Drug Design, Development and Therapy

Dovepress
open access to scientific and medical research

Open Access Full Text Article

CLINICAL TRIAL REPORT

Influences of Propofol, Ciprofol and Remimazolam on Dreaming During Anesthesia for Gastrointestinal Endoscopy: A Randomized Double-Blind Parallel-Design Trial

Rui Zhou[1,2,*], Lijuan Fu[2,*], Shu Liu[2,*], Sanjie Gao[2], Zhifu Zhao[2], Wencai Jiang[2], Li Liu[2], Weiqiao Ren[2], Dongmei Xiang[2], Xing You[2], Chunyong Tang[2], Yukai Zhou[2], Yanqing Song[2], Juan Xie[2], Li Xie[2], Ru Yu[2], Xianjie Zhang[2], Dan Zhou[2], Jia Han[2], Leqiang Xia[2], Lize Xiong[1]

[1]Shanghai Key Laboratory of Anesthesiology and Brain Functional Modulation, Translational Research Institute of Brain and Brain-Like Intelligence, Clinical Research Center for Anesthesiology and Perioperative Medicine, Department of Anesthesiology and Perioperative Medicine, Shanghai Fourth People's Hospital, School of Medicine, Tongji University, Shanghai, 200434, People's Republic of China; [2]Department of Anesthesiology, Deyang People's Hospital, Deyang, 618000, People's Republic of China

*These authors contributed equally to this work

Correspondence: Leqiang Xia, Department of Anesthesiology, Deyang People's Hospital, No. 173, Section 1, North Taishan Road, Deyang, Sichuan, 618000, People's Republic of China, Tel +8613547098458, Email xialq123184@163.com; Lize Xiong, Shanghai Fourth People's Hospital, No. 1279, Sanmen Road, Shanghai, 200434, People's Republic of China, Tel +86-21-55603002, Fax +86-21-56660851, Email mzkxlz@126.com; lizexiong@tongji.edu.cn

Purpose: To compare the influences of propofol, ciprofol and remimazolam on dreaming during painless gastrointestinal endoscopy.

Methods: This study was a single-center, prospective, parallel-design, double-blind, randomized clinical trial. Between May 2023 and October 2023, patients undergoing elective painless gastrointestinal endoscopy were recruited and randomly allocated into one of the three groups. Demographic data, intraoperative information, incidence of dreaming, insufficient anesthesia and intraoperative awareness, type of dream, patient satisfaction score, adverse events, and improvement of sleep quality were collected.

Results: The difference in incidence of dreaming among the three groups was not significant (33.33% vs 48.33% vs 41.67%, p=0.061). The number of patients with intraoperative hypotension in the propofol group was larger than that of the remimazolam group (32 vs 12, p=0.001). However, the cases of intraoperative hypotension between propofol group and ciprofol group or ciprofol group and remimazolam group were comparable (32 vs 22, p=0.122; 22 vs 12, p=0.064). The percentage of insufficient anesthesia between propofol group and remimazolam group was significant (13.33% vs 1.67%, p=0.001), while no statistical difference was detected between propofol group and remimazolam group or ciprofol group and remimazolam group (13.33% vs 5.00%, p=0.025; 5.00% vs 1.67%, p=0.150). The ability of propofol to improve sleep quality at 1st post-examination day was significantly better than that of remimazolam (86.21% vs 72.88%, p=0.015), while it was not significant between propofol group and ciprofol group or ciprofol group and remimazolam group (86.21% vs 80.36%, p=0.236; 72.88% vs. 72.88%, p=0.181). Incidence of intraoperative awareness, intraoperative hypoxia, type of dream, satisfaction score, adverse events during recovery, and sleep improvement on the 7th post-examination day was not significant among the groups.

Conclusion: Anesthesia with propofol, ciprofol and remimazolam, respectively, for gastrointestinal endoscopy did not induce statistical difference in the incidence of dreaming, despite that all of them are more likely to induce pleasant dreams.

Keywords: propofol, ciprofol, remimazolam, endoscopic sedation, dreaming

Introduction

New cases of gastrointestinal tumors in 2020 were about 3 million with a striking 1.7 million deaths globally.[1] In China, lung cancer, liver cancer, stomach cancer, breast cancer and colon cancer are the five leading causes of cancer-related death, and the incidence of colon cancer is increasing rapidly.[2] Gastrointestinal endoscopy has been regarded as an

Received: 22 January 2024
Accepted: 14 May 2024
Published: 29 May 2024

effective way for early detection of gastrointestinal tumors.[3–5] In recent years, owing to the popularity of painless techniques conducted by anesthesia, great advances have been made in comfort medicine. As a result, cases of painless gastrointestinal endoscopy have also increased dramatically. Studies showed that about one-fifth to one-quarter of the patients had dreams during painless colonoscopies, while pleasant dreams accounted for only about one-third.[6,7] It was reported that dreams during anesthesia were affected by different anesthetics, depth of anesthesia, age, gender, preoperative psychological state and other factors.[6–10]

Propofol is the preference for painless gastrointestinal endoscopy due to its advantages of rapid anesthetic induction, rapid recovery, and low incidence of postoperative nausea and vomiting. Meanwhile, evidence indicated that propofol was related to euphoria during painless endoscopy.[11–13] The euphoria induced significant increased happiness, relaxation and declined anxiety, which was connected with the more positive attitude of patients towards the results of endoscopy.[12] Besides, propofol was regarded as a main factor for dream formation and recall during general anesthesia.[14] Previous studies found that 12% to 40% of patients who underwent propofol-based anesthesia reported dreaming.[14–16] However, the proportion of neutral or negative dreams was about 65%.[7] Moreover, the adverse effects of propofol were obvious, including respiratory depression, circulatory depression, bradycardia and injection pain.

Ciprofol, a novel intravenous anesthetic with a similar chemical structure to propofol, has characteristics of rapid onset and recovery. Studies indicated that 0.4–0.5 mg/kg ciprofol induced equivalent effects of sedation or anesthesia in comparison with 2.0 mg/kg propofol, which means the potency of ciprofol is 4–5 times that of propofol.[17,18] Though the overall safety profile and adverse events were similar between ciprofol and propofol, injection pain of ciprofol was much less observed.[19,20]

Remimazolam is a new benzodiazepine sedative that has been increasingly applied in sedation and general anesthesia. It was reported that 0.4 mg/kg remimazolam induced 100% successful induction of general anesthesia and no injection pain was observed.[21] Chen et al[22] proposed remimazolam as a priority over propofol in gastrointestinal endoscopy owing to its faster recovery and fewer adverse events. More importantly, remimazolam could be safely used in high-risk patients undergoing colonoscopy.[23]

Obviously, ciprofol and remimazolam have unique advantages over propofol, which is of clinical significance. However, few studies reported dreams during ciprofol or remimazolam anesthesia. Thus, we designed this randomized double-blinded parallel-design trial to investigate dreaming during painless gastrointestinal endoscopy under the three anesthetics, respectively.

Methods

Ethics and Registration

The study protocol was approved by the Ethics Committee of Deyang People's Hospital, Deyang city, Sichuan province, China (Date: April 20, 2023; Registration number: 2023–04-031-K01). This trial was registered on the Chinese Clinical Trial Registry prior to patient enrollment (Registration number: ChiCTR2300071565; Principal investigator: Leqiang Xia; Date of registration: May 18, 2023). Investigators explained the study to all subjects and got written informed consent. The whole study procedure was conducted in Deyang People's Hospital and was in line with the Declaration of Helsinki. The unabridged study protocol is described in our previous article.[24]

Subjects

Patients who intended to undergo elective painless gastroscopy, colonoscopy or gastroenteroscopy were considered to be recruited into this trial. Inclusion criteria were as follows: 18 to 65 years old, ASA status I to II, respiration rate 12 to 18 cycles/min, heart rate 50 to 100 beats/min, systolic blood pressure ≥90 mmHg, diastolic blood pressure ≥60 mmHg, SpO_2 >95% when inhaling air. Exclusion criteria included allergies to the related drugs or drug adjuvants, contraindications to deep sedation or anesthesia, medication of opioid analgesics within 1 month, drinking more than 14 units of alcohol per week (1 unit = 360 mL beer or 45 mL spirits with 40% alcohol or 150 mL wine), difficult airway, pregnant or lactating women, serious mental illness or emotional disorder, and disability to finish the interviews. Researchers detailedly introduced this study to all subjects before enrollment.

Randomization and Masking

A randomized sequence was generated by SPSS 23.0 by an independent investigator. The numbers were encoded to represent the three groups in a 1:1:1 ratio and then sealed in opaque envelopes. The anesthesiologist responsible for anesthesia opened the envelopes in order and gave interventions according to the grouping information. Since the patients lay on the side and the vein access was sheltered, the patients were blinded to grouping. The examination area was separated by an opaque curtain, another anesthesiologist monitored the vital signs and anesthesia depth of the patients, gave guidance to the anesthesia management, and documented related events. The nurse anesthetist who took charge of interviews and follow-ups did not get into the examination room. Therefore, the subjects and observers were blinded.

Study Procedure

The eligible patients received a Hospital Anxiety and Depression Scale (HADS) survey before the endoscopy. After positioning in a standard posture, patients were sent into the examination room, non-invasive blood pressure, SpO_2, electrocardiogram and Narcotrend index were continuously monitored. The oxygen flow was 8 L/min. The subjects were then randomly allocated into the propofol group, ciprofol group and remimazolam group according to the grouping information. Anesthesia induction was initiated by sufentanil (0.06–0.08 μg/kg), followed by propofol (1.5–2 mg/kg), ciprofol (0.3–0.5 mg/kg) or remimazolam (0.2–0.3 mg/kg). When the Narcotrend index reached C, endoscopy was started by a skillful gastroenterologist. Before the value of Narcotrend changed to B, top-ups were administered. Hypoxia was treated with jaw thrust maneuver and manual ventilation. Dopamine was applied to improve hypotension. Patients were transferred to the post-anesthesia care unit (PACU) for recovery.

In the PACU, a nurse anesthetist who was well trained and blinded to the grouping interviewed the patients. The incidence of dreaming and intraoperative awareness was determined on the basis of modified Brice questionnaire. Type of dream (positive, negative, or neutral) and evaluation of anesthesia (0 to 10 points, extremely unsatisfied to extremely satisfied) were obtained consequently. Side effects during recovery like hypotension, hypoxia, nausea, vomiting, drowsiness, dizziness and other discomforts were treated by the senior anesthesiologist. The nurse anesthetist accordingly recorded them. Improvement (yes or no) in sleep quality of 1st and 7th post-examination days was collected by telephone call of the nurse anesthetist.

Outcomes

The primary outcome was the incidence of dreaming. Secondary outcomes were as follows: type of dreams, improvement of sleep quality, satisfaction score of patients, incidence of insufficient anesthesia (defined as Narcotrend index changed to A or B) and intraoperative awareness. Safety evaluation was reflected by the incidence of hypotension and hypoxia during examination and adverse events during recovery.

Statistical Analysis and Sample Size

Data storage and analysis were performed by the SPSS software. Categorical variables were presented as number of cases or percentage, and analyzed with Chi-Square test. Continuous variables were firstly verified by the Kolmogorov–Smirnov test to determine the normality of the data distribution. Normally distributed data were depicted as mean ± standard deviation (SD), and one-way analysis of variance (ANOVA) was used to test the differences, followed by LSD-*t* test for pairwise comparisons. Abnormally distributed data were shown as median (inter-quartile range), and Kruskal–Wallis test was applied to determine significance, followed by Wilcoxon test for pairwise comparisons.

According to the preliminary study in which 60 cases were included, incidence of dream was 25%, 45% and 35% in propofol group, ciprofol group and remimazolam group, respectively. Sample size was calculated by Compare K Proportions model on http://powerandsamplesize.com/. Given that type I error (α) was 0.05 and power (1-β) was 0.8, 114 cases were needed in each group (allocation ratio 1:1:1) to detect the differences in dreaming incidence. Concerning 5% dropout, we recruited 360 subjects. Statistical significance was defined as $p<0.05$. The adjusted value of α' for pairwise comparison was 0.017.

Results

Three hundred and sixty patients were finally recruited (172 males, 47.8%) between May 21, 2023, and October 10, 2023. Generally, 118 patients (32.8%) underwent gastroscopy, 58 (16.1%) colonoscopy, and 184 (51.1%) gastroenteroscopy. Table 1 shows the detailed demographic and baseline data. All patients came to the primary endpoint, 14 (4 in propofol group, 8 in ciprofol group and 2 in remimazolam group) did not respond to the sleep quality of the 1st post-examination day, and we failed to acquire the sleep quality of the 7th post-examination day from 26 (8 in propofol group, 8 in ciprofol group and 10 in remimazolam group) subjects. The schedule of this trial was presented in Figure 1.

Demographic, Baseline and Intraoperative Data

There were no significant differences in sex, age, anxiety score, depression score, kind of endoscopy, time to adequate anesthesia, and the incidence of hypoxia among the three groups (Table 1). However, the differences in body weight, incidences of hypotension and insufficient anesthesia were significant (Table 1). Furthermore, the incidence of hypotension between propofol group and remimazolam group was significantly different (26.67% vs 10.00%, p=0.001, Figure 2a), while between propofol group and ciprofol group or ciprofol group and remimazolam group it was comparable (26.67% vs 18.33%, p=0.122; 18.33% vs 10.00%, p=0.064; Figure 2a). The difference in percentage of insufficient anesthesia reflected by Narcotrend index between propofol group and remimazolam group was significant (13.33% vs 1.67%, p=0.001, Figure 2b), while cases of insufficient anesthesia between propofol group and ciprofol group or ciprofol group and remimazolam group were similar (13.33% vs 5.00%, p=0.025; 5.00% vs 1.67%, p=0.150; Figure 2b).

Postoperative Interview

In total, 6 subjects (2 in each group) were considered to have intraoperative awareness. One hundred and forty-eight patients (40 in propofol group, 58 in ciprofol group, and 50 in remimazolam group) reported that they had a dream. The incidence of dreaming among the three groups was not significant (33.33% vs 48.33% vs 41.67%, p=0.061, Table 2). In all groups, most of the dreams were positive or pleasant. Only 2 patients in the remimazolam group experienced unpleasant dreams. The types of dreams among the three groups were comparable (Table 2).

According to the interview, adverse events during recovery included dizziness and drowsiness. In the propofol group, the number of dizziness, drowsiness, both dizziness and drowsiness, and none adverse events was 22, 48, 8 and 42,

Table 1 Demographic, Baseline and Intraoperative Data

Parameters	Group Propofol	Group Ciprofol	Remimazolam Group	*P* value
Sex (n, %)				
Male	66, 55.00	52, 43.33	54, 45.00	0.147[a]
Female	54, 45.00	68, 56.67	66, 55.00	
Age (mean±SD)	48.72±9.97	48.02±12.05	49.65±8.90	0.474[b]
Body weight	62.74±11.19	59.28±11.20	58.32±9.42	0.004[b*]
Anxiety score	4.77±1.42	4.61±1.34	4.93±1.35	0.204[b]
Depression score	2.98±2.07	2.58±2.21	2.53±1.81	0.169[b]
Endoscopy type (n, %)				
Gastroscopy	34, 28.33	38, 31.67	46, 38.33	0.143[a]
Colonoscopy	18, 15.00	16, 13.33	24, 20.00	
Gastroenteroscopy	68, 56.67	66, 55.00	50, 41.67	
Time to adequate anesthesia(s)	37.05±4.64	36.91±6.61	42.71±6.39	<0.001[b*]
Hypotension (n, %)	32, 26.67	22, 18.33	12, 10.00	0.004[a*]
Hypoxia (n, %)	24, 20.00	28, 23.33	18, 15.00	0.260[a]
Insufficient anesthesia (n, %)	16, 13.33	6, 5.00	2, 1.67	0.001[a*]
Examination duration(min)	11(6, 15)	9.5(5, 12)	8(6, 13)	0.010[c*]
Drug consumption(mg)	170.0(120.0, 200.0)	30(25, 37.5)	20.0(17.5, 25.0)	–

Notes: [a]Chi-Square test; [b]ANOVA; [c]Kruskal–Wallis test. *Difference among the groups is significant.

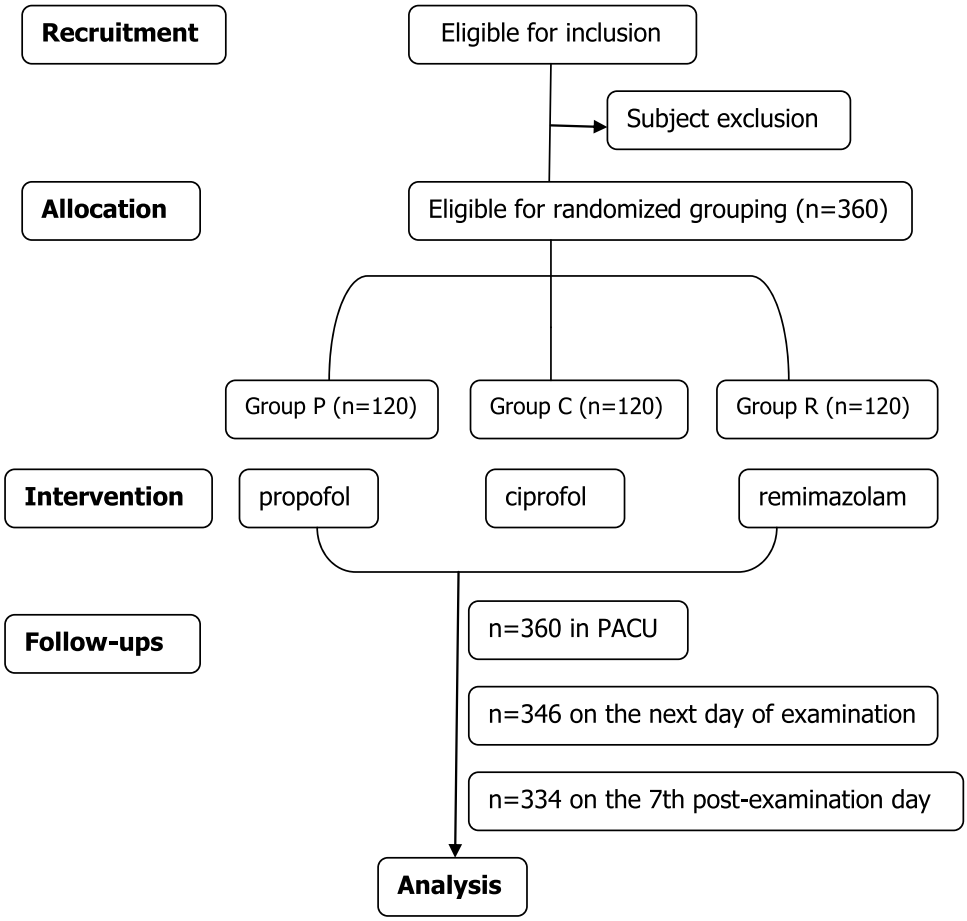

Figure 1 Flowchart of this study.
Abbreviation: PACU, post-anesthesia care unit.

respectively (Table 2). While it was 40, 36, 8 and 36 in ciprofol group, and 26, 46, 14 and 34 in remimazolam group, respectively (Table 2). The incidence of adverse effects during recovery was comparable (Table 2). All medication protocol won a high satisfaction score with no statistical difference (10(9, 10) vs 10(9, 10) vs 10(9, 10), p=0.077, Table 2).

The sleep quality of post-anesthesia was described as improved or unimproved according to the feelings of subjects. Generally, a large proportion of subjects felt improvement of sleep quality on the 1st post-examination day in every group. However, there was significant difference among the propofol group, ciprofol group and remimazolam group (86.21% vs 80.36% vs 72.88%, p= 0.039, Table 2). Propofol provided an equivalent improvement of sleep quality on the 1st post-examination day to ciprofol (86.21% vs 80.36%, p= 0.236, Figure 2c), while performed a better effect than remimazolam did (86.21% vs 72.88%, p= 0.012, Figure 2c). Remimazolam showed similar ability with ciprofol in improving sleep (72.88% vs 80.36%, p= 0.181, Figure 2c). However, sleep improvement on the 7th post-examination day was not significant among the groups (44.64% vs 41.07% vs 38.18%, p=0.619, Table 2).

Discussion

In the present study, we determined the influences of different anesthetics on dreaming in people who underwent a painless gastrointestinal endoscopy. We found that incidences of dreaming were of no significant difference among propofol, ciprofol or remimazolam anesthesia for gastrointestinal endoscopy. But it is more likely to induce happy dreams by the above-mentioned three anesthetics. Results of this study indicated that about one-third of patients under propofol anesthesia had a dream, which is in accordance with several previous studies.[14,16] Propofol induced dreaming

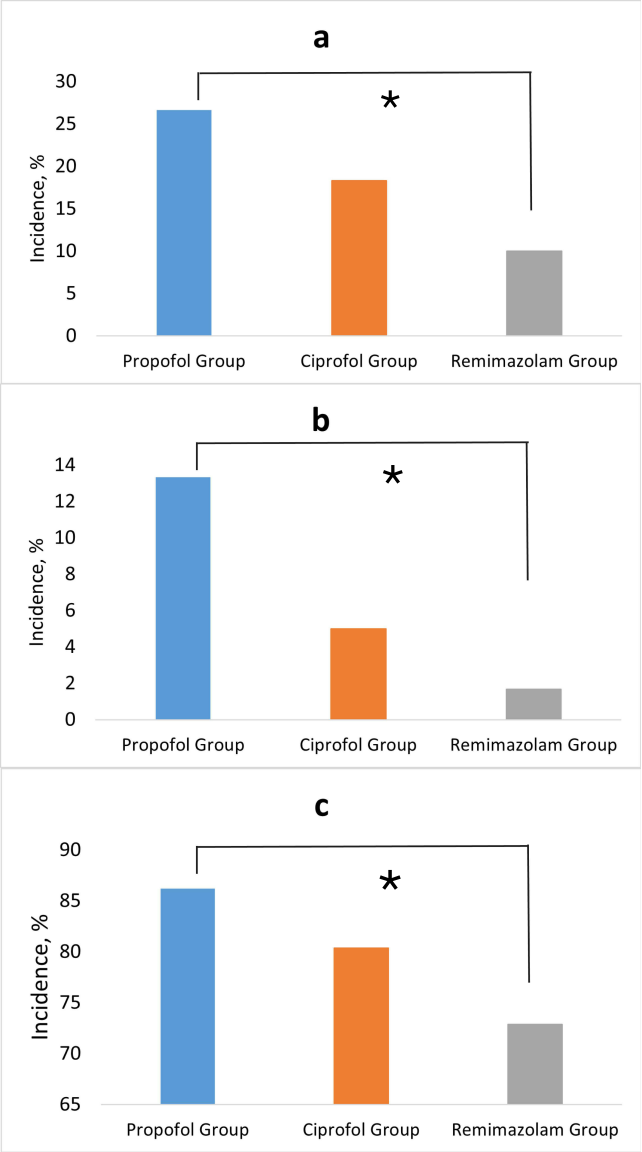

Figure 2 Incidence of intraoperative hypotension (**a**), insufficient anesthesia (**b**) and sleep improvement of the 1st day of post-examination (**c**). *p<0.017.

was reported to be related to anesthetics, depth of anesthesia, age, gender, preoperative psychological state and other factors.[6–10] However, the baseline information of our study was comparable among the groups. Matus et al[8] found that the Bispectral Index value of dreamers at 2 min after endoscopy initiation was lower than that of non-dreamers. We monitored the depth of anesthesia by Narcotrend which was applied in remimazolam and propofol sedation.[25,26] Twenty-four patients with inadequate sedation (16 in propofol group, 6 in ciprofol group and 2 in remimazolam group) were detected. Inadequate anesthesia might be the reason for the relatively lower incidence of dreaming. A recent study focused on propofol sedation induced euphoria indicated that pleasant dream was associated with a higher Morphine-Benzedrine Group (MBG) score, which means that there are positive relations among propofol, pleasant dreams and euphoria.[13] In this study, almost all dreams were positive or pleasant, which is similar to a previous study.[27]

Semblable to propofol, ciprofol is a new gamma-aminobutyric acid (GABA) receptor agonist. Most notably, ciprofol is well known for little injection pain and high potency.[17–20] Moreover, the present study showed that nearly half of the subjects experienced dreams under ciprofol anesthesia, and no unpleasant or negative ones were recorded. However, we could not infer that these fond dreams led to higher satisfaction of patients.

Table 2 Postoperative Interview Parameters

Parameters	Propofol Group	Ciprofol Group	Remimazolam Group	*P* value
Intraoperative awareness (n, %)	2, 1.67	2, 1.67	2, 1.67	1[a]
Dreaming (n, %)	40, 33.33	58,48.33	50, 41.67	0.061[a]
Type of dream (n, %)				
Positive	36, 90.00	56, 96.55	46, 92.00	0.185[a]
Negative	0, 0	0, 0	2, 4.00	
Neutral	4, 10.00	2, 3.45	2, 4.00	
Adverse events (n, %)				
Dizziness	22, 18.33	40, 33.33	26, 21.67	0.079[a]
Drowsiness	48, 40.00	36, 30.00	46, 38.33	
Both dizziness and drowsiness	8, 6.67	8, 6.67	14, 11.67	
None	42, 35.00	36, 30.00	34, 28.33	
Satisfaction score (median, inter-quartile range)	10(9, 10)	10(9, 10)	10(9, 10)	0.077[b]
Sleep quality improvement T1 (n, %)	100, 86.21	90, 80.36	86, 72.88	0.039[a*]
Sleep quality improvement T2 (n, %)	50, 44.64	46, 41.07	42, 38.18	0.619[a]

Notes: [a]Chi-Square test; [b]Kruskal–Wallis test; T1: 1st day of post-examination; T2: 7th day of post-examination. *There is significant difference among the groups.

Benzodiazepines exert an anterograde amnesia effect through a direct or an indirect way during sedation.[28] Previous studies established that remimazolam induced deep anesthesia that facilitated painless endoscopy.[21–23] Similarly, our results showed that remimazolam was eligible for gastroscopy, colonoscopy and gastroenteroscopy. However, remimazolam was less likely to lead to hypotension. In addition, about 40% of subjects under remimazolam anesthesia had a dream. Although two of them experienced negative or unpleasant dreams, no patient gave a low satisfaction score to the anesthesia procedure.

The overall incidence of intraoperative awareness under anesthesia was estimated to range from 1/20,000 to 1/1000 and was influenced by anesthetic, patient and surgery factors.[29,30] In the present study, Narcotrend index indicated that part of patients (16 in propofol group, 6 in ciprofol group and 2 in remimazolam group) experienced insufficient anesthesia. Though we administered top-ups according to Narcotrend index, intraoperative awareness might emerge before top-ups functioning. However, the groups had equal incidence of intraoperative awareness (2 cases in each group). This mismatching incidence of insufficient anesthesia and intraoperative awareness might be explained by a theory that intraoperative awareness was thought to occur occasionally during general anesthesia.[31] Nevertheless, intraoperative awareness did not decrease the evaluation of anesthesia of these patients in our study.

There were some limitations in this study. Firstly, we enrolled patients undergoing gastroscopy, colonoscopy and gastroenteroscopy rather than one kind of specific endoscopy. The stimulus intensity, duration, and drug consumption were diverse for the three kinds of examination. However, proportions among the groups showed no significant difference. Sample size was also calculated from a preliminary test that contained the three kinds of endoscopy. Secondly, we did not exclude patients whose examination time was too long, because for all patients, top-ups were administered to maintain a moderate Narcotrend value. Thirdly, the outcomes mostly depend on subjective indicators and the estimation of improvement in sleep quality was relatively simple. Because there are no objective measurements to assess dream, emotion and satisfaction. Considering the compliance of patients and way of follow-up, we evaluated the improvement of sleep quality by simply asking yes or no rather than scales. This method is more suitable for patients with lower educational levels. In addition, in keeping with trial registration, subgroup analyses were not conducted.

Conclusion

Propofol, ciprofol and remimazolam resulted in nonstatistical difference in the incidence of dreaming during painless gastrointestinal endoscopy, but tended to induce pleasant dreams. However, dreaming, quality of dreams, and

intraoperative awareness did not impact the evaluation of patients for anesthesia. In addition, remimazolam was less likely to contribute to intraoperative hypotension and improvement of sleep quality of the 1st post-operative day than propofol.

Data Sharing Statement

The database of this study can be obtained by contacting the corresponding authors.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of Deyang People's Hospital on April 20, 2023, with a registration number 2023-04-031-K01. Trial registration was conducted in the Chinese Clinical Trial Registry on May 18, 2023 (www.chictr.org.cn; registration number: ChiCTR2300072987). All the subjects provided their written informed consent. The study protocol was designed in line with the CONSORT guidelines and performed in accordance with the Declaration of Helsinki.

Acknowledgments

We appreciate the support from the Endoscopy Center and Department of Digestive System in Deyang People's Hospital.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This study was supported by "Xinglin Scholar" Hospital Project of Chengdu University of Traditional Chinese Medicine (YYZX2022077, Leqiang Xia), and Scientific and technological innovation 2030 – major project of Brain Science and Brain-Like Intelligence Technology (2021ZD0202804, Lize Xiong).

Disclosure

The authors declare that there are no existing or potential conflicts of interest in this work.

References

1. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2021;71(3):209–249. doi:10.3322/caac.21660
2. Cao W, Chen HD, Yu YW, et al. Changing profiles of cancer burden worldwide and in China: a secondary analysis of the global cancer statistics 2020. *Chin Med J*. 2021;134(7):783–791. doi:10.1097/CM9.0000000000001474
3. Chen R, Liu Y, Song G, et al. Effectiveness of one-time endoscopic screening programme in prevention of upper gastrointestinal cancer in China: a multicentre population-based cohort study. *Gut*. 2021;70(2):251–260. doi:10.1136/gutjnl-2019-320200
4. Zhang N, Li Y, Chang X, et al. Long-term effectiveness of one-time endoscopic screening for esophageal cancer: a community-based study in rural China. *Cancer*. 2020;126(20):4511–4520. doi:10.1002/cncr.33119
5. Liu M, He Z, Guo C, et al. Effectiveness of intensive endoscopic screening for esophageal cancer in China: a community-based study. *Am J Epidemiol*. 2019;188(4):776–784. doi:10.1093/aje/kwy291
6. Eer AS, Padmanabhan U, Leslie K. Propofol dose and incidence of dreaming during sedation. *Eur J Anaesthesiol*. 2009;26(10):833–836. doi:10.1097/EJA.0b013e32832c500c
7. Xu G, Liu X, Sheng Q, et al. Sex differences in dreaming during short propofol sedation for upper gastrointestinal endoscopy. *Neuroreport*. 2013;24(14):797–802. doi:10.1097/WNR.0b013e3283644b66
8. Matus H, Kvolik S, Rakipovic A, et al. Bispectral index monitoring and observer rating scale correlate with dreaming during propofol anesthesia for gastrointestinal endoscopies. *Medicina*. 2021;58(1):62. doi:10.3390/medicina58010062
9. Yoshida A, Fujii K, Yoshikawa T, et al. Factors associated with quality of dreams during general anesthesia: a prospective observational study. *Journal of Anesthesia*. 2021;35(4):1–5. doi:10.1007/s00540-021-02942-8
10. Stait ML, Leslie K, Bailey R. Dreaming and recall during sedation for colonoscopy. *Anaesth Intensive Care*. 2008;36(5):685–690. doi:10.1177/0310057X0803600509

11. Kim JH, Byun H, Kim JH. Abuse potential of propofol used for sedation in gastric endoscopy and its correlation with subject characteristics. *Korean J Anesthesiol*. 2013;65(5):403–409. doi:10.4097/kjae.2013.65.5.403
12. Brechmann T, Maier C, Kaisler M, et al. Propofol sedation during gastrointestinal endoscopy arouses euphoria in a large subset of patients. *United Eur Gastroenterol J*. 2018;6(4):536–546. doi:10.1177/2050640617736231
13. Zhao K, Yang N, Yue J, et al. Factors associated with euphoria in a large subset of cases using propofol sedation during gastrointestinal endoscopy. *Front Psychiatry*. 2023;14:1001626. doi:10.3389/fpsyt.2023.1001626
14. Gyulaházi J, Varga K, Iglói E, et al. The effect of preoperative suggestions on perioperative dreams and dream recalls after administration of different general anesthetic combinations: a randomized trial in maxillofacial surgery. *BMC Anesthesiol*. 2015;15(1):11. doi:10.1186/1471-2253-15-11
15. Leslie K, Sleigh J, Paech MJ, et al. Dreaming and electroencephalographic changes during anesthesia maintained with propofol or desflurane. *Anesthesiology*. 2009;111(3):547–555. doi:10.1097/ALN.0b013e3181adf768
16. Cascella M, Fusco R, Caliendo D, et al. Anesthetic dreaming, anesthesia awareness and patient satisfaction after deep sedation with propofol target controlled infusion: a prospective cohort study of patients undergoing day case breast surgery. *Oncotarget*. 2017;8(45):79248–79256. doi:10.18632/oncotarget.17238
17. Teng Y, Ou MC, Wang X, et al. Efficacy and safety of ciprofol for the sedation/anesthesia in patients undergoing colonoscopy: phase IIa and IIb multi-center clinical trials. *Eur J Pharm Sci*. 2021;164:105904. doi:10.1016/j.ejps.2021.105904
18. Liu Y, Yu X, Zhu D, et al. Safety and efficacy of ciprofol vs propofol for sedation in intensive care unit patients with mechanical ventilation: a multi-center, open label, randomized, Phase 2 trial. *Chin Med J*. 2022;135(9):1043–1051. doi:10.1097/CM9.0000000000001912
19. Chen BZ, Yin XY, Jiang LH, et al. The efficacy and safety of ciprofol use for the induction of general anesthesia in patients undergoing gynecological surgery: a prospective randomized controlled study. *BMC Anesthesiol*. 2022;22(1):245. doi:10.1186/s12871-022-01782-7
20. Zhong J, Zhang J, Fan Y, et al. Efficacy and safety of Ciprofol for procedural sedation and anesthesia in non-operating room settings. *J Clin Anesth*. 2023;85:111047. doi:10.1016/j.jclinane.2022.111047
21. Dai G, Pei L, Duan F, et al. Safety and efficacy of remimazolam compared with propofol in induction of general anesthesia. *Minerva Anestesiol*. 2021;87(10):1073–1079. doi:10.23736/S0375-9393.21.15517-8
22. Chen SH, Yuan TM, Zhang J, et al. Remimazolam tosilate in upper gastrointestinal endoscopy: a multicenter, randomized, non-inferiority, Phase III trial. *J Gastroenterol Hepatol*. 2021;36(2):474–481. doi:10.1111/jgh.15188
23. Rex DK, Bhandari R, Lorch DG, et al. Safety and efficacy of remimazolam in high risk colonoscopy: a randomized trial. *Dig Liver Dis*. 2021;53(1):94–101. doi:10.1016/j.dld.2020.10.039
24. Xia LQ, Zhou R, Deng R, et al. Dreaming during gastrointestinal endoscopy under propofol, ciprofol, or remimazolam anesthesia: study protocol for a parallel-design double-blind, single-center trial. *Trials*. 2024;25(1):2. doi:10.1186/s13063-023-07873-1
25. Xiao Y, Wei R, Chen L, et al. Efficacy and safety of remimazolam for procedural sedation during ultrasound-guided transversus abdominis plane block and rectus sheath block in patients undergoing abdominal tumor surgery: a single-center randomized controlled trial. *BMC Anesthesiol*. 2022;22(1):381. doi:10.1186/s12871-022-01927-8
26. Weber F, Prasser C. Investigating propofol-sufentanil interaction using clinical endpoints and processed electroencephalography: a prospective randomized controlled trial. *Minerva Anestesiol*. 2019;85(3):271–278. doi:10.23736/S0375-9393.18.12326-1
27. Tuncali B, Pekcan YO, Celebi A, et al. Addition of low-dose ketamine to midazolam-fentanyl-propofol-based sedation for colonoscopy: a randomized, double-blind, controlled trial. *J Clin Anesth*. 2015;27(4):301–306. doi:10.1016/j.jclinane.2015.03.017
28. Viana KA, Daher A, Maia LC, et al. What is the level of evidence for the amnestic effects of sedatives in pediatric patients? A systematic review and meta-analyses. *PLoS One*. 2017;12(7):e0180248. doi:10.1371/journal.pone.0180248
29. Sebel PS, Bowdle TA, Ghoneim MM, et al. The incidence of awareness during anesthesia: a multicenter United States study. *Anesth Analg*. 2004;99(3):833–839. doi:10.1213/01.ANE.0000130261.90896.6C
30. Pandit JJ, Andrade J, Bogod DG, et al. Association of anaesthetists of Great Britain and Ireland. 5th national audit project (NAP5) on accidental awareness during general anaesthesia: summary of main findings and risk factors. *Br J Anaesth*. 2014;113(4):549–559. doi:10.1093/bja/aeu313
31. Czarko K, Kwiatosz-Muc M, Fijałkowska A, et al. Intraoperative awareness--comparison of its incidence in women undergoing general anaesthesia for caesarean section and for gynaecological procedures. *Anaesthesiol Intensive Ther*. 2013;45(4):200–204. doi:10.5603/AIT.2013.0039