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Attenuation of Pneumoperitoneum-Induced Hypertension by Intraoperative Lidocaine Infusion in Laparoscopic Cholecystectomy

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ABSTRACT

Background: Laparoscopy has now become the standard technique and is considered gold standard for cholecystectomy but the intraoperative requirements of laparoscopic surgery produce significant physiological changes, which pose many challenges for the anesthesiologist.

Objective: The aim of this work was to evaluate the effect of intraoperative IV lidocaine infusion for attenuation of pneumoperitoneum-induced hypertension.

Patients and Methods: After approval of the Medical Ethical Committee at Al-Azhar University Hospitals, Department of Anesthesia, and after patient written consent, 90 patients of American Society of Anesthesiologists (ASA) physical status I or II, scheduled for laparoscopic cholecystectomy were enrolled in this randomized, controlled, prospective, double-blind, clinical trial study.

Results: Regarding the intraoperative and postoperative hemodynamics, in the present study it was observed that patients who received intravenous lidocaine (1.5 mg/kg bolus before skin incision and abdominal inflation followed by 1 mg/kg/h or 2 mg/kg/h and stopped immediately after abdominal deflation) were associated with a reduction in intraoperative BP and HR without any associated hemodynamic instability in comparison to patients who did not received lidocaine with no statistically significant difference between the two doses of lidocaine. **Conclusion:** This study showed that the intraoperative infusion of lidocaine of two different doses in patients undergoing laparoscopic cholecystectomy was associated with attenuation of blood pressure, heart rate, decreases the intensity of postoperative pain, and early recovery of bowel function without causing significant adverse effects, with more satisfaction for both patients and surgeons.

Keywords: Pneumoperitoneum-induced hypertension, Intraoperative lidocaine infusion, Laparoscopic cholecystectomy.

INTRODUCTION

Normal intra-abdominal pressure (IAP) is 0 to 5 mmHg. Increases in IAP above 10 mmHg are clinically significant, and above 15 mmHg can result in an abdominal compartment syndrome, which affects multiple organ systems [(1)].

Pneumoperitoneum (the act of insufflating the peritoneal cavity with gas, most often carbon dioxide; CO_2) and different patient positions required for laparoscopic surgery results in various pathophysiological changes. Both mechanical and neurohumoral factors contribute to these alterations in cardiovascular and respiratory physiology. The increase in intra-abdominal pressure (IAP) produced by pneumoperitoneum, results in direct mechanical effects on blood flow [(2)].

Systemic absorption of CO_2 (most common pneumoperitoneum), and reverse Trendelenburg position cause pathophysiological changes in various systems of the body leading to increase in plasma level of norepinephrine, epinephrine, and plasma renin activity. All these factors together contribute to increase in heart rate, mean arterial pressure, and increased systemic and pulmonary vascular resistance along with reduced cardiac output [(3)].

Hypertensive episodes are dangerous because of their potential risk for hemorrhagic stroke, pulmonary edema and cardiac decompensation. The true incidence of hypertensive episodes is unknown, but its incidence seems to be higher at the beginning of insufflations, when the increasing intra-abdominal pressure increases the venous return by reducing the blood volume in the splanchnic vasculature [(4)].

Intravenous lidocaine is known as having anti-inflammatory analgesic, antihyperalgesic properties and is used for attenuating stress response to laryngoscopy and intubation [(5)]. The prolonged analgesic effect of lidocaine, which extends well beyond the infusion time, could potentially also be explained by sustained concentrations of lidocaine in the cerebrospinal fluid. In addition, lidocaine metabolites have analgesic effects by inhibiting the glycine [(6)].

The origin of pain after laparoscopic cholecystectomy is complicated. Thus, a combination of inflammatory, incisional, somatic, and visceral components, multimodal analgesic regimens and various treatments are suggested, which include opioids, non-steroidal anti-inflammatory drugs (NSAIDs), dexamethasone, injection of local anesthetics into the surgical wound, and removal of residual carbon dioxide[(7)].

The analgesic properties of lidocaine can persist even after the reduction of its plasma levels, favoring the theory of the blockade of nervous conduction [(8)].

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AIM OF THE WORK

The aim of this work was to evaluate the effect of intraoperative IV lidocaine infusion for attenuation of pneumoperitoneum-induced hypertension (primary outcome). And its effect on recovery time, time to first postoperative analgesic requested, time of return of bowel function (The secondary outcomes) in patients undergoing laparoscopic cholecystectomy.

PATIENTS AND METHOD

Study design:

90 patients of American Society of Anesthesiologists (ASA) physical status I or II, scheduled for laparoscopic cholecystectomy were enrolled in this randomized, controlled, prospective, double-blind, clinical trial study.

Ethical approval:

Approval of the Medical Ethical Committee at Al-Azhar University Hospitals, Department of Anesthesia was obtained. All patients gave their written informed consents prior to their inclusion in the study. Study protocol was explained to the patients before taking their consent.

Setting:

The study was carried out in Al-Azhar University Hospitals (Al-Huseen and Sayed Galal Hospital).

In our study, 90 patients were randomly divided into three equal groups:

Lidocaine group (group L1): patients received lidocaine 2% 1.5 mg/kg IV bolus before pneumoperitoneum followed by lidocaine infusion (1 mg/kg/h). 100 mg diluted in 50 ml syringe pump. (Every 1 cm of syringe pump contain 2 mg of lidocaine 2%). The lidocaine infusion was stopped at the time of abdominal deflation.

Lidocaine group (group L2): patients received lidocaine 2% 1.5 mg/kg IV bolus before pneumoperitoneum followed by lidocaine infusion (2 mg/kg/h). 100 mg diluted in 50 ml syringe pump. (Every 1 cm of syringe pump contain 2 mg of lidocaine 2%). The lidocaine infusion was stopped at the time of abdominal deflation.

Placebo group (group P): received equal volumes of saline.

Inclusion criteria:

1- ASA I to II patients.
2- Aged between 18 and 60 years.
3- Patients undergoing laparoscopic cholecystectomy.

Exclusion criteria:

1- Declining to give written informed consent.
2-Advanced respiratory, renal, hematological, hepatic or cardiovascular diseases.
3- Chronic opioid usage.
4- Patients with allergies to local anesthetics and opioids.
5- Being obese or underweighted (body mass index>30 or <18.5).
6- Pregnant women, and mentally retarded cases.

Preoperative assessment: Full history taking, physical examination including chest and heart examination as well as reviewing the patient's investigations (CBC, S. creatinine, blood urea, SGOT, SGPT, PT, PTT, INR, ECG, and chest X-Ray). After accessible IV line by cannula 18 G in forearm. For premedication, patients were given 40 mg risk (omeprazole) and 3 mg midazolam IV.

Monitoring: Basic monitoring for all patients (5 leads ECG, NIBP, pulse oximetry, capnography for end tidal CO_2, and temperature monitoring).

Drugs for GA: Propofol, Atracurium, Fentanyl, Isoflurane, Atropine, Neostigmine and Lidocaine 2%.

Equipment for general anesthesia (GA): I.V line, I.V fluids, suction apparatus, airways, laryngoscope with different size blades, endotracheal tubes of variable sizes, electrical cardioversion (DC) and equipment for difficult intubation, syringe pump

Drugs for the technique: Saline 0.9%, Lidocaine 2%, Fentanyl, atropine.

Anesthetic technique: The technique of general anesthesia was standardized for all patients.

Induction: After 3-5 minutes preoxygenation, all patients received fentanyl 2 µg/kg and after 2 minutes propofol was given in dose 2 mg/kg throughout 90 seconds and atracurium 0.5 mg/kg was used to facilitate orotracheal intubation.

Maintenance: After tracheal intubation, anesthesia was maintained with 1.2% isoflurane in O_2 via a closed circuit system. Mechanical ventilation was provided by Dragger anesthesia machine and the respiratory rate and tidal volume were adjusted to maintain the end-tidal CO_2 around 35 mmHg. Neuromuscular blockade was maintained with i.v. atracurium at a dose of 0.1 mg/kg for muscular relaxation, which was administered at 20 min intervals. CO_2 pneumoperitoneum was established and maintained to a pressure of 14 mmHg throughout the laparoscopic surgery using an automatic insufflation unit. All groups were received fasting and maintenance fluid by i.v. drip.

Patient position: The patients were in supine position and in reverse Trendelenburg position and slightly to the left and undergoing laparoscopic cholecystectomy.

Recovery: At the end of surgery, inhalational anesthesia was stopped, then the residual neuro-muscular block was reversed with neostigmine (0.05 mg/kg) and atropine (0.02 mg/kg) and when the patient fulfilled extubation criteria, the endotracheal tube was withdrawn and patient was transferred to the PACU.

The following parameters were measured:

The primary outcome:

Intraoperative measurements: systolic and diastolic arterial blood pressures. Heart rates; and the SpO_2 of the patients was recorded before induction, before inflation, every 5 minutes, after abdominal deflation and after extubation.

The secondary outcomes: **Recovery time** (time required for regaining of consciousness after stoppage of inhalational).

Postoperative management: All the patients were admitted to the PACU. Additionally, i.v. morphine 3 mg/dose was given to patients if the VAS score was ≥ 3 up to a total dose of 0.15 mg/kg.

Postoperative measurements:

1. Hemodynamic parameters (NIBP and HR) was recorded every 4 hours interval for 12 hours postoperative.
2. Time to first postoperative analgesic requested.
3. Adverse effects. All the adverse events related to surgery and the anesthetic technique was also recorded, e.g. light-headedness, perioral numbness, sedation, nausea, vomiting, and pruritus. Any episodes of bradycardia (HR<40 % beats/min from base line), hypotension (SBP<40 % mm Hg from base line), nausea and vomiting were recorded during the first 12 hours after surgery. If there was nausea or vomiting; 10 mg intravenous metoclopramide was given.
4. VAS score was recorded every 4 hours for 12 hours.
5. Functional gastrointestinal recovery (either time to defecation, time to first flatus, or time to first bowel movement/sounds).
6. Patients satisfaction *(3 points)*: complete satisfaction, partial satisfaction or no satisfaction.

Visual analogue scale (VAS): The patient was simply instructed and asked to correlate the degree of his pain on a scale for pain assessment graded from 0 to 10 (0 as "no pain" to 10 as "worst imaginable pain"). To indicate how much pain they are currently feeling. The far left end (0) indicates 'No pain' and the far right end (10) indicates 'Worst pain ever'.

7. ***Surgeon satisfaction:*** After the operation, the surgeon, who didn't know what medication was given, was asked to qualify the operative conditions according to the following numeric scale: 1= poor, 2= fair, 3= Good and 4= Excellent.

Statistical analysis:

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following tests were done:

- A one-way analysis of variance (ANOVA) when comparing between more than two means.
- Post Hoc test: least significant difference (LSD) was used for multiple comparisons between different variables.
- Chi-square (x^2) test of significance was used in order to compare proportions between qualitative parameters.
- The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following:
  - P-value <0.05 was considered significant.
  - P-value <0.001 was considered as highly significant.
  - P-value >0.05 was considered insignificant.

RESULTS

Demographic data of the three groups of patients showed no statistically significant differences as regard age, sex, weight and ASA state as shown in the table (1).

Table (1): Comparison between groups according to demographic data.

Demographic data	Group L1 (n=30)	Group L2 (n=30)	Group P (n=30)	P-value
Sex				
Female	25 (83.3%)	24 (80.0%)	25 (83.3%)	>0.05
Male	5 (16.7%)	6 (20.0%)	5 (16.7%)	
Age (years)				
Mean±SD	41.27±8.32	42.16±7.93	41.11±9.13	>0.05
Range	26-60	24-60	25-60	
Weight (cm)				
Mean±SD	78.07±8.58	76.80±6.53	76.40±8.07	>0.05
Range	60-94	56-90	59-95	
ASA				
I	24 (80.0%)	27 (90.0%)	25 (83.3%)	>0.05
II	6 (20.0%)	3 (10.0%)	5 (16.7%)	

Systolic Blood pressure

At base line till the time to before inflation showed no statistical difference among the groups. There was a statistically significant decrease in systolic blood pressure in lidocaine groups compared to control group from start of infusion to postoperative at 8 hours as shown in table (2).

Table (2): Comparison between groups according to systolic blood pressure (mmHg).

Systolic blood pressure (mmHg)		**Group L1 (n=30)**	**Group L2 (n=30)**	**Group P (n=30)**	**P-value**
Base line Mean±SD Range		132.17±4.48 122-139	131.83±4.45 122-138	132.03±5.14 122-139	>0.05
Intra operative	**Induction** Mean±SD Range	103.20±6.32 89-120	103.30±6.37 89-120	102.10±6.42 89-120	>0.05
	Before inflation Mean±SD Range	106.07±5.61 99-122	105.50±2.86 111-122	107.73±7.68ab 89-120	>0.05
	start of infusion Mean±SD Range	98.93±3.90 89-107	99.23±4.52 89-111	125.37±15.69ab 80-150	<0.001**
	At 5min. Mean±SD Range	102.63±4.77 90-112	104.30±4.96 90-112	127.40±15.00ab 85-155	<0.001**
	At 10 min. Mean±SD Range	102.63±4.77 90-112	103.13±5.04 90-112	125.93±12.01ab 90-150	<0.001**
	At 15 min. Mean±SD Range	96.10±4.33 89-111	95.97±3.03 89-100	123.27±10.88ab 89-145	<0.001**
	At 20 min. Mean±SD Range	95.93±4.31 89-111	96.63±4.24 89-111	120.57±9.33ab 100-140	<0.001**
	At 25 min. Mean±SD Range	96.23±2.73 89-100	96.43±2.78 89-100	120.17±7.18ab 101-140	<0.001**
	At 30 min. Mean±SD Range	96.23±5.13 89-111	96.37±5.09 89-111	122.30±7.49ab 100-144	<0.001**
	After deflation Mean±SD Range	115.70±3.12 111-122	115.43±3.49 111-122	121.97±6.74 100-136	<0.001**
	After extubation Mean±SD Range	116.80±5.57 111-135	115.57±2.94 111-122	124.10±7.45 100-140	0.003*
Post-operative	**Postoperative At 4 hrs.** Mean±SD Range	115.20±3.06 111-122	115.27±3.13 111-122	128.73±7.50 100-144	<0.001**
	Postoperative At 8 hrs. Mean±SD Range	115.03±2.74 111-120	115.03±2.92 110-120	127.43±7.41 100-142	<0.001**
	Postoperative At 12 hrs. Mean±SD Range	124.70±2.52 111-120	125.00±2.77 111-120	126.57±8.58 100-148	>0.05

*P-value >0.05 NS; *p-value <0.05 S; **p-value <0.001 HS*

***a**: significant difference with group L1, **b**: Significant difference with group L2*

Diastolic Blood pressure

At base line till the time before inflation showed no statistical difference among the groups. There was a statistically significant decrease in diastolic blood pressure in lidocaine groups compared to control group from start of infusion to postoperative at 8 hours as shown in table (3).

Table (3): Comparison between groups according to diastolic blood pressure (mmHg).

Diastolic blood pressure (mmHg)		**Group L1 (n=30)**	**Group L2 (n=30)**	**Group P (n=30)**	**P-value**
Base line Mean±SD Range		76.03±10.38 64-99	75.93±10.43 64-99	74.00±10.45 60-97	>0.05
Intraoperative	**Induction** Mean±SD Range	63.93±7.71 55-90	63.83±7.75 55-90	64.07±6.52 55-80	>0.05
	Before inflation Mean±SD Range	60.90±8.27 54-90	58.83±5.09 54-75	61.30±8.39ab 55-90	>0.05
	start of infusion Mean±SD Range	60.20±3.20 54-68	60.03±3.22 54-68	80.30±10.79ab 50-90	<0.001**
	At 5min. Mean±SD Range	61.87±5.99 54-87	60.93±6.13 54-87	78.37±9.66ab 60-90	<0.001**
	At 10 min. Mean±SD Range	61.87±5.99 54-87	62.33±7.48 54-87	74.93±7.87 63-90	<0.001**
	At 15 min. Mean±SD Range	58.30±2.45 54-63	58.13±2.36 54-62	75.10±8.07ab 58-88	<0.001**
	At 20 min. Mean±SD Range	58.20±2.35 54-63	58.60±1.94 55-63	69.97±8.60ab 60-87	<0.001**
	At 25 min. Mean±SD Range	58.13±2.18 54-62	58.17±2.18 54-62	71.63±8.65ab 60-90	<0.001**
	At 30 min. Mean±SD Range	58.57±2.40 55-63	58.57±2.40 55-63	69.90±7.10ab 61-85	<0.001**
	After deflation Mean±SD Range	60.00±7.18 54-90	61.20±7.54 54-90	69.60±5.86ab 55-80	<0.001**
	After extupation Mean±SD Range	64.13±12.38 54-99	61.73±10.16a 55-90	69.40±6.09ab 50-80	0.011*
Post-operative	**Postoperative At 4 hrs.** Mean±SD Range	61.37±8.97 54-90	62.47±10.35 55-90	69.70±5.78ab 55-80	<0.001**
	Postoperative At 8 hrs. Mean±SD Range	63.30±11.57 54-90	64.50±12.45 54-90	69.43±6.56 55-83	0.014*
	Postoperative At 12 hrs. Mean±SD	60.83±9.05 54-90	62.23±10.46 54-90	65.43±5.46 55-80	>0.05

*P-value >0.05 NS; *p-value <0.05 S; **p-value <0.001 HS*

***a**: significant difference with group L1, **b**: Significant difference with group L2*

Heart Rate

At base line till the time before inflation showed no statistical difference among the groups. There was a statistically significant decrease in heart rate in lidocaine groups compared to control group from start of infusion to postoperative at 8 hours as shown in table (4).

Table (4): Comparison between groups according to heart rate (Beat/min).

Heart Rate (beat/min)		**Group L1 (n=30)**	**Group L2 (n=30)**	**Group P (n=30)**	**P-value**
Base line Mean±SD Range		82.60±7.45 65-97	82.83±7.63 65-97	81.63±7.35 65-97	>0.05
Intraoperative	**Induction** Mean±SD Range	68.13±6.20 58-78	68.07±6.41 58-78	71.30±8.15 60-92	>0.05
	Before inflation Mean±SD Range	79.53±7.07 61-88	78.50±6.42 61-88	81.47±8.08 65-91	>0.05
	start of infusion Mean±SD Range	68.77±5.00 60-78	68.60±4.12 64-78	87.30±10.77ab 61-112	0.023*
	At 5min. Mean±SD Range	68.80±4.73 60-76	69.07±4.49 63-76	92.00±12.73ab 54-111	<0.001**
	At 10 min. Mean±SD Range	72.57±3.38 64-79	71.67±3.68 64-78	91.23±13.34ab 55-122	<0.001**
	At 15 min. Mean±SD Range	75.57±2.43 68-79	75.53±2.46 68-79	91.63±13.53ab 53-116	<0.001**
	At 20 min. Mean±SD Range	75.40±2.80 68-79	75.77±2.50 68-79	91.40±13.02ab 59-117	<0.001**
	At 25 min. Mean±SD Range	75.50±2.87 68-79	75.40±2.79 68-79	89.97±10.92ab 70-117	<0.001**
	At 30 min. Mean±SD Range	75.67±2.88 68-79	75.57±3.24 68-79	91.07±11.36ab 72-112	<0.001**
	After deflation Mean±SD Range	67.97±6.26 58-78	67.87±6.13 58-78	83.20±11.42ab 70-115	<0.001**
	After extupation Mean±SD Range	77.53±3.34 73-84	77.67±3.56 73-84	91.83±8.58ab 80-115	<0.001**
Post- operative	**Postoperative At 4 hrs.** Mean±SD Range	77.53±3.34 73-84	77.47±3.26 73-84	81.27±7.67ab 73-100	0.007*
	Postoperative At 8 hrs. Mean±SD Range	77.63±3.70 73-84	77.73±3.63 73-84	81.13±7.04 71-97	0.019*
	Postoperative At 12 hrs. Mean±SD Range	78.07±3.55 73-84	77.47±3.36 73-84	79.97±7.09 70-97	>0.05

*P-value >0.05 NS; *p-value <0.05 S; **p-value <0.001 HS*

***Post HOC**: **a**: significant difference with group L1, **b**: Significant difference with group L2*

Postoperative pain (VAS):

VAS pain scores throughout the first 12 hrs postoperative showed highly statistically significant decrease in VAS in immediate till 12 hrs postoperative in lidocaine groups as shown in table (5).

Table (5): Comparison between groups according to VAS score postoperative.

VAS score postoperative	Group L1 (n=30)	Group L2 (n=30)	Group P (n=30)	Kruskal Wallis	P-value
After operative					
Mean±SD	2.33±0.48	2.35±0.48	3.83±0.65		
Median (IQR)	2 (1)	2 (1)	4 (1)ab	76.765	<0.001**
Range	2-3	2-3	3-5		
After 4hrs.					
Mean±SD	2.67±0.66	2.70±0.65	3.83±0.83		
Median (IQR)	3 (1)	3 (1)	4 (1)ab	25.509	<0.001**
Range	2-4	2-4	3-6		
After 8hrs.					
Mean±SD	2.67±0.71	2.80±0.76	3.93±0.98		
Median (IQR)	3 (1)	3 (1)	3.5 (2)ab	21.310	<0.001**
Range	2-4	2-4	3-5		
After 12hrs.					
Mean±SD	2.73±0.69	2.80±0.71	3.67±0.76		
Median (IQR)	3 (1)	3 (1)	4 (1)ab	15.609	<0.001**
Range	2-4	2-4	2-5		

*Using: One Way Analysis of Variance; *p-value <0.05 S*

***a**: significant difference with group L1, **b**: Significant difference with group L2*

Patients' satisfaction:

There was statistically significant difference among the studied groups as shown in table (6).

Table (6): Comparison between groups according to patients' satisfaction.

Patients satisfaction	Group L1 (n=30)	Group L2 (n=30)	Group P (n=30)	P-value
Complete	14 (46.7%)	12 (40.0%)	4 (13.3%)	0.025*
Partial	12 (40.0%)	13 (43.3%)	14 (46.7%)	
No	4 (13.3%)	5 (16.7%)	12 (40.0%)	

**p-value <0.05 S;*

DISCUSSION

In the current study; the heart rate, and BP were significantly attenuated in patient that received two different doses of lidocaine as compared to patient received saline, but there was no statistically significant difference between two doses of lidocaine. The hemodynamic response to skin incision and abdominal inflation is well known and the use of lidocaine for its attenuation is well described. Thus this study further confirms that intravenous lidocaine blunts reflexes for skin incision and abdominal inflation.

Another study by **El-Tahan and colleagues** [(9)] carried out on pregnant women undergoing cesarean delivery concluded that lidocaine infusion was safe and associated with significant decrease in neuroendocrine response to surgical trauma.

The analgesic effects of lidocaine in surgical trauma could be due to decrease of the neuronal transmission at the site of injury, attenuating the neurogenic response, and by the intrinsic systemic anti-inflammatory properties. Besides, depending on the dose, lidocaine can reduce cytokine-induced cellular damage through mechanisms that involve mitochondrial adenosine triphosphate (ATP)-gated potassium channels [(10)].

Regarding the intraoperative and postoperative hemodynamics, in the present study it was observed that patients who received intravenous lidocaine (1.5 mg/kg bolus before skin incision and abdominal inflation followed by 1 mg/kg/h or 2 mg/kg/h and stopped immediately after abdominal deflation were associated with a reduction in intraoperative BP and HR without any associated hemodynamic instability in comparison to patients who did not received lidocaine with no statistically significant difference between the two doses of lidocaine.

That was consistent with **Kaba *et al.*** [(11)] study which observed the patients that received bolus injection of 1.5 mg/kg lidocaine at induction of anesthesia, then a continuous infusion of 2 mg/kg/h intraoperatively and 1.33 mg/kg/h for 24 h postoperatively. Their averaged mean arterial pressure and heart rate were slightly lower in the

lidocaine groups: 91 ±7 versus 85 ±6 mmHg (P = 0.030) and 69 ± 4 versus 63 ± 4 beats/min (P= 0.002), respectively.

As regard time to first rescue analgesia and recovery time, it was longer in lidocaine infusion treated patients which could be attributed to the increased depth of anesthesia and prevention of the induction of central hyperalgesia by intravenous lidocaine, that was consistent with **Baral *et al.*** [12] who administered lidocaine (1.5 mg/kg as slow i.v. bolus injection followed by a continuous infusion of 1.5 mg /kg/hour).

Also our study results are in accordance with **Mraovic *et al.*** [13] **and Omar and Aboushanab** [14], as they have noticed that extubation time was longer in the lidocaine infusion treated patients, which can be explained by blunting of the cough reflex by lidocaine.

The present work demonstrated that lidocaine infusion decreased the VAS score, less postoperative nausea and vomiting (PONV) and complication in patient undergoing laparoscopic cholecystectomy with no statistically significant difference between the two doses of lidocaine. Another study by **Solimana *et al.*** [15] showed that lidocaine was associated with better outcome as it decreased postoperative pain during the first 24 h, decreased PONV, decreased the total dose of fentanyl, and resulted in increased patient satisfaction.

In agreement with our study **Ezzeldin *et al.*** [16] found that patients who received lidocaine at a rate of (2 mg/kg/h) provides analgesia and low pain scores after laparoscopic cholecystectomy.

In accordance with our study **Saadawy *et al.*** [17] who conducted the same study with the same operation (laparoscopic cholecystectomy) and the same dose of lidocaine 2 mg/kg/h. One hundred and twenty patients were divided into three equal groups to receive either magnesium, lidocaine, or saline. They found that the lidocaine group had lower VAS score and total morphine consumption in the first 24 h postoperatively. Moreover, they concluded that they had the least PACU stay.

Moreover, in accordance with our study, **Dogan *et al.*** [18] conducted a similar study with laparoscopic cholecystectomy with lidocaine infusion at a rate of 1.5 mg/kg/h. Sixty patients were divided into two equal groups to receive either lidocaine or esmolol. They found that the lidocaine group had a lower VAS score and total analgesia consumption postoperatively.

However, our results are partly in contrast to the findings of **Farag *et al.*** [19]**,** who reported that perioperative i.v. lidocaine (2 mg/kg/h and in the PACU for no more than 8 h) in patients having complex spine surgery can reduce opioid requirements by approximately 25% only comparable to that reported for major abdominal surgery, and greater than that reported in previous studies in non-abdominal surgery studies. This may be attributed to types of operation and no bolus dose prior to surgical stimuli. Also in **de Oliveira *et al.*** [20] study, intravenous lidocaine (2 mg kg/h without initial bolus infusion was initiated at the time of induction of anesthesia and continued until the end of the operation) did not improve postoperative analgesia in patients undergoing open abdominal hysterectomy, similar to some studies, probably because of the short infusion time (intraoperative only) and absence of initial bolus dose.

As regard recovery of the bowel function it was reduced in lidocaine groups as compared to control group

In accordance with the present study **Kwon *et al.*** [21] as they noticed that intravenous lidocaine facilitates the recovery of the bowel function after a laparoscopic hysterectomy by reducing the flatus time and defecation time.

Also, in agreement with the current study **Kuo *et al.*** [8] who administered (i.v. lidocaine 2 mg/kg were started 30 min before surgery then 3 mg/kg/h till end of operation) demonstrated a faster return of flatus, a reduction in early VAS pain scores, but not earlier hospital discharge. Another smaller study of 22 patients by **Harvey *et al.*** [22] showed a faster recovery of bowel movement and earlier discharge in the lidocaine group,

At the end of the study we noticed a significant increase in patient satisfaction in lidocaine infusion treated patients in comparison to control patients. Furthermore there was a decrease in overall visual analogue scale pain scores 12 hours after surgery. This is possibly due to decrease postoperative pain intensity and morphine requested interval. That was consistent with **Harvey *et al.*** [22] as they concluded that patients in lidocaine groups appeared to report less pain as reflected by a decrease in overall visual analogue scale pain scores 24 hours after surgery.

CONCLUSION

This study showed that the intraoperative infusion of lidocaine of two different doses (1.5 mg/kg bolus with 1 mg/kg/h or 2 mg/kg/h intraoperative infusion) in patients undergoing laparoscopic cholecystectomy was associated with attenuation of blood pressure, heart rate, decreases the intensity of postoperative pain, and early recovery of bowel function without causing significant adverse effects, with more satisfaction for both patients and surgeons. Therefore it can be considered as an inexpensive, easy, relatively safe and effective modality as a part of multimodal approach for

attenuation of blood pressure, heart rate in patients undergoing laparoscopic cholecystectomy. But there was no difference between the two doses so using the smallest dose is recommended.

RECOMMENDATION

More studies are needed to confirm these results and evaluate the beneficial effects of lidocaine in patients undergoing other types of surgery.

Moreover, the appropriate dose, the onset time, and the duration of lidocaine infusion required to attenuation of BP in laparoscopic cholecystectomy remain to be determined.

REFERENCES

1. **Smith TC (2010):** Local anesthetic agents. Pharmacology. In Tim Smith, Colin Pinnock and Ted Lin (editors): Fundamentals of Anesthesia, 3rd ed., published by Cambridge University Press.
2. **Kotwani DM, Kotwani MB, Beena K *et al.* (2017):** Comparative clinical study of the effect of oral clonidine premedication on intraoperative haemodynamics in the patients undergoing laparoscopic cholecystectomy. Int Surg J., 4(3):950-960.
3. **Kataria AP, Joginder PA, Ramita K *et al.* (2016):** Efficacy of dexmedetomidine and fentanyl on pressor response and pneumoperitoneum in laparoscopic cholecystectomy Anesthesia. Essays and Researches, 10(3): 446-450**.**
4. **Gutt CN, Oniu T, Mehrabi A *et al.* (2014):** Circulatory and respiratory complications of carbon dioxide insufflations. Digestive Surgery, 21(2): 95-105.
5. **El-Sayed W, Hasanein R (2016):** Intraoperative lidocaine infusion attenuates tourniquet induced hypertension in patients undergoing anterior cruciate ligament reconstruction under general anesthesia. Egyptian Journal of Anaesthesia, 32: 345–350.
6. **Werdehausen R, Kremer D, Brandenburger T *et al.* (2012):** Lidocaine metabolites inhibit glycine transporter 1: A novel mechanism for the analgesic action of systemic lidocaine? Anesthesiology**,**116:147–58.
7. **Lim SH, Jang EH, Kim MH, Cho K, Lee JH, Lee KM *et al.*(2011):** Analgesic effect of preoperative versus intraoperative dexamethasone after laparoscopic cholecystectomy with multimodal analgesia. Korean J Anesthesiol., 61: 315-9.
8. **Kuo CP, Jao SW, and Chen KM** (**2006**) Comparison of the effects of thoracic epidural analgesia and i.v. infusion with lidocaine on cytokine response, postoperative pain and bowel function in patients undergoing colonic surgery. Br J Anaesth., 97:640-46.
9. **El-Tahan MR, MowafiI H, Al Sheikh HI *et al.* (2012):** Efficacy of dexmedetomidine in suppressing cardiovascular and hormonal responses to general anaesthesia for caesarean delivery: A dose-response study. International Journal of Obstetric Anesthesia, 21(3):222-9.
10. **Oliveira CMB, Issy AM and Sakata RK (2010):** Intraoperative Intravenous Lidocaine. Rev Bras Anestesiol Elsevier Editora Ltda.**,** 60(3): 325-333.
11. **Kaba A, Laurent SR, Detroz BJ *et al.* (2007).** Intravenous lidocaine infusion facilitates acute rehabilitation after laparoscopic colectomy. Anesthesiology, 106: 11–18.
12. **Baral BK, Bhattarai BK, Rahman TR *et al.* (2010):** Perioperative intravenous lidocaine infusion on postoperative pain relief in patients undergoing upper abdominal surgery. Nepal Med Coll J., 12(4): 215-220.
13. **Mraovic B, Simurina T, Mikulandra S *et al.* (2010):** Effects of IV lidocaine administered prior to extubation on early and late recovery after breast surgery. Eur J Anaesth**.,** 27:8.
14. **Omar AM, Aboushanab OH (2013):** Effect of intravenous lidocaine infusion on sevoflurane requirements as monitored by bispectral index: A randomized double-blinded controlled study. Egyptian Journal of Anesthesia, 29: 235-239.
15. **Solimana HF, Ahmed R, Gharbiyab C (2015)** Efficacy of systemic lidocaine infusion compared with systemic ketorolac infusion in improvement of recovery after laparoscopic bariatric surgery Ain-Shams Journal of Anesthesiology, 08:334–340.
16. **Ezzeldin S, Hatem A, Mohamed IA *et al.* (2018):** The effect of intraoperative lidocaine infusion on perioperative opioid consumption for laparoscopic cholecystectomy Menoufia Medical Journal, 31:83–86.
17. **Saadawy IM, Kaki AM, Abd El Latif AA *et al.* (2010):** Lidocaine vs. Magnesium: effect on analgesia after a laparoscopic cholecystectomy. Acta Anaesthesiol Scand., 54: 549-56.
18. **Dogan SD, Ustun FE, Sener EB *et al.* (2016):** Effects of lidocaine and esmolol infusions on hemodynamic changes, analgesic requirement, and recovery in laparoscopic cholecystectomy operations. Braz J Anesthesiol., 66:145–150.
19. **Farag E, Ghobrial M, Sessler DI *et al.* (2013):** Effect of Perioperative Intravenous Lidocaine Administration on Pain, Opioid Consumption, and Quality of Life after Complex Spine Surgery. The American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins. Anesthesiology, 119(4):932-40.
20. **de Oliveira CM, Issy AM and Sakata RK (2015):** Intraoperative Intravenous Lidocaine. Rev Bras Anestesiol Elsevier Editora Ltda., 60(3): 325-333.
21. **Kwon MI, Keon SK**, **Bong JL *et al.* (2008):** The Effect of Perioperative Intravenous Lidocaine Infusion on the Recovery of the Bowel Function after a Laparoscopic Hysterectomy Department of Anesthesiology and Pain Medicine, College of Medicine, Kyung Hee University, Seoul, Korea.
22. **Harvey KP, Adair JD, Isho M *et al.* (2009):** Can intravenous lidocaine decrease postsurgical ileus and shorten hospital stay in elective bowel surgery? A pilot study and literature review. Am J Surg., 198(2):231-36.