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CLINICAL STUDY ON PERIOPERATIVE IV LIGNOCAINE INFUSION ON POST OPERATIVE ANALGESIA IN PATIENTS UNDERGOING SURGERY FOR GASTROINTESTINAL MALIGNANCIES.

Dr. Madiha Nusrat MBBS, PG Student, Resident, Dept. of Anaesthesialogy, GMCH Aurangabad.

Dr. Kalyanam Dayasagar MBBS, PG Student, Resident, Dept. of Anaesthesialogy, GMCH Aurangabad.

Dr. Ramakant Alapure MBBS, MD Anaesthesiology, Associate Professor, Dept. of Anaesthesiology, Govt Cancer Hospital, GMCH Aurangabad.

ABSTRACT **Background And Aims:** Optimal perioperative pain management is crucial in cancer patients undergoing surgery for gastrointestinal malignancies. This study aimed to assess the efficacy of perioperative intravenous lidocaine infusion on postoperative pain intensity and analgesic requirement in these patients. **Methods:** This prospective, randomized, single-blinded study included 60 patients aged 18-60 years, ASA physical status I or II, undergoing elective surgery for gastrointestinal malignancies. Patients were randomized into two groups: Group A (n=30) received intravenous lidocaine 1.5 mg/kg bolus followed by 1.5 mg/kg/h infusion until 1 hour after surgery, while Group B (n=30) received an equal volume of normal saline. The primary outcomes were postoperative pain scores (Visual Analogue Scale) and analgesic requirement over 24 hours. Hemodynamic parameters and sedation scores were also evaluated. **Results:** The lidocaine group had significantly lower pain scores until 6 hours postoperatively ($p<0.05$) and required rescue analgesia much later than the control group (793±429 min vs. 87±126.61 min, $p<0.0001$). The total dose of rescue analgesic (fentanyl) was significantly less in the lidocaine group (59±26.04 µg vs. 117.16±47.26 µg, $p<0.005$). The lidocaine group showed better attenuation of hemodynamic responses to intubation and extubation ($p<0.05$). However, it had higher sedation scores until 4 hours postoperatively ($p<0.05$). The incidences of bradycardia and hypotension were not statistically significant. **Conclusion:** Perioperative intravenous lidocaine infusion provided excellent analgesia, opioid-sparing effects, and hemodynamic stability in patients undergoing surgery for gastrointestinal malignancies, although increased sedation was observed.

KEYWORDS : Pain, Lignocaine infusion, Post Operative analgesia, Opioid sparing effect,Gastrointestinal malignance.

INTRODUCTION

Cancer patients undergoing surgery for gastrointestinal malignancies often experience chronic pain originating from primary tumor invasion or its pressure effects. [1] Inadequate postoperative pain management leads to patient suffering, increased healthcare costs, prolonged hospital stay, delayed recovery, and adverse effects on respiratory, cardiovascular, gastrointestinal, urinary, and neuroendocrine systems. [2-8] Optimal postoperative analgesia is associated with reduced postoperative cognitive impairment, lower risk of chronic postsurgical pain, early mobilization and rehabilitation, decreased clinical expenses, and improved quality of life. [9-14]

The concept of pre-emptive analgesia, which inhibits nociceptors before they are sensitized, preventing central alterations induced by afferent input after surgery and receptor changes responsible for central sensitization, neuropathic pain, hyperalgesia, and allodynia, has gained popularity. [13,16-21] In gastrointestinal cancer surgeries, long-standing preoperative pain and NSAID consumption can lead to opioid dependence or resistance. Deranged coagulation profiles and compromised liver and kidney functions limit the use of regional anesthesia or newer nerve block techniques. [22]

Intravenous (IV) lignocaine infusion has been suggested as a suitable alternative to overcome these limitations while achieving opioid-free analgesia. [22] Lignocaine is easily available, inexpensive, simple, and safe to administer without requiring expertise, with additional benefits such as preventing propofol-induced injection pain, protecting against bronchial reactivity by bronchotracheal relaxation during surgery, and increasing the depth of general anesthesia. [25,33,34,35] Its high therapeutic index [30-32] makes it an attractive subject for clinical research. [22] This study aimed to determine the risk-benefit profile of perioperative IV lignocaine infusion on postoperative analgesia in patients undergoing surgery for gastrointestinal malignancies.

MATERIALS AND METHODS

This prospective, randomized, single-blinded study included 60 patients aged 18-60 years, ASA physical status I or II, undergoing elective surgical procedures for gastrointestinal malignancies. After obtaining institutional ethics committee approval and written informed consent, patients were randomized into two groups using a computer-generated random number table and the opaque sealed envelope technique: Group A (n=30) received intravenous lignocaine, and Group B (n=30) received placebo. Exclusion criteria were emergency surgeries, uncontrolled systemic diseases (hypertension, diabetes mellitus, asthma, chronic obstructive pulmonary disease), G6PD deficiency, pregnancy, breastfeeding, hepatic or renal dysfunction, cardiac dysrhythmias/AV blocks/WPW syndrome, hypersensitivity to study medication, and ASA grade III and IV.

All patients underwent routine pre-anesthetic evaluation, and baseline vital parameters were recorded. Patients were familiarized with the study, including the use of the visual analog scale (VAS) for pain assessment. In the operating room, standard monitoring was applied, and baseline parameters were noted. Intravenous access was secured, and Ringer's lactate was started at 10 ml/kg.

Group A received intravenous 2% Lignocaine 1.5 mg/kg bolus 30 minutes before incision, followed by an infusion of 1.5 mg/kg/h until 1 hour after surgery completion. Group B received an equal volume of normal saline 0.9% infusion. Both groups received general anaesthesia with Inj. Fentanyl 2ug/kg, Inj. Midaz 0.02mg/kg as premedication; Inj. Propofol 2mg/kg, Inj. Scoping 2 mg/kg as induction agents; Inj. Vecuronium and Sevoflurane as maintenance along with Inj. Paracetamol and Inj. Tramadol 1mg/kg. Heart rate, systolic and diastolic blood pressure, mean arterial pressure, SpO2, and ECG were monitored perioperatively.

Postoperatively, patients were evaluated for analgesia and recovery up to 24 hours. Pain scores were assessed hourly using the VAS (0-10) until the patient had a VAS ≥ 4, when rescue analgesia (fentanyl 25 µg bolus + infusion) was administered as required. The duration of analgesia was measured from the completion of local anesthetic administration until the first need for rescue analgesia. Patients were observed for side effects such as arrhythmias, hyper/hypotension, bradycardia, nausea, and vomiting, and treated accordingly.

Data analysis was performed using SPSS version 20 (Statistical Package for the social Sciences). Continuous variables were compared using the unpaired Student's t-test, and qualitative data were compared using the chi-square test. Demographic data, hemodynamic data, duration of analgesia, and postoperative analgesia were evaluated using the independent sample Student's t-test. A p-value < 0.05 was considered statistically significant.

RESULTS:

The demographic data were comparable between the two groups (Table 1). The mean VAS pain scores at rest were significantly lower in

the lignocaine group compared to the control group until 6 hours after extubation ($p<0.05$), but beyond that time point VAS scores between two groups were comparable ($p>0.05$) (Figure 1). The first dose of rescue analgesia (fentanyl) was required at 13 hours in the lignocaine group versus 1.452 hours in the control group ($p<0.0001$). The total 24-hour rescue analgesic dose was significantly less in the lignocaine group (59±26.04 µg vs. 117.16±47.26 µg, $p<0.005$).

The lignocaine group showed better attenuation of the sympathetic response during laryngoscopy, intubation, and extubation. The mean heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) remained significantly lower in the lignocaine group compared to the control group during the entire infusion period ($p<0.001$), although within the clinically acceptable range. The Ramsay sedation scores were significantly higher in the lignocaine group until 4 hours after extubation ($p<0.05$) but comparable between groups beyond that time point ($p>0.05$) (Figure 2).

In the lignocaine group, the incidence of bradycardia was 6.67%, and hypotension was 13.33%. No other side effects like headache, dizziness, perioral numbness, or seizures were observed. The incidence of postoperative complications was not significant between the groups.

DISCUSSION:

To attain desired clinical effects, plasma levels of lignocaine between 0.5 to 5 mcg/ml are required. Based on evidences from previous studies showing plasma levels of lignocaine remain well below toxic levels after giving bolus of 1.5mg/kg followed by infusion at the rate 1.5 mg/kg/hr, we decided to select this particular dose and duration of lignocaine infusion.

At baseline, there were no significant differences in hemodynamic parameters between the groups. After intubation, at 0, 5 and 15minutes, the heart rate, SBP, DBP increases in both groups, but it is significantly lower in the lignocaine group than in the control group at all time points ($p < 0.0001$). But after intubation at 0 minutes mean MAP increased in control group, but the MAP in Lignocaine group decreased significantly ($p < 0.005$); at 5 and 15 minutes post-intubation the MAP in lignocaine group is significantly less than in the control group ($p < 0.05$). This suggests that lignocaine effectively reduces the sympathetic response to intubation. At the completion of surgery, the heart rate decreases in both groups, but it is still lower in the lignocaine group than in the control group, although the difference is not significant ($p = 0.0766$). But At the completion of surgery, mean SBP, DBP and MAP in both groups is comparable ($p = 0.6301$, $p = 0.8309$, $p = 0.8786$ respectively). After extubation, the heart rate, SBP increases again in both groups, but it is significantly lower in the lignocaine group than in the control group at 0, 15 and 30 minutes post-extubation ($p < 0.05$). But after extubation, at 0 minutes mean DBP and mean MAP increased in control group, but the DBP and MAP in the Lignocaine group decreased significantly ($p<0.05$); at 15 minutes and 30 minutes post-extubation the DBP and MAP in lignocaine group is significantly less than in the control group(p-value < 0.05).

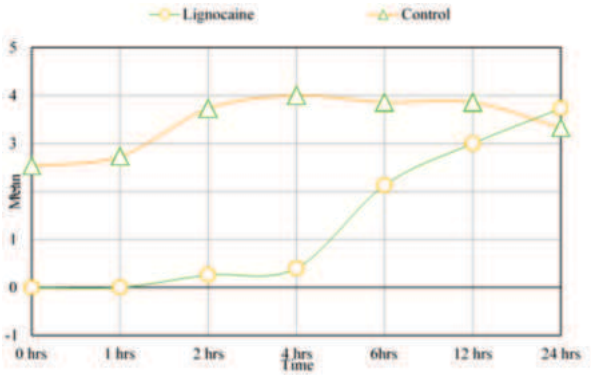

Figure 1 - Comparison of variation in mean Visual Analogue Scale score after extubation.

This indicates that lignocaine also attenuates the stress response to extubation. The heart rate, SBP, DBP and MAP in lignocaine group is lower than in control group upto 2 hrs post extubation ($p < 0.02$). This difference in heart rate between 2 groups can be explained by the lignocaine infusion which was administered upto 60 min post extubation.

Our study shows that lignocaine has beneficial effects on heart rate, SBP, DBP and MAP after intubation and extubation, as it reduces the magnitude and duration of the haemodynamic response to these procedures. Thus our study further confirms that lignocaine blunts direct laryngoscopic intubation reflexes and extubation reflexes.

Krishna murthy et al[29] had shown similar results in their study. Kaba et al[15], Baral BK et al[22] and Lauwick et al[27] also observed and described hemodynamic stability obtained by iv lignocaine infusion in their studies.[29,36-39]

We measured the post operative pain by Visual analogue scale at 0, 1, 2, 4, 6, 12 and 24 hrs at rest. In our study mean pain scores were significantly less in lignocaine group as compared to control group not only upto 4 hrs after extubation ($P<0.0001$, highly significant), but also upto 6 hrs after extubation (2.13 ± 1.81 vs 3.86 ± 1.96 $p = 0.0005$). Pain scores between 2 groups after 6 hrs are comparable between 2 groups ($p > 0.05$, not significant). The highest pain score observed in lignocaine group was 3.73 ± 1.36 at 24 hrs as compared to control group in which highest pain score was 4 ± 1.66 at 4 hrs postoperatively. The mean score in the control group decreased to 3.33 ± 1.98 at 24 hrs, this change can be explained by higher requirement of rescue analgesic in the control group. Many patients from the control group requested for analgesia by 2 hrs postoperatively (87 ± 126.61 min) and by the end of 24 hrs they had already been administered by 117.16 ± 47.26 ug of rescue analgesic.

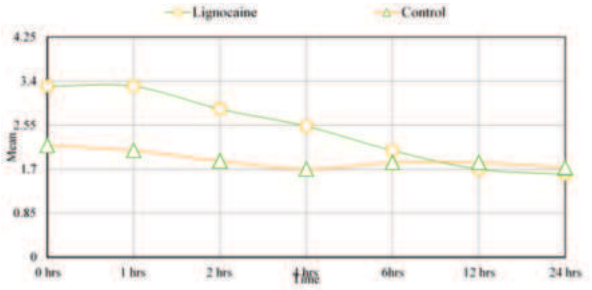

Figure 2 - Comparison of variation in Ramsey Sedation Scale after extubation at different time

Kaba et al [15]study showed that patients in the lidocaine group reported less pain during mobilisation and when coughing and less abdominal discomfort. C.Cooke et al [28] in their study showed that Intravenous lidocaine was associated with lower pain scores at rest at 24 h compared with placebo in the open subgroup. In the meta analysis of Louise Vigneault et al [26] the WMD between groups for pain control at rest was statistically significant at six hours and at 12 hr but not at 24, 48, or 72 hr.

Despite the fact that in our study all patients were of gastrointestinal malignancies undergoing major abdominal surgeries experienced pain requiring management (VAS > 4) much later (793 ± 429 min) than control group (87 ± 126.61 min) ($p<0.0001$, highly significant); the total dose of rescue analgesic administered in the lignocaine group was much less (59 ± 26.04 ug VS 117.16 ± 47.26 ug) than the control group. The lignocaine group showed significantly less consumption of fentanyl.

In the study carried out by B.K.Baral et al [22] in patients undergoing upper abdominal surgery, the total mean analgesic (Diclofenac) requirement in lidocaine group was significantly less than that in normal saline group. In the meta analysis carried out by Louise MD et al [26] the mean Morphine dose received in the control group was 46.4 mg and a reduction in morphine of 8.4 mg was observed in the IVLI group compared with the control group.

In our study patients in the Lignocaine group were observed to have significantly higher Ramsay Sedation Score (RSS) than the Control group at 0, 1, 2, and 4 hours after extubation ($p<0.05$), indicating that Lignocaine had a significant effect on increasing sedation levels during these times. However at 6, 12, and 24 hours post-extubation, there was no significant difference in RSS between the two groups ($p>0.05$), indicating that the effect of Lignocaine on sedation levels diminished over time. This is consistent with the literature that suggests that Lignocaine has a short half-life of about 1.5 hours and is rapidly metabolised by the liver. Therefore, its effect on sedation is expected to wear off within a few hours after discontinuation of infusion.

The similar observations were made by BK Baral et al[22],K D Oliveira et al [24], and S Weibel et al [23] in their studies and this sedation can be explained by the central nervous system depressant effect of lignocaine or the sedative effect of our rescue analgesic (fentanyl) [40,41].

We observed two incidences of bradycardia (HR < 50 managed by Inj. Glycopyrrolate 0.2 ug) and four of hypotension (MAP < 65) which were not significant statistically ($p > 0.05$). We assume that the possible reasons for these incidences were absence of any noxious stimuli while the patient was in deeper planes of anaesthesia (we observed these incidences happen when time between intubation and surgical stimulus was longer than usual or after extubation). We also assume that being suffering from gastrointestinal malignancies our study population has nutritional deficiencies, malabsorption leading to hypoproteinemia, anaemia which in turn leading to more free drugs being available. Hemodynamic parameters came back to normal as soon as the incision was taken in one case and after Inj Glycopyrrolate 0.2 ug in another. Hypotension was corrected by fluid therapy alone.

The study had several limitations worth noting. Firstly, the efficacy of intravenous lignocaine was not compared to thoracic epidural anesthesia, which is another common modality for perioperative pain management. Additionally, the study did not assess the potential inhalational agent-sparing effect of lignocaine infusion. While all patients underwent exploratory laparotomy, the exact surgical procedures performed (resection and anastomosis, abdominoperineal resection with colostomy, cytoreductive surgery, or feeding gastro/jejunostomy) were not accounted for or compared between groups. Furthermore, the duration of surgical procedures and consequently, the duration of lignocaine infusions, were not recorded. The time taken for extubation was also not compared between the two groups. Lastly, the Visual Analogue Scale (VAS) scores were only evaluated at rest and not during movement, which could have provided additional insight into the efficacy of lignocaine infusion for different pain modalities.

Table 1 - Demographic Data Of 2 Groups

Variables	Lignocaine Group (A)	Control Group (B)	p-value
Age in years	47.73 ± 9.93 (28 - 70)	44.6 ± 9.18 (24 - 59)	0.2098
Gender M/F	13/17	16/14	0.438
ASA Grade I/II	7/23	14/16	0.058

Summary

In conclusion perioperative lignocaine infusion in patients undergoing surgeries for gastrointestinal malignancies provides excellent analgesia with prolonged pain free periods, significant sparing of opioids along with hemodynamic stability during intubation and extubation. But lignocaine produces significant perioperative sedation, bradycardia and hypotension in the patients, who may need close monitoring in the high dependency unit.

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