Original Research Article

Indian Journal of Anesthesia and Analgesia
2019; 6(5) (Part - II): 1857-1862
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6519.53

A Comparative Study to Evaluate the Efficacy of three Different Doses of Intraoperative Infusion of Intravenous Preservative Free Lidocaine in Patients Undergoing Laparoscopic Cholecystectomy

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Abstract

Background: Surgical stress and pain elicit a consistent and well-defined metabolic response, involving release of neuroendocrine hormones and cytokines, which leads to a myriad of detrimental effects. Lidocaine is a local anesthetic and antiarrhythmic which has anti-inflammatory, analgesic and anti-hyperalgesic properties. There are studies comparing differentt doses of infusion for varying periods of time, our study was aimed to evaluate the efficacy of intraoperative infusion of three different doses of intravenous Lidocaine in patients undergoing Laparoscopic cholecystectomy. *Methods:* Forty-eight inpatients were divided into 3 groups of 16 each. All the groups received intravenous lidocaine infusion of 1.5 mg/kg bolus over 10 min, 30 min before the skin incision followed by 1 mg/kg/hr in Group A, 2 mg/kg/hr in Group B and 3 mg/kg/hr in Group C infusion throughout the surgery and continued for 1 hour after the skin closure. The outcome measures are the time at which first visual analogue scale (VAS) was more than 4 requiring rescue analgesia of Inj Tramadol, total number of doses and side effects of lignocaine in 24 hours of postoperative period. *Results:* Onset of breakthrough pain (VAS>4) was significantly prolonged in Group C than Group A and B. Time for first rescue analgesia was significantly prolonged in Group C than Group A and Group B. Overall Analgesic consumption was significantly lower in Group C than other groups. *Conclusion:* Intraoperative infusion of intravenous preservative free Lidocaine at 3 mg/kg/hour is more efficient than 2 mg/kg/hour and 1 mg/kg/hour in controlling postoperative pain and reduces the requirement of postoperative analgesics.

Keywords: Lignocaine infusion; Pain; Postoperative analgesia.

How to cite this article:

Shobha Dhayalan, Asha Narayan Gowda, Krishna Prasad Prabhu. A Comparative Study to Evaluate the Efficacy of three Different Doses of Intraoperative Infusion of Intravenous Preservative Free Lidocaine in Patients Undergoing Laparoscopic Cholecystectomy. Indian J Anesth Analg. 2019;6(5 P-II):1857-1862.

Introduction

Acute postoperative pain is a complex physiologic reaction to tissue injury, visceral distension or disease which is manifested by autonomic, psychological and behavioral responses that result in patient specific unpleasant, unwanted sensory and subjective emotional experience. Moderate to severe acute pain, regardless of site, can affect nearly every organ function and may adversely influence postoperative morbidity and mortality. Opioids remain the primary pharmacologic therapy for moderate to severe postoperative pain with side effects such as nausea, vomiting[1], constipation, urinary retention and ventilatory depression. Non-opioid analgesics NSAIDS, COX-1 and COX-2 inhibitors is used to treat minor or moderate acute postoperative pain. These are hepatotoxic, affect platelet function with gastrointestinal bleeding risk.[2] Local anesthetic (LA) are increasingly being

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Received on 12.07.2019, **Accepted on** 16.08.2019

used in the treatment of chronic malignant and non malignant pain.[3] It provides effective postoperative analgesia, reduces opiate consumption, accelerates the recovery of bowel function and facilitates rehabilitation after surgery with a good safety margin.[4] There are studies conducted on the varying doses of preservative free lidocaine infusion from 1.5–5 mg/kg/hr[5-7] on the requirement of postoperative analgesics. Our study is aimed to evaluate the efficacy of intraoperative infusion of three different doses of intravenous (IV) lidocaine.

Materials and Methods

This randomized double blind clinical study was approved from Institutional Ethical Committee. Sample size was calculated assuming a difference in total analgesic requirement of at least 20% with different doses of IV lidocaine infusion. With the alpha error 0.05 and 80% power we found 14 patients were required in each group. We included 16 patients in each group to compensate for dropout. Forty-eight patients fulfilling inclusion criteria who were willing to give informed consent were included in the study. Then patients were divided into three groups of 16 patients each by using the computer generated randomization table (http://www.randomizer.org). Allocation concealment done by sealed envelope method into 3 study groups. Patients providing written informed consent voluntarily, posted for elective laparoscopic cholecystectomy, between 18 and 60 yrs of either sex, ASA Grade I and II with body mass index between 19 and 28 were included in the study. Patients with known hepatic or renal dysfunction, any cardiac dysrhythmias or atrioventricular block, allergic to the study drug were excluded from the study. During the preoperative assessment education regarding use of VAS was given to the patients. All patients were kept nil per orally for 8 hours. On arrival to the pre-operation room, intravenous access was secured. Non Invasive Blood Pressure (NIBP), Pulse Oximetry and Electrocardiogram (ECG) were connected. The baseline systolic, diastolic and mean arterial blood pressures (SBP, DBP and MAP), heart rate (HR) and oxygen saturation (SpO_2) were recorded. Drug infusion was prepared by the anesthesiologist who was not involved in the study. All the subjects in all the three groups received intravenous preservative free lidocaine bolus infusion at the dose of 1.5 mg/kg over 10 minutes, 30 minutes before the skin incision. Bolus dose was followed by continuous infusion as follows:

Group A received a continuous IV infusion at the dose of 1 mg/kg/hour, throughout the surgery and continued for 1 hour after the skin closure via infusion pump.

Group B received a continuous IV infusion at the dose of 2 mg/kg/hour, throughout the surgery and continued for 1 hour after the skin closure via infusion pump.

Group C received a continuous IV infusion at the dose of 3 mg/kg/hour, throughout the surgery and continued for 1 hour after the skin closure via infusion pump.

On arrival to the operating room, NIBP, Pulse Oximetry and ECG were connected. SBP, DBP, MAP, HR and SpO_2 monitoring continued perioperatively. Intubation was done according to the Institute protocol. Persistent intraoperative tachycardia and hypertension was managed by deepening the plane of anesthesia with additional opioids who were excluded from further analysis. The patient was extubated once the consciousness regained and was transferred to the post-anesthesia care unit (PACU), where the infusion was continued for 1 hour following surgical skin closure. In PACU, hemodynamic variables and any signs of adverse effects like light headedness, perioral numbness, nausea and vomiting, Ramsay sedation score, arrhythmias, hypotension and Aldrete score were monitored and recorded at every 15 minute interval. Aldrete score more than or equal to 8 is taken as a discharge criteria from PACU to the surgical wards. In surgical wards hemodynamic variables and any signs of adverse effects were recorded every 2 hours for 24 hours after the discontinuation of intravenous lidocaine infusion. Intensity of pain was assessed and recorded immediately after extubation and then at the interval of 15 minutes for one hour in the immediate postoperative period and at the interval of 120 minutes for 24 hours after the discontinuation of lidocaine infusion. The intensity of pain was assessed with VAS by asking the patient to indicate on the 10 cm line at the point that corresponded to the level of pain intensity they felt. The distance in centimeter from no pain end of VAS (Appendix)[8] to the patient's mark was used as a numerical index of the severity of pain. Time for first rescue analgesia was recorded when patient's VAS score was more than 4 and was treated with Inj.Tramadol 50 mg IV. Further VAS score was assessed at the minimal interval of 2 hours in the first 24 hours and Inj.Tramadol was administered when the VAS score was more than 4. The total dose of analgesia consumed in 24 hours was recorded. Any adverse effects were monitored.

Statistical Analysis

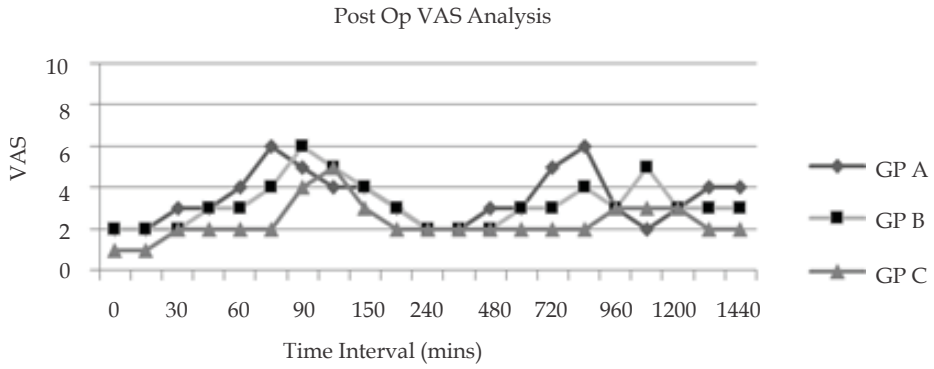
Data was entered into Microsoft excel sheet and was analyzed using SPSS 21 version software. Categorical data was represented in the form of frequencies and proportions. Chi-square test was used as test of significance for parametric data ANOVA test was used as test of significance for non-parametric data. p value of < 0.05 was considered to be statistically significant.

Results

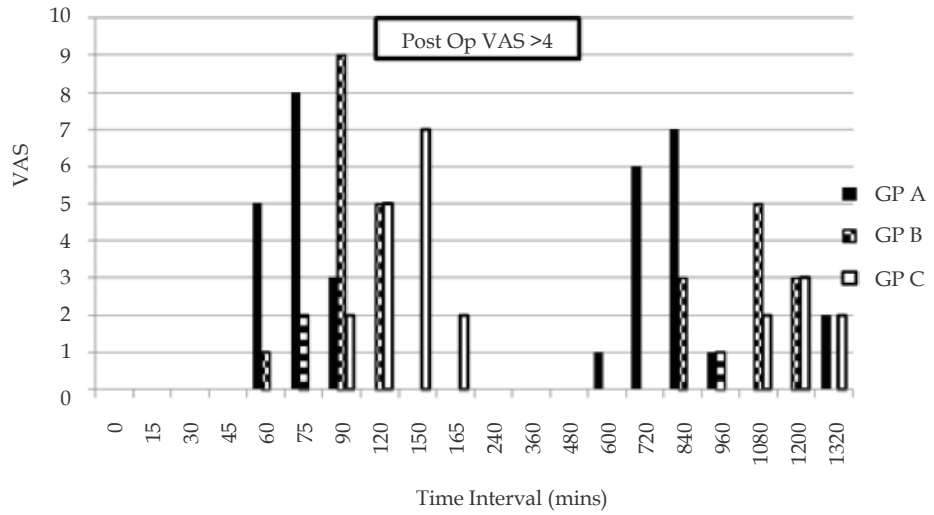
Demographic data (Table 1) did not differ significantly with respect to age, gender, ASA score, height, BMI and duration of surgery between the groups. Onset of breakthrough pain (VAS > 4) was significantly prolonged in Group C than Group A and B. Subsequent VAS were significantly

Table 1: Demographic Characteristics

	GP A	GP B	GP C
Age (yrs)	45.25 ± 5.56	43.94 ± 9.09	42.69 ± 7.49
Sex (M:F)	03:13	02:14	02:14
Weight (kg)	62.19 ± 6.96	61.44 ± 7.24	62.56 ± 5.96
Height (m)	1.64 ± 0.15	1.57 ± 0.20	1.59 ± 0.21
BMI (kg/m^2)	23.81 ± 2.67	23.92 ± 3.22	24.27 ± 2.33
ASA (1:2)	09:07	10:06	10:06
Duration of surgery (mins)	58.75 ± 9.57	58.13 ± 10.46	59.38 ± 9.258



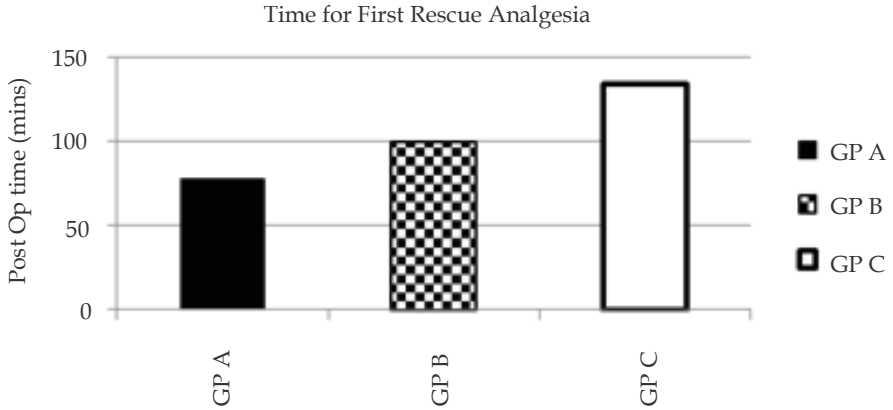
Graph 1: Postoperative VAS analysis



Graph 2: Postoperative VAS >4

Table 2: Time for First Rescue Analgesia

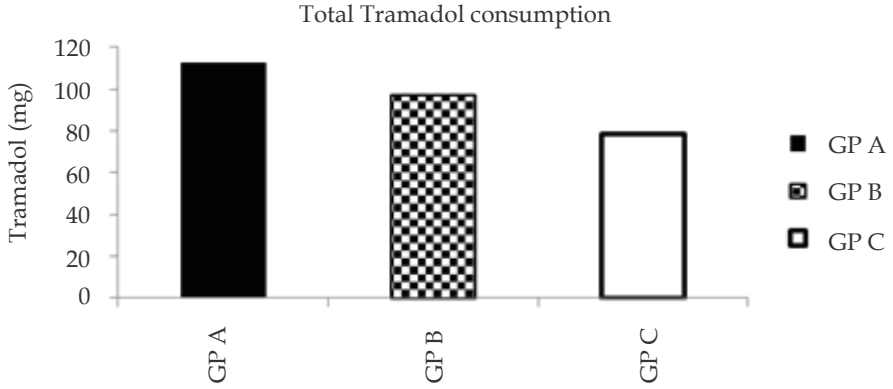
	GP A	GP B	GP C	*p* value
Time for First Rescue Analgesia (min)	77.81 ± 12.51	99.38 ± 17.21	134.06 ± 22.89	0.001*



Graph 3: Time for first rescue analgesia

Table 3: Total Tramadol Consumption in 24 Hours

	GP A	GP B	GP C	*p* value
Total tramadol consumption (mg)	112.50 ± 22.36	96.88 ± 22.12	78.13 ± 25.62	0.001*



Graph 4: Total analgesia consumed in first 24 hours

lower in Group C than Group A and B. Number of patients with VAS > 4 was significantly lower in Group C than other two Groups (Graph 1 and 2). Majority of the patients received their first rescue analgesia by around 75 min in Group A, 120 min in Group B and around 150 min in Group C (Table 2, Graph 3). Total tramadol consumption was 112 mg in Group A, 97 mg in Group B and 78 mg in Group C ($p < 0.001$) which was significantly lower than in Group A and B in first 24 hours (Table 3, Graph 4). There was delayed recovery in Group C when compared to other two groups.

Discussion

Lidocaine when administered intravenously reduces acute pain by decreasing ileus and postoperative nausea and vomiting.[9] IV lidocaine has analgesic[10], anti inflammatory[11] and anti hyperalgesic properties.[12] Molecular and genetic studies indicate that LA primarily inhibit glycine receptors.[13] LA block the generation, propagation and oscillations of electrical impulses in electrically excitable tissue both peripherally and centrally.[14,15]

Safety level of the IV lidocaine was considered with respect to the study[10,16,17] when administered as infusion where the plasma level of lidocaine was below the toxic level.

In our study, patients posted for elective laparoscopic cholecystectomy under general anesthesia with perioperative IV lidocaine being administered at 3 mg/kg infusion for 1 hour post skin closure had significantly prolonged onset of break through pain with VAS > 4 than in patients who received 1 mg/kg/hr and 2 mg/kg/hr infusion. Our study showed opioid sparing properties like nausea and vomiting which can delay the hospital discharge, increasing the expenditure[18,19] and patient dissatisfaction. Postoperative analgesic requirement was significantly lower in Group C than with Group A and B. But with lidocaine infusion of 3 mg/kg had delayed awakening from patients being less responsive to endotracheal tube. But study has showed PACU discharge was not delayed[20] in Group C. Perioperative lidocaine had the advantage of blunting sympathetic responses to tracheal intubation and extubation.[21] Complications related to lignocaine infusion was not noticed in our study.

Conclusion

With higher dosage of lignocaine infusion, rescue analgesia and total analgesic requirement was significantly lower. It improved postoperative pain scores in patients. It can be used as an alternative to epidural administration where it is difficult or contraindicated. Lidocaine provides the advantage of not requiring time and expertise in performing tranversus abdominal blocks.[22] Perioperative lidocaine improves postoperative quality of recovery in patients undergoing ambulatory surgery.[23] It is less expensive, easy to administer and relatively safe so can be used as an alternative intervention with wide potential applicability.

Limitations

We have not measured serum lidocaine levels. Also the effect of short-term lidocaine infusion on duration of hospital stay was not studied.

Source of support: Nil

Presentation at a meeting: Nil

Conflicts of interest: None

Appendix:

Visual Analogue Scale (VAS)

Ranging from zero (No pain) to ten (Maximal pain)

0 – No pain

1,2 – Mild, annoying pain

3,4 – Nagging, uncomfortable troublesome pain

5,6 – Distressing, miserabe pain

7,8 – Intense, dreadful horrible pain

9,10 – Worst possible unbearabe, excruciating pain

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