

EC₅₀ and EC₉₅ of Remifentanyl for Inhibiting Bronchoscopy Responses in Elderly Patients During Fiberoptic Bronchoscopy Under Ciprofol Sedation: An Up-and-Down Sequential Allocation Trial

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Background: Opioids are used to suppress cough during fiberoptic bronchoscopy (FOB). However, evidence regarding the optimal dose of remifentanyl during FOB under ciprofol sedation is limited. This study aimed to investigate the effective concentration (EC) of remifentanyl required to suppress bronchoscopy responses during FOB under ciprofol sedation in elderly patients.

Materials and Methods: Elderly patients aged 60 to 90 years with American Society of Anesthesiologists (ASA) physical status I–III, scheduled for FOB, were enrolled. Patients were assigned to either the male or the female group. Remifentanyl was administered intravenously prior to ciprofol administration. The endpoints included responses to FOB, such as vocal cords movement, coughing, and body movement. The EC₅₀ and EC₉₅ values of remifentanyl required to alleviate the responses to FOB were calculated using Dixon's up-and-down method for both male and female groups. Probit analysis was used to generate a dose-response curve.

Results: Thirty-nine patients (19 males and 20 females) were enrolled. The EC₅₀ values (plasma concentration) of remifentanyl for blunting FOB responses under ciprofol sedation were 3.25 (2.75 to 3.26) ng/mL and 2.25 (1.75 to 2.25) ng/mL in males and females, respectively ($p = 0.0023$). Probit analysis indicated that the EC₅₀ of remifentanyl required to suppress responses to FOB under ciprofol sedation was 3.102 [95% confidence interval (CI): 2.694 to 3.749] ng/mL and 2.052 [95% CI: 1.345 to 2.750] ng/mL in males and females, respectively. The EC₉₅ of remifentanyl required to suppress responses to FOB under ciprofol sedation was 3.741 [95% CI: 3.366 to 7.699] ng/mL and 2.943 [95% CI: 2.456 to 9.533] ng/mL in males and females, respectively.

Conclusion: The results indicate differences between males and females in the EC₅₀ and EC₉₅ of remifentanyl needed to suppress responses to FOB under ciprofol sedation while preserving spontaneous breathing in elderly patients.

Trial Registration: The study was registered with chictr.org.cn (ChiCTR2300077720; 17th November 2023).

Keywords: remifentanyl, ciprofol, bronchoscopy, anesthesia, effective concentration

Introduction

The acceleration of global aging places a significant burden on the healthcare systems.¹ In particular, the prevalence of pulmonary diseases is rapidly increasing, affecting most older individuals. Clinically, fiberoptic bronchoscopy (FOB) is one of the most effective methods for diagnosing and treating this condition. Current guidelines recommend performing this procedure under sedation to minimize cough reactions and perioperative stress.^{2,3} Propofol is commonly used for sedation. However, propofol has several shortcomings, including injection pain and circulatory and respiratory depression, highlighting

the need for alternatives.⁴ Ciprofol is a novel intravenous general anesthetic. By binding to gamma-aminobutyric acid-A receptors (GABA_ARs), ciprofol induces effective sedation with a rapid onset and offset, and no injection pain at the injection site.^{5–7} Ciprofol also protects the heart by reducing oxidative stress in mice.⁸ Ciprofol has been successfully used for general anesthesia^{6,9–11} and sedation in intensive care unit patients.⁷

Opioids, including alfentanil and remifentanil, are commonly used for cough suppression during FOB.^{12,13} The combination of ciprofol and remifentanil has been successfully used in younger patients undergoing FOB.¹⁴ However, data on the optimal dose of remifentanil for suppressing bronchoscopy responses during FOB under deep sedation with ciprofol in elderly patients are lacking. The purpose of this study was to investigate the EC₅₀ and EC₉₅ of remifentanil required to suppress responses to FOB through the laryngeal mask (LMA) under ciprofol sedation while preserving spontaneous breathing in elderly patients. We hypothesized that differences exist between males and females in the EC₅₀ and EC₉₅ of remifentanil required to suppress responses to FOB in elderly patients.

Materials and Methods

The protocol was approved by the Medical Ethics Committee of the First Affiliated Hospital of Guangxi Medical University (2023-E606-01) and registered at chictr.org.cn (ChiCTR2300077720, 17th November 2023). The trial adhered to the TREND Statement and Declaration of Helsinki. All participants provided written informed consent and were informed of the purpose of the study.

Patients

From the 17th November 2023 until the 30th December 2023 patients requiring diagnostic bronchoscopy at the First Affiliated Hospital of Guangxi Medical University were consecutively enrolled in the study. The inclusion criteria were as follows: age 60–90 years and American Society of Anesthesiologists (ASA) 1–III physical status. Exclusion criteria included contraindications to bronchoscopy, difficult airways, severe airway stenosis and acute infection, opioid allergy, severe hypertension (systolic blood pressure ≥ 180 mmHg, or diastolic blood pressure ≥ 110 mmHg), severe arrhythmia (manifested as sinus bradycardia with a ventricular rate of <50 beats per minute, atrioventricular block or ventricular block of degree II or above, or other arrhythmias with a high risk of sinus arrest, such as sick sinus syndrome), New York Heart Association Class III or higher with severe heart failure, liver dysfunction characterized by abnormal biochemical indicators of liver function, preoperative consciousness state that is difficult to determine independently or accurately, a history of psychotropic drug use, or any other criteria deemed inappropriate by the researchers for inclusion in this study.

Study Design

This study was an Up-and-Down Sequential Allocation Trial. Patients were assigned to female and male groups. The EC₅₀ (plasma concentration) of remifentanil required to suppress responses to FOB was obtained by calculating the average of the midpoint dose of each pair of patients after seven inflection points were obtained, and was calculated by probit analysis, according to a modified Dixon's up-and-down method.^{15,16} Based on the pre-experimental results, the initial plasma concentration of remifentanil was set to 2 ng/mL. The next plasma concentration of remifentanil was increased or decreased by 0.5 ng/mL based on the responses to FOB. After seven inflection points were completed, recruitment was terminated.

Sedation and Bronchoscopy

All patients fasted for less than 8 hours before general anesthesia. Premedication was not administered. Standard monitors included electrocardiography, non-invasive blood pressure (NIBP), pulse oxygen saturation (SpO₂), automatic respiratory rate (RR), end-tidal carbon dioxide (ETCO₂), and bispectral index (BIS). Before starting anesthesia induction, all patients received supplemental oxygen through a face mask at a flow rate of 6 L/min for 3 min. Remifentanil was administered by using a target-controlled infusion pump. The initial plasma concentration of remifentanil was increased or decreased by 0.5 ng/mL based on the previous responses to FOB. After the effective concentration of remifentanil balanced with plasma concentration, all patients received an initial intravenous bolus of 0.4 mg/kg ciprofol and maintained between 0.2–1.0 mg/kg/h.^{17–19} When the

BIS ≤ 60 , a LMA was inserted with bare hands, and the position was verified by chest auscultation and capnography. The BIS was maintained within 50–60 during the anesthesia maintenance stage. All FOB procedures were performed through the LMA by two experienced endoscopists. The type of flexible bronchoscopes used was determined by the endoscopist according to clinical need. During the FOB, endotracheal lidocaine (20 mg/mL) was administered using a syringe. The target zones for lidocaine included the vocal cords (40 mg), trachea (100 mg), main carina (40 mg), right main bronchi (40 mg), and left main bronchi (40 mg).

Assessment of Bronchoscopy Responses

The bronchoscopy reaction was assessed using a bronchoscopy score. The bronchoscopy score included three variables: vocal cord movement, cough severity, and limb movement. Each variable was scored on a 4-point scale. Vocal cord movement was graded as 1 (complete relaxation of the vocal cords), 2 (vocal cords inward during inhalation), 3 (vocal cords outward during inhalation), or 4 (vocal cords completely closed). Cough severity was graded as 1 (no coughing), 2 (coughing once or twice in sequence), 3 (coughing three or four times in sequence), and 4 (coughing more than five times in sequence). Limb movement was graded as 1 (no movement in the upper limb, lower limb, or trunk), 2 (one movement in the upper limb, lower limb, or trunk), 3 (two movements in the upper limb, lower limb, or trunk), or 4 (all movements in the upper limb, lower limb, or trunk). All scores were assessed at the first FOB insertion through the LMA. The final bronchoscopy scores were 3 (optimal score) to 12 (worst score).

Study Endpoints

The primary outcome was the incidence of bronchoscopy reaction. Bronchoscopy reaction was defined as a final bronchoscopy score > 6 . The secondary outcomes included vital signs at the following time points: at 5 min before anesthesia induction (baseline), at loss of consciousness (LOC), at BIS ≤ 60 , at the completion of LMA insertion, at the start of FOB, at the end of FOB, and at the time of eyes opening. Other secondary outcomes included administration of anesthetic drugs, duration of anesthesia and FOB procedures, and the minimum spontaneous breathing rate and SpO₂. The adverse events included needing assisted ventilation, respiratory depression (defined as meeting at least one of the following criterias: respiratory rate [RR] ≤ 8 breaths/min; apnea; SpO₂ $\leq 90\%$ [≥ 15 s]), hypotension ($\geq 20\%$ decrease in the mean arterial blood pressure (MBP) from baseline), hypertension ($\geq 20\%$ increase in the MBP from baseline), sinus tachycardia (> 100 beats/min), sinus bradycardia (< 50 beats/min), injection pain, delirium, hiccup, postoperative nausea and vomiting, and awareness.

Statistical Analysis

Statistical analysis was performed using GraphPad Prism 9.0 (GraphPad, La Jolla, CA, USA) and SPSS (version 25.0; IBM, Chicago, IL, USA). Normally distributed continuous data (tested by the Kolmogorov–Smirnov test) are presented as mean $\pm$ standard deviation. Normally distributed continuous data, such as MBP, heart rate (HR), and RR, were compared using repeated-measures analysis of variance. Other normally distributed continuous data were compared using an unpaired *t* test. Non-normally distributed data are presented as median (interquartile range) and were compared using the Mann–Whitney *U*-test. Categorical data are presented as *n* (%) and were compared using Fisher's exact test. Statistical significance was defined as *p* < 0.05 .

Results

Patients

We screened 46 elderly patients consecutively from the 17th November 2023 until the 30th December 2023. Ultimately, 19 males and 20 females of them agreed to participate in the study. None of the 39 patients were excluded from the analysis. The demographic characteristics of the patients are presented in Table 1. No differences were found in terms of age, body mass index (BMI), or ASA physical status between the groups. However, there were differences in the weight (*p* = 0.0012) and height (*p* < 0.0001) between the groups. No difference was found in the indication for FOB or diagnostic procedures between the groups (Table 2).

Table 1 Demographic Characteristics of Patients

Characteristic	Overall (n=39)	Male (n=19)	Female (n=20)	p value
Age, years	68.79±5.944	68.95±5.977	68.65±6.063	0.8783
Weight, kg	55.95±12.85	62.47±9.137	49.75±12.97	0.0012
Height, cm	158.7±8.703	165.1±6.900	152.7±5.244	< 0.0001
BMI, kg/m ²	22.50±3.128	22.94±2.971	22.09±3.212	0.3964
ASA physical status, n				0.4971
II	7	3	4	
III	32	16	16	

Note: Data are expressed as mean ± standard deviation or numbers of patients.

Abbreviations: BMI, body mass index; ASA, American Society of Anesthesiologists.

Table 2 Indication for Fiberoptic Bronchoscopy and Diagnostic Procedures

Characteristic	Male (n=19)	Female (n=20)	p value
Indication for FOB			0.810
Pneumonia	2 (10.53%)	3 (15.0%)	
Chronic cough	1 (5.26%)	0 (0%)	
Suspicion of malignancy	8 (42.11%)	8 (40.0%)	
Cancer	4 (21.05%)	5 (25.0%)	
COPD	2 (10.53%)	0 (0%)	
Bronchiectasis	0 (0%)	2 (10%)	
Hemoptysis	1 (5.26%)	1 (5.0%)	
Fever	1 (5.26%)	1 (5.0%)	
Diagnostic procedures			0.780
EI + BBi	1 (5.26%)	1 (5.0%)	
BAL	0 (0%)	2 (10.0%)	
BBi+ BAL	6 (31.58%)	4 (20.0%)	
BBi+BBi+BBi+BBi	1 (5.26%)	0 (0%)	
EI + BAL + BB+ TBLB	10 (52.63%)	11 (55.0%)	
Photodynamics therapy	1 (5.26%)	2 (10.0%)	

Note: Variables are expressed as n (%).

Abbreviations: BAL, Bronchoalveolar lavage; BBi, bronchoscopic biopsy; BBi, bronchia brushings; COPD, Chronic obstructive pulmonary disease; EI, Endobronchial inspection; TBLB, Transbronchial lung biopsy.

EC₅₀ and EC₉₅

The seven inflection points are shown in Figure 1. The EC₅₀ values of remifentanyl for the blunting FOB reaction under sedation with ciprofol were 3.25 (2.75 to 3.26) ng/mL and 2.25 (1.75 to 2.25) ng/mL in males and females, respectively ($p = 0.0023$).

A dose-response curve from the probit analysis of the remifentanyl dose and the probability of no bronchoscopy reaction is shown in Figure 2. The EC₅₀ values of remifentanyl in the male and female groups were compared. Probit analysis showed the EC₅₀ of remifentanyl required to suppress responses to FOB under deep sedation with ciprofol was 3.102 [95% confidence interval (CI): 2.694 to 3.749] ng/mL and 2.052 [95% CI: 1.345 to 2.750] ng/mL in males and females, respectively. EC₉₅ of remifentanyl required to suppress responses to FOB under deep sedation with ciprofol were 3.741 [95% CI: 3.366 to 7.699] ng/mL and 2.943 [95% CI: 2.456 to 9.533] ng/mL in males and females, respectively.

Medication

The medications are listed in Table 3. No difference was observed in the administration of ciprofol or remifentanyl. The dosage of endotracheal lidocaine used was similar between the groups. The mean or median duration of FOB, anesthesia, and recovery were similar between the groups.

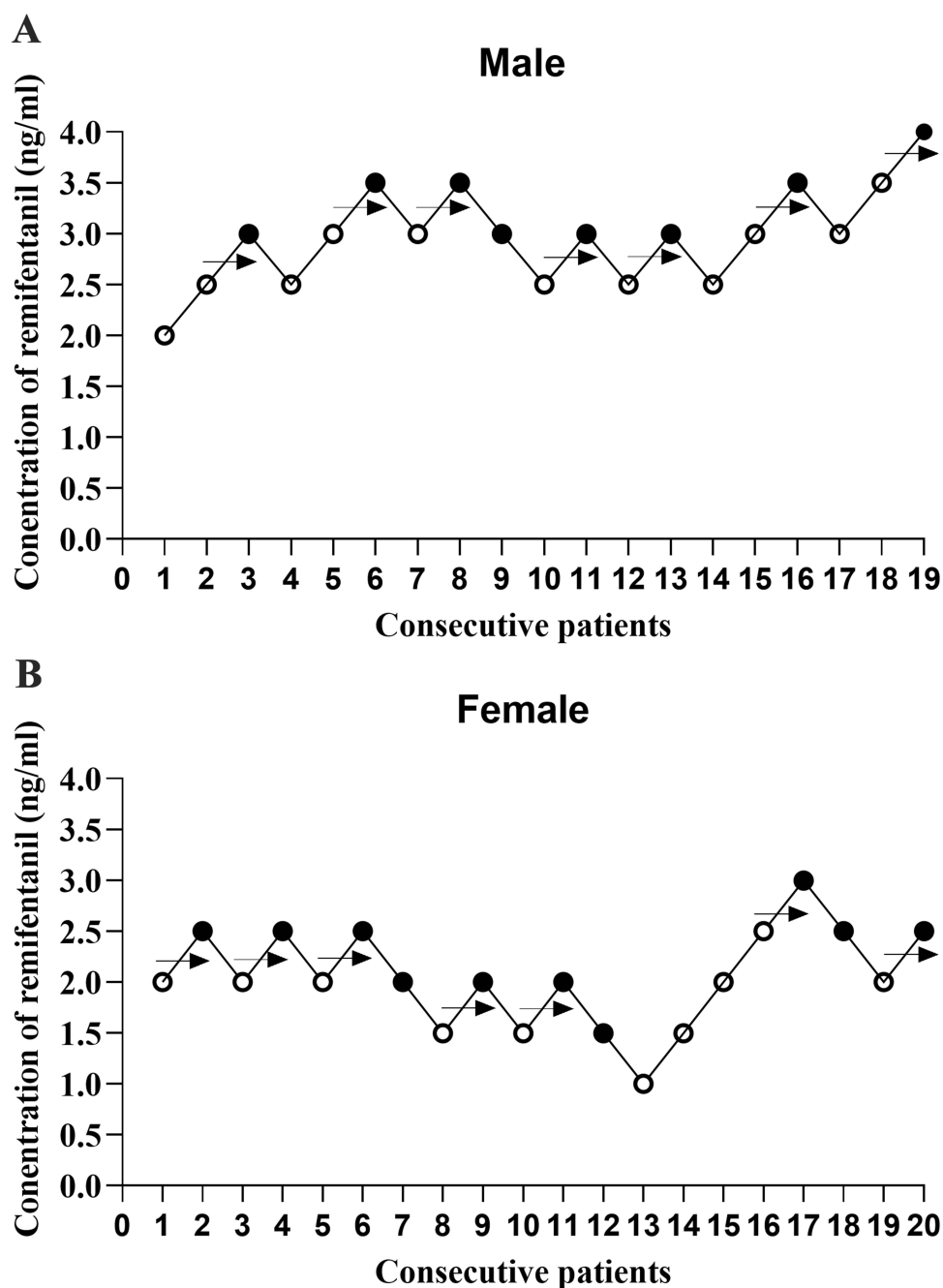


Figure 1 The dose of remifentanyl in consecutive male (A) and female (B) patients undergoing fiberoptic bronchoscopy. The response of patients was presented as black (negative) or white (positive) circle. The arrow indicated the inflection point of the bronchoscopy reaction from positive to negative. Each group completed seven inflection points.

Vital Signs During Bronchoscopy

Vital signs are presented in Figure 3 and Table 3. The MBP ($p < 0.05$) and HR ($p < 0.001$) were higher in the male group than in the female group at BIS ≤ 60 . No other between-group differences in vital signs were observed at any of the time points. There was no difference between the groups in terms of minimum respiratory rate and minimum SpO₂.

Adverse Events

Adverse events are presented in Table 4. No difference was found in the proportion of patients developed at least one adverse events between males ($n = 17$ [89.47%]) and females ($n = 15$ [75.0%]) ($p = 0.4075$). The most adverse events

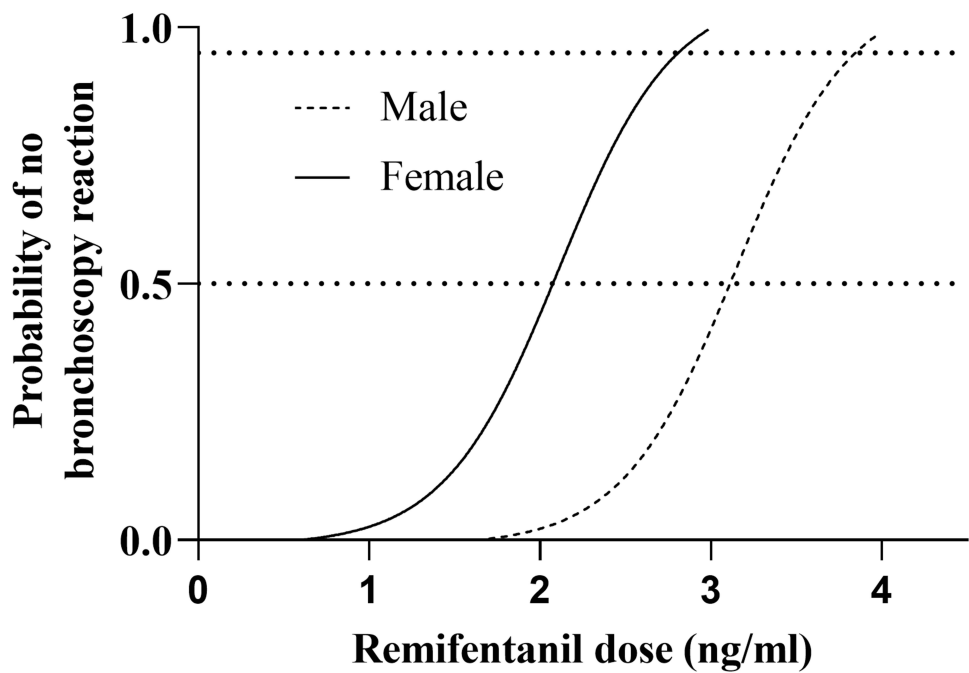


Figure 2 A dose-response curve from the probit analysis of remifentanyl dose and the probability of no bronchoscopy reaction. The EC₅₀ of remifentanyl in male and female groups was compared.

were respiratory depression (males, n = 15 [78.95%] vs females, n = 14 [70.0%]; $p > 0.7164$) and hypotension (males, n = 14 [73.68%] vs females, n = 14 [70.0%]; $p > 0.9999$), but there was no difference between groups. Three and two patients need assisted ventilation in the male and female groups, respectively ($p = 0.6614$). Six patients developed sinus tachycardia in female group (males: n = 0 [0%] vs females: n = 6 [30.0%]; $p = 0.0202$). There were no differences between the groups in terms of hypertension, sinus bradycardia, or hiccups. None of the patients developed injection pain, delirium, PONV, or awareness during FOB.

Discussion

The current study investigated the optimal dose of remifentanyl required to suppress responses to FOB through LMA under ciprofol sedation. The results suggested that there was a difference between males and females regarding the EC₅₀ and EC₉₅ of remifentanyl required to suppress responses to FOB through LMA under deep sedation with ciprofol while preserving spontaneous breathing in elderly patients.

Remifentanyl-based drugs are commonly used for anesthesia and pain control. The median EC₅₀ of remifentanyl required to inhibit noxious stimulation during propofol anesthesia has been reported. For example, the EC₅₀ of

Table 3 Medication and Breathing Characteristics During Fiberoptic Bronchoscopy

Characteristics	Male (n=19)	Female (n=20)	p value
Administration of ciprofol (mg)	39.30 (32.60 to 46.26)	33.20 (28.68 to 43.68)	0.3088
Administration of remifentanyl (ug)	216.0 (170.0 to 280.0)	188.5 (115.6 to 242.1)	0.2010
Dosage of Endotracheal lidocaine (mg)	260.0 (260.0 to 260.0)	260.0 (260.0 to 260.0)	>0.9999
Duration of FOB (min)	26.85 ± 15.80	27.60 ± 15.48	0.8817
Duration of anesthesia (min)	32.00 (19.62 to 37.00)	32.00 (24.50 to 37.75)	0.6612
Duration of recovery (min)	9.081 ± 3.581	8.700 ± 4.044	0.7579
Minimum breathing rate (breaths/min)	8.0 (6.0 to 8.0)	8.0 (6.25 to 9.75)	0.5668
Minimum SpO ₂ (%)	99 (96 to 100)	99 (94 to 100)	0.6195

Note: Variables are presented as mean ± standard deviation or median (interquartile range).
Abbreviations: FOB, fiberoptic bronchoscopy; SpO₂, pulse oxygen saturation.

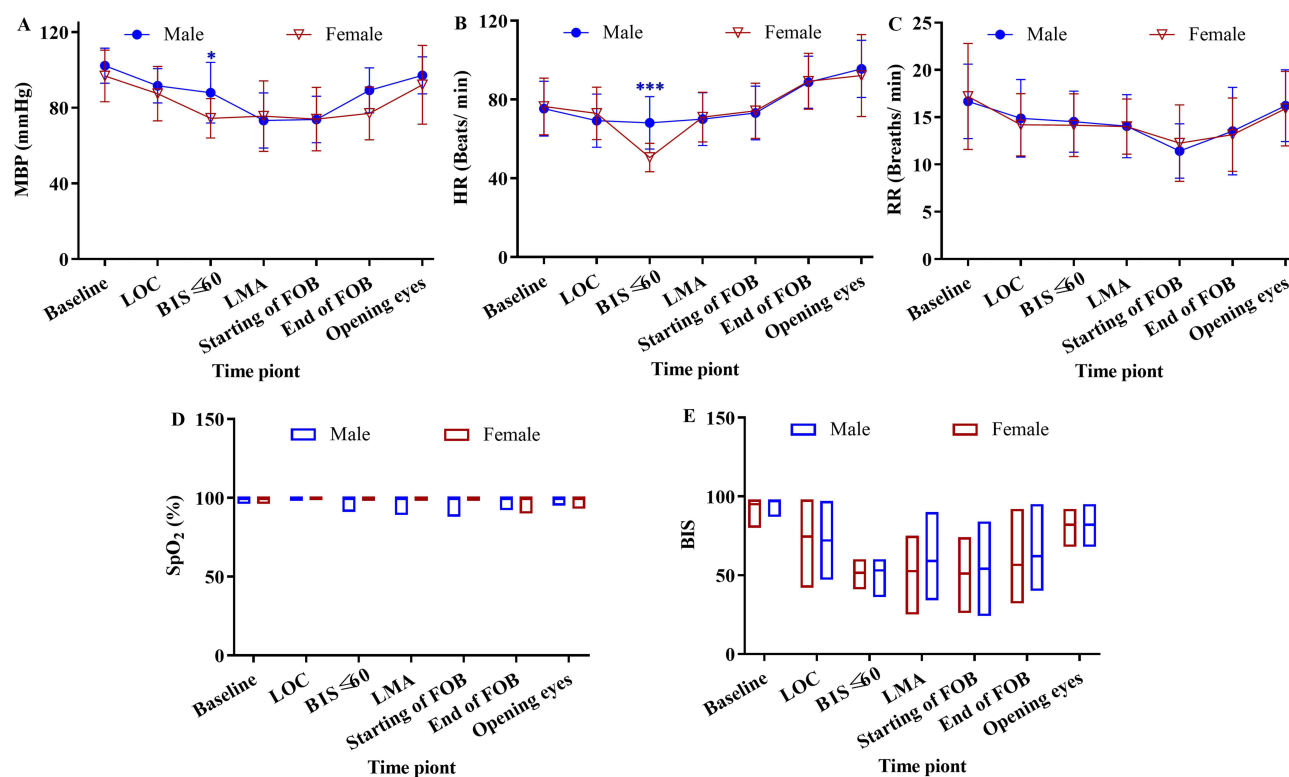


Figure 3 Vital signs of patients. Variables are presented as mean $\pm$ standard deviation (A–C) or median (interquartile range) (D and E). * $P < 0.05$, *** $P < 0.001$. (A) Drug: $F(1, 259) = 9.908$, $p = 0.0018$; Time: $F(6, 259) = 18.74$, $p < 0.0001$; Time $\times$ Drug: $F(6, 259) = 1.643$, $p = 0.1357$; (B) Drug: $F(1, 259) = 1.333$, $p = 0.2493$; Time: $F(6, 259) = 27.45$, $p < 0.0001$; Time $\times$ Drug: $F(6, 259) = 2.599$, $p = 0.0183$; (C) Drug: $F(1, 259) = 0.02038$, $p = 0.8886$; Time: $F(6, 259) = 7.480$, $p < 0.0001$; Time $\times$ Drug: $F(6, 259) = 0.1959$, $p = 0.9778$; (D) Drug: $F(1, 259) = 0.9756$, $p = 0.3242$; Time: $F(6, 259) = 2.431$, $p = 0.0265$; Time $\times$ Drug: $F(6, 259) = 0.8971$, $p = 0.4975$; (E) Drug: $F(1, 259) = 2.475$, $p = 0.1169$; Time: $F(6, 259) = 92.08$, $p < 0.0001$; Time $\times$ Drug: $F(6, 259) = 0.6991$, $p = 0.6506$.

Abbreviations: MBP, mean arterial blood pressure; RR, respiratory rate; HR, heart rate; SpO₂, pulse oxygen saturation; LOC, loss of consciousness; BIS, bispectral index; LMA, laryngeal mask; FOB, fiberoptic bronchoscopy.

remifentanyl required to inhibit CO₂ pneumoperitoneum was 4.17 ng/mL in females and 5.00 ng/mL in males.²⁰ The EC₅₀ of remifentanyl required to blunt sympathetic responses to tracheal intubation and skin incision was 5 and 2 ng/mL, respectively.²¹ However, the EC₅₀ for blunting sympathetic responses to tracheal intubation was 1.86 ng/mL in patients

Table 4 Adverse Events During Fiberoptic Bronchoscopy

Characteristic	Male (n=19)	Female (n=20)	p value
Respiratory depression	15 (78.95%)	14 (70.0%)	0.7164
RR $\leq$ 8 (breathing/ min)	15 (78.95%)	14 (70.0%)	0.7164
Apnea	1 (5.26%)	1 (5%)	>0.9999
SpO ₂ $\leq$ 90% ($\geq$ 15s)	2 (10.53%)	2 (10.0%)	>0.9999
Assisted ventilation	3 (15.79%)	2 (10.0%)	0.6614
Hypertension	1 (5.26%)	1 (5.0%)	>0.9999
Hypotension	14 (73.67%)	14 (70.0%)	>0.9999
Sinus tachycardia	0 (0%)	6 (30%)	0.0202
Sinus bradycardia	4 (21.05%)	2 (10.0%)	0.4075
Injection pain	0 (0%)	0 (0%)	>0.9999
Delirium	0 (0%)	0 (0%)	>0.9999
Hiccup	0 (0%)	1 (5.0%)	0.4872
PONV	0 (0%)	0 (0%)	>0.9999
Awareness	0 (0%)	0 (0%)	>0.9999

Note: Variables are expressed as n (%).

Abbreviations: PONV, postoperative nausea and vomiting; RR, respiratory rate; SpO₂, pulse oxygen saturation.

with Parkinson's Disease (PD) and 3.20 ng/mL in those without PD.²² The EC₅₀ for blunting the response to skin incision was 2.17 ng/mL in patients with PD and 3.09 ng/mL in those without PD.²² To our knowledge, this study is the first to investigate the EC₅₀ and EC₉₅ of remifentanyl required to suppress responses to FOB through the LMA under deep sedation with ciprofol while preserving spontaneous breathing in elderly patients. Our results indicated that the EC₅₀ of remifentanyl for blunting FOB reaction under sedation with ciprofol was 3.25 ng/mL and 2.25 ng/mL in males and females, respectively. These findings suggest that inhibiting different degrees of noxious stimulation requires varying EC₅₀ values of remifentanyl during propofol-based anesthesia, whereas inhibiting the same noxious stimulation requires different EC₅₀ values of remifentanyl between propofol-based anesthesia and ciprofol-based anesthesia. The differences in weight and height between the groups had a minor impact on the EC₅₀ of remifentanyl, which was calculated and adjusted for these covariates in the Minto model.

Sex differences influence the efficacy of opioid. Males need higher doses of opioids to achieve the same therapeutic effect.^{23–25} For example, males required more remifentanyl than females for LMA insertion under propofol anesthesia.²⁶ The EC₅₀ of remifentanyl required to inhibit response to CO₂ pneumoperitoneum was higher in males than in females under propofol anesthesia.²⁰ The EC₅₀ of remifentanyl required to prevent emergence cough was higher in male patients compared to female patients.²⁷ Our results suggest that the EC₅₀ and EC₉₅ of remifentanyl required to suppress responses to FOB through LMA under deep sedation with ciprofol, while preserving spontaneous breathing in elderly patients, were lower in females than in males. These results reinforce the concept that sex differences affect responses to opioid treatment. Several reasons may contribute to this disparity. First, variations in physiology and pharmacology between males and females impact on drug efficacy. Females have a higher percentage of fat and a lower percentage of water than males, affecting drug distribution. Second, female hormones affect the affinity for mu-opioid receptors. Females have a higher binding affinity to mu-opioid receptors (MORs) and a greater response to MORs agonists than males.^{28–30} Third, when exposed to acute psychological pressure and experimental tasks, females had lower cortisol responses than males. Finally, sex differences affect the activity of nonspecific esterase responsible that metabolize remifentanyl.³¹

The major adverse events included respiratory depression and hypotension. However, no differences were observed between the groups. Ciprofol is a novel entrant similar to propofol. By binding to GABAARs, ciprofol achieves sedative or anesthetic effects with a rapid onset and offset.³² Ciprofol induces cardiovascular depression by inhibiting vascular tension and myocardial contractions. Opioid-induced respiratory depression (OIRD) is the most common complication associated with opioids.³³ By activating MORs on neurons in respiratory circuits, opioids inhibit chemosensory respiratory responses, leading to respiratory depression.^{34–36} The respiratory rate and tidal volume decreased.^{37,38} The incidence of hypotension and respiratory depression was higher than that reported in previous studies,^{32,39–41} but was consistent with the findings of Zhong et al.⁴² We attribute this to the following reasons. First, the higher incidence of hypotension may be due to the absence of saline infusion before anesthesia. Second, the initial dosage of ciprofol was fixed (0.4 mg/kg). The ED₅₀ of ciprofol required to inhibit responses during upper gastrointestinal endoscopy decreased with increasing age in elderly patients.⁴³ Ignoring age differences, a fixed dosage of ciprofol may increase the incidence of cardiopulmonary depression. Third, the combination of ciprofol and remifentanyl may increase the risk of respiratory and hemodynamic adverse events due to their synergistic cardiopulmonary depressant properties, similar to the combination of propofol and remifentanyl.⁴⁴ Fourth, the different definitions of cardiopulmonary inhibition led to varying outcomes. In our study, respiratory depression was defined as meeting at least one of the following criteria: RR ≤ 8 breaths/min, apnea, or SpO₂ ≤ 90% (≥ 15s). Hypotension was defined as a ≥ 20% decrease in the MBP from the baseline, differing from definitions in other reports.

This study had several limitations. First, we did not directly measure the actual blood EC of remifentanyl. Instead, we calculated the EC using the Minto pharmacokinetic model. This model has been widely used in clinical settings with acceptable levels of inaccuracies and biases. Second, the limitations of the “up-and-down” method may affect the reliability of the EC₅₀ and EC₉₅ of remifentanyl. Further studies should measure the actual blood EC of remifentanyl. Finally, all the patients were enrolled from the same region. Therefore, our results cannot be directly generalized to other ethnicities.

Conclusion

The results suggested a difference between males and females in the EC₅₀ and EC₉₅ of remifentanyl required to suppress responses to FOB via LMA under deep sedation with ciprofol, while preserving spontaneous breathing in elderly patients.

Abbreviation

ASA, American Society of Anesthesiologists; BAL, Bronchoalveolar lavage; BBi, bronchoscopic biopsy; BBr, bronchia brushings; BIS, bispectral index; BMI, body mass index; CI, confidence interval; COPD, Chronic obstructive pulmonary disease; EC, effective concentration; EI, Endobronchial inspection; ETCO₂, end-tidal carbon dioxide; FOB, fiberoptic bronchoscopy; GABA_ARs, gamma-aminobutyric acid-A receptors; HR, heart rate; LMA, laryngeal mask; LOC, loss of consciousness; MBP, mean arterial blood pressure; PONV, postoperative nausea and vomiting; RR, respiratory rate; SpO₂, pulse oxygen saturation; TBLB: Transbronchial lung biopsy.

Data Sharing Statement

Data are available from the corresponding author (Xuehai Guan) upon request. All data are included in this published article.

Author's Contribution

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

Funding

This study was supported by the Guangxi Zhuang Autonomous Region Health Commission's Self Fund Research Project on Western Medicine (Z-A20230492), the Clinical Research "Climbing" Program of the First Affiliated Hospital of Guangxi Medical University (YYZS2022005), the Traditional Chinese medicine appropriate technology development and promotion project of Guangxi Zhuang Autonomous Region (GZSY22-59), and the Natural Science Foundation of Guangxi Zhuang Autonomous Region (2022GXNSFAA035628, 2024GXNSFAA010222).

Disclosure

The authors report no conflicts of interest in this work.

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