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Efficacy and safety of esketamine combined with propofol for conscious sedation in painless colonoscopy: a prospective, randomized, double-blind controlled clinical trial

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Abstract

Background We explored the efficacy and safety of esketamine combined with propofol for conscious sedation in painless colonoscopy.

Methods A total of 195 patients who underwent painless colonoscopy surgery were randomly divided into three groups: the propofol deep sedation group (group DS), the sufentanil combined with propofol for conscious sedation (group CS_1) and the esketamine combined with propofol for conscious sedation (group CS_2). The primary outcomes of this study included the incidence of hypoxemia, hypotension, hypertension, and bradycardia and excellent and good rates of anaesthesia during colonoscopy. The secondary outcomes included perioperative changes in vital signs (MAP, HR, and SpO_2), anaesthesia induction time, dischargeable time, patient and endoscopist satisfaction scores, and incidence of postoperative nausea and vomiting (PONV), drowsiness, dizziness, propofol injection pain, assisted ventilation and vasoactive medications.

Results The incidence of intraoperative hypoxemia in the DS group was significantly greater than that in the CS_1 and CS_2 groups ($\chi2 = 7.081$, $P = 0.029$). The incidence of hypotension in the CS_2 group was significantly lower than that in the DS and CS_1 groups ($\chi2 = 16.278$, $P < 0.001$). The risk of hypoxemia was 5.727 times higher in Group DS than in Group CS_2 (OR 5.727; 95%CI 1.203–27.273), and the risk of hypotension was 9.864 times higher in Group DS than in Group CS_2 (OR 9.864; 95%CI 2.770–35.120). The risk of hypotension in Group CS_1 was 5.167 times that in Group CS_2 (OR 5.167; 95%CI 1.396–19.117). The incidence of propofol injection pain, assisted ventilation, ephedrine usage and drowsiness in the DS group was significantly greater than that in the CS_1 and CS_2 groups ($\chi2 = 57.618$, $P < 0.001$; $\chi2 = 9.544$, $P = 0.008$; $\chi2 = 14.820$, $P = 0.001$; $\chi2 = 37.257$, $P < 0.001$). The incidence of dizziness during recovery in the CS_1 group was significantly greater than that in the DS and CS_2 groups ($\chi2 = 6.594$, $P = 0.037$). The dischargeable time

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in the DS group was significantly greater than that in the CS_1 and CS_2 groups (F = 53.039, $P < 0.001$). The satisfaction scores of the endoscopist and patients in the DS group were significantly lower than those in the CS_1 and CS_2 groups (F = 17.390, $P < 0.001$; F = 19.282; $P < 0.001$).

Conclusions In conclusion, esketamine combined with propofol for conscious sedation can be safely and effectively used for painless colonoscopy and has fewer complications.It is recommended for painless colonoscopy.

Keywords Esketamine, Conscious sedation, Deep sedation, Painless colonoscopy, Safety, Efficacy

Introduction

Currently, colorectal cancer ranks third among all malignant tumours, and its mortality (approximately 9.2%) ranks second [1]. Colorectal endoscopy biopsy is the main screening method for colorectal cancer. During routine colonoscopy, patients often show significantly increased blood pressure, tachycardia and restlessness due to tension, abdominal distension and abdominal pain stimulation, which increases the risk of complications during colorectal endoscopy [2]. Painless colonoscopy significantly reduces patients' fear and anxiety about endoscopy, provides good operating conditions for endoscopists, and improves the detection rate and review rate of positive patients to a certain extent [3].

Deep sedation is mainly used for painless enteroscopy, and propofol is commonly used [4]. However, propofol is associated with dose-resistant respiratory depression, hypotension, a prone response reaction, and an increased risk of reflux aspiration in suppressing laryngeal reflection [5, 6]. In conscious sedation, sedative and analgesic drugs are used to mildly inhibit the central nervous system. Patients respond to verbal stimulation with a normal tone of voice and can complete position changes with the instructions of the endoscopist, thus allowing the colonoscopy operation to proceed smoothly [4]. This technology has good clinical value for patients who may be at risk from deep sedation [5].

Recently, Wang et al. found that dexmedetomidine combined with oxycodone could be used safely as a conscious sedation method for colonoscopy in obese patients [7]. The most appropriate drug for conscious sedation still needs to be explored. Esketamine is the right monomer of ketamine (S-ketamine). It is an N-methyl-D-aspartate receptor (NMDA) antagonist. Esketamine is suitable for short procedures as well as outpatient painless diagnostic techniques due to its rapid onset of action and rapid clearance from the body. It has a sympathomimetic effect and can excite the heart, relax bronchial smooth muscle, and relieve bronchospasm and airway oedema, thus reducing the circulatory and respiratory depression of propofol [8, 9].

Ma et al. found that esketamine combined with propofol reduced propofol consumption and increased cardiovascular stability compared with fentanyl [10]. A recent meta-study showed that low-dose esketamine (0.25 mg/kg) combined with propofol (1-3.5 mg/kg) was safe and effective for painless gastrointestinal endoscopy in adults, but the harm brought by high-dose propofol and the waste of drugs should not be ignored [11]. Most clinical studies on esketamine combined with propofol in painless gastroenteroscopy have used deep sedation [10–13], and few studies have focused on the efficacy and safety of esketamine combined with propofol conscious sedation in colonoscopy. Therefore, our study aimed to explore the efficacy and safety of esketamine combined with propofol for conscious sedation in painless colonoscopy and to provide a reference basis for clinical medication. We hypothesized that esketamine combined with propofol for conscious sedation would reduce the incidence of hypoxemia and that its use in painless colonoscopy would be effective and safe.

Methods

Study design

This was a single-centre, prospective, double-blind, randomized controlled clinical trial. Control groups of this study were groups DS (propofol deep sedation) and CS_1 (sufentanil combined with propofol for conscious sedation), and the experimental group was group CS_2 (sufentanil combined with propofol for conscious sedation). The study was performed following the tenets of the Declaration of Helsinki. Approval to conduct the study was obtained from the Ethics Committee of the First Affiliated Hospital of Hunan University of Medicine (Ref. No. LL-SOP-003-FJ02). Written informed consent was acquired from all patients. The study was registered with the Chinese Clinical Trial Registry (http://www.chictr.org.cn; registration number, ChiCTR2200064552; principal investigator, Lizhu Xiao; registration date, October 11, 2022) before patient recruitment. This study was conducted according to the relevant CONSORT guidelines (supplementary File 1).

Patients

A total of 195 patients who underwent painless colonoscopy in the digestive endoscopy room were enrolled from the First Affiliated Hospital of Hunan University of Medicine from November 1, 2022, to February 28, 2023. The patients were aged 18–60 years with a body mass index (BMI) of 18–25 kg/m^2, had grade I-II physical

status based on the American Society of Anaesthesiologists (ASA) criteria, and consented to participate in this trial. The exclusion criteria for the study were as follows: severe asthma attacks; acute airway inflammatory response within 2 weeks; anticipated or known difficult airway; allergy to analgesics or sedatives; anaesthesia drug dependence or addiction; serious mental or psychological illness; impaired consciousness; pregnancy or lactation; elevated intracranial pressure; poorly controlled hypertension; aneurysms; and arteriovenous malformations.

Patients withdrew from the study with the following symptoms: withdrawal of informed consent by the patient; patient's request to stop the trial at any stage of the trial; serious violation of medication protocol due to loss of infusion pathway or other reasons; failure to complete a colonoscopy for any reason; loss of follow-up during trial follow-up; other conditions identified by the investigators, including serious adverse events.

Randomization and blinding

This study used simple randomization for random grouping. Randomization was performed using computer-generated random numbers, and patient allocation ratio was 1:1:1. Group assignments were performed by opaque sealed envelopes prepared by a research nurse not involved in the study. The experimental drugs are drawn by the nurse using syringes of the same size and capacity and prepared in a separate dispensing room. After preparation, the drug was placed in the medicine tray and covered with a treatment towel. A non-blind anesthesiologist administered the experimental drug according to the study protocol, and the whole process of drug administration was obscured. All outcome assessments and perioperative data collection were performed by a research assistant. All participants, including assessors, research assistant, gastrointestinal endoscopist, nurses, and patients were all fully blinded to group allocation.

Intervention and procedure

Preparation before anaesthesia

Routine preoperative bowel preparations (including 6 h of food fasting and 2 h for clear fluid fasting and diarrhoea) were performed. After the patient entered the room, venous access to the upper limb was established, and the compound sodium chloride was injected at a rate of 4–6 mL/min. We used a Mindray BeneVision N12 multifunctional monitor to monitor heart rate (HR), blood pressure (BP), and oxygen saturation (SpO_2). Five minutes before the induction of sedation, we provided a continuous oxygen supply (4–5 L/min) and intravenous administration of 0.01 mg/kg penehydine hydrochloride to relieve smooth muscle spasm during colonoscopy.

Anaesthesia management

A research nurse, who not involved in the study, allocated the liquid according to the patient's body weight, extracted sufentanil and esketamine with a 5mL syringe and diluted to 5mL respectively, and extracted 50mL propofol with a 50mL syringe. Patients in the DS group were injected with 5mL normal saline, and 1 min later, 1.5-2.0 mg/kg propofol (10 mg/10 seconds) was injected to maintain the target level of sedation (MOAA/S score [4] ≤ 2). Patients in the CS_1 and CS_2 groups were injected with 0.1 μg/kg sufentanil (diluted to 5 ml) or 0.2 mg/kg esketamine (diluted to 5 ml), respectively, and 1 min later, 0.5–0.8 mg/kg propofol (10 mg/10 seconds) was injected to maintain the target level of sedation (MOAA/S score 4 or 5). The time between the start of anaesthetic induction and the patient's sedation level reaching the target level was recorded as the anaesthesia induction time. Thereafter, additional doses of 0.3 mg/kg propofol were given intravenously as a bolus to sustain a targeted level of sedation. Each additional propofol should be administered at least 1 min apart. The whole process of drug administration was obscured. All patients underwent enteroscopy by the same attending gastrointestinal endoscopist in the gastrointestinal endoscopy unit.

Perioperative changes in vital signs, including MAP (mean arterial pressure), HR (heart rate), and SpO_2 (oxygen saturation), were recorded at the beginning of induction (T_0), immediately after colonoscopy implantation (T_1), immediately before tracheal intubation (T_2), during colonoscopy transsplenic flexure (T_3), and at the end of colonoscopy in patients (T_4).

We provided mandibular support whenever the SpO_2 was <95% during colonoscopy. A continuous decrease in SpO_2 of <90% for a duration of >30 s was defined as hypoxemia. We immediately opened the airway and assisted ventilation with pressure. We defined hypotension as a decrease in systolic blood pressure (SBP) > 20% of the baseline value (the basal blood pressure measured when the patient made an appointment for colonoscopy in an outpatient clinic), and we injected 3–5 mg of ephedrine. We defined hypertension as an increase in systolic blood pressure (SBP) > 20% of the baseline value, and we injected 10–50 μg of nitroglycerin. We intravenously injected 0.3–0.5 mg of atropine if the HR dropped below <50 bpm, which was defined as bradycardia. We recorded the use of assisted ventilation (jaw rest and mask ventilation), ephedrine, atropine, and nitroglycerin during colonoscopy.

We used the anaesthesia effect level standard to evaluate the anaesthetic effect of colonoscopy. Excellent: no significant limb movement or quiet expression during colonoscopy. Good: small limb movement and slight facial pain during colonoscopy. Poor: large limb movement or/and facial pain during colonoscopy. The formula

for calculating the rates of excellent and good anaesthesia effectiveness was as follows: the rate of excellent and good anaesthesia efficacy = (the number of excellent patients + the number of good patients)/the total number of patients in each group*100%.

Anaesthesia awakening

After completion of the colonoscopy, the endoscopist completed the satisfaction questionnaire. Patients were transferred to the recovery unit and continuously monitored until discharge. Patients completed the questionnaire when they reached an Aldrete score ≥ 9. Endoscopist satisfaction and patient satisfaction scores were assessed on a verbally administered numerical rating scale (NRS, 0–10; 0 = no satisfaction, 10 = the most severe satisfactiona) [4].

Outcomes

The primary outcomes of this study included the incidence of hypoxemia, hypotension, hypertension, and bradycardia and excellent and good rates of anaesthesia during colonoscopy. The secondary outcomes included perioperative changes in vital signs (MAP, HR, and SpO_2), anaesthesia induction time, incidence of adverse reactions during recovery (PONV, drowsiness, and dizziness), patient and endoscopist satisfaction scores, incidence of propofol injection pain, incidence of assisted ventilation and vasoactive medications, and dischargeable time (defined as the time from the end of the examination to an Aldrete score ≥ 9).

Sample size calculation

We used PASS 15 software for sample size calculations. A review of the literature revealed that common and high-risk adverse reactions during painless colonoscopy include hypoxemia. The incidence of hypoxemia during deep sedation with propofol was 22.0%, while for patients receiving sufentanil combined with conscious sedation with propofol, the incidence was 2.5%. According to the pretrial data, the incidence of hypoxemia in patients receiving esketamine combined with propofol conscious sedation was 2.0%. We set the type I error rate (α) to 0.05 and the test power (1-β) to 0.8, resulting in a calculated sample size of 49 individuals per group. Considering a 20% dropout rate, the adjusted sample size was 62 individuals per group. To account for potential exclusions or withdrawals, the trial plans to enrol 198 participants, with 66 participants in each group.

Statistical analysis

Collected data were organized, tabulated, and statistically analysed using SPSS statistical version 22 software (SPSS Inc., USA). We expressed measurement data that conformed to the normal distribution as means ± standard deviations (SD). Between-group comparisons were performed using one-way analysis of variance (ANOVA), while within-group comparisons utilized repeated measures analysis of variance. We expressed non-normal distribution measurement data as median (M) and interquartile distance (IQR), and performed comparisons between groups by the Mann−Whitney U test. We expressed count data as n (%), and compared groups by chi-squared test. The odds ratio (OR) and 95% confidence interval (CI) were calculated using crosstab analysis. A *P*-value < 0.05 was considered statistically significant.

Results

Patient selection and patient characteristics

Of 198 patients assessed for eligibility, three patients were excluded because of not meeting inclusion criteria. The remaining 195 patients were randomly assigned to the different study groups (Fig. 1). All patients completed colonoscopy and achieved the target level of sedation. The demographic characteristics of the patients, including age, BMI, colonoscopy time, sex, and ASA physical status, were not significantly different among the three groups (Table 1).

Comparison of safety indicators, efficacy indicators

The incidence of hypoxemia in the DS group was significantly greater than that in the CS_1 and CS_2 groups ($p < 0.05$). The incidence of hypotension in the CS_2 group was significantly lower than that in the DS and CS_1 groups ($p < 0.05$). There was no significant difference in the incidence of bradycardia, hypertension, excellent or good anaesthesia among the three groups (Table 2).

The risk of hypoxemia was 5.727 times higher in Group DS than in Group CS_2 (OR 5.727; 95%CI 1.203–27.273), and the risk of hypotension was 9.864 times higher in Group DS than in Group CS_2 (OR 9.864; 95%CI 2.770–35.120). The risk of hypotension in Group CS_1 was 5.167 times that in Group CS_2 (OR 5.167; 95%CI 1.396–19.117) (Table 2).

Comparison of SpO2, MAP and HR at different time points

A comparison of the SpO_2 between the groups revealed that the SpO_2 in the CS_2 group was significantly greater than that in the DS group at T_1 and T_2 ($p < 0.05$) (Fig. 2). The MAP of the CS_2 group was significantly greater than that of the DS group at T_1, T_2, T_3 and T_4 ($p < 0.05$), and that of the CS_2 group was significantly greater than that of the CS_1 group at T_1, T_2 and T_3 ($p < 0.05$) (Fig. 3). A comparison of the HR between the groups revealed that the HR in the CS_1 group was significantly lower than that in the DS and CS_2 groups at T_1, T_2, T_3 and T_4 ($p < 0.05$) (Fig. 4).

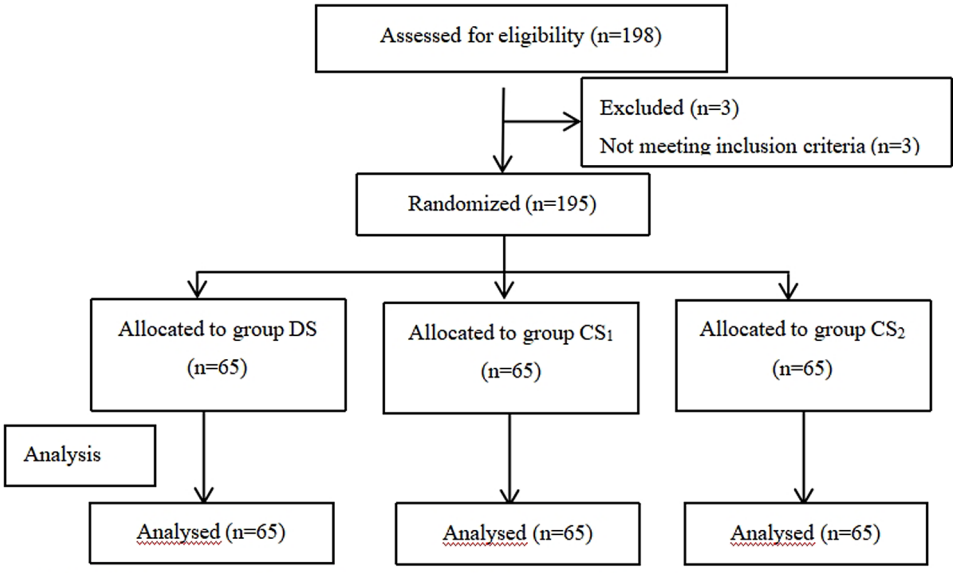

Fig. 1 A flow diagram showing the experimental design used in the study

Table 1 Demographic characteristics of the participants

	Group DS	Group CS_1	Group CS_2	χ^2/F	*p* value[a, b]
Age (years)	47.7 ± 11.4	48.2 ± 11.5	48.9 ± 11.8	0.180	0.835
BMI (kg/m^2)	22.3 ± 2.1	22.0 ± 2.3	22.8 ± 1.8	2.188	0.115
Colonoscopy time (min)	11.8 ± 4.3	12.4 ± 4.2	11.5 ± 3.5	0.808	0.447
Sex (M/F)	30/35	29/36	25/40	0.878	0.645
ASA I/II (n)	17/48	14/51	19/46	1.764	0.414

Abbreviations BMI, body mass index; *ASA*, American Society of Anaesthesiologists

[a] One-way analysis of variance

[b] Chi-square test

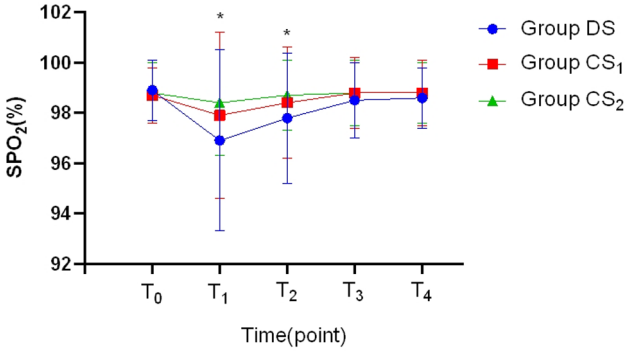

Fig. 2 SpO_2 changes at different time points among the three groups. Figure legends, compared group DS with group CS_2, $^*p < 0.05$ was considered significant

Comparison of adverse reactions during recovery, and

Table 2 Comparison of safety indicators, efficacy indicators among the three groups of patients [n(%), OR(95%CI)]

	Group DS	Group CS_1	Group CS_2	χ^2	*p* value[b]	OR(95%CI)		
						Group DS vs. Group CS_1	Group DS vs. Group CS_2	Group CS_1 vs. Group CS_2
Safety indicators								
Hypoxemia	10(15.4)	4(6.2)*	2(3.1)*	7.081	0.029	2.773(0.822–9.349)	5.727(1.203–27.273)	2.066(0.365–11.692)
Hypotension	21(32.3)	13(20.0)	3(4.6)*#	16.278	< 0.001	1.909(0.858–4.248)	9.864(2.770–35.120)	5.167(1.396–19.117)
Bradycardia	2(3.1)	1(1.5)	2(3.1)	0.411	0.814	2.032(0.180-22.975)	1.000(0.137–7.322)	0.492(0.044–5.566)
Hypertension	0(0.0)	1(1.5)	1(1.5)	1.010	0.603	0 (NA)	0 (NA)	1.000(0.061–16.336)
Efficacy indicators								
Excellent and good anaesthesia effect	64(98.5)	63(96.9)	62(95.4)	1.032	0.597	2.032(0.180-22.975)	3.097(0.314–30.579)	1.524(0.246–9.437)

[b] Chi-square test

Note Compared with the DS group, $^*p < 0.05$ was considered significant. Compared with the CS_1 group, $^\#p < 0.05$ was considered to indicate statistical significance

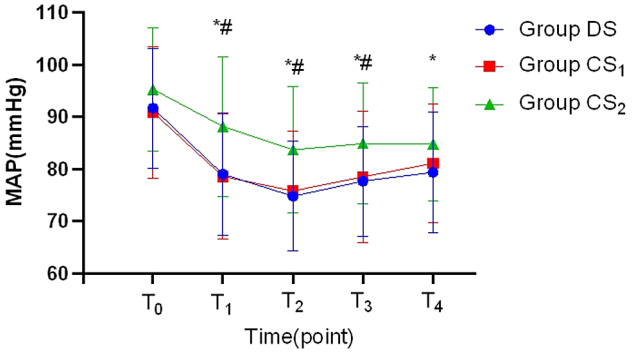

Fig. 3 MAP changes at different time points among the three groups. Figure legends, compared group DS with group CS_2, $^{*}p<0.05$ was considered significant. Compared group CS_1 with group CS_2, $^{\#}p<0.05$ was considered to indicate statistical significance

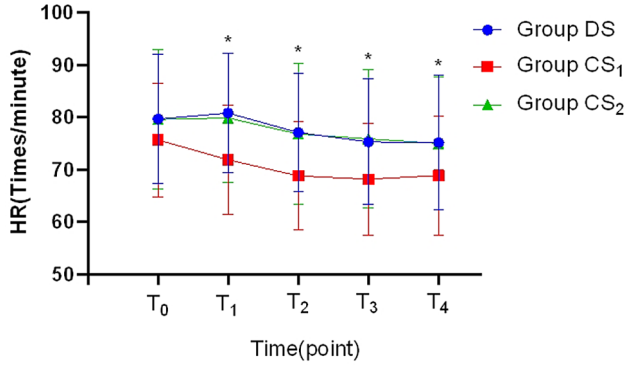

Fig. 4 HR changes at different time points among the three groups. Figure legends, compared group CS_1 with groups DS and CS_2, $^{*}p<0.05$ was considered significant

Table 3 Comparison of adverse reactions during recovery, and intraoperative management among the three groups of patients [n(%)]

	Group DS	Group CS_1	Group CS_2	χ^2	*p* value[b]
Adverse reactions during recovery					
PONV	1(1.5)	4(6.2)	2(3.1)	2.074	0.354
Drowsiness	45(69.2)	19(29.2)*	13(20.0)*	37.257	< 0.001
Dizziness	20(30.8)	31(47.7)*	18(27.7)#	6.594	0.037
Propofol injection pain	46(70.8)	12(18.5)*	9(13.8)*	57.618	< 0.001
Intraoperative management					
Assisted ventilation	16(24.6)	6(9.2)*	5(7.7)*	9.544	0.008
Ephedrine	14(21.5)	5(7.7)*	1(1.5)*	14.820	0.001
Nitroglycerin	0(0.0)	1(1.5)	1(1.5)	1.010	0.603
Atropine	2(3.1)	1(1.5)	2(3.1)	0.411	0.814

[b] Chi-square test

Note: Compared with the DS group, $^{*}p<0.05$ was considered significant. Compared with the CS_1 group, $p<0.05$ was considered to indicate statistical significance

Table 4 Comparison of anaesthesia induction time, dischargeable time, and satisfaction scores of patients and endoscopists among the three groups of patients $[\bar{x} \pm s]$

	Group DS	Group CS_1	Group CS_2	F	*p* value[a]
Anaesthesia induction time, min	2.3 ± 0.4	2.2 ± 0.2	2.3 ± 0.2	1.030	0.359
Discharge time, min	24.3 ± 5.4	17.4 ± 3.6*	17.8 ± 3.7*	53.039	< 0.001
Endoscopist satisfaction scores	8.9 ± 0.6	9.5 ± 0.6*	9.4 ± 0.7*	17.390	< 0.001
Patients satisfaction scores	9.1 ± 0.7	9.7 ± 0.5*	9.6 ± 0.6*	19.282	< 0.001

a: One-way analysis of variance

Note: Compared with the DS group, $^{*}p<0.05$ was considered significant

intraoperative management

The incidence of drowsiness during recovery, propofol infusion pain, assisted ventilation and ephedrine usage in the DS group was significantly greater than that in the CS_1 and CS_2 groups ($p<0.05$). The incidence of dizziness during recovery in the CS_1 group was significantly greater than that in the DS and CS_2 groups ($p<0.05$). There was no significant difference in the incidence of PONV during recovery, or nitroglycerine or atropine usage among the three groups (Table 3).

Comparison of anaesthesia induction time, dischargeable time, and satisfaction scores between patients and endoscopists

The dischargeable time in the DS group was significantly greater than that in the CS_1 and CS_2 groups ($p<0.05$). The satisfaction scores of patients and endoscopists in the DS group were significantly lower than those in the CS_1 and CS_2 groups ($p<0.05$). There was no significant difference in anaesthesia induction time among the three groups (Table 4).

Discussion

The findings of the present study indicated that the incidence of hypoxemia in patients receiving deep sedation with propofol was 15.4%, which was significantly greater than that in patients receiving conscious sedation with sufentanil combined with propofol (6.2%) or esketamine combined with conscious sedation with propofol (3.1%). First, propofol acts on GABA (γ- Aminobutyric) receptors to reduce respiratory variability in a dose-dependent manner. Higher doses of 2 mg/kg propofol during deep sedation increase the risk of hypoxemia [14]. Second, esketamine retains respiratory variability to maintain spontaneous breathing and has sympathomimetic activity that can relax bronchial smooth muscles and inhibit bronchospasm contraction caused by histamine release, thereby effectively alleviating airway oedema

and reducing the incidence of hypoxemia [15]. Jonkman et al. reported that low-dose ketamine can reduce the incidence of respiratory depression after opioid use [16]. Kamp et al. showed that the combined use of esketamine and propofol is better than the combined use of opioids and propofol because the latter may increase the possibility of respiratory depression [17]. In this study, there was no significant difference in the incidence of hypoxemia between the sufentanil combined with propofol for conscious sedation group and the esketamine combined with propofol for conscious sedation group. Notably, the risk of hypoxemia was 5.727 times higher in Group DS than in Group CS_2. Conscious sedation with esketamine combined with propofol shows promise in maintaining spontaneous breathing with lower respiratory depressant effects than deep sedation.

A previous study indicated that the occurrence of cardiopulmonary complications due to propofol sedation during endoscopy varies between 20% and 60%, depending on the surgical procedure and sedation approach [12]. In this study, the propofol deep sedation group had a hypotension incidence of 32.3%. The combination of sufentanil with propofol has been shown to have a synergistic effect on circulatory suppression [18]. Therefore, the incidence of hypotension in patients receiving sufentanil combined with propofol conscious sedation was still 20% greater in this study. Esketamine, known for its sympathetic nerve characteristics, can counteract the haemodynamic suppression effect of propofol [14]. Therefore, the incidence of hypotension (4.6%) in the esketamine combined with propofol conscious sedation group was the lowest in this study and was significantly lower than that in the DS and CS_1 groups. The risk of hypotension was 9.864 times higher in Group DS than in Group CS_2 ,and the risk of hypotension in Group CS_1 was 5.167 times that in Group CS_2. Animal studies have demonstrated that ketamine treatment in rats leads to the release of dopamine amino acid precursors, activation of dopamine activity, and increased vascular tone and heart rate [19]. Research has shown that esketamine can lead to notable elevations in both systolic and diastolic blood pressure, with a particular emphasis on the rise in systolic blood pressure [20]. This finding aligns with the theory that increased cardiac output may be a possible underlying mechanism [21]. However, the increase in blood pressure after esketamine administration is transient and rarely causes serious cardiovascular events [22]. In this study, only 1.5% of the patients in the esketamine combined with propofol for conscious sedation group had hypertension, and there was no significant difference in the incidence of hypertension among the three groups. Overall, the findings suggest that conscious sedation with esketamine combined with propofol can effectively reduce the occurrence of hypotension in patients without increasing the risk of hypertension. It can be safely used for painless colonoscopy.

The study results indicated that there was no significant difference in the incidence of bradycardia among the three groups. Intravenous administration of 0.01 mg/kg penehyclidine hydrochloride 5 min before the examination helped alleviate the vagal reflex caused by colonoscopy stimulation, potentially reducing the occurrence of arrhythmias [4, 23]. Furthermore, the combination of conscious sedation with esketamine and propofol did not increase the likelihood of bradycardia, as esketamine can increase sympathetic nerve tone and heart rate.

The study revealed that the efficacy of anaesthesia with esketamine combined with propofol conscious sedation in group CS_2 was comparable to that in groups DS and CS_1, demonstrating similar effectiveness in achieving anaesthesia induction and facilitating smooth entry into the microscope. Esketamine, the dextrorotatory enantiomer of ketamine, exhibits sedative and analgesic effects twice as potent as those of racemic ketamine. While low doses primarily produce sedation and analgesia, high doses result in significant anaesthetic effects [24]. Clinical trials have shown that esketamine can reduce opioid requirements and alleviate severe pain during liver tumour ablation [25]. Additionally, subanaesthetic doses of esketamine have been shown to improve postoperative pain management and are commonly used in painless digestive endoscopy procedures [26].

The present study revealed that patients in group CS_2 had significantly greater SpO_2 levels than did those in group DS at T_1 and T_2, suggesting that the respiratory depression caused by esketamine combined with propofol conscious sedation postanaesthesia induction was minimal. In group CS_2, both the mean arterial pressure (MAP) and heart rate (HR) were greater at T_1, T_2, and T_3. Due to the sympathomimetic effect of esketamine combined with propofol, conscious sedation has mild circulatory depression effects. Previous studies have shown that deep sedation with subanaesthetic doses of esketamine and propofol can maintain haemodynamic stability during painless gastrointestinal endoscopy [27], painless abortion [14], and bronchoscopy [28], consistent with the findings of this study.

The results indicate that the conscious sedation group had a significantly shorter dischargeable time than did the deep sedation group. There was no significant difference between the sufentanil combined with propofol conscious sedation group and the esketamine combined with propofol conscious sedation group. On the one hand, conscious sedation is characterized by low drug dosage and rapid recovery [4]. On the other hand, compared to ketamine, esketamine has a quick onset of action and short recovery time when used in small doses [24]. Therefore, conscious sedation with esketamine and

propofol results in faster recovery than deep sedation, leading to significantly shorter hospital discharge times.

The study showed that the incidence of drowsiness during recovery from conscious sedation with esketamine combined with propofol (20%) was significantly lower than that in the deep sedation group (69.2%). Additionally, the occurrence of dizziness during recovery (27.7%) was notably lower than that in the group receiving conscious sedation with sufentanil combined with propofol (30.8%). The five most common adverse effects of esketamine were dizziness, psychomimetic symptoms, sensory disturbances, vertigo, and nausea (incidence ranging from 20.9 to 26.1%) [13, 29], and the results of this study were similar. A study by Wang et al. revealed a lower incidence of adverse events (e.g., dizziness, nausea, vomiting, and headache) in patients who received esketamine for sedation during gastroscopy than in those who received racemic ketamine and that a low dose of esketamine reduces the incidence of adverse events due to the dose-dependent side effects of esketamine [24].

Previous research has indicated that the incidence of propofol injection pain ranges from 25 to 74% [30]. In this study, the deep sedation group had a significantly greater incidence of propofol injection pain (70.8%) than did the conscious sedation group (18.5% in group CS_1 and 13.8% in group CS_2), suggesting that the conscious sedation regimen during painless colonoscopy can lower the occurrence of propofol injection pain. Common methods to prevent propofol injection pain include pretreatment with opioid analgesics for central analgesia and early intravenous lidocaine to provide local anaesthetic effects on the vascular endothelium [31]. A randomized controlled trial demonstrated that low-dose esketamine pretreatment at 0.15 mg/kg effectively relieved propofol-induced injection pain as effectively as lidocaine, with the main mechanism likely being a peripheral local anaesthetic effect via the vascular endothelium rather than a central analgesic effect [32]. Furthermore, Ueki et al. showed that the free propofol concentration was positively correlated with the incidence of propofol injection pain [33], suggesting that the use of lower doses of propofol in the conscious sedation group in the present study resulted in a decrease in the intravascular concentration of free propofol such that the incidence of propofol injection pain was reduced.

The study also revealed that endoscopist satisfaction and patient satisfaction in conscious sedation groups were significantly greater than those in the deep sedation group. Patients under conscious sedation can easily adjust their position according to the endoscopist's instructions, facilitating the smooth progress of colonoscopy [4]. Recovery is rapid, adverse reactions during the recovery period are minimal, and the waiting time for patients to wake up is shortened for endoscopists, leading to higher satisfaction levels. Consistent with the findings of this study, Su et al. also reported that conscious sedation and analgesia were safe and provided satisfactory comfort during surgery, with high patient satisfaction scores [34].

Limitations of the study

The present study had several limitations. Psychotomimetic symptoms, a common adverse effect of esketamine, were not assessed in the study due to the absence of observable symptoms during the pretest. Further investigation is needed to determine whether different dosages or dosing regimens may lead to psychotomimetic symptoms. Additionally, postoperative long-term conditions, such as postoperative recovery quality, were not followed up in this study and should be explored in future research. Given that this was a single-centre study, a multicentre study with a larger sample size is necessary to validate the findings.

Conclusions

In conclusion, esketamine combined with propofol for conscious sedation can be safely and effectively used for painless colonoscopy and has fewer complications.It is recommended for painless colonoscopy.

Abbreviations

ASA	The American Society of Anesthesiologists
BMI	Body mass index
CS	Conscious Sedation
DS	Deep Sedation
ECG	Electrocardiogram
HR	Heart Rate
MAP	Mean Arterial Pressure
MOAA/S	Modified Observers Assessment of Alertness/Sedation scale
NMDA	N-methyl-D-aspartate receptor
NRS	Numerical Rating Scale
PONV	Postoperative Nausea and Vomiting
SpO2	Saturation of Pulse Oxygenation
SBP	Systolic Blood Pressure
SPSS	Statistical Product and Service Solutions
GABA	γ- Aminobutyric

Supplementary Information

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Supplementary Material 1

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Not applicable.

Author contributions

Lizhu XIAO, Jiaoling ZHANG, and Zhaoguo LIU conducted data collection. Zhaoguo LIU, Lizhu XIAO, Xiaohua ZOU and Jiefu TANG conducted data analysis. Lizhu XIAO and Xiaohua ZOU wrote the main manuscript text and Zhaoguo LIU prepared figures 1–4 and table 1–3. Xiaohua ZOU, Jiefu TANG, Lizhu XIAO, Zhenghua ZHANG, Jing LU, Zhaoguo LIU and Kang LU contributed to the revision. All authors reviewed the manuscript and have approved the final copy of the manuscript.

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Data availability
The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Approval to conduct the study was obtained from the Ethics Committee of the First Affiliated Hospital of Hunan University of Medicine (Ref. No. LL-SOP-003-FJ02). Written informed consent was acquired from all patients. All methods were performed following the relevant guidelines and regulations.

Consent for publication
Not applicable.

Registration
The study protocol was registered with the Chinese Clinical Trial Registry (http://www.chictr.org.cn; registration number, ChiCTR2200064552; principal investigator, Lizhu Xiao; registration date, October 11, 2022, no protocol amendment or study changes after start of the trial).

Competing interests
The authors declare no competing interests.

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