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Research Article

HEMODYNAMIC RESPONSES TO INTUBATION, EXTUBATION, AND POST-OPERATIVE ANALGESIA AFTER INTRAVENOUS LIGNOCAINE IN LAPAROSCOPIC CHOLECYSTECTOMY SURGERIES: A RANDOMIZED CONTROL STUDY

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ABSTRACT

Objectives: The study aimed to evaluate the effect of intravenous (IV) lignocaine on hemodynamic responses to intubation, extubation, and post-operative analgesia in laparoscopic cholecystectomy surgeries.

Methods: This prospective, randomized, double-blinded study was conducted in patients for elective laparoscopic cholecystectomy surgery in a tertiary care hospital in Tamil Nadu. Group A (n=60) received 0.9% normal saline for perioperative IV infusion, and Group B (n=60) received preservative-free lignocaine 2% (20 mg/mL) as IV infusion. Hemodynamic responses were recorded to intubation, extubation, and post-operative analgesia in both groups. Visual analog scale (VAS) scores and pain-free period were also compared.

Results: Pulse rate (PR) and mean arterial pressure (MAP) were significantly increased in both groups during laryngoscopy and intubation, though the rise of both in the lignocaine group was significantly less than in the normal saline group ($p<0.0001$). Similarly, both PR and MAP were significantly increased during extubation in both groups ($p<0.0001$). However, the rise of both parameters in the lignocaine group was significantly less as compared to the normal saline group ($p<0.0001$). VAS scores in the immediate post-operative period were better in the lignocaine group than in the normal saline group. The mean pain-free period was less than an hour in the normal saline group, while it was approximately 4 h in the lignocaine group ($p<0.0001$).

Conclusion: This study concluded that IV infusions of lignocaine significantly increased the pain-free period post-operatively. So for those who are not affordable for epidural block, lignocaine IV infusion is a better alternative for post-operative analgesia.

Keywords: Lignocaine, Infusion, Intubation, Extubation, Hemodynamic changes.

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INTRODUCTION

Providing sufficient pain treatment after surgery is one of the important anesthesiologists' duties. Opioids are no longer the primary means of post-operative analgesia; instead, a multimodal strategy is becoming more popular. Laparoscopic cholecystectomy, despite being a minimally invasive surgery, causes many patients to suffer from moderate to severe pain. For some people, lignocaine may be useful in the treatment of pain. All the studies so far have taken into consideration only a single parameter of lignocaine utility, either attenuation of hemodynamic changes secondary to intubation and extubation or post-operative analgesia.

Evidence of intravenous (IV) lidocaine's potential to lessen post-operative pain is dates back to the 1960s. Further work in the 1980s showed that low-dose intraoperative IV lidocaine reduced post-operative pain scores. In the realm of managing chronic pain, especially neuropathic pain, lidocaine infusions have been used more recently. Perioperative IV infusion of lignocaine has been used as a method to control post-operative pain [1]. In clinical trials, IV lidocaine has been effective in providing long-lasting pain relief, in particular after major abdominal surgery such as laparoscopic colectomy and prostatectomy [2]. A recent meta-analysis confirmed these findings in abdominal surgery [3]. Lidocaine infusion may also reduce opiods, anesthetic requirements, and minimum alveolar concentration (MAC) by 20–40%, with economic benefits [2-5].

Even with continuous IV administration, the half-life of lidocaine was approximately 1.5–2 h [6]. Although the exact mechanism and analgesic-sparing effect of parenterally administered lidocaine are unclear, some authors speculate that it acts more as an antihyperalgesic than as a direct analgesic. Central sensitization was known to be induced by the mechanosensitive nociceptor class of receptors.

IV lignocaine is one of the oldest, cheapest, and most easily available drugs used for attenuating the hemodynamic response to laryngoscopy, intubation, and extubation [7-9]. Though the effects of lignocaine on controlling both hemodynamic changes during tracheal intubation and extubation and providing post-operative analgesia have been studied and established separately, it would be highly advantageous if one could use both of these effects simultaneously. Hence, the present study was planned to evaluate the effect of IV lignocaine on hemodynamic responses to intubation, extubation, and post-operative analgesia in laparoscopic cholecystectomy surgeries.

METHODS

This prospective, randomized, double-blinded study was conducted after ethics committee approval and informed consent from all patients between the ages of 30 and 60 years. ASA 1 and 2 patients were electively scheduled for elective laparoscopic cholecystectomy surgery in a tertiary care hospital in Tamil Nadu for a period of 1 year. Patients with predicted difficult tracheal intubation, a BMI <18 or >25 kg/m^2,

and whenever the surgical procedure necessitated the conversion of laparoscopic to open cholecystectomy were excluded from the study.

Randomization was done using a computer-generated random number. In this study, both the patient and the investigator were blinded. The patients were divided into groups A and B of 60 patients each.

1. Group A: 0.9% normal saline was used for perioperative IV infusion
2. Group B: preservative-free lignocaine 2% (20 mg/mL) (xylocard) used as an IV infusion started at a dose of 1.5 mg/kg of lignocaine given as a bolus over 10 min before induction, followed by a continuous infusion of 1.5 mg/kg/h till 1 h post-operatively.

Sample size

Sample size was calculated by using the formula n=2σ2 (Zα+Zβ) 2/Δ2, where Zα=1.96, Zβ=1.28, and Δ= difference in mean pain-free period =175 min. We conducted a pilot study on 10 patients in each group and found there was a difference of 175 min in post-operative pain-free period. The primary objective of the study was to compare the post-operative pain-free period between the lignocaine group and the normal saline group. An effect size of 0.52 was kept for the workup of the sample size. With a two-tailed distribution, level significance at 5%, power of 80%, and an allocation ratio of 1:1, the required sample size was 60 in each group.

Procedure

All the patients were subjected to a thorough pre-anesthetic checkup, including a detailed history, a complete physical examination, and routine investigations. Routine investigations include a complete blood count, blood urea, serum creatinine, serum electrolytes, blood glucose, chest X-ray, electrocardiography (ECG), blood group, and type.

On the morning of surgery, one of the anesthesia post-graduates who were not involved in the delivery of anesthesia care prepared a 60-mL syringe and labeled each syringe with the time and date of preparation and the subject's ID number. The 60-mL syringe contained either 1200 mg of lidocaine (20 mg/mL) or 0.9% normal saline solution.

All the patients were pre-medicated with a tablet of alprazolam 0.5 mg orally at night day before surgery. Once it was determined, the subject was ready for surgery; the subject was transported to the operative suite and positioned on the surgical table. Standard monitors, including ECG, arterial oxygen saturation (SaO^2), and non-invasive blood pressure (NIBP) devices, were placed, and baseline vital signs were recovered by the investigator. An 18-gauge wide-bore IV cannula was inserted. All subjects were pre-oxygenated with 100% oxygen through face mask for 3 min before induction of anesthesia. After the lignocaine bolus was finished, pre-oxygenation with 100% oxygen was initiated for 3 min, and general anesthesia was then given. Ringer lactate is given as IV fluids for both group patients as per fasting guidelines. Patients were induced with 2 mcg/kg of IV fentanyl, 2 mg/kg of IV propofol and relaxed with 0.5 mg/kg of atracurium, and their trachea was intubated. In cases of uncontrolled hemodynamics, patients were supplemented with fentanyl and inhalation agents. Anesthesia was maintained with a mixture of oxygen, nitrous oxide (40% and 60%, respectively), and sevoflurane inhalation with MAC-1. The sevoflurane and nitrous oxide were stopped at the conclusion of the surgery. Anti-nausea medications were administered as 0.1 mg/kg of ondansetron, and neuromuscular blockade was antagonized using IV neostigmine, 0.05 mg/kg, and glycopyrrolate, 0.01 mg/kg. Patients were extubated and subsequently shifted to the recovery room. Heart rate (HR), non-invasive mean arterial pressure (MAP), NIBP, oxygen saturation, 3 lead electrocardiograms, end tidal carbon dioxide, temperature, and MAC were recorded intra-operatively.

After endotracheal extubation, subjects were transported to the post-anesthesia care unit (PACU). Total surgical time (measured in minutes from surgical incision to skin closure), anesthesia time (measured as arrival time in the operating room to arrival in the PACU, in minutes), medications given, and the start and stop time of the study drug infusion were documented by the investigator. Injection tramadol 1 mg/kg (maximum 50 mg) I.M. was administered as a rescue analgesic when the visual analog scale (VAS) ≥4 was reported by the patient during the post-operative period.

Hemodynamic assessments were recorded immediately before starting the infusion of lignocaine, prior to induction of anesthesia, post-induction, after tracheal intubation, and subsequently at 1, 3, and 5 min after intubation. Similarly, they were recorded immediately prior to the administration of the reversal agent and subsequently at 1, 3, and 5 min after tracheal extubation.

While the duration of the pain-free period was recorded to evaluate post-operative analgesia, the pain-free period as VAS <4 was taken, as the period from the conclusion of surgery to the first requirement of an injection of tramadol. The attending nursing staff recorded VAS scores by visual analog pain scale every 15 min in the initial 1st h and then every 2 h until 24 h in the post-operative period or whenever the patient complained of pain. The nursing records of patients were reviewed at the end of the 24-h in post-operative period to note VAS scores. In this study, skin infiltration with local anesthetic was avoided in both groups, which may affect the post-operative pain-free period and may lead to overdosage.

Statistical analysis

Data were entered in MS-Excel (a spreadsheet). Data validation and analysis were done by the statistical software Statistical Package for the Social Sciences, Version 16.0. All the continuous variables were assessed for normality using a test called Shapiro–Wilk's test. If the continuous variables met the assumptions of normality, they were expressed as mean±standard deviation, otherwise median (interquartile range). The categorical variables were all reported as proportions or percentages. The comparison of normally (Gaussian) distributed continuous variables among the categories was done by the "t" test. All the categorical comparison was taken care by the Chi-square test or Fisher's exact test based on the number of observations present. All $p<0.05$ were considered statistically significant.

RESULTS

There were 60 patients in each group. The mean age, weight, and duration of surgery in the normal saline group were comparable to lignocaine group ($p>0.05$). Gender distribution and ASA physical status were also comparable in both groups ($p>0.05$) (Table 1).

Pulse rate (PR) and MAP were significantly increased during laryngoscopy and intubation in both groups, though the rise of both in the lignocaine group was significantly less than in the normal saline group ($p<0.0001$). Similarly, both PR and MAP were significantly increased during extubation in both groups ($p<0.0001$). However, the rise of both parameters in the lignocaine group was significantly less as compared to the normal saline group ($p<0.0001$) (Figs. 1-4).

Table 1: Demographic details of both the groups

Parameters	Normal saline (n=60) (%)	Lignocaine (n=60) (%)	p-value
Age group (Years)			
≤40	7 (11.7)	8 (13.3)	0.917
41–50	30 (50.0)	31 (51.7)	
>50	23 (38.3)	21 (35.0)	
Sex			
Male	19 (31.7)	22 (36.7)	0.707
Female	41 (68.3)	38 (63.3)	
ASA grade			
1	36 (60)	38 (63.3)	0.851
2	24 (40)	22 (36.7)	
Weight (Kg)			
	58.92±6.11	59.45±5.73	0.625
	64.60±4.70	63.70±5.20	0.322

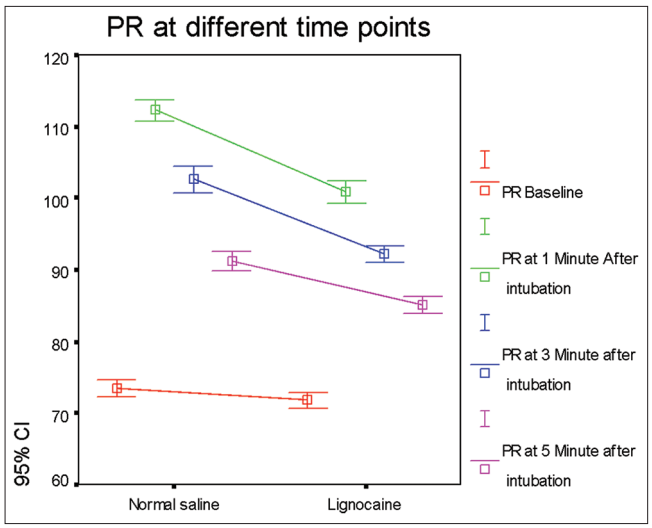

Fig. 1: Comparison of pulse rate between two groups at intubation

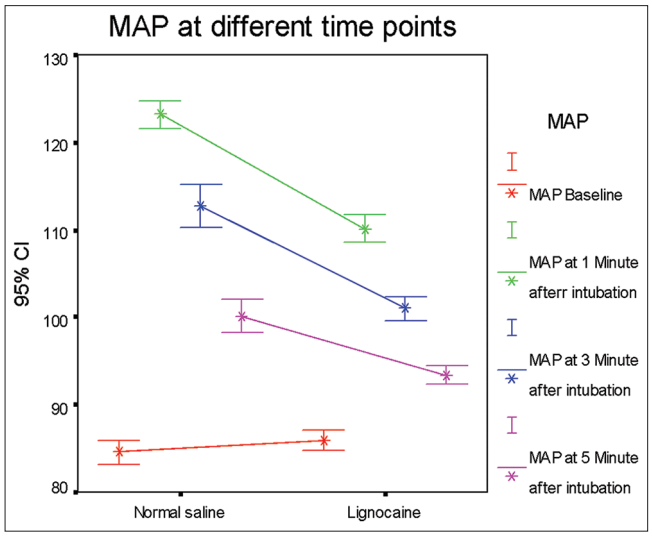

Fig. 2: Comparison of mean arterial pressure at intubation between two groups

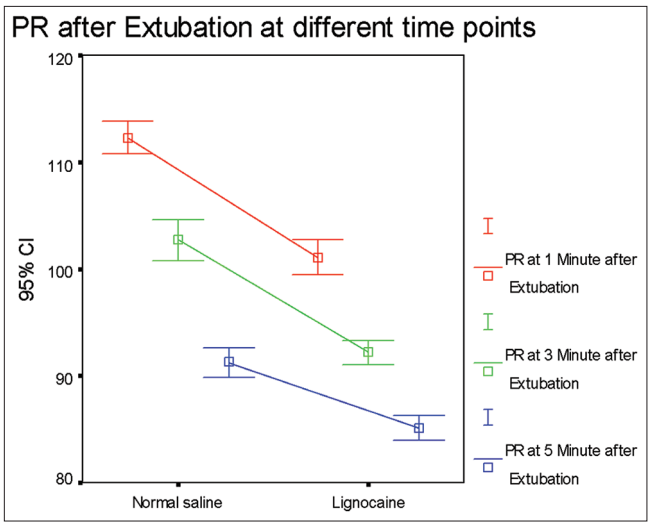

Fig. 3: Comparison of pulse rate between two groups after extubation

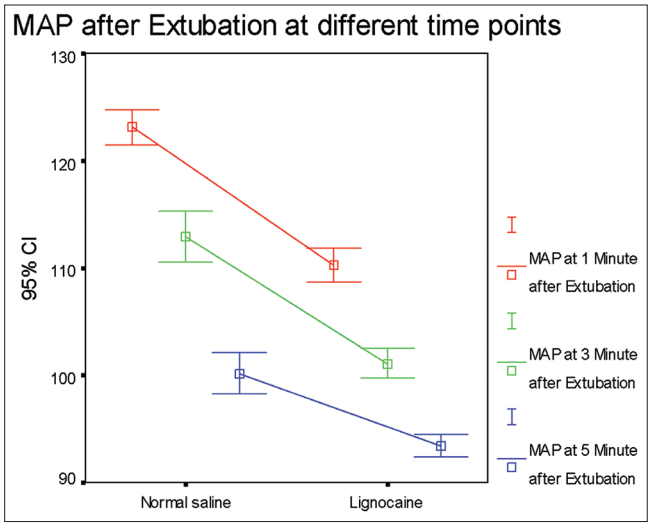

Fig. 4: Comparison of mean arterial pressure between two groups after extubation

VAS scores in the immediate post-operative period were better in the lignocaine group than normal in the saline group. The mean pain-free period was less than an hour in the normal saline group, while it was approximately 4 h in the lignocaine group (p<0.0001). None of the patients complained of lignocaine-related side effects such as perioral numbness, metallic taste, seizures, and cardiac arrhythmias (Table 2).

Table 2: Comparison of visual analog scores and pain-free period between groups

Parameters	Groups	Mean±SD	p-value
VAS at 30 min	Normal saline	1.3±0.5	0.0001*
	Lignocaine	0.4±0.5	
VAS at 1 H	Normal saline	4.4±0.6	0.0001*
	Lignocaine	1.2±0.7	
Pain free period (minutes)	Normal saline	49.9±6.4	0.0001*
	Lignocaine	227.4±11.6	

*Significant, VAS: Visual analog scale

DISCUSSION

Various agents, such as opioids, beta-adrenergic blockers, calcium channel antagonists, clonidine, and dexmeditomedine, have been used to blunt the hemodynamic response to laryngoscopy and intubation, but they all have limitations [10,11]. The role of lidocaine infusions peri-operatively for intra-abdominal surgery at comparable doses has been studied in recent publications. They demonstrated reduced post-operative pain, in addition to faster return of bowel function and a shortened hospital stay [12,13] short-term IV infusions of lidocaine are safe [14]. Lignocaine attenuated the hemodynamic response to tracheal extubation by its direct myocardial depressant effect, central stimulant effect, and peripheral vasodilatory effect, and finally it suppressed the cough reflex, an effect on synaptic transmission [15]. So we considered lignocaine in our study.

In the present study, the dosage of lignocaine was fixed, and the total duration was limited to 180 min to safeguard against its toxicity. Several trials on the analgesic effect of lignocaine involved giving a 1.5 mg/kg bolus dose after intubation, followed by an infusion for 6–24 h following surgery at a rate that varied from 1.5 mg/kg/h to 3 mg/kg/h. They reported plasma lignocaine levels varying from 1 to 3.8 µg/mL [2]. Since the facility of measuring plasma levels of lignocaine was not available at our institute, we presumed similar plasma lignocaine levels in the present study. Similar to this, only bolus doses of lignocaine ranging from 1 to 2 mg/kg were employed in many investigations on the impact

of lignocaine on regulating hemodynamic alterations; these doses often came before tracheal intubation and extubation [16].

Wallace *et al*. administered a computer-controlled lidocaine infusion to target plasma concentrations of 0.5, 1, 1.5, 2, and 2.5 mcg/mL. There was a significant plasma concentration-dependent decrease in pain scores starting at 1.5 mcg/mL [17]. In the present study, serum lignocaine levels were not measured, assuming similar, safer, and more effective serum lignocaine levels.

Hemodynamic changes (increased blood pressure and HR, and cardiac arrhythmia) in mechanical stimulation due to tracheal intubation and extubation are claimed to be caused by sympathoadrenal activity and catecholamine discharge. Pharyngeal and laryngeal nerves are still stimulated by tracheal intubation, despite enough deep anesthesias. These stimulations trigger a wide range of sympathetic activations in the nervous system via the vagus and glossopharyngeus nerves. Tracheal intubation is considered a stressful situation for a person undergoing general anesthesia, which could be detrimental to patients with cardiac problems. Tachycardia and hypertension induced by tracheal intubation and extubation decrease myocardial perfusion and increase oxygen consumption, both of which disrupt myocardial function [18].

In the present study, there was a significantly less rise in PR and MAP in the lignocaine group as compared to the normal saline group. This attenuating effect on both PR and MAP has been reported previously, either with the use of lignocaine alone or in combination with esmolol [1,19]. In addition, during tracheal intubation and extubation, the lignocaine group showed a considerably lower rise in PR and MAP than the normal saline group did in this trial. Different investigators have found the utility of lignocaine in attenuating the hemodynamic response associated with extubation [20,21]. Other studies have reported better results with drugs like diltiazem or a combination of lignocaine and verapamil [21,22]. The cough-suppressant action of lignocaine may be the cause of the attenuating effect, as it may raise BP and PR during extubation by irritating the trachea.

The pain-free period postoperatively was significantly less in the lignocaine group as compared to the normal saline group in this study. There were studies in favor of lignocaine infusion being used for post-operative pain relief [2,15,23]. A systemic review of randomized controlled trials on the impact of IV lignocaine infusion on post-operative analgesia and recovery from surgery concluded that IV lignocaine infusion in the perioperative period was safe, and such patients had lower pain scores, reduced post-operative analgesic requirement, decreased intraoperative anesthetic requirements, faster return of bowel function, and decreased length of hospital stay [24]. IV lignocaine inhibits neuronal excitability in dorsal horn neurons and lowers spike activity, amplitude, and conduction time in both myelinated A and unmyelinated C fibers, which may be the cause of this analgesic effect [25]. Local anesthetics also have a broad spectrum of anti-inflammatory properties due to their impact on the immune system and other cell types. Local anesthetics have strong anti-inflammatory qualities that outperform conventional non-steroidal anti-inflammatory drugs and steroid anti-inflammatory treatments in a number of ways [26]. Similarly, intraperitoneal administration of local anesthetics has been shown to induce potent inhibition of peritonitis [6]. Since lignocaine or bupivacaine may affect the degree of post-operative discomfort, they were not used to infiltrate the incision sites in this investigation and thereby affect analgesic requirements. It could also predispose to lignocaine overdosage.

This study attempted to examine the effects of perioperative lidocaine infusion on pain, as measured by the VAS score and as subjectively reported by patients undergoing laparoscopic gynecologic outpatient surgery. The study's findings are in line with earlier investigations that suggested intraoperative lidocaine infusion might lessen post-operative discomfort.

Limitations

In the present study, the inability to measure plasma lignocaine levels was prevented us from using the different dose and duration combinations of lignocaine. In the present study, the analgesic action of IV lignocaine was studied till 1st 24 h post-operatively only and did not include the pediatric and elderly populations.

CONCLUSION

This study concluded that IV infusions of lignocaine had significantly increased the pain-free period postoperatively. Hence, it can be used as a multimodal analgesic approach for post-operative analgesia. Lignocaine is cheap and easily available, so for those who are not affordable for epidural block, lignocaine IV infusion is a better alternative for post-operative analgesia.

AUTHORS' CONTRIBUTION

All the authors contributed to the preparation of the final manuscript.

CONFLICTS OF INTEREST

None.

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Nil.

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