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Effects of Intraoperative Lignocaine Infusion on Heamodynamics and Postoperative Analgesic Requirement after Day Case Laparoscopic Surgery

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Abstract

Background: ***Intravenous lignocaine is an amide local anaesthetic known for its analgesic, anti-hyperalgesic, anti-inflammatory and anti-arrhythmic properties. During perioperative period of laparoscopic surgeries haemodynamic alteration occurs due to laryngoscopy, intubation, and surgical excision, gas insufflation during pneumo-peritoneum, inadequate analgesia and inadequate depth of anaesthesia. Intravenous lignocaine is often administered to suppress the haemodynamic response and as an analgesic agent. We aimed to evaluate the effect of intravenous infusion of lignocaine on haemodynamic response and post-operative analgesic requirement.***

Objectives: ***The purpose of this study was to evaluate the effect of intravenous infusion of lignocaine on haemodynamic and postoperative analgesic requirements after laparoscopic day case surgeries.***

Material and method: ***Four hundred Sixty (460) patients were selected who's were going to be operated for laparoscopic surgeries (Laparoscopic Cholecystectomy, laparoscopic Hernioplasty, laparoscopic appendicectomy, Diagnostic laparoscopy due to infertility) were grouped into exposed (Group L) who were received lignocaine infusion @1mg/kg/hr and controlled (Group C) who were received placebo. Systematic random sampling was employed.***

Results: ***Demographic characteristics were comparable between the groups p>0.05. In lignocaine group intraoperative mean systolic blood pressure, mean diastolic blood pressure, mean arterial blood pressure and mean heart rate were significantly lower than control group (p<0.05). Twenty four hour mean VAS score (0 – 10 cm) at immediate recovery, 1st, 2nd, 3rd, 6th, 12th and 24th hour were lower in lignocaine group (p<0.05). The mean time of first analgesic requirement were longer (120 minutes) in lignocaine group compared to 40 minutes in control group (p<0.001) and the mean total tramadol consumption is less in lignocaine group (p<0.001).***

Conclusion: ***Intra operative lignocaine infusion causes more haemodynamic stability and decreases postoperative pain score, required longer time for first analgesic requirement and reduced total analgesic consumption in laparoscopic surgeries.***

Keywords: ***Day case laparoscopic surgery, Heamodynamics, Lignocaine infusion, Post-operative analgesic requirement.***

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Introduction

During perioperative period, patients become haemodynamically unstable due to laryngoscopy, intubation, and surgical excision, gas insufflation during pneumoperitoneum, inadequate analgesia and inadequate depth of anaesthesia.[1,2] As a result many

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complications like tachycardia, hypertension, myocardial ischemia, arrhythmia, myocardial infarction, and cerebral hemorrhages can be occurring.[1,2] To prevent development of these unwanted effects, various measures such as administration of topical anaesthesia, IV lignocaine, vasodilators, alfa$_2$ agonists, beta-adrenergic blockers, opioids, and increasing the depth of anaesthesia have been implemented. For the control of this type of unfavorable haemodynamic changes developed secondary to intubation, lignocaine can be administered intravenously before the induction of anaesthesia and several studies have demonstrated its preventive effects on postoperative pain[2, 3, 4].

In laparoscopic surgeries pneumoperitoneum was made by carbon dioxide insufflation. The effects of pneumoperitoneum patient become haemodynamically unstable due to insufflating gas causes peritoneal stressing which causes bradyarrythmia and causes catecholamine secretion which increases blood pressure, as a result increase bleeding tendency from the dissection site. It is essential to control blood pressure during laparoscopic surgery. On the other hand in laparoscopic surgeries pain is associated with incisions for the operative ports, operative field and upper abdominal, shoulder tip, and postural high back pain after laparoscopy are likely to be caused by gas retained in the peritoneal cavity. For these causes in laparoscopic surgeries patient become more haemodynamically unstable.

Pain after laparoscopy is treated optimally with local anesthetic, paracetamol, NSAIDs, and opioids if required[4].

There are different techniques have been implemented to reduce postoperative pain following laparoscopic day case surgery, including non-steroidal anti-inflammatory drugs, administration of Opioids, and neuraxial anesthesia. But, most of the time they did not show consistent efficacy. Thus, multimodal analgesia regime was recommended for pain management after laparoscopic surgery[5]. Besides of decreasing cost and side effect of opioids, use of lignocaine infusion also support the principle of multimodal analgesia where a variety of analgesic medication and techniques that target different mechanisms of action in the peripheral or central nervous system might have additive or synergistic effects or alternative analgesia and more effective pain relief compared with single-modality interventions.[6-8]

Lignocaine was initially used as an antiarrhythmic agent. But now a day's intravenous infusion of lignocaine considered as a useful adjunct in perioperative pain management[9,10]. Intravenous infusion of lignocaine can be administered intraoperatively or postoperatively as a component of multimodal pain strategy. In the perioperative period when lignocaine administered as an intravenous infusion, have been found its analgesic properties at concentration levels 0.5–5 ìg/ml [10]. Therapeutic plasma level of lignocaine 1.4 – 6.0 ìg/ml where the toxic plasma level 8 - 12 ìg/ml[11].

The mechanisms of action of lignocaine include the following: blockade of sodium channels, glycinergic action, blockade of N-methyl- D- aspartate (NMDA) receptors, reduction in substance P and others[12,13]. The exact molecular mechanisms of lignocaine action in modifying both acute and chronic pain are still somewhat elusive[13]. Lignocaine is thought to reduce pain and hyperalgesia in neuropathic pain states.[14] It may inhibit spontaneous impulse generation from injured peripheral nerves and dorsal root ganglions proximal to the injured fibres[15, 16]. It is thought to suppress poly-synaptic reflexes in the dorsal horn, hence resulting in decreased nociception. [17] In the electrophysiological experiments, intravenous lignocaine inhibits the excitatory postsynaptic currents evoked by noxious pinch stimuli[17]. Intravenous systemic lignocaine may exhibit a central mode of action[18]. Lignocaine is thought to have a slight negative chronotropic effect on the heart. The compound exhibits a biphasic action on smooth muscle of peripheral blood vessels, with vaso-constriction at low concentrations and vasodilation at higher concentrations[19].

Though many studies have compared the effects of intravenous infusion of lignocaine on haemodynamic responses, comparative studies related to their effects on recovery and analgesia, but in our study, we have aimed to see the effects of intraoperative intravenous infusion of lignocaine on haemodynamic changes, and postoperative analgesic requirements.

Material & methods:

This prospective observational study was conducted from 1st July '2022 to 30th June '2023 at the department of Anaesthesiology and Surgical ICU, BIRDEM General

Hospital, Shahbagh, Dhaka, Bangladesh. After institutional ethical committee approval and informed written consent, a total number of 460 adult patients' age 18 – 50 years, with ASA physical status I & II scheduled for various elective laparoscopic day case surgeries under general anaesthesia were enrolled in this study. Patient who have allergy for local anesthetics and has history of chronic opioid use, Liver dysfunction, and renal insufficiency has been excluded from study.

The subjects were allocated randomly into two groups, using a computer-generated randomization code. The lignocaine group (Group L) received an IV lignocaine infusion and the control group (Group C) received placebo.

The base line blood pressure and heart rate were recorded from the same noninvasive monitor and cardiac rate and rhythm were also monitored from a continuous display of E.C.G from lead II. All patients were reassured and the anaesthetic procedure was explained on the day before the operation. Intravenous access established in all patients in the operating room. After that the lignocaine group (Group L) received an IV lignocaine infusion bolus at a rate of 1.5 mg/kg over 5 minute just before induction followed by 1 mg/kg/hour continuous infusion. The control group (Group C) was received i.v. infusion of 0.1 ml/kg 0.9% normal saline over 5 minute just before induction followed by 0.1 ml/kg/hour continuous infusion. Each patient received General anaesthesia with induction dose of inj.Fentanyl 2 µgram/kg, inj. Propofol 2mg/kg and muscle relaxant inj.Atracurium 0.5mg/kg. After induction, general anaesthesia was maintained by 60% N_2O and 40% O_2 and Isoflurane MAC 0.2 – 1%. An incremental dose of muscle relaxant inj. Atracurium 1/4th of initial dose was given every 20 minutes interval. Every patient was received Inj. paracetamol 15mg/kg and 10 mg IV metoclopramide just twenty minutes after induction. Dosages of all anesthetic agents were tapered 50% at the start of skin suturing and discontinued at the last skin suture. The effects of muscle relaxants were reversed using 0.04 mg/kg neostigmine and 0.02 mg/kg atropine. The infusion of both group were terminated immediately after extubation.

Monitoring of heart rates (HR), systolic blood pressure (SBP), diastolic blood pressure(DBP), and mean arterial blood pressure (MABP), were recorded preoperatively (t1), just before induction (t2), after the intubation at 1 minute (t3) and 5 minute (t4) and, during the surgical incision (t5), after the surgical incision at 5 minute (t6), 10 minute (t7), 15 minute (t8), 20 minute (t9), 30 minute (t10), 40 minute (t11), 50 minute (t12), and 60 minute(t13), before extubation (t14), and after the extubation at 5 minute (t15)and 10 minute(t16).

In post-operative ward patients were asked to mark their pain level based on 0-10cm Visual analogue scale (VAS) score as soon as patient fully respond to verbal command and recovered from full cognitive ability. VAS score were recorded at immediate recovery, 1st hour, 2nd hour, 3rd hour, 6th hour, 12th hour and 24th hour at post-operative ward after end of surgery. A time in minutes from end of surgery to first analgesia request were also recorded together with total analgesia consumed in the first 24 hours. In postoperative period pain was managed by inj. tramadol hydrochloride IV according to patient requirement. Duration of surgery and duration of anesthesia were also recorded.

Data processing:

Data were collected using a pretested observational checklist. Data collectors were one Diploma in Anaesthesia (DA) 2nd year student and one DA 1st year student and they supervised by principle investigator. The data were reviewed from completed structured data retrieval form to ensure completeness and quality of data. After data quality was assured, forms were collected and assigned consecutive number (code) for ease of data entry. The Data was entered using the Epi-Info version 7.0 and clean-up has been made to check accuracy, consistency and errors identified were corrected and finally transported to SPSS V 20 for analysis.

Shapiro Wilk test with p value <0.05 for non-normally distributed data and histogram with bell-shaped were used to test for normal distributions of data while homogeneity of variance were assessed using Levene's test for equality of variance. Numeric data were described in terms of mean ± SD for symmetric data like age, heart rate(HR) and median (Inter-quartile range) for asymmetric numeric data like 24 hour VAS score and total analgesia consumption. A comparison of numerical variables between the study groups was done using the Student's t test for independent samples with parametric distribution and Mann-Whitney test for non-parametric distribution. For comparing categorical data, chi-square

test was performed. P values less than 0.05 were considered statistically significant.

Operational definitions:

Postoperative pain: A patient complaining pain and any pain score other than zero within 24 hours

Intra-operative haemodynamic changes: Changes in heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) during surgery

Duration of surgery: Time in minutes from skin incision to end of surgery

Duration of anesthesia: A time in minutes it takes from preoxygenation to extubation

Time to first analgesic requirement: A time in minutes from the end of surgery to a first time analgesia were given

Total analgesia consumption: Total dose of anti-pain medication given within the first 24 hour after end of surgery

Result:

Four hundred sixty (460) patients who underwent laparoscopic day case surgery were enrolled in this study. Among them 256 male and 204 female. ASA categorization (I, II) of group L were 144/86 and of group C were 136/94 patients. Demographic data for each group was similar (Table I). Two hundred fifty three patients (55%) underwent cholecystectomy, ninety two patients (20%) underwent diagnostic laparoscopy due to primary infertility, sixty nine (15%) patients underwent inguinal hernioplasty & fourty six patients (10%) underwent appendicectomy (Table II). Mean duration of surgery for cholecystectomy 54.8 minutes, for diagnostic laparoscopy due to primary infertility 45.6 minutes, for inguinal hernioplasty 55.6 minutes & for appendicectomy 54.8 minutes (Table II). Mean duration of anaesthsia for cholecystectomy 66.4 minutes, for diagnostic laparoscopy 58.5 minutes, for inguinal hernioplasty 68.2 minutes & for appendicectomy 62.4 minutes (Table II).

Intraoperative mean heart rates (HR) (Fig. 1), mean systolic blood pressure (SBP) (Table III), mean diastolic blood pressure (DBP) (Table IV), and mean arterial blood pressure (MABP) (Fig. 2) were lower in both group but in lignocaine group were more lower than control group which was statistically significant ($P < 0.05$).

The mean values of postoperative VAS pain scores were lower in the lignocaine group in comparison to the control group, which was statistically significant at immediate recovery, 1st hour, 2nd hour, 3rd hour, 6th hour, 12th hour and 24th hour ($p<0.05$) (Table 5). The mean time of first analgesic requirement was longer (120 minutes) in lignocaine group in compared to control group (40 minutes) which was statistically significant. ($p<0.001$) (Table VI). In comparison to analgesic consumption, in lignocaine group every patient were received single dose of 100mg tramadol hydrochloride IV in 24 hours post operative period according to their demand where in control group 120 (105 male & 15 female) patients were received single dose of 100 mg tramadol hydrochloride IV and 105 (25 male & 80 female) patients were received double dose of 100 mg tramadol hydrochloride IV and rest of 05 female patient were received third dose of 100 mg tramadol hydrochloride IV according to their demand, which showed total analgesic consumption were lower in lignocaine group in comparison with control group which was statistically highly significant($p< 0.001$) (Table 6). No cases of cardiac depression or central nervous system toxicity occurred by local anaesthetic. Our postoperative repeated visits for early detection of pain and provide increased patient satisfaction.

Table-I

Demographic variables

Variables	Group-L (n=230)	Group-C (n=230)	p value
Age (years)	40.8 ± 7.5	44.5 ± 8.7	0.068^{ns} *
Sex (M/F)	126/104	130/100	0.78^{ns} **
Weight (kg)	63.30±8.44	64.67±7.13	0.55^{ns} *
ASA (I/II)	144/86	136/94	0.271^{ns} **

All values were presented as mean± SD or in frequencies. Data were analyzed using unpaired * student t-test & ** Chi-square test. Statistically significance was set at p-value <0.05. (S=significance, NS=not significant)

Table-II

Distribution of the patients by type and duration of operation (n=460)

Types of operation	Frequency	Duration of operation (minute) Mean±SD	Duration of anaesthesia (minute) Mean±SD
Cholecystectomy	253(55%)	54.8±1.12	66.4±1.12
Diagnostic laparoscopy	92(20%)	45.6±0.85	58.5±0.85
Hernioplasty	69(15%)	55.6±0.75	68.2±0.75
Appendicectomy	46(10%)	54.8±0.65	62.4±0.65
Total	460(100%)	52.7±0.60	63.87±0.60

All values were presented as mean ± SD or in frequencies. Data were analyzed using unpaired student t-test. Statistically significance was set at p-value <0.05. (S=significance, NS=not significant)

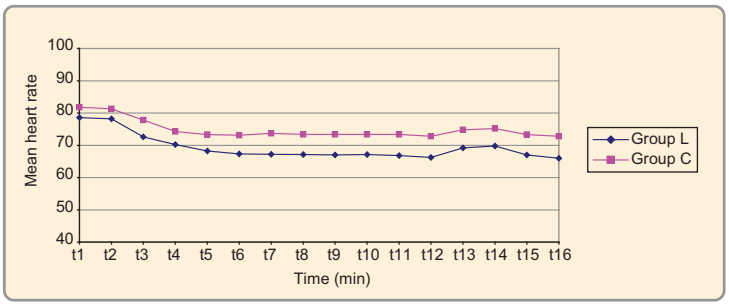

Figure-1: *Line diagram showing mean heart rate in two groups*

The mean heart rate at different time in intraoperative period compared between two groups. Statistical significant were observed in between groups ($p < 0.05$)

Table-III

Comparison of mean systolic blood pressure of the study respondents (n=460)

Time	Group-L (n=230) Mean±SD	Group-C (n=230) Mean±SD	p value
t1	124.90±7.0	127.30±5.7	0.09
t2	124.70±5.7	126.50±4.7	0.21
t3	123.33±7.60	125.84±8.13	0.001
t4	121.33±6.60	123.84±7.13	0.001
t5	120.54±6.90	123.67±7.84	0.001
t6	119.78±5.39	122.92±6.55	0.001
t7	119.72±5.35	122.86±6.51	0.001
t8	118.62±4.70	122.39±4.36	0.001
t9	117.86±3.95	121.74±4.12	0.001
t10	117.24±3.40	120.76±4.10	0.001
t11	118.30±4.57	120.20±4.07	0.001
t12	118.72±4.68	121.46±4.50	0.001
t13	116.88±3.95	120.76±4.12	0.001
t14	121.28±3.40	124.80±4.10	0.001
t15	120.30±4.57	122.20±4.07	0.001
t16	117.42±4.70	121.19±4.36	0.001

P value of d" 0.05 was considered significant, P value e" 0.05 was considered non-significant. P value < 0.001 was considered highly significant. Mann-Whitney test

Table-IV

Comparison of mean diastolic blood pressure of the study respondents (n=460)

Time	Group-L(n=230) Mean±SD	Group-C(n=230) Mean±SD	p value
t1	80.60±6.0	83.10±4.7	0.09
t2	80.90±4.5	83.70±3.4	0.21
t3	78.22±3.91	81.52±3.02	0.001
t4	70.60±3.82	70.60±3.82	0.001
t5	68.42±6.72	75.74±5.72	0.001
t6	69.52±5.42	72.80±6.74	0.001
t7	68.46±4.33	72.21±5.91	0.001
t8	69.82±4.19	73.30±4.74	0.001
t9	70.54±3.94	73.80±4.11	0.001
t10	69.84±4.21	73.32±4.76	0.001
t11	68.15±3.75	73.41±3.34	0.001
t12	67.33±3.24	72.52±3.40	0.001
t13	68.74±3.10	72.20±3.27	0.001
t14	76.22±3.91	79.52±3.02	0.001
t15	70.60±3.82	70.60±3.82	0.001
t16	67.74±3.10	72.42±3.40	0.001

P value of ≤0.05 was considered significant, P value ≥0.05 was considered non-significant. P value < 0.001 was considered highly significant. Mann-Whitney test

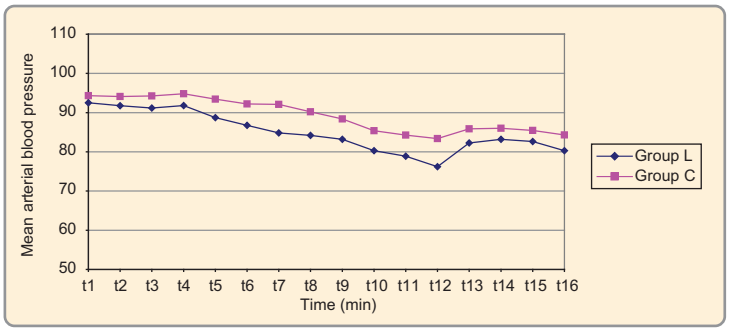

Figure- 2: *Line diagram showing intraoperative mean arterial blood pressure in two groups*

The mean arterial blood pressure at different time in intraoperative period compared between two groups. Statistical significant were observed in between groups (p< 0.05)

Table-V

Changes in VAS scores in both groups (n=460)

VAS	Group-L (n=230)	Group-C (n=230)	p value
Immediate recovery	3.00 ± 1.62	4.2 ± 1.08	0.011
1st hour postoperative	3.27±1.66	4.60±1.64	0.015
2nd hour postoperative	2.40 ± 0.72	3.70 ± 1.12	0.001
3rd hour postoperative	2.30±1.66	3.6±1.68	0.001
6th hour postoperative	2.20± 0.74	3.30 ± 1.14	<0.0001
12th hour postoperative	2.01 ± 1.10	3.00 ± 1.64	0.029
24th hour postoperative	1.40± 0.62	2.02± 1.02	0.02

P value of ≤0.05 was considered significant, P value ≥0.05 was considered non-significant. P value < 0.001 was considered highly significant. Mann-Whitney test

Table-VI

Mean time to the first request for postoperative analgesia and mean total dose of analgesic in the first 24 hours in both groups (n=460)

Variables	Group-L (n=230)	Group-C (n=230)	p value
First request for analgesia (min)	120 ± 18.7	40 ± 16.7	<0.001
Total analgesia consumption	100	150	< 0.001

P value of ≤0.05 was considered significant, P value ≥0.05 was considered non-significant. P value < 0.001 was considered highly significant. Mann-Whitney test

Discussion:

The present study showed that intraoperative haemodynamic were more stable in lignocaine group compared to control group (p = <0.0001). Numerous trials have evaluated the effects of IV lignocaine on intraoperative haemodynamic and anaesthetic requirement. [20, 21] The administration of a bolus dose of IV lignocaine, followed by an IV infusion was associated with a decreased requirement of volatile anaesthetic agents, as compared to saline and intraoperative systolic and mean arterial pressure and heart rate were significantly lower in the Lignocaine group. While there is a growing body of evidence supporting the use of IV lignocaine in accelerating rehabilitation and improving outcomes after abdominal surgery[22, 23, 24]. In contrast to the present study, Gupta et al. studied three groups: clonidine group received intravenous clonidine (2 ìg/kg, 30 min before laryngoscopic intubation); lignocaine group received intravenous lignocaine (1.5 mg/kg, 90 s before the intubation); and control group received normal saline (NS). They evaluated systolic blood pressure (SBP), diastolic (DBP), MAP, and HR measured at the baseline, pre-induction and at 3, 5, and 10 min. The rise in BP and HR from the baseline to one minute after intubation was significantly less in both lignocaine and clonidine groups as compared to the control group; however, the lignocaine group maintained haemodynamic around the baseline better than the clonidine group. [25] S.D. Dogan et al. study found that lignocaine and esmolol equally depressed haemodynamic responses to intubation. Even though haemodynamic responses to extubation were suppressed more effectively in the lignocaine group relative to the esmolol group[26].

The present study also showed that the mean VAS score at immediate recovery, 1st hour, 2nd hour, 3rd hour, 6th hour, 12th hour and 24th hour postoperative ward were lower in lignocaine group compared to control group (p<0.05). But in 6th hour of postoperative ward the mean VAS score in lignocaine group was 2.20± 0.74 in compared to control group 3.30 ± 1.14 which was highly significant (p<0.0001). The first analgesic requirement was longer in lignocaine group compared to control group and the total analgesic consumption were also lower in lignocaine group in compared to control group which were statistically significant (p = <0.001). A meta-analysis in China aimed to assess the efficacy and safety of intravenous infusion of lignocaine for pain management after cholecystectomy concluded that there were significant difference between groups in terms of VAS scores at 24 hours, (p<0.05) and significant difference were found regarding opioid consumption at 24 hours, (p=0.009)[27]. Our study also supports the findings of the study done in Nepal with the mean pain VAS scores in lignocaine group remained significantly less than that in control group with mean VAS score at 3rd hour is 2.5 ± 1.4 and 3.6 ± 1.7 respectively (p<0.001). [28] The analgesic efficacy of lignocaine is due to a selective depression of pain transmission in the spinal cord and a reduction in tonic neural discharge of active peripheral nerve fibers[29, 30].

Our study demonstrate the mean time for the request of the first dose of analgesic was significantly longer in lignocaine group than in control group 120 minutes vs. 40 minutes, (p<0.001). Our finding is comparable with study done in Nepal which shows mean time for the first analgesic request time was longer in lignocaine group compared to control group, 60.97 ± 18.05minutes vs. 15.73 ± 7.46 minutes, respectively, (p<0.001)[28].

Koppert et al. analyzed the effects of perioperative lignocaine infusion in major abdominal surgeries and found that, in patients who had received lignocaine infusion at a rate of 1.5 mg/kg/h following a loading dose of 1.5 mg/kg 30 min before surgical incision up to the end of surgery demanded fewer numbers of PCA and less morphine administered via PCA, and the total consumption of morphine was relatively lower compared with the control group[31]. In our study, we also found that the duration of first analgesic requirement is longer and the total amount of analgesic consumption significantly lower in lignocaine infusion group. A double-blinded study by Saadawy and collaborators in 120 patients submitted to laparoscopic cholecystectomy using the lignocaine infusion for post-operative pain management showed that, there was lower need of morphine use at the second postoperative hour. In our study shown that the lignocaine group had lower dose of analgesic consumption in postoperative period. The scientific reason for result similarity between the studies is that lignocaine and its metabolites interacts with peripheral and central voltage-gated sodium channel on intracellular face of membrane blocking the start and conduction of neural impulse potential and morphine sparing effect[32, 33].

Intravenous lignocaine as an anaesthetic adjuvant may have the ability to maintain intraoperative haemodynamic stability and to improve the impact of multimodal analgesic regimens in laparoscopic surgery. We expect our results will have implications for the assessment of the impact of intraoperative intravenous lignocaine administration in patients undergoing laparoscopic day case surgery.

There are several strengths to this study. First, we have investigated the combination of an IV loading dose and a continuous infusion of lignocaine on intraoperative haemodynamic and postoperative analgesics requirement. Second, the original trial was conducted under strict methodology, which minimizes the risk of bias and third, as the study was conducted in tertiary level teaching hospital and first time in Bangladesh, so it will be very helpful for the management of intraoperative haemodynamic and postoperative analgesia for other hospitals in home and abroad.

Conclusion:

In this study we found that intra-operative use of lignocaine causes more haemodynamic stability, decreases the intensity of postoperative pain, reduces the postoperative analgesics requirement, prolongs first analgesic requirement and as a part of multimodal approach for post-operative analgesia in patients underwent laparoscopic day case surgery.

Limitations:

Our study however, does have several limitations. First, it was very difficult to measure the plasma concentration of lignocaine to understand its pharmacokinetics and second, the original trial investigated generally healthy patients (ASA I, II) undergoing elective laparoscopic day case surgeries. The results may not be applicable in patients with underlying comorbidities, including cardiac diseases, obesity or those undergoing emergency or other types of surgeries.

Declaration:

We, the undersigned, declare that this paper is our original work has never been published in any Journal and we understand that plagiarism will not be tolerated and all directly quoted material has been appropriately referenced.

Conflicts of interest:

The authors declare no conflicts of interest.

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