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Clinical Application Effect of Ciprofol Combined with Low-dose Esketamine in Painless Gastrointestinal Endoscopy

Dongyu Zhang, Qi Feng, Weiyan Huang, Xuefu Tang, Changhui Shao, Shan Ou*

Chengdu Integrated TCM & Western Medicine Hospital (Chengdu First People's Hospital, Chengdu Traditional Chinese Medicine Hospital), Chengdu 610000, Sichuan, China

**Author to whom correspondence should be addressed.*

Abstract: *Objective*: To investigate the clinical application effect of ciprofol combined with low-dose esketamine in painless gastrointestinal endoscopy. *Methods*: A retrospective analysis was conducted on the clinical data of 160 patients who underwent painless gastrointestinal endoscopy at the Digestive Endoscopy Center of Chengdu Integrated Traditional Chinese and Western Medicine Hospital from June 2023 to June 2024. The patients were divided into a control group (ciprofol + sufentanil, n=80) and a study group (ciprofol + esketamine, n=80) based on the anesthesia protocol they received. Hemodynamic indicators [mean arterial pressure (MAP), heart rate (HR), and blood oxygen saturation (SpO2)], anesthesia-related indicators, sedation effectiveness, and the incidence of adverse events were observed and compared between the two groups at different time points during the examination. *Results*: The fluctuations in HR and MAP at three time points (after induction, during endoscope insertion, and during the examination) were significantly smaller in the study group than in the control group (all $P<0.05$), indicating more stable hemodynamics. The total amount of sedative drugs used, the number of additional sedative doses administered, and the time spent in the post-anesthesia care unit were significantly lower in the study group than in the control group (all $P<0.05$). There was no significant difference in the success rate of sedation between the two groups (98.75% vs. 96.25%, $P>0.05$). The incidence of adverse events was lower in the study group than in the control group (3.75% vs. 13.75%, $P<0.05$). *Conclusion*: The use of low-dose esketamine as an adjuvant analgesic drug based on ciprofol sedation can effectively maintain hemodynamic stability, reduce the amount of sedative drugs used, facilitate rapid recovery of patients, and lower the risk of adverse events.

Keywords: Ciprofol; Esketamine; Sufentanil; Painless gastrointestinal endoscopy; Hemodynamics

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1. Introduction

Gastrointestinal endoscopy plays a crucial role in the diagnosis and treatment of digestive system diseases in

modern medicine. However, traditional endoscopy can cause severe discomfort such as nausea, vomiting, and abdominal pain in patients, easily triggering negative emotions such as anxiety and fear, thereby reducing patient tolerance and compliance with follow-up examinations [1]. Ciprofol, a novel GABAA receptor agonist, is a structurally modified version of propofol. It exhibits significantly superior anesthetic potency compared to propofol, while simultaneously reducing the risk of adverse events such as injection pain and hypotension, demonstrating enhanced safety. Its application in clinical anesthesia is becoming increasingly widespread. However, to suppress the stimulation caused by endoscopic procedures on patients, it is still routine clinical practice to combine other analgesic drugs. Commonly used drugs include sufentanil, and when used in combination with GABAA receptor agonists as opioid analgesics, they can produce a synergistic respiratory depressant effect, which remains a core concern for perioperative safety [2]. In view of this, this study conducted a retrospective analysis of the clinical data of 160 patients who underwent painless gastrointestinal endoscopy at the Digestive Endoscopy Center of Chengdu Integrated Traditional Chinese and Western Medicine Hospital from June 2023 to June 2024. Based on ciprofol sedation, the study aimed to explore the clinical efficacy of its combined use with low-dose esketamine in painless gastrointestinal endoscopy, with the goal of providing more effective and safer anesthesia options for clinical practice.

2. Materials and methods

2.1. General information

A retrospective analysis was conducted on the clinical data of 160 patients who underwent painless gastrointestinal endoscopy at the Digestive Endoscopy Center of our hospital from June 2023 to June 2024. Patients were divided into a control group (ciprofol + sufentanil, n=80) and a study group (ciprofol + esketamine, n=80) based on the anesthesia regimen they received. A comparison of the general information between the two groups is shown in **Table 1**, indicating comparability. This study has been approved by the Medical Ethics Committee of Chengdu Integrated Traditional Chinese and Western Medicine Hospital (Ethics Approval Number: KT No. 017, 2022).

Table 1. Comparison of baseline demographic and clinical characteristics between the two groups [$\bar{x}$ ±s, n]

Group	n	Age	Gender (Male/Female, n)	Body Mass Index (kg/m²)	ASA Physical Status (I/II, n)
Study Group	80	45.12 ± 11.28	38/42	23.45 ± 2.91	62/18
Control Group	80	46.35 ± 10.94	41/39	23.98 ± 3.35	59/21
χ^2/t		-0.700	0.225	-1.068	0.305
P		0.485	0.635	0.287	0.581

2.2. Inclusion criteria

① Patients who undergo elective diagnostic or therapeutic painless gastrointestinal endoscopy in our hospital; ② Aged between 18 and 65 years old; ③ Classified as American Society of Anesthesiologists (ASA) physical status I/II; ④ Complete clinical data, anesthesia records, and recovery room records.

2.3. Exclusion criteria

① Patients with allergies to drugs involved in this study; ② Patients with severe cardiovascular, respiratory, liver, or kidney diseases; ③ Pregnant or lactating women; ④ Patients with a history of drug abuse or alcohol dependence;

⑤ Patients with uncontrolled hypertension; ⑥ Patients with a history of mental disorders such as schizophrenia, severe depression, epilepsy, or neurological diseases.

2.4. Methods

Both groups of patients were routinely fasted for 8 hours and abstained from drinking for 4 hours. After entering the room, a peripheral intravenous access was established and connected to a monitor to routinely monitor the patient's vital signs. All patients received oxygen via nasal cannula with an oxygen flow rate set at 2 L/min. In the control group, 0.1 μg/kg of sufentanil was intravenously administered 2 minutes before anesthesia induction, followed by an intravenous injection of 0.4-0.5 mg/kg of ciprofol emulsion injection. Induction success was considered when the patient's eyelash reflex disappeared. During the procedure, intermittent additional doses of 5-10 mg of ciprofol were administered based on the patient's body movement, heart rate, and blood pressure changes to maintain the depth of sedation. In the study group, 0.2 mg/kg of esketamine was intravenously administered 2 minutes before anesthesia induction, followed by a slow intravenous injection of 0.4-0.5 mg/kg of ciprofol emulsion injection. Induction success was also considered when the patient's eyelash reflex disappeared. Intermittent additional doses of 5-10 mg of ciprofol were administered to maintain the depth of sedation.

2.5. Observation indicators

2.5.1. Hemodynamic parameters

The heart rate (HR), mean arterial pressure (MAP), and blood oxygen saturation (SpO2) of the two groups of patients were monitored and compared at five time points: T0 (when entering the anesthesia room), T1 (immediately after successful induction), T2 (when inserting the endoscope), T3 (at the midpoint of the examination), and T4 (when withdrawing the endoscope).

2.5.2. Anesthesia-related indicators

The total dosage of sedative drugs (total administered dose of ciprofol), the number of additional doses of sedative drugs, and the duration of stay in the post-anesthesia care unit were recorded for both groups of patients.

2.5.3. Clinical sedation efficacy

The Modified Observer's Assessment of Alertness/Sedation (MOAA/S) [3] was used for evaluation. Patients were classified into six levels ranging from 0 to 5 based on their responses to external stimuli, with higher scores indicating lower levels of sedation depth. In this study, successful sedation was defined as maintaining an MOAA/S score of 3 (responding only to loud or repeated vocal stimuli) or lower during endoscopic examination, without the need for auxiliary ventilation methods such as jaw thrust.

2.5.4. Adverse events

The occurrence of adverse events such as hypotension, respiratory depression, and psychotic-like symptoms was observed in both groups of patients.

2.6. Statistical methods

Data analysis was performed using SPSS 24.0 statistical software. After confirming normal distribution through the Shapiro-Wilk test, measurement data such as hemodynamic parameters and total dosage of sedative drugs

were expressed as mean ± standard deviation ($\bar{x}$ ±s), and comparisons between groups were made using the independent samples t-test. Count data such as sedation success rate and incidence of adverse events were expressed as rates (%), and differences between the two groups were compared using the χ^2 test or Fisher's exact probability method. A *P*-value < 0.05 was considered statistically significant.

3. Results

3.1. Comparison of hemodynamic indicators between the two groups of patients

The SpO2 levels of both groups of patients remained within the normal range at all observed time points in this study, with no statistically significant differences (all $P > 0.05$). At T0, the mean arterial pressure (MAP) and heart rate (HR) levels were comparable between the two groups. At T1, both groups showed a decrease, with the control group experiencing a greater decrease in MAP and HR than the study group (all $P < 0.05$). At T2 and T3, the MAP and HR levels in the study group were higher than those in the control group (all $P < 0.05$). At T4, both groups showed a trend towards recovery in MAP and HR, with the study group maintaining relatively higher levels (all $P > 0.05$). See **Table 2**.

Table 2. Comparison of hemodynamic indicators between the two groups at different time points ($\bar{x}$ ±s)

Indicator	Group	T0 (Pre-anesthesia)	T1 (Post-induction)	T2 (During Scope Insertion)	T3 (During Examination)	T4 (During Scope Removal)
MAP (mmHg)	Study (n=80)	94.28 ± 8.15	88.15 ± 7.92*	87.33 ± 8.01*	89.24 ± 7.55*	91.16 ± 8.23
	Control (n=80)	93.95 ± 8.33	80.48 ± 9.14	81.05 ± 8.86	82.81 ± 8.49	89.52 ± 8.57
HR (bpm)	Study (n=80)	75.82 ± 10.21	72.11 ± 9.85*	73.25 ± 9.53*	74.39 ± 9.17*	74.55 ± 9.88
	Control (n=80)	76.45 ± 10.56	65.56 ± 10.12	67.88 ± 9.94	68.17 ± 9.76	73.81 ± 10.03
SpO_2 (%)	Study (n=80)	99.15 ± 0.88	98.85 ± 0.95	98.65 ± 1.02	98.78 ± 0.99	99.02 ± 0.91
	Control (n=80)	99.27 ± 0.85	98.58 ± 1.10	98.41 ± 1.19	98.55 ± 1.08	98.95 ± 0.96

Note: Compared with the control group in the same period, *P<0.05.

3.2. Comparison of anesthesia-related indicators between the two groups

The total dosage of sedative drugs, the number of intraoperative top-ups, and the duration of stay in the post-anesthesia care unit were significantly lower in the study group than in the control group, with statistically significant differences (all P<0.05). See **Table 3**.

Table 3. Comparison of anesthesia-related indicators between the two groups

Group	n	Total Sedative Dosage (mg)	Number of Supplemental Doses (times)	PACU Stay Time (min)
Study Group	80	35.88 ± 8.14	1.15 ± 0.88	20.36 ± 4.58
Control Group	80	45.48 ± 9.67	1.95 ± 1.24	24.12 ± 5.12
t-value		-6.793	-4.706	-4.896
P-value		<0.001	<0.001	<0.001

3.3. Comparison of sedation efficacy between the two groups

According to the MOAA/S score, 79 patients in the study group were judged to have successful sedation, while 77 patients in the control group were judged to have successful sedation. The sedation success rate in the study group was higher than that in the control group (98.75% vs. 96.25%), but the difference was not statistically significant (χ^2=0.256, *P*=0.613).

3.4. Comparison of the incidence of adverse events between the two groups

The incidence of adverse events in the study group was lower than that in the control group (3.75% vs. 13.75%), with a statistically significant difference (*P*<0.05). See **Table 4**.

Table 4. Comparison of the incidence of adverse events between the two groups (n, %)

Group	n	Hypotension	Respiratory Depression	Psychiatric-like Symptoms	Total Incidence
Study Group	80	1	1	1	3 (3.75%)
Control Group	80	6	4	1	11 (13.75%)
χ^2 value					5.010
P-value					0.025

4. Discussion

With the continuous development and deepening of the concept of comfortable medical care, the ideal anesthesia regimen for painless gastrointestinal endoscopy not only provides reliable sedative and analgesic effects but also minimizes interference with patients' physiological functions to ensure the stability of perioperative physiological indicators[4]. This study, based on the new-generation sedative drug ciprofol, focuses on the selection of adjuvant analgesic drugs, aiming to clarify the clinical value of low-dose esketamine compared with the traditional opioid drug sufentanil[5]. The results are as follows.

In this study, compared with the control group, the study group exhibited smaller fluctuations in MAP and HR during anesthesia induction and at key intraoperative stimulation stages (endoscope insertion, biopsy), along with a lower incidence of adverse events. This suggests that the anesthesia regimen combining ciprofol with low-dose esketamine offers better hemodynamic stability and higher safety. The underlying reason is that as a highly selective GABAA receptor agonist, Ciprofol exhibits weaker cardiovascular inhibitory effects compared to an equivalent dose of Propofol. Meanwhile, Esketamine can slightly increase heart rate and blood pressure through NMDA receptor antagonism and sympathetic nervous system activation, thereby counteracting, to a certain extent, the cardiovascular depression caused by Ciprofol [6]. Compared to the control group using opioid drugs, the study group also avoided respiratory depression resulting from the activation of μ-opioid receptors, demonstrating better hemodynamic stability and reducing the risk of adverse events such as respiratory depression and hypotension [7]. In terms of anesthetic efficacy, both groups achieved a high rate of successful anesthesia (both above 95%). The reason is that Ciprofol's unique cyclopropyl structure endows it with a receptor affinity and anesthetic potency approximately 4 to 5 times that of Propofol [8]. Additionally, the use of Esketamine in the study group can reduce or reset central sensitization caused by continuous painful stimuli through NMDA receptor antagonism [9]. The combination of these two agents produces a synergistic effect in sedation and analgesia, not only more effectively suppressing the noxious stimuli from endoscopic procedures but also reducing the dosage and frequency of additional

sedative drugs required to maintain sedation, thereby lowering the risk of accumulation and laying the foundation for faster recovery. The low dose of Esketamine used in this study resulted in no significant difference in the incidence of psychotomimetic symptoms between the study group and the control group, and the overall incidence of adverse events was lower. This finding is consistent with the study by Xue [10] and, to a certain extent, alleviates clinical concerns regarding its psychiatric side effects.

5.Conclusion

In conclusion, the anesthetic regimen combining Ciprofol with low-dose Esketamine demonstrates definite anesthetic effects in painless gastrointestinal endoscopy procedures, along with excellent hemodynamic stability. It reduces the risk of adverse events such as respiratory depression and hypotension, facilitating rapid patient recovery.

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Disclosure statement

The authors declare no conflict of interest.

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