Perioperative Intravenous Lidocaine Infusion for Postlaparoscopic Cholecystectomy Pain

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ABSTRACT

Objective: To compare intravenous lidocaine infusion adjunct to NSAID and Acetaminophen with regular analgesics for postoperative mean pain score and mean ambulation time after laparoscopic cholecystectomy.

Study Design: Randomised controlled trial.

Place and Duration of Study: Department of General Surgery, Islamabad Medical Complex, (IMC), from March 2020 to December 2021.

Methodology: Sixty (n=60) adult patients, both males and females between the ages of 18-60 years planned for laparoscopic cholecystectomy, were selected and randomly allocated to two groups of treatment (Lidocaine and Ringer Lactate). The control group did not receive any other placebo other than Ringer Lactate infusion. Both groups received Intramuscular Diclofenac 12 hourly and intravenous acetaminophen infusion 8 hourly. Postoperative pain 2, 6, 12 and 24 hours (h) and mean ambulation time were compared in both groups.

Results: Mean VAS (Visual Analogue Scale) of group 1 versus group 2 at 2 h, 6 h, 12 h and 24 h were 3.47 ± 0.82 *vs.* 6.27 ± 0.52 (p=<0.001), 2.7 ± 0.75 *vs.* 4.8 ± 0.8 (p<0.001), 2.0 ± 0.49 *vs.* 3.93 ± 0.94 (p<0.001), 0.73 ± 0.82 *vs.* 2.2 ± 0.61 (p<0.001). Time for spontaneous ambulation after surgery was 5.57 ± 1.55 hours for Group 1 versus 7.3 ± 1.9 hours for Group 2 (p<0.001).

Conclusion: Pain scores at all-time intervals were lower, and ambulation time was shorter in patients who received intravenous infusion of lidocaine as compared to patients who received only regular analgesics for laparoscopic cholecystectomy.

Key Words: *Ambulation time, Laparoscopic cholecystectomy, Postoperative pain.*

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INTRODUCTION

Despite recent advances, postoperative pain is still a dilemma for many physicians and surgeons till this day. It immensely affects postoperative respiratory function, early mobilisation time, wound healing and length of hospital stay. Not only that, it has a psychological effect on the patient, making them anxious and worried which is a hurdle towards recovery. In pain control protocols, NSAIDs and acetaminophen are commonly used and the beneficial role of these drugs in the management of pain has been well-defined.[1] Current guidelines recommend NSAIDS for instance Diclofenac and Ibuprofen which can be administered intramuscularly, per oral and rectal, also Acetaminophen which is given *via* intravenous route. When these medications do not work then intravenous opiates are used.

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They have ominous effects in the time after surgery because of possible delayed recovery and respiratory depression, even requiring mechanical ventilation which is why they are usually avoided and used as a last resort. Certain patient populations like people with obstructive sleep apnea, elderly, obese, and individuals getting opioid or sedative drugs are at additional risk for developing respiratory depression.[2-4]

There has been a lot of research done abroad to evaluate the role of systemic lidocaine in regulating acute pain after surgery. lidocaine is an amino amide kind of local anaesthetic drug and class 1B antiarrhythmic medicine.[5] Because of its fast onset of action and intermediate time of action, perioperative usage of lidocaine for pain relief after surgery is a topic of curiosity and attention because perioperative systemic lidocaine has advantageous post-operative effects on pain management. It has been stated before to prevent post-operative pain when administered either as a single dose or as small infusions. The mechanism of lidocaine infusion in the blood is that it blocks a part of neuronal sodium channels however the polymorphonuclear granulocyte (PMN), does not express sodium channels. In its place, intrusion with additional molecular targets that are involved with inflammatory signals seems to be the possible mechanism. Nonetheless, the effects

of neurons also show a part, for example intravenous lidocaine inhibits excitatory responses in the spinal cord neurons of rats through a process possibly involving receptors of strychnine-sensitive glycine.

Due to the high prevalence of cholelithiasis and other gall-bladder diseases, cholecystectomy is now done with minimally invasive techniques using laparoscopic instruments and it is a very popular procedure performed in hospitals these days. According to some studies, intravenous infusion of lidocaine is shown to have a beneficial role in the recovery of laparoscopic cholecystectomy.[6-8] The main aim of this research was to measure the effectiveness of systemic lidocaine adjunct to NSAID with Acetaminophen for the management of acute pain after surgery. Less opioid requirements[9-13] and early ambulatory time after laparoscopic cholecystectomy, may make this procedure be performed as a daycare case.

METHODOLOGY

This study was done at the Department of General Surgery, Islamabad Medical Complex (IMC), from March 2020 to December 2021. The sample size was calculated using WHO software and the difference in postoperative pain in the last studies, which came out to be a total of 60 patients, 30 in each group. Postoperative VAS score in lidocaine group at 6 hours was 2.37±0.93, and that in the control group was 3.27±1.26. Keeping mean difference between the two groups 0.90±0.33 in WHO software 7.4, using confidence interval of 95% and power 80%, and ratio of sample size 1 between both groups, the sample size turned out 30 for each group. Permission for the study was taken from the Ethical review committee (ERC) of IMC and protocol for the study was approved from the research department of CPSP (College of Physicians and Surgeons of Pakistan) for dissertation as part of partial fulfilment of training requirements.

Patients scheduled for laparoscopic cholecystectomy were included. Patients with age less than 18 years or more than 60 years, who have ASA physical status 3 and greater, patients with liver compromise (Child & Pugh A to C), patients having renal failure (creatinine above normal range), patients with cardiac compromise (dysrhythmias /atrioventricular block), morbid obesity (BMI >40 Kg/m^2), history of seizures, and severe mental deficiency were excluded. Patients allergic to local anaesthetics and to all the medicines utilised in the research and patients with acute calculus cholecystitis were also excluded from the study.

Protocol of study included consent from patients to enroll into the study, randomisation by balloting into group 1 (lidocaine group) or group 2 (Control group). All patients received preoperative antibiotics, Acetaminophen and NSAIDS during and after the surgery. Patients in Group 1 received bolus of lidocaine 1mg/kg at the initiation of anaesthesia then followed by uninterrupted infusion at 2mg/Kg/hour using infusion pump. Heart rate and blood pressure were monitored on a cardiac monitor by Postgraduate trainee (PG) during surgery in the main OT and then postoperatively in PACU (Post Anaesthesia Care Unit) infusion of lidocaine was continued for 1 hour after surgery. Both groups received Intramuscular Diclofenac 12 hourly and intravenous acetaminophen infusion 8 hourly. Opioid was given if patient's pain was severe as per VAS score of 7 or more at any time in post-operative period and was recorded. VAS for pain was used to measure postoperative pain at 2 hours, 6 hours, 12 hours, and 24 hours after surgery by the on-call postgraduate surgery trainee who had no knowledge of which group the patient belonged to. Time for the first spontaneous ambulation of the patient was also recorded after surgery for both groups. All data was collected on predesigned performas by PG to maintain sanctity of data and maintenance of patient care. After completion of the study, data was entered on SPSS and analysed. Continuous and categorical data were stated in means ± SD and frequency and percentages respectively. Comparison among the two groups was done using t-test or chi-square test for continuous or categorical variables respectively. The p-values were calculated using student t-test for continuous variables and chi-square test for categorical variables. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 60 patients were designated for the study and divided into Group 1 (lidocaine infusion Group) and Group 2 (Control) by balloting. Mean age of patients was 41.7 ± 8.58 years. Out of total patients, 49(81.7%) were females and 11(18.3%) were males with mean weight 71.2 ± 12.4 Kg.

All cases were admitted through OPD for elective cholecystectomy. None of the cases belonged to ASA 3 or higher group. Baseline characteristics of both groups were identical and statistically not significant.

Mean VAS of group 1 *versus* group 2 at 2 hours, 6 hours, 12 hours, and 24 hours were 3.47 ± 0.82 *vs.* 6.27 ± 0.52 (p<0.001), 2.7 ± 0.75 *vs.* 4.8 ± 0.8 (p<0.001), 2.0 ± 0.49 *vs.* 3.93 ± 0.94 (p<0.001), 0.73 ±0.82 *vs.* 2.2 ±0.61 (p<0.001). Time for spontaneous ambulation after surgery was 5.57 ± 1.55 hours for group 1 versus 7.3 ± 1.9 hours for group 2 (p<0.001, Table I).

Table I: Comparison of outcome variables in both groups.

Variable	Cases (n=30)	Controls (n=30)	p-value
Mean VAS at 2 hours	3.47 ± 0.82	6.27 ±0.52	<0.001
Mean VAS at 6 hours	2.7 ± 0.75	4.8 ± 0.8	<0.001
Mean VAS at 12 hours	2.0 ± 0.49	3.93 ± 0.94	<0.001
Mean VAS at 24 hours	0.73 ± 0.82	2.2 ± 0.61	<0.001
Ambulation time (hours)	5.57 ± 1.55	7.3 ± 1.9	<0.001

p-values were calculated using student t-test.

DISCUSSION

Cholecystectomy is the most common operating room procedure performed in hospitals these days and is generally performed with minimally invasive techniques using laparoscopic instruments. Ninety percent of cholecystectomies in USA are done using minimally invasive technique that is laparoscopic.[14] This procedure results in less pain in postoperative period, improved cosmetic

results, and lesser time in hospital and early return to work compared to open cholecys-tectomy.[15] The best approach to control perioperative pain should consist of strategy to reduce opioid requirements. Overprescription of opioids has reached an alarming level across the world,[16] and surgery may become the factor for long-standing and preventable practice of opioids in a lot of patients.[17,18] According to some studies, intravenous infusion of lidocaine is shown to have a beneficial role in the recovery of laparoscopic cholecystectomy in terms of acute pain after surgery, need for opioids and early ambulatory time after the surgery. However, the evidence is scarce and to date, it is not established if systemic lidocaine has a helpful part in managing acute postoperative pain following laparoscopic cholecystectomy. The present study was designed to compare intravenous lidocaine infusion adjunct to adjunct to NSAID and acetaminophen with regular analgesics for postoperative mean pain score and mean ambulation time after laparoscopic cholecystectomy. Total sixty (n=60) adult patients, both males and females between the ages of 18-60 years planned for laparoscopic cholecystectomy were registered and randomly allocated to two treatment groups (Lidocaine and Ringer Lactate). Postoperative pain 2, 6, 12, and 24 hours and mean ambulation time were matched in both the groups. The outcomes of this study showed that mean VAS was considerably lower in lidocaine group as compared to the ringer lactate group at 2 hours, 6 hours, 12 hours, and 24 hours were 3.47±0.82 *vs.* 6.27±0.52 (p<0.001), 2.7±0.75 *vs.* 4.8±0.8 (p<0.001), 2.0±0.49 *vs.* 3.93±0.94 (p<0.001), and 0.73±0.82 *vs.* 2.2±0.61 (p<0.001) respectively.

Time for spontaneous ambulation was also significantly shorter after surgery was 5.57±1.55 hours for group 1 *versus* 7.3±1.9 hours for group 2 (p<0.00).

The results are alike with previously published figures on the topic. In a similar study among local population, Shahzad *et al.* compared fewer doses of systemic lidocaine and placebo for total pain score in postoperative period and total analgesic necessity in patient having open cholecystectomy. Patients were casually assigned to either saline group (S) or lidocaine infusion (L). Their result showed that the total need for analgesia and total VAS pain score were revealed to be considerably less in the lidocaine infusion (L) group (p-values 0.04 and 0.29 respectively), as related to the control group.[5]

In another similar study, Chen *et al.* reported that VAS score at postoperation immediately, PACU 30 minutes, postoperative 2, 6, 12, 24h in lidocaine group were 2.76±0.97, 2.37±0.93, 2.10±1.12, 1.76±0.97, and 1.20±0.76 respectively, which were lower than those in the control group (3.83±1.34, 3.27±1.26, 3.06±1.20, 2.63±0.88, and 1.90±0.84 respectively; all p<0.05). The time of PACU retention, postoperative ambulation and first intestine venting were 39.90 ± 8.06 minutes, 11.93±1.68 hours and 10.16±1.05 hours respectively in the lidocaine group, were also shorter than those in the control group ([48.23±10.04 minutes, 13.16±1.58 hour, and 11.13±1.30 hour, all p<0.05]).[19]

In a recent meta-analysis of 5 RCTs comprising of 274 patients, Zhao JB *et al.* studied the safety and effectiveness of intravenous lidocaine infusion for the management of pain following laparoscopic cholecystectomy. Outcomes of their study revealed noteworthy differences between groups relating to scores of visual analogue scale at 12-hour (weighted mean difference [WMD] =-0.743, 95% CI: -1.246 to -0.240, p = 0.004), 24-hours (WMD=-0.712, 95% CI: -1.239 to -0.184, p = 0.008), and 48 hours (WMD=-0.600, 95% CI: -0.972 to -0.229, p = 0.002) following laparoscopic cholecystectomy. Important variations were established concerning the use of opioids at 12 hour (WMD=-3.136, 95% CI: -5.591 to -0.680, p = 0.012), 24 hours (WMD=-4.739, 95% CI: -8.291 to -1.188, p = 0.009), and 48 hours (WMD=-3.408, 95% CI: -5.489 to -1.326, p = 0.001) after laparoscopic cholecystectomy. Authors concluded that IV infusion of lidocaine considerably lessened scores of pain and requirement for opioid following laparoscopic cholecystectomy. Side effects due to perioperative lidocaine infusion like visual disturbances, lightheadedness, neurologic changes, cardiac dysrhythmias, and dizziness are very rare. This study had very few side effects in the lidocaine group.

Li *et al.* in another recent meta-analysis of randomised controlled trials directed to define the safety and effectiveness of intravenous infusion of lidocaine for the management of acute pain following laparoscopic cholecystectomy.[7] They included six RCTs in the meta-analysis and the main investigative outcome was score of visual analogue scale (VAS) and opioids requirements at 12 hours, 24 hours, and 48 hours. Another point was the duration of stay in the hospital and side effects related to opioids. Their results showed that systemic lidocaine was related with fewer score of pain and less consumption of opioids at 12 hours, 24 hours, and 48 hours after laparoscopic cholecystectomy. Authors established that IV lidocaine use was capable to lessen acute pain after surgery, the overall need for opioids and side effects due to opioids after laparoscopic cholecystectomy.[7]

Song *et al.* measured the outcome of perioperative intravenous infusion of lidocaine on the intensity of pain, response of cytokine, and bowel function following laparoscopic cholecystectomy. A total of eighty patients scheduled for laparoscopic cholecystectomy were randomly allocated to be given intravenous infusion of lidocaine or an equivalent amount of saline. Their results revealed that lidocaine considerably lessened the intensity of pain at 2 hours (lidocaine 3.01±0.65 cm *vs.* placebo 4.27±0.58 cm, p = 0.01) and 6 hours (lidocaine 3.38±0.42 cm *vs*. placebo 4.22±0.67 cm, p = 0.01) and overall consumption of fentanyl 24 hours following surgery (lidocaine 98.27±16.33 µg *vs*. placebo 187.49±19.76 µg, p = 0.005).[8]

Bakan *et al.* explored whether intravenous anaesthesia comprising of lidocaine and dexmedetomidine could be used instead of opioid, perhaps another method for laparoscopic cholecystectomy and will require less fentanyl after surgery and fewer frequency of nausea and vomiting in postoperative period. Total eighty adult patients undergoing laparoscopic cholecystectomy

were assigned randomly into two groups to either have anaesthesia devoid of opioid with propofol, lidocaine and dexmedetomidine infusions (Group DL) or anaesthesia containing opioid with propofol and remifentanil, infusions (Group RF). Their results showed that even though with increased time to recovery, Group DL had considerably fewer scores for pain, analgesic needs and requirement for ondansetron.[20]

The present results and several other similar studies highlighted that perioperative intravenous infusion of lidocaine improves postoperative control of pain and lessens the use of opioid analgesic following laparoscopic cholecystectomy. Nevertheless, there are few limitations and restrictions in this study. Sample size was comparatively smaller and secondly, we did not take into account the total amount of opioid utilised in after surgery as outcome variable. Although the present subject did not have side effects and there was no death of any patient as lidocaine infusion had been administered within safe dosage according to body weight, it is still important to emphasise that it is an off-license intravenous analgesia. Whenever administered to patients, it should be done with caution and constant monitoring. Foo *et al.* and his team published a paper in which they extensively analysed the efficacy and safety of systemic lidocaine for pain recovery after surgery.[21] It contains important recommendations regarding its use in patients. The authors suggest further studies with larger sample size to validate current study results, dosage and safety for intravenous lidocaine administration before recommending its routine use.

CONCLUSION

This study showed lower pain scores at all-time intervals and shorter ambulation time in patients who received intravenous infusion of lidocaine when compared with patients in the control group who received only regular analgesics for laparoscopic cholecystectomy.

FUNDING:
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ETHICAL APPROVAL:
Ethical approval of this study was obtained from the ethical committee of Islamabad Medical Complex, NESCOM.

PATIENTS' CONSENT:
Written informed consent were taken from all the patients participating in this study.

COMPETING INTEREST:
All authors declare no competing interest.

AUTHORS' CONTRIBUTION:
FTZS: Contributed to the design, data acquisition, interpretation, and drafting of the manuscript.
RS: Contributed to analysis, interpretation of data for the work, drafting, and revising it critically for important intellectual content.
FTZN, RS, RS, MZS, AJ, AJ: Approved the final version of the manuscript to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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