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Haemodynamic Responses Following Lidocaine Infusion on Hypertensive Patient Undergoing Laparoscopic Cholecystectomy

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Abstract

Many pharmacological methods have been evaluated to attenuate the adverse haemodynamic responses resulting from airway manipulation and pneumoperitoneum. Intravenous lidocaine infusion is one of them; bolus dose of intravenous lidocaine is used to reduce haemodynamic changes resulting from intubation and extubation reflex whereas intraoperative infusion of lidocaine has been used for post-operative analgesia in laparoscopic cholecystectomy. This randomized controlled trial was conducted to observe the effectiveness of lidocaine infusion in obtundation of haemodynamic responses on hypertensive patient undergoing laparoscopic cholecystectomy. A total number of 80 patients were enrolled in this study. Patients were allocated into two groups by computer generated random chart according to a 1:1 ratio. The patients of group A were given general anaesthesia with placebo normal saline infusion and the patients of group B were given general anaesthesia with lidocaine infusion (1.5mg/kg). Mean differences of blood pressure (SBP & MAP) and heart rate at different time periods from baseline were compared between two groups. The demographic profiles were almost similar between the groups ($p>0.05$). In comparison between two groups, heart rate, systolic blood pressure and mean arterial pressure rise from baseline value was more in normal saline group (group A) than lidocaine test group (group B) during peri-intubation, pneumoperitoneum and peri-extubation period. Statistical difference was significant between two groups ($p<0.05$) in different haemodynamic parameters. Adverse events such as tachycardia premature ventricular contraction (PVC) and hypertension were observed much more in group A, which was higher than that of group B. We observed that administration of lidocaine infusion attenuates haemodynamic responses of hypertensive patient during laparoscopic cholecystectomy.

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Introduction

In operation theatre, anesthesiologists always face a challenge to minimize the alteration of haemodynamics. Changes of haemodynamics are inevitably related to general anesthesia. Laryngoscopy, tracheal intubation and subsequent extubation are often associated with several unwanted haemodynamic responses such as an increase arterial blood pressure, heart rate, arrhythmias and raised intracranial and intraocular pressure.[1,2] Prevention of haemodynamics alteration due to pneumoperitoneum in laparoscopic cholecystectomy remains an important issue. The control and modification of these haemodynamic changes have opened a whole new chapter in the

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field of anesthesiology. Several modifications in technique have been tried to attenuate these responses. Various pharmacological agents like nitroglycerine[3], beta blockers[4], opioids[5], magnesium sulfate[6], clonidine and dexmedetomidine[7] are used to provide haemodynamic stability during pneumoperitoneum with varying success rate.

Many studies have showed some drawback. For sedative effect of opioid agent, even if short-acting, may cause delayed extubation[8], postoperative nausea vomiting that result in patient discomfort and postoperative ileus development. Though statistical differences between oral clonidine and iv lidocaine for attenuation of haemodynamic responses are nil after intubation in controlled hypertensive patients, but the rate of complications including mouth dryness, bradycardia, and orthostatic hypotension are significantly higher in the clonidine group before induction of anesthesia.[9] Many cardiac patients are prescribed β-blockers, which increase the risk for Brady-arrhythmias.[10]

Lidocaine is a synthetic aminoethyl amide and a local anesthetic agent. Lidocaine typically begins working within 1.5 minutes (IV) and lasts for an hour. Intravenous lidocaine has analgesic, anti-hyperalgesia, anti-inflammatory and antiarrhythmic effects.[11,12] A variety of mechanisms mediate these properties, including voltage gated sodium channel blockade and inhibition of N-Methyl-D-Aspartate receptors.[13] Intravenous lidocaine might be a potential option to treat complex pain following laparoscopic cholecystectomy.[14]

Most of the studies addressing cardiovascular effects of CO_2 pneumoperitoneum have been performed in healthy subjects, who seem to tolerate pneumoperitoneum without untoward problem.[18] Many studies on lidocaine are available showing postoperative analgesic effect[15,16] but very few previous studies have demonstrated about the effect of lidocaine infusion on attenuation of intraoperative haemodynamics change due to pneumoperitoneum.

Per-operative intravenous lidocaine infusion can be a method to minimize tachycardia, abnormal heart rhythm and elevation of blood pressure that arise during laparoscopic cholecystectomy. reducing the minimum alveolar concentration of volatile anesthetics by up to 40%. Several studies have demonstrated its preventive effects on postoperative pain.[15,16] Hence, the present study was designed to find out the effectiveness of intraoperative lidocaine infusion on changes in heart rate, cardiac rhythm, systolic blood pressure and mean arterial pressure in hypertensive patient during laparoscopic cholecystectomy, that means intraoperative haemodynamic stability.

Methods

This randomized controlled trial was carried out between March 2018 and September 2020 in Dhaka Medical College Hospital, Dhaka, Bangladesh. After obtaining approval permission for intervention from the ethical committee of Dhaka Medical College, 80 consecutive ASA class II well controlled hypertensive patients undergoing elective laparoscopic cholecystectomy were allocated for the study. During pre-anaesthetic visits participants were included according to inclusion and exclusion criteria. The patients were excluded if they had

Ischemic heart disease, Cardiac arrhythmia, abnormal liver or renal function, allergy to lidocaine, BMI > 40 kg/m^2 and pagnancy. Following providing information about the study aim, objectives and procedure, written consent was taken from each participant. Histories taking focusing on clinical features, disease duration along with physical examinations were done. Relevant investigations had been checked carefully. Patients on regular antihypertensive medication whose arterial blood pressure remained ≤140/90 during the preoperative anesthetic visit before surgery were approached about participation the study. Patient allocations into two groups were done by computer generated chart according to a 1:1 ratio. The on-duty anaesthesiologist who would collect the intraoperative data as well as the patients would be blinded to the drug solution administered.

All the patients would have kept nil per orally for 8 hours before surgery and Hartmann's solution infusion was commenced through 18-gauge intravenous (IV) cannula. Then patient was premeditated with injection midazolam 0.025 mg/kg intravenously, injection omeprazole 40 mg and injection ondansetron 8 mg intravenously at preoperative room. Drug solution was also prepared at preoperative room according to group allocation. Then patient was transferred to operation table where all the standard monitoring was attached. Baseline haemodynamic parameters like heart rate, heart rhythm and blood pressure (SBP, DBP and MAP) were checked with automated machine. After recording baseline parameters, injection lidocaine or normal saline bolus was given before induction of anaesthesia over 5 minutes according to group allocation with syringe pump.

The controlled group (group A) received 6ml 0.9% normal saline as bolus over 5 minutes, followed by 6 ml/h normal saline as placebo. The lidocaine test group (group B) received 2% lidocaine 1.5 mg/kg iv bolus (made to a volume of 6 ml with normal saline) over 5 minutes, followed by infusion at a rate of 1.5 mg/kg/hour (pre-diluted in normal saline made to a volume of 6 ml/hour). Group A received 6ml 0.9% normal saline as bolus over 5 minutes, followed by 6 ml/hour normal saline as placebo for per-operative intravenous infusion.[1] Group B received 2% lidocaine 1.5 mg/kg iv bolus (made to a volume of 6 ml with normal saline) administered over a period of 5 minutes.[1] Thereafter an infusion at a rate of 1.5 mg/kg/hr (pre-diluted in normal saline made to a volume of 6 ml/hour) continued through a syringe pump. Then participants were pre-oxygenated with 100% oxygen for 3 minutes after completion of bolus dose according to group allocation. Anaesthesia was induced with fentanyl 2 mcg/ kg, propofol 2 mg/kg or in a dose sufficient to cause loss of verbal command. The laryngoscopy and intubation were facilitated with suxamethonium 1.5 mg/kg as early as possible. Then haemodynamic parameters were monitored and recorded with automated machine as mentioned at 1st minute, 3rd minute, and 5th minute following intubation. Controlled ventilation was performed with a mechanical ventilator. Maintenance of anesthesia was done with halothane at an inspired concentration of 0.60% in an inhaled mixture of 65% nitrous oxide and 35% oxygen. Supplemental neuromuscular block was provided with injection vecuronium 0.1 mg/kg bolus dose and maintained by one third of bolus given intermittently or as per needed.

Intraperitoneal pressure was kept between 12 to 14 mm Hg during intraperitoneal insufflation of carbon dioxide. After creation of pneumoperitoneum again haemodynamic parameters were recorded with automated machine at 1st min, 3rd min, 5th min, 10th min and 15th min but continued careful observation throughout the operation. All adverse events during operation were recorded and treated properly. Peropertive hypertension was treated initially with deepening of general anaesthesia, then by adding 25 mcg injection fentanyl intravenously. Per-operative hypotension was treated accordingly cause. At first by increasing intravenous fluid flow. Then by reducing halothane and nitrous oxide. If above measures had failed, then injection phenylephrine 50 mcg by intravenous bolus. When premature ventricular contractions (PVCs) were noticed on ECG monitor, we alerted surgeons to stop surgery and to stop CO_2 insufflation. Simultaneously we provided 100% oxygen, reduced halothane and nitrous and carefully observed. When the above measures failed, injection lidocaine 2 mg/kg bolus was given. Surgery was started again when cardiac rhythm became normal. Bradycardia was managed by reducing halothane and by injection atropine 0.6 mg intravenously. At the end of operation, the laparoscope was withdrawn, and the inflated carbon dioxide was carefully evacuated by manual compression of the abdomen.

The effect of residual neuromuscular blocking agent was reversed at the end of surgery using neostigmine 0.05 mg/kg and glycopyrronium bromide 0.01mg/kg. Lidocaine infusion was terminated just after extubation. Haemodynamic changes were lastly recorded with automated machine during extubation, 3rd and 5th minute after extubation.

Statistical analyses were carried out by using the Statistical Package for Social Sciences version 26.0 for Windows (SPSS Inc., Chicago, Illinois, USA). A statistical analysis was performed for all data. The mean values were calculated for continuous variables. The qualitative observations were expressed by frequencies and percentages. Mean differences of BP and heart rate at different time periods from baseline were calculated within group and between groups. Chi-square test (X2- test) was done for qualitative variables and quantitative variables were tested by t-test. P-value <0.05 was considered as significant.

This study was approved by the Ethical Review Committee of Dhaka Medical College, Dhaka, Bangladesh.

Results

Table-I shows that no statistical difference was found in demographic variables of patients (n=80) between two groups (P>0.05) but females are predominant in both groups.

Table-I: Demographic profile for the patients (n=80)

Criteria	Group A (n=40)	Group B (n=40)	P value
Age (year)	45.5±6.80	44.3±5.35	0.378
Sex (F/M)	25/15	24/16	0.053
BMI (kg/m^2)	24.5±6.34	23.9±5.23	0.393

Table-II shows the changes in heart rate during peri-intubation period. Rise of heart rate in group

B was minimum from baseline but more rise of heart rate occurred in group A. Statistical difference was significant (P<0.05) between two groups. Table-III shows comparison to changes in heart rate (HR) during pneumoperitoneum was significant between two groups (P<0.05). Heart rate reduced in both groups from intubation value, but more reduction occurred in lidocaine test group (group B) than normal saline infusion group (group A).

Table II: Changes of heart rate before and after intubation of both groups

Time of observation	Group A (n=40)	Group B(n=40)	P value
Baseline	83.90±6.43	82.60±7.22	0.398
Just after intubation	115.43±6.55	93.38±6.20	0.001*
After intubation at 1st minute	102.23±6.46	82.53±5.84	0.001*
After intubation at 3rd minute	93.38±6.20	71.70±6.21	0.001*
After intubation at 5th minute	79.55±7.62	69.60±6.08	0.001*

Table-III: Changes of heart rate after pneumoperitoneum of both groups

Time of observation	Group A	Group B	P value
1st minute	93.85±6.78	70.40±9.38	0.001*
3rd minute	88.80±7.34	71.05±10.21	0.001*
5th minute	84.23±8.20	72.58±8.03	0.001*
10th minute	80.33±7.10	68.88±6.82	0.001*
15th minute	81.30±7.47	70.58±6.17	0.001*

Table-IV shows changes in heart rate during and after extubation. Rise of heart rate noticed in group A due to extubation reflex but this reflex was minimized in group B. After extubation at 5th minute heart rate difference reduced between two groups. Significant changes were observed in systolic blood pressure (mmHg) before and after intubation of both groups (Table-V).

Table-IV: Changes of heart rate (Beat/min) during and after extubation of both groups

Time of observation	Group A (n=40)	Group B (n=40)	P value
During extubation	95.38±7.90	85.98±6.21	0.031*
after extubation at 3rd minute	90.40±7.36	77.90±14.06	0.001*
after extubation at 5th minute	81.35±6.85	73.78±8.96	0.271

Table-V: Changes in Systolic blood pressure (mmHg) before and after intubation of both groups

Time of observation	Group A (n=40)	Group B (n=40)	P value
Baseline	140.50± 10.02	141.90± 9.65	0.526
Just after intubation	159.50± 7.61	143.93± 8.33	0.001*
After intubation at 1st minute	145.60± 6.57	133.60± 8.40	0.001*
After intubation at 3rd minute	133.98± 7.869	120.05± 6.68	0.001*
After intubation at 5th minute	128.55± 8.961	119.00± 6.15	0.001*

When we compared during pneumoperitoneum between two groups, systolic blood pressure markedly rises in group A than group B. Difference of SBP was large during pneumoperitoneum between groups. The difference was statistically significant (P<0.05) (Table-VI). Table-VII shows changes in SBP during and after extubation. More rise of SBP noticed in group A due to extubation reflex but this reflex was minimized in group B. The statistical difference was significant (P<0.05). Table-VIII shows comparison of mean arterial pressure (MAP) before and after intubation. Mean arterial pressure (MAP) change due to intubation

reflex in group B was minimum, but it was significantly (P<0.05) higher from baseline value in comparison to group A.

Table-VI: Changes in Systolic blood pressure (mmHg) after pneumoperitoneum of both groups

Time of observation	Group A (n=40)	Group B (n=40)	P value
1st minute	147.48±8.29	125.55±8.05	0.001*
3rd minute	144.73±8.16	127.03±4.67	0.001*
5th minute	141.40±6.50	126.48±5.03	0.001*
10th minute	140.82±7.66	128.05±4.96	0.001*

Table-VII: Changes in Systolic blood pressure (mmHg) during and after extubation period of both groups

Time of observation	Group A (n=40)	Group B (n=40)	P value
During extubation	148.93±7.68	138.73±8.86	0.001*
3rd minute after extubation	134.05±7.12	123.58±8.42	0.001*
5th minute after extubation	128.07±8.54	117.13±6.52	0.001*

Table-VIII: Changes in Mean arterial pressure (MAP) (mmHg) before and after intubation of both groups

Time of observation	Group A (n=40)	Group B (n=40)	P value
Baseline	89.00±8.23	87.70±7.65	0.467
Just after intubation	125.05±7.70	109.03±4.77	0.001*
After intubation at 1st minute	122.85±5.24	105.80±3.96	0.001*
After intubation at 3rd minute	113.00±4.42	99.00±3.74	0.001*
After intubation at 5th minute	99.83±5.34	90.98±6.25	0.001*

Table-IX shows comparison of mean arterial pressure (MAP) during pneumoperitoneum between two groups. The rise of mean arterial pressure (MAP) due to stress response was effectively prevented in lidocaine infusion group (group B) than placebo normal saline infusion group (group A). MAP change was significantly lower in group B than group A (p<0.05). Table-X shows changes in MAP during and after extubation. Rise of MAP noticed in group A due to extubation reflex but this reflex was minimized effectively in group B. The statistical difference for MAP change between two groups was significant (P<0.05). In case of group A 5% (2 out of 40) patients had developed premature ventricular contraction (PVC), 37.5% (15 out of 40) patients had developed tachycardia and 32.5% (13 out of 40) patients developed hypertension. 15% (6 out of 40 patients) of patients had developed bradycardia and 5% (2 out of 40) of patients developed hypotension in group B (Table-XI).

Table-IX: Changes in mean arterial pressure (mmHg) after pneumoperitoneum of both groups

Time of observation	Group A (n=40)	Group B (n=40)	P value
1st minute	103.53±8.36	90.70±11.53	0.001*
3rd minute	104.68±9.13	96.83±12.36	0.001*
5th minute	98.38±10.49	90.90±12.95	0.001*
10th minute	92.13±10.71	85.68±14.21	0.001*
15th minute	88.30±8.89	83.75±10.86	0.001*

Table-X: Changes in Mean arterial pressure (mmHg) during and after extubation of both groups

Time of observation	Group A (n=40)	Group B (n=40)	P value
During extubation	123.43±11.21	102.94±7.65	0.001*
After extubation at 3rd minute	105.76±8.43	96.83±5.23	0.001*
After extubation at 5th minute	96.39±9.32	87.58±5.72	0.001*

Table-XI: Abnormal rhythm and adverse events observed

Observed events	Group A (n=40)		Group B (n=40)	
	Frequency	%	Frequency	%
Bradycardia	2	5%	6	15%
Tachycardia	15	37.5%	1	2.5%
PVC	2	5%	0	0%
Hypotension	1	2.5%	2	5%
Hypertension	13	32.5 %	1	2.5 %

Discussion

During intubation, heart rate and blood pressure usually increases due to airway manipulation. In this study heart rate and blood pressure increased in both groups due to intubation reflex from baseline value (P>0.05) but the rate of changed was more group A than group B as group B received lidocaine bolus and infusion. This study reveals that lidocaine infusion successfully attenuated haemodynamic changes during peri-intubation period. The result was statistically significant all the time during peri-intubation period (P<0.05). This study is consistent with the study of Jain & Khan[1] who found that intravenous lidocaine 1.5mg/kg bolus and 1.5mg/kg/hour maintenance was effective in attenuating haemodynamic responses such as heart rate and blood pressure. With regard to studies of lidocaine, Abou-Madi *et al.*[17] administered lidocaine 1.5 mg/kg and 0.75 mg/kg intravenously 30 seconds before laryngoscopy and intubation and reported that the 0.75 mg/kg dosage was not effective, but lidocaine 1.5 mg/kg was effective in preventing hypertension and tachycardia. However, Pathak *et al.*[18] found that lidocaine 2mg/kg was not effective in preventing hypertension and tachycardia. The reason might be- they used only bolus dose of lidocaine but in our study, we used both bolus and infusion of lidocaine. Our result is also dissimilar with Samaha *et al.*[19] who compared esmolol and lidocaine and found neither esmolol 1.5 mg/kg or lidocaine 1.5 mg/kg given intravenously 2 min before intubation could prevent hypertension (P>0.05). Their time of lidocaine starting might be inappropriate. However, we started lidocaine bolus and infusion 5 minutes before induction of anaesthesia. Hollmann & Durieux found partial effectiveness of lidocaine.[20] In their study they found that lidocaine 200mg given 2 minutes before intubation prevented hypertension only but not tachycardia. This might happen as lidocaine causes vasodilation.

In the present study, lidocaine effectively blunted the haemodynamic consequences resulting from pneumoperitoneum as lidocaine attenuates stress response effectively. Our result is consistent with the study of Anis *et al.*[21] that showed that lidocaine infusion as well as dexmedetomidine infusion reduced the elevation of mean values of systolic blood pressure, diastolic blood pressure, mean arterial pressure and heart rate during pneumoperitoneum. In a recent study, Hegazy *et al.*[22] used two different doses of lidocaine (1.5 mg/kg bolus with 1 mg/kg/h or 2 mg/kg/h intraoperative infusion) in comparable to normal saline infusion to see the effectiveness of lidocaine in alleviating haemodynamic changes caused by pneumoperitoneum.

Our study showed that in case of heart rate, systolic blood pressure and mean blood pressure during peri-extubation period, lidocaine effectively blunted extubation reflex that mean prevent rise of heart rate and blood pressure but in normal saline study group significant rise of heart rate

and blood pressure were noted (P<0.05). Few minutes after extubation heart rate difference between groups became reduced (P>0.05). Our study is consistent with the study of Khezri *et al.*[23] who experimented on two groups that received either 2% injection lidocaine 1.5 mg/kg IV or intratracheally. Heart rate, systolic blood pressure, bucking, and number of coughs were continuously monitored for 30 min post-extubation. Similarly, Bidwai *et al.*[24] and Marret *et al.*[25] observed that patients who received lidocaine did not have an elevation in heart rate and blood pressure at or after extubation when compared with the saline group. However, in another study, Khan *et al.*[26] found that labetalol is safer and more effective than nitroglycerin and lidocaine to attenuate the endotracheal intubation reflex in hypertensive patients.

Conclusion

To summarize, we found that administration of lidocaine infusion attenuates haemodynamic responses of hypertensive patient during laparoscopic cholecystectomy. It also demonstrated that patients receiving lidocaine infusion had better stability in heart rate, cardiac rhythm, systolic blood pressure and mean arterial pressure during laparoscopic cholecystectomy.

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