Original Article

Effect of intravenous lignocaine infusion on propofol requirement using a closed-loop anaesthesia delivery system: A randomised controlled study

Address for correspondence:
Dr. Goverdhan D. Puri,
Department of Anaesthesia and Intensive Care,
Level 4, Nehru Hospital,
PGIMER, Sector 12,
Chandigarh - 160 012, India.
E-mail: gdpuri007@gmail.com

Submitted: 14-Aug-2024
Revised: 19-Mar-2025
Accepted: 28-Mar-2025
Published: 14-May-2025

Access this article online

Website: https://journals.lww.com/ijaweb

DOI: 10.4103/ija.ija_830_24

Quick response code

Jijo Francis, Goverdhan D. Puri, Tanvir Samra, Vighnesh Ashok, Rajarajan Ganesan

Department of Anaesthesia and Intensive Care, Post Graduate Institute of Medical Education and Research, Chandigarh, India

ABSTRACT

Background and Aims: Closed-loop anaesthesia delivery systems (CLADS) have made total intravenous anaesthesia easier, safer and more precise. lignocaine is a local anaesthetic with analgesic properties. This study aimed to compare the consumption of propofol and fentanyl delivered using CLADS in patients administered intraoperative lignocaine infusion. **Methods:** In this randomised trial, 70 females (18–60 years) undergoing elective breast surgery between March 2021 and December 2022 were randomised into two groups: a group administered lignocaine (1.5 mg/kg bolus followed by infusion of 2 mg/kg/h) and a placebo group. In both groups, propofol was administered using CLADS with a target bispectral index (BIS) set at 50 and an initial set fentanyl concentration of 2 ng/ml. The data were analysed using measures of central tendency and dispersion. **Results:** The mean total consumption of propofol (mg/kg/h) was 6.0 [standard deviation (SD): 1.4] [95% confidence interval (CI): 5.54, 6.46] in the lignocaine group and 6.2 (SD: 1.7) (95% CI: 5.64, 6.76) in the placebo group ($P = 0.719$). The mean dose of propofol (mg/kg) to achieve target BIS of 50 at induction was 2.00 (SD: 0.39) (95% CI: 1.87, 2.13) in the lignocaine group and 1.95 (SD: 0.38) (95% CI: 1.82, 2.08) in the placebo group ($P = 0.515$). The total dose of intraoperative fentanyl, as well as the performance parameters of CLADS (Median Performance Error, Median Absolute Performance Error and Wobble), time to extubation, time to rescue analgesia and duration of post-anaesthesia care unit stay were similar in both groups. **Conclusion:** There were no significant additive anaesthetic or analgesic effects of intraoperative lignocaine given during breast surgery, where anaesthesia was maintained with propofol, fentanyl and nitrous oxide.

Keywords: Anaesthesia, CLADS, closed-loop anaesthesia delivery system, fentanyl, lignocaine, propofol

INTRODUCTION

Intravenous (IV) lignocaine infusion has been evaluated extensively for its analgesic, anti-inflammatory and immune-modulatory effects.[1] It has been shown to reduce the intraoperative requirements of both volatile and IV anaesthetic agents.[2,3] A major limitation of all earlier studies evaluating the role of IV lignocaine on IV anaesthetic requirements has been the use of manually titrated infusion systems, which introduce bias. The use of closed-loop control systems for IV drug delivery ensures a stable anaesthetic depth and accounts for the interindividual variations due to pharmacokinetic (PK) and pharmacodynamic (PD) differences in the patient population.[4]

A closed-loop anaesthesia delivery system (CLADS) is one such automated anaesthesia delivery system

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Francis J, Puri GD, Samra T, Ashok V, Ganesan R. Effect of intravenous lignocaine infusion on propofol requirement using a closed-loop anaesthesia delivery system: A randomised controlled study. Indian J Anaesth 2025;69:587-93.

that incorporates a two-drug PK/PD model for the simultaneous administration of propofol and fentanyl.[5,6] The usual initial set fentanyl concentration is 2 ng/ml (Schafer PK model for fentanyl), and the target bispectral index (BIS) is 50. However, the in-built algorithm monitors changes in BIS, heart rate and blood pressure and raises or lowers the effect site concentration of propofol and fentanyl to maintain haemodynamics.[5,6]

To the best of our knowledge, there are no studies evaluating the effect of intraoperative IV lignocaine infusion on the intraoperative requirements of propofol and fentanyl administered via closed-loop delivery systems. We hypothesised that IV lignocaine infusion in patients administered general anaesthesia using CLADS would reduce intraoperative propofol requirements. The primary objective was thus to compare intraoperative total consumption of propofol in mg/kg/h between the lignocaine group (1.5 mg/kg bolus followed by infusion of 2 mg/kg/h) and placebo in female patients aged 18–60 years administered general anaesthesia for total mastectomy. The secondary objectives of our study were to compare intraoperative fentanyl consumption, performance characteristics of CLADS, time to extubation, time to rescue analgesia and duration of post-anaesthesia care unit (PACU) in patients administered general anaesthesia with and without lignocaine infusion.

METHODS

This double-arm, placebo-controlled, parallel-group randomised controlled trial was conducted between March 2021 and November 2021 in a tertiary care research and referral hospital. Ethical approval for this study was obtained from the Institutional Ethics Committee (vide approval number INT/IEC/2021/SPL-249, dated 13 February 2021). Prospective registration was made with the Clinical Trials Registry-India (vide registration number CTRI/2021/03/032074, dated 17 March 2021, accessible at www.ctri.nic.in). Written informed consent was obtained from all study participants, and the study was conducted in accordance with the principles outlined in the Declaration of Helsinki (2013) and the Good Clinical Practice guidelines. Patients aged 18–60 years, classified as American Society of Anesthesiologists Physical Status (ASA-PS) I/II, scheduled for total mastectomy with or without axillary clearance under general anaesthesia were included after they gave written informed consent. Patients with known allergies to lignocaine, those with hepatic and/or renal dysfunction and those with a history of substance abuse and/or psychiatric illness were excluded from the study.

Patients were consecutively screened for potential enrolment and then randomly allocated into one of the two groups. Randomisation was done using computer-generated codes using Statistical Package for the Social Sciences (SPSS) statistics software version 29.0 [International Business Machines Corporation (IBM Corp.), Armonk, NY, USA], with the allocation sequence concealed in sealed envelopes. The study drugs were prepared by an investigator who was not involved in the perioperative care of the patient. The patients, attending anaesthesiologists and surgeons were blinded to group allocation. Participants in the lignocaine group received a bolus of IV lignocaine 2% (1.5 mg/kg) 90 sec before induction of general anaesthesia, followed by a maintenance infusion of 2 mg/kg/h of IV lignocaine 2% intraoperatively. Participants in the placebo group received a bolus of 0.075 ml/kg of 0.9% normal saline 90 sec before induction of general anaesthesia, followed by a maintenance infusion of 0.1 ml/kg/h of 0.9% saline intraoperatively. According to these calculations, the volume of the bolus dose of lignocaine and the normal saline placebo was the same in both groups, as was the total infusion rate administered per hour. The infusions were administered using a syringe driver infusion pump with the display screen showing the volume administered shielded from the attending anaesthesiologist. Furthermore, lignocaine and normal saline are both colourless solutions and the attending anaesthesiologist and the surgeons were, thus, unaware of the drug being infused. A sample calculation of the bolus and infusion doses for a 70-kg patient is shown in Supplementary Table 1.

All study participants were fasted preoperatively according to standard nil per os guidelines. Monitors (including electrocardiogram, non-invasive blood pressure, continuous pulse oximetry and BIS) were attached, and baseline vital signs were recorded. General anaesthesia was administered using CLADS. Induction was achieved with CLADS using an initial set fentanyl concentration of 2 ng/ml (Schafer PK model for fentanyl) and a set target BIS of 50. Following the achievement of the initial set target of fentanyl, CLADS automatically controlled further dosing of fentanyl to maintain the heart rate and blood pressure within around 20% of baseline. The

administration of propofol was based on continuous feedback from BIS. However, delivery was interrupted in cases of hypotension as per the device's built-in safety mechanism. Tracheal intubation was achieved using atracurium 0.5 mg/kg, and further dosing was administered as per neuromuscular monitoring. The lungs were ventilated using volume-controlled ventilation mode with a 50:50 oxygen-nitrous oxide mixture. Intraoperative vitals and anaesthetic drug consumption data were recorded automatically using CLADS, as per the proforma. All patients were actively warmed intraoperatively using a forced warm air blanket applied to the lower half of the body. All intraoperative key events (start of anaesthesia, start of surgery, end of surgery and end of anaesthesia) were marked as event flags in the log file. The performance parameters of CLADS in maintaining the target BIS, heart rate and mean arterial pressure were measured by Median Performance Error (MDPE), Median Absolute Performance Error (MDAPE), Wobble and global score, the measures of variations in target parameters as well as stability of the performance of the controlling algorithm, as performed in our earlier studies evaluating CLADS.[7] Wobble is an index of time-related changes in performance, measuring intrasubject variability in performance errors. MDAPE indicates the inaccuracy of the device, while the median of PE (MDPE) reflects the bias. Divergence demonstrates the effect of drug concentrations over time. A positive value indicates a progressive widening of the gap between predicted and measured concentrations, whereas a negative value reveals that the measured concentrations converge on the predicted values.

All three infusions were switched off during skin closure. Residual neuromuscular blockade was reversed using IV neostigmine 50 μg/kg and glycopyrrolate 10 μg/kg. The trachea was extubated when the patient was fully awake, obeying commands and exhibiting adequate recovery of muscle power. CLADS was disconnected, and the patients were transferred to PACU for further observation and monitoring.

Postoperatively, the patient's vital signs were monitored, including electrocardiogram for heart activity, non-invasive blood pressure for blood pressure, oxygen saturation for blood oxygen levels and respiration for breathing rate. Pain was measured using a visual analogue scale (VAS; 1 – no pain at all to 10 – extreme pain) every 15 min. Rescue analgesia in the form of paracetamol 1 g IV was given if the VAS score was >4. Nausea or vomiting was treated with rescue antiemetic ondansetron 0.1 mg/kg. Any other significant postoperative events were noted and documented. Data collection was continued for 12 h postoperatively. The postoperative data was collected by an independent observer blinded to group allocation and otherwise not involved in the study.

For sample size calculation, OpenEpi: Open-Source Epidemiologic Statistics for Public Health (developed by Emory University's Rollins School of Public Health, www.OpenEpi.com) was used. The sample size was calculated based on the evidence that the mean dose of propofol required for anaesthesia maintenance using the closed-loop system is 4.7 [standard deviation (SD): 1.69] [95% confidence interval [CI]: 4.356, 5.044) mg/kg/h.[8] Considering a power of 90% and an alpha of 0.05, to detect a 30% decrease in propofol dosage among patients who receive lignocaine, we required 56 patients for the study. We aimed to recruit at least 73 patients to account for potential dropouts.

Statistical analysis was performed using SPSS version 22.0 (IBM Corp., Armonk, NY, USA). Shapiro–Wilk test was applied to check the normal distribution of continuous data. Mean and SD were calculated for normally distributed continuous data. Otherwise, the median and interquartile range were calculated. Categorical variables are described in terms of frequency and percentages. Normally distributed continuous variables (patient demographic data, duration of anaesthesia and surgery, fentanyl and propofol consumption, and extubation parameters) were compared between two studies using the Student's *t*-test. The performance characteristics of CLADS, namely MDPE, MDAPE, Wobble and global score, exhibited a skewed distribution; therefore, these continuous variables were compared using the Mann–Whitney *U* test. A two-tailed *P* value ≤0.05 was considered statistically significant, with a 95% CI.

RESULTS

A total of 73 patients from March 2021 to December 2022 were consecutively screened for eligibility, and all were successfully recruited and randomised. Three patients (two in the lignocaine group and one in the placebo group) were subsequently excluded from the analysis because of a violation of the study protocol due to technical issues with machinery. A total of 70 patients (35 in each group) were included in the final analysis [Figure 1].

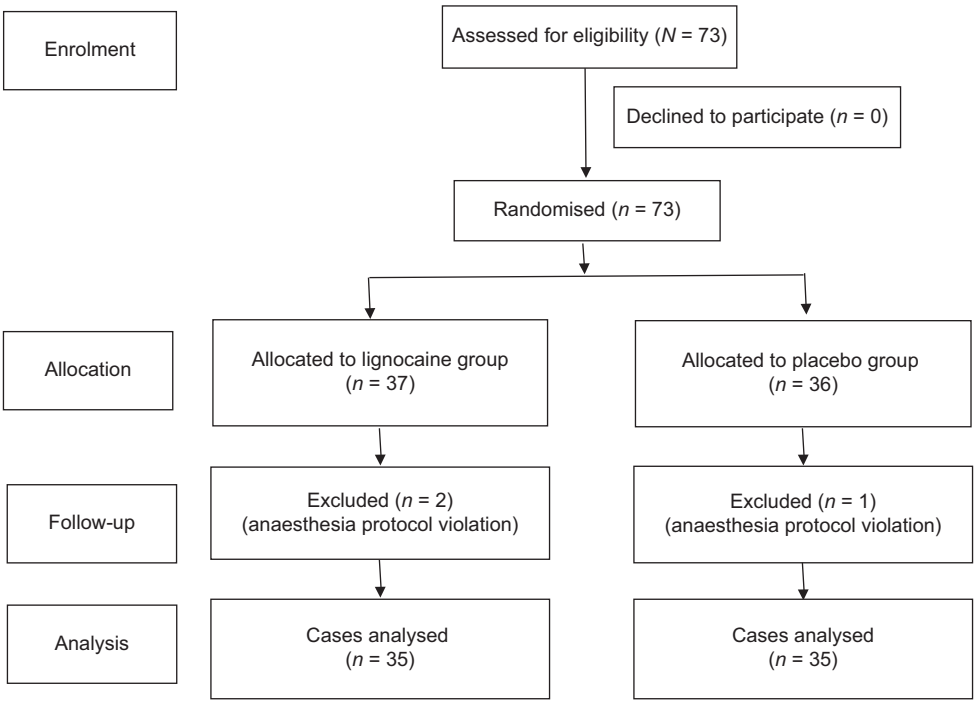

Figure 1: CONSORT (Consolidated standards of reporting trials) figure

The demographic parameters and surgical profiles were comparable between the two groups [Table 1]. There was no significant difference in the drug administration profile of propofol between the two groups. No significant difference was found in propofol consumption between the two groups [Table 2]. The mean dose of propofol at which loss of consciousness (LOC) was marked was 105.2 (SD: 22.9) (95% CI: 97.61, 112.79) mg in the lignocaine group and 103.2 (SD: 28.6) (95% CI: 93.72, 112.68) mg in the placebo group (P = 0.755). The mean value of BIS at which LOC was marked was 74.4 (SD: 7.3) (95% CI: 71.98, 76.82) in the lignocaine group and 75.1 (SD: 7.4) (95% CI: 72.65, 77.55) in the placebo group (P = 0.710).

The mean total dose of intraoperative fentanyl was 209.9 (SD: 74.3) (95% CI: 185.28, 234.51) µg and 192.8 (SD: 65.5) (95% CI: 171.10, 214.50) µg in the lignocaine group and placebo group, respectively, and the difference was not statistically significant [Table 2]. The total dose of intraoperative fentanyl administered at induction to reach the initial target effect-site concentration (ITC) of 2 ng/ml was also comparable in both groups. The mean time to reach ITC in seconds was 232 (SD: 100) (95% CI: 198.87, 265.13) in the lignocaine group versus 227 (SD: 140) (95% CI: 180.62, 273.38) in the placebo group (P = 0.862). The performance parameters of CLADS in maintaining BIS, heart rate and mean arterial pressure, as measured by MDPE, MDAPE and Wobble, were similar in both groups [Table 3].

The extubation parameters (BIS at skin closure, reversal of neuromuscular blockage and extubation, and time to extubation) and the postoperative recovery profile (time to rescue analgesia and duration of PACU stay) were all comparable between the two groups [Table 4]. None of the patients had any episode of postoperative nausea and/or vomiting or any adverse events that could be attributed to the systemic administration of lignocaine.

DISCUSSION

In this single-centre randomised controlled trial involving 70 patients undergoing total mastectomy (with/without axillary clearance), the addition of IV lignocaine (1.5 mg/kg bolus followed by 2 mg/kg/h) resulted in no significant difference in the intraoperative requirements of propofol and fentanyl administered using CLADS.

The global score (a measure of the overall inefficiency of the closed-loop system control), time to extubation after reversal, and duration of stay in the PACU were higher in the placebo group; however, the differences were not statistically significant. It is worth noting, however, that the study was not adequately powered

Table 1: Demographic and surgical profile

Variable	Lignocaine group (*n*=35)	Placebo group (*n*=35)	*P*
Age (years)	47.9 (7.7) (45.349, 50.451)	45.6 (9.3) (42.519, 48.681)	0.263
Weight (kg)	63.9 (12.3) (59.825, 67.975)	62.5 (11.0) (58.856, 66.144)	0.610
Height (cm)	157.7 (7.4) (155.248, 160.152)	159.3 (4.5) (157.809, 160.791)	0.296[a]
BMI (kg/m^2)	25.7 (4.5) (24.209, 27.191)	24.7 (4.7) (23.143, 26.257)	0.370
ASA-I and II	22	27	0.373
Anaesthesia time (min)	137.2 (41.2) (123.551, 150.849)	127.7 (38.1) (115.078, 140.322)	0.320
Surgery time (min)	109.5 (37.7) (97.010, 121.990)	100.2 (38.6) (87.412, 112.988)	0.313

[a]Values expressed as mean (standard deviation) (95% CI) and frequency. Anaesthesia time=time from start of fentanyl till shift out of patient to PACU, surgery time=time from skin incision to closure. *P*<0.05 considered significant and Student's *t*-test used. ASA=American Society of Anesthesiologists, BMI=body mass index, CI=confidence interval, PACU=post-anaesthesia care unit

Table 2: Propofol and fentanyl consumption

Variable	Lignocaine group (*n*=35)	Placebo group (*n*=35)	*P*
Propofol			
Total dose to reach target BIS of 50 (mg)	126.1 (26.2) (117.420, 134.780)	121.5 (32.5) (110.733, 132.267)	0.520
Drug dosage/BW (mg/kg)	2.00 (0.39) (1.871, 2.129)	1.95 (0.38) (1.824, 2.076)	0.515
Time to reach target BIS of 50 (min)	2.2 (1.8) (1.604, 2.796)	2.4 (1.3) (1.969, 2.831)	0.598
Intraoperative propofol consumption (mg)	890.4 (396.7) (758.976, 1021.824)	841.7 (396.6) (710.309, 973.091)	0.609
Average drug infusion rate (mg/kg/h)	6.0 (1.4) (5.536, 6.464)	6.2 (1.7) (5.637, 6.763)	0.719
Fentanyl			
Drug to reach ITC (µg)	76.5 (16.9) (70.901, 82.099)	76.5 (23.4) (68.748, 84.252)	0.995
Drug dosage/BW (µg/kg)	1.21 (0.22) (1.137, 1.283)	1.23 (0.30) (1.131, 1.329)	0.675
Intraoperative fentanyl consumption (µg)	209.9 (74.3) (185.285, 234.515)	192.8 (65.5) (171.100, 214.500)	0.310
Average drug infusion rate (µg/kg/h)	1.53 (0.58) (1.338, 1.722)	1.56 (0.70) (1.328, 1.792)	0.850

Values expressed as mean (standard deviation) (95% CI). *P*<0.05 considered significant and Student's *t*-test used. BIS=bispectral index, BW=body weight, CI=confidence interval, ITC=initial target effect site concentration

Table 3: Performance characteristics

Variable	Lignocaine group (*n*=35)	Placebo group (*n*=35)	*P*
BIS MDPE	–4 (-6, -2)	−2 (−6, 2)	0.095
BIS MDAPE	12 (10, 16)	14 (11.25, 17.75)	0.310
BIS Wobble	10 (10, 14)	12 (10, 15)	0.923
Percentage time in maintenance mode where BIS was within±10 of target	76 (63, 82)	69 (55, 77)	0.311
HR MDPE	1 (−1, 3)	0 (−2.75, 2)	0.224
HR MDAPE	5 (4, 6)	5 (4, 7)	0.375
HR Wobble	4 (3, 5)	5 (3, 6)	0.284
MAP MDPE	0 (−2, 4)	1 (−0.75, 4)	0.357
MAP MDAPE	6 (4, 9)	6 (4, 8)	0.592
MAP Wobble	6 (4, 7)	5.5 (4, 7.75)	0.864
Global score	29.2 (24.3, 47.0)	36.7 (28.7, 61.1)	0.816

Values expressed as median (first, third quartile) and compared using Mann–Whitney *U* test. *P*<0.05 significant. BIS=bispectral index, HR=heart rate, MAP=mean arterial pressure, MDAPE=Median Absolute Performance Error, MDPE=Median Performance Error, PE=performance error. PE=[(measured BIS−target BIS)/target BIS]× 100. $MDPE_i$=median {PE_{ij}, j=1,…, Ni}. $MDAPE_i$=median {$|PE|_{ij}$, j=1,…, Ni}. $Wobble_i$=median {$|PE_{ij}-MDPE_i|$, j=1, …, Ni}, where i=subject number, j=jth (one) measurement of observation period and N=total number of measurements. (the median absolute deviation of each PE from MDPE. Global score={(MDAPE+wobble)/% of the time BIS value between 40 and 60}×100

Table 4: Extubation and postoperative parameters

Variable	Lignocaine group (*n*=35)	Placebo group (*n*=35)	*P*
BIS at the end of skin closure[a]	60 (60, 67.5)	60 (55, 64)	0.127[c]
BIS at reversal[a]	66 (62, 71)	68 (63, 73)	0.893[c]
BIS after extubation[a]	80 (76.5, 86.5)	78 (76, 80)	0.206[c]
Time to extubation after reversal (min)[b]	2.9 (0.6) (2.701–3.099)	3.1 (0.8) (2.835–3.365)	0.559[d]
Time taken for VAS >4 (min)[b]	26.6 (26) (17.986–35.214)	29 (22) (21.712–36.288)	0.685[c]
Duration of stay in PACU[b]	59.14 (30.88) (48.910–69.370)	63.71 (32.14) (53.062–74.358)	0.546[c]

[a]Values expressed as median (first, third quartile). [b]Values expressed as mean (standard deviation)(95% confidence interval); *P*<0.05 significant. [c]Mann–Whitney *U* test. [d]Student's *t*-test. BIS=bispectral index, PACU=post-anaesthesia care unit, VAS=visual analogue scale

for the above parameters; therefore, further research with a larger sample size is necessary.

IV administration of lignocaine has been shown to reduce the intraoperative requirements of volatile agents.[2,3] The effect of IV lignocaine infusion on the intraoperative requirements of propofol is less specific. No statistically significant difference was reported by Altermatt *et al*.[9] in the total dose of propofol and plasma levels of propofol measured in arterial samples at the termination of infusions with IV lignocaine in patients undergoing laparoscopic cholecystectomy. However, the total and maintenance doses of propofol, the incidence of hypoxia and postoperative pain were significantly reduced when lignocaine was co-administered for sedation in the elderly for gastroscopy.[10]

Altermatt *et al*.[9] used a mixture of oxygen and air as carrier gases for patients undergoing laparoscopic surgeries during general anaesthesia, while we used a combination of oxygen and nitrous oxide for patients undergoing breast surgery. If the hypnotic-sparing effect of lignocaine is secondary to its anti-nociceptive effect, the use of nitrous oxide, which is a moderate analgesic, could have influenced the results of our study. Altermatt *et al*.[9] used a bolus dose of fentanyl intraoperatively based on alterations in haemodynamics for analgesia. In our study, we have used a closed-loop fentanyl delivery system.

Lignocaine has been shown to possess analgesic, anti-hyperalgesic and anti-inflammatory properties.[1] It suppresses spontaneous impulses generated from injured nerve fibres at the surgical site and from the proximal dorsal root ganglion.[11-13] Systemic administration of lignocaine lowers postoperative pain scores, decreases opioid consumption and improves the quality of recovery.[14-18] However, a Cochrane systematic review and meta-analysis concluded that the effect of systemic lignocaine on the pain scores is uncertain in the first 24 h after surgery, and after 24 h, lidocaine has no effect on the quality of postoperative analgesia.[19]

Our study was conducted on a homogeneous group of patients undergoing a specific surgical procedure. A closed-loop drug delivery system was used for the administration of propofol and fentanyl intraoperatively. This minimised operator bias ensured consistent and reliable maintenance of the depth of anaesthesia and analgesia.

The therapeutic range for serum lignocaine is considered to be 2.5–3.5 μg/ml with toxicity symptoms starting at >5 μg/ml. Studies conducted with 3 mg/kg/h dosages report higher incidences of adverse events. So, we used 2 mg/kg/h. Our study, however, has limitations. We did not measure plasma concentrations of propofol, fentanyl or lignocaine in our research. Real-time measurements of these drug concentrations and their temporal analysis could have provided more insight into the effect of lignocaine on hypnosis and analgesia. Furthermore, without plasma concentration measurement, the possibility also exists that our dosage was inadequate to reach therapeutic efficacy for our population, as the dosage for lignocaine may vary from individual to individual and from population to population.

CONCLUSION

IV administration of lignocaine infusion following a bolus does not affect the total dose of propofol and fentanyl used intraoperatively in patients undergoing total mastectomy with/without axillary clearance in which induction and maintenance of general anaesthesia were done using CLADS.

Study data availability

De-identified data may be requested with reasonable justification from the authors (via email to the corresponding author) and will be shared after approval, in accordance with the authors' institution's policy.

Financial support and sponsorship

This work was funded and supported by the Department of Anaesthesia and Intensive Care, Post Graduate Institute of Medical Education and Research, Chandigarh, India.

Conflicts of interest

There are no conflicts of interest.

ORCID

Jijo Francis: https://orcid.org/0009-0007-7820-6147
Goverdhan Dutt Puri: https://orcid.org/0000-0002-9763-4055
Tanvir Samra: https://orcid.org/0000-0002-6301-1992
Vighnesh Ashok: https://orcid.org/0000-0001-5185-5656
Rajarajan Ganesan: https://orcid.org/0000-0002-9984-7150

REFERENCES

1. Castro I, Carvalho P, Vale N, Monjardino T, Mourão J. Systemic anti-inflammatory effects of intravenous lidocaine in surgical patients: A systematic review and meta-analysis. J Clin Med 2023;12:3772. doi: 10.3390/jcm12113772
2. Nakhli MS, Kahloul M, Guizani T, Zedini C, Chaouch A, Naija W. Intravenous lidocaine as adjuvant to general anesthesia in renal surgery. Libyan J Med 2018;13:1433418. doi: 10.1080/19932820.2018.1433418
3. Batko I, Kościelniak-Merak B, Tomasik PJ, Kobylarz K. Lidocaine reduces sevoflurane consumption and improves recovery profile in children undergoing major spine surgery. Med Sci Monit 2020;26:e919971. doi: 10.12659/MSM.919971
4. Hosseinirad S, van Heusden K, Dumont GA. Evaluating inter-individual variability captured by the Eleveld pharmacokinetics model. J Clin Monit Comput 2024;38:505-18
5. Mahajan V, Samra T, Puri GD. Anaesthetic depth control using closed loop anaesthesia delivery system vs. target controlled infusion in patients with moderate to severe left ventricular systolic dysfunction. J Clin Anesth 2017;42:106-13.
6. Biswas I, Mathew PJ, Singh RS, Puri GD. Evaluation of closed-loop anesthesia delivery for propofol anesthesia in pediatric cardiac surgery. Pediatr Anesth 2013;23:1145-52.
7. Castellanos Peñaranda C, Casas Arroyave FD, Gómez FJ, Pinzón Corredor PA, Fernández JM, Velez Botero M, *et al*. Technical and clinical evaluation of a closed loop TIVA system with SEDLineTM spectral density monitoring: Multicentric prospective cohort study. Perioper Med 2020;9:1. doi: 10.1186/s13741-019-0130-2
8. Hegde HV, Puri GD, Kumar B, Behera A. Bi-spectral index guided closed-loop anaesthesia delivery system (CLADSTM) in pheochromocytoma. J Clin Monit Comput 2009;23:189-96.
9. Altermatt FR, Bugedo DA, Delfino AE, Solari S, Munoz HR, Cortinez LI. Evaluation of the effect of intravenous lidocaine on propofol requirements during total intravenous anaesthesia as measured by bispectral index. Br J Anaesth 2012;108:979-83.
10. Hu S, Wang M, Li S, Zhou W, Zhang Y, Shi H, *et al*. Intravenous lidocaine significantly reduces the propofol dose in elderly patients undergoing gastroscopy: A randomized controlled trial. Drug Des Devel Ther 2022;16:2695-705.
11. Li Y, Xu J, Xu Y, Zhao XY, Liu Y, Wang J, *et al*. Regulatory effect of general anesthetics on activity of potassium channels. Neurosci Bull 2018;34:887-900.
12. Jayakar SS, Zhou X, Chiara DC, Dostalova Z, Savechenkov PY, Bruzik KS, *et al*. Multiple propofol-binding sites in a γ-aminobutyric acid type A receptor (GABAAR) identified using a photoreactive propofol analog. J Biol Chem 2014;289:27456-68.
13. Daykin H. The efficacy and safety of intravenous lidocaine for analgesia in the older adult: A literature review. Br J Pain 2017;11:23-31.
14. McKay A, Gottschalk A, Ploppa A, Durieux ME, Groves DS. Systemic lidocaine decreased the perioperative opioid analgesic requirements but failed to reduce discharge time after ambulatory surgery: Anesth Analg 2009;109:1805-8.
15. Ghimire A, Subedi A, Bhattarai B, Sah BP. The effect of intraoperative lidocaine infusion on opioid consumption and pain after totally extraperitoneal laparoscopic inguinal hernioplasty: A randomized controlled trial. BMC Anesthesiol 2020;20:137. doi: 10.1186/s12871-020-01054-2
16. Plass F, Nicolle C, Zamparini M, Issa GAI, Fiant AL, Roux YL, *et al*. Effect of intra-operative intravenous lidocaine on opioid consumption after bariatric surgery: A prospective, randomised, blinded, placebo-controlled study. Anaesthesia 2021;76:189-98.
17. Habibi A, Alipour A, Gholipour Baradari A, Gholinataj A, Habibi MR, Peivandi S. The effect of adding lidocaine to patient controlled analgesia with morphine on pain intensity after caesarean section with spinal anesthesia: A double-blind, randomized, clinical trial. Open Access Maced J Med Sci 2019;7:1946-50.
18. Koshyari H, Asthana V, Agrawal S. Evaluation of lignocaine infusion on recovery profile, quality of recovery, and postoperative analgesia in patients undergoing total abdominal hysterectomy. J Anaesthesiol Clin Pharmacol 2019;35:528-32.
19. Weibel S, Jelting Y, Pace NL, Schnabel A, Hollmann MW, Hahnenkamp K, *et al*. Continuous intravenous perioperative lidocaine infusion for postoperative pain and recovery in adults. Cochrane Database Syst Rev 2018;6:CD009642. doi: 10.1002/14651858.CD009642.pub3

Supplementary Table 1: Example of bolus dose and infusion rate calculation in a 70-kg patient
For an example, patient weighing 70 kg
Bolus dose of 2% lignocaine: 1.5 mg × 70=105 mg=105/20 ml=5.25 ml
Bolus dose of 0.9% normal saline: 0.075 ml × 70=5.25 ml
Infusion rate of 2% lidocaine: 2 × 70 mg/h=140 mg/h=140/20 ml/h=7 ml/h
Infusion rate of 0.9% normal saline: 0.1 × 70 ml/h=7 ml/h