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Intravenous lidocaine decreased oxygen-desaturation episodes induced by propofol-based sedation for gastrointestinal endoscopy procedures: a prospective, randomized, controlled trial

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Abstract

Background As a popularly used analgesic adjuvant, intravenous (IV) lidocaine could reduce the consumption of propofol in painless gastrointestinal (GI) endoscopy. However, whether IV lidocaine could affect the incidence of oxygen-desaturation episodes (ODE) during painless GI endoscopy is still unknown. Therefore, we tested the hypothesis that IV lidocaine could decrease the incidence of propofol-induced ODE and involuntary movements in patients during GI endoscopy.

Methods Three hundred twenty-two patients scheduled for GI endoscopy were randomly divided into lidocaine group and control group. After midazolam and sufentanil injection, a bolus of 1.5 mg/kg lidocaine was given and followed by continuous infusion of 4 mg/kg/h in lidocaine group, whereas the same volumes of saline solution in control group. Then, propofol was titrated to produce unconsciousness. The primary outcome was the incidence of ODE during the procedure. The secondary outcomes were the incidence of different degree of hypoxia and corresponding treatments and the involuntary body movements.

Results A total of 300 patients were finally included in the analysis, 147 patients in lidocaine group and 153 in control group. The incidence of ODE was 22% in lidocaine group and 39% in control group (OR:0.052; 95%CI: 0.284–0.889; $P=0.018$). IV lidocaine also improved the occurrence of different degree of hypoxia ($P=0.017$) and needed few treatments ($P=0.028$). The incidence of involuntary body movements (14% vs 26%, $P=0.013$) and adverse circulatory events was decreased by IV lidocaine.

Conclusions IV lidocaine adjuvant to propofol-based sedation could reduce the incidence of oxygen-desaturation episodes and involuntary body movements, with fewer adverse circulatory events.

Trial registration Chinese Clinical Trial Registry ChiCTR2100053818. Registered on 30 November 2021.

Keywords Lidocaine, Oxygen-desaturation, Involuntary movements, Propofol, Painless, Gastrointestinal endoscopy

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Background

Gastrointestinal (GI) endoscopy has been regarded as the gold standard for screening and diagnosis of GI diseases. With the increasing demand of patients for painless medical care, procedure sedation and anesthesia (PSA) has become a popular method to mitigate patients' discomfort and pain during GI endoscopy. Despite PSA is considered safe generally, the occurrence of adverse effects is still inevitable [1–3]. Limb movement, respiratory depression and cardiovascular events often occur in patients undergoing PSA, especially in the combined examination of gastroscopy and colonoscopy, due to the longer operation time and stronger stimulation. Both painless and safety are equally important for GI endoscopy. Therefore, more safety and efficacy drugs used in painless GI endoscopy are needed.

With the rapid action and short half-life pharmacologic characteristic, propofol has been the main sedative drug recommended for PSA. However, hypoxemia commonly occurs during propofol sedation due to respiratory depression and shared channels with gastroscopy [4–6]. Once hypoxia is severe or lasts for a longer time, patients, especially the older, may face the risk of permanent neurologic damage, arrhythmia, cardiorespiratory arrest, or even death [7–9]. As some studies have shown, propofol consumption, aging, high body mass index (BMI), sleep apnea syndrome, and operation time were independent risk factors for hypoxia [5, 10]. Therefore, adjuvant drugs with less side effects on cardiovascular function, while reducing the dosage of propofol, are increasingly used in painless GI endoscopy. For example, opioids and benzodiazepines used with propofol can significantly decrease propofol requirements, but hypoxemia and hypotension still frequently occur [11–14]. Ketamine combined with propofol reduce propofol consumption and decrease cardiopulmonary depression events, but it produces schizophrenia and dissociative states, and increases the time to recovery as well [15, 16]. In addition, dexmedetomidine has been used in PSA also. However, it leads to bradycardia and hypertension which will also endanger patient safety [17–19].

Intravenous (IV) lidocaine is always used for curing arrhythmia, it also has been popularly used as an adjuvant to propofol sedation at present. Previous studies have shown that IV lidocaine can reduce visceral pain, decrease opioid consumption, accelerate the recovery of postoperative intestinal function and promote the rehabilitation after visceral surgery [20, 21]. Possessing some properties, such as increasing ventilatory response to carbon dioxide (CO_2) and anti-nociceptive action [22], intraoperative application of IV lidocaine can reduce the dosage of propofol [23–25], prevent postoperative coughing and sore throat in adults [26]. Our previous research had also found that IV lidocaine could reduce the median effective dose (ED_{50}) of propofol during gastroscopy [27]. Although there are several previous studies that evaluated the effect of IV lidocaine on the doses of propofol in GI endoscopy [28], the procedure of these studies were ERCP or coloscopy or others, and the main outcome were the dosage of propofol. Although the impact of hypoxia incidence has been observed in the past studies, these studies either did not have a clear definition of hypoxia and did not control the occurrence of different degrees of hypoxia as a secondary outcome indicator. The more obvious drawback is that some factors that clearly affect hypoxia incidence, such as the body mass index (BMI), STOP-BANG score, and patient airway evaluation, were not well documented. This leads to deficiencies in existing research. Therefore, our study is not only feasible, but also necessary. It needs to further study the incidence of oxygen-desaturation episodes during propofol sedation with lidocaine under a uniform and strict trial.

We hypothesized that IV lidocaine adjuvant to propofol sedation could decrease the ODE in GI procedure patients. Other indicators including the incidence of involuntary body movements, propofol consumption, circulatory adverse events, lidocaine relevant adverse symptoms, endoscopist and patient satisfaction were compared between lidocaine group and control group.

Materials and methods

This study was a single-center, double-blind, randomized, placebo-controlled trial conducted in the endoscopy unit of Beijing Friendship Hospital affiliated to Capital Medical University, Beijing, China. All enrolled participants were required to sign written informed consent. The study complied the Declaration of Helsinki and adhered to CONSORT guidelines. The protocol was approved by the Ethics Committee of the Beijing Friendship Hospital Affiliated to Capital Medical University (2020-P2-159–02), registered at Chinese Clinical Trial Registry (ChiCTR2100053818), and published on Trials [29].

Patients who planned to undergo both painless gastroscopy and colonoscopy, histopathology would be taken if necessary, were enrolled in this study and met the following inclusion criteria: 18–65 years old, American Society of Anesthesiologists physical status classification I–III, body mass index (BMI) < 30 kg/m^2, STOP-Bang score < 5, heart rate (HR) > 50 beats/min without history of atrioventricular block, liver and kidney function well, without local anesthetic in the past 24 h, without analgesics and hypnotics in the past 7 days, volunteer to participate in this research and sign the informed consent concerning their participation in the study. Exclusion criteria were as following: patients aged > 65 years or < 18 years, had participated in other clinical trials within the past

four weeks, allergic to lidocaine, pregnancy or lactation, couldn't understand the VAS score, severe central nervous system disease and severe mental illness, taking sedative, analgesic or hypnotics in the past week, considered unsuitable to participate in this study by the investigator (such as abnormally long operation time, and not meeting the target sedative depth during the procedure).

Three hundred twenty-two patients were randomly allocated to the lidocaine group or the saline control group at a ratio of 1:1 by a computer-generated sequence. Only the nurse who kept grouping envelops knew the grouping information, she was responsible for configuring and covering trail drugs. The anesthesiologist, endoscopist, the patient, as well as the assessor, were all blinded to the grouping.

The gastrointestinal endoscopy was performed by a fixed team, including 3 experienced endoscopists, all of whom are attending physicians and have completed over 500 procedures. The sedation based on propofol was conducted by a fixed team of anesthesiologists. After entering the endoscopic operating room, all patients were anesthetized and according to the following strategies, such as Fig. 1 shows, and the data were collected and stored at the same time.

All participants followed the clinical procedure below: Routine monitors were performed: electrocardiogram, noninvasive blood pressure (BP), peripheral oxygen saturation, respiratory rate, and waveform capnography. With patients in a left lateral position, 6 L/min oxygen via a nasal cannula was supplied at least 3 min. At the moment of 60 s before the administration of propofol, midazolam 0.02 mg/kg, sufentanil 0.1 μg/kg, and then the intervention medicines were given intravenously in turn to patients of both groups. In group L, lidocaine will be administrated at 1.5 mg/kg (0.15 ml/kg, 10 mg/ml) as initial dose within 10 s, then followed by 4 mg/kg/h (0.4 ml/kg/h) infusion until the ileocecal area was exposed. According to the Lidocaine Instructions, the maximum loading of intravenous lidocaine within 1 h is 4.5 mg/kg or 300 mg. In Group C, normal saline will be administrated at 0.15 ml/kg, and the following infusion speed is 0.4 ml/kg/h, the same volume with lidocaine, until the ileocecal area was exposed. Induction: An initial bolus of propofol (adjusted to the patient's age: 1.0 mg/kg for age > 50; 1.5 mg/kg for age < 50) was administered slowly. Then Modified Observer's Assessment of Alertness/sedation (MOAA/S) was evaluated [30]. A repeated dose of 10–20 mg propofol was injected if MOAA/S > 2 until the patients' MOAA/S score was ≤ 1 before the operation start. Sedation maintains after the operation start: additional propofol (0.5 mg/kg) was repeated in any case occurs, including coughing, grimaces, involuntary body movements, MAP or HR increased by 20%, or MOAA/S score > 1. By the time our colonoscope reached the ileocecal area, most of the difficult procedures during the examination had already been completed, and the uncertainty of the procedure for retracting the colonoscope was low, and it could generally be completed within 2 min. In order to give the patient a recovery time, we stopped the infusion of lidocaine at this time. When the operation completed, all patients were transferred to the post-anesthesia care unit (PACU).

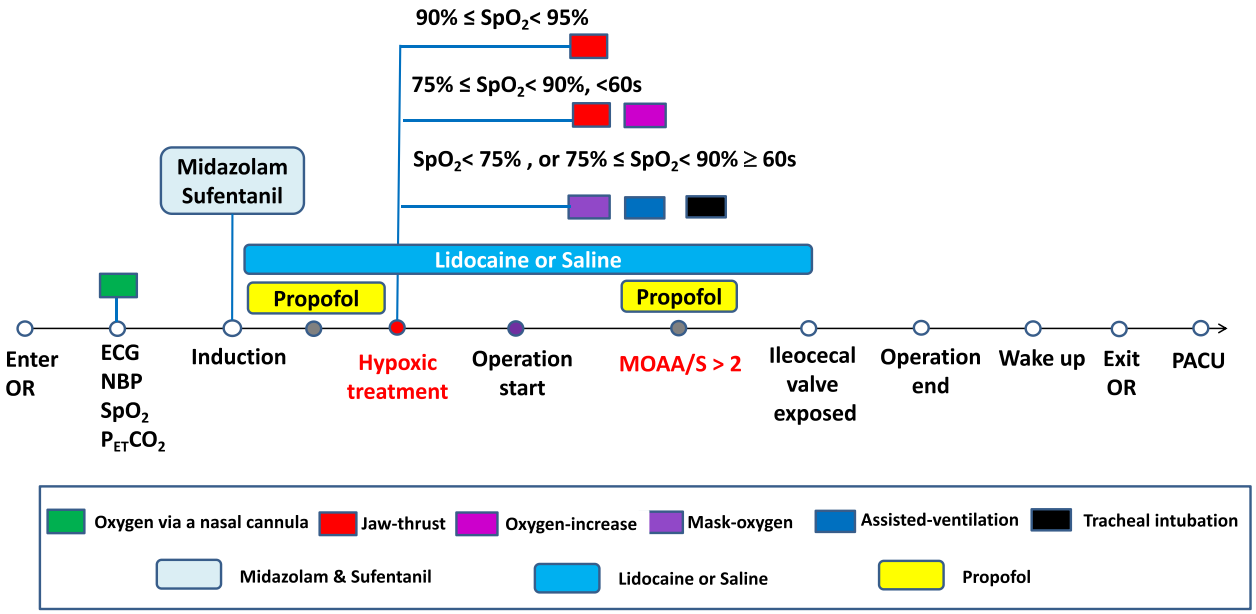

Fig. 1 Administration and hypoxic treatment protocol

Oxygen-desaturation episodes was defined that occurrence of $SpO_2 < 90\%$ for more than 10 s after induction [26]. The subclinical respiratory depression was defined as $90\% \leq SpO_2 < 95\%$ for more than 15 s, it was improved using jaw-thrust maneuver. If hypoxia ($75\% \leq SpO_2 < 90\%$ for > 10 s) developed, it was treated both with the jaw-thrust maneuver and increasing the oxygen flow from 6 to 10 L/min. Once the severe hypoxia ($SpO_2 < 75\%$ or $75\% \leq SpO_2 < 90\%$ for ≥ 60 s) occurred [2, 6], patients were rescued by assisted mask ventilation, even tracheal intubation if necessary [27].

The primary outcome was the occurrence of ODE, when $SpO_2 < 90\%$ exceeded 10 s [26]. The duration of the ODE and the related inventions were recorded. The secondary outcomes were as follows: The incidence of subclinical respiratory depression, hypoxia, severe hypoxia and related treatments; the incidence of the following events (coughing, grimaces, and involuntary body movements) in patients during anesthesia; the circulatory adverse events and the related treatments during the procedure; the propofol dose of induction, the total propofol dose requirements; the time of induction, procedure time (the time between insertion of the gastroscope and colonoscope peeps into the ileocecal area), awake time (the time from the colonoscope peeping into the ileocecal area to the patients could be called to wake up); the score of endoscopist satisfaction and patient satisfaction; lidocaine related side effects were recorded and treated, such as tongue numbness, metallic taste, tinnitus, anaphylaxis, nausea, and vomiting.

The sample size was estimated based on the results of our previous pilot study of nearly 80 cases. From our pilot study, the incidence of ODE in the control group was about 50%. We hypothesized that compared with the control group, IV lidocaine could reduce the incidence of ODE by 30%. We calculated that 134 patients per group were required, with a power of 90% and a level of significance of 0.05. We aimed to recruit a total of 300 patients finally considering about 10% dropout rate.

The statistical analysis was performed using the SPSS 23.0 software by the statistician. Continuous variables were summarized with mean (SD) or median (IQR). Compared baseline characteristics using absolute standard mean differences (SMD), defined as absolute difference in means, medians, or proportions divided by the pooled standard deviation. Baseline variables with SMD more than 0.226 ($1.96\ X\ (\sqrt{\frac{1}{150}+\frac{1}{150}}) = 0.226$) were considered imbalanced and were adjusted for all analyses. Categorical variables were reported as frequencies and percentages and were analyzed with the Fisher's exact test or χ^2 as appropriate. A repeated-measures analysis of variance was used to analyze repeatedly measured data such as MBP and HR. $P < 0.05$ was considered statistically significant. Univariate logistic regression analysis was initially used to identify possible risk factors for the occurrence of deoxygenation saturation episodes. Then, the covariates with a P-value ≤ 0.05 in the univariate analysis were subjected to multivariate logistic regression to ultimately determine the risk factors associated with the deoxygenation saturation event.

Results

Figure 2 shows the participant flow diagram clearly. From December 1, 2021, to December 31, 2022, a total of 350 patients were enrolled. Twenty-eight patients were excluded because of the following reasons: seven for hypnotics, one for anxiolytics, seven for STOP-Bang score > 5, eight for BMI ≥ 30 kg/m^2, one for Pre-excitation syndrome, four for single endoscopy. Then 322 participants were randomized to the lidocaine group or control group. Fourteen patients were withdrawn from the Group L: three for long operation time (meaning lidocaine overdose), one for monitoring data missing, one for not meeting the target sedative depth, nine for not meeting the trial standards of drug administration and oxygen inhalation. Eight patients were excluded from Group C, one for long operation time, one for monitoring data missing, one for conscious sedation, five for not meeting the trial standards of drug administration and oxygen inhalation. Thus, 147 patients in Group L and 153 in Group C were included in the final analyses.

Table 1 shows the demographic characteristics of the two groups. There was no significant difference between the two groups about gender, age, height, weight, BMI, ASA status, cormorbidity, general anesthesia history, smoking and alcohol intake history ($P > 0.05$). Moreover, patient airway characteristics were well balanced in terms of BMI, mallampati status, mouth opening length, cervical motion, jaw mobility, tooth-problem, and STOP-Bang score ($P > 0.05$).

During the whole procedure of gastrointestinal endoscopy, the incidence of ODE was 22% (32/147 cases) in the Lidocaine group and 39% (59/153 cases) in the Control group (difference, −16.7%, $P = 0.009$). According to definitions of different degree of hypoxic, there were 19 (13%) cases happened subclinical respiratory depression in Lidocaine group and 17 cases (11%) in Control group. In Lidocaine group, 30 patients (20%) developed hypoxia and 2 patients (1%) happened severe hypoxia, whereas 56 patients (37%) occurred hypoxia and 3 patients (1%)

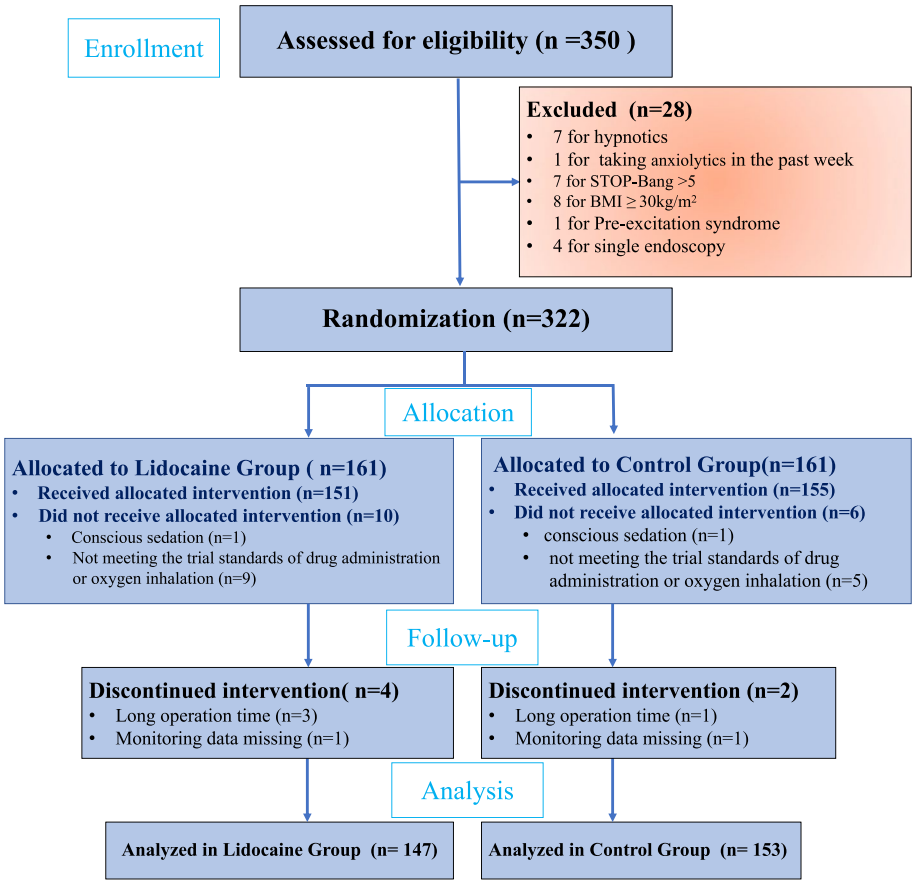

Fig. 2 Flow Diagram

occurred severe hypoxia in the Control group, $P=0.017$. Above all are showed in Table 2.

We also adopted different treatments for different degrees of hypoxia. Neither endotracheal intubation nor laryngeal mask was applied in any patient. In Table 2, intravenous lidocaine significantly decreased the hypoxia treatments by 11% (lidocaine vs control: 39/147 vs 58/153, $P=0.028$). 18 patients were helped with jaw-thrust maneuver, 17 with jaw-thrust maneuver and oxygen flow-increase, 4 with mask-assisted ventilation in Lidocaine group, 15, 42 and 1 in the Control group respectively, $P=0.009$.

Table 3 summarized the details of propofol doses and perioperative status. IV lidocaine decreased the induction dosage of propofol by 23% (Lidocaine vs control: 69 ± 21 vs 90 ± 24 mg, $P<0.001$), and the total consumption of propofol by 22% (Lidocaine vs control: 129 ± 47 vs 165 ± 56 mg, $P<0.001$). No difference was found in the whole procedure time. However, intravenous lidocaine leaded patients to reach the target depth of sedation slightly slower by 5 s (Lidocaine vs control: 109 ± 20 vs 104 ± 14 s, $P<0.01$), whereas it did not extend the awake time (Lidocaine vs control: 181 ± 144vs 210 ± 150 s, $P=0.097$).

During the whole procedure, 17 cases (11%) experienced coughing in the control group, whereas only 2 patients in the Lidocaine group, $P=0.001$. The incidence of involuntary body movements was lower in Lidocaine group than that in the control group (Lidocaine vs Control: 14% vs 26%, $P=0.013$).

The MAP and HR before induction were similar between the two groups. Compared with baseline, induction decreased MAP and HR in both groups ($P<0.01$). However, MAP dropped less ($P<0.01$) in Lidocaine group compared with Control group (Fig. 3). There was no difference in the cases of arrhythmia, decreased blood pressure (MAP < 65 mmHg), or decreased heart rate (HR < 50 bpm) between the two groups. No lidocaine related side effects such as tongue numbness, metallic taste, tinnitus, anaphylaxis, was found in both groups. 5 patients happened vomiting in Lidocaine group, and 5 patients in Control group also.

Table 1 Demographics and Baseline characteristics

Characteristics	Lidocaine Group (*n* = 147)	Control Group (*n* = 153)	SMD
Gender			
M	55 (37.4)	59 (38.6)	0.010
F	92 (62.6)	94 (61.4)	
Age, yr	50.0 ± 9.8	49.6 ± 9.2	0.030
Height, cm	165.6 ± 7.7	166.5 ± 8.4	0.113
Weight, kg	64.4 ± 10.5	66.1 ± 10.2	0.164
BMI, kg/m^2	23.4 ± 2.9	23.7 ± 2.7	0.098
ASA classification, n/%			
I	41 (27.9)	57 (37.3)	0.085
II	106 (72.1)	96 (62.7)	
Complications, n/%			
Hypertension/Diabetes/CD	35 (23.8)	34 (22.2)	0.027
Chronic pharyngitis	5 (3.4)	3 (2.0)	0.034
History of gatroenteroscopy	48 (32.7)	54 (35.3)	0.058
Mallampati status, n/%			
I	23 (15.6)	16 (10.5)	0.125
II	116 (79.0)	121 (79.1)	
III	8 (5.4)	16 (10.5)	
Jaw mobility, n/%			
Good	126 (85.7)	128 (83.7)	0.049
Poor	19 (12.9)	23 (15.0)	
Worst	2 (1.4)	2 (1.3)	
STOP-Bang score, median (IQR)	1(1–2)	1(1–2)	0.087
Smoking history, n/%			
No	128(87.0)	129 (84.3)	0.053
≤ 10 cigarettes /d	12(8.2)	14 (9.2)	
> 10 cigarettes /d	7(4.8)	10 (6.5)	
Alcohol intake history, n/%			
Yes	35 (23.8)	34 (22.2)	0.030
No	112 (76.2)	119 (77.8)	
Procedure time, min	19.0 ± 6.7	19.6 ± 7.3	0.099

SMD absolute standard mean difference, SMD more than 0.226 were considered imbalanced. Values are presented as mean ± SD or number (%). *BMI* body mass index. *ASA* American Society of Anesthesiologists. *CD* Cardiovascular Diseases. Jaw mobility classification: Good, the mandibular incisors can move forward over the maxillary incisors; Poor, the mandibular incisors move forward only to align with the maxillary incisors; Worst, the mandibular incisors could not move forward beyond the maxillary incisors. STOP-Bang score: snoring, tired or sleepy, observed apneas, and high blood pressure, BMI > 35 kg/m^2, age > 50 years old, neck circumference > 40 cm (16 inches), and gender (male)

With VAS score evaluation method showed in Table 3, the proportion of endoscopists with a satisfaction score of 10 points in the lidocaine group was higher than that in the control group (lidocaine vs control: 83% vs 67%, $P = 0.001$). On the contrary, most patients were satisfied with the sedation in both groups (lidocaine vs control: 96% vs 94%, $P = 0.470$). In the Lidocaine group 5 patients complained of postoperative pain and 1 patient dissatisfied with the sedation. In the control group, 5 patients reported pain, 1 patient could recall intraoperative pain, and 3 patients dissatisfied with the sedation.

According to the definition of ODE, 91 patients (30%) developed ODE among all participants. All perioperative factors that may affect the occurrence of ODE based on clinical status were analyzed by univariate logistic regression analysis, showed in Table 4. In terms of the occurrence of ODE, the differences in intravenous lidocaine, gender, BMI, smoking history, comorbidity, total propofol dose, procedure time were statistically significant ($P < 0.05$). There was no correlation between the incidence of ODE and ASA, age, mallampati status, patients' jaw mobility, alcohol intake history, STOP-Bang.

Then, multivariate logistic regression analysis was performed on factors with $P < 0.05$. The results showed that only IV lidocaine administration was a definite protective factor associated with reduced incidence of ODE (odds ratio (OR) = 0.502; 95%confidence interval (CI), 0.284–0.889; $P = 0.018$; Fig. 4]. BMI and procedure time were risk factors that increase the occurrence of ODE (BMI: OR = 1.188; CI = 1.076–1.311, $P = 0.001$; Procedure time: OR = 1.054; CI = 1.007–1.103 l, $P = 0.025$). Male gender, smoking history, comorbidity, and total propofol dosage were all not influencing factors.

Discussion

In this prospective, randomized, controlled study, we evaluated the effect of intravenous lidocaine on the incidence of ODE during GI endoscopy. Compared with control group, IV lidocaine reduced the incidence of ODE from 39 to 22% during GI procedure and needed fewer hypoxic treatments. Moreover, IV lidocaine decreased the inductive and total requirements of propofol, and the incidence of coughing and involuntary body movements. Endoscopists' satisfaction was improved at the same time. Besides, IV lidocaine improved the circulatory adverse events, and did not produce the lidocaine related side effects. Therefore, for patients undergoing painless gastrointestinal endoscopy, IV lidocaine adjuvant to PSA would be a more beneficial choice for patients' efficacy and safety.

Propofol has always been the preferred sedative for painless GI endoscopy due to its fast onset, strong sedative effect, short half-life, fast recovery. However, propofol consumption was one of the independent risk factors for hypoxia [5, 10]. Discomfort caused by gastroscopy and colonoscopy is mainly due to visceral injury caused by colon dilation and traction. To make patients painless

Table 2 The incidence of oxygen-desaturation episodes and corresponding treatment

Variable	Lidocaine Group ($n=147$)	Control Group ($n=153$)	RR (95% CI)	*P* value
The primary outcome				
Oxygen-desaturation episodes	32 (22)	59 (39)	2.256 (1.355–3.754)	0.002
The secondary outcomes				
Degree of hypoxia				
Subclinical respiratory depression	19 (13)	17 (11)		0.017
Hypoxia	30 (20)	56 (37)		
Severe hypoxia	2 (1)	3 (1)		
No	96 (65)	97 (63)		
Treatments of hypoxia				
Jaw-thrust maneuver	18 (12)	15 (10)		0.009
Jaw-thrust maneuver and oxygen flow-increase	17 (12)	42 (28)		
Mask-assisted ventilation	4 (3)	1 (1)		
Tracheal intubation	0	0		-

Values are presented as number (%, proportion)

Oxygen-desaturation episodes: SpO2 < 90% for more than 10 s after induction

Subclinical respiratory depression: 90% ≤ SpO2 < 95% for more than 15 s

hypoxia: 75% ≤ SpO2 < 90% for no more than 10 s

Severe hypoxia: SpO2 < 75% or 75% ≤ SpO2 < 90% for more than 60 s

and immobile, we often combine propofol sedation with midazolam or opioid drugs, but this also increases the risk of respiratory depression [11–14, 16]. The clinical manifestations of respiratory depression by opioid drugs include hypoventilation (decrease respiratory rate and volume), hypercapnia and respiratory acidosis, and decreased oxygen saturation [11, 14]. Opioids also decrease upper airway patency and reduce ventilatory responses to hypoxia and hypercapnia. Numerous clinical studies have confirmed that even low-dose sufentanil as a supplement to propofol sedation may lead to unacceptable frequent hypotension and oxygen desaturation [11–14, 16].

Many studies have shown that IV lidocaine can effectively alleviate visceral pain [20, 21] and reduce the need for propofol during surgery under total intravenous anesthesia [23–25]. In present study, the propofol requirements dose was still significantly reduced [lidocaine 128 (47) mg vs saline 165 (56) mg, $P=0.000$]. It is worth noting that the reduction in propofol dosage did not come at the cost of sacrificing working conditions, as the satisfaction levels of the two groups of endoscopists were similar. Deoxygenation events incidences were as high as 12% to 33% during deep sedation [6, 13, 31, 32]. In present study, 91 patients (30.3%) developed oxygen-desaturation ($SpO_2<90\%$ for 10 s) totally, IV lidocaine (21.8%) decreased the incidence of ODE compared with control group (38.5%). Our results were different with a meta-analysis which found that IV lidocaine didn't affect the incidence of ODE when used in sedation for GI endoscopy [28]. The reasons of this difference were as following: Firstly, we chose patients who performed gastroscopy and colonoscopy both which means the procedure was longer, but the procedure in the meta-analysis were ERCP or ESD ect, the procedure was different, so the stimulation and duration were different, so as to the dosages of lidocaine and propofol were also different. Secondly, the primary of present study was the incidence of ODE, and we not only provide a clear definition of the occurrence of ODE ($SpO_2<90\%$, and > 10 s), but also set different treatment measures for each occurrence of hypoxia. But the primary outcome in the studies in the meta-analysis was the dosage of propofol and the incidence of desaturation was secondary outcome. Thirdly, we recorded in detail the factors that affect ODE, such as airway conditions. Possible influencing factors such as bigger BMI and STOP-BANG were excluded. But these information were not mentioned in the studies [28]. The above factors may lead to the results of present study: IV lidocaine reduced the incidence of ODE, which differed from the meta-analysis.

Although there is no direct evidence to prove the exact mechanism by which IV lidocaine reduces the occurrence of hypoxia, numerous clinical studies have

Table 3 Perioperative medication and satisfaction status

Variable	Lidocaine Group ($n=147$)	Control Group ($n=153$)	Difference (95%CI)	*P* value
Anesthesia status				
Propofol induction dose, mg	69 ± 21	90 ± 24	21(15 to 26)	0.000
Total propofol requirements, mg	128 ± 47	165 ± 56	37 (25to 48)	0.000
Average propofol consumption, mg/kg/h	6.7 ± 2.3	8.2 ± 2.8	1.4 (0.9 to 2.1)	0.000
The total lidocaine dose, mg	182 ± 4	-		
The time of induction, seconds	109 ± 20	104 ± 14	−6 (−10 to −2)	0.004
The time of colonoscopy exit, sec	213 ± 57	216 ± 57	7 (−10 to 16)	0.652
Awake time, seconds	181 ± 144	210 ± 150	28 (−5 to 62)	0.097
Special events during anesthesia, n/%				
Coughing	2 (1)	17 (11)		0.001
Grimaces	5 (3)	4 (3)		0.746
Involuntary body move	20 (14)	39 (26)		0.013
Circulatory adverse Events				
Arrhythmias	2 (1)	2 (1)		0.000
MAP < 65 mmHg	9 (6)	12 (8)		
HR < 50 bpm	0 (0)	1 (1)		
No	136 (93)	138 (90)		
Endoscopists' satisfaction				
Good (10 points)	122(83)	102 (67)		0.001
Worse (7–9 points)	20 (14)	30 (20)		
Worst (1–6 points)	5 (3)	21 (14)		
Patients' satisfaction				
Good (10 points)	141 (96)	144 (94)		0.47
Worse (7–9 points)	5 (3)	6 (4)		
Worst (1–6 points)	1 (1)	3 (2)		
Lidocaine related side effects	0	0		-

Values are presented as mean ± SD or number (%). Procedure time: the time between insertion of the gastroscope and colonoscope peeps into the ileocecal area. Awake time: the time from the colonoscope peeps into the ileocecal area to the patients could be called to wake up. MAP: Mean arterial pressure. HR: Heart rate. Lidocaine related side effects included tongue numbness, metallic taste, tinnitus, anaphylaxis. Average propofol consumption = The total propofol dose requirements/Weight/Procedure time. The time of colonoscopy exit: Time for colonoscopy to exit from ileocecal valve to exenteral

found that IV lidocaine had analgesic effect that could be beneficial in perioperative settings. A large amount of evidence confirms that IV lidocaine has anti-inflammatory, opioid protective effects, the ventilatory response to carbon dioxide [22], and the combination of these features leads to a series of effects, such as reducing postoperative pain and opioid consumption, shortening the duration of digestive intestinal obstruction, and producing significant propofol sparing [22, 23, 25, 26], finally reducing the incidence of ODE. In our preliminary experiment, it was found that IV lidocaine significantly reduced the median effective dose (ED_{50}) of propofol for successful endoscope insertion in adult patients [29]. In present study, the inductive dose and total dose of propofol were all significantly decreased by IV lidocaine by 22.9%. As the rapid increase in intravenous concentration of propofol is the main cause of respiratory depression during PSA. The effect of IV lidocaine, which reduced the induction and maintenance dose of propofol, had a protective effect on respiratory depression, thereby reducing the occurrence of oxygen-desaturation.

According to the definition of ODE, we also performed multivariate logistic regression analysis. It indicated that IV lidocaine was the protective risk factor whereas BMI and procedure time were the non-protective risk factors for ODE, which was consist with one previous article [2]. It suggested that age over 65 years, higher BMI, and ASA III may increase the incidence of ODE during endoscopic. While in our study, it was relevant to our criterion of including only ASA I–II patients and age under 65 years. The new discovery is that IV lidocaine may be a protective supplement to PSA for decreasing the ODE.

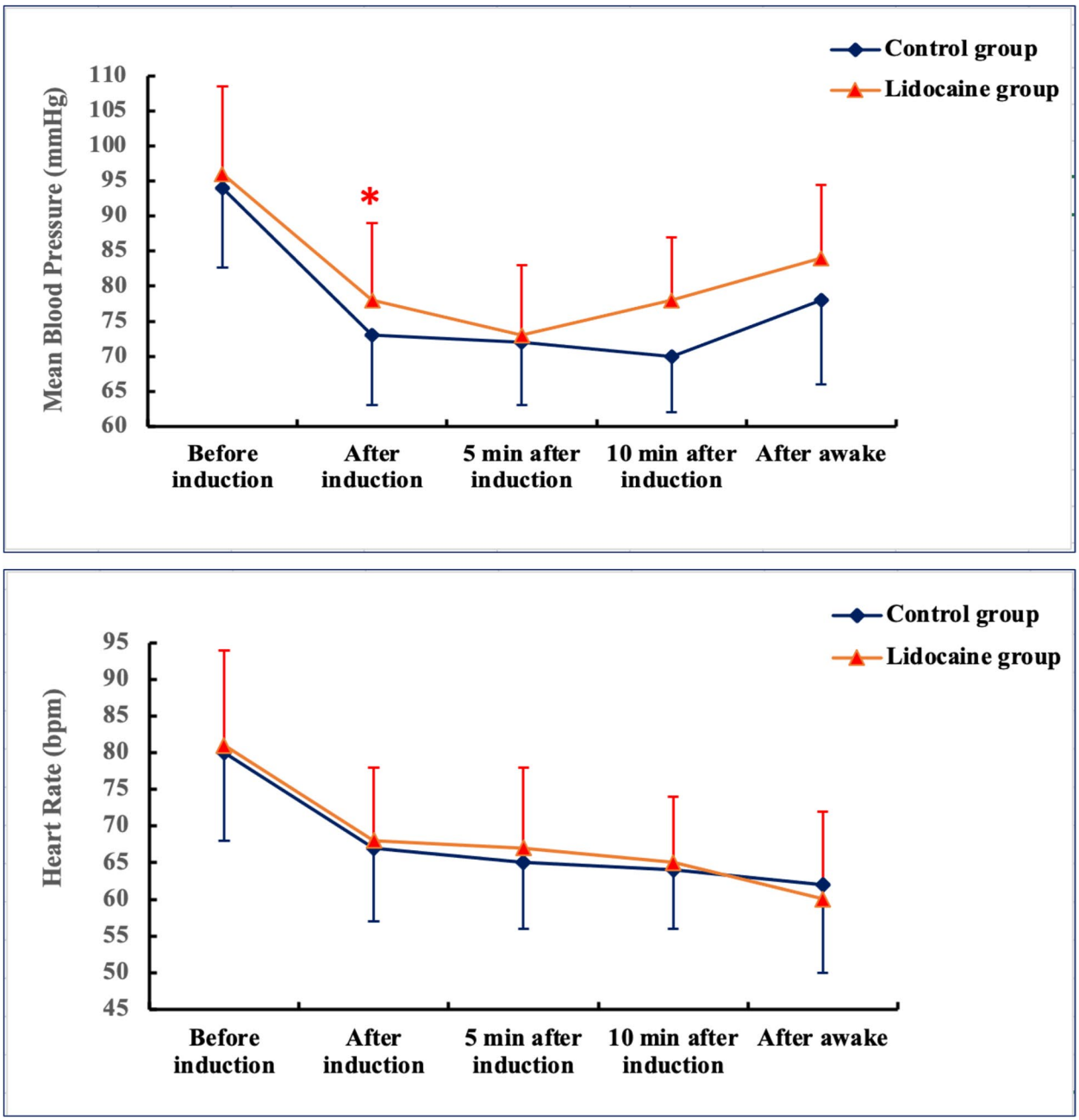

Fig. 3 MAP and HR

We also found that ODE was linked to BMI. Due to the physiologic changes of the airways that fat infiltration of the upper airway and its surrounding structures, patients with higher BMI are prone to predisposing upper airway narrowing [25]. We found that IV lidocaine might play a helpful role on reducing the incidence of coughing during GI procedure, which was consistent with one previous report, demonstrating that IV lidocaine with a dose of 1 mg/kg can significantly (78.8%) suppress fentanyl-induced cough in pediatric patients before general anesthesia [33]. A possible mechanism is that IV lidocaine may deactivate peripheral cough receptors in the trachea and hypopharynx [34].

Involuntary body movements were also decreased by IV lidocaine down to 11.9% with the better endoscopist satisfaction in our research, may benefiting from that it might attenuates peripheral nociceptors sensitization

Table 4 Results of univariate analysis of risk factors for Oxygen-desaturation episodes

Items	Oxygen-desaturation episodes (*n* = 91)	Non-Oxygen-desaturation episodes (*n* = 209)	Diffenrence (95% CI)	*P* value
IV Lidocaine	32 (35)	115 (55)		0.002
Male gender	41 (45)	144 (69)		0.000
Age, y	50 ± 9	50 ± 10	1.196 (−2.436 to 2.273)	0.946
BMI, kg/m^2	25 ± 2	23 ± 3	0.348 (−2.022 to −0.654)	0.000
ASA, n/%	63 (69)	139(66)		0.644
Mallampati status				
I	15 (17)	24 (12)		0.498
II	69 (76)	169 (81)		
III	7 (8)	16 (8)		
Jaw mobility				
Good	72 (80)	183 (88)		0.096
Poor	18 (12)	23 (29)		
Worst	1 (1)	3 (3)		
Smoking history				
No	66 (73)	191 (91)		0.000
≤ 10	21 (23)	7 (3)		
> 10	4 (4)	13 (6)		
Alcohol intake history	68 (75)	163 (78)		0.537
Hypertension/Diabetes/CD	26 (29)	42 (20)		0.000
Chronic pharyngitis	2 (2.2)	6 (2.9)	0.760 (0.151 to 3.840)	0.739
STOP-Bang score, median (IQR)	1(1, 2)	1(0, 2)	0.864 (0.429 to 1.742)	0.683
The total propofol dose requirements, mg	164 ± 60	140 ± 51	−23.600 (−37.831 to −9.369)	0.001
Procedure time, minutes	21 ± 8	19 ± 6	−2.403 (−4.316 to −0.490)	0.014
Average propofol consumption, mg/kg/h	6.6 ± 2.1	6.1 ± 1.9	0.252 (0.038 to 1.031)	0.035

Values are presented as mean ± SD or or median (IQR). BMI: body mass index. STOP-Bang score: snoring, tired or sleepy, observed apneas, and high blood pressure, BMI > 35 kg/m2, age > 50 years old, neck circumference > 40 cm (16 inches), and gender (male). Procedure time: the time between insertion of the gastroscope and colonoscope peeps into the ileocecal area. Average propofol consumption = The total propofol dose requirements / Weight / Procedure time

and central hyperexcitability through its sodium channel blocking action to treat acute and chronic pain [35].

The dose of IV lidocaine used in this study was an induction dose of 1.5 mg/kg and a maintenance dose of 4 mg/kg/h. This dose was used within the recommended range of guidelines (1–5 mg/kg/h) [36]. Although the dose we have chosen may be higher than the recommended dose of 1.5 mg/kg/h in another guideline, this guideline is for long-term medication (< 24 h) to assist postoperative analgesia [37]. We believe that our infusion duration was within 30 min, and even at higher concentrations, it is safe compared to long-term adjuvant postoperative analgesia. In addition, similar doses to our medication were found in other studies of colonoscopy, and demonstrated that 4 mg/kg/h for 30 min did not produce any toxic reactions [38, 39]. Few adverse events of IV lidocaine had been reported in clinical studies and analysis [40]. We also found that IV lidocaine could improve the cases of arrhythmia, MAP and HR's degree of decline, may also resulting from the effect of propofol sparing.

However, IV lidocaine prolonged the inductive time, not the awake time, which possibly because of IV lidocaine requiring sufficient time to take effect and not slowing the distribution half-life of propofol. In addition, the propofol-sparing effect may also contribute to it.

And during the whole anesthesia period, no lidocaine related side effect such as tongue numbness, metallic taste, tinnitus, anaphylaxis, appeared among the two groups. It should be due to the fact that the dose of IV lidocaine we used was much lower than its' toxic dose [38]. So, IV lidocaine did not make patients' satisfaction worse.

This study had some limitations. Firstly, there was no objective indicators to measure sedation levels during the procedure such as BIS or EEG monitoring. We used the subjective observation technique MOAA/S score as our sedation indicator, there could be slightly differences in the judgment of sedation depth; Secondly, this study recruited relatively healthy patients with normal liver and kidney function (ASA I or II). We did not extend to older or frail or more severe ill patients (ASA III or IV) who are

Influence Factors	OR	95% CI	*P* value
IV Lidocaine	0.46	(0.263, 0.803)	0.006
Male	1.322	(0.733, 2.384)	0.354
BMI	1.179	(1.081, 1.306)	< 0.001
Smoking history(≤ 10 cigarettes /d)	1.315	(0.528, 3.273)	0.556
Smoking history (> 10 cigarettes /d)	0.538	(0.155, 1.864)	0.328
Hypertension/Diabetes/CAD	1.5	(0.824, 2.731)	0.184
Average propofol consumption, mg/kg/h	1.028	(0.894, 1.181)	0.702

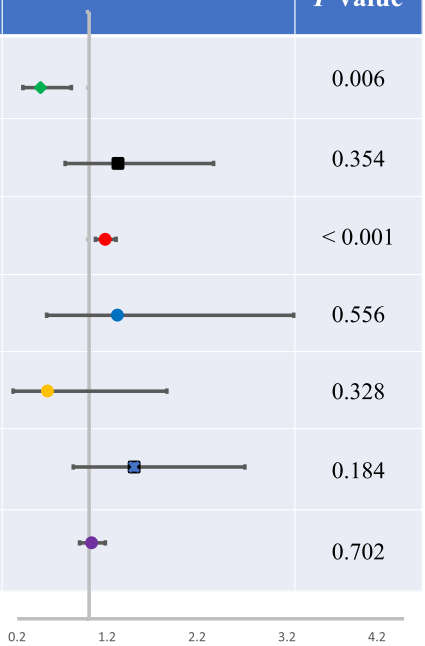

Fig. 4 Revised forest plot

more prone to respiratory and cardiovascular suppression when exposed to propofol and are more sensitive to intravenous lidocaine injection.

Conclusions

To conclude, IV lidocaine adjuvant to propofol-based sedation during the GI endoscopy could reduce the incidence of ODE and involuntary body movements, with less adverse events. So, the addition of intravenous lidocaine to PSA could be a beneficial way for painless GI endoscopy.

Abbreviations

IV	Intravenous
GI	Gastrointestinal
ODE	Oxygen-desaturation episodes;
PSA	Procedure sedation and anesthesia
BMI	Body mass index
CO_2	Carbon dioxide;
ED50	Median effective dose
HR	Heart rate
BP	Blood pressure
MOAA/S	Modified Observer's Assessment of Alertness/sedation
PACU	Post-anethesia care unit
OR	Odds ratio
CI	Confidence interval

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Authors' contributions

XRQ and YXQ prepared the manuscript and implemented the anesthesia. LXA designed, interpreted the data and finally approved the version to be published. KZ and WWH was responsible for the implementation of anesthesia for some participants and participated in postoperative follow-up and data collection. All authors read and approved the final manuscript.

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Data availability

The data sets used and/or analyzed during the present study are available from the corresponding author on reasonable request. The email of corresponding author is anlixin8120@163.com.

Declarations

Ethics approval and consent to participate

This study protocol was approved by the Institutional Ethics Committee of Beijing Friendship Hospital, Capital Medical University (Approval No: 2020-P2-159–02), registered on the Chinese Clinical Trial Registry (http://www.chictr.org.cn; registration number: ChiCTR2100053818; registered on 30 November, 2021). Written informed consent was obtained from all patients.

Consent for publication

Not Applicable.

Competing interests

The authors declare no competing interests.

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References

1. Wang S, Shen N, Wang Y, Cheng N, Li L, Pan S, et al. Bilevel positive airway pressure for gastroscopy with sedation in patients at risk of hypoxemia: A prospective randomized controlled study. J Clin Anesth. 2023;85:111042.
2. Chen DX, Yang H, Wu XP, Niu W, Ding L, Zeng HL, et al. Comparison of a Nasal Mask and Traditional Nasal Cannula During Intravenous Anesthesia for Gastroscopy Procedures: A Randomized Controlled Trial. Anesth Analg. 2022;134(3):615–23.
3. Shao LJ, Zou Y, Liu FK, Wan L, Liu SH, Hong FX, et al. Comparison of two supplemental oxygen methods during gastroscopy with propofol monosedation in patients with a normal body mass index. World J Gastroenterol. 2020;26(43):6867–79.
4. Wei J, Zhang X, Min K, Zhou H, Shi X, Deng H, et al. Supraglottic Jet Oxygenation and Ventilation to Minimize Hypoxia in Patients Receiving Flexible Bronchoscopy Under Deep Sedation: A 3-Arm Randomized Controlled Trial. Anesth Analg. 2024;138(2):456–64.
5. Shao LJ, Hong FX, Liu FK, Wan L, Xue FS. Prospective, randomized comparison of two supplemental oxygen methods during gastroscopy with propofol mono-sedation in obese patients. World J Clin Cases. 2021;9(20):5479–89.
6. Zheng HR, Zhang XQ, Li LZ, Wang YL, Wei Y, Chen YM, et al. Multicentre prospective cohort study evaluating gastroscopy without sedation in China. Br J Anaesth. 2018;121(2):508–11.
7. Smith HL, Sapsford DJ, Delaney ME, Jones JG. The effect on the heart of hypoxaemia in patients with severe coronary artery disease. Anaesthesia. 1996;51(3):211–8.
8. Eertmans W, De Deyne C, Genbrugge C, Marcus B, Bouneb S, Beran M, et al. Association between postoperative delirium and postoperative cerebral oxygen desaturation in older patients after cardiac surgery. Br J Anaesth. 2020;124(2):146–53.
9. Bartels K, Kaizer A, Jameson L, et al. Hypoxemia Within the First 3 Postoperative Days Is Associated With Increased 1-Year Postoperative Mortality After Adjusting for Perioperative Opioids and Other Confounders. Anesth Analg. 2020;131(2):555–63.
10. Simons JC, Pierce E, Diaz-Gil D, Malviya SA, Meyer MJ, Timm FP. Effects of Depth of Propofol and Sevoflurane Anesthesia on Upper Airway Collapsibility, Respiratory Genioglossus Activation, and Breathing in Healthy Volunteers. Anesthesiology. 2016;125(3):525–34.
11. Montandon G. The pathophysiology of opioid-induced respiratory depression. Handb Clin Neurol. 2022;188:339–55.
12. Miao Y, Zheng M, Li Q, Xiong L, Feng J, Liu X, Fan G, Chaturvedi R, Zhang F, Yin N. Comparison of propofol-esketamine versus propofol-sufentanil for deep sedation and analgesia in children with autism: A randomized double-blind clinical trial. Autism Res. 2024;17(7):1356–64.
13. van Schaik EPC, Blankman P, Van Klei WA, Knape HJTA, Vaessen PHHB, Braithwaite SA, et al. Hypoxemia during procedural sedation in adult patients: a retrospective observational study. Can J Anaesth. 2021;68(9):1349–57.
14. Dossa F, Medeiros B, Keng C, Acuna SA, Baxter NN. Propofol Versus Midazolam with or Without Short-Acting Opioids for Sedation in Colonoscopy: A Systematic Review and Meta-Analysis of Safety, Satisfaction, and Efficiency Outcomes. Gastrointest Endosc. 2020;91(5):1015–26.
15. Krystal JH, Karper LP, Seibyl JP, Freeman GK, Delaney R, Bremner JD. Subanesthetic effects of the noncompetitive NMDA antagonist, ketamine, in humans. Psychotomimetic, perceptual, cognitive, and neuroendocrine responses. Arch Gen Psychatrie. 1994;51(3):199–214.
16. Singh SA, Prakash K, Sharma S, Dhakate G, Bhatia V. Comparison of propofol alone and in combination with ketamine or fentanyl for sedation in endoscopic ultrasonography. Korean J Anesthesiol. 2018;71(1):43–7.
17. Edokpolo LU, Mastriano DJ, Serafin J, Weedon JC, Siddiqui MT, Dimaculangan DP. Discharge readiness after Propofol with or without Dexmedetomidine for colonoscopy: a randomized controlled trial. Anesthesiology. 2019;131(2):279–86.
18. Singh J, Pathania J, Bodh V, Sharma R, Kumar R, Sharma B. Etomidate-ketamine versus dexmedetomidine-ketamine for entropy-guided procedural sedation during endoscopic retrograde cholangiopancreatography procedures: A randomized single blind study. Indian J Gastroenterol. 2023;42(2):177–84.
19. Inatomi O, Imai T, Fujimoto T, Takahashi K, Yokota Y, Yamashita N, et al. Dexmedetomidine is safe and reduces the additional dose of midazolam for sedation during endoscopic retrograde cholangiopancreatography in very elderly patients. BMC Gastroenterol. 2018;18:166.
20. Kim DH, Park JY, Yu J, Lee SA, Park S, Hwang JH, et al. Intravenous Lidocaine for the Prevention of Postoperative Catheter-Related Bladder Discomfort in Male Patients Undergoing Transurethral Resection of Bladder Tumors: A Randomized, Double-Blind. Controlled Trial Anesth Analg. 2020;131(1):220–7.
21. Meaney ED, Reid L, Srivastava D. A survey on the use of intravenous lidocaine infusion for acute pain in Scottish Hospitals. Br J Pain. 2020;14(2):98–103.
22. Labaille T, Clergue F, Samii K, Ecoffey C, Berdeaux A. Ventilatory response to CO2 following intravenous and epidural lidocaine. Anesthesiology. 1985;63(2):179–83.
23. Li X, Lv X, Jiang Z, Nie X, Wang X, Li T, et al. Application of Intravenous Lidocaine in Obese Patients Undergoing Painless Colonoscopy: A Prospective, Randomized, Double -Blind. Controlled Study Drug Des Devel Ther. 2020;27(14):3509–18.
24. Wu F, Zhan L, Xu W, Bian J. Effect of intravenous lidocaine on outcomes in patients receiving propofol for gastrointestinal endoscopic procedures: an updated systematic review and meta-analysis. Eur J Clin Pharmacol. 2024;80(1):39–52.
25. Liu J, Liu X, Peng LP, Ji R, Liu C, Li YQ. Efficacy and safety of intravenous lidocaine in propofol-based sedation for ERCP procedures: a prospective, randomized, double-blinded, controlled trial. Gastrointest Endosc. 2020;92(2):293–300.
26. Yang SS, Wang NN, Postonogova T, Yang GJ, McGillion M, Beique F, et al. Intravenous lidocaine to prevent postoperative airway complications in adults: a systematic review and meta-analysis. Br J Anaesth. 2020;124(3):314–23.
27. Qi XR, Sun JY, An LX, Zhang K. Effect of intravenous lidocaine on the ED_{50} of propofol for inserting gastroscope without body movement in adult patients: a randomized, controlled study. BMC Anesthesiol. 2022;22(1):319.
28. Hung KC, Yew M, Lin YT, Chen JY, Wang LK, Chang YJ, et al. Impact of intravenous and topical lidocaine on clinical outcomes in patients receiving propofol for gastrointestinal endoscopic procedures: a meta-analysis of randomised controlled trials. Br J Anaesth. 2022;128(4):644–54.
29. Qi XR, Sun JY, An LX, Zhang K, Xue FS. Effects of intravenous lidocaine on hypoxemia induced by propofol-based sedation for gastrointestinal endoscopy procedures: study protocol for a prospective, randomized, controlled trial. Trials. 2022;23(1):800.
30. Chernik DA, Gillings D, Laine H, Hendler J, Silver JM, Davidson AB, et al. Validity and reliability of the Observer's Assessment of Alertness/Sedation Scale: study with intravenous midazolam. J Clin Psychopharmacol. 1990;10(4):244–51.
31. Lin Y, Zhang X, Li L, Wei M, Zhao B, Wang X, et al. High-flow nasal cannula oxygen therapy and hypoxia during gastroscopy with propofol sedation: a randomized multicenter clinical trial. Gastrointest Endosc. 2019;90(4):591–601.
32. Wadhwa V, Issa D, Garg S, Lopez R, Sanaka MR, et al. Similar Risk of Cardiopulmonary Adverse Events Between Propofol and Traditional Anesthesia for Gastrointestinal Endoscopy: A Systematic Review and Meta -analysis. Clin Gastroenterol Hepatol. 2017;15(2):194–206.
33. Golmohammadi M, Shajiee S, Sane S, Valie M. Comparison of the effects of pretreatment intravenous fentanyl or intravenous lidocaine on suppression of fentanyl-induced cough in children: a randomized, double-blind, controlled clinical trial. Electron Physician. 2018;10(6):6877–83.
34. Poulton TJ, James FM 3rd. Cough suppression by lidocaine. Anesthesiology. 1979;50:470–2.

35. Vacher E, Kosela M, Song-Smith C, Morell-Ducos F, Fayaz A. Lidocaine infusions in chronic pain management: A prospective case series analysis. Br J Pain. 2022;16(3):270–80.
36. Beaussier M, Delbos A, Maurice-Szamburski A, Ecoffey C, Mercadal L. Perioperative Use of Intravenous Lidocaine. Drugs. 2018;78(12):1229–46.
37. Foo I, Macfarlane AJR, Srivastava D, Bhaskar A, Barker H, Knaggs R, et al. The use of intravenous lidocaine for postoperative pain and recovery: international consensus statement on efficacy and safety. Anaesthesia. 2021;76(2):238–50.
38. Forster C, Vanhaudenhuyse A, Gast P, Louis E, Hick G, Brichant JF, Joris J. Intravenous infusion of lidocaine significantly reduces propofol dose for colonoscopy: a randomised placebo-controlled study. Br J Anaesth. 2018;121(5):1059–64.
39. Chen M, Lu Y, Liu H, Fu Q, Li J, Wu J, Shangguan W. The propofol-sparing effect of intravenous lidocaine in elderly patients undergoing colonoscopy: a randomized, double-blinded, controlled study. BMC Anesthesiol. 2020;20(1):132.
40. Willis-Gray MG, Husk KE, Brueseke TJ, Connolly A, Geller EJ. Lidocaine Use in Vaginal Surgery and Risk of Toxicity. Female Pelvic Med Reconstr Surg. 2020;26(9):546–9.

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