Original Article

# Evaluation of lignocaine infusion on recovery profile, quality of recovery, and postoperative analgesia in patients undergoing total abdominal hysterectomy

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## Abstract

**Background and Aims:** Multimodal analgesia entrains the use of drugs in perioperative period producing adequate pain relief without affecting the quality of recovery by decreasing drug-related adverse effects. Systemic lignocaine has effective analgesic, anti-inflammatory, and anti-hyperalgesic properties and improves the quality of recovery after surgery.

**Material and Methods:** Ninety women scheduled for elective transabdominal hysterectomy under general anesthesia were randomized to receive infusion of lignocaine (1.5 mg/kg over 15 min followed by a 2 mg/kg/h infusion until the end of surgery) (Group 1) or normal saline (10 mL over 15 min followed by infusion 1 mL/kg/h till end of surgery) (Group 2). Standard anesthesia techniques were used in both the groups. The patients received inj. tramadol for postoperative analgesia. Perioperative hemodynamics, extubation variables, postoperative analgesic requirement, and quality of recovery score were evaluated.

**Results:** Hemodynamics were maintained in both the groups. Time for extubation was also similar. Demand for first postoperative analgesic was after 70.8 ± 70.4 min (Group 1) and 40.7 ± 30.0 min (Group 2) ($P = 0.006$). Total tramadol usage was 477.0 ± 133.2 mg (Group 1) and 560.0 ± 115.0 mg (Group 2) ($P < 0.001$). Return of bowel function was faster in Group 2 compared with Group 1 (37.1 ± 5 vs 41.8 ± 7.4 h, $P < 0.001$). The median (interquartile range) recovery score (QoR-40) was 184 (178–191) in Group 1 and 178 (171–180) in Group 2 ($P < 0.001$).

**Conclusion:** Perioperative use of intravenous infusion of lignocaine is associated with decreased analgesic requirement postoperatively, and improved quality of recovery score signifying greater patient satisfaction.

**Keywords:** Lignocaine infusion, postoperative analgesia, quality of recovery score

## Introduction

Postoperative pain results due to releases of inflammatory, visceral, and neuropathic mediators as a result of surgical trauma producing structural and functional changes in pain pathways resulting in hyperalgesia and central sensitization.[1,2] Effective analgesia is the backbone of rehabilitation from surgery. However, undertreatment of acute postoperative pain is common and hence decreases the overall satisfaction of patients undergoing surgical procedures.

Multimodal analgesia entrains the use of combination of drugs in perioperative period thereby producing better pain relief and a decrease in individual drug-related adverse effects.[3] Lignocaine has analgesic, anti-inflammatory, and anti-hyperalgesic properties. Analgesic effects are mediated by the suppression of spontaneous

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impulse generation from injured nerve fibers and proximal dorsal root ganglion. The mechanism includes inhibition of Na channels, NMDA, and G-protein-coupled receptors. The anti-inflammatory effects are attributable to the blockade of neural transmission at the site of tissue injury, resulting in the attenuation of neurogenic inflammation, and to the intrinsic anti-inflammatory property.[4,5] Use of lidocaine infusion in abdominal surgery is associated with reduction in anesthetic and opioid requirements in perioperative and postoperative periods.

With this background, we conducted this study with the aim to evaluate the effects of lignocaine infusion on the quality of recovery score undergoing abdominal hysterectomy under anesthesia in Indian patients.

## Material and Methods

The prospective randomized trial was conducted after Institutional Ethics Committee approval and written informed consent from the patients. A total of 90 American Society of Anesthesiologists (ASA) I and II female patients, 30–65 years of age scheduled for elective transabdominal hysterectomy under general anesthesia were included. Exclusion criteria included body mass index >35 kg/m$^2$, history of allergic reaction to local anesthetic agents especially lignocaine, history of preoperative use of opioids, and chronic use of nonsteroidal analgesics, psychotropic drugs, and beta-blockers. Patients with history of uncontrolled hypertension, A-V conduction block, and history of sleep apnea were also excluded.

On shifting the patients to the operation room, standard monitoring (electrocardiograph, pulse oximetry, noninvasive blood pressure, and Bispectral index BIS (Bispectral Index)) was attached. The patients were randomized by computer-generated table of random number into two groups, to receive lignocaine 1.5 mg/kg intravenously over 15 min followed by intravenous infusion of 2 mg/kg/h till the end of the surgery (Group 1) and normal saline 10 mL over 15 min followed by infusion of 1 mL/kg/h till the end of the surgery (Group 2). The test drug infusion was started according to group allotment after establishing an intravenous infusion, over a period of 15 min. The infusion of the test drugs was started after fixing of endotracheal tube and continued over the perioperative period. Induction of anesthesia was achieved with fentanyl 2 μg/kg and propofol 1–1.5 mg/kg till loss of verbal commands. Neuromuscular blockade was achieved with 0.1 mg/kg of vecuronium. Endotracheal intubation was completed with cuffed endotracheal tube of size 7–7.5. Maintenance of anesthesia was achieved with 66% $N_2O$ in $O_2$, incremental concentration of isoflurane, and intermittent boluses of fentanyl 1 μg/kg and vecuronium 1 mg. Ventilation was achieved to maintain end-tidal carbon dioxide between 33 and 36 mmHg. BIS in the perioperative period was maintained between 40 and 60. Any decrease in BIS was maintained by altering the concentration of isoflurane. At the end of the surgery, the infusions were stopped. After thorough oral suction and with resumption of spontaneous effort and BIS value between 80 and 100, neuromuscular blockade was reversed by administration of neostigmine (0.05 mg/kg) and glycopyrollate (0.01 mg/kg). Intravenous paracetamol 1 g was administered in all the cases 15 min before expected extubation for postoperative analgesia.

Time for eye opening, response to verbal commands, and removal of endotracheal tube after administration of reversal agents were noted.

In the postoperative period, analgesia was maintained with tramadol 100 mg IV 8 hourly. Rescue analgesia in the form of additional bolus of tramadol 100 mg was administered when visual analog scale ≥5. The total doses of tramadol received in the first 24 h were noted. The patients were also monitored for nausea, vomiting, first passage of flatus, and any other complication.

A 40-point quality of recovery score (QoR-40) was assessed on postoperative day 5 to ascertain the quality of recovery and the total score was calculated for each patient.

The primary objective of the study was to assess the QoR40 score on day 5 after surgery, while the secondary objectives were to access the influence of lignocaine infusion on perioperative hemodynamics, extubation variables, and postoperative analgesia.

The *sample size calculation* was based on a previous study,[6] to detect a difference of 10 in QoR-40 score with a power of 80% and α of 0.05; 42 patients were needed in each group. We took 45 patients in each group to compensate for any drop-out.

The data were analyzed statistically using software Microsoft office Excel 2007 and SPSS IBM version 22. Quantitative data were expressed as mean and standard deviation, while qualitative data were expressed in terms of median and range or frequencies and percentages. The means of the continuous variables were compared using independent sample *t*-test. Hemodynamic changes were compared with the help of repeated measure analysis of variance and *post hoc* test with Bonferroni's method. When data were not normally distributed, nonparametric test (Kruskal–Wallis) was used. $P < 0.05$ was considered to be significant.

## Results

The demographic profile, duration of surgery, and anesthesia are shown in Table 1. Hemodynamic variation among the

groups is shown in Figures 1 and 2. Baseline heart rate (HR) was similar in both the groups. A fall in HR was observed in both the groups from the baseline value after induction of anesthesia. Intubation caused an increase in the HR. Baseline values of mean arterial pressure (MAP) were similar in both the groups. A fall in MAP was observed after induction of anesthesia. Tracheal intubation caused an increase in MAP, thereafter it remained stable throughout the perioperative period.

**Table 1: Demographic profile**

| | Group 1 (*n*=45) | Group 2 (*n*=45) |
|---|---|---|
| ASA I/II | 34/11 | 31/13 |
| Age in years | 45.6±7.4 | 45.0±7.6 |
| Weight (kg) | 61.8±9.9 | 58.0±6.9 |
| DOA (min) | 111.7±15.3 | 104.5±19.7 |
| DOS (min) | 109.0 ±15.4 | 101.7±19.7 |

*ASA=American Society of Anesthesiologists; DOA=Duration of anesthesia, DOS=Duration of surgery. The data is presented as mean ± standard deviation or numbers*

**Table 2: Recovery parameters**

| | Group 1 (*n*=45) | Group 2 (*n*=45) | *P* |
|---|---|---|---|
| T1(min) | 2.8±2.0 | 2.8±1.8 | 0.241 |
| T2 (min) | 3.6±2.7 | 4.5±3.4 | 0.113 |
| T3 (min) | 3.4±2.4 | 4.6±3.3 | 0.395 |
| T4 (min) | 10.2±3.2 | 11.1±3.4 | 0.142 |
| Return of bowel motility (h) | 41.8±7.4 | 37.1±5.7 | 0.001 |

*The data is presented as mean ± Standard deviation; T1=Time of extubation after reversal of neuromuscular blockade (T0); T2=Time of eye opening after T0; T3=Time of verbal response after T0; T4=Time to achieve alderate score ≥9 after T0*

**Table 3: Postoperative analgesic requirement**

| | Group 1 (*n*=45) | Group 2 (*n*=45) | *P* |
|---|---|---|---|
| Time for requirement of first analgesic (min) | 70.8±70.4 | 40.7±30.0 | 0.006 |
| Total dosage (mg) | 477.0±133.2 | 560.0±115.0 | 0.001 |

*SD=Standard deviation*

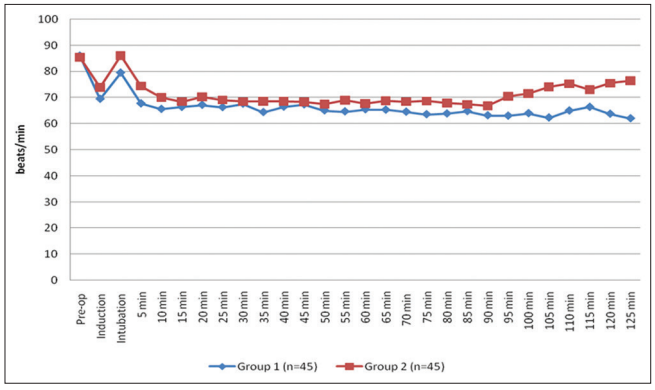


**Figure 1:** Heart rate variability in study groups

Table 2 shows the extubation variables among the groups. The values were comparable in the two groups.

The need for first analgesic in the postoperative period occured later in Group 1 compared to Group 2. The total dosage of postoperative tramadol usage for analgesia was higher in Group 2 [Table 3].

Return of bowel function was faster in the control group compared with lignocaine group.

The median [interquartile range (IQR)] recovery score (QoR-40) was 184 (178–191) in Group 1 and 178 (171–180) in Group 2, and the difference was statistically significant ($P < 0.001$).

## Discussion

Our study demonstrated usefulness of perioperative infusion of lignocaine in controlling pain, in improving the quality of recovery in Indian subjects undergoing total abdominal hysterectomy under general anesthesia.

Intravenous administration of lidocaine in perioperative period produces analgesia by different mechanisms. Increase in concentration of acetylcholine in cerebrospinal fluid, leading to exacerbation of inhibitory descending pain pathway,[7] blocking of muscarinic receptors M3,[8] inhibition of glycine receptors,[9] release of endogenous opioids,[10,11] reduction of the inflammatory response to tissue ischemia, and decreased release of cytokines in response to tissue damage[12] are some of the mechanisms proposed for the analgesic effects of lignocaine infusion. Lignocaine is also responsible for direct or indirect reduction of postsynaptic depolarization mediated by N-methyl-D-aspartate receptors.[13]

The effects of intravenous lignocaine depend on dosage, route of delivery, and blood supply at the site of injection. The

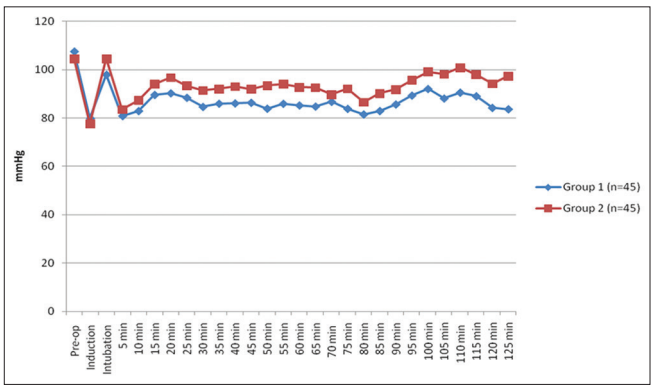


**Figure 2:** Mean blood pressure changes in study groups

peak serum levels are achieved after 20–30 min irrespective of the site, 60%–80% plasma bound, with a $V_d$ of 0.6–4.5 L/kg. Binding fraction also depends on the plasma levels of the acute phase reactant alpha-1-glycoprotein. A plasma level of 0.5–5 μg/mL is needed for clinical effects,[14] while a level of >5 μg/mL produces toxicity. The aim of intravenous therapy is to achieve effective therapeutic steady-state concentration with minimal side effects.[15] Bolus administration prior to infusion achieves faster plasma concentration and thus therapeutic concentration. The infusion should be based on body weight and should be reduced after 24 h to prevent toxicity.

Lignocaine infusion is associated with hemodynamic stability. It has a direct myocardial depressant effect, a peripheral vasodilating effect, and an effect on synaptic transmission and depth of anesthesia thereby preventing swings in HR and blood pressures.[16] In our study, infusion of lignocaine leads to a decrease in blood pressure from baseline after induction of anesthesia with fixed dose of propofol. Intubation leads to an increase in HR and mean blood pressure thereby stabilizing and remaining constant during the perioperative period. Ali *et al.* in their study on use of intravenous lignocaine in laproscopic cholecystectomy found that MAP and HR were significantly lower in lignocaine group compared with placebo after intubation and pneumoperitonium. Similar effects on hemodynamics were observed in other studies.[17,18]

The study of neuromuscular recovery and extubation after lignocaine infusion has been sparsely studied. Our study demonstrated no prolongation of neuromuscular paralysis and extubation time. Response to verbal commands/eye opening and time to achieve alderate score of ≥9 were similar in the two groups. In their study, Omar[19] studied the effects of systemic lidocaine infusion on train-of-four ratios during recovery from general anesthesia. They found a reduction of 15% in cumulative dose of rocuronium intraoperatively in patients receiving lidocaine.

Postoperative analgesia by lignocaine infusion has been widely reported and is multifactorial. In their study Tauzin-Fin and Bernard studied the effect of adding lignocaine infusion to standard anesthesia protocol in a total of 47 patients admitted in two phases and planned for laproscopic nephrectomy. Lignocaine infusion was continued for 24 h postoperatively and was associated with significant reduced morphine consumption and postop pain score and hyperalgesic extent on days 1, 2, and 4 postoperatively. Six-minute walk test and passage of first flatus were also significantly enhanced in patients receiving iv lignocaine infusion. Similar results were seen by Kim *et al*. in their patients undergoing lumbar surgery and by Yon *et al*. in patients for subtotal gastrectomy.[20-22]

Our study was corresponding to these studies in terms of reduced analgesic need and better postoperative analgesia. The difference with these studies was the nature of analgesic used (tramadol vs morphine), use of intermittent bolus versus patient-controlled analgesia, and duration of lignocaine infusion (perioperative vs perioperative with upto 24 h postoperatively). Few authors,[23,24] however, have not reported the beneficial effect of postoperative analgesia with use of lignocaine infusion.

Early return of bowel function was described as one of the criteria for fast-track surgery and early discharge from hospital. The data on bowel motility after surgery with perioperative lignocaine infusion have been conflicting. Release of inflammatory mediators during surgery, large volume fluid resuscitation, prolonged surgery, and postoperative use of opioids for analgesia have been postulated as factors responsible for ileus. Herroeder *et al*.[25] postulated that lignocaine through its effects on proinflammatory mediators was responsible for early bowel moments. This effect was, however, not seen in patients undergoing peripheral and abdominal surgeries.[26,27] Our study is in line with the later group as we found that the recovery of bowel function and passage of flatus were actually delayed as compared with the control group.

The QoR-40 is a global measure of quality of recovery incorporating five dimensions of health: patient support, comfort, emotions, physical independence, and pain; each item is graded on a 5-point Likert scale.[28] QoR-40 scores range from 40 (extremely poor quality of recovery) to 200 (excellent quality of recovery). The quality of recovery is directly related to patient satisfaction. Avoidance of postoperative discomfort and complications, early feeding and ambulation, early return to home, improved mental health of patient, enhancing patient satisfaction to modality of anesthetic used perioperatively. Our study demonstrated a better QoR-40 score with use of perioperative lignocaine than in the control group. This may be a result of pharmacological effects of lignocaine on inflammation, analgesic requirement, and nausea/vomiting. Our study corresponds to a study by De Oliveira *et al*. who found that intravenous infusion of lignocaine provides better recovery.[29]

Few limitations of our study were the inability to study the effects of lignocaine infusion on anesthetic consumption and use of PCA for better control of pain in the postoperative period. Continuous infusion of postoperative tramadol may have further improved patient satisfaction, Second, the QoR score could have been assessed at shorter intervals, that is, 24–48 h rather than on the fifth day to assess factors affecting the emotional aspect of recovery.

In conclusion, we observed that the use of intraoperative infusion of lignocaine is associated with early recovery, decreased postoperative analgesic requirement, and better patient satisfaction.

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## Conflicts of interest

There are no conflicts of interest.

## References

1. Kehlet H, Jensen TS, Woolf C. Persistent postsurgical factors and prevention. Lancet 2006;367:1618-25.
2. Carr D, Goudas LC. Acute pain. Lancet 1999;353:2051-8.
3. Macintyre PE, Schug SA, Scott DA, Visser EJ, Walker SM. Acute pain and injury response. In: Macintyre PE, Schug SA, Scott DA, Visser EJ, Walker SM, editors. Acute Pain Management: Scientific Evidence. 3rd ed. Melbourne: ANZCA and FPM; 2010. p. 15.
4. McCarthy GC, Megalla SA, Habib AS. Impact of intravenous lidocaine infusion on postoperative analgesia and recovery from surgery a systematic review of randomized controlled trials. Drugs 2010;70:1149-63.
5. Vigneault L, Turgeon AF, Cote D, Lauzier F, Nichole PC, Zarychanski R, *et al*. Perioperative intravenous lidocaine infusion for postoperative pain control: A meta-analysis of randomized controlled trials. Can J Anaesth 2011;58:22-37.
6. Oliveria GSD Jr, Ahmad S, Fitzgerald PC, Marcus RJ, Altman CS, Panjwani AS, *et al*. Dose ranging study on the effect of preoperative dexamethasone on postoperative quality of recovery and opioid consumption after ambulatory gynaecological surgery. Br J Anaesth 2011;107:362-71.
7. Abelson KS, Hoglund AU. Intravenously administered lidocaine in therapeutic doses increases the intraspinal release of acetylcholine in rats. Neurosci Lett 2002;317:93-6.
8. Hollmann MW, Ritter CH, Henle P, De Klaver M, Kamatchi GL, Durieux ME. Inhibition of m3 muscarinic acetylcholine receptors by local anaesthetics. Br J Pharmacol 2001;133:207-16.
9. Biella G, Sotgiu ML. Central effects of systemic lidocaine mediated by glycine spinal receptors: An iontophoretic study in the rat spinal cord. Brain Res 1993;603:201-6.
10. Coda B, Bausch S, Haas M, Chavkin C. The hypothesis that antagonism of fentanyl analgesia by 2-chloroprocaine is mediated by direct action on opioid receptors. Reg Anesth 1997;22:43-52.
11. Cohen SP, Mao J. Is the analgesic effect of systemic lidocaine mediated through opioid receptors? Acta Anaesthesiol Scand 2003;47:910-1.
12. De Klaver MJ, Buckingham MG, Rich GF. Lidocaine attenuates cytokine-induced cell injury in endothelial and vascular smooth muscle cells. Anesth Analg 2003;97:465-70.
13. Nagy I, Woolf CJ. Lignocaine selectivity reduces C fibre evoked neuronal activity in rat spinal cord *in vitro* by decreasing N-methyl-D-aspartate and neurokinin receptor-mediated postsynaptic depolarizations; implications for the development of novel centrally acting analgesics. Pain 1996;64:59-70.
14. Collinsworth KA, Kalman SM, Harrison DC. The clinical pharmacology of lidocaine as an antiarrhythymic drug. Circulation 1974;50:1217-30.
15. Weinberg L, Peake B, Tan C, Nikfarjam M. Pharmacokinetics and pharmacodynamics of lignocaine: A review. World J Anesthesiol 2015;4:17-29.
16. Abou-Madi MN, Keszler H, Yacoub JM. Cardiovascular reactions to laryngoscopy and tracheal intubation following small and large intravenous doses of lidocaine. Can Anaesth Soc J 1977;2:12-9.
17. Ali QE, Siddiqui OA, Khan YA. Effects of Xylocard pretreatment on hemodynamics in patients undergoing laparoscopic cholecystectomy. RMJ 2010;35:188-91.
18. Baral BK, Bhattarai BK, Rahman TR, Singh SN, Regmi R. Perioperative intravenous lidocaine infusion on postoperative pain relief in patients undergoing upper abdominal surgery. Nepal Med Coll J 2010;12:215-20.
19. Omar AM. Effect of systemic lidocaine infusion on train-of-four ratios during recovery from general anesthesia. Egyptian J Anaesth 2012;28:281-6.
20. Tauzin-Fin P, Bernard O. Benefits of intravenous lidocaine on post-operative pain and acute rehabilitation after laparoscopic nephrectomy. J Anaesthesiol Clin Pharmacol 2014;30:366-72.
21. Kim KT, Cho DC, Sung JK, Kim YB, Kang H, Song KS, *et al*. Intraoperative systemic infusion of lidocaine reduces postoperative pain after lumbar surgery: A double-blinded, randomized, placebo-controlled clinical trial. Spine J 2014;14:1559-66.
22. Yon JH, Choi GJ, Kang H, Park JM, Yang HS. Intraoperative systemic lidocaine for pre-emptive analgesics in subtotal gastrectomy: A prospective, randomized, double-blind, placebo-controlled study. Can J Surg 2014;57:175-82.
23. Bryson GL, Charapov I, Krolczyk G, Taljaard M, Reid D. Intravenous lidocaine does not reduce length of hospital stay following abdominal hysterectomy. Can J Anaesth 2010;57:759-66.
24. Choi SJ, Kim MH, Jeong HY, Lee JJ. Effect of intraoperative lidocaine on anesthetic consumption, and bowel function, pain intensity, analgesic consumption and hospital stay after breast surgery. Korean J Anesthesiol 2012;62:429-34.
25. Herroeder S, Pecher S, Schonherr ME, Kaulitz G, Hahnenkamp K, Friess H, *et al*. Systemic lidocaine shortens length of hospital stay after colorectal surgery: A double-blinded, randomized, placebo-controlled trial. Ann Surg 2007;246:192-200.
26.. Choi SJ, Kim MH, Jeong HY, Lee JJ. Effect of intraoperative lidocaine on anesthetic consumption, and bowel function, pain intensity, analgesic consumption and hospital stay after breast surgery. Korean J Anesthesiol 2012;62:429-34.
27. Wuethrich PY, Romero J, Burkhard FC, Curatolo M. No benefit from perioperative intravenous lidocainein laparoscopic renal surgery: A randomised, placebo-controlled study. Eur J Anaesthesiol 2012;29:537-43.
28. Myles PS, Weitkamp B, Jones K, Melick J, Hensen S. Validity and reliability of a postoperative quality of recovery score: The QoR-40. Br J Anaesth 2000;84:11-5.
29. De Oliveira GS Jr, Duncan K, Fitzgerald P, Nader A, Gould RW, McCarthy RJ. Systemic lidocaine to improve quality of recovery after laparoscopic bariatric surgery: A randomized double-blinded placebo-controlled trial. Obes Surg 2014;24:212-8.