Clinical Investigation

Effect of peri-operative intravenous infusion of lignocaine on haemodynamic responses to intubation, extubation and post-operative analgesia

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ABSTRACT

Background and Aims: Lignocaine in intravenous (IV) bolus dose has been used for minimising haemodynamic changes associated with intubation and extubation. Furthermore, IV infusion has been used for post-operative analgesia. We investigated whether IV peri-operative lignocaine (bolus and infusion) would be able to produce both the effects simultaneously in elective laparoscopic cholecystectomies. **Methods:** In this randomised prospective study, 60 patients undergoing elective laparoscopic cholecystectomy were randomly divided into two groups of 30 each. In Group A, patients received 6 ml normal saline as bolus over 10 min followed by 6 ml/h infusion whereas in Group B, patients received preservative free 2% lignocaine 1.5 mg/kg IV bolus (made to a volume of 6 ml with normal saline) administered over a period of 10 min and thereafter an infusion at a rate of 1.5 mg/kg/h (pre-diluted in normal saline made to a volume of 6 ml/h. $P < 0.05$ was considered as significant. **Results:** The rise in pulse rate (PR) and mean arterial pressure (MAP) were less in Group B as compared to the Group A ($P < 0.05$) during intubation as well as during extubation. Furthermore, the Group B had significant longer mean pain-free post-operative period of 5½ h as compared to 54.43 min in the Group A ($P < 0.05$). **Conclusion:** Administration of lignocaine infusion attenuates the rise in PR as well as MAP during the peri-intubation and peri-extubation period. Furthermore, infusion of lignocaine significantly increases the mean pain-free period post-operatively.

Key words: Analgesia, haemodynamics, intubation, lignocaine, tracheal extubation

INTRODUCTION

Laryngoscopy, tracheal intubation and subsequent extubation are often associated with an increase in arterial blood pressure (BP), heart rate, arrhythmias, and raised intracranial and intraocular pressure. Factors responsible for such changes are different for intubation and extubation. A variety of drugs have been recommended for the control of these haemodynamic events, including lignocaine, esmolol, alfentanil, and fentanyl.[1]

Lignocaine given as bolus dose just prior to tracheal intubation[2-8] or extubation[9-13] has been effectively used to decrease haemodynamic responses associated with them. In addition, peri-operative intravenous (IV) infusion of lignocaine has been used as a method to control post-operative pain.[14-17]

Despite being a minimally invasive surgery, many patients suffer from moderate to severe pain after laparoscopic cholecystectomy. Lignocaine may be helpful in pain management for such patients.[14]

All the studies so far have taken into consideration only a single parameter of lignocaine utility, that is, either attenuation of haemodynamic changes secondary to intubation/extubation or post-operative analgesic efficacy.

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The primary objective of the present study was to observe whether a regimen of IV lignocaine of pre-operative bolus dose followed by peri-operative infusion can reduce the haemodynamic changes during tracheal intubation and extubation as well as attenuate post-operative pain following elective laparoscopic cholecystectomy.

METHODS

Following approval by Board of Studies and Hospital Ethical Committee, 60 female patients belonging to American Society of Anaesthesiologists physical status I and II with age ranging between 20 and 50 years and weighing between 40 and 70 kg, undergoing elective laparoscopic cholecystectomy (non-malignant) were selected for the study.

Patients with cardio-respiratory, renal, hepatic or endocrine disease or those having predicted difficult tracheal intubation were excluded from the study. Furthermore, whenever the surgical procedure necessitated the conversion of laparoscopic to open cholecystectomy or surgical time exceeded 180 min, such patients were excluded from the study. A day before surgery, after giving oral informed consent to take part in the study, patients were instructed by an anaesthesiologist about numeric pain rating scale (NRS), identifying 0 as 'no pain' and 10 as 'worst imaginable pain'. Furthermore, the patients were asked to report effects such as lightheadedness, perioral numbness, metallic taste, sedation, nausea, vomiting, and pruritus post-operatively. The patients were randomly divided (by chit- in- a- box technique) into two groups of 30 patients each. All the cases were done by same surgeon and anaesthesia given by the same team. Data collection was done by a team member who was blinded to the group of patient. Surgeon and the nursing staff in the recovery room were also blinded about the patient's group.

Ten min prior to induction of anaesthesia, in Group A, patients received 6 ml normal saline as bolus over 10 min, followed by 6 ml/h infusion while in Group B, patients received preservative free lignocaine 2% (Xylocard® 2%, Astra Zeneca, Bangalore, India) 1.5 mg/kg IV bolus (made to a volume of 6 ml with normal saline) administered over a period of 10 min and thereafter an infusion at a rate of 1.5 mg/kg/h (pre-diluted in normal saline made to a volume of 6ml/h). It was continued till the end of 1st post-operative hour. The maximum duration of infusion was kept to 180 min (including 1 h post-operative infusion) as a safeguard against potential lignocaine toxicity.

All patients were pre-medicated with injection midazolam 0.025 mg/kg IV, injection ketorolac 0.5 mg/kg intramuscular (IM) (maximum of 30 mg), and injection ondansetron 0.1 mg/kg IV. Pre-oxygenation with 100% oxygen for 3 min was started after completion of lignocaine bolus. Patients were induced with 2 mg/kg of IV propofol and relaxed with 0.1 mg/kg of vecuronium bromide and trachea intubated. Anaesthesia was maintained with a mixture of oxygen and nitrous oxide (40% and 60%, respectively) and an infusion of propofol in step down manner. The propofol infusion and nitrous oxide were stopped at the conclusion of the surgery. After reversal of residual neuromuscular blockade with a mixture of neostigmine and glycopyrrolate, patient's trachea was extubated. Patients were subsequently shifted to the recovery room. The attending nursing staff recorded numeric pain scale every 15 min in the initial 1st h and then every 2 h or whenever patient complained of pain. First dose of ketorolac 0.5 mg/kg (maximum 30 mg) IM was administered when the NRS ≥4 was reported by the patient. Subsequently, if NRS was ≥4, the patient received injection ketorolac IM 6 hourly. Despite administration of ketorolac, if patient reported NRS ≥4, then injection pentazocine 0.25mg/kg was administered.

Haemodynamic assessment was done using pulse rate (PR) and mean arterial pressure (MAP) while post-operative analgesia was assessed by recording pain-free period. Complications, if any were recorded. PR, systolic and diastolic BP were recorded immediately before starting the infusion of lignocaine, prior to induction of anaesthesia, post-induction, after tracheal intubation, and subsequently at 3, 5, 10 min after intubation. Similarly, they were recorded immediately prior to the administration of reversal agent, post-extubation, and subsequently at 3, 5, 10 min after tracheal extubation. Pain-free period (NRS <4) was taken as period from the conclusion of surgery to the first requirement of injection ketorolac.

The nursing records of patients were reviewed at the end of 24 h to note the total amount of ketorolac and pentazocine injections administered.

We conducted a pilot study on 20 patients with 10 patients in each group and presumed the difference

in the haemodynamic variable MAP and effect size to be true (MA*P* values were 100 ± 7 in Group A and 96 ± 9 in Group B at the end of study). These patients were not included in the study. The sample size was calculated by the method of change which is a repeated measure analysis of variance (two-way ANOVA) on the basis of MAP the haemodynamic variable. With α as 5% and β as 10% in order to achieve a relative efficiency of 3.056 and assuming the correlation of 0.7 between baseline and follow-ups, we needed to include 56 cases, 28 in each group. Hence, it was decided to include 60 cases (for 5% dropout rate), randomly allocated into two groups by chit in a box technique.

The data in tables is represented as mean ± standard deviation. The continuous data are analysed using Student's *t*-test or Mann–Whitney test as appropriate. To observe the change over period of time, repeated measure analyses followed by *post-hoc* comparison by the least significant difference method are employed. Besides this, the log transformation was also applied where necessary. Value of $P < 0.05$ was considered as significant in this study.

RESULTS

There were 30 patients in each group. Mean age, weight, and duration of surgery in Group A (34.53 years, 51.77 kg, and 53.37 min, respectively) were comparable to Group B (34.97 years, 53.90 kg, and 54.80 min, respectively) [Table 1].

During laryngoscopy and intubation, the haemodynamic parameters (PR and MAP) rose significantly in both the groups, though the rise of both in Group B was significantly less than Group A [Tables 2, 3].

Similarly, during extubation, both PR and MAP rose significantly in both the groups as compared to the immediate pre-reversal value within the same group. However, the rise of both the parameters in Group B was significantly less as compared to Group A [Tables 2 and 3]. The mean pain-free period was less than an hour in Group A, while it was approximately 5½ hours in Group B ($P < 0.05$) [Table 4].

In the post-operative period, the requirement of injection ketorolac was 66.77 mg in Group A and 27.72 mg in Group B in 24 h. ($P < 0.001$) while requirement of pentazocine, as a rescue analgesic, was 13.87mg in Group A and 7.51mg in Group B ($P = 0.01$) [Table 4].

Table 1: Demographics

Variable	Group A	Group B
Age (years)	34.43±9.71	34.97±11.06
Weight (kg)	52.00±10.31	53.90±9.06
Duration of surgery (min)	53.37±8.47	54.80±9.14

Table 2: Changes in pulse rate during peri-intubation and peri-extubation period

Time of observation	Group A (per min)	Group B (per min)	*P*
Before infusion of drug	91.87±13.77	86.60±16.69	0.19
Before induction	91.90±13.01	86.93±13.78	0.16
Post-induction	90.03±10.42	85.80±12.40	0.16
Post-intubation			
Immediate	115.57±13.44*	105.13±13.49	0.00
3 min	98.37±10.68*	89.43±13.75	0.01
5 min	93.83±20.74	84.83±13.14	0.05
10 min	86.50±12.42	80.13±11.75	0.05
Prior to reversal	90.03±10.42	85.40±15.21	0.26
Post-extubation			
Immediate	118.17±17.19*	109.83±12.83	0.04
3 min	99.13±15.99	97.43±12.29	0.65
5 min	91.17±15.46	89.43±11.47	0.62
10 min	87.53±14.78	84.0±13.18	0.33

* indicates *P* value less than 0.05

Table 3: Changes in MAP during peri-intubation and peri-extubation period of both groups

Time of observation	Group A (mm Hg)	Group B (mm Hg)	*P*
Before infusion of drug	98.51±8.18	95.89±7.20	0.19
Before induction	98.38±7.85	95.69±6.68	0.16
Post-induction	82.78±8.19	86.71±8.75	0.08
Post-intubation			
Immediate	124.69±11.75*	105.82±5.04*	<0.001
3 min	106.02±8.07*	96.93*±6.98*	<0.001
5 min	100.29±7.58	95.91*±7.37	0.03
10 min	97.47±7.79	94.29±5.74	0.08
Prior to reversal	102.93±6.55	96.42±6.62	<0.001
Post-extubation			
Immediate	124.76±10.05	108.44±5.98	<0.001
3 min	110.11±7.78	99.47±5.69	<0.001
5 min	101.49±9.17	97.71±6.07	0.07
10 min	99.98±6.82	95.47±8.59	0.03

MAP – Mean arterial pressure, * indicates *P* value<0.05

Table 4: Comparison of analgesic requirement of both the groups in 24 h

Parameter	Group A	Group B	*P*
Pain-free period (NRS <4) (min)	54.43±99.70	329.70±372.46	<0.001
Ketorolac requirement (mg)	60.77±17.48	27.72±16.42	<0.001
Pentazocine requirement (mg)	13.87±9.12	7.51±7.61	0.01

NRS – Numeric pain rating scale

None of the patients complained of lignocaine-related side effects such as perioral numbness or metallic taste. The incidence of light-headedness and nausea was comparable in both the groups. Three patients in the Group B demonstrated drowsiness in the post-operative period lasting between 10 and 17 min.

DISCUSSION

Though the effect of lignocaine in controlling both haemodynamic changes during tracheal intubation/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. The purpose of this trial was to ascertain whether our regimen of initial bolus dosage followed by low dose continuous infusion of lignocaine would be significantly effective for both these aspects.

The nature of surgery was kept identical (laparoscopic cholecystectomy) to prevent any variation in intensity of post-operative pain and haemodynamic changes. Only female patients were chosen for this study to prevent any gender-based bias in the assessment of post-operative pain.

The dosage of lignocaine was fixed and the total duration was limited to 180 min to safeguard against its toxicity. In different studies on analgesic action of lignocaine, bolus dose of 1.5mg/kg was given after intubation followed by infusion at rate varying from 1.5mg/kg/hr to 3mg/kg/hr for 6 to 24 hours post-operatively. They reported plasma lignocaine levels varying from 1-3.8 μg/ml.[15,16,17] Since facility of measuring plasma levels of lignocaine was not available at our institute, we presumed similar plasma lignocaine levels in the present study.

Similarly, in different studies on the effect of lignocaine on controlling haemodynamic changes, only bolus dose of lignocaine varying from 1 to 2 mg/kg were used, usually preceding tracheal intubation/extubation.[2-13]

In the present study, there was significantly less rise in PR and MAP in Group B as compared to Group A. This attenuating effect on both PR and MAP has been reported previously, either with use of lignocaine alone[5] or in combination with esmolol.[18] Other studies have reported significant effect on either PR[4,18] or MAP alone.[8] In contrast, other studies have reported that lignocaine has no significant attenuating effect on hemodynamic parameters.[19,20] The attenuating effect has been attributed to lignocaine causing arteriolar vasodilatation,[3] mitigating autonomic reaction,[4] having cough suppressant activity,[4,14,21,22] and increasing the depth of general anaesthesia.[6]

In this trial, it was also seen that during tracheal extubation there was significantly less rise in PR and MAP in the Group B as compared to the Group A. Different investigators have found the utility of lignocaine in attenuating the haemodynamic response associated with extubation.[10,12,18] Other studies have reported better results with drugs like diltiazem[9] or combination of lignocaine with verapamil.[13] The attenuating effect of lignocaine might be due to its cough suppressant activity, which could increase BP and PR at the time of extubation due to tracheal irritation.

The pain-free interval and analgesic requirement in the first 24 h post-operatively was significantly less in the Group B as compared to the Group A of this study. There are studies in favour of lignocaine infusion being used for post-operative pain relief.[14,15] But other studies didn't find any significant analgesic effect of lignocaine infusion.[16,23] A systemic review of randomised controlled trials on impact of IV lignocaine infusion on post-operative analgesia and recovery from surgery concluded that IV lignocaine infusion in the peri-operative period is safe and such patients had lower pain scores, reduced post-operative analgesic requirement, decreased intraoperative anaesthetic requirement, faster return of bowel function, and decreased length of hospital stay.[24]

This analgesic action may be because IV lignocaine suppresses neuronal excitability in dorsal horn neurons, depresses spike activity, amplitude, and conduction time in both myelinated A and unmyelinated C fibres,[25] and decreases the neural response to post-operative pain by blockade or inhibition of nerve conduction.[16]

In the present study, infiltration of the incision sites was not done with lignocaine or bupivacaine as it may interfere with the intensity of post-operative pain and thereby affect analgesic requirement. It could also predispose to lignocaine over dosage.

We studied the analgesic action of IV lignocaine only till 24 h post-operatively and found it to be significant.

Other studies have reported significant analgesic action varying from 2 to 48 hours post-operatively[14,16,17] while one study reported such effect only on 2nd and 3rd postoperative day.[15] This difference may be attributed to the difference in the type of surgery, that is the amount of tissue trauma involved, in different studies.

In the present trial, 3 out of 30 patients receiving lignocaine infusion demonstrated excessive drowsiness in the post-operative period. This observation has also been noted in other studies.[15,26]

There were certain limitations to our study. Inability to measure plasma lignocaine levels prevented us from using the different dose and duration combinations of lignocaine. We had to use a non-steroidal anti-inflammatory drug, ketorolac, IM for analgesia as the availability of opioids is a limiting factor at our institute. We studied the analgesic action of IV lignocaine till first 24 h post-operatively only. Our study did not include parameters such as total hospital stay, early ambulation, and total cost effectiveness for the patient. Further study is warranted to examine whether similar results can be achieved in other surgical procedures, including those associated with significant opioid use or prolonged ileus.

CONCLUSION

Administration of lignocaine 1.5 mg/kg bolus followed by 1.5 mg/kg/h infusion attenuates the rise in PR and MAP during the peri-intubation and peri-extubation period. It also increases the duration of pain-free period and reduces the requirement of analgesic in the post-operative period after laparoscopic cholecystectomy.

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Announcement

Conference Calender - 2015

Name of the conference: 63rd Annual National Conference of the Indian Society of Anaesthesiologists, ISACON 2015
Date: 25th to 29th December 2015
Venue: B. M. Birla Auditorium & Convention Centre, Jaipur, India
Organising Secretary: Dr. Suresh Bhargava
Contact: +91 98290 63830
E-mail: suresh3559@yahoo.com
Website: www.isacon2015jaipur.com

Name of the conference: TRISZAC 2015, 31st Annual Conference of Indian Society of Anaesthesiologists, South Zone and 39th Annual Conference of ISA Kerala State Chapter
Date: 6th to 9th August 2015
Venue: Hotel KTDC Samudra & Uday Samudra Beach Hotel, Kovalam, Trivandrum
Organising Secretary: Dr. Gopakumar D
Contact: +91 98476 39616
E-mail: triszac2015@yahoo.in
Website: www.triszac2015.com

Name of the conference: 16th North Zone ISACON 2015
Date: 16th to 18th October 2015
Venue: Dr. Rajendra Prasad Govt. Medical College, Kangra, TANDA (HP)
Organising Chairman: Dr. Sudarshan Kumar

Name of the conference: 7th Central Zone Conference & 29th MP State Conference 2015
Date: 3rd to 4th October 2015
Venue: Motel Shiraz, MP Nagar, Bhopal
Organising Secretary: Dr. Surendra Raikwar
Contact: +91 94065 33300, +91 89591 13801
E-mail: mpisaconcentzone2015@gmail.com, drskraikwar@gmail.com, centralzonempisacon2015@gmail.com
Website: www.isampchapter.com

Name of the conference: ISA JAC 25th East Zone Conference
Date: 6th to 8th November 2015
Venue: Hotel The Stadel, Kolkatta
Organising Secretary: Dr. Subhendu Sarkar
Contact: +91 98311 71162
E-mail: subhendusarkar757@gmail.com, sarkar_subhendu@yahoo.com

Name of the conference: 7th Annual Conference of ICA
Date: 13th to 15th November 2015
Venue: Hotel Savera, Dr. Radhakrishnan Road, Chennai 600004
Organising Secretary: Dr. K. Balakrishnan
Contact: +91 98410 29259
E-mail: ica2015@gmail.com (visit isaweb.in ISA > ICACON2015)

Name of the conference: KISACON2015, 31st Annual Conference of Indian Society of Anaesthesiologists, Karnataka State Chapter
Date: 9th to 11th October 2015
Venue: S N Medical College, Bagalkot
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E-mail: rameshkoppaldr@gmail.com
Website: www.kisacon2015.com

Name of the conference: 48th Gujarat State Conference of Indian Society of Anaesthesiologists 2015 (GISACON 2015)
Date: 9th to 11th October 2015
Venue: Shanku's Water World Resort (Ahmedabad-Mehsana Highway)
Organising Chairman: Dr. R G Agrawal
Organising Secretary: Dr. H G Bhavsar
Contact: +91 98242 33694
E-mail: info@gisacon2015.com
Website: www.gisacon2015.com

Name of the conference: ukisacon 2015 Uttrakhand State ISA Conference 2015
Date: 27th to 29th November 2015
Venue: Max Hospital, Dehradun
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Name of the conference: 28th Assam State Branch ISA Conference ABISACON 2015
Date: 3rd to 4th October 2015
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Name of the conference: 6th National Airway Conference 2015 (NAC 2015)
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Name of the conference: AORA2015 5th National Conference of Academy of Regional Anaesthesia of India
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Name of the conference: AOACON
Date: 11th to 13th September 2015
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