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Comparison of the safety and efficacy of ciprofol monotherapy versus combined propofol for painless gastroscopy

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Abstract: Traditional sedatives like Propofol can lead to adverse effects. This study compares the safety and efficacy of Ciprofol monotherapy versus combined Propofol for painless gastroscopy. Patients underwent painless gastroscopy at our hospital from January 2023 to December 2023 were studied. Sedation quality, adverse events, patient satisfaction, cognitive function, pain, anxiety, gastrointestinal side effects, and endoscopic quality and so on was recorded and assessed. A retrospective analysis was conducted on patients undergoing painless gastroscopy from January to December 2023. Participants (n = 200) were categorized into Ciprofol (n = 102) and Combined Propofol (n = 98) groups. The Ciprofol group exhibited longer sedation onset (4.35 ± 1.71 min) but significantly quicker recovery (12.64 ± 4.54 min) compared to the combined group. Adverse events of nausea (2.94% vs 10.20%, p = 0.037) and vomiting (1.96% vs 9.18%, p = 0.025) were less frequent in the Ciprofol group, although satisfaction scores were similar between groups. Cognitive function, pain, anxiety levels and gastrointestinal side effects was comparable. Endoscopy quality measures showed no significant differences. Cyclophenol monotherapy is a viable alternative to combine Propofol, offering a reduced incidence of adverse effects and quicker recovery without compromising procedure quality or cognitive outcomes.

Keywords: Safety; Efficacy; Ciprofol, propofol, painless gastroscopy.

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INTRODUCTION

Gastroscopy, is a routinely performed procedure enabling direct visualization and assessment of the upper gastrointestinal tract. It is pivotal in diagnosing and managing various gastrointestinal disorders such as peptic ulcers, malignancies, and inflammatory diseases (Wang *et al.*, 2022). Historically, patient discomfort and procedural anxiety has underscored the need for effective sedation practices, to ensure both patient compliance and procedural success. Studies have reported that the use of propofol combined with sufentanil for anesthesia in children's gastroscopy can improve the sedation effect, with a low adverse reaction rate and greatly reduce the patient's tension, anxiety and fear (Wang *et al.*, 2023). As medical practice evolves, the focus has shifted toward finding sedation methods that enhance patient comfort while minimizing recovery time and adverse effects (Yu *et al.*, 2022).

Propofol, a commonly used intravenous anesthetic agent, is often favored for its rapid onset and short duration of action, which makes it suitable for outpatient procedures like gastroscopy (Wang *et al.,* 2020). Meta-analysis study shows, propofol is associated with adverse effects such as hypotension and respiratory depression, and can often lead to nausea and vomiting post-procedure (Chang *et al.*, 2023). Propofol is frequently combined with other agents, aiming at reduce dosage and alleviate side effects. However, the search for an optimal sedative regimen continues (Sun *et al.*, 2023; Li and Zhou, 2022). Enter Ciprofol, a relatively new sedative-hypnotic agent that is gaining attention for its potential advantages over traditional sedatives like Propofol (Sun *et al.*, 2023). Ciprofol is structurally akin to Propofol but with molecular modifications intended to enhance its pharmacokinetic profile. Ciprofol is a short-acting intravenous sedative based on the structural modification of propofol. Cyclopofol has high efficacy, good selectivity and few adverse reactions and has good clinical application potential (Lu *et al.*, 2023). Our retrospective study aims at comparing the application of Ciprofol monotherapy and combined Propofol regimens for painless gastroscopy.

MATERIALS AND METHODS

Patient and groups

This retrospective study examined the clinical data of patients who underwent painless gastroscopy at our hospital over the period from January 2023 to December 2023. The patients were categorized into two groups according to the anesthetic administered: the Ciprofol group (n=102) and the combined group (n=98). As the study was retrospective and relied solely on de-identified patient data, informed consent was waived. This decision was in lignment with regulatory and ethical standards for retrospective research and the waiver was duly authorized by the Institutional Review Board and Ethics Committee.

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This approach ensured that the study posed no risk or negative impact on patient care.

The inclusion criteria for the study were as follows: indication and eligibility for painless gastroscopy, an American Society of Anesthesiologists (ASA) physical status classification of I or II, age of 18 years or older, normal liver and kidney function, comprehensive clinical data, and normal mental and cognitive function. The exclusion criteria were a history of allergy or contraindications to anesthetic drugs, severe dysfunction of major organs such as the heart, liver, or kidneys, a history of chronic pain, long-term opioid use, language, hearing, or mental disorders, and a gastroscopy examination duration exceeding 30 minutes. The sedation procedures for all included patients were administered by a single, experienced professional anesthesiologist. Similarly, the gastroscopies were performed by the same experienced gastroenterologist. Data collection and verification were conducted by two independent researchers to ensure accuracy and reliability. Except for the anesthesiologist responsibility for sedation, all other participants were blinded to the study's grouping and specific drug types used.

Anesthesia procedures for Gastroscopy

Upon entering the operating room, patients were routinely monitored using ECG, non-invasive blood pressure, and SpO_2, and an intravenous line was established. Oxygen was administered at a rate of 3 L/min via a face mask. In the Ciprofol group, patients received a slow intravenous injection of ciprofol, dosed at 0.5-0.6 mg/kg, administered over 30 seconds (batch number: 20210804, Sichuan Hisun Pharmaceutical Co., Ltd., China). In contrast, the Combined group initially received a slow intravenous injection of ciprofol at 0.5μg/kg, followed by a slow injection of 1.5 mg/kg propofol (batch number: 21905082, Xi'an Libang Pharmaceutical Co., Ltd., China). The gastroscopy procedure commenced once the Modified Observer's Assessment of Alertness/Sedation (MOAA/S) score was ≤1. If the sedation achieved was inadequate, an additional single dose of 5 mg of Ciprofol was administered. In cases where systolic blood pressure (SBP) dropped below 90 mmHg or decreased by more than 30% from baseline, dopamine (batch number: 2101221, Yabang Pharmaceutical Co., Ltd.) was intravenously administered at 1-2mg per dose. If the heart rate fell below 50 beats per minute, atropine (batch number: 21052006, Anhui Changjiang Pharmaceutical Co., Ltd.) was administered intravenously at 0.25-0.50 mg. For SpO_2 levels falling below 90%, breathing was assisted using jaw thrust or bag-mask ventilation.

Clinical indicators

General patient information and disease-related characteristics, such as age, gender, body mass index (BMI), smoking history, alcohol consumption history, education level, presence of hypertension, diabete, history of previous gastrointestinal diseases, liver disease, and regular medication usage rates, was extracted from the medical records system. Statistical analyses were conducted to evaluate various intraoperative and postoperative factors, including the onset time of sedation, procedure duration, recovery time, incidence of adverse events and postoperative gastrointestinal side effects. Patient satisfaction was evaluated using a hospital-developed satisfaction scale, which ranged from 1 to 10. Higher scores on this scale corresponded to greater levels of patient satisfaction. Cognitive function was evaluated postoperatively using the Montreal Cognitive Assessment (MoCA) scale. The MoCA scale comprises 11 items spanning eight cognitive domains, including attention and concentration, executive functions, memory, language, visuospatial skills, abstract thinking, calculation and orientation. The total score possible on the MoCA is 30 points. Scores of 26 or higher indicate normal cognitive function, while scores between 21 and 25 signify moderate cognitive impairment and scores from 0 to 20 suggest severe cognitive impairment. The memory item carries a total score of 5 points, the attention item totals 6 points, and the executive function item has a maximum score of 5 points. Higher scores denote better cognitive function. The Cronbach's alpha coefficient for the MoCA was 0.87, indicating good internal consistency (Khatib N *et al.*, 2024). The Visual Analogue Scale (VAS) was utilized to assess postoperative pain in both groups at 1 hour and 4 hours after the procedure. Pain levels were categorized as follows: no pain (0 points), mild pain (1-3 points), moderate pain (4-6 points), severe pain (7-9 points), and acute severe pain (10 points). The VAS demonstrated a Cronbach's alpha of 0.94, indicating high reliability (Naunheim MR *et al.*, 2020). Anxiety levels in patients were evaluated both preoperatively and postoperatively using the Hamilton Anxiety Rating Scale (HAMA). A score of 0-7 is considered normal, 8-14 indicates mild anxiety, 15-21 suggests moderate anxiety and scores exceeding 22 signify severe anxiety. The HAMA demonstrated a Cronbach's alpha of 0.92, reflecting high reliability (Dos Santos ERP *et al.*, 2023). The visibility during the procedure was evaluated using the following criteria: (1 point) no adherent mucus with a clear view; (2 points) a small amount of mucus without obscuring the view; (3 points) a large amount of adherent mucus that obscures vision, requiring a saline rinse of up to 30mL; (4 points) thick adherent mucus that obscures vision, necessitating a saline rinse of more than 30mL. Two gastroenterologists, each with over 10 years of endoscopic experience, independently reviewed the images of all patients in a blinded and randomized manner. The visibility score for each section of the stomach was the average of the scores assigned by both physicians. The total visibility score (TVS) represented the sum of the scores from the cardia, fundus, body, and antrum, ranging from 4 to 16, with lower scores indicating better visibility.

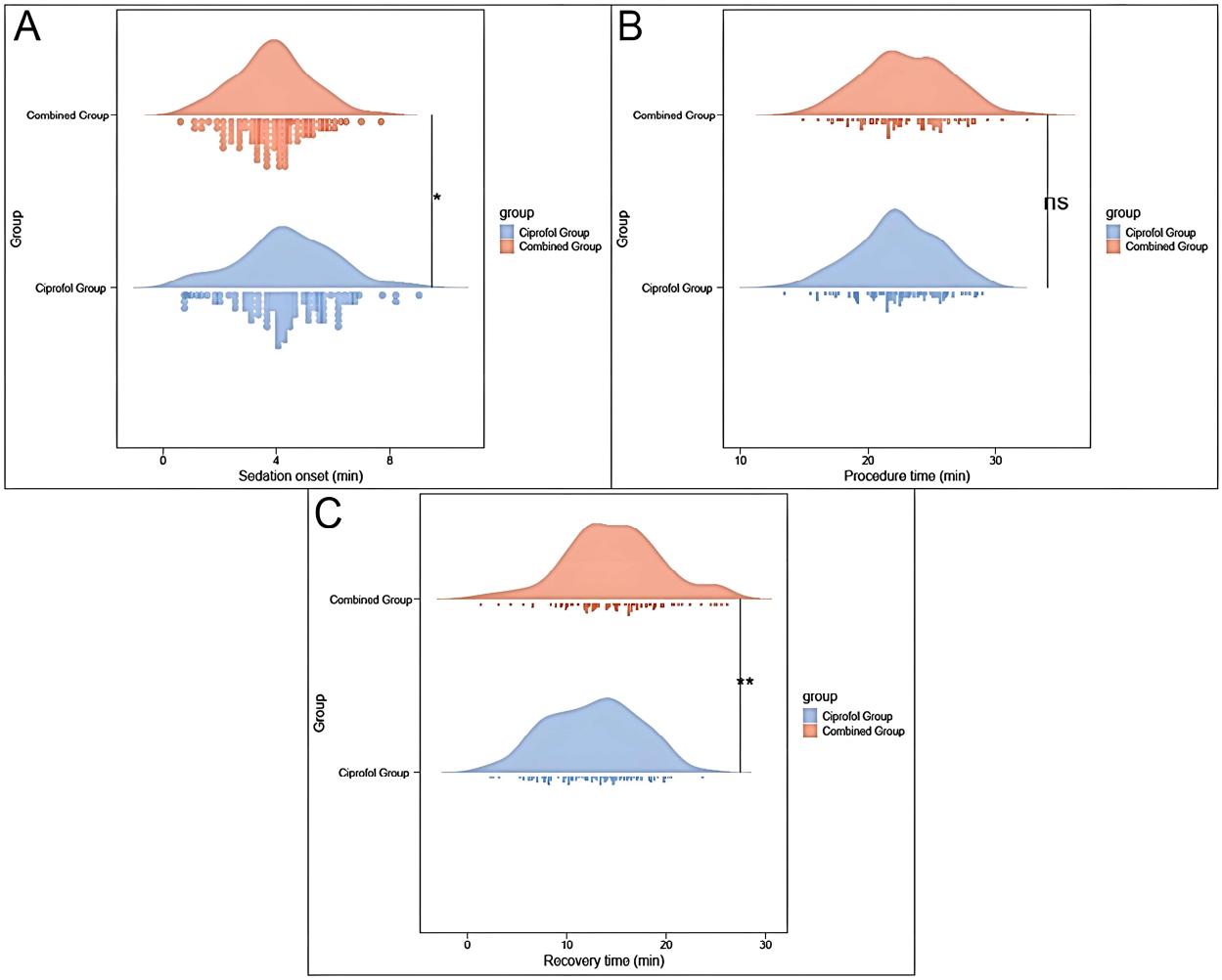

Fig. 1: Efficacy in Sedation Quality. A: Sedation onset (min); B: Procedure time (min); C: Recovery time (min).

The endoscopist's satisfaction with the procedure was rated on a scale of 1 to 10, with higher scores reflecting better performance and smoother workflow. Using G*Power 3.1.9.7, a post hoc power analysis was conducted for t-tests based on the "Means: Difference between two independent means (two groups)" option. The analysis was set to two-tailed mode with an effect size (d) of 0.5 and an alpha error probability (α) of 0.05. After entering the sample sizes for the two groups, the calculated power (1-β error probability) was determined to be 0.940.

ETHICAL APPROVAL

This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Huai'an First People's Hospital affiliated with Nanjing Medical University (JS-HA-008).

STATISTICAL ANALYSIS

Data analysis was conducted using SPSS statistical software, version 29.0 (SPSS Inc., Chicago, IL, USA). Categorical data were expressed as [n (%)]. For these data, the chi-square test was employed using the basic formula when the sample size was ≥40 and the theoretical frequency (T) was ≥5, with the test statistic denoted by χ^2. If the sample size was ≥40 but 1≤T < 5, the chi-square test was adjusted using a correction formula. In instances where the sample size was < 40 or T < 1, Fisher's exact test was utilized. Continuous variables were initially tested for normality using the Shapiro-Wilk method. Normally distributed continuous data were presented as the mean (X ± s). For data not normally distributed, the Wilcoxon rank-sum test was applied, and results were reported as the median (25% quantile, 75% quantile). A p-value of less than 0.05 was considered indicative of statistical significance.

RESULTS

Demographic and basic data

The demographic characteristics of both groups were statistically similar, ensuring comparability across age, gender, BMI, smoking status, alcohol consumption, and education level, indicating well-matched cohorts in terms of baseline characteristics (table 1).

Table 1: Demographic Data of Participants

Parameter	Ciprofol Group (n = 102)	Combined Group (n = 98)	t/χ^2	P
Age (years)	45.67 ± 8.35	44.98 ± 8.12	0.592	0.554
Gender (Male, %)	56 (54.90%)	56 (57.14%)	0.102	0.750
BMI (kg/m²)	24.89 ± 3.12	25.16 ± 3.45	0.565	0.573
Smoking Status (%)			0.259	0.878
- Non-smokers	72 (70.59%)	67 (68.37%)		
- Former smokers	15 (14.71%)	17 (17.35%)		
- Current smokers	15 (14.71%)	14 (14.29%)		
Alcohol Consumption (%)			0.196	0.907
- Non-drinkers	61 (59.80%)	61 (62.24%)		
- Social drinkers	31 (30.39%)	27 (27.55%)		
- Regular drinkers	10 (9.80%)	10 (10.20%)		
Education Level (%)			0.083	0.959
- High school	51 (50.00%)	47 (47.96%)		
- Undergraduate	31 (30.39%)	31 (31.63%)		
- Postgraduate	20 (19.61%)	20 (20.41%)		

Table 2: Baseline Disease-Related Characteristics

Parameter	Ciprofol Group (n = 102)	Combined Group (n = 98)	X^2	P
History of Hypertension (%)	26 (25.49%)	26 (26.53%)	0.028	0.867
History of Diabetes (%)	18 (17.65%)	20 (20.41%)	0.248	0.619
Pre-existing Gastrointestinal Disorders (%)	15 (14.71%)	16 (16.33%)	0.100	0.752
Hepatic Disorders (%)	10 (9.80%)	8 (8.16%)	0.164	0.685
Regular Use of Medications (%)			0.420	0.811
- Antihypertensives	43 (42.16%)	43 (43.88%)		
- Antidiabetics	18 (17.65%)	14 (14.29%)		
- Other chronic medications	41 (40.2%)	41 (41.84%)		

Table 3: Adverse Events Incidence

Adverse Event	Ciprofol Group (n = 102)	Combined Group (n = 98)	X^2	P
Hypotension (%)	10 (9.80%)	15 (15.31%)	1.383	0.240
Bradycardia (%)	5 (4.90%)	10 (10.20%)	2.025	0.155
Respiratory Issues (%)	8 (7.84%)	12 (12.24%)	1.076	0.300
Nausea (%)	3 (2.94%)	10 (10.20%)	4.338	0.037
Vomiting (%)	2 (1.96%)	9 (9.18%)	5.017	0.025

Table 4: Cognitive Function Post-Procedure

Parameter	Ciprofol Group (n = 102)	Combined Group (n = 98)	t	P
Memory (1-5)	3.82 ± 1.12	3.61 ± 1.23	1.297	0.196
Attention (1-6)	3.51 ± 1.15	3.34 ± 1.25	1.025	0.307
Executive function (1-5)	3.76 ± 1.05	3.58 ± 1.15	1.155	0.249

Table 5: Post-Operative Pain Scores

Parameter	Ciprofol Group (n = 102)	Combined Group (n = 98)	t	P
Pain score 1 hour post-procedure (0-10)	2.05 ± 0.96	2.16 ± 1.06	0.803	0.423
Pain score 4 hours post-procedure (0-10)	1.54 ± 0.83	1.63 ± 0.85	0.766	0.444

Table 6: Patient Anxiety Levels

Parameter	Ciprofol Group (n = 102)	Combined Group (n = 98)	t	P
Pre-procedure anxiety (0-10)	4.83 ± 1.45	4.62 ± 1.34	1.096	0.275
Post-procedure anxiety (0-10)	2.24 ± 0.82	2.31 ± 0.83	0.543	0.588

Table 7: Gastrointestinal Side Effects

Parameter	Ciprofol Group (n = 102)	Combined Group (n = 98)	X^2	P
Bloating (%)	6 (5.88%)	9 (9.18%)	0.785	0.376
Abdominal pain (%)	7 (6.86%)	12 (12.24%)	1.684	0.194
Constipation (%)	4 (3.92%)	10 (10.20%)	3.030	0.082
Flatulence (%)	5 (4.90%)	8 (8.16%)	0.875	0.350
Diarrhea (%)	3 (2.94%)	7 (7.14%)	1.078	0.299
Dyspepsia (%)	4 (3.92%)	6 (6.12%)	0.152	0.697
Acid reflux (%)	2 (1.96%)	5 (5.10%)	0.678	0.410

Table 8: Quality of Endoscopy

Parameter	Ciprofol Group (n = 102)	Combined Group (n = 98)	t	P
Visibility score (4-16)	15.04 ± 2.76	15.27 ± 2.75	0.589	0.556
Endoscopist satisfaction (0-10)	9.48 ± 0.62	9.54 ± 0.55	0.714	0.476

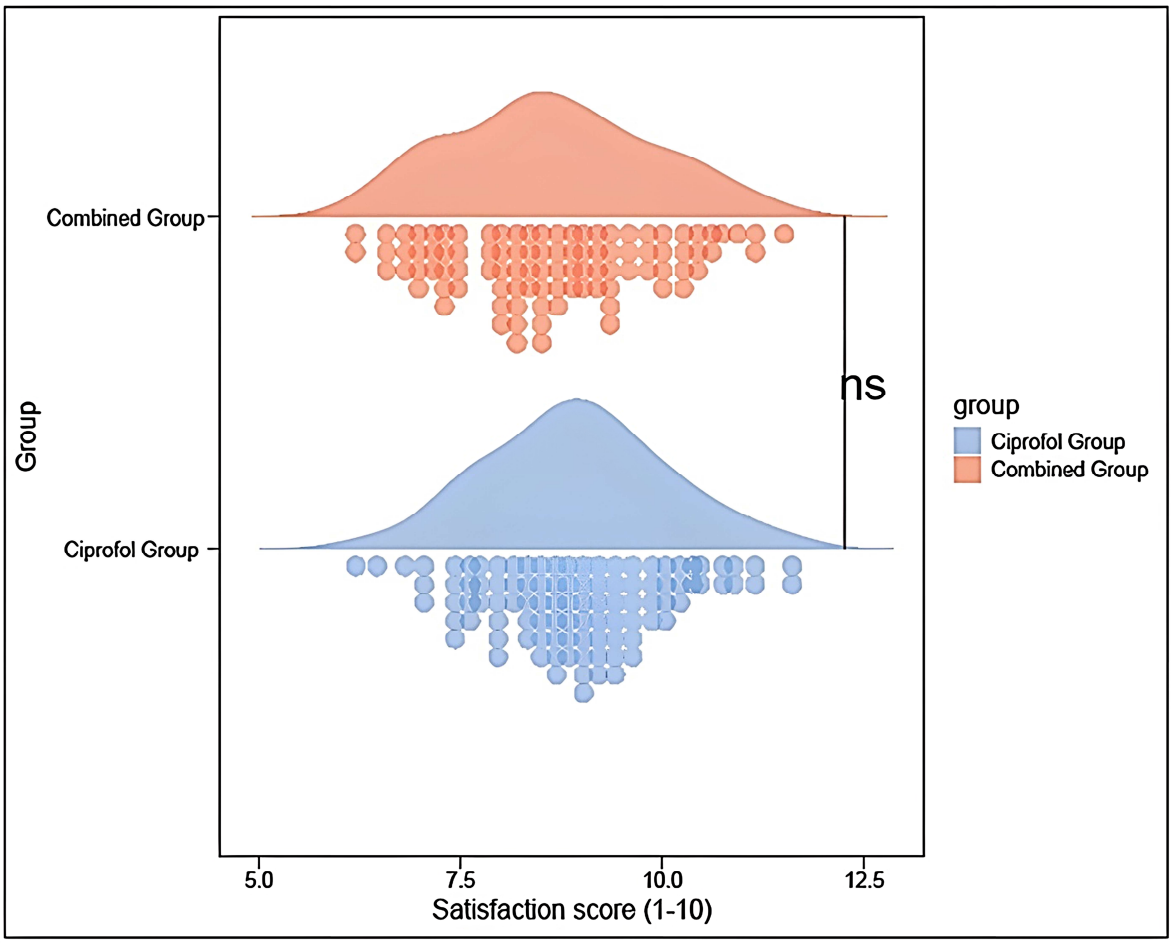

Fig. 2: Patient satisfaction scores

Baseline disease-related characteristics

These data of history of hypertension, history of Diabetes, pre-existing gastrointestinal gisorders, hepatic disorders, and regular use of medications confirm that both cohorts were well-matched in terms of baseline disease-related characteristics (table 2).

Efficacy in sedation quality

The Ciprofol group experienced a longer sedation onset time of 4.35±1.71 minutes compared to 3.85±1.35 minutes in the Combined group, with the difference reaching statistical significance (t=2.315, P=0.022) (fig. 1). Conversely, the recovery time was significantly shorter in the Ciprofol group, averaging 12.64±4.54 minutes versus 14.72±4.83 minutes in the Combined group (t=3.148, P=0.002). Procedure time did not differ significantly between the groups, with the Ciprofol group averaging 22.31±3.25 minutes and the Combined group 23.02±3.41 minutes (t=1.502, P=0.135), indicating comparable durations for the procedures across the study groups.

Adverse events incidence

The findings indicate a lower incidence of nausea and vomiting in the Ciprofol group, with other adverse events being comparable between the groups (table 3).

Patient satisfaction scores

The mean satisfaction score in the ciprofol group was 8.93±1.13, while in the Combined group, it was 8.63 ± 1.25 (t = 1.826, P=0.069) (fig. 2). Although the ciprofol group exhibited a slightly higher satisfaction score, this difference was not sufficient to reach statistical significance, suggesting comparable patient satisfaction levels between the two sedation regimens.

Cognitive function post-procedure

The findings indicate that cognitive function, including memory, attention, and executive function, was similarly preserved in both groups following the procedure (table 4).

Post-operative pain scores

These results indicate comparable post-operative pain levels between the two sedation regimens, consistent across both time points assessed (table 5).

Patient anxiety levels

The findings suggest that both sedation regimens were similarly effective in managing patient anxiety levels before and after the procedure (table 6).

Gastrointestinal side effects

There was no significant difference in Bloating, Abdominal pain, Constipation, Flatulence, Diarrhea, Dyspepsia, Acid reflux between the two groups ($p>0.05$). These results suggest similar gastrointestinal side effect profiles for both sedation regimens (table 7).

Quality of endoscopy

There were no significant differences in Visibility score and Endoscopist satisfaction between the two groups ($p > 0.05$). These results indicate that both sedation regimens provided comparable quality of endoscopy as assessed by visibility and endoscopist satisfaction (table 8).

DISCUSSION

The objective of this study was to compare the safety and efficacy of ciprofol monotherapy versus combined Propofol for painless gastroscopy, with a focus on sedation quality, adverse events, patient satisfaction, cognitive function, pain and anxiety levels, gastrointestinal side effects and the quality of endoscopy.

One of the primary findings was related to the onset and recovery times of sedation. The ciprofol group demonstrated a longer sedation onset time but a significantly shorter recovery period compared to the combined propofol group. This discrepancy might be attributed to the pharmacokinetic properties of the drugs involved. Ciprofol, a newer sedative-hypnotic agent, is known for its rapid onset followed by quick metabolism and clearance, which can contribute to a more expedited recovery. A single dose of painless gastroscopy for general anesthesia is 0.4-0.5mg/kg, and a single dose of propofol is 2mg/kg (Currò, 2024). This characteristic is potentially advantageous in outpatient settings where quick turnover is desirable (Dong *et al.*, 2022). Conversely, the combination of propofol and ciprofol could delay metabolism and clearance, leading to a more prolonged recovery due to the synergistic or potentially competing effects of the two drugs in hepatic metabolism Enzymes responsible for the metabolism of these agents might be saturated or inhibited to varying extents, prolonging Propofol's effects (Yan 2023; Qiu 2023).

In terms of adverse events, the ciprofol group experienced a significantly lower incidence of nausea and vomiting compared to the combined group. This finding may be linked to the different pharmacodynamic properties of ciprofol compared to Propofol (Su *et al.*, 2023). Nausea and vomiting are common side effects associated with propofol, potentially exacerbated when combined with other sedatives. A prospective observational cohort study of 1670 children undergoing painless gastroscopy showed the incidence rates of negative postoperative behavioral changes (NPOBCs) on the 1st, 14th and 30th day were 14.13%, 4.55% and 2.14%, respectively (YanYing *et al.*, 2023). Ciprofol's distinct chemical structure could result in fewer interactions with the neurotransmitter systems involved in nausea and vomiting reflexes, or a lower degree of emetogenic potential at the doses used in this study. These differences underline ciprofol's potential advantage in minimizing certain adverse effects in clinical settings, improving patient comfort and satisfaction.

The slight, albeit statistically insignificant, superiority in patient satisfaction scores for the ciprofol group could be correlated with the reduced adverse effects and quicker recovery time. Patient experience during procedures is heavily influenced by both the occurrence of adverse effects and the recovery process. The smoother and quicker recovery associated with Ciprofol may directly enhance patient perceptions of the procedure, leading to higher satisfaction scores (Xia 2024; Wang 2019). This is crucial in patient-centered care, where experiential factors significantly sway patient preferences and treatment adherence.

Cognitive function post-procedure was comparable between groups, which may be expected given the similarity in the sedative depth achieved by both regimens. Both groups maintained normal cognitive function following the procedure. This suggests that neither sedative regimen exerted protracted neurocognitive effects, which is an important safety consideration in outpatient procedures (Zheng *et al.*, 2023). The maintenance of cognitive function aligns with the rapid metabolic clearance of the anesthetics used, minimizing the risk of prolonged cognitive impairment post-sedation.

Post-operative pain scores did not differ significantly between the two groups at 1 and 4 hours post-procedure. This might indicate that both sedative regimens provide adequate pain control for the types of procedural stimuli encountered during gastroscopy. Considering that sedation primarily affects consciousness rather than pain perception directly, the provision of analgesia during gastroscopy would rely more on local anesthetics or adjunct analgesics if needed (Lin 2023; Yan 2023). The lack of difference in pain perceptions might suggest that neither regimen affects pain-related neurophysiological pathways differentially, supporting their equivalence for this outcome.

Anxiety levels, another critical component of patient experience, were similarly managed by both sedation regimens. Pre and post-procedure anxiety scores were comparable, suggesting both ciprofol and combined propofol regimens are effective at anxiety attenuation. Anxiety during gastroscopy is common due to the invasiveness and discomfort associated with the procedure. A prospective, double-blind, randomized controlled clinical trial of 162 patients showed that propofol has good sedation, low incidence of adverse effects, small fluctuations in heart rate and blood pressure, and less anxiety (Tang 2024; Feng 2024). Sedatives serve dual purposes in this context: to ensure unawareness of the procedure and to mitigate anxiety related to the event itself (Zhang *et al.*, 2023). The equivalency observed in our study likely reflects that both regimens reach the necessary sedative depth to effectively manage anxiety related to the procedure.

Gastrointestinal side effects showed a non-significant trend with fewer occurrences in the Ciprofol group. This is noteworthy given the commonness of such side effects with sedative medications (Zhang R *et al.*,2024). The mechanisms by which Ciprofol and Propofol induce gastrointestinal side effects could differ; Propofol is known for relaxing smooth muscle tone, which might impact gastrointestinal motility and increase the likelihood of gastrointestinal symptoms. A study of 100 patients with nalbuphine +Propofol anesthesia for gastroscopy showed that the incidence of Nausea, Vomiting, Abdominal distension and Abdominal pain was 20% and 16%, respectively. 15% and 12% (Zheng *et al.*, 2023). Ciprofol might have a lesser effect on these systems or act on alternative pathways, reducing the frequency of such symptoms (Mi SC *et al.*, 2023). Though the differences weren't statistically significant, they point towards potential clinical advantages that merit further research in larger, more powered studies.

Regarding the quality of endoscopy, measured by visibility and endoscopist satisfaction, there were no significant differences between the two groups. This suggests that the quality of sedation, in terms of stillness and cooperativeness provided by both regimens, was comparable. Endoscopic procedures require patients to be sufficiently sedated to prevent movement, which can affect the endoscopic view and procedure duration. Both regimens appeared to cater adequately to such procedural requirements, highlighted by similar visibility scores and high endoscopist satisfaction ratings across groups. The findings imply that in terms of procedural conditions, endoscopists might not find one regimen superior to the other in routine clinical practice.

While our study provides crucial insights, several aspects warrant additional discussion. The retrospective nature of the study, while robust in review, limits our ability to draw causal inferences. Prospective studies would be necessary to confirm causality and further delineate mechanistic differences. Additionally, our study’s generalizability might be limited to the specific cohort typical within our institution, indicating a need for further studies in diverse populations.

CONCLUSION

In conclusion, the findings from this study suggest that ciprofol monotherapy is a viable alternative to combined propofol for painless gastroscopy, offering advantages in terms of reduced adverse effects and a quicker recovery without compromising procedure quality or cognitive outcomes. Future research may explore these dynamics using prospective designs and explore personalized sedation protocols considering individual patient risk profiles and preferences. This will enhance the ability to offer tailored, effective and safe sedation choices for elective procedures such as gastroscopy.

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