Cite as: Fu XH, Yang Z, Wang L, Zhao SL, Yang C. Effect of different doses of nalmefene pre-administration on respiratory depression during painless gastrointestinal endoscopy [J]. Chin J Clin Res, 2025, 38(12):1827-1831,1835.

DOI: 10.13429/j.cnki.cjcr.2025.12.008

Effect of different doses of nalmefene pre-administration on respiratory depression during painless gastrointestinal endoscopy

FU Xinghuo*, YANG Zan, WANG Li, ZHOU Suli, YANG Chun

**Department of Anesthesiology and Perioperative Medicine, The First Affiliated Hospital with Nanjing Medical University, Nanjing, Jiangsu 210029, China*

Corresponding author: YANG Chun, E-mail: chunyang@njmu.edu.cn

Abstract: Objective To explore the effect of different doses of nalmefene pre-administration on vital sign and respiratory depression of patients during painless gastroenteroscopy under fentanyl combined with propofol anesthesia. **Methods** A total of 195 patients who underwent painless gastroenteroscopy in Taizhou Fourth People's Hospital from August 2024 to December 2024 were randomly divided into three groups: physiological saline group (Group S, n=65), 0.1 μg/kg nalmefene group (Group N1, n=65), and 0.2 μg/kg nalmefene group (Group N2, n=65). Two min before induction, patients in Group N1 and Group N2 received an intravenous injection of 0.1 μg/kg and 0.2 μg/kg nalmefene respectively, while patients in Group S were given the same volume of physiological saline. All three groups adopted the anesthesia scheme of fentanyl combined with propofol for anesthesia induction and propofol for maintenance. The primary observation indicator was the incidence of respiratory depression during the examination. Secondary observation indicators included vital signs [respiratory rate (RR), saturation of peripheral oxygen (SpO_2), mean arterial pressure (MAP), and heart rate at pre-anesthesia (T0), when the endoscope entered the esophageal inlet (T1), and upon awakening (T2)], anesthesia indicators [time to awakening, time to discharge from the procedure room, propofol dosage], satisfaction, and adverse anesthesia reactions (body movement responses, jaw thrust intervention, and nausea and vomiting). **Results** The incidence of respiratory depression was 18.5% (12/65) in Group S, 6.2% (4/ 65) in Group N1, and 3.1% (2/65) in Group N2, with statistically significant differences among the three groups (χ^2= 10.282, P=0.006). However, the difference between Group N1 and Group N2 was not statistically significant (P> 0.05). At T1, the RR, SpO_2, and MAP in Group N1 and Group N2 were higher than those in Group S, and the RR and heart rate in Group N2 were higher than those in Group N1, with statistically significant differences (P<0.05). The time to awakening and time to discharge from the procedure room in Group S were significantly longer than those in Group N1 and Group N2, with statistically significant differences (P<0.05). Group N1 and Group N2 were superior to Group S in terms of the incidence of jaw thrust intervention and anesthesiologist satisfaction, with statistically significant differences (P<0.05). **Conclusion** Pre-injection of both 0.1 μg/kg and 0.2 μg/kg nalmefene can stabilize patients' RR and reduce the incidence of respiratory depression, with the 0.2 μg/kg nalmefene pre-injection showing better efficacy.

Keywords: Nalmefene; Pre-injection; Painless gastroenteroscopy; Respiratory depression; Propofol Fund program: Jiangsu Provincial Outstanding Youth Fund Project (BK20240054)

With the advancement of medical technology and the increasing patient demand for pain-free diagnosis and treatment, the application of painless gastrointestinal endoscopy in clinical diagnosis and treatment is also growing. It involves administering appropriate anesthetic agents to render the patient unconscious and pain-free during the procedure, thereby enhancing patient comfort and compliance [1-2]. However, the use of anesthetic agents also brings a series of potential risks, such as respiratory depression, delayed recovery, hypotension, etc. [3]. Balanced anesthesia can reduce the required dose of each anesthetic, thereby lowering the likelihood of adverse reactions. The classic regimen for endoscopic procedures primarily combines propofol with opioids. It has been reported that under such an anesthetic regimen, the incidence of adverse reactions during painless gastroscopy combined with colonoscopy increases four-fold [4].

Nalmefene hydrochloride is a specific opioid receptor antagonist that exerts antagonistic effects on μ, δ, and κ opioid receptors. When administered at low doses (<0.25 μg/kg), it exhibits the strongest affinity for the μ2 opioid receptor. It competitively binds to opioid receptors, blocking the effects of endogenous or exogenous opioid substances, thereby reversing adverse reactions such as respiratory depression, excessive sedation, and hypotension induced by opioids. Importantly, it does not produce significant agonist effects and does not affect postoperative analgesia [5-8]. This study aims to evaluate the effects of different low-dose nalmefene pretreatment on respiratory depression during painless gastrointestinal endoscopy under anesthesia with fentanyl combined with propofol, thereby providing a more scientific and accurate theoretical basis for future clinical medication use.

1 Materials and Methods

1.1 Clinical Data

This study was approved by the Ethics Committee of Taizhou Fourth People's Hospital (Approval No.: 2024-EC/TZFH-047) and has been registered with the Chinese Clinical Trial Registry (ChiCTR2400088347). Patients or their family members voluntarily provided informed consent.

Inclusion criteria: (1) American Society of Anesthesiologists (ASA) physical status classification I–II; (2) Age 20–65 years; (3) Body mass index (BMI) 18–30 kg/m²; (4) Patients and their families are aware of all study requirements and voluntarily cooperate.

Exclusion criteria: (1) Contraindications to the use of anesthetic agents; (2) Recent upper respiratory tract infection; (3) Severe hypertension or arrhythmia; (4) Presence of psychiatric disorders or severe systemic diseases.

A total of 195 patients scheduled for painless gastrointestinal endoscopy at Taizhou Fourth People's Hospital from August to December 2024 were selected as the study subjects. They were randomly divided into three groups: Normal Saline group (Group S, n=65), 0.1 μg/kg Nalmefene group (Group N1, n=65), and 0.2 μg/kg Nalmefene group (Group N2, n=65).

1.2 Preoperative Preparation

Patients were instructed to fast for 6 hours and abstain from clear liquids for 2 hours before the procedure. Upon arrival in the endoscopy suite, patients assumed the left lateral position. A peripheral intravenous line was established using a 24G cannula, and oxygen was administered via nasal cannula at a flow rate of 2–4 L/min. Continuous monitoring of electrocardiogram (ECG), blood pressure, peripheral oxygen saturation (SpO_2), and respiratory rate (RR) was performed using a monitor (Mindray Medical).

1.3 Anesthesia Method

Anesthesia was administered by the same anesthesiologist for all cases, and the gastrointestinal endoscopy was performed by the same experienced endoscopist. Two minutes before anesthesia induction, patients in Group N1 received an intravenous pretreatment of 0.1 μg/kg nalmefene hydrochloride, Group N2 received 0.2 μg/kg nalmefene hydrochloride, and Group S received an equal volume of normal saline.

All three groups then received a slow intravenous injection of 1 μg/kg fentanyl over 20 seconds, followed by a slow intravenous bolus of 1.5 mg/kg propofol at approximately 0.5 mL/s. The anesthesiologist assessed the patient's sedation level every 10 seconds using the Modified Observer's Assessment of Alertness/Sedation (MOAA/S) scale. Endoscopy commenced when the MOAA/S score was ≤ 2 and the eyelash reflex was absent.

During the procedure, propofol was continuously infused at 4–6 mg/(kg·h). If movement occurred during the procedure, an additional 20 mg bolus of propofol was administered. In the perioperative period, if blood pressure decreased by more than 20% from the preoperative baseline or if the mean arterial pressure (MAP) was<60 mmHg, ephedrine 6 mg was immediately administered intravenously. If bradycardia occurred (heart rate<50 beats/min), atropine 0.5 mg was administered. If respiratory depression occurred (respiratory rate<10 breaths/min or SpO_2<95%), the oxygen flow rate was increased, and jaw thrust was applied. If the condition did not improve within 10 seconds, the examination was terminated, the endoscope was withdrawn, and assisted ventilation was provided using a facemask.

After the procedure, all patients were transferred to the Post-anesthesia Care Unit (PACU). An anesthesia nurse assessed them every 30 seconds until the modified Aldrete score was ≥ 9, at which point they could leave the PACU [9].

1.4 Observation Indicators

The following were recorded and compared: (1) Total propofol dosage, recovery time (time from last drug administration to eye opening on command), and discharge time from the PACU (time from last drug administration to achieving a modified Aldrete score ≥ 9) [9]; (2) RR, SpO_2, MAP, and heart rate at the following time points: before anesthesia (T0), when the endoscope entered the esophageal inlet (T1), and upon recovery (T2); (3) Post-anesthesia adverse events including respiratory depression, movement response, jaw thrust intervention, and nausea/vomiting; (4) Patient satisfaction, anesthesiologist satisfaction, and endoscopist satisfaction. Satisfaction was assessed using a verbal rating scale (0–10), with a score ≥ 8 considered satisfactory [10].

1.5 Statistical Methods

Data analysis was performed using SPSS 27.0 software. Normally distributed measurement data are expressed as $\bar{x} \pm s$ Comparisons among multiple groups were conducted using one-way analysis of variance (ANOVA), between-group comparisons were made using independent samples t-test, and within-group comparisons were made using paired t-test. Non-normally distributed measurement data are expressed as $M(P_{25},P_{75})$ and compared using the Kruskal-Wallis H test. Comparisons of repeated measures data were performed using generalized estimating equations. Count data are expressed as case (%) and compared among groups using the chi-square test. P<0.05 was considered statistically significant.

2 Results

2.1 Comparison of general Data

There was no significant difference among three groups in gender, age, BMI, ASA classification (P>0.05). See **Table 1.**

2.2 Comparison of Vital Signs

At T1, the RR, SpO_2 and MAP in Group N1 and Group N2 were significantly higher than those in Group S (P<0.05). RR and heart rate in Group N2 was higher than that in Group N1 (P<0.05). See **Table 2**.

2.3 Comparison of Adverse Reaction

Compared with Group S, Group N1 and Group N2 had lower incidence of respiratory inhibition and mandibular support intervention. There was no statistically significant difference in the incidence of intraoperative motor reactions among the three groups (P>0.05); No nausea or vomiting occurred in the Group N2, the incidence rate of nausea or vomiting was significantly lower than that in Group S (6.2%), with significant difference (P<0.05). See **Table 3**.

2.4 Comparison of Anesthesia Indicators

There was no statistically significant difference in the dosage of propofol among the three groups of patients (P>0.05); The awakening time and release time of Group S were significantly longer than those of Group N1 and Group N2, and the difference was statistically significant (P<0.05). See **Table 4**.

Tab.1 Comparison of general data among three groups (n=65)

Group	Gender (M/F, case)	Age (years,$\bar{x}$±s)	BMI (kg/m^2,$\bar{x}$±s)	ASA (I/II, cases)
Group S	24/41	49.3±9.1	23.7±2.3	14/51
Group N1	27/38	50.7±8.1	23.2±2.5	11/54
Group N2	29/36	49.4±9.3	23.5±2.6	13/52
χ^2/F value	0.805	0.497	0.825	0.458
***P* value**	0.672	0.609	0.440	0.795

Tab.2 Comparison of vital signs among three groups at different time points [n=65, $M(P_{25}, P_{75})$]

Group	MAP (mmHg)			HR (times/min,$\bar{x}$±s)			RR (times/min)			SpO_2 (%)		
	T0	T1	T2	T0	T1	T2	T0	T1	T2	T0	T1	T2
Group S	87.0 (78.5,101.5)	69.0 (61.0,77.5)	77.0 (68.5,86.0)	76.4±11.9	67.1±8.1	70.0±8.6	19.0 (19.0,20.0)	14.0 (12.0,15.0)	18.0 (18.0,19.0)	98 (98,99)	97 (95,97)	98 (98,99)
Group N1	92.0 (86.0,100.0)	78.0 (72.0,88.5)[a]	81.0 (75.0,86.5)	76.3±12.4	68.2±9.6	69.5±9.1	19.0 (18.0,20.0)	15.0 (13.0,16.0)[a]	18.0 (18.0,19.0)	98 (98,99)	98 (96,99)[a]	99 (98,99)
Group N2	90.0 (78.0,100.0)	79.0 (66.0,85.0)[a]	81.0 (69.0,89.0)	78.5±12.8	72.0±9.1[ab]	72.6±9.3	19.0 (18.5,20.0)	16.0 (15.0,17.0)[ab]	18.0 (17.0,19.0)	98 (98,99)	98 (96,99)[a]	99 (98,99)
***F* value**	1.865	11.247	1.424	0.661	5.384	2.181	1.232	31.818	1.222	1.434	7.128	2.381
***P* value**	0.158	<0.001	0.243	0.518	0.005	0.116	0.294	<0.001	0.297	0.241	0.001	0.095

Note: Compared with Group S, [a]P<0.05; Compared with Group N1, [b]P<0.05.

Tab.3 Comparison of adverse events among three groups [case(%)]

Group	Respiratory Inhibition	Nausea or Vomiting	Intraoperative Motor Reactions	Mandibular Support Intervention
Group S	12(18.5)	4(6.2)	8(12.3)	16(24.6)
Group N1	4(6.2)[a]	1(1.5)	5(7.6)	4(6.2)[a]
Group N2	2(3.1)[a]	0[a]	6(9.2)	2(3.1)[a]
χ^2 value	10.282	5.337	0.816	17.625
***P* value**	0.006	0.069	0.665	<0.001

Note: Compared with Group S, [a]P<0.05.

Tab.4 Comparison of anesthesia indicators among three groups [n=65, $M(P_{25},P_{75})$]

Group	Awakening time(min)	Leaving time(min)	Propofol Dosage (mg, $\bar{x}$±s)
Group S	7.0(6.0,8.0)	15.0(13.0,16.0)	102.9±23.6
Group N1	5.5(5.0,6.0)[a]	13.5(13.0,14.5.0)[a]	104.5±21.8
Group N2	5.5(5.0,6.0)[a]	13.0 12.5,13.5)[ab]	105.6±22.3
***F* value**	43.004	25.230	0.233
***P* value**	<0.001	<0.001	0.792

Note: Compared with Group S, [a]P<0.05; Compared with Group N1, [b]P<0.05.

Tab.5 Comparison of satisfaction among three groups [n=65,case(%)]

Group	Patient Satisfaction	Anesthesiologist Satisfaction	Endoscopist Satisfaction
Group S	58(89.2)	53(81.5)	64(98.5)
Group N1	62(95.4)	61(93.8)[a]	64(98.5)
Group N2	64(98.5)[a]	63(96.9)[a]	65(100.0)
χ^2 value	5.395	10.282	1.010
***P* value**	0.067	0.006	0.603

Note: Compared with Group S, [a]P<0.05.

3 Discussion

Gastrointestinal endoscopy is currently the primary method for screening digestive tract tumors [11] and can significantly reduce the incidence of gastric cancer in populations [12]. In the context of comfortable medical care, painless endoscopic examinations have become a mainstream trend. Propofol, due to its advantages of rapid onset and recovery, has become the anesthetic of choice for outpatient painless gastrointestinal endoscopy. However, rapid or high-dose administration can easily cause respiratory and circulatory depression. Therefore, it is often used in combination with other drugs to balance sedation and analgesia needs and improve medication safety [13-14]. The anesthetic method combining propofol and fentanyl while preserving spontaneous respiration, as the most classic approach for painless gastrointestinal endoscopy, can perfect and enhance sedation and analgesic effects. However, it simultaneously increases the probability and severity of respiratory depression. Under conditions where resuscitation facilities in outpatient endoscopy suites are less comprehensive than in operating rooms, this anesthetic technique also carries certain safety risks [15-16].

Low-dose nalmefene can selectively antagonize the binding of opioid drugs to μ2 and κ receptors [17-18]. In recent years, some scholars have proposed combining opioid analgesics with low-dose opioid receptor antagonists. By competitively binding to opioid receptors and blocking the effects of endogenous or exogenous opioid substances, this can reduce side effects such as respiratory depression, hypotension, and pruritus induced

by opioid analgesics without affecting their analgesic efficacy [19-20]. This study observed the occurrence of respiratory depression in patients undergoing painless gastrointestinal endoscopy by pretreating with different doses of nalmefene. The results showed that pretreatment with 0.1 μg/kg and 0.2 μg/kg nalmefene both reduced the incidence of respiratory depression in patients, with few adverse reactions and a stable anesthesia process. Among these, pretreatment with 0.2 μg/kg nalmefene yielded the best results. This study has certain limitations. The number of patients included in the analysis is relatively limited. Subsequent research is necessary to further expand the sample size to more effectively control potential biases in the study results and enhance the accuracy and reliability of the research.

In summary, for outpatient painless gastrointestinal endoscopy, preemptive intravenous injection of low-dose nalmefene is safe and feasible. This intervention can effectively stabilize the patient's respiratory rate, reduce the probability of respiratory depression, while significantly shortening the recovery time and improving the quality of recovery. Notably, this method does not adversely affect the sedation and analgesia during anesthesia. It also reduces adverse reactions such as nausea/vomiting and hypotension, greatly enhancing the safety and comfort of outpatient painless examinations, and holds high clinical application value.

Conflict of Interest None

References

[1] Tang LL, Ye CX, Wang N, et al. The Median effective doses of propofol combined with two different doses of nalbuphine for adult patients during painless gastroscopy[J]. Front Pharmacol, 2022, 13:1014486.

[2] Zheng LL, Wu XY, Gu W, et al. Development and validation of a hypoxemia prediction model in middle-aged and elderly out patients undergoing painless gastroscopy[J]. Sci Rep, 2025, 15(1):17965.

[3] Deng J, Yu YF, Tang ZG, et al. Efficacy and safety of low-dose esketamine for painless gastrointestinal endoscopy inadults: a systematic evaluation and meta-analysis[J]. Front Pharmacol, 2024, 15:1364546.

[4] Sneyd JR, Absalom AR, Barends CRM, et al. Hypotension during propofol sedation for colonoscopy: are trospective exploratory analysis and meta-analysis[J]. Br J Anaesth, 2022, 128(4):610-622.

[5] WangY, ZhaoL, WuM, et al. Different doses of nalmefene combined with hydromorphone hydrochloride for postoperative analgesia after colorectal surgery: a randomized controlled study[J]. BMC Surg, 2024, 24(1):3.

[6] Li GT, Yan H, Li WS, et al. Nalmefene effectively relieves thoracic epidural opioid-induced pruritus without affecting analgesia: a randomized controlled clinical trial[J]. J Thorac Dis, 2025, 17(4):2028-2037.

[7] Tournier N, Pottier G, Caillé F, et al. Nalmefene alleviates theneuroimmune response to repeated binge-like ethanol exposure: aTSPO PET imaging study in adolescent rats[J]. Addict Biol, 2021, 26(3):e12962.

[8] Windisch KA, Morochnik M, Reed B, et al. Nalmefene, a muopioid receptor antagonist/kappa opioid receptor partial agonist, potentiates cocaine motivation but not intake with extended access self-administration in adult male mice[J]. Neuropharmacology, 2021, 192:108590.

[9] Wang BH, Liu FZ, Li XM. Dose of remimazolam in painless gastroenteroscopy in elderly patients under bispectral index monitoring [J]. Chin J Clin Res, 2024, 37(4):519-524. **[In Chinese]**

[10] Yi QL, Mo HZ, Hu H, et al. Comparison of ciprofol and propofol in elderly patients undergoing gastroscopy [J]. J Clin Anesthesiol, 2022, 38(7):712-715. **[In Chinese]**

[11] Bray F, Laversanne M, Sung H, et al. Global cancer statistics2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries[J]. CA Cancer J Clin, 2024, 74(3):229-263.

[12] Li P, Qi X, Bai RH, et al. The spatiotemporal associations between esophageal and gastric cancers provide evidence for its joint endoscopic screening in China: a population-based study[J]. BMC Med, 2024, 22(1):364.

[13] Koo BW, Na HS, Park SH, et al. Comparison of the safety and efficacy of remimazolam and propofol for sedation in adults undergoing colonoscopy: a meta-analysis of randomized controlled trials[J]. Medicina(Kaunas), 2025, 61(4):646.

[14] Yang YC, Shuai DC, Han J, et al. Sedative effect of low-dose remidazolam combined with propofol in elderly patients received gastrointestinal endoscopy [J]. Chin J Clin Res, 2023, 36(8):1205-1209. **[In Chinese]**

[15] Sidhu R, Turnbull D, Haboubi H, et al. British Society of Gastroenterology guidelines on sedation in gastrointestinal endoscopy[J]. Gut, 2024, 73(2):219-245.

[16] Hardman B, Karamchandani K. Management of anesthetic complications outside the operating room[J]. Curr Opin Anaesthesiol, 2023, 36(4):435-440.

[17] Fan YZ, Duan YL, Chen CT, et al. Advances in attenuating opioidinduced respiratory depression:a narrative review[J]. Medicine (Baltimore), 2024, 103(29):e38837.

[18] Ma XW, Liu JY, Tang Y, et al. The efficacy of nalmefene on anesthetic recovery of patients:a study protocol for a multicenter randomized controlled trial[J]. Trials, 2023, 24(1):156.

[19] Wang J, Zheng K, Wen Q, et al. Sufentanil combined with nalmefene reduce the adverse events in recovery period of patients undergoing uvulopalatopharyngoplasty-a randomized controlled trial[J]. Heliyon, 2023, 9(2):e13241.

[20] Yan H, Chen JJ, Luo JW, et al. Prophylatic use of IV nalmefeneto prevent epidural opioid-induced pruritus: a multicenter, randomized clinical trial[J]. J Clin Anesth, 2024, 92:111301.

Submission received: 2025-04-03/ **Revised:** 2025-07-29

·论 著·

不同剂量纳美芬预给药对无痛胃肠镜检查中呼吸抑制的影响

付星火[1,2]， 杨赞[2]， 王莉[2]， 周素利[1]， 杨春[1]
1. 南京医科大学第一附属医院麻醉与围术期医学科，江苏 南京 210029；
2. 泰州市第四人民医院麻醉科，江苏 泰州 225300

摘要：目的 探讨在芬太尼复合丙泊酚麻醉下无痛胃肠镜检查中不同剂量纳美芬预给药对患者生命体征及呼吸抑制的影响。**方法** 选择2024年8月至2024年12月在泰州市第四人民医院行无痛胃肠镜检查的患者195例，随机分为生理盐水组（S组，n=65）、0.1 μg/kg纳美芬组（N1组，n=65）和0.2 μg/kg纳美芬组（N2组，n=65）。在诱导前2 min，N1组和N2组患者分别静脉注射0.1 μg/kg和0.2 μg/kg纳美芬，S组患者给予同体积的生理盐水。三组均采用芬太尼复合丙泊酚麻醉诱导和丙泊酚维持的麻醉方案。主要观察指标为检查过程中呼吸抑制的发生率，次要观察指标包括生命体征[麻醉前（T0）、内镜进入食管入口时（T1）、苏醒时（T2）时的呼吸频率（RR）、外周血氧饱和度（SpO_2）及平均动脉压（MAP）、心率]、麻醉指标[苏醒时间、离室时间、丙泊酚用量]、满意度以及麻醉不良反应（体动反应、托下颌干预及恶心呕吐）。**结果** S组呼吸抑制发生率为18.5%（12/65），N1组为6.2%（4/65），N2组为3.1%（2/65），三组差异有统计学意义（χ^2=10.282，P=0.006），但N1组和N2组差异无统计学意义（P>0.05）。T1时，N1组和N2组的RR、SpO_2及MAP高于S组，N2组的RR及心率高于N1组，差异有统计学意义（P<0.05）。S组苏醒时间与离室时间显著长于N1组和N2组，差异有统计学意义（P<0.05）。N1组和N2组在托下颌干预发生率、麻醉医生满意度方面优于S组，差异有统计学意义（P<0.05）。**结论** 0.1 μg/kg和0.2 μg/kg纳美芬预注射均可稳定患者的RR，降低呼吸抑制的发生率；其中0.2 μg/kg纳美芬效果更佳。

关键词： 纳美芬；预给药；无痛胃肠镜；呼吸抑制；丙泊酚
中图分类号： R614 **文献标识码：** A **文章编号：** 1674-8182(2025)12-1827-05

Effect of different doses of nalmefene pre-administration on respiratory depression during painless gastrointestinal endoscopy

FU Xinghuo*, YANG Zan, WANG Li, ZHOU Suli, YANG Chun
*Department of Anesthesiology and Perioperative Medicine, The First Affiliated Hospital with Nanjing Medical University, Nanjing, Jiangsu 210029, China
Corresponding author: YANG Chun, E-mail: chunyang@njmu.edu.cn

Abstract: Objective To explore the effect of different doses of nalmefene pre-administration on vital sign and respiratory depression of patients during painless gastroenteroscopy under fentanyl combined with propofol anesthesia. **Methods** A total of 195 patients who underwent painless gastroenteroscopy in Taizhou Fourth People's Hospital from August 2024 to December 2024 were randomly divided into three groups: physiological saline group (Group S, n=65), 0.1 μg/kg nalmefene group (Group N1, n=65), and 0.2 μg/kg nalmefene group (Group N2, n=65). Two min before induction, patients in Group N1 and Group N2 received an intravenous injection of 0.1 μg/kg and 0.2 μg/kg nalmefene respectively, while patients in Group S were given the same volume of physiological saline. All three groups adopted the anesthesia scheme of fentanyl combined with propofol for anesthesia induction and propofol for maintenance. The primary observation indicator was the incidence of respiratory depression during the examination. Secondary observation indicators included vital signs [respiratory rate (RR), saturation of peripheral oxygen (SpO_2), mean arterial pressure

DOI：10.13429/j.cnki.cjcr.2025.12.008
基金项目： 江苏省杰出青年基金项目（BK20240054）
通信作者： 杨春，E-mail：chunyang@njmu.edu.cn
出版日期： 2025-12-20

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(MAP), and heart rate at pre-anesthesia (T0), when the endoscope entered the esophageal inlet (T1), and upon awakening (T2)], anesthesia indicators [time to awakening, time to discharge from the procedure room, propofol dosage], satisfaction, and adverse anesthesia reactions (body movement responses, jaw thrust intervention, and nausea and vomiting). **Results** The incidence of respiratory depression was 18.5% (12/65) in Group S, 6.2% (4/65) in Group N1, and 3.1% (2/65) in Group N2, with statistically significant differences among the three groups (χ^2=10.282, P=0.006). However, the difference between Group N1 and Group N2 was not statistically significant (P>0.05). At T1, the RR, SpO_2, and MAP in Group N1 and Group N2 were higher than those in Group S, and the RR and heart rate in Group N2 were higher than those in Group N1, with statistically significant differences (P<0.05). The time to awakening and time to discharge from the procedure room in Group S were significantly longer than those in Group N1 and Group N2, with statistically significant differences (P<0.05). Group N1 and Group N2 were superior to Group S in terms of the incidence of jaw thrust intervention and anesthesiologist satisfaction, with statistically significant differences (P<0.05). **Conclusion** Pre-injection of both 0.1 μg/kg and 0.2 μg/kg nalmefene can stabilize patients' RR and reduce the incidence of respiratory depression, with the 0.2 μg/kg nalmefene pre-injection showing better efficacy.

Keywords: Nalmefene; Pre-injection; Painless gastroenteroscopy; Respiratory depression; Propofol

Fund program: Jiangsu Provincial Outstanding Youth Fund Project (BK20240054)

随着医疗技术的不断发展和患者对无痛化诊疗需求的提升,无痛胃肠镜检查在临床诊断和治疗中的应用也日益增加。其通过给予适当的麻醉药物,使患者在检查过程中处于无意识、无痛苦的状态,提高了患者的舒适度和依从性[1-2]。然而,麻醉药物的使用也带来了一系列潜在风险,如呼吸抑制、苏醒延迟、低血压等[3]。平衡麻醉可以减少每种麻醉药所需的剂量,从而降低发生不良反应的可能性。内镜检查的经典方案主要为丙泊酚与阿片类药物的结合,据报道,在此麻醉方案下无痛胃镜联合结肠镜检查时不良反应的发生率增加了4倍[4]。

盐酸纳美芬是一种特异性的阿片受体拮抗剂,对μ、δ、κ阿片受体均有拮抗作用。当小剂量(<0.25 μg/kg)预注时对μ2阿片受体的亲和力最强。它能够竞争性地与阿片受体结合,阻断内源性或外源性阿片类物质的作用,从而逆转阿片类药物引起的呼吸抑制、镇静过度、低血压等不良反应,同时不产生明显的激动效应,对术后镇痛没有影响[5-8]。本研究旨在评估不同小剂量纳美芬预注在芬太尼复合丙泊酚麻醉下的无痛胃肠镜检查中对呼吸抑制的影响,从而为今后的临床用药提供更为科学准确的理论依据。

1　资料与方法

1.1　*临床资料*　本研究经泰州市第四人民医伦理委员会批准(2024-EC/TZFH-047),并已在中国临床试验注册中心注册(ChiCTR2400088347)。患者或家属自愿签署知情同意书。纳入标准:(1)美国麻醉医师协会(American Society of Anesthesiologists, ASA)分级Ⅰ~Ⅱ级;(2)年龄20~65岁;(3)身体质量指数(body mass index, BMI)18~30 kg/m^2;(4)受试者及其家属对本次研究要求均知晓且都自愿配合。排除标准:(1)存在麻醉药物使用禁忌;(2)近期有上呼吸道感染;(3)严重高血压或心律失常;(4)存在精神障碍或严重系统性疾病者。选择2024年8月至12月在泰州市第四人民医院行无痛胃肠镜检查的患者共195例作为研究对象,随机分为3组:生理盐水组(S组,n=65)、0.1 μg/kg纳美芬组(N1组,n=65)和0.2 μg/kg纳美芬组(N2组,n=65)。

1.2　*术前准备*　指导患者在检查前禁饮2 h,禁食6 h。到达腔镜室后,行左侧卧位,使用24G留置针开通外周静脉,并通过鼻导管以2~4 L/min供氧。使用监护仪(迈瑞医疗)对心电图、血压、外周血氧饱和度(saturation of peripheral oxyen, SpO_2)和呼吸频率(respiratory rate, RR)进行连续监测。

1.3　*麻醉方法*　麻醉始终由同一位麻醉医生进行,胃肠镜检查也由同一位经验丰富的内窥镜医师操作。在麻醉诱导前2 min,N1组患者静脉预注射0.1 μg/kg盐酸纳美芬,N2组患者预注射0.2 μg/kg盐酸纳美芬,S组患者给予同体积生理盐水。三组患者均先在20 s内缓慢静脉注射1 μg/kg芬太尼,随后缓慢静脉推注1.5 mg/kg丙泊酚,速度约0.5 mL/s。麻醉医生使用改良观察者警觉性/镇静评估(Modified Observer's Assessment of Alertness/Sedation, MOAA/S)量表每10 s评估1次患者镇静水平。当MOAA/S评分≤2分时,且睫毛反射消失后行内窥镜检查。术中丙泊酚以4~6 mg/(kg·h)持续泵注。若术中出现体动反应,则追加20 mg丙泊酚。围手术期如果血

压较术前基线下降超过20%或平均动脉压（mean arterial pressure，MAP）<60 mmHg时，立即静脉推注麻黄碱6 mg/次。若出现心动过缓患者（心率<50次/min），则给予阿托品0.5 mg/次。如果出现呼吸抑制（呼吸频率低于每分钟10次或SpO_2<95%），应增加氧气流量、托下颌。如果10 s后病情没有改善，则应停止检查退出胃肠镜，使用面罩加压辅助通气。检查结束后所有患者均被转移到麻醉后监护病房（postanesthesia care unit，PACU），由麻醉护士每30 s对其进行一次评估，直到改良的Aldrete评分≥9分时方可离开PACU[9]。

1.4　观察指标　记录并比较：（1）三组丙泊酚用量、苏醒时间（最后一次给药至睁眼配合）、离室时间（最后一次给药至改良Aldrete评分≥9分[9]）；（2）记录麻醉前（T0）、内镜进入食管入口时（T1）、苏醒时（T2）的呼吸频率（respiratory rate，RR）、SpO_2、MAP和心率；（3）麻醉后不良事件包括呼吸抑制、体动反应、托下颌干预以及恶心呕吐。（4）记录患者满意度、麻醉医生满意度以及内镜医生满意度。以口诉评分法进行满意度评分（0～10分），评分≥8分为满意[10]。

1.5　统计学方法　采用SPSS 27.0软件对研究数据进行统计分析。符合正态分布的计量资料以$\bar{x}\pm s$表示，多组间比较采用单因素方差分析，两组间比较采用独立样本t检验，组内比较采用配对t检验。不符合正态分布的计量资料以$M(P_{25},P_{75})$表示，比较采用Kruskal-Wallis H检验，重复测量资料比较采用广义估计方程。计数资料以例（%）表示，组间比较采用χ^2检验。P<0.05为差异有统计学意义。

2　结　果

2.1　一般资料比较　三组性别、年龄、BMI、ASA分级的比较差异无统计学意义（P>0.05）。见表1。

2.2　生命体征比较　T1时，N1组和N2组的RR、SpO_2、MAP高于S组，差异有统计学意义（P<0.05）；N2组的RR及心率高于N1组，差异有统计学意义（P<0.05）。见表2。

2.3　不良反应比较　与S组比较，N1组和N2组呼吸抑制及托下颌干预发生率较低，差异有统计学意义（P<0.05）；术中体动反应的发生率3组差异无统计学意义（P>0.05）；N2组中未出现恶心呕吐，发生率低于S组的6.2%（4/65），差异有统计学意义（P<0.05）。见表3。

2.4　三组患者麻醉指标比较　三组患者丙泊酚用量比较，差异无统计学意义（P>0.05）；S组苏醒时间与离室时间显著长于N1组和N2组，差异有统计学意义（P<0.05）。见表4。

表1　三组一般资料比较　（n=65）

Tab.1　Comparison of general data among three groups　（n=65）

组别	性别（男/女，例）	年龄（岁，$\bar{x}\pm s$）	BMI（kg/m^2，$\bar{x}\pm s$）	ASA分级（Ⅰ/Ⅱ，例）
S组	24/41	49.3±9.1	23.7±2.3	14/51
N1组	27/38	50.7±8.1	23.2±2.5	11/54
N2组	29/36	49.4±9.3	23.5±2.6	13/52
χ^2/F值	0.805	0.497	0.825	0.458
P值	0.672	0.609	0.440	0.795

表2　三组不同时间点生命体征比较　［n=65，$M(P_{25},P_{75})$］

Tab.2　Comparison of vital signs among three groups at different time points　［n=65，$M(P_{25},P_{75})$］

组别	MAP（mmHg）			心率（次/min，$\bar{x}\pm s$）		
	T0	T1	T2	T0	T1	T2
S组	87.0(78.5,101.5)	69.0(61.0,77.5)	77.0(68.5,86.0)	76.4±11.9	67.1±8.1	70.0±8.6
N1组	92.0(86.0,100.0)	78.0(72.0,88.5)[a]	81.0(75.0,86.5)	76.3±12.4	68.2±9.6	69.5±9.1
N2组	90.0(78.0,100.0)	79.0(66.0,85.0)[a]	81.0(69.0,89.0)	78.5±12.8	72.0±9.1[ab]	72.6±9.3
$\chi^2/F_{组间/时间/交互}$值		2.073/98.326/0.897			1.539/91.578/0.665	
$P_{组间/时间/交互}$值		0.128/<0.001/0.474			0.217/<0.00180.642	
组别	RR（次/min）			SpO_2（%）		
	T0	T1	T2	T0	T1	T2
S组	19.0(19.0,20.0)	14.0(12.0,15.0)	18.0(18.0,19.0)	98(98,99)	97(95,97)	98(98,99)
N1组	19.0(18.0,20.0)	15.0(13.0,16.0)[a]	18.0(18.0,19.0)	98(98,99)	98(96,99)[a]	99(98,99)
N2组	19.0(18.5,20.0)	16.0(15.0,17.0)[ab]	18.0(17.0,19.0)	98(98,99)	98(96,99)[a]	99(98,99)
$\chi^2/F_{组间/时间/交互}$值		1.807/131.045/0.749			1.268/44.319/0.828	
$P_{组间/时间/交互}$值		0.166/<0.001/0.559			0.286/<0.001/0.508	

注：与S组比较，[a]P<0.05；与N1组比较，[b]P<0.05。

2.5　满意度的比较　N2组在患者满意度优于S组，在麻醉医生满意度方面优于N1组和S组，差异有统计学意义（P<0.05）。见表5。

表3　三组不良反应比较　［n=65，例（%）］

Tab.3　Comparison of adverse events among three groups ［n=65，case（%）］

组别	呼吸抑制	恶心呕吐	体动反应	托下颌干预
S组	12（18.5）	4（6.2）	8（12.3）	16（24.6）
N1组	4（6.2）[a]	1（1.5）	5（7.6）	4（6.2）[a]
N2组	2（3.1）[a]	0[a]	6（9.2）	2（3.1）[a]
χ^2值	10.282	5.337	0.816	17.625
P值	0.006	0.069	0.665	<0.001

注：与S组比较，[a]P<0.05。

表4　三组患者麻醉指标比较　［n=65，$M(P_{25},P_{75})$］

Tab.4　Comparison of anesthesia indicators among three groups ［n=65，$M(P_{25},P_{75})$］

组别	苏醒时间（min）	离室时间（min）	丙泊酚用量（mg，$\bar{x}\pm s$）
S组	7.0（6.0，8.0）	15.0（13.0，16.0）	102.9±23.6
N1组	5.5（5.0，6.0）[a]	13.5（13.0，14.5）[a]	104.5±21.8
N2组	5.5（5.0，6.0）[a]	13.0（12.5，13.5）[ab]	105.6±22.3
χ^2/F值	43.004	25.230	0.233
P值	<0.001	<0.001	0.792

注：与S组比较，[a]P<0.05；与N1组比较，[b]P<0.05。

表5　三组满意度的比较　［n=65，例（%）］

Tab.5　Comparison of satisfaction among three groups ［n=65，case（%）］

组别	患者满意	麻醉医生满意	内镜医生满意
S组	58（89.2）	53（81.5）	64（98.5）
N1组	62（95.4）	61（93.8）[a]	64（98.5）
N2组	64（98.5）[a]	63（96.9）[a]	65（100.0）
χ^2值	5.395	10.282	1.010
P值	0.067	0.006	0.603

注：与S组比较，[a]P<0.05。

3　讨　论

胃肠镜是目前消化道肿瘤筛查的主要方式[11]，可显著降低人群胃癌发病率[12]。在舒适化医疗的大背景下，无痛内镜检查已成为主流趋势。丙泊酚因其起效快、恢复快等优势，已成为门诊无痛胃肠镜的首选麻醉药，但快速或大剂量给药容易造成呼吸循环系统抑制，因此常与其他药物复合使用，以平衡镇静与镇痛需求，提升用药安全性[13-14]。丙泊酚复合芬太尼并保留自主呼吸的麻醉方法作为无痛胃肠镜麻醉中最为经典的麻醉方式，可以完善并增强镇静和镇痛效果，但同时也会增加呼吸抑制的概率和程度。在门诊腔镜室的抢救条件不如手术室完善的情况下该项麻醉技术亦存在着一定的安全隐患[15-16]。

小剂量纳美芬可以高选择性拮抗阿片类药物与μ2受体及κ受体的结合[17-18]。近年来，有学者提出使用阿片类镇痛药时可以复合小剂量阿片受体拮抗剂，通过竞争性地与阿片受体结合，阻断内源性或外源性阿片类物质的作用，从而减少阿片类镇痛药引起的呼吸抑制、低血压、瘙痒等副作用，但同时不影响其镇痛效果[19-20]。本研究通过预注射不同剂量的纳美芬来观察无痛胃肠镜中患者呼吸抑制的情况，结果显示，0.1 μg/kg 和 0.2 μg/kg 的纳美芬预注射均可降低患者呼吸抑制的发生率，不良反应少，麻醉过程平稳，其中以 0.2 μg/kg 的纳美芬预注射效果最佳。本研究存在一定局限性，纳入分析的患者数量相对有限，后续研究有必要进一步扩大样本规模，从而更有效地控制研究结果的潜在偏倚，提升研究的准确性与可靠性。

综上所述，在门诊无痛胃肠镜检查中，预先静脉注射小剂量纳美芬是安全可行的。这一操作能够有效稳定患者RR，降低呼吸抑制的发生概率，同时显著缩短苏醒时长，提升苏醒质量。值得一提的是，该方式不会对麻醉期间的镇静与镇痛效果产生不良影响，还能减少恶心呕吐、低血压等不良反应，极大地提高了门诊无痛检查的安全性与舒适度，具有很高的临床应用价值。

利益冲突　无

参考文献

［1］ Tang LL, Ye CX, Wang N, et al. The Median effective doses of propofol combined with two different doses of nalbuphine for adult patients during painless gastroscopy［J］. Front Pharmacol, 2022, 13: 1014486.

［2］ Zheng LL, Wu XY, Gu W, et al. Development and validation of a hypoxemia prediction model in middle-aged and elderly outpatients undergoing painless gastroscopy［J］. Sci Rep, 2025, 15（1）: 17965.

［3］ Deng J, Yu YF, Tang ZG, et al. Efficacy and safety of low-dose esketamine for painless gastrointestinal endoscopy in adults: a systematic evaluation and meta-analysis［J］. Front Pharmacol, 2024, 15: 1364546.

［4］ Sneyd JR, Absalom AR, Barends CRM, et al. Hypotension during propofol sedation for colonoscopy: a retrospective exploratory analysis and meta-analysis［J］. Br J Anaesth, 2022, 128(4): 610-622.

［5］ Wang Y, Zhao L, Wu M, et al. Different doses of nalmefene combined with hydromorphone hydrochloride for postoperative analgesia after colorectal surgery: a randomized controlled study［J］. BMC Surg, 2024, 24(1): 3.

［6］ Li GT, Yan H, Li WS, et al. Nalmefene effectively relieves thoracic epidural opioid-induced pruritus without affecting analgesia: a randomized controlled clinical trial［J］. J Thorac Dis, 2025, 17(4): 2028-2037.

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[8] 陈熹，冯甜甜，张金辉，等. 环泊酚用于烧伤切痂植皮手术全身麻醉诱导的有效性及安全性：随机对照试验[J]. 药物评价研究，2024，47(9)：2116-2121.
[9] Sousonis V, Asvestas D, Vavouris E, et al. The use of intracardiac echocardiography in catheter ablation of atrial fibrillation[J]. Curr Cardiol Rep, 2024, 26(9): 893-901.
[10] 中华医学会消化内镜学分会麻醉协作组. 常见消化内镜手术麻醉管理专家共识[J]. 临床麻醉学杂志，2019，35(2)：177-185.
[11] 蒋婷婷，刘月，徐漫，等. 复合丙泊酚时阿芬太尼抑制胃镜置入反应的半数有效剂量[J]. 临床麻醉学杂志，2022，38(8)：791-794.
[12] 回宇峰，谭思琪，孙莹杰. 环泊酚联合阿芬太尼用于支气管镜检查术患者的临床研究[J]. 中国临床药理学杂志，2024，40(19)：2806-2810.
[13] Gan TJ, Bertoch T, Habib AS, et al. Comparison of the efficacy of HSK3486 and propofol for induction of general anesthesia in adults: a multicenter, randomized, double-blind, controlled, phase 3 noninferiority trial[J]. Anesthesiology, 2024, 140(4): 690-700.
[14] 王龙江，庞轩，郑紫晨，等. 环泊酚联合艾司氯胺酮麻醉用于支气管内超声检查的安全性研究[J]. 实用药物与临床，2024，27(7)：525-531.
[15] 梅凤美，杨坤，吴姗姗，等. 环泊酚与丙泊酚在经鼻内镜垂体瘤切除术中的比较[J]. 临床神经外科杂志，2023，20(5)：531-535.
[16] Zeng Y, Wang DX, Lin ZM, et al. Efficacy and safety of HSK3486 for the induction and maintenance of general anesthesia in elective surgical patients: a multicenter, randomized, open-label, propofol-controlled phase 2 clinical trial[J]. Eur Rev Med Pharmacol Sci, 2022, 26(4): 1114-1124.
[17] 胡泽凡，岳定雄，胡忠诚，等. 环泊酚复合纳布啡在门诊无痛人工流产术中的应用[J]. 临床麻醉学杂志，2023，39(12)：1328-1331.
[18] Li J, Wang X, Liu J, et al. Comparison of cipepofol (HSK3486) versus propofol for the induction of deep sedation during gastroscopy and colonoscopy procedures: a multi-centre, non-inferiority, randomized, controlled phase 3 clinical trial[J]. Basic Clin Pharmacol Toxicol, 2022,131(2):138-148.

收稿日期：2024-11-26 **修回日期**：2025-02-11 **编辑**：李方

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[7] Tournier N, Pottier G, Caillé F, et al. Nalmefene alleviates the neuroimmune response to repeated binge-like ethanol exposure: a TSPO PET imaging study in adolescent rats[J]. Addict Biol, 2021, 26(3): e12962.
[8] Windisch KA, Morochnik M, Reed B, et al. Nalmefene, a mu opioid receptor antagonist/kappa opioid receptor partial agonist, potentiates cocaine motivation but not intake with extended access self-administration in adult male mice[J]. Neuropharmacology, 2021, 192: 108590.
[9] 王伯花，刘凤芝，李希明. 脑电双频指数监测下瑞马唑仑在老年患者无痛胃肠镜检查中的剂量[J]. 中国临床研究，2024，37(4)：519-524.
[10] 易强林，莫怀忠，胡慧，等. 环泊酚与丙泊酚在老年患者无痛胃镜检查中的比较[J]. 临床麻醉学杂志，2022，38(7)：712-715.
[11] Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries[J]. CA Cancer J Clin, 2024, 74(3): 229-263.
[12] Li P, Qi X, Bai RH, et al. The spatiotemporal associations between esophageal and gastric cancers provide evidence for its joint endoscopic screening in China: a population-based study[J]. BMC Med, 2024, 22(1): 364.
[13] Koo BW, Na HS, Park SH, et al. Comparison of the safety and efficacy of remimazolam and propofol for sedation in adults undergoing colonoscopy: a meta-analysis of randomized controlled trials[J]. Medicina (Kaunas), 2025, 61(4): 646.
[14] 杨亚崇，帅世超，韩静，等. 小剂量瑞马唑仑复合丙泊酚在老年患者胃肠镜诊疗中的镇静效果[J]. 中国临床研究，2023，36(8)：1205-1209.
[15] Sidhu R, Turnbull D, Haboubi H, et al. British Society of Gastroenterology guidelines on sedation in gastrointestinal endoscopy[J]. Gut, 2024, 73(2): 219-245.
[16] Hardman B, Karamchandani K. Management of anesthetic complications outside the operating room[J]. Curr Opin Anaesthesiol, 2023, 36(4): 435-440.
[17] Fan YZ, Duan YL, Chen CT, et al. Advances in attenuating opioid-induced respiratory depression: a narrative review[J]. Medicine (Baltimore), 2024, 103(29): e38837.
[18] Ma XW, Liu JY, Tang Y, et al. The efficacy of nalmefene on anesthetic recovery of patients: a study protocol for a multicenter randomized controlled trial[J]. Trials, 2023, 24(1): 156.
[19] Wang J, Zheng K, Wen Q, et al. Sufentanil combined with nalmefene reduce the adverse events in recovery period of patients undergoing uvulopalatopharyngoplasty-a randomized controlled trial[J]. Heliyon, 2023, 9(2): e13241.
[20] Yan H, Chen JJ, Luo JW, et al. Prophylatic use of IV nalmefene to prevent epidural opioid-induced pruritus: a multicenter, randomized clinical trial[J]. J Clin Anesth, 2024, 92: 111301.

收稿日期：2025-04-03 **修回日期**：2025-07-29 **编辑**：王宇