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Research Article

Comparison of the Clinical Effects of Ciprofol, Propofol, and Etomidate in the Combined Painless Gastroscopy and Enteroscopy: A Randomized Controlled Trial

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Abstract

Background: Propofol and etomidate are commonly used for sedation during painless gastroenteroscopy, but both have significant side effects. Cycline is a new sedative with minor side effects. This study aims to observe the clinical effects of ciprofol, propofol, and etomidate in the combined painless gastroscopy and enteroscopy. *Methods*: We randomly divided 600 outpatients aged 18-70 years, with a body mass index 18-30 kg/m^2, and an ASA score of I-II, who underwent painless gastroenteroscopy, into three groups: propol group, etomidate group, and cyclizine group, with 200 cases in each group. All groups were pre-injected with 01 ug/kg sufentanil injection intravenously. The propofol group was given 2 mg/kg propofol injection intravenously, theomidate group was given 0.2 mg/kg etomidate injection intravenously, and the cyclizine group was given 0.4 mg cyclizine injection intravenously. The injection time for all groups was 30±5 seconds. The examination began when the MOAA/S score was 0-1 or the corneal reflex disappeared. 1. We observed the incidence of injection pain, onset time, sedation success rate, incidence of movement, incidence of respiratory depression, circulatory inhibition, awakening time, PACU time, and satisfaction of the examiner and the patient in all three groups; We observed the adverse reactions such as muscle pain and intraoperative awareness in the patients of all three groups. *Results*: 1. There were no differences in basic information of the patients in the three groups. The sedation success rate in all three groups was 100%. There were no significant differences in the time, awakening time, and PACU time among the three groups (P>0.05); 2. The incidence of injection pain, respiratory depression, circulatory inhibition in the propofol group was higher than that in the etomidate group and the cyclizine group, with significant differences (P<.05). However, there were no significant differences between the etomidate group and the cyclizine group. The satisfaction of the patients and the exam in the cyclizine group was higher (P<0.05); 3. Although there were no significant differences in the incidence of adverse reactions among three groups, the incidence of muscle tremor and muscle pain in the etomidate group was significantly higher than that in the propofol group and the cycline group, with significant differences (P<0.05). *Conclusion*: The clinical effect of ciprofol for painless gastroenteroscopy is significantly better than that of propofol and etomidate, and suitable for promotion in outpatient painless gastroenteroscopy.

Keywords

Ciprofol, Propofol, Etomidate, Gastroscopy and Enteroscopy, Clinical Effects

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1. Introduction

Gastrointestinal endoscopy is the gold standard for diagnosing most digestive system diseases, and painless gastrointestinal endoscopy accounts for over 90% of the total gastrointestinal endoscopy examinations [1]. Currently, propofol and/or etomidate are commonly used anesthetic drugs for gastrointestinal endoscopy both domestically and internationally. Although both drugs can achieve anesthesia for gastrointestinal endoscopy, they each have their own advantages and disadvantages. Propofol has a fast onset and recovery, but its strong injection pain and significant inhibitory effects on the circulatory and respiratory systems have long been criticized by anesthesiologists. Etomidate has milder circulatory and respiratory inhibitions compared to propofol, but its recovery time is slightly longer, and it has problems such as muscle tremors, muscle pain, and suppression of adrenal cortical function after large-scale use [2]. Therefore, finding a new generation of intravenous anesthetic drugs superior to propofol and etomidate is an important way to improve anesthetic quality and patient satisfaction. Ciprofol is the first innovative intravenous anesthetic compound in China. Clinical phase II and III study data show that its potency is five times that of propofol [3], and its onset and recovery times are comparable. It provides a new option for the development of comfortable medical care. However, there are few clinical studies on whether ciprofol has more advantages in painless gastrointestinal endoscopy compared to traditional propofol and etomidate. Although some studies have hinted at certain advantages of ciprofol in painless gastrointestinal endoscopy, the sample size is small and the evidence is insufficient. Therefore, this study takes adult patients with ASA physical status classification I - II undergoing combined painless gastrointestinal endoscopy as the research objects to compare the clinical effects of ciprofol with propofol and etomidate in terms of onset time, recovery time, incidence of respiratory depression, circulatory depression, incidence of injection pain, and patient satisfaction in painless gastrointestinal endoscopy, and analyze the data to provide more clinical evidence for clinical application.

2. Materials and Methods

2.1. General Information

600 patients who underwent combined painless gastrointestinal endoscopy in our hospital from February to December 2022 were selected. Inclusion criteria: aged 18 - 70 years old, BMI 18 - 30 kg/m ², ASA physical status classification I - II. Exclusion criteria: those with severe dysfunction of organs such as the heart, lungs, liver, and kidneys; those with existing or potential allergies or contraindications to the drugs used in this study; those who have been taking hormones, non-steroidal anti-inflammatory drugs, and opioid drugs for a long time. Exclusion criteria during the study: those who need treatment under gastrointestinal endoscopy. This study was approved by the Ethics Committee of our hospital, complied with GCP management regulations, and all patients signed informed consent forms.

2.2. Anesthesia and Treatment

The 600 patients included in the study were randomly divided into the propofol group (P group), the etomidate group (E group), and the ciprofol group (H group), with 200 cases in each group. All patients had an intravenous access established in the preparation room. After entering the examination room, routine monitoring of electrocardiogram (ECG), non-invasive blood pressure (NIBP), heart rate (HR), and blood oxygen saturation (SpO2) was carried out, and oxygen was inhaled through a face mask at a flow rate of 5 L/min. All patients were pre-administered with sufentanil 0.1 μg/kg (specification: 1 mL, 50 μg, manufacturer: Yichang Humanwell Pharmaceutical Co., Ltd.) intravenously. The P group was slowly (30 ± 5 s) injected with 2 mg/kg propofol injection (specification: 20 mL, 200 mg, manufacturer: Yangtze River Pharmaceutical Group Co., Ltd.); the E group was slowly (30 ± 5 s) injected with 0.2 mg/kg etomidate injection (specification: 10 mL, 20 mg, manufacturer: Jiangsu Nhwa Pharmaceutical Co., Ltd.); the H group was slowly (30 ± 5 s) injected with 0.4 mg/kg ciprofol injection (specification: 20 mL, 50 mg, manufacturer: Sichuan Hisun Pharmaceutical Co., Ltd.). After the MOAA/S score was 0 - 1 or the corneal reflex disappeared, the gastrointestinal endoscopy operation was started. The gastroscopy was performed first, followed by the colonoscopy. During the examination, drugs were supplemented as appropriate according to the length of time and the patient's reaction: the H group was supplemented with 0.1 mg/kg ciprofol, the P group was supplemented with 0.5 mg/kg propofol, and the E group was supplemented with 0.05 mg/kg etomidate. If hypotension (systolic blood pressure decreased by 30% compared to the baseline value or systolic blood pressure was lower than 90 mmHg) occurred during the examination, metaraminol 0.2 mg was injected intravenously each time; if sinus bradycardia (HR < 45 times/min) occurred, atropine 0.3 - 0.5 mg was injected intravenously; if the patient had hypoxemia (SpO2 < 90%), the abdomen was first lifted and then lowered to move the diaphragm up and down. If the condition could not be improved after 1 minute, during the gastroscopy, the endoscopist was instructed to withdraw the gastroscope and perform assisted ventilation by pressurized oxygen inhalation through a face mask. If it was during the colonoscopy, direct pressurized oxygen inhalation through a face mask was carried out. After all patients completed the examination, they were sent to the PACU to be observed until they woke up and then left the endoscopy center.

2.3. Observation Indicators

Observation indicators included: incidence of injection pain, onset time, success rate of sedation, incidence of respiratory depression, circulatory depression, recovery time, satisfaction of examiners and patients, and overall adverse events. Respiratory depression was defined as a respiratory interval > 20 s; hypoxemia was defined as Spo2 < 90%. Circulatory depression included hypotension (systolic blood pressure lower than 30% of the preoperative value or < 90 mmHg) and bradycardia (< 50 times/min). Adverse events included muscle tremors, body movement reactions, postoperative nausea, vomiting, somnolence, restlessness, shivering, muscle pain, and intraoperative awareness.

2.4. Statistical Methods

SPSS 26.0 software was used to analyze the data. For measurement data, normal distribution and homogeneity of variance were first tested. Data that conformed to normal distribution and homogeneity of variance were represented by mean ± standard deviation ($x \pm s$), and one-way analysis of variance was used. For data with intra-group comparison and normal distribution, repeated measurement analysis of variance was used. Categorical data were described in the form of frequencies or percentages, and chi-square test or Fisher's exact probability test was used. A P value < 0.05 was considered to indicate a statistically significant difference.

3. Results

In the P group, 3 examinees were converted to receive treatment during the process, so finally 197 cases were included in the analysis. In the E group, 5 examinees were converted to treatment, and thus 195 cases were included in the end. In the H group, 4 examinees were converted to treatment, with 196 cases being included for further analysis.

3.1. Comparison of General Information of Examinees in the Three Groups

There were no statistically significant differences in age, gender, ASA classification, height, weight, and past medical history among the examinees in the three groups (P > 0.05), Which are shown in Table 1.

Table 1. *Comparison of General Information of Examinees in the Three Groups ($x \pm s$).*

Characteristics		P group (N=197)	E group (N=195)	H group (N=196)	P-value
Age (year)		45.6±6.5	43.1±6.2	44.2±6.1	0.845
Sex (men/women)		105/92	107/88	102/94	0.812
ASA grade (I/II)		164/33	165/30	160/36	0.813
Weight (kg)		64.5±8.5	64.5±8.5	65.2±8.8	0.765
Height (cm)		162.1±11.2	162.1±11.2	161.2±10.8	0.723
Comorbidity	Cerebrovascular disease	9/197	10/195	8/196	
	Heart disease	22/197	23/195	20/196	
	Lung disease	20/197	18/195	22/196	
	Endocrine diseases	6/197	5/195	2/196	
	Total	57/197	56/195	52/196	0.613

3.2. Comparison of Clinical Effects Among the Three Groups of Examinees

Compared with the ciprofol group and the etomidate group, the incidence of injection pain in the propofol group was significantly increased, and the difference was statistically significant (P < 0.001). Further analysis revealed that the incidence of injection pain in the ciprofol group was higher than that in the etomidate group, but the difference was not statistically significant (P > 0.05). Compared with the propofol group, the incidences of respiratory depression and circulatory depression in the etomidate group and the ciprofol group were lower (P < 0.05). Compared with the etomidate group and the propofol group, the satisfaction of both examinees and examiners in the ciprofol group was higher (P < 0.05), Which are shown in Table 2.

Table 2. *Comparison of Clinical Effects among the Three Groups of Examinees (% x ±s).*

Characteristics	P group (N=197)	E group (N=195)	H group (N=196)	P-value
Incidence of injection pain	70/197 (35.5%)	23/195 (11.8%)	41/196 (20.9%)	＜0.001$^{*\#}$
Onset time (min)	1.2±0.2	1.3±0.2	1.1±0.2	0.453
Sedation success rate	197/197	195/195	196/196	-
Incidence of respiratory depression	35/197 (17.8%)	14/195 (7.2%)	18/196 (9.2%)	＜0.05$^{*\#}$
Incidence of circulatory inhibition	136/197 (69.0%)	25/195 (12.8%)	36/196 (18.4%)	＜0.05$^{*\#}$
Recovery time (min)	10.2±3.2	13.1±3.3	9.8±3.1	0.033$^{\#}$
PACU time (min)	22.4±5.1	23.5±5.5	21.6±5.0	0.345
Examiner satisfaction	7.8±0.2	7.1±0.1	9.4±0.2	＜0.05^{*a}
Examinee satisfaction	7.9±0.1	7.2±0.2	9.2±0.2	＜0.05^{*a}

Note: Regarding injection pain, when comparing Group H with Group P, P* < 0.001; when comparing Group E with Group P, $P^{\#}$ < 0.001. Regarding respiratory and circulatory depression, when comparing Group H with Group P, P* < 0.05; when comparing Group E with Group P, $P^{\#}$ < 0.05. Regarding satisfaction, when comparing Group H with Group P, P* < 0.05; when comparing Group H with Group E, P^{a} < 0.05.

3.3. Comparison of the Incidence of Other Adverse Events Among the Three Groups of Examinees

The overall incidence of adverse events in the ciprofol group is significantly lower than that in the propofol group and the etomidate group, and the difference is statistically significant (P < 0.05), Which are shown in Table 3.

Table 3. *Comparison of the occurrence of adverse events among the three groups of examinees (cases/total number).*

Characteristics	P group (N=197)	E group (N=195)	H group (N=196)	P-value
Motor response	8/197	18/196	5/196	<0.05$^{-\#\ -a}$
Tremor	1/197	15/196	0/196	<0.05$^{-\#\ -a}$
nausea	10/197	12/196	5/196	0.127
Vomiting	9/197	11/196	3/196	0.232
Lethargy	8/197	9/196	5/196	0.656
Agitation.	12/197	15/196	8/196	0.564
Shivering	4/197	5/196	3/196	0.876
Pain (muscle pain)	0/197	8/196	0/196	0.000$^{-\#\ -a}$
Intraoperative awareness	0/197	0/196	0/196	-
Cumulative incidence	7.5%	11.2%	3.7%	<0.05$^{-\#\ -a\ *}$

Note: Chi-square test was used for count data. A P < 0.05 indicates that the difference is statistically significant. When comparing Group E with Group P, $P^{-\#}$ < 0.05; when comparing Group E with Group H, P^{-a} < 0.05; when comparing Group H with Group P, P* < 0.05.

4. Discussion

Gastrointestinal endoscopy is the most commonly used examination method for the digestive tract. Traditional gastrointestinal endoscopy diagnosis and treatment adopts surface anesthesia. Patients often experience discomfort, cough, nausea, vomiting and other painful sensations. This not only affects the accuracy of the examination and easily leads to complications but also makes it difficult for some patients to accept and be afraid of undergoing diagnosis and treatment

again [4]. With the improvement of people's living standards, the emphasis on personal health and the increase in requirements for comfort, more and more patients choose gastrointestinal endoscopy. At present, intravenous anesthetic drugs are mostly used to enable patients to complete the examination under a light anesthesia state. The whole process is comfortable, quiet and painless for patients. This study found that the clinical effect of ciprofol combined with sufentanil for painless gastrointestinal endoscopy is significantly better than that of propofol and etomidate combined with sufentanil and is a more effective anesthesia scheme for painless gastrointestinal endoscopy.

Propofol and etomidate are one of the most commonly used drugs for endoscopic sedation. They can be used alone or in combination with opioid drugs. Several studies have reported that propofol and etomidate combined with sufentanil and other adjuvant analgesic drugs can reduce the total dose of the required sedatives and reduce severe adverse events [5, 6]. Therefore, in this study, sufentanil 0.1 μg/kg was given before ciprofol, propofol and etomidate. During the examination, all patients were adequately sedated.

Ciprofol is a new type of intravenous anesthetic. Similar to propofol, it enhances the ion channel mediated by gamma-aminobutyric acid A receptor (GABA), causes chloride ion influx and induces hyperpolarization of the nerve cell membrane, thereby realizing central nervous system inhibition [7]. Related studies have shown that ciprofol has the advantages of rapid onset, strong potency, less respiratory depression and injection pain, and patients have higher comfort and satisfaction [8]. In this study, it was found that the injection pain of patients using ciprofol was reduced, which is similar to the results of previous studies [8, 9]. It may be related to the unique structure of ciprofol itself. The high concentration of propofol in the aqueous phase is one of the reasons for injection pain. Ciprofol has a higher lipid solubility than propofol, and the concentration of free molecules in the emulsion is significantly lower than that of propofol, which may be the reason for the reduction of injection pain. Further research found that the incidence of injection pain of ciprofol is higher than that of etomidate. This may be related to the thinner indwelling needle used in outpatient examinations and the fact that the volume of ciprofol injected intravenously in the same time is larger than that of etomidate. In addition, there is no statistically significant difference in the sedation success rate between patients using propofol and ciprofol for sedation, and the induction time and recovery time are similar, which is similar to the results of previous studies [10]. It may be related to the similar molecular structure and pharmacokinetics of ciprofol and propofol. Hypotension and respiratory depression are common anesthetic complications in gastroscopy. The effect of ciprofol on the cardiovascular system is similar to that of propofol, which can produce transient hypotension. Multiple mechanisms may be involved, including peripheral vasodilation, reduction of ventricular preload, sympathetic nerve activity or myocardial contractility [11, 12]. Whether ciprofol has a similar mechanism of action to propofol remains uncertain and requires further research. Hypoxia may be caused by respiratory depression, apnea or airway obstruction, with an incidence of 1.5 - 70%, making it the most common cardiopulmonary complication in endoscopy. In this trial, compared with the propofol group, the incidence of respiratory system complications (including respiratory depression, apnea and hypoxemia) of ciprofol was lower. The possible reason is that ciprofol produces less respiratory depression in the central nervous system or airway collapse. However, this speculation requires further research in the near future.

This study also evaluated the occurrence of adverse events in the three groups. The results showed that the incidence of body movement, muscle tremor and muscle pain in the etomidate group was higher than that in the propofol group and the ciprofol group. In addition, this study also evaluated the satisfaction rates of endoscopists and patients. The results showed that compared with the etomidate group and the propofol group, the satisfaction of the examinees and examiners in the ciprofol group was higher. This may be because the evaluation of satisfaction by endoscopists focuses more on whether patients have body movement, cough and other factors that lead to the suspension or termination of the examination, while patients focus more on the comfort after the examination, that is, mainly related to nausea, vomiting, abdominal distension, abdominal pain, muscle pain, etc. during the recovery room period.

5. Conclusion

Ciprofol is a new type of anesthetic sedative, which has good sedative effect during painless gastroscopy and colonoscopy with low incidence of injection pain, mild inhibition of respiration and circulation, and low incidence of other adverse reactions, leading to high satisfaction for both examiners and. It can compensate for the deficiencies of propofol and etomidate, and therefore is suitable for widespread clinical use.

Abbreviations

BMI	Body Mass Index
ASA	American Society of Anesthesiologists
MOAA/S	Modified Observer's Assessment of Alertness/Sedation Scale
PACU	Post - Anesthesia Care Unit
GABA	Gamma - Aminobutyric Acid

Conflicts of Interest

In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received

from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work. Human subjects: Consent was obtained by all participants in this study.

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