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Impact of Peroperative Intravenous Lidocaine on Postoperative Analgesia in Laparoscopic Cholecystectomy

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Key words:
Lidocaine, Postoperative Analgesia, Laparoscopic Cholecystectomy

Abstract:

The present study was undertaken to evaluate the outcome of peroperative intravenous lidocaine in reducing the intensity of postoperative pain after laparoscopic cholecystectomy.This prospective randomized clinical trial study was conducted in the Department of Anaesthesiology, Sir Salimullah Medical College Mitford Hospital (SSMC MH), Dhaka between April 2014 to September 2014. A total of 80 patients of chronic cholecystitis or cholelithiasis undergoing laparoscopic cholecystectomy in SSMC MH, Dhaka were consecutively included in the study and were randomly assigned to two study groups. Patients in the study group received I/V lidocaine administration @ 3 mg/kg/h and those in the control group received normal saline (0.9% saline) in the same volume by a different observer. When compared the changes in haemodynamic variables from baseline to endpoint of the study shows that there was no significant difference between the groups in terms of heart rate, systolic, diastolic and mean blood pressures except a sudden rise of the parameters at 5 minutes after induction. However, the systolic blood pressure of study group experienced a slight reduction from 30 minutes onwards to the end of the observation and differed significantly from the corresponding SBPs of the control group. The mean BP of both the groups also showed similar trend like systolic BPs.The SpO_2 in both study and control groups was maintained at 99 to 100% throughout the study. The study concluded that peroperative infusion of nontoxic dose of lidocaine decreases the intensity of postoperative pain and reduces the postoperative analgesics(inj. Pethidine) requirement without causing any significant adverse effects.

Introduction:

The effective modality for postoperative pain management has still remained a subject of ongoing debate due to its uniqueness and associated complex physiological consequences with somatic, autonomic and behavioral manifestations[1]. Optimal postoperative pain relief is not only needed for patients' comfort and satisfaction but also to facilitate their early mobilization and rehabilitation. Moreover, optimal postoperative pain relief has been found to be associated with less postoperative cognitive impairment, enhanced quality of life, reduced risk of chronic/persistent post-surgical pain with better

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overall outcome and reduced clinical expenses[2,3,4,5].

Many patients still suffer from moderate to severe pain after laparoscopic cholecystectomy (LC) [6]. Different treatments have been used to relieve pain, including non steroidal antI inflammatory drugs, opioids, and local anesthetics, but none has been consistently satisfactory. This may be because post-LC pain results from a combination of inflammatory, incisional, somatic and visceral components[7].

In previous studies, it was found that pre-incisional intramuscular (IM) treatment with 40 mg of dextromethorphan (DM) provided good pain management in patients who underwent upper abdominal surgery, LC, and modified radical mastectomy by diminishing central sensitization[8,9] . But multimodal analgesia has become a current trend in postoperative pain management[5].This implies that a single antagonist may not be sufficient to prevent postoperative pain if other pathways are not blocked.

Lidocaine is an amide local anesthetic agent that works by blocking sodium channels in the neural cascade and exhibits inhibitory effects on the neuropeptide chemical mediators, which influence the complex phenomenon of pain[10, 11, 12]. Blocking systemic inflammatory responses to surgical stress may result in preservation of bowel motility[13,14]. Recent investigations suggest that intravenous (I/V) lidocaine, given as a single dose or as a continuous infusion has influence on biochemical pain processes, while preserving the gastrointestinal motility[15]. Despite these findings, there are conflicting results with regard to lidocaine efficacy in the provision of analgesia and reduction in postoperative paralytic ileus, which demands a formal study.

Lidocaine may provide a multimodal approach to pain management for the post-laparoscopic cholecystectomy patients. Groudine et al.[16] studied I/V lidocaine administration (3 mg/kg/h) in patients undergoing radical retropubic prostatectomy and concluded that lidocaine reduced the neural response to pain by blockade or inhibition of nerve conduction. In addition to blocking nerve transmission, lidocaine has significant anti inflammatory properties[17]. Moreover, intravenous (I/V) lidocaine might be an effective modality for treating visceral pain. Therefore, lidocaine might be a potential drug for treating the complex pain processes after laparoscopic cholecystectomy[18]. However, the efficacy of lidocaine in this regard has not been formally tested in the context of our population. That purpose the present study is intended to evaluate the efficacy of intravenous lidocaine on postoperative pain in patients undergoing laparoscopic cholecystectomy.

Materials & methods:

The study was conducted in the Department of Aanaesthesiology, Sir Salimullah Medical College Mitford Hospital (SSMC MH), Dhaka over a period of six months from April 2014 to September 2014.The ethical clearance was taken ((Memo No. MEU-SSMC/2014/35)from the institutional ethics committee of our institute for the study. The prospective randomized clinical trial was carried over the patients of chronic cholecystitis or cholelithiasis undergoing laparoscopic cholecystectomy. The sample size was calculatedat at 5% level of significance and 80% power.

We included a total of 80 patients by the criteria that the adult patients (age 18 years onwards) with ASA grade I & II who were scheduled for laparoscopic cholecystectomy under general anesthesia. We excluded the patients who were ASA grade III & above, having acute preoperative pain other than biliary colic, clinically diagnosed acute pancreatitis, scheduled to undergo any surgical procedure expected to produce more trauma than LC alone,required chronic pain treatment preoperatively,have current or recent cancer or any condition that would contraindicate participation in a surgical study of this nature and patients with contraindications for lidocaine or who had received opioids or non-steroidal anti-inflammatory drugs within 1 week.

The study commenced after obtaining approval of the Ethics Committee of our Institution and patients' informed consent. Patients with ASA physical status I or II scheduled for elective LC

were included and were randomly divided into 2 groups using lottery method. Preoperatively, all patients were instructed as how to use a visual analog scale (VAS) to measure pain scores for pain assessment.

Patients in the study group (Group-L) received I/V lidocaine administration @ 3 mg/kg /h and those in the control group (Group-C) received normal saline (0.9% saline) in the same volume by a different observer. The infusions were started at the start of induction of anaesthesia and continued until the end of skin closure. The drug was prepared by another anesthesiologist. The investigator and the anesthesiologist who performed the general anaesthesia were blinded to the study groups.

On arrival to Operation Theater, routine monitoring (ECG, Pulse oxymetry, NIBP) was started and baseline parameters like heart rate, mean arterial blood pressure (MAP) and arterial oxygen saturation (SpO2) were recorded. For all patients, general anesthesia was induced with IV fentanyl (2 μg/kg), thiopental (5 mg/kg). Tracheal intubation was facilitated with succinylcholine (1.5 mg/kg). Anesthesia was maintained with halothane 0.6% in oxygen (40%) with N_2O (60%) via Bain circuit. Vecuronium bromide (0.1 mg/kg) was used for muscle relaxation. The mean arterial blood pressure was maintained within the range of ±20% of the basal mean arterial blood pressure. Respiratory frequency and tidal volume were adjusted to maintain the end-tidal CO_2 level at 35–45 mmHg. No additional opioids were given during the operation. CO_2 was insufflated by the surgeon into the peritoneal cavity to create pneumoperitoneum. Intra-abdominal pressure was maintained upto 14 mmHg throughout the laparoscopic procedure. The patients were mechanically ventilated. At the end of surgery, residual neuromuscular blockade was antagonized with neostigmine (0.05 mg/kg) and atropine (0.02 mg/kg), and the endotracheal tube was removed when the patient started to breathe spontaneously and smoothly. Heart rate, MAP and SPO_2 were also being recorded throughout the procedure at an interval of 5 minutes for first half an hour and then at an interval of ten minutes. Postoperative oxygen (100%) was given by mask for 5 minutes.

Inj. pethidine (1.5 mg/kg) IM injection was used for postoperative pain relief, if requested. A 0-10 cm VAS (with end-points labeled “no pain” and “worst possible pain”) was used to assess pain intensity at rest and during coughing at 1, 2, 4, 12, 24, and 48 h after completion of surgery. The outcome variables studied were the time to first pethidine injection, total pethidine consumption, the first time to the passage of flatus by patients’ self-report, and side-effects related to pethidine (drowsiness, dizziness, nausea, and vomiting) and lidocaine (cardiac arrhythmia, light headed, drowsiness, perioral numbness, metal taste, dryness of the mouth, nausea, muscular twitch, tinnitus, and visual disturbances) for 48 h after the operation. All observations were made by an independent observer who remained blinded to study and control groups. Side effects were treated as required.

ERC clearance: ERC clearance (Memo No. MEU-SSMC/2014/35 & dated 09/03/2014) was obtained.

Data processing Statistical analysis: Data were processed and analyzed using SPSS (Statistical Package for Social Sciences). The test statistics used to analyze the data were descriptive statistics, Chi-square ($\div^2$) Probability Test, Student’s t-Test and Repeated Measure ANOVA. For all analytical tests, the level of significance was set at 0.05 and $p < 0.05$ was considered significant. The summarized data were presented in the form of tables and charts.

Results:

The mean ages of the groups were 41.2 ± 11.4 and 45.2 ± 15.0 years respectively ($p = 0.178$). There was no significant difference between the groups in terms of weight ($p = 0.364$). All the haemodynamic variables like heart rate, systolic and diastolic blood pressures, mean BP were almost homogeneously distributed between groups at baseline ($p = 0.735$, $p = 0.252$, $p = 0.070$ and $p=0.117$ respectively) . The oxygen saturation was almost 99.9% in both groups ($p = 0.053$). Majority of the subjects in either group had ASA grade-I with no significant intergroup difference ($p = 0.264$) (Table I).

Table I: Comparison of baseline characteristics between groups

Baseline Characteristics	Group L (n = 40)	Group C (n = 40)	p-value
Age (years) #	41.2 ± 11.4	45.2 ± 15.0	0.178
Weight (kg) #	56.2 ± 6.7	57.7 ± 7.5	0.364
ASA grade*			
Grade I	34(85.0)	30(75.0)	0.264
Grade II	6(15.0)	10(25.0)	
Heart rate (beat/ minute) #	77.0 ± 6.0	77.4 ± 4.4	0.735
Systolic blood pressure (mmHg)	123.0 ± 10.1	125.5 ± 9.3	0.252
Diastolic blood pressure (mmHg) #	77.8 ± 7.1	80.7 ± 7.6	0.070
Mean BP (mmHg) #	93.2 ± 7.5	95.9 ± 7.7	0.117
SpO_2 (%)#	99.9 ± 0.5	100.0± 0.00	0.053

Figures in the parentheses indicate corresponding %; * Chi-squared Test (c^2) was done to analyzed the data.#Data was analyzed using Unpaired t-Test and were presented as mean ± SD.

Comparison of changes in heart rates from baseline to endpoint of the study shows that there was no significant change in the parameter at any level of evaluation either within or between groups, except a sudden rise of heart rate at 5 minutes after induction (Fig. 1).

Table II depict the changes in SBP at different time interval following induction. While the systolic blood pressure of control group was more or less stable throughout observation, the blood pressure of study group experienced a significant fluctuation from 30 minutes onwards to end of the observation and differed significantly from the corresponding SBPs of the control group.

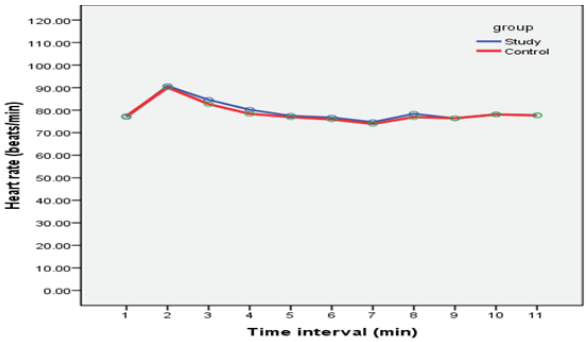

Fig.-1. *Monitoring of heart rate at different time interval*

Table II: *Systolic blood pressure at different time interval between groups*

Systolic blood pressure# (mmHg)	Group L(n = 40)	Group C(n = 40)	p-value
At baseline 123.0±10.1	125.5 ± 9.3	0.252	
5 minutes after induction	133.6 ± 9.7	135.0 8.2	0.473
10 minutes after induction	123.8 10.4	127.0 ± 8.5	0.130
15 minutes after induction	119.8 ± 9.4	123.3 9.8	0.107
20 minutes after induction	116.9 9.6	121.5 ± 8.9	0.030
25 minutes after induction	115.3 ± 9.9	122.8 8.2	<0.001*
30 minutes after G/A	115.7 11.5	123.0 ± 8.1	0.002*
40 minutes after G/A	120.6 ± 5.3	126.0 7.6	0.001*
At the end of surgery	116.8 9.7	123.5 ± 8.0	0.001*
At 30 minutes postoperatively	118.7 ± 7.4	126.0 7.6	<0.001*
At 1 hours postoperatively	118.3 ± 7.7	125.0 ± 6.2	<0.001*

Data was analyzed using Student's t-Test andwas presented as mean ± SD.*statistically significant.

Table III showed that mean BP of both the groups went up sharply at 5 minutes after induction and then fell sharply to baseline level at 10 minutes after induction. Thereafter both the groups experienced a gradual fall of mean BP up to 30 minutes after general anesthesia and then followed a plateau up to the end of the study.

Table III: *Mean BP at different time intervals between groups*

Mean blood pressure# (mmHg)	Group L(n = 40)	Group C(n = 40)	p-value
At baseline	93.2 ± 7.5	95.9 ± 7.7	0.117
5 minutes after induction	101.8 ± 6.6	103.1 ± 7.2	0.403
10 minutes after induction	94.7 ± 7.5	96.4 ± 7.5	0.327
15 minutes after induction	91.2 ± 6.6	92.7 ± 7.7	0.368
20 minutes after induction	88.6 ± 6.9	91.1 ± 6.9	0.116
25 minutes after induction	87.3 ± 6.8	90.8 ± 5.8	0.014*
30 minutes after G/A	86.4 ± 7.2	90.2 ± 6.3	0.014*
40 minutes after G/A	88.2 ± 4.3	90.0 ± 5.2	0.001*
At the end of surgery	86.7 ± 5.6	89.9 ± 4.3	0.005*
At 30 minutes postoperatively	88.7 ± 3.9	90.6 ± 3.6	0.032*
At 1 hours postoperatively	89.2 ± 5.6	90.4 ± 4.0	0.199

Data was analyz+ed using **Student's t-Test** andwas presented as **mean ± SD**.* statistically significant.

The pain VAS was reported to be significantly lower in the group L than that in group C at all levels of evaluation from 1 to 24 hours postoperatively. Thereafter the intensity of pain equalizes. Time to first pethidine injection was much delayed in the former group than that in the latter group ($p = 0.001$). Total pethidine consumption was much lower in group L compared to that in group C ($p < 0.001$). However, the groups were almost homogeneous in terms of time to first passage of flatus and postoperative hospital stay ($p = 0.802$ and $p = 0.858$ respectively).

Table IV: Comparison different Outcome between groups

Outcome#	Group L (n = 40)	Group C (n = 40)	p-value
Pain VAS (0-10cm) 1 hour postoperatively	1.9 ± 0.2	2.1 ± 0.4	0.004*
Pain VAS (0-10cm) 2 hour postoperatively	2.5 ± 0.5	3.2 ± 0.5	<0.001*
Pain VAS (0-10cm) 4 hour postoperatively	2.8 ± 0.4	3.1 ± 0.4	<0.001*
Pain VAS (0-10cm) 12 hour postoperatively	2.7 ± 0.4	3.1 ± 0.2	<0.001*
Pain VAS (0-10cm) 24 hour postoperatively	2.0 ± 0.0	2.3 ± 0.4	0.001*
Pain VAS (0-10cm) 48 hour postoperatively	1.0 ± 0.0	1.0 ± 0.0	0.951
Time to 1st pethidine injection (hr)	4.33 ± 0.75	2.5 ± 0.67	0.001*
Total pethidine consumption (mg)	78.7 ± 12.5	111.3 ± 10.9	<0.001*
Time to 1st passage of flatus (hr)	22.3 ± 6.7	24.1 ± 2.2	0.802
Postoperative hospital stay (days)	2.0 ± 0.0	2.0 ± 0.0	0.858

Data was analyzed using Unpaired t-Test and were presented as mean ± SD.* statistically significant

Discussion:

Postoperative pain is a unique and common type of acute pain. Studies have indicated that appropriate pain treatment protocols reduce postoperative morbidity, improve the results of the surgery, and decrease hospital costs[4,5]. Besides, adequate relief of postoperative pain is associated with positive long-term effects for patients, such as, reduced postoperative cognitive changes, better quality of life, and reduced risk of chronic or persistent postoperative pain.[19,20] Still it is demonstrated that approximately half to two-thirds of the patients undergoing abdominal surgeries experience moderate to severe pain, indicating that, despite the development of new drugs and implementation of new analgesic techniques, postoperative pain is poorly evaluated and treated.[21,22]

In the present study all the haemodynamic variables like heart rate, systolic, diastolic and mean blood pressures were almost homogeneously distributed between groups at baseline with oxygen saturation being almost 100% in both groups. Majority of the subjects in either group had ASA grade-I. Comparison of changes in haemodynamic variables from baseline to endpoint of the study shows that there was no significant difference between the groups in terms of heart rate, systolic, diastolic and mean blood pressures except a sudden rise of the parameters at 5 minutes after induction. However, the systolic blood pressure of study group experienced a slight reduction from 30 minutes onwards to the end of the observation and differed significantly from the corresponding SBPs of the control group. The mean BP of both the groups also showed similar trend like systolic BPs – a sharp rise and a sharp fall at 5 and 10 minutes after induction respectively. Thereafter both the groups experienced a gradual fall of mean BP up to 30 minutes after general anesthesia and then followed a plateau up to the end of the study. The SpO2 in both study and control groups was maintained at 99 to 100% throughout the study.

The intensity of pain was lower in the study group than that in control group at all levels of evaluation from 1 to 24 hours postoperatively. It means that the peroperative intravenous infusion of lidocaine reduces postoperative pain intensity and analgesic requirement without causing any significant adverse effects including longer hospital stay in patients undergoing laparoscopic surgery. Ali and associates[23] in an attempt to evaluate the efficacy of single bolus dose of xylocard(lidocaine) before induction to provide perioperative hemodynamic stability in patients undergoing laparoscopic cholecystectomy. Mean arterial pressure and heart rate in patients who received xylocard (study group) before induction were significantly lower after intubation and throughout the period of pneumoperitoneum than the patients who received normal saline (control group). No significant difference in the parameters of recovery was observed between the two groups.

Our study supports the findings of the studies by Groudineet al[16] and Kabaet al[1] which showed impressive effect on postoperative pain with reduction in total pain scores compared with control groups. Koppertet al[3]also demonstrated the preventive effects of perioperative intravenous lidocaine infusion on postoperative pain and reduced analgesic consumption after major abdominal surgery.

Thus, the findings of the present study and those of other investigators clearly show and confirm postoperative analgesic effects of perioperative lidocaine infusion. The intravenous lidocaine in most of the previous studies has been administered perioperatively (i.e.during the presence of significant nociceptive input) and the infusion maintained for varying durations postoperatively. Kabaet al[1]and Cassuto et al[24]administered lidocaine in small-dose regimen starting 30 minutes before surgery and continuing for 24 hours after surgery. While Koppertet al[3]and Groudineet al[16] administered lidocaine starting prior to anaesthesia and surgery and continuing until 1h postoperatively. We also started the lidocaine infusion at induction of anaesthesia and continued until the skin closure was done. We did not observe any significant haemodynamic changes in any group in our study except at the time corresponding to laryngoscopy and endotracheal intubation. Although, haemodynamic response to direct laryngoscopy and endotracheal intubation is well-known.

Finally it can be concluded that peroperative infusion of nontoxic dose of lidocaine decreases the intensity of postoperative pain and reduces the postoperative analgesics requirement without causing any significant adverse effects.

Conclusion:

From the findings of the study it can be concluded that preoperative continuous infusion of lidocaine decreases the intensity of postoperative pain and reduces the postoperative analgesics requirement

without causing any significant complications. Therefore, peroperative intravenous lidocaine infusion could be considered as an inexpensive, easy, relatively safe and effective modality as a part of multimodal approach for postoperative analgesia in patients undergoing laparoscopic cholecystectomy.

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Conflicts of interest:
There are no conflicts of interest.

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