ORIGINAL ARTICLE

A Prospective Randomized Study to Evaluate the Analgesic Efficacy and Quality of Recovery of Perioperative Intravenous Lignocaine Infusion in Laparoscopic Surgeries

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Abstract

Background: The role of intravenous lignocaine perioperatively is studied to evaluate whether it has an opioid-sparing effect, component of a multimodal analgesia regimen, enhancing recovery, and early discharge of the patients undergoing laparoscopic surgery.

Materials and methods: A randomized prospective double-blind study was done on 80 ASA I/II adult patients of both sexes in the age group 18–60 years scheduled for elective laparoscopic surgery under general anesthesia over a period of 6 months. Group L was administered lignocaine 1.5 mg/kg i.v. bolus followed by and 1.5 mg/kg/hour i.v. infusion and group NS 10 mL of 0.9% normal saline i.v. instead of lignocaine.

Results: The intubation response, length of hospital stay, ambulation time, time of the return of bowel movements, use of rescue analgesics, use of opioids, and visual analog scores (VAS) in the saline group were significantly higher as compared to the lignocaine group.

Conclusion: Intravenous lignocaine as bolus and infusion demonstrated a significant decrease in the hemodynamic parameters following intubation and postextubation, provided opioids-sparing role, showed lower VAS scores, fewer rescue analgesics over 24 hours, significantly early bowel movements, ambulation, and discharge.

Keywords: Analgesia, Laparoscopic surgeries, Lignocaine.

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Introduction

Laparoscopic surgeries, being minimally invasive have a major advantage of early ambulation, reduced hospital stay, and better recovery scores. Though the incidence of pain in laparoscopic surgeries is of shorter duration and lower intensity than open surgeries (46–54%) it needs to be treated effectively.[1,2] High-quality analgesia is essential to enhance early recovery and discharge. Most often opioid analgesics are considered intra- and postoperatively at varying intervals owing to the multifactorial causes of pain in laparoscopic surgeries in combination with multimodal analgesia. This is attributed to tissue injury (visceral pain), peritoneal irritation largely due to (1) pneumoperitoneum, (2) blood left in the abdomen after surgery, (3) diaphragmatic irritation, (4) also owing to the possible source of pain in laparoscopy from sustained intraoperative pressure on capillary beds in abdominal and possibly retroperitoneal viscera causing nociception.[3] The adverse effects of opioids (nausea, vomiting, sedation, urinary retention, etc.) limit the benefits and warrant the need for alternative modalities like intraperitoneal instillation of local anesthetic, truncal blocks, wound infiltration, and intravenous drugs such as lignocaine, magnesium, dexamethasone, or ketamine. More recent research has demonstrated that lignocaine decreases pain scores, analgesic consumption, and side effects of opioids but also promotes enhanced recovery after surgery (ERAS). These effects include early ambulation, early feeding (reduced ileus), and patient satisfaction. Lignocaine acts as effective analgesia through its anti-inflammatory effects, anti-hyperalgesic effects, inhibition of nociceptive transmission, and stimulation of inhibitory descending pathways.

Several studies and meta-analyses of these studies have been published and show that perioperative lignocaine infusion is indeed effective but the evidence supporting its use varies as per the surgical procedure. Perioperative i.v. infusion of lignocaine has been used as a method to control postoperative pain.[4–7]

The i.v. use of lignocaine for its anti-hyperalgesic and analgesic properties in the dose of (1.3–3) mg/kg/hour has been used in the past.[4,5] Most of the studies done in major and minor laparoscopic surgeries have used a dose of 2 mg/kg i.v. lignocaine and have shown satisfactory results with prolonged infusions of up to 24 hours and had a lower incidence of side effects. Modern postoperative care is focused on multimodal management to enhance recovery. Various drugs including lignocaine, esmolol, alfentanil, and fentanyl have been recommended for the control of hemodynamic events caused by laryngoscopy, tracheal intubation, and subsequent extubation. The usage of multimodal analgesia, reduced opioid consumption, resuming early oral intake, promoting early ambulation, and better patient experience would help to achieve ERAS. Lignocaine as an intravenous bolus dose

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has been used for minimizing hemodynamic changes associated with intubation and extubation.[8,9] Furthermore, i.v. infusion has been used for postoperative analgesia. We investigated whether i.v. perioperative lignocaine (bolus and infusion) would be able to provide adequate analgesia in addition to obtunding pressor response and improving the quality of recovery in laparoscopic surgeries.[10–13] We chose a lower dose of 1.5 mg/kg of i.v. lignocaine bolus and 1.5 mg/kg/hour of infusion for a limited duration after surgery to assess whether it would be as effective and thereby to assess the role of i.v. lignocaine as an analgesic and whether it enhances postoperative recovery and is a suitable alternative to sparing use of opioids.

Materials and Methods

After approval of our institutional ethics committee, a randomized prospective double-blind study was done on 80 ASA physical status 1 and 2 adult patients of both sexes in the age group 18–60 years scheduled for elective laparoscopic surgery under general anesthesia. The data were collected in a pretested proforma after obtaining written informed consent from the patient for the study. The primary objective was to evaluate the analgesic efficacy of intraoperative lignocaine-infused patients, the effectiveness of lignocaine infusion on the pressor response at intubation and extubation, and the effect of intravenous lignocaine on postoperative analgesia. The secondary objectives included observing any side effects of intravenous lidocaine infusions, the role of i.v. lignocaine on return of bowel movements postoperatively and its effect on the time to discharge from the hospital. The study population of 80 patients was randomly allocated into two groups based on a computerized randomization table, with 40 patients in each group.

The two groups (1) Group L—Lignocaine 1.5 mg/kg i.v. bolus diluted to 10 mL with normal saline and 1.5 mg/kg/hour i.v. infusion was continued till 15 minutes postoperatively prepared in a 20-mL syringe. (2) Group NS—10 mL of 0.9% normal saline i.v. bolus and infusion of normal saline at a similar volume infusion rate as it would be with 1.5 mg/kg/hour of lignocaine till 15 minutes postoperatively prepared in a 20-mL syringe. To facilitate blinding the initial drug either lignocaine 1.5 mg/kg or saline was given as a 10-mL volume. The person administering the drug and the evaluator were different.

The Inclusion Criteria Considered was

Age 18–60 years, males or females, ASA 1 or 2, elective laparoscopic surgeries, duration of surgery of 2 hours, elective laparoscopic surgeries, BMI 18–26.

Exclusion Criteria

Patient refusal, pregnant females, and known allergy to study drugs were excluded from the study.

Statistical Methods

Software PS: power and sample size calculation software was used. Descriptive statistical analysis was carried out in the study to explore the distributions of several characteristics of the cases studied. Results on categorical data were shown as *n* (% of cases) and the data on continuous measurements were presented on mean ± standard deviation OR median (minimum–maximum). The statistical significance of the difference of various categorical variables across two groups was tested using the Chi-square test. Inter-group statistical significance was assessed of difference of various continuous measurements, independent sample *t*-test was used after confirming the underlying normality assumption. The *p* values < 0.05 were considered to be statistically significant. All the hypotheses were formulated using two-tailed alternatives against each null hypothesis. The entire data were statistically analyzed using Statistical Package for Social Sciences (SPSS version 16.0, Inc., Chicago, USA) for MS Windows.

Conduct of Anesthesia

After 3 minutes of preoxygenation with 6 L/minute, lignocaine i.v. 1.5 mg/kg bolus was administered in group L and saline likewise in group NS. General anesthesia was administered using inj. propofol 2 mg/kg, inj. fentanyl 2 µg/kg, and inj. rocuronium 0.9 mg/kg. Orotracheal intubation was performed and lungs were ventilated with nitrous oxide, oxygen, and inhalational agent and MAC maintained at 0.8 to 1.2. After induction, inj. dexamethasone 0.1 mg/kg i.v. was administered and infusions were started as per randomization intraoperatively till 15 minutes postoperatively. Intraoperatively inj. paracetamol 1 g i.v. and anti-emetic ondansetron 0.1 mg/kg i.v. were administered. To ensure the same infusion rate in both groups (e.g., 1.5 mg/kg/hour for 60 kg person comes to be 90 mg). So in group L 200 mg of lignocaine was diluted till 20 mL with normal saline and was started at 9 mL/hour and in group NS saline infusion was also started at 9 mL/hour as per lignocaine group calculation. Intraoperative tachycardia and hypertension if >20% of baseline warranted a check of MAC, relaxation, and if adequate inj. fentanyl 0.25 µg/kg i.v. as titrated bolus was given to all patients to manage the intraoperative pain. Port sites were locally infiltrated with 0.2% ropivacaine with a volume of 5 mL per port site. At the end of the surgery, neuromuscular block was antagonized in all patients with neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg and was extubated in the operating room. All patients were observed in the recovery room and visual analog score (VAS), number of rescue analgesics, duration of hospital stay, amount of opioid used, duration of ileus, and postoperative nausea and vomiting (PONV) was assessed and noted at 0, 2, 4, 6, 12, 18, and 24 hours. Rescue analgesics required by the patient according to the VAS (≥3) were assessed after completion of surgery. Our first rescue analgesic was inj. diclofenac 75 mg slow i.v. bolus in case of VAS (≥3) and second rescue analgesic was given if there was no relief beyond 30 minutes of first analgesic rescue, i.e., inj. tramadol 50 mg i.v. Several postoperatively adverse effects of lignocaine like dizziness, drowsiness, tinnitus, blurred or double vision, vomiting and sensation of heat, cold, numbness; twitching, tremors, and convulsions were noted. Duration of ileus was assessed by checking the first return of bowel movement by noting the time of passing flatus since the surgery was completed. Ambulatory time was measured as the time interval between postoperative periods to the start of ambulation of the patient. The duration of hospital stay was also noted in both groups (Fig. 1).

Results

The two groups were comparable with regards to demographics: age, sex, BMI, duration of surgery, various surgeries in each group (Tables 1 and 2). The intubation response in the saline group was significantly higher as compared to the lignocaine group. The hemodynamic parameters after extubation in the lignocaine group were significantly lower than the saline group, though not in the DBP after extubation (Table 3). The use of additional fentanyl in the lignocaine group was significantly less as compared to the saline group with a *p* value of 0.002 (Table 4). The average dose of additional fentanyl used was 15.83 µg in the lignocaine group *vs*

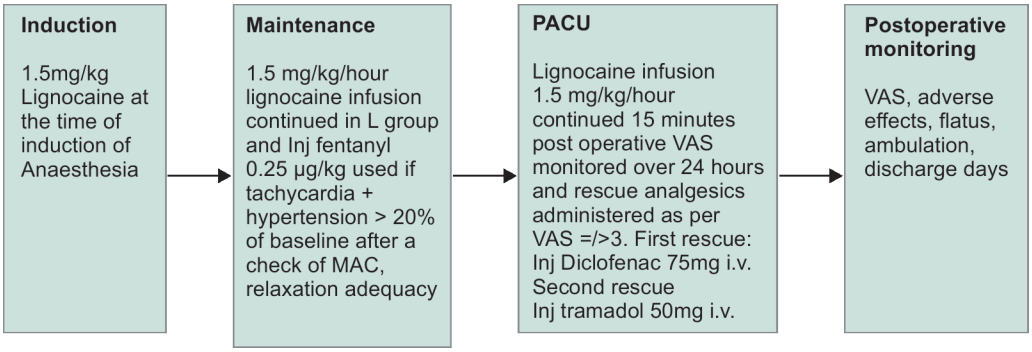

Fig. 1: Outline of the study procedure

Table 1: Age, sex, and BMI demographic characteristics of patients in two groups

Characteristics	*Group L*	*Group NS*	*p value*
Number of patients	40	40	
Age (in years) Mean ± S.D.	40.3 ± 12.01	41.7 ± 7.83	0.462
Range	42	30	
BMI	22.05 ± 1.10	22.15 ± 1.16	0.838
Range	4	5	
Sex			
Number of males	22 (55.0 %)	19 (47.5%)	0.502
Number of females	18 (45.0%)	21(52.5 %)	
Surgery duration (minute)	107.1	105.5	0.757

Table 2: Types of surgeries in two groups

Surgery	*L*	*NS*	*All*	*p value*	*Statistical significance*
Diagnostic lap	3	1	4	0.286	NS
Lap appendix	13	12	25		
Lap cholecystectomy	14	14	28		
Lap cystectomy	3	4	7		
Lap inguinal hernia	3	5	8		
Lap myomectomy	1	2	3		
Lap umbilical hernia	3	2	5		
All	40	40	80		

Table 3: Vitals noted in both the groups before intubation (BI), after intubation (AI), and after extubation (AE)

Variables	*Group L*	*Group NS*	*p value*	*Statistical significance*
Vitals after intubation (BI) in both the groups				
HR (BI)	72.22 ± 4.08	73.40 ± 5.35	0.273	NS
SBP (BI)	125.55 ± 5.18	123.5 ± 10.83	0.5	NS
DBP (BI)	73.03 ± 6.56	75.55 ± 8.22	0.133	NS
MAP (BI)	88.22 ± 5.39	91.25 ± 7.88	0.52	NS
Vitals after intubation (AI) in both the groups				
HR (AI)	82.33 ± 9.75	87.63 ± 6.84	0.043	S
SBP (AI)	124.23 ± 12.36	142.25 ± 9.81	0.0001	S
DBP (AI)	82.25 ± 11.48	79.80 ± 6.11	0.239	NS
MAP (AI)	95.39 ± 10.48	100.22 ± 5.22	0.0001	S
Vitals after extubation (AE) in both the groups				
HR (AE)	88.53 ± 6.92	98.30 ± 7.09	0.0001	S
SBP (AE)	124.40 ± 8.52	149.58 ± 8.1	0.0001	S
DBP (AE)	82.38 ± 7.04	84.05 ± 4.82	0.218	NS
MAP (AE)	95.53 ± 5.66	105.55 ± 4.29	0.0001	S

33.37 µg in the saline group which was almost double as compared with the lignocaine group.

Visual analog scores were significantly lower in the lignocaine group at 0, 2, and 6 hours though at 4 hours was not statistically significant. At 0 hours, 65% of patients in the lignocaine group had a VAS <3 which was significant whereas 95% of patients in the saline group had a VAS of >2. Likewise, at 2 hours, 79.5% of patients in the lignocaine group had a VAS < 3 which was significant whereas 60% of patients in the saline group had a VAS of <3 (Table 5). Inadequate pain relief (VAS ≥ 3) in both the groups warranted a rescue analgesia. The number of patients requiring diclofenac in the lignocaine group (67.5%) as the first rescue was significantly less as compared to the saline group (95%) ($p = 0.002$). Likewise, the use of tramadol as a second rescue was significantly higher in the NS group as compared to the lignocaine group. Thirty-five percent of patients needed tramadol in group L vs 72.5% in NS group ($p = 0.001$). Bowel movements in the saline group (568.0 ± 44.09 minutes) were significantly delayed as compared to the lignocaine group (434.0 ± 42.71 minutes) ($p = 0.0001$). Ambulation time in the lignocaine group was significantly earlier than the saline group, i.e., 14.5 hours in the lignocaine group as compared to 16.2 hours in the saline group ($p = 0.003$). Thus, the length of hospital stay was significantly longer in the saline group which was 1.83 days as compared with the lignocaine group which was 1.62 days ($p = 0.0001$).

Table 4: Distribution of EXFENT used in patients between two groups

	Group		
EXFENT	*L*	*NS*	*p value*
Used	12	37	0.002
Not used	28	3	
Total	40	40	

Table 5: Comparison of VAS between both groups at 0, 2, 4, and 6 hours

	Group			
	L (%)	*NS (%)*	*p value*	*Statistical*
VAS 0 hours				
0	6 (15.0)	0 (0.0)	0.0001	S
1	16 (40.0)	0 (0.0)		
2	4 (10.0)	2 (5.0)		
3	14 (35.0)	12 (30.0)		
4	0 (0.0)	21 (52.5)		
5	0 (0.0)	5 (12.5)		
Total	40 (100.0)	40 (100.0)		
VAS 2 hours				
0	13 (33.3)	10 (25.0)	0.009	S
1	11 (25.6)	1 (2.5)		
2	8 (20.5)	13 (32.5)		
3	8 (20.5)	16 (40.0)		
Total	40 (100)	40 (100.0)		
VAS 4 hours				
0	17 (43.6)	22 (55.0)	0.068	NS
1	13 (33.3)	13 (32.5)		
2	7 (15.4)	0 (0.0)		
3	3 (7.7)	5 (12.5)		
Total	40 (100)	40 (100.0)		
VAS 6 hours				
0	29 (72.5)	24 (60.0)	0.046	S
1	7 (17.5)	16 (40)		
2	1 (2.5)	0 (0.0)		
3	3 (7.5)	0 (0.0)		
Total	40 (100.0)	40 (100.0)		

Discussion

The increasing use of laparoscopy for major and minor surgeries has made it essential to provide efficient pain control, a better quality of recovery, early ambulation, and limit the hospital stay. Usage of intravenous lignocaine in acute pain came from its established role in chronic pain. Lignocaine interrupts neuronal transmission by blocking sodium channels in nervous tissue. Animal studies have suggested that the systemic effect of lignocaine is mainly by preventing depolarization of the neuronal membrane which is prior damaged or dysfunctional. Systemic lignocaine prevents the proliferation of new active sodium channels in traumatized or scarred tissue, thereby blocking their firing.[14] Lignocaine has analgesic, anti-hyperalgesic, and anti-inflammatory properties. It is proposed to reduce central sensitization and decrease *N*-methyl-D-aspartate receptor-mediated post-synaptic depolarization. Studies have also shown a significant decrease in systemic inflammatory markers.[1,5,15]

Hemodynamics

Wilson way back in 1991 concluded through their study that 1.5 mg/kg i.v. lignocaine 4 minutes before intubation completely obtunded the pressor response but not the chronotropic response to intubation.[16] Kindler and colleagues stated that lignocaine in combination with esmolol attenuated the heart rate and pressor response *vs* only heart rate by esmolol though may be accompanied by hypotension.[17] Intravenous injection of lignocaine in a dose 1 mg/kg, 2 minutes before tracheal extubation prevented both coughing and increase in arterial pressures and heart rate during and after extubation as studied by Bidwai et al.[18] The decrease in the heart rate, SBP, and DBP (blunting of the sympathoadrenal response) with i.v. lignocaine has been substantial when in combination with opioids as noted in various studies[16,19,20]

In our study, a significant decrease in laryngoscopic response to heart rate and mean arterial pressure were observed in group L as compared to group NS during intubation. A decrease in HR (82.33 ± 9.75) in group L as compared to HR (87.63 ± 6.84) in group NS was found during intubation with a *p* value of 0.043 (Table 3). Jain and Khan observed similar results in patients undergoing elective laparoscopic cholecystectomy at 1.5 mg/kg i.v. bolus administered and thereafter an infusion at a rate of 1.5 mg/kg/hour.[8] They found that in the lignocaine group there was a change in heart rate postintubation (105.13 ± 13.49) and postextubation (109.83 ± 12.83) which was significantly lower than respective heart rates with postintubation (115.57 ± 13.44) and postextubation (118.17 ± 17.19) with the saline group with a p value < 0.005. Murthy and Kumar studied laparoscopic surgeries with a dose of 1.5 mg/kg lignocaine i.v. bolus followed by an infusion dose of 1.5 mg/kg/hour till 1 hour postoperatively.[9] They too found a significantly lower heart rate in the lignocaine group after intubation and postextubation with a *p* value of <0.001. Whereas no changes in DBP were noted in both the groups at intubation and postextubation. Hence, according to our observation, intravenous lignocaine was effective in reducing the pressor response, specifically the SBP and MAP.

Various studies have noted lignocaine on controlling hemodynamic changes have shown similar results periintubation and periextubation.[8,9,21] Other studies have reported a significant effect on either PR[17,22] or MAP alone.[16,23] In contrast to it, few other studies have also noted no significant attenuating effect of lignocaine on the hemodynamic parameters.[24,25] Such phenomena can be attributed to the action of lignocaine in causing arteriolar vasodilatation,[26] downregulating the autonomic reaction,[21] having cough suppressant activity,[22,27] and increasing the depth of general anesthesia.[28]

Intraoperative Use of Opioids

In our study, we have observed that the use of i.v. bolus and i.v. infusion of lignocaine has shown an opioid-sparing role and enhanced recovery. We observed reductions in pain scores. Thirty percent of patients in group L required fentanyl intraoperatively as compared to 92.5% of patients in group NS (p value = 0.002) (Table 4). The NS group needed double the dose (15.83 vs 33.37 µg) which was needed in group L. McKay et al. found that there was a 30% reduction of the amount of opioid use in patients undergoing ambulatory surgeries which were significant and comparable to our study and suggest an opioid-sparing role of lignocaine.[29] Ventham et al. in their meta-analysis noted lowered 24-hour opioids consumption, lower pain scores at 2, 12, and 24 hours with i.v. lignocaine following laparoscopic surgery and was similar to our study.[30] Patients undergoing laparoscopic bariatric surgeries required significantly lower morphine (10 mg) requirement and this facilitated better quality of recovery scores in the lignocaine group (1.5 mg/kg i.v. bolus and 2 mg/kg/hour i.v. infusion).[11] Intravenous lignocaine attenuated the postoperative pain and decreased the morphine consumption after abdominal surgery due to prevention of central hyperalgesia and likewise reduced opioid requirement very significantly in laparoscopic cholecystectomy vs intraperitoneal lignocaine.[1,31] In our study, in both the groups, the port sites were infiltrated postoperatively, though intraperitoneal instillation was not practiced.

Dose and Duration of Infusion

Perioperative lignocaine in a dose ranging from 0.5 to 1.5 mg/kg bolus followed by 1.5 to 3 mg/kg/hour has over the years shown to have reduced pain (noted as lower VAS pain scores) in various open and laparoscopic abdominal surgeries.[6,32–35] Lignocaine infusions of 2 mg/kg/hour reduced pain and the requirement of opioids over the first 24 hours. Longer duration of infusions provided a proportionate reduction in opioids use but showed no benefit of continuing infusions beyond 24 hours.[33] Overall requirement of analgesics was lowered by 35% when lignocaine infusions were continued up to 1-hour post-surgery, whereas further reduced up to 83% when infusions were run for 24 hours.[35] The duration of the analgesic action of i.v. lignocaine varied between 2 hours and 48 hours postoperatively,[15,27,36] whereas one study also reported no immediate effect but analgesic action seen on day 2 and 3 postoperatively.[1] Its effects were seen after i.v. lignocaine is most effective when the infusion is administered intraoperatively and this effect may persist for days to weeks beyond the infusion time and the plasma half-life thus suggesting that other mechanisms (prevention of the hypersensitivity of the central or peripheral nervous system or both) do exist apart from voltage-gated sodium channels.[1,37,38] The type of surgery may be liable to explain the difference in observations. Previous studies have shown that lignocaine has best effect when administered during the presence of a significant nociceptive input.[11,12]

VAS

Reduction in pain was significantly lower in group L at 0, 2, and 6 hours and further reduction was seen at 12 and 24 hours as compared with the NS group in our study. Differing analgesic efficacy of lignocaine would be noted in the context of different surgical procedures. It has shown most effectiveness after major open surgeries after prolonged infusions owing to its anti-inflammatory effects.[5] Intravenous lignocaine has similar beneficial effects on the outcome as epidural anesthesia after laparoscopic cholecystectomy, thus highlighting its analgesic role which significantly reduced opioid consumption, postoperative pain, and fatigue scores.[5]

A decrease in VAS, fentanyl consumption, proportionate reduction in the shoulder tip pain without any adverse effect in i.v. lignocaine groups in laparoscopic cholecystectomy and appendicectomy[13,39] Studies have shown analgesic efficacy of lignocaine relates to the afferent (sensory) innervation of the manipulated tissues. Intravenous lignocaine has the potential to improve postoperative analgesia following abdominal surgical procedures associated with visceral pain or postoperative ileus. Analgesic efficacy was not observed in laparoscopic fundoplication as it was surgical manipulation of a diaphragm which has more somatic sensory innervation *via* the phrenic nerve.[40]

Rescue Analgesics

In our study, we found that 67.5% of patients in group L needed first rescue analgesia as compared to group NS whereas 95% of patients required first rescue analgesic (p value = 0.002). The time of the first request for additional analgesia in the lignocaine group was longer than saline group (9.56 ± 2.06 vs 1.82 ± 0.9 hours) in spinal surgery using a bolus dose of 2 mg/kg before induction followed by 3 mg/kg/hour infusion till the end of surgery.[41] Our study also showed similar results but with a low dose of lignocaine used, was observed to have lower pain scores at 0, 2, 4, 6, 12, and 24 hours as compared to saline and significantly lower at 0, 2, and 6 hours. We observed a significant difference in the number of patients requiring second rescue analgesics in group L and group NS.

Reviewing literature there have been inconsistent reports of the analgesic benefits of intravenous lignocaine. Benefits have been noted in colorectal, abdominal, complex spine surgeries, ischemic pain, post-amputation pain, breast surgery[32,42–47] additionally for postoperative pain relief.[1,27] Some studies including hip arthroplasty and open abdominal hysterectomy have not shown a statistically significant reduction in pain.[48,49]

Therefore, although opioid analgesics play an important part in pain management their use may be associated with an increase in postoperative complications which delays discharge of the patient. Consequently, as in our study, lignocaine was noted to be a suitable non-opioid alternative which appears to be a part of multimodal pain relief regimen especially when we encounter instances of patient refusal or contraindication of epidural or regional techniques.[50]

Bowel Function/Ileus

Reduction in nausea and vomiting, early resumption of oral intake, and early ambulation are guided by the early return of bowel function. Opioids have a higher predisposition to nausea and vomiting though our study did not show a difference in the PONV

score. The ability of lignocaine to shorten the duration of ileus is attributed to a direct excitatory effect on intestinal smooth muscle which may be a consequence of the blockade of inhibitory reflexes originating from the myenteric plexus.[51] Postoperative ileus is consequent to active abdominal reflexes that are maintained in any inflammatory response.[52] Duration of ileus is not related to the duration of that particular surgery. Peritoneal surgery mediates the release of prostaglandins, kinins, and histamine, all of which further activate afferent nerve fibers.[51] Amide local anesthetics are potent anti-inflammatory drugs (inhibiting migration of granulocytes and release of lysosomal enzymes) with prolonged duration of action after the serum levels have decreased.[51] Amide anesthetics given to attenuate postoperative ileus need not be administered epidurally to be beneficial.[15] Lignocaine-treated patients (bolus and infusion up to 1-hour post-op) experienced flatulence in a significantly shorter time, were more comfortable, and with a shorter hospital stay after radical prostate surgery with no adverse effects of the infusion.[15] Perioperative lignocaine infusion shortens the duration of post-op ileus by 8 hours[6,35] and reduces PONV by 10–20%.[6,34] In our study, the mean time for the return of bowel movement in group L was early (434 ± 42.71) minutes/7.2 hours as compared with group NS (568 ± 44.09) minutes/9.4 hours ($p < 0.05$). Marret et al. noted that the duration of postoperative ileus was decreased in cases by 8.36 hours as compared to controls with a $p < 0.001$ which concurs with our study.[6] Contrastingly in a meta-analysis done by Ventham et al. did not observe a significantly earlier return of bowel movement in both cases and controls possibly due to a variety of different surgeries.[30] We took the passing of flatus as an indicator of the return of bowel function whereas their study noted the time as until resumption of diet which again was dependent on the type of surgeries the patients have undergone and possibly surgical team protocol. This may be due to the heterogeneity in the type of surgery.[30] Significant reduction in time to return of normal diet, reduced ileus and hospital stay may be considered as a cost-effective strategy though we have not computed the same. This meta-analysis observed diet resumption was quicker in six studies but no differences in time until first bowel movement (seven studies) or time until flatus (eight studies) that could be attributable to major and minor laparoscopic surgeries in the meta-analysis.[30] Koppert et al. concluded that perioperative lignocaine (starting 30 minutes before 1-hour post-op infusion) resulted in the early return of bowel function, less overall pain, and thus shorter hospital course though not significant.

Ambulation

In our study, we found the mean ambulatory time in group L was (14.5 ± 2.86) hours as compared to group NS (16.2 ± 1.96) hours (p value = 0.003). Lauwick et al. studied the functional walking capacity in laparoscopic surgeries with a bolus dose of 1.5 mg/kg i.v. lignocaine and fentanyl 1.5 µg/kg i.v. bolus followed by 2 mg/kg/hour infusion in comparison with inj. fentanyl 3 µg/kg i.v. bolus.[7] They found that the 2-minute walk test significantly decreased by an average of 60% in both groups on a postoperative day 1, but patients in the lignocaine group ambulated 26 minutes earlier ($p = 0.009$) which concurs with our study. This highlights an opioid-sparing early ambulation. Our study also showed similar results in terms of earlier ambulation but with a lower dose of infusion of 1.5 mg/kg/hour as compared with the above study. This may suggest that an infusion of <2 mg/kg/hour would be sufficient to facilitate ambulation as an endpoint of effective postoperative analgesia. Though we have encouraged early ambulation in both groups, it has been as per the patient comfort and we have not noted time duration or a walk test for the same.

Discharge

Our study noted the mean time of discharge in group L as (39.05 ± 5.69) hours as compared with group NS (44.45 ± 2.81) hours with a p value (0.0001). A meta-analysis noted a shorter length of stay of 5.40 hours in the i.v. lignocaine group like in our study.[6] Similarly, studies have recorded a reduction in hospital stay ranging from 26 minutes to 20 hours in abdominal surgeries and laparoscopic bariatric cases ($p = 0.03$), respectively.[6,11] After a bolus dose and continuous infusion of 2 mg/kg/hour for 4 hours postoperative, Herroeder et al. noted a significant acceleration of bowel function and a decreased hospital stay by 24 hours.[4] We have observed similar results by a lower dose of i.v. lignocaine bolus and infusion for a period of 15 minutes after surgery. Length of hospital stay was shorter in the lignocaine group (3.15 ± 1.08 days) as compared to the control group (4.55 ± 1.31 days) in patients undergoing spine surgery ($p = 0.001$).[41] The mean length of hospital stay as noted in various laparoscopic surgeries was shorter in the lignocaine group but was not significant.[30,40] The difference in the above studies from our study with regards to mean length of hospital stay may be due to heterogeneity in types of surgeries in their study, attributes to multiple local factors, culture and practices followed.[30,40] The meta-analysis by Ventham et al. in laparoscopic surgeries recently showed no difference in length of hospital stay (9 studies, 453 participants) though noted a significantly reduced incidence of nausea and vomiting (12 studies, 647 participants).[30] A low-dose lignocaine infusion started before induction and continued for 15 minutes postoperatively can have an impressive effect on pain, bowel function, and hospital stay.[15] Various studies and reviews inferred perioperative i.v. lignocaine reduced postoperative analgesia, aided opioids-sparing role, reduced intraoperative anesthetic requirement (less inhalational agents), resulted in an earlier return of bowel function, obtunded production of interleukins for up to 72 hours, and reduced hospital stay.[35,42] Shorter hospital stay after retropubic radical prostatectomy have shown benefits in significant cost-savings up to 32% per patient.[53]

Side Effects of Lignocaine Infusion

Toxicity resulting from perioperative i.v. lidocaine infusion such as neurologic changes (confusion, euphoria, tinnitus, lightheadedness), dizziness and visual disturbances (blurring of vision),[29] and cardiac dysrhythmias[42] is exceedingly rare.[6,34,35] Ventham et al. noted one cardiac side effect in the i.v. lignocaine group amongst 742 patients studied in the meta-analysis.[30] Lidocaine plasma levels of approximately 2 mg/mL were noted after bolus and infusions of the dose we used in our study with no related side effects except for sedation or excessive drowsiness for an hour in some studies.[1,8,54] Intravenous lignocaine can blunt sympathetic responses to tracheal extubation which may cause delayed awakening as patients are less responsive to the endotracheal tube.[55] Various studies with an infusion rate varying between 1.5 and 3 mg/kg/hour for 6 to 24 hours postoperatively reported plasma lignocaine levels varying from 1 to 3.8 mg/mL,[1,15,36,56] which were well below toxic levels (5 pg/mL).[57] Signs of toxicity occurs at a plasma concentration of >5 µg/mL which was not achieved even when i.v. lignocaine was given continuously for over 14 days in case of severe migraine.[58] Some studies have limited infusions to a duration of 180 minutes to avoid the possibility of toxicity in case serum levels are not monitored.[8] Our study showed no such side effects. The dual advantage

we observed of using lignocaine was, firstly reducing opioid requirement during surgery and secondly limiting the immediate postoperative side effects of opioids. Our study in addition also underlines the safety of lignocaine infusions used perioperatively.

Conclusion

Multimodal analgesia is the norm currently practiced and has been evolving since the emergence of literature on the sparing use of opioids. Limitations of the running infusions in the wards concerning safety prompted us to study the effects of short-duration infusions on overall patient recovery after laparoscopic surgeries. Our study showed i.v. lignocaine 1.5 mg/kg infusion plays an important role in lowering the pain scores, reducing the requirement of rescue analgesics with no side effects, and enhanced recovery in terms of early bowel movements, ambulation, and shorter hospital stay. Perioperative benefits of i.v. lignocaine as a preemptive analgesia is a suitable option to the multimodal analgesia regimen, especially when there are limitations in the usage of regional anesthesia (contraindications, refusal, or failures) or opioids. In conclusion, intravenous lignocaine 1.5 mg/kg i.v. bolus followed by 1.5 mg/kg/hour infusion demonstrated a significant decrease in the hemodynamic parameters following intubation and postextubation, provided opioids-sparing role, showed lower VAS, fewer rescue analgesics over 24 hours, significantly early bowel movements, earlier ambulation, and discharge. Shorter PACU stays and long-term effects of shorter duration of varying dosages of lidocaine infusions need study to evaluate its usefulness in the patient recovery.

Limitations of Our Study

Larger sample size and inclusion of major gastrointestinal surgeries would be beneficial in understanding the role of lignocaine better. The hospital stay is likely to have skewed distribution and be affected by local factors, culture and practice. The results of this study cannot be extrapolated to other settings such as orthopedic surgery or major open abdominal surgeries. The requirement of an inhalational agent or total cost savings perioperatively was not studied. Blood serum levels were not studied though at similar doses the literature review documented safe blood levels. The duration of our study is limited to 24 hours, whereas beyond this time duration the effect is yet to be ascertained.

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