery by reducing postoperative pain and complications, shortening hospital stays, and enhancing patient satisfaction without compromising safety when compared to conventional opioid based general anesthesia.

## **COMPETING INTERESTS DISCLAIMER:**

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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