

Effects of Intravenous Lidocaine in Total Intravenous Anesthesia for Colonoscopy: a Double-Blind Randomized Controlled Study

Pretimon Kimpee, Subundit Injampa, Tanat Chotijarumaneewong, Napanont Kiatmongkolkul, Tatchakorn Promboon

Ramathibodi Medical School, Chakri Naruebodindra Medical Institute, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Samut Prakan, Thailand

Abstract

Background: Total intravenous anesthesia (TIVA) is widely used as an anesthetic technique in patients undergoing colonoscopy. Lidocaine can reduce visceral pain and potentiates the ventilatory responses to carbon dioxide. This study aimed to evaluate the efficacy and safety of lidocaine combined with propofol during a colonoscopic procedure.

Methods: Sixty-one patients underwent elective colonoscopy under TIVA with IV fentanyl 0.5 mcg/kg and propofol 1 mg/kg followed by 2 mg/kg/h as a maintenance infusion with titration as needed. The patients were also randomized to receive 1.5 mg/kg of IV lidocaine followed by 2 mg/kg/h (group L) or 0.3 mL/kg of IV normal saline followed by 0.4 mL/kg/h (group N). The primary outcome was the total dose of propofol used. The secondary outcomes were complications and adverse events.

Results: Data for 60 patients were available for analysis. There was no statistically significant difference in the median total dose of propofol used between the two groups or in episodes of apnea and desaturation. The mean difference in mean arterial pressure at 5 min after scope insertion was significantly smaller in group N than in group L. There was no statistically significant between groups in terms of the decrease in heart rate from baseline, or any adverse events.

Conclusion: Intravenous lidocaine 1.5 mg/kg followed by lidocaine 2 mg/kg/h did not decrease the dose of IV propofol used during a colonoscopic procedure. However, it was able to reduce the risk of hypotension in the early induction phase.

Keywords: colonoscopy, lidocaine, propofol, total intravenous anesthesia

Introduction

Total intravenous anesthesia (TIVA) is a popular anesthetic technique for patients undergoing colonoscopy. The aim of sedation is to provide analgesia while avoiding hemodynamic instability. Midazolam, fentanyl, and propofol are commonly used for sedation because of their rapid onset and short duration of action.¹ Unfortunately, these agents have a synergistic depressive effect on respiration.² There is a considerable body of literature on the ability of dexmedetomidine or ketamine combined with propofol to reduce respiratory and cardiovascular complications during a colonoscopy procedure.^{3,4} Nevertheless, dexmedetomidine increases the incidence of hypotension and bradycardia while ketamine induces hallucination after the procedure and prolongs the recovery time, resulting in patient dissatisfaction. Lidocaine can be combined with propofol during colonoscopy to reduce inflammation and visceral pain and to potentiate the ventilatory response to carbon dioxide.^{5,6}

There are no published recommendations regarding the appropriate dose of lidocaine for a colonoscopy procedure; according to the American Pain Society, intravenous (IV) administration of lidocaine 1.5 mg/kg as a loading dose followed by 1.5-2 mg/kg/h as a maintenance infusion in patients undergoing abdominal surgery can decrease bowel ileus and postoperative pain without local anesthetic systemic toxicity.⁷ The aim of this study was to determine whether administration of lidocaine can reduce the total dose of propofol administered and the incidence of respiratory complications during a colonoscopic procedure.

Methods

The study was reviewed and approved by the Ethics Committee of the Faculty of Medicine Ramathibodi Hospital (approval number MURA2021/165; date of approval, March 8, 2021) and retrospectively registered in the Thai Clinical Trial Registry September 2, 2021 (<https://www.thaiclinicaltrials.org/show/TCTR20210902012>). The study adhered to the CONSORT statement and was performed in accordance with the Declaration of Helsinki. All patients provided written informed consent before enrollment in the study. Patients with lidocaine allergy, epilepsy, arrhythmias, desaturation (baseline oxygen saturation <95%), hepatic dysfunction (increase in aspartate aminotransferase or alanine aminotransferase to more than twice the upper limit of normal), or renal dysfunction (glomerular filtration rate <45 mL/min/1.73 m²), those using analgesics or hypnotics for longer than 3 months, and those engaging in drug abuse were excluded. This prospective randomized controlled study was performed at Chakri Naruebodindra Medical Institute and included patients aged 18-75 years with American Society of Anesthesiologists physical status I, II, or III who were scheduled for colonoscopy under TIVA between March and October 2021.

Patients who did not meet all the inclusion criteria and/or met at least one exclusion criterion and those who wished to withdraw before randomization were deemed to be screen failures. Patients were randomly assigned using a computer-generated randomization method into a lidocaine (L) group and a normal saline (N) group. Allocation concealment was performed using the sealed envelope

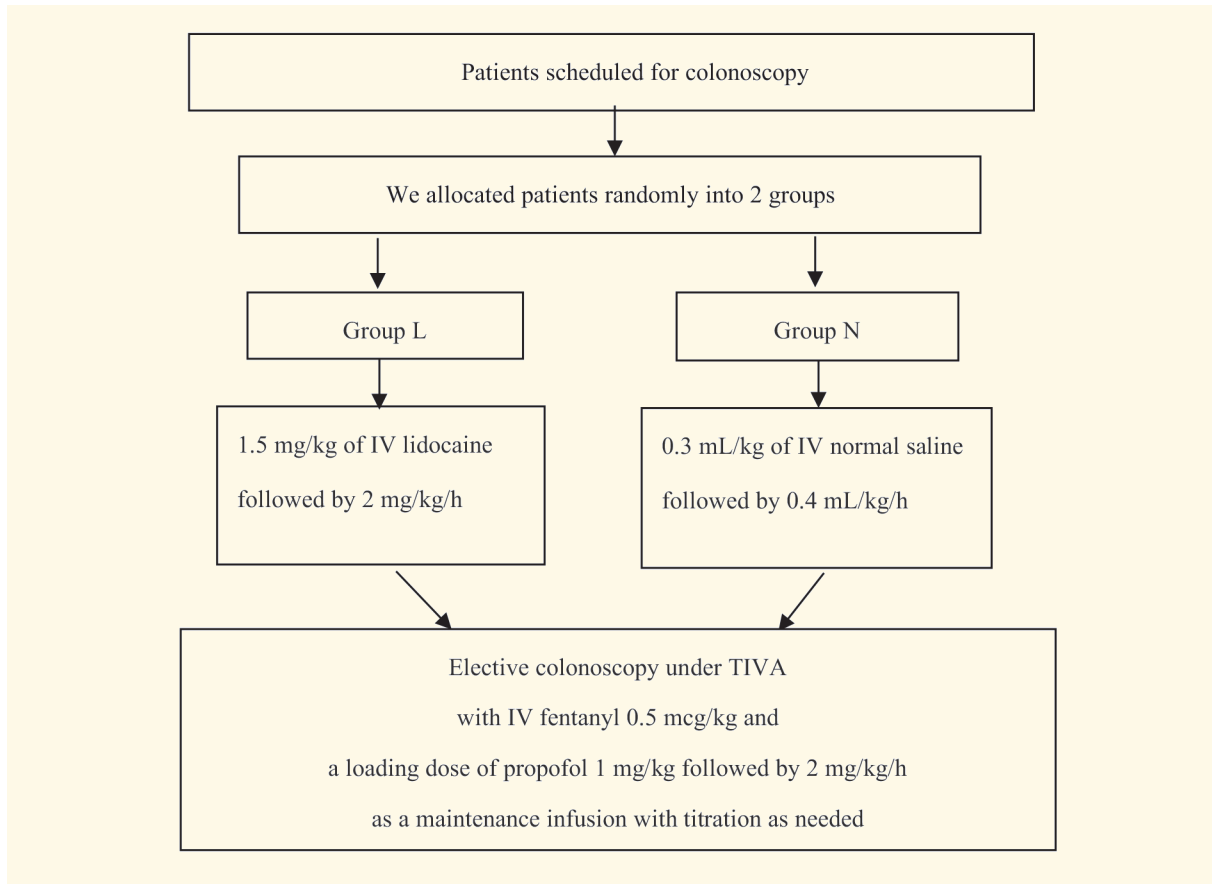


Figure 1 Protocol flow chart

method. A nurse anesthetist who was not involved in collection of data prepared the drugs according to group allocation, after which an anesthesiologist who was not involved in the data analysis-maintained anesthesia and collected the data. Standard monitoring was performed in the colonoscopy room.

All patients were hydrated by infusion of Ringer's acetate solution at a maintenance rate and supplemented with oxygen 3 L/min via nasal cannula as usual care. In both groups, TIVA was induced using IV fentanyl 0.5 mcg/kg and propofol 1 mg/kg (Propofol®-Lipuro; B. Braun, Melsungen, Germany), and moderate-to-deep sedation was maintained intraoperatively by IV infusion of propofol 2 mg/kg/h. Patients in

group L also received 0.5% lidocaine (prepared by diluting 2% preservative-free lidocaine hydrochloride in normal saline) at 0.3 mL/kg as an IV loading dose over 5 min before induction followed by a maintenance infusion of 0.4 mL/kg/h. In group N, patients received an equal loading volume and infusion rate of normal saline instead of 0.5% lidocaine (Figure 1). Blood pressure, heart rate (HR), respiratory rate, and oxygen saturation were recorded at 5 min intervals during the procedure.

If HR increased by >20 bpm, mean arterial pressure (MAP) increased by 10 mmHg, or the patient moved, a 20-30-mg IV bolus of propofol was administered and the rate of propofol infusion was increased by 0.5 mg/kg/h. If hypo-

tension (MAP <65 mmHg or <20% of baseline) occurred, 6 mg of ephedrine was administered. If bradycardia (HR <50 bpm or <10% of baseline) developed, 0.6 mg of atropine was administered. If desaturation (oxygen saturation <95%) occurred or the apneic time was >10 sec, the anesthesiologist performed an airway maneuver and facemask ventilation with a fraction of inspired oxygen of 1.0 until oxygen saturation was >95%. After the colonoscopy was completed, the patient was transferred to the post-anesthesia care unit (PACU), where vital signs were monitored and readiness for discharge was assessed using the Modified Aldrete Score.

The primary outcome was the total dose of propofol used during the colonoscopy. The secondary outcomes were incidence of apnea, desaturation, and adverse events from lidocaine infusion, including hemodynamic instability, the sedation score on arrival in the PACU, time to awakening, postoperative nausea and vomiting, post-colonoscopy pain (assessed using a numeric rating scale) and the patient and endoscopist satisfaction score (both 0-10) and were compared between the two study groups. Study outcomes were analyzed by intention-to-treat.

Statistical analysis

Continuous variables are expressed as the mean±standard deviation or as the median (interquartile range [IQR]). Comparisons were performed using the Student's t-test or the Wilcoxon rank-sum test as appropriate. Numeric variables are shown as the number (percentage). The other variables were compared between groups using the chi-square test or Fisher's exact test. Repeated measures data were compared between groups using linear mixed model

analysis. All statistical analyses were performed using SPSS for Windows version 21.0 (IBM Corp., Armonk, NY, USA). *P*-values <0.05 were considered statistically significant. A previous study reported that intravenous lidocaine allows for a nearly 50% reduction in propofol dose requirements, with a mean of 200±109 mg in the saline group and 128±53 mg in the lidocaine group.⁸ A sample size that would have 80% power based on a type I error of 0.05 was calculated based on this report. Allowing for an approximately 30% dropout rate, the required sample size was determined to be 30 in each group.

Results

A CONSORT flowchart of the study is shown in Figure 2. Sixty-one patients were enrolled in the study between March and October 2021. One patient was found to have a cardiac arrhythmia and hypertension in the colonoscopy room and was excluded before randomization. There were no significant between-group differences in demographic characteristics, except that there were more women group L than in group N (Table 1). There was no significant difference in the median total dose of propofol administered between group L and N (Table 2). Furthermore, there was no significant between-group difference in the median propofol loading dose or in the median propofol maintenance dose.

In terms of the secondary outcomes, the frequency of apneic episodes in group L was similar to that in group N (three patients with one episode per person in group L; three patients with one episode per person and one with two

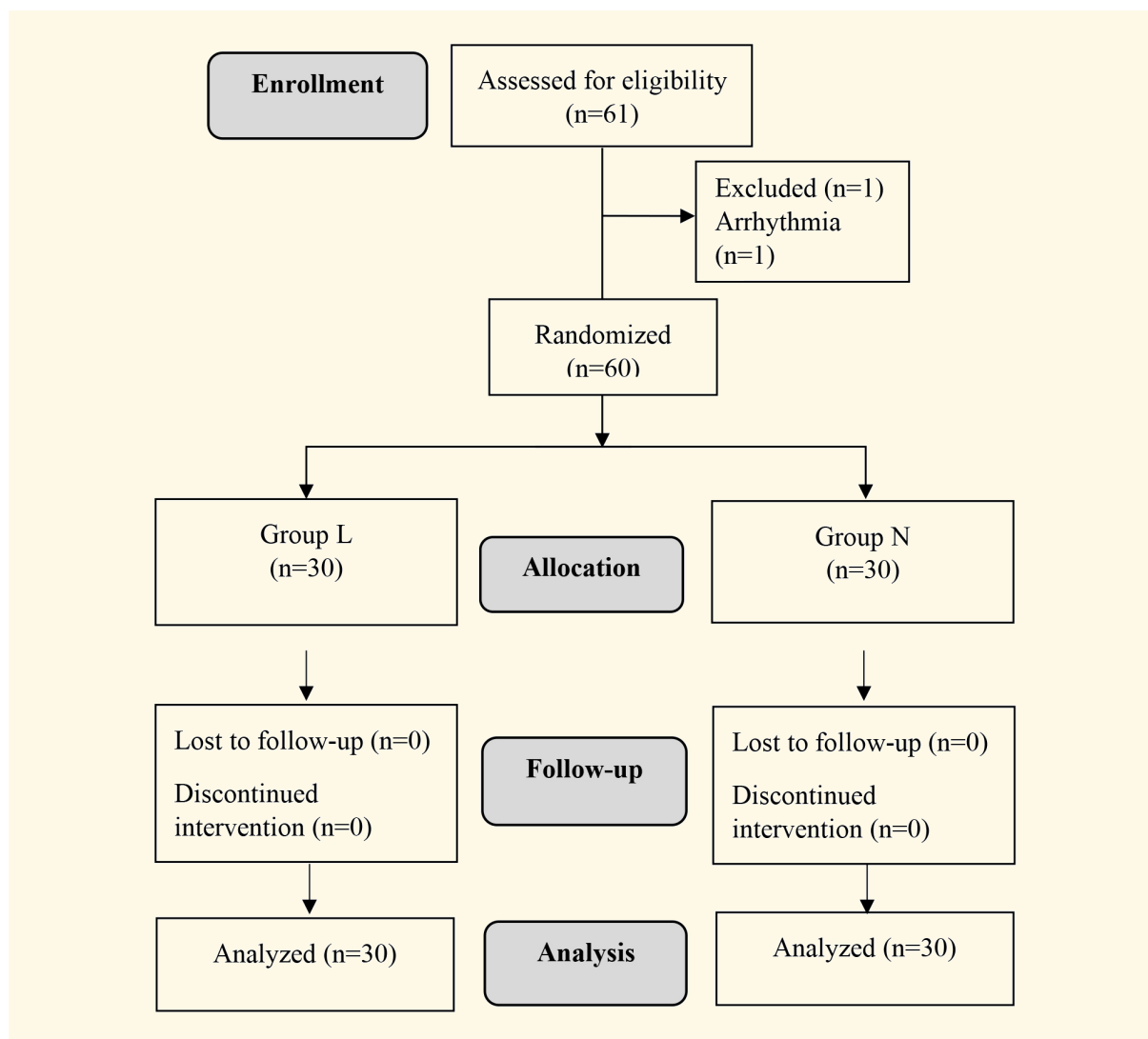


Figure 2 CONSORT flow chart

episodes per person in group N). Four patients in group L and two in group N had desaturation, but the difference was not significant (Table 3).

There was no statistically significant between-group difference in frequency of episodes of hemodynamic instability (hypotension and bradycardia). However, episodes of hypotension seemed to be more frequent in group N ($P=0.071$). MAP decreased from baseline at the time of starting colonoscopy and at 5 min after colonoscopy by significantly greater amounts in

group N ($P=0.055$ and 0.033 , respectively) (Figure 3). At both these time points, there was no statistically significant between-group difference in the decrease in HR from baseline (Figure 4).

There was no significant difference in other postoperative adverse events between the two groups (Table 3). No cardiac arrhythmias or symptoms of local anesthetic systemic toxicity, such as dizziness, drowsiness, metallic taste, oral paresthesia, or blurred vision, were detected during colonoscopy.

Table 1 Demographic and clinical characteristics

	Group L (n=30)	Group N (n=30)	P-value
Age (yr), mean±SD	57.0±11.8	56.7±10.9	0.901
Female, n (%)	22 (73.3)	14 (46.7)	0.035*
Body mass index (kg/m ²), mean±SD	24.4±5.4	24.9±3.3	0.707
ASA physical status, n (%)			0.411
I	4 (13.3)	3 (10.0)	
II	16 (53.3)	21 (70.0)	
III	10 (33.3)	6 (20.0)	
Mallampati score, n (%)			0.211
I	9 (30.0)	13 (43.3)	
II	18 (60.0)	12 (40.0)	
III	2 (6.7)	5 (16.7)	
IV	1 (3.3)	0	
Operation time (min), mean±SD	32.6±16.1	33.5±14.1	0.832
Intravenous fluid (mL), median (IQR)	300 (200-400)	300 (200-450)	0.582

Data are shown as the mean±standard deviation, number (%), or median (interquartile range) as appropriate. ASA = American Society of Anesthesiologists, **P* <0.05, statistically significant.

Table 2 Drugs and dosages administered

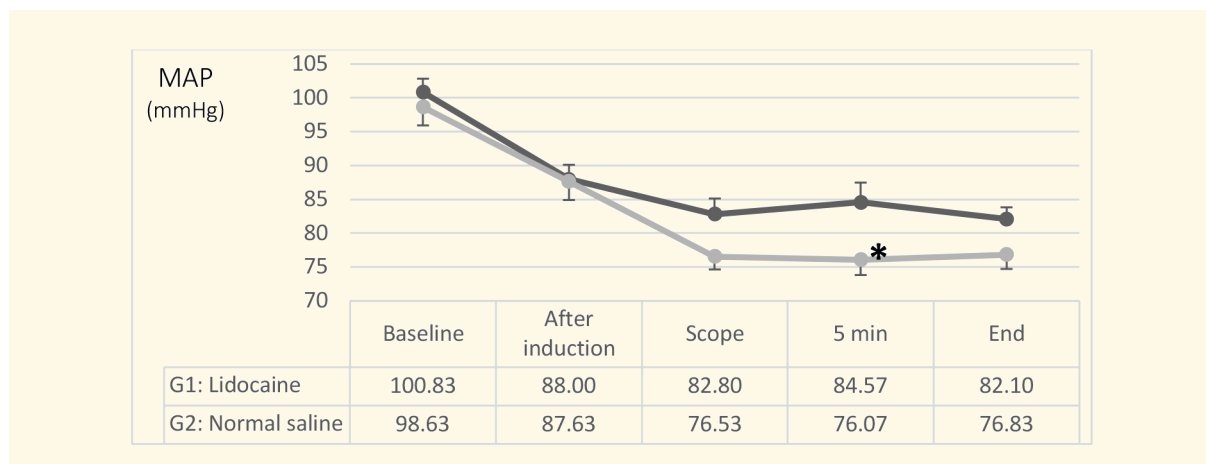
	Group L (n=30)	Group N (n=30)	P-value
Fentanyl (mcg), median (IQR)	32.5 (25-40)	35 (30-40)	0.356
Total propofol (mg), median (IQR)	180 (150-270)	200 (150-250)	0.953
Propofol for loading (mg), median (IQR)	60 (55-70)	67.5 (60-70)	0.103
Propofol for infusion (mcg/kg/min), median (IQR)	73.2 (64.5-90.3)	62.9 (47.3-93.6)	0.294
Lidocaine (mg), mean±SD	154.2±42.5	0	

Data are shown as the mean±standard deviation or as the median (interquartile range).

Table 3 Intraoperative and postoperative events, and patient and endoscopist satisfaction

	Group L (n=30)	Group N (n=30)	P-value
Intraoperative events			
Apnea, n (%)			
1 episode	3 (10.0)	3 (10.0)	>0.999
2 episodes	0	1 (3.3)	
Desaturation, n (%)			
1 episode	2 (6.7)	2 (6.7)	0.547
2 episodes	2 (6.7)	0	
Hypotension, n (%)			
1 episode	5 (16.7)	2 (6.7)	0.071
2 episodes	0	4 (13.3)	
3 episodes	1 (3.3)	3 (10.0)	
Bradycardia, n (%)			
1 episode	3 (10.0)	6 (20.0)	0.472
Postoperative events			
Sedation score, mean±SD	2.4±1.0	2.2±0.9	0.500
Time to awakening (min), mean±SD	6.8±8.9	5.1±7.4	0.442
Nausea and vomiting, n (%)	0	0	1.000
Numeric rating scale score (0-10), median (IQR)	0 (0-1)	0 (0-0)	0.279
Patient satisfaction (0-10), median (IQR)	10 (10-10)	10 (10-10)	0.700
Endoscopist satisfaction (0-10), median (IQR)	10 (9-10)	10 (9-10)	0.942

Data are shown as the mean±standard deviation or median (interquartile range). Sedation score: 1, awake; 2, asleep but easily aroused; 3, drowsy but arousable; 4, somnolent and difficult to arouse⁹



* $P < 0.05$, statistically significant. MAP = mean arterial pressure

Figure 3 Mean MAP at each time point (black line, lidocaine group; gray line, normal saline group)

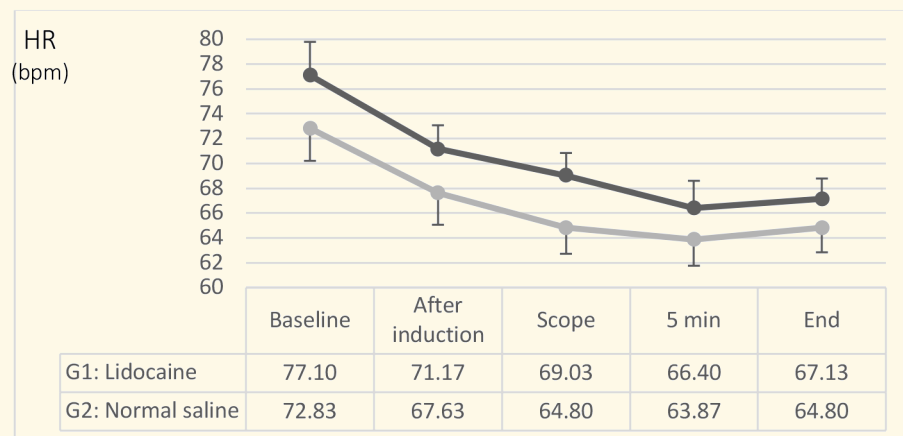


Figure 4 Mean HR at each time point (black line, lidocaine group; gray line, normal saline group)

Discussion

The main finding of this study was that administration of IV lidocaine combined with propofol and fentanyl did not reduce the total dose of propofol during colonoscopy. This finding is in contrast with the statistically significant reduction in the total dose of propofol administered simultaneously with IV lidocaine during a colonoscopic procedure when compared with placebo in previous randomized controlled studies^{8,10,11} and in a systematic review and meta-analysis.¹²

The dosage and combination of sedative drugs used in this study (fentanyl 0.5 mcg/kg iv and propofol 1 mg/kg IV as a loading dose followed by a maintenance infusion of 2-4 mg/kg/h) were decided based on usual practice for a colonoscopic procedure at our hospital. In view of concerns about lidocaine toxicity, we chose a lower dose of lidocaine for IV infusion (a loading dose of 1.5 mg/kg followed by a 2 mg/kg/h maintenance infusion) as recommended by

the American Pain Society.⁷ Hence, our regimen was different from that used in the previous studies^{8,10,11} and might explain why IV lidocaine did not reduce the propofol requirement in our study. However, we did not measure the plasma concentration of propofol or lidocaine and did not monitor the accuracy of the sedation level using the Bispectral Index or target-controlled infusion. A previous study found that using lidocaine can reduce propofol dose by up to almost 50%. However, they used ketamine instead of fentanyl, which could have a more sedative effect. Moreover, a recent study found that adding intravenous lidocaine combined with propofol and sufentanil in elderly patients undergoing colonoscopy could significantly reduce propofol consumption by 13.2%.¹³ Our study found that lidocaine reduced propofol by around 10%, but it might not have had enough power to confirm this.

Unlike previous studies, our trial included a patient with American Society of Anesthesiologists physical status III and the duration of

colonoscopy procedure was longer, which might have affected our results. Additionally, the difference in sex distribution between our two study groups may have affected our results due to physiological and pharmacological differences.^{14,15} But after adjusting for baseline characteristics, the results still showed no significant changes. It has been reported that lidocaine has a significant propofol-sparing effect and increases the ventilatory response to carbon dioxide.⁶ We did not detect a reduction in desaturation or in apnea complications as secondary outcomes. Even though we designed the power of the sample size based on a relevant study⁸ in which the patient population had characteristics that were very similar to those in our patients, the main aim of the previous study was to detect a reduction in the requirement for propofol.

In terms of the frequency of episodes of events and degree of decrease from baseline, the only hemodynamic parameters recorded in our study were MAP and HR. We found no statistically significant between-group difference in the frequency of episodes of hypotension. However, there was a significant decrease in MAP from baseline at 5 min after colonoscopy in the N group but not in the L group, which suggests that lidocaine can improve hypotension when after propofol is used. There was also no statistically significant between-group difference in the extent of the decrease in HR from baseline. In term of postoperative complications, we did not find a significant between-group difference in the sedation score on arrival in the PACU, time to awakening, postoperative nausea and

vomiting, post-colonoscopy pain, or satisfaction when scored by patients and endoscopists.

This study has some limitations. First, plasma propofol and lidocaine concentrations were not measured and sedation levels could not be measured accurately. Second, an opioid was subsequently combined with propofol in our sedation protocol, which might have interfered with a propofol-sparing effect of lidocaine and be the reason why using lidocaine did not affect the ventilatory response to carbon dioxide. Third, the power and design of the study were insufficient to assess incidence of apnea and desaturation. These will need to be investigated further in the future.

Conclusion

Administration of IV lidocaine 1.5 mg/kg as a loading dose followed by a maintenance infusion 2 mg/kg/h could not decrease the total dose of propofol used for sedation during colonoscopy. Additionally, lidocaine could improve hypotension in the early phase of induction but had no effect on other hemodynamic parameters or on the adverse event rate.

Acknowledgements

The authors are grateful to Assistant Professor Dr. Rattaphol Seangrung and Assistant Professor Dr. Sunthiti Morakul (Anesthesiologist, Department of Anesthesiology, Ramathibodi Hospital, Mahidol University) for supporting this study. They also thank Edanz (www.edanz.com/ac) for editing a draft of this manuscript.

References

1. Early DS, Lightdale JR, Vargo JJ, et al. Guidelines for sedation and anesthesia in GI endoscopy. *Gastrointest Endosc.* 2018;87:327-37.
2. Sonnenberg A. Sedation in colonoscopy. *Gastroenterol Hepatol.* 2016;12:327-9.
3. Nishizawa T, Suzuki H, Hosoe N, Ogata H, Kanai T, Yahagi N. Dexmedetomidine vs propofol for gastrointestinal endoscopy: a meta-analysis. *United European Gastroenterol J.* 2017;5:1037-45.
4. Seleem WM, El Hossieny KM, Abd-Elsalam S. Evaluation of different sedatives for colonoscopy. *Curr Drug Saf.* 2020;15:20-4.
5. 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.
6. Labaille T, Clergue F, Samii K, Ecoffey C, Berdeaux A. Ventilatory responses to CO₂ following intravenous and epidural lidocaine. *Anesthesiology.* 1985;63:179-83.
7. Chou R, Gordon DB, de Leon-Casasola OA, et al. Management of postoperative pain: a clinical practice guideline from the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. *J Pain.* 2016;17:131-57.
8. Forster C, Vanhaudenhuyse A, Gast P, et al. Intravenous infusion of lidocaine significantly reduces propofol dose for colonoscopy: a randomised placebo-controlled study. *Br J Anaesth.* 2018;121:1059-64.
9. Pasero C. Assessment of sedation during opioid administration for pain management. *J Perianesth Nurs.* 2009;24:186-90.
10. Chen M, Lu Y, Liu H, et al. The propofol-sparing effect of intravenous lidocaine in elderly patients undergoing colonoscopy: a randomized, double-blinded, controlled study. *BMC Anesthesiol.* 2020;20:132.
11. Li X, Lv X, Jiang Z, et al. Application of intravenous lidocaine in obese patients undergoing painless colonoscopy: a prospective, randomized, double-blind, controlled study. *Drug Des Devel Ther.* 2020;14:3509-18.
12. Kamal F, Khan MA, Lee-Smith W, et al. Efficacy and safety of supplemental intravenous lidocaine for sedation in gastrointestinal endoscopic procedures: systematic review and meta-analysis of randomized controlled trials. *Gastrointest Endosc.* 2021;93:1241-9.
13. Li M, Ke W, Zhuang S. Effect of intravenous lidocaine on propofol consumption in elderly patients undergoing colonoscopy: a double-blinded, randomized, controlled trial. *BMC Anesthesiol.* 2022;22:61.
14. Filipescu D, Ștefan M. Sex and gender differences in anesthesia: relevant also for perioperative safety? *Best Pract Res Clin Anaesthesiol.* 2021;35:141-53.
15. Diego LADS. Anesthesia and women's peculiarities. *Rev Assoc Med Bras.* 2023;69(Suppl1):e2023S103.