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Perioperative Use of Intravenous Lidocaine Infusion to Decrease Postoperative Opioids in Colorectal Surgery: A Randomized Prospective Study

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Abstract

Pain is defined as an unpleasant sensory and emotional sensation provoked by real tissue damage and manifested by autonomic, psychological, and behavioral reactions. Improvement of postoperative pain control remains a significant challenge among clinicians. 40 patients aged 30-60 years, ASA 1-2 scheduled for colorectal surgery, were divided into two groups 20 patients each. Lidocaine group: (n= 20) received bolus intravenous lidocaine 20 min before incision with a dose of 1.5mg/kg followed by lidocaine infusion with a dose of 1.5mg/kg/h. Control group: (n= 20) receive intravenous lidocaine only. After premedication with a bolus dose of lidocaine at induction, the heart rate was lower in the interventional group compared with the control one until 12 hours post-operatively, then returned to be equal by 24 hours. Between recovery and one hour postoperative, intraoperative serial differences were significant only for the intervention group. After premedication and during the operation until 24 hours, postoperative mean blood pressure was significantly higher among controls. This returns to be equal by 48 hours and beyond. The postoperative VAS score and analgesic requirements were significantly lower in the lidocaine infusion group. Perioperative lidocaine infusion provides analgesia, low pain score, and decreases postoperative opioid consumption in laparoscopic colorectal surgery.

Keywords: Anesthesia, Lidocaine infusion, Colorectal surgery, Pain, Analgesia.

INTRODUCTION

Pain is a complex of unpleasant sensory, emotional, and cognitive sensations caused by real tissue damage (Terman GW, et al. 2001). It is provoked by a noxious stimulus that gives impulses that reach the brain through the ascending pathway in the spinal cord. The primary afferents called the nociceptors are located in the nerve endings and end in the dorsal horn in the spinal cord. These nerves could be classified into small myelinated A-delta fibers and unmyelinated C fibers. The nociceptors when stimulated produce action potential that is transferred through these primary afferents, leading to the release of excitatory amino acids, neurotrophins, and peptides such as substance P, neurokinin A, and calcitonin gene-related peptide (CGRP) from the nerve endings in the dorsal

horn of the spinal cord (Vranken JH 2012). The communication between the neurons of the pain pathways is mainly via chemical neurotransmitters. Several neurotransmitters and their receptors transmit and modulate the sensation of pain. Painful damage causes inflammatory changes that lead to the activation of inflammatory mediators that cause depolarization of the nociceptive membrane by the opening up of voltage and ligand-gated ion channels (Aggugia M. 2003).

The N-Methyl-D- aspartate (NMDA) receptors have a great role in the propagation of chronic pain and it is responsible for hyperalgesia and allodynia sensations (Woolf CJ. 2011) (Coull JA, et al. 2005). The gamma-aminobutyric acid (GABA) secreted by the inhibitory neurons, affects pain transmission at the superficial layers of the dorsal horn by presynaptic inhibition of pain fibers and blocks the release of excitatory amino acids (Gwak YS, et al. 2011)

Two mechanisms modulate the feeling of pain within the central nervous system, which are the inhibitory and excitatory mechanisms. The majority of them are inhibitory and are activated with the initiation of nociceptive information to decrease pain sensations (Gassner M, et al. 2009).

The descending pathway exists from the nucleus raphe magnus has inhibitory effects via activating 5-HT1A and 5-HT7 receptors and excitatory effects by 5-HT2A and 5-HT3 receptors) on pain transmission (Doly S, et al. 2005). Trauma caused by surgery results in the release of cytokines initiating local inflammatory responses and promoting tissue healing (Lin E, et al. 2000).

The degree of tissue damage is correlated with the increase of Interleukin-6 (IL-6), which is detected early as an initial response to injury (Gebhard F, et al. 2000). Lidocaine is an amide type of local anesthetic that has an antiarrhythmic, analgesic, anti-inflammatory, and anti-hyperalgesia effect. It blocks intracellular sodium channels of neurons, interrupting the propagation of impulses in neural axons, and inhibits NMDA activation by blocking glutamate/glycine, and by inhibiting protein kinase C (Hahnenkamp K, et al. 2006).

Other studies have reported that IV lidocaine can cause the reduction of cytokines, and postoperative pain intensity (Kuo CP, et al. 2006). Furthermore, low doses of intravenous lidocaine (plasma level below 5µg/ml) are ineffective on normal nerve conduction and are associated with fewer opioid side effects (Wu CT, et al. 2005). The sodium channels are the main site of action of lidocaine (Canavero S, et al. 2006). The painkiller effect and anti-inflammatory action can act via calcium and potassium channels and receptors through G protein coupling (Heavner JE 2007).
Some lidocaine metabolites, like monoethylglycinexylidide (MEGX), may have an analgesic effect (Werdehausen R, et al. 2012).

Surgical procedures on the abdomen have a higher incidence of postoperative pain and gastrointestinal motility dysfunction. Laparoscopic colorectal surgery has become a common surgery, as it is associated with less pain and less analgesic use, low incidence of infection, rapid recovery, and short hospital stay (Lloyd GM, et al. 2010). Proper pain control is the mainstay of postoperative care that facilitates early mobility and feeding (White PF 2002). Other studies used preoperative intravenous lidocaine infusion as an alternative approach and have reported a beneficial effect on pain management postoperatively and significantly improved the general outcomes including the spare consumption of opioids (Lauwivk S, et al. 2008), and early recovery of bowel mobility (Harvey KP, et al. 2009), particularly after urological surgeries (Groudine SB, et al. 1998), and shortens the hospital stay after colorectal surgeries (Herroedr S, et al. 2007).

Intravenous lidocaine infusion is used as an adjunct to provide anesthesia with less opioid consumption, inhalation, and neuromuscular-blocking agents (Dennis PB, et al. 2020).

The vision of this study is to compare with other studies and research results, considering the differences in environmental factors, resources, size of samples, dose of lidocaine, and duration of surgery. The primary endpoint of this study was to evaluate postoperative pain scores and the need for postoperative analgesia.

MATERIALS AND METHODS

After obtaining our institutional ethics committee approval and written informed consent from each patient, 40 male patients aged 30-60 years, ASA 1-2 scheduled for colorectal surgery were involved in this randomized prospective study divided into two groups, 20 patients each.
The participants included in this study had no hepatic, renal, or cardiac diseases or allergies to local anesthetics.

Patients with intraoperative hypotension (mean blood pressure <60mmHg) or bradycardia (heart rate < 40 beats/min), urticaria, or arrhythmia associated with lidocaine infusion were excluded.

Both groups were premedicated by midazolam to overcome any effect of anxiety on vital signs.

Lidocaine group: (n= 20) received bolus IV lidocaine 20 min before incision with a dose of 1.5mg/kg followed by lidocaine infusion of 1.5mg/kg/h until skin closure.

Control group: (n= 20) were untreated with lidocaine.

General anesthesia was induced with propofol 2mg/kg IV, rocuronium 0.8mg/kg IV with oxygen, and sevoflurane mask ventilation followed with oral endotracheal intubation.

Anesthesia was maintained with sevoflurane with oxygen and medical air 1L: 1L.

Fentanyl was given to the patients in either group during the maintenance of anesthesia as needed according to vital signs. Patients were monitored throughout the operation with BP, HR, SPO2, end-tidal sevoflurane, and end-tidal CO_2. Sevoflurane concentration was adjusted according to the hemodynamic values. HR and BP were maintained within 20% of preoperative values. End-tidal CO2 was between 35-45 mmHg. Perioperative fluid with lactate ringer solution at a rate of 6-8 ml/kg/h. Intraoperatively, the vital signs are taken and recorded every 5 minutes in the first 30 minutes then every 15 for the rest of surgery. At the end of the surgery, the muscle relaxant was reversed with sugammadex (2mg/kg). In the post-anesthesia care unit (PACU) postoperative pain control with IV tramadol was provided within 20 min after surgery and supplemented after recovery as needed. The total amount and frequency of analgesics and opioid-associated side effects such as nausea and vomiting were registered. Postoperative pain was assisted by a visual analog scale (VAS) which ranged from 0-10 at 1st, 2nd, 3rd, 4th, 5th, 6th, 12th, 24th, 48th, and 72nd hours postoperatively. For statistical analysis, SPSS version 20.0 was used. The parametric variables are presented as mean ± SD or frequency (%) and analyzed by student t-test. Statistical analysis is performed with an ANOVA test. $P< 0.05$ was considered as statistically significant. This study aims to evaluate the effects of perioperative intravenous lidocaine infusion on postoperative pain and opioid consumption in patients undergoing colorectal surgeries.

RESULTS

Both groups were matched regarding age. Age was homogeneous across study groups, Table (1) and Figure (1). No patient was excluded from the study, as all fit the inclusion criteria.

Table (1). Age parameters of study groups

Parameter	Group	
	Intervention group	Control group
Mean	46.85	47.60
SD	10.241	7.185

t = -0.268, P = 0.790 (Non-significant)

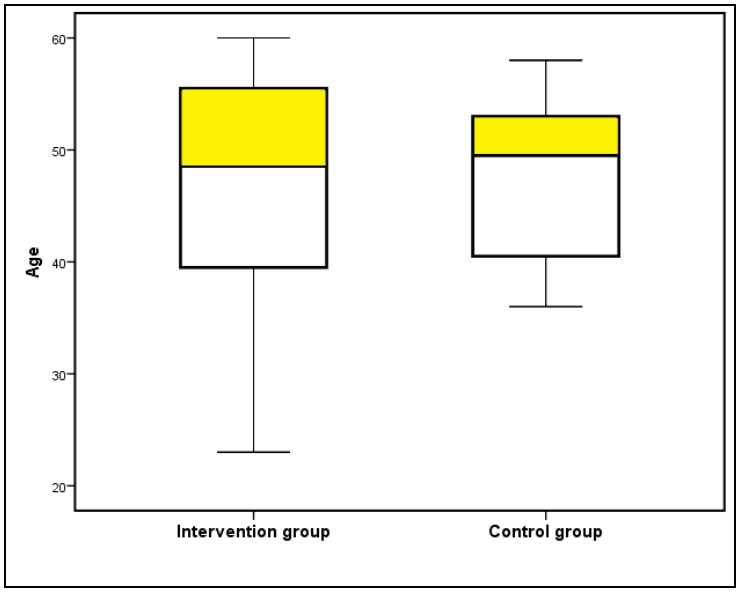

Figure (1). Plot of age parameter across study groups

When comparing the heart rate among both groups, there are no differences between the two groups in baseline heart rate before premedication. After premedication with a bolus dose of lidocaine and induction, the heart rate was lower among the interventional group compared with the control one until 12 hours postoperative. This returns to be equal by 24 hours and beyond. The intraoperative serial difference was significant along perioperative measurements for both groups (Friedman test X2 =27.76, P < 0.001 for controls versus Friedman test X2 = 88.742, P < 0.001 for intervention group), Table (2).Between recovery and one-hour post-operative, Intraoperative serial difference was significant only for the intervention group (Wilcoxon signed rank test
Z = - 1.132, P = 0.258 for controls versus Z = -2.953,
P = 0.003 for the intervention group). Figure (2).

Table (2). Serial preoperative and intraoperative heart rate measurement inter-group comparison

Time	Mean (SD)		T	P
	Intervention group	Control group		
5mn before premed.	82.15 (5.214)	80.75 (9.066)	0.599	0.554
5mn after induction	72.80 (5.248)	80.50 (7.508)	-3.759	0.001*
at the time of incision	72.30(5.686)	81.45 (8.042)	-4.155	<0.001*
15mn	70.30 (5.555)	77.35 (5.631)	-3.986	<0.001*
30mn	70.45 (8.256)	81.20 (7.784)	-4.237	<0.001*
45mn	69.80 (7.851)	85.30 (10.931)	-5.151	<0.001*
60mn	67.70 (5.172)	80.20 (7.509)	-6.131	<0.001*
Recovery	67.80 (5.317)	83.25 (6.180)	-8.475	<0.001*

* The difference is significant at the level of confidence 95% or higher.

Table (3). Serial post-operative heart rate measurement inter-group comparison

Time	Mean (SD)		T	P
	Intervention group	Control group		
1	70.25(4.387)	84.35(8.381)	-6.666	<0.001*
4	73.90(4.621)	80.05(6.452)	-3.465	0.001*
5	74.80(4.444)	81.55(6.493)	-3.837	<0.001*
6	76.15(4.727)	82.45(6.962)	-3.348	0.002*
12	77.30(4.635)	82.70(6.775)	-2.942	0.006*
24	78.60(4.173)	81.35(6.011)	-1.681	0.101
48	79.85(4.499)	80.20(6.330)	-0.202	0.841
72	80.75(4.494)	80.05(6.403)	0.400	0.691

* The difference is significant at the level of confidence 95% or higher.

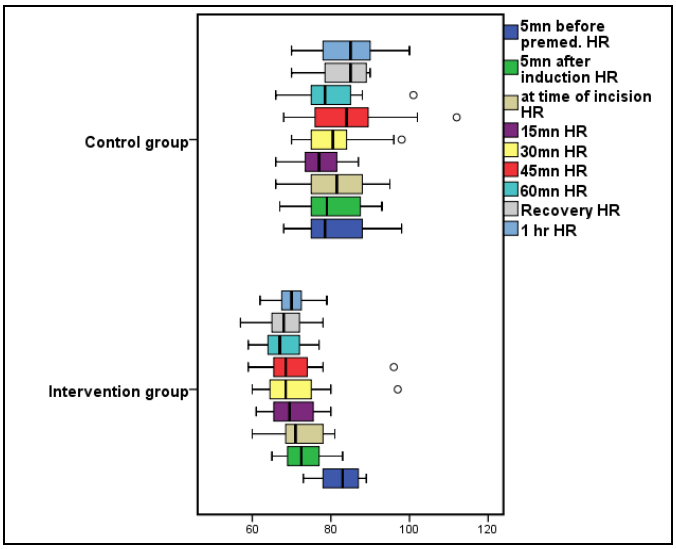

Figure (2). Plot for heart rate serial measurements in both study groups

There is no difference in baseline mean blood pressure between the two groups, but after premedication, induction, and during the operation until 24 hours, postoperative mean blood pressure was significantly higher among the control group. This returns to be equal by 48 hours and beyond. Serial differences were significant along intraoperative measurements for both groups (Friedman test X2 =77.53, P < 0.001 for controls versus Friedman test X2 = 91.2, P < 0.001 for the intervention group). Table (4). Between recovery and one-hour post-operative, serial differences were significant only for the intervention group (Wilcoxon signed rank test Z = - 1.072, P = 0.284 for controls versus Z = - 3.488, P < 0.001 for the intervention group), Figure (3).

Table (4). Serial preoperative and intraoperative mean blood pressure measurement groups comparison

Time	Mean (SD)		T	P
	Intervention group	Control group		
5min before premedication	98.151(1.189)	102.10 (6.640)	-1.358	0.183
5 min after induction	86.05 (5.605)	91.45 (5.735)	-3.011	0.005*
time of incision	85.959(5.671)	93.90 (5.857)	-4.361	<0.001*
15 min	83.85(6.141)	92.70 (4.589)	-5.162	<0.001*
30 min	83.30(8.986)	97.90 (7.490)	-5.582	<0.001*
45 min	82.45(6.653)	98.80 (6.396)	-7.923	<0.001*
60 min	79.45(5.615)	96.05 (4.893)	-9.968	<0.001*
Recovery time	79.75(5.893)	99.35 (5.489)	-10.88	<0.001*

* The difference is significant at a level of confidence of 95% or higher.

Postoperative mean blood pressure was tremendously lower among the interventional group until 24 hours and then there were no differences.

Table (5). Serial post-operative mean blood pressure measurement inter-group comparison

Time (hour)	Mean (SD)		T	P
	Intervention group	Control group		
1	84.95 (5.951)	98.40 (6.116)	-7.048	<0.001*
4	89.25 (6.812)	97.55 (6.219)	-4.024	<0.001*
5	90.65 (5.480)	98.70 (6.053)	-4.409	<0.001*
6	91.15 (6.150)	99.30 (6.530)	-4.063	<0.001*
12	93.25 (6.463)	99.60 (5.276)	-3.404	0.002*
24	94.95 (6.403)	99.90 (5.515)	-2.620	0.013*
48	96.10 (6.874)	98.65 (6.310)	-1.222	0.229
72	97.10 (6.782)	98.30 (6.097)	-0.588	0.560

* The difference is significant at a level of confidence of 95% or higher.

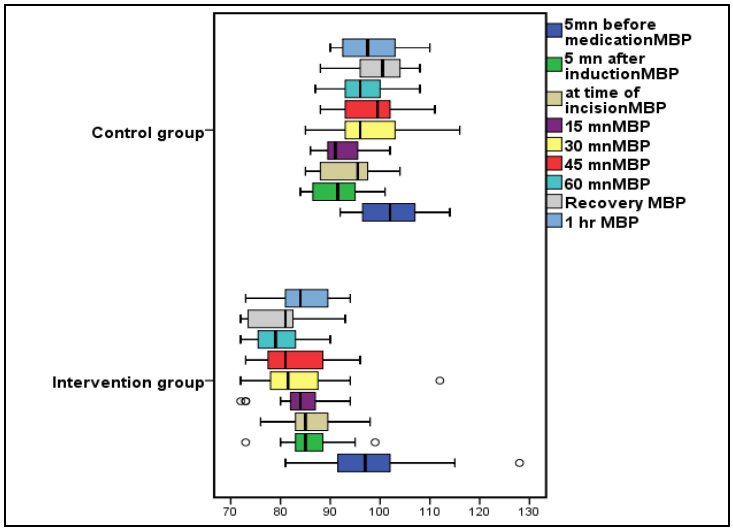

Figure (3). Plot for mean blood pressure serial measurements in both study groups

The postoperative VAS was significantly lower in the lidocaine group Table (6), and also decreased the analgesic requirements in the lidocaine group as compared with the control group postoperatively Table (8), and also, noted that rocuronium was used less frequently in the interventional group Figure (9).

Table (6): VAS parameters of study groups

Parameter	Group	
	Intervention group	Control group
Mean	1.47	3.19
SD	0.46	0.22

t = -15.081, P <0.001 (Significant)

The average of the visual analogue scale was lower among the interventional group.

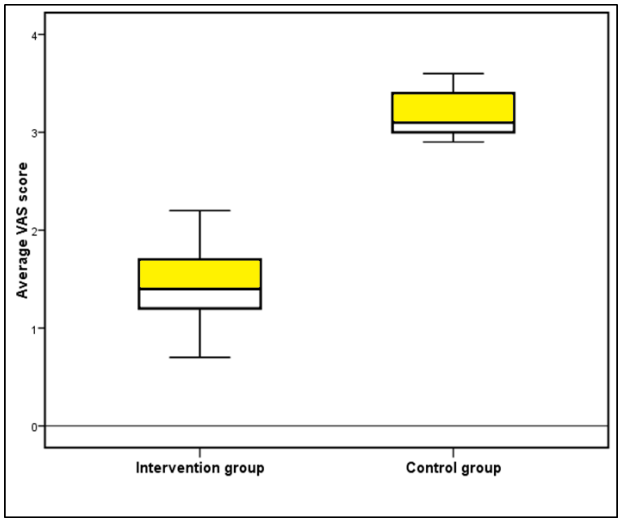

Figure (4). Plot of average VAS score parameters across study groups.

The 72 hours postoperative VAS was significantly higher among control except for hour 3.
Table (7). The intragroup serial difference was significant only for the control group (Friedman test X2 =12.686,
P = 0.002 for controls versus Friedman test X2 = 4.0, P = 0.135 for the intervention group), Figure (5).

Table (7). Serial postoperative visual analogue scale measurement inter-group comparison

Time (hour)	Mean (SD)		T	P
	Intervention group	Control group		
1	0.10. (308)	3.70 (1.895)	-8.388	<0.001*
2	0.00 (0.000)	2.05 (2.585)	-3.547	0.002*
3	0.00 (0.000)	0.50 (1.539)	-1.453	0.163
4	0.5 (5.686)	2.4 (0.883)	-7.400	<0.001*
5	1.00 (1.124)	3.50 (1.395)	-6.240	<0.001*
6	1.05 (1.099)	3.55 (1.276)	-6.638	<0.001*
12	2.5 (5.999)	4.4 (0.883)	-6.208	<0.001*
24	3.00 (1.298)	4.2 (0.410)	-3.943	0.001*
48	3.2 (0.834)	3.7 (5.444)	-2.604	0.014*
72	3.2 (5.786)	3.9 (0.308)	-3.442	0.002*

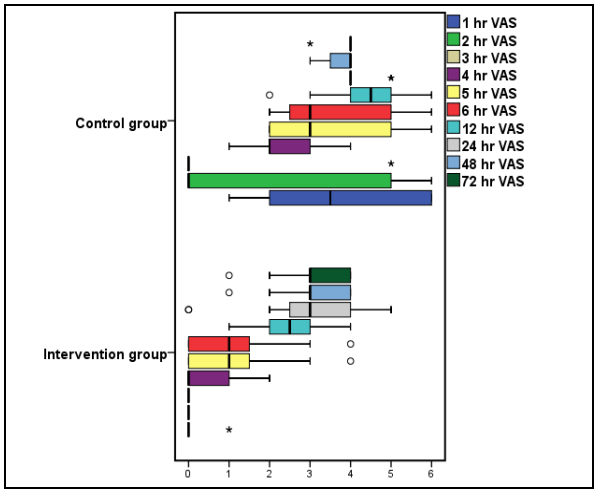

Figure (5). Plot for visual analogue scale serial measurements in both study groups.

The mean of required tramadol doses in the control group was almost more than half that of the interventional group.

Table (8). Total tramadol dose parameters of study groups

Parameter	Group	
	Intervention group	Control group
Mean in mg	662.50	1152.50
SD in mg	129.650	105.724

t = -13.099, P <0.001 (Significant)

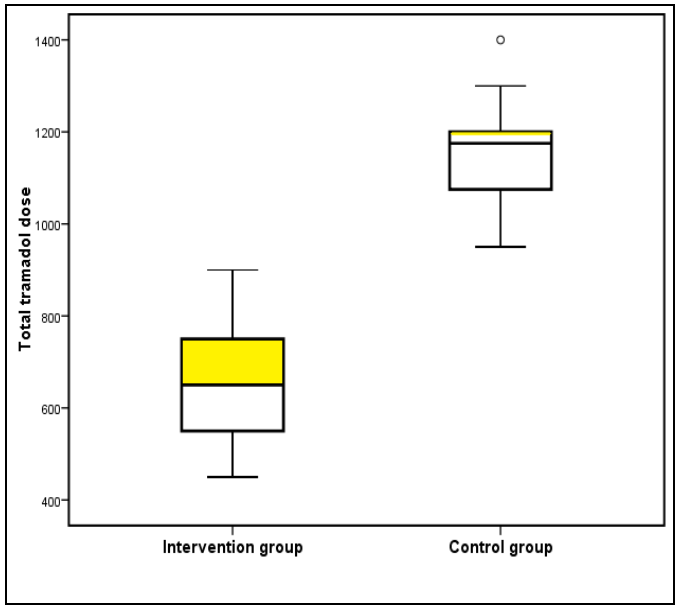

Figure (6). Plot of total required tramadol parameters across study groups

During 10 hours postoperative, the dose of tramadol was significantly higher among control except for hours 3, 4, and 8, Table (9). The intragroup serial difference was significant only for control group (Friedman test X2 =13.6, P = 0.004 for controls versus Friedman test X2 = 3.0, P = 0.392 for the intervention group), Figure (7).

Table (9). Serial total doses of tramadol inter-group comparison

Time (hour)	Mean (SD)		T	P
	Intervention group	Control group		
1	0.00 (0.000)	42.50 (46.665)	-4.073	0.001*
2	0.00 (0.000)	35.00 (46.169)	-3.390	0.003*
3	0.00 (0.000)	7.50 (24.468)	-1.371	0.186
4	2.501 (1.180)	0.00 (0.000)	1.000	0.330
5	2.501 (1.180)	30.00 (41.039)	-2.891	0.009*
6	5.001 (5.390)	37.50 (48.327)	-2.866	0.009*
7	67.50 (33.541)	95.00 (35.909)	-2.503	0.017*
8	112.50 (58.208)	140.00(50.262)	-1.599	0.118
9	222.50 (47.226)	385.00 (36.635)	-12.159	<0.001*
10	250.00 (51.299)	380.00 (41.039)	-8.850	<0.001*

* The difference is significant at the level of confidence 95% or higher.

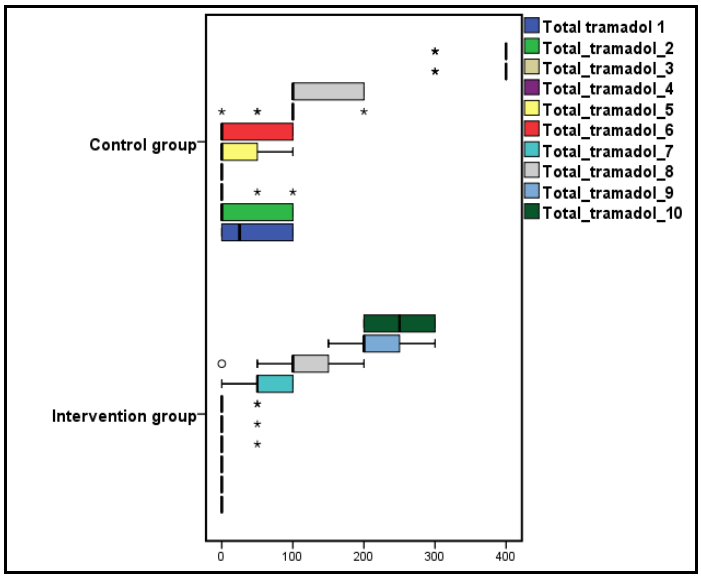

Figure (7). Plot for tramadol dose serial measurements in both study groups

The control group has a higher frequency of rocuronium usage. Intervention group; 1 – 5 times per patient, mean = 2.4 (SD=1.1) and median of 2 times per patient. Control group; 3 – 6 times per patient, mean = 4.4 (SD= 0.9) and median of 4.5 times per patient.

The difference was statistically significant (Mann-Whitney U test statistic = 38.5, P <0.001) Figure (8). Highest proportions of patients in the intervention group were reported with the least frequency of rocuronium use and the inverse in the control group, Figure (9).

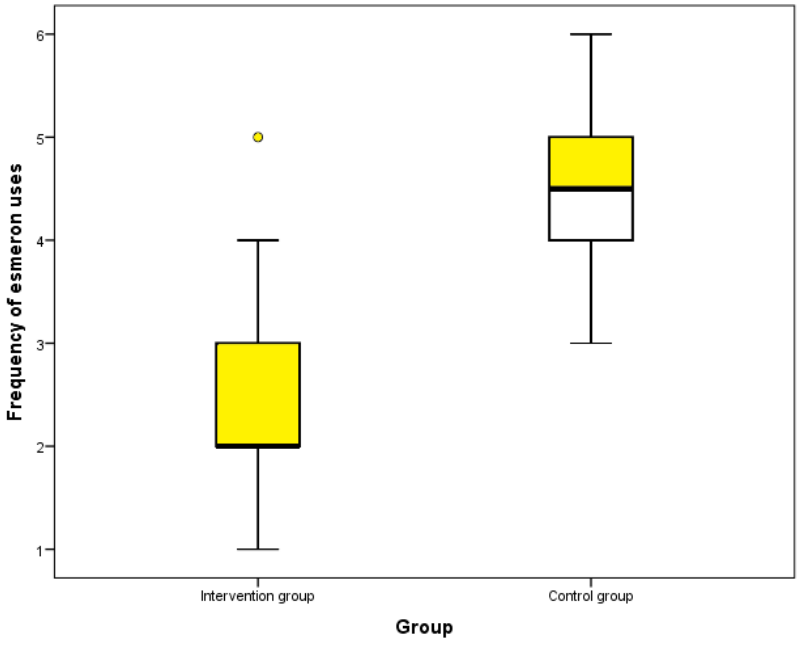

Figure (8): Plot for frequency of rocuronium use in both study groups.

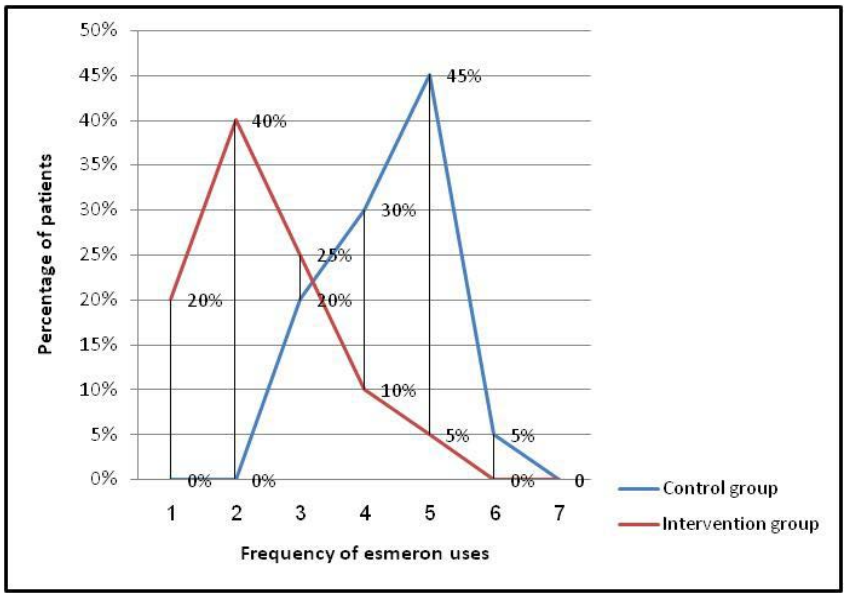

Figure (9). Plot for rates of patients in both study groups according to each frequency of rocuronium usage.

DISCUSSION

The current study suggests the use of perioperative lidocaine infusion in patients undergoing laparoscopic colorectal surgeries, and that laparoscopic surgery improves postoperative analgesia and reduces postoperative opioid consumption. The uses of lidocaine beyond local and regional tissue anesthesia are well established. Given intravenously, it is effective in obtunding the sympathetic response to laryngoscopy and reducing the pain of propofol injection. (Keats AS, et al. 1951) first documented a positive analgesic effect on postoperative pain. Investigation and interest in perioperative IV local anesthetic infusion has continued. A systematic review of multiple studies done in 2010 documented a low incidence of pain when IV lidocaine infusions were given during general anesthesia (McCarthy GC, et al. 2010). According to this study, IV lidocaine infusion in the perioperative period is safe and results in a low incidence of pain, reduced postoperative analgesic consumption, and decreased intraoperative anesthetic requirement.

The effect of lidocaine might be due to the suppression of neuronal excitability in dorsal horn neurons, inhibiting the spike activity, amplitude, and conduction time in both myelinated A and unmyelinated C fibers. The dosage of lidocaine in this study was similar to a study by (Groudine, et al. 1998). The current study revealed a significantly low incidence of tachycardia and MBP in the interventional group when compared with the control group. This finding is in accordance with (Lauwivk S, et al. 2008). Whereas (Kaba A, et al. 2007) and (Groudine SB, et al. 1998), didn't find any significant analgesic effect of lidocaine infusion.

CONCLUSION

Perioperative lidocaine infusion has a beneficial effect on patients who have undergone laparoscopic colorectal surgery, provides analgesia, low pain score, and decreases postoperative opioid consumption.

Based on the results of this study, it is recommended to consider intravenous lidocaine perioperatively to provide analgesia, low pain score, and decrease postoperative opioid consumption in laparoscopic colorectal surgery.

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Author contributions: Contribution is equal between authors.

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