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CLINICAL TRIAL REPORT

The Efficacy and Safety Profile of Balanced Propofol Sedation for Bronchoscopy

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Purpose: We conducted a prospective, real-world study to evaluate the efficacy and safety of balanced propofol sedation (BPS) in bronchoscopy and identify an advantageous sedation regimen for such procedures.

Patients and Methods: The participants were placed in four groups based on their sedation regimen (exposure factor): the M-S group (midazolam + sufentanil for traditional sedation), R-S group (remimazolam + sufentanil for traditional sedation), M-S-P group (midazolam + sufentanil + propofol for BPS), and R-S-P group (remimazolam + sufentanil + propofol for BPS). The primary outcomes included satisfaction metrics (satisfaction of the patients, endoscopic physicians, and nurses) and follow-up questionnaires. The secondary outcomes included time metrics (induction time, recovery time, and discharge time), dosage metrics (induction dose, maintenance dose, and total dose of each sedative), completion rate of sedation, intraprocedural dose, and frequency of lidocaine spray in the airway, and incidence of adverse reactions.

Results: In total, 418 subjects were included in this study. Compared to traditional sedation, both BPS groups significantly increased the satisfaction of patients, endoscopic physicians, and nurses ($P < 0.05$) and reduced the incidence of intraprocedural wakefulness ($P < 0.05$). Additionally, induction and recovery of the BPS group were rapid, with high sedation completion rates and no increase in the incidence of intraprocedural and postprocedural adverse reactions ($P < 0.05$). The RSP group was better than the MSP group in terms of various time metrics and postprocedural adverse reactions.

Conclusion: BPS can be safely and effectively applied during bronchoscopy, with remimazolam and sufentanil combined with a small dose of propofol being an optimal medication regimen.

Keywords: balanced propofol sedation, bronchoscopy, remimazolam, midazolam, procedural sedation

Introduction

Balance propofol sedation (BPS), a technique proposed by gastroenterologists, involves the use of low-dose benzodiazepines (typically midazolam) along with opioids and a small dose of propofol to achieve the desired sedation level.[1] BPS provides easily adjustable sedation depth, minimal cardiorespiratory depression, rapid recovery, and high satisfaction among both patients and physicians.[2,3] The proposal of BPS has offered new perspectives for procedural sedation.

Bronchoscopy is a prevalent invasive diagnostic and therapeutic procedure for respiratory diseases. It often results in significant discomfort in patients during the procedure. Multiple guidelines suggest bronchoscopy under sedation or anesthesia.[4,5] The shared airway between the operator and the patient, the complexity of diagnostic procedures, and the presence of respiratory ailments in patients all increase the risk of sedation. Thus, selecting the appropriate sedative agents and the optimal level of sedation is crucial for bronchoscopic sedation.[6]

Commonly used sedatives for bronchoscopy include midazolam and propofol; both have certain limitations. The combination of midazolam with opioids for moderate sedation is a traditional sedation regimen. The increasing complexity of bronchoscopic procedures has increased patient discomfort, making it difficult for many patients to cooperate under traditional sedation.[7] According to recent regulatory changes, midazolam has been reclassified from a Class II to a Class I psychotropic drug (effective from July 1, 2024), further constraining its clinical application.[8] Propofol, known for its rapid

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onset and recovery, is considered an ideal agent for procedural sedation.[9] However, its cardiorespiratory depression effect is dose-dependent, and the safe dosage range is narrow. Thus, it poses significant risks and management challenges when used alone or in conjunction with opioids.[10] BPS has the advantages of minimal cardiopulmonary inhibitory effect and high patient and doctor satisfaction. These advantages make it theoretically suitable for bronchoscopy. Previous studies have already confirmed the safety of BPS in bronchoscopy, but its efficacy in bronchoscopic sedation needs to be investigated.[11]

Compared to midazolam, remimazolam, a novel ultrashort-acting benzodiazepine classified as a Class II psychotropic drug, offers rapid onset and offset and minimal cardiorespiratory depression. However, the feasibility of replacing midazolam with remimazolam in BPS needs to be determined.

In this prospective real-world study, we evaluated the efficacy and safety of BPS in bronchoscopy and identified the better sedation regimen for bronchoscopy.

Materials and Methods

Methods

This was a single-center, prospective real-world study aimed at monitoring and comparing the sedation effects and safety indicators of different sedation protocols during bronchoscopy to identify the optimal sedation regimen for bronchoscopy. The study was approved by the Ethics Committee of Qingdao University Affiliated Hospital (QYFYEC2023-111) and registered on clinicaltrials.gov (NCT06116955). The study adhered to the ethical principles outlined in the Declaration of Helsinki. All participants signed informed consent forms before the procedure.

This study included patients aged 18 years or older who underwent bronchoscopy at Qingdao University Affiliated Hospital (Laoshan Branch) between September and December 2023. The exclusion criteria were as follows: (1) patients with contraindications or allergies to anesthetics; (2) patients with a history of alcohol abuse or drug misuse; (3) patients with contraindications for cricothyroid membrane puncture; (4) patients with mental or neurological disorders or those with significant communication difficulties, poor comprehension, and inability to cooperate with the doctors; (5) patients requiring laryngeal mask insertion, tracheal intubation, or rigid bronchoscopy; (6) patients who refused sedation or did not provide signed informed consent.

Before the bronchoscopy procedure, patients at our hospital were given a choice between conventional and painless bronchoscopy. Patients undergoing conventional bronchoscopy received moderate sedation with benzodiazepines combined with sufentanil under the guidance of a bronchoscopy doctor, known as traditional sedation. Patients opting for painless bronchoscopy receive deep sedation via BPS administered by an anesthesiologist. Our hospital introduced remimazolam for clinical use in November 2023, replacing midazolam, which was previously used for bronchoscopy sedation. All patients were divided into four groups according to their sedation protocols: the M-S group (midazolam + sufentanil for traditional sedation), R-S group (remimazolam + sufentanil for traditional sedation), M-S-P group (midazolam + sufentanil + propofol for BPS), and R-S-P group (remimazolam + sufentanil + propofol for BPS).

All patients were administered 0.1 μg/kg of sufentanil (Sufentanil Citrate Injection, Humanwell Healthcare (Group) Co, China, national medicine permission number: H20050580) and 8 mg of ondansetron.

M-S group: Patients receive 2 mg of midazolam (Midazolam Injection, Jiangsu Nhwa Pharmaceutical Co, China, national medicine permission number: H10980025) if they are under 65 years old (and 1 mg if they are 65 years old or older). If the desired level of moderate sedation was not achieved, an additional 1 mg of midazolam was administered, with a maximum of three supplemental doses within 12 min, each dose was separated by at least 2 min.

R-S group: Patients were given 5 mg of remimazolam (Remimazolam Tosilate for Injection, Jiangsu Hengrui Pharmaceuticals Co, China, national medicine permission number: H20190034) if they were under 65 years old (and 2.5 mg if they were 65 years old or older). If moderate sedation was not achieved, an additional 2.5 mg of remimazolam was administered, with a maximum of five supplemental doses within 15 min, each dose was separated by at least 1 min.

M-S-P group: Patients received 0.05 mg/kg midazolam if they were under 65 years old (≤2 mg if they were 65 years old or older), followed by administration of propofol (Propofol Injectable Emulsion, Jiangsu Yingke Biopharmaceutical Co, China, national medicine permission number: H20203504) after 3 min at doses ranging from 5–10 mg until deep

sedation was achieved. During the procedure, propofol was continuously infused at a rate of 0.15–0.2 mg/(kg*h) to maintain deep sedation.

R-S-P group: Patients were administered 0.05 mg/kg remimazolam if they were under 65 years old (≤2.5 mg if they were 65 years old or older), followed by a continuous infusion of remimazolam at 0.1 mg/(kg*h). Propofol was then administered at doses of 5–10 mg to achieve deep sedation, with continuous infusion of 0.15–0.2 mg/(kg*h) propofol to maintain this level.

The Modified Observer's Alertness/Sedation Scale (MOAA/S, as detailed in Table 1) was used to monitor and adjust the sedation level. Moderate sedation is defined as a MOAA/S score of 3–4, whereas deep sedation is indicated by a score of 1–2.[12,13] If a patient failed to tolerate the examination at the designated sedation level, the examination was halted, or the anesthesiologist decided to deepen the sedation to a general anesthesia level, based on the patient's condition.

Before initiating the procedure, lidocaine gel was administered intranasally, followed by intratracheal surface anesthesia by applying 3–5 mL of 2% lidocaine solution via cricothyroid puncture. When the bronchoscope reached the carina, 2 mL of 2% lidocaine solution was separately administered into the left and right main bronchi through the bronchoscope. During the procedure, a 2% lidocaine solution was intermittently sprayed into the airway via the bronchoscope as needed. The total dosage of lidocaine used throughout the examination did not exceed 8 mg/kg.[14]

All patients were required to fast before the procedure and were administered oxygen via a mask (5 L/min) before induction. During bronchoscopy via the nasal approach, an oropharyngeal airway was placed postinduction, with oxygen administration (5 L/min) via the mask through the oropharyngeal airway until the patient was ready to leave the room. The electrocardiogram, pulse rate, pulse oximetry, and noninvasive blood pressure were continuously monitored from the moment the patient entered the room.

Post-examination, the patients were transferred to a recovery area where oxygen administration and cardiac monitoring continued. The period from the end of the procedure until the patient achieved a Modified Observer's Assessment of Alertness/Sedation (MOAA/S) score of 5 was defined as the recovery time. Patients with a modified Aldrete score of 9 or higher were eligible for discharge, with the time from wakefulness to discharge defined as the discharge time.

Primary outcomes included satisfaction of the patient, endoscopic doctor, and nurse, as well as, patient follow-up questionnaires. Satisfaction surveys use the visual analog scale (VAS) for quantification (ranging from 0–10, with 0 indicating the least satisfaction and 10 indicating the most satisfaction). Patient satisfaction surveys were conducted before discharge, whereas those for endoscopic doctors and nurses were completed immediately after the examination. Follow-up questionnaires were filled in via telephone calls 24 hours after the examination. The secondary outcomes included the rate of successful sedation (proportion of patients who completed bronchoscopy at the targeted sedation level), time metrics (induction time, recovery time, and discharge time), dosage metrics (induction, maintenance, and total doses of midazolam, remimazolam, and propofol), additional doses and frequency of 2% lidocaine administered during the procedure and the dosage and frequency of supplemental propofol administered. Safety metrics included the incidence of adverse reactions during and after the procedure.

Sample Size Calculation

Based on the pre-experiment results, the mean ± standard deviation of the patient satisfaction VAS score was 6.0 ± 3.0 in the M-S group, 6.3 ± 3.1 in the R-S group, 9.3 ± 1.2 in the M-S-P group, and 9.5 ± 0.5 in the R-S-P group. Because the number of patients undergoing painless bronchoscopy is greater than that of patients undergoing ordinary bronchoscopy,

Table 1 Modified Observer's Assessment of Alertness and Sedation (MOAA/S) score[12,13]

Score	Responsiveness
5	Responds readily to their name called in a normal tone ("alert")
4	Lethargic response to their name called in a normal tone
3	Responds only after their name is called loudly and/or repeatedly
2	Responds only after mild prodding or shaking
1	Responds only after a painful trapezius squeeze
0	Does not respond to a painful trapezius squeeze

we recruited research subjects at a ratio of 1:1:5:5. Moreover, we utilized PASS 2021 to estimate the sample size for the comparison of multiple sample means, with a two-sided α=0.05 and a confidence level of 90%. This calculation determined a total sample size of 98 cases for the study. Considering a 10% dropout rate, the total sample size required was adjusted to 110 cases, with 9 cases in the M-S group, 9 cases in the R-S group, 46 cases in the M-S-P group, and 46 cases in the R-S-P group. To enhance the precision of the study results, consultation with statistical experts led to a final determination of a sample size of 330 cases, with 27 cases in the M-S group, 27 cases in the R-S group, 138 cases in the M-S-P group, and 138 cases in the R-S-P group.

Statistical Analysis

Statistical analysis was conducted using SPSS.26, with the Kolmogorov test used to assess the normality of all measured data. As all measured data in this study were skewed, they were expressed as the median (interquartile range) [M(QR)] and analyzed by the Kruskal–Wallis rank sum test. Qualitative data were analyzed using Chi-square tests or Fisher's exact test and expressed as counts and percentages, with ordinal data analyzed using the Kruskal–Wallis rank sum test. All results were considered to be statistically significant at $P < 0.05$. For patients who required rescue medication due to sedation failure or those who were lost to follow-up, an intention-to-treat (ITT) analysis was performed based on the primary outcome measures. Secondary outcome measures were analyzed using a per-protocol (PP) approach.

Results

General Information

In total, 418 subjects were included in this study, comprising 24 subjects in the M-S group, 31 in the R-S group, 154 in the M-S-P group, and 209 in the R-S-P group. The detailed inclusion and exclusion process is illustrated in Figure 1. Except for a slightly greater BMI in the R-S-P group than in the M-S-P group (23.5 kg*m-2 vs 22.4 kg*m-2, P = 0.040), no statistically significant differences were found in age, sex, ASA classification, underlying diseases, or history of bronchoscopy among the groups. Pulmonary shadows and pneumonia were the primary reasons for bronchoscopy. Bronchoscopy lavage and biopsy were the most common procedures, whereas EBUS and transbronchial treatments were mostly performed under BPS because of their longer duration, greater patient discomfort, and requirements for patient cooperation. Consequently, the BPS groups (M-S-P group and R-S-P group) had slightly longer examination times than the traditional sedation groups (M-S group and R-S group) (17.0 min vs 14.0 min, P = 0.002) (Table 2).

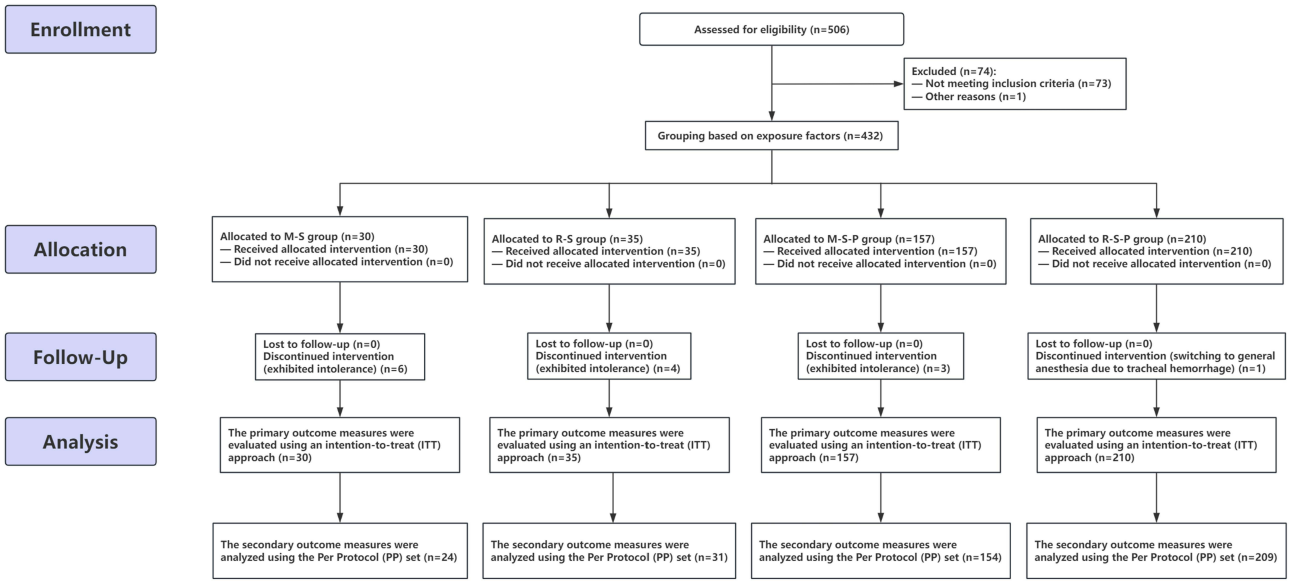

Figure 1 CONSORT trial flow diagram.

Table 2 The Baseline Characteristics of the Patients

Patient Baseline Characteristics	M-S Group (n = 24)	R-S Group (n = 31)	M-S-P Group (n = 154)	R-S-P Group (n = 209)	P
Age, M (QR)/years	60.5(13.0)	61.0(21.0)	63.0(15.0)	64.0(13.0)	0.705
BMI, M (QR)/kg*m^{-2}	21.5(6.5)	23.1(5.1)	22.4(4.7)	23.5(4.3)[c]	0.040
Gender, %(n)					0.067
Male	58.3%(14)	64.5%(10)	57.1%(88)	70.3%(147)	
Female	41.7%(10)	35.5%(11)	42.9%(66)	29.7%(62)	
ASA, %(n)					0.346
I	8.3%(2)	3.2%(1)	11.7%(18)	14.8%(31)	
II	54.2%(13)	48.4%(15)	53.9%(83)	49.3%(103)	
III	37.5%(9)	32.3%(10)	28.6%(44)	30.6%(64)	
IV	0.0%(0)	16.1%(5)	5.8%(9)	5.3%(11)	
History of bronchoscopy, %(n)					0.678
Yes	12.5%(3)	25.8%(8)	19.5%(30)	19.1%(40)	
No	87.5%(21)	74.2%(23)	80.5%(124)	80.9%(169)	
Diagnosis, %(n)					0.002
Atelectasis	0.0%(0)	0.0%(0)	0.6%(1)	0.5%(1)	
Lung shadow	29.2%(7)	19.4%(6)	48.1%(74)[b]	52.6%(110)[b]	
Pulmonary infection	50.0%(12)	54.8%(17)	26.0%(40)[b]	24.4%(51)[ab]	
Pulmonary fibrosis	0.0%(0)	0.0%(0)	1.3%(2)	0.0%(0)	
Bronchiectasis	8.3%(2)	6.5%(2)	6.5%(10)	2.9%(6)	
Silicosis	0.0%(0)	0.0%(0)	0.0%(0)	0.5%(1)	
Asthma	4.2%(1)	0.0%(0)	0.0%(0)	0.0%(0)[a]	
Hemoptysis	4.2%(1)	6.5%(2)	2.6%(4)	2.9%(6)	
Enlargement of mediastinal lymph nodes	4.2%(1)	0.0%(0)	5.2%(8)	1.4%(3)	
Post lung surgery	0.0%(0)	3.2%(1)	0.0%(0)	0.0%(0)	
Airway stenosis	0.0%(0)	3.2%(1)	3.2%(5)	5.3%(11)	
Airway foreign body	0.0%(0)	0.0%(0)	1.3%(2)	1.4%(3)	
Tracheal fistula	0.0%(0)	0.0%(0)	3.2%(5)	1.4%(3)	
Postoperative follow-up of bronchoscopy treatment	0.0%(0)	6.5%(2)	1.9%(3)	6.7%(14)	
Procedure, %(n)					
Bronchoalveolar lavage	100.0%(24)	93.5%(29)	89.0%(137)	85.2%(178)	0.120
Bronchopulmonary biopsy	54.2%(13)	29.0%(9)	50.6%(78)	49.8%(104)	0.144
EBUS	4.2%(1)	3.2%(1)	24.7%(38)[b]	21.5%(45)	0.010
Tracheoscopy treatment	0.0%(0)	0.0%(0)	18.8%(29)	20.1%(42)[b]	0.005
Total time, M (QR)/min	15.5 (18.0)	12.0 (8.0)[c]	17.0 (19.0)[b]	16.0 (16.0)[b]	0.003

Notes: [a]Compared to the M-S group, the difference was significant; [b]Compared to the R-S group, the difference was significant; [c]Compared to M-S-P, the differences were significant (P < 0.05).

Satisfaction and Follow-Up Questionnaire

The median patient satisfaction score for both BPS groups was 10, which was significantly higher than that of the M-S group and R-S group (10.0 vs 10.0 vs 6.0 vs 7.0, P < 0.001) (Figure 2a). Endoscopists and endoscopy nurses reported higher satisfaction VAS scores in the BPS groups than in the traditional sedation groups (P < 0.001) (Figure 2b and c). In the follow-up questionnaire, 50.0% of the patients in the M-S group reported average sedation effects, which represented a significantly greater proportion of patients than those recorded in the other three groups (P < 0.001), in which 43.3% indicated a need for substantial improvement in sedation (P < 0.001). Patients in both BPS groups reported no memory of the bronchoscopy procedure and no discomfort during the procedure. In contrast, 85.7% of the patients in the R-S group and 76.7% of those in the M-S group reported different degrees of memory of the procedure, with 77.1% and 73.3% of patients in the R-S and M-S groups, respectively, experiencing mild to unbearable discomfort, which was significantly greater than that reported by the BPS group (P < 0.001). Additionally, 50.0% of the M-S group patients and 19.7% of the M-S-P group patients reported mild effects on daily life due to sedation, with 26.7% and 7.0%, respectively, reporting significant effects, both of which were significantly greater than those reported in the R-S and R-S-P groups (P < 0.001) (Table 3).

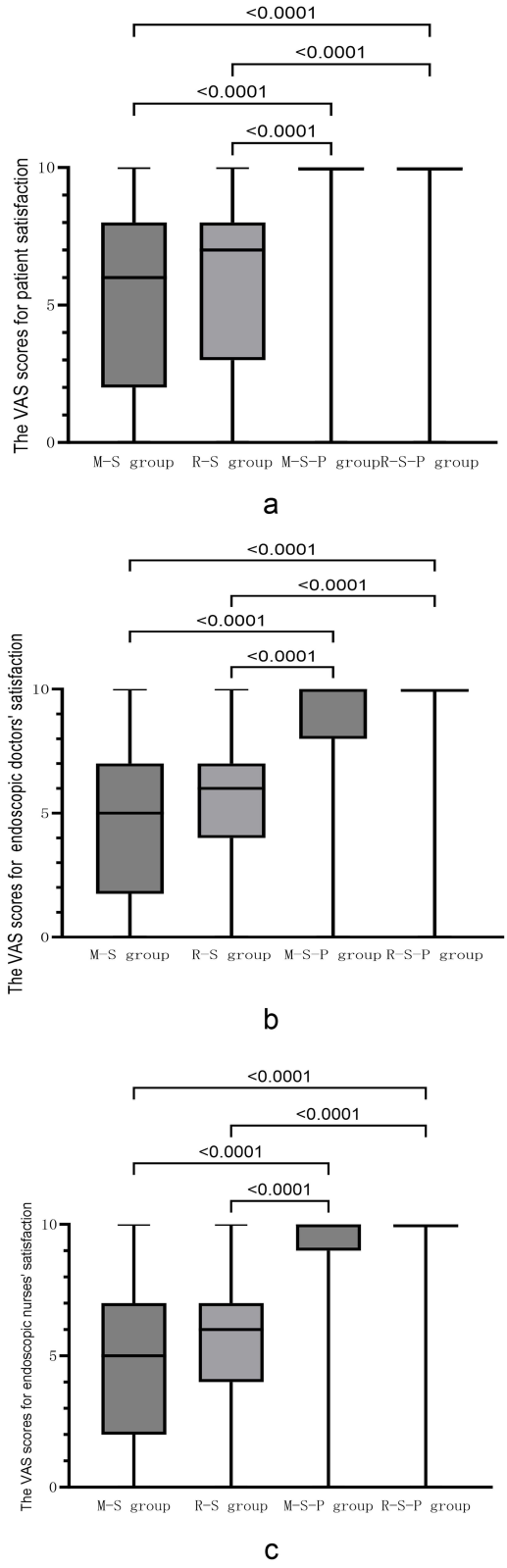

Figure 2 Box plots of the VAS scores for satisfaction. (**a**): Box plots of the VAS scores for the satisfaction of patients; (**b**): Box plots of the VAS scores for the satisfaction of endoscopic doctors; (**c**): Box plots of the VAS scores for the satisfaction of endoscopic nurses.

Table 3 Patient Follow-Up Questionnaires

Patient Follow-up Questionnaires (n,%)	M-S Group (n = 30)	R-S Group (n = 35)	M-S-P Group (n = 157)	R-S-P Group (n = 210)	P
Sedation Quality			[ab]	[abc]	0.000
Excellent	16.7%(5)	25.7%(9)	94.3%(148)	99.5%(209)	
Good	33.3%(10)	42.9%(15)	3.8%(6)	0.0%(0)	
Average	50.0%(15)	31.4%(11)	1.9%(3)	0.5%(1)	
Adjustment Necessity for Sedation			[ab]	[abc]	0.000
No adjustment required	30.0%(9)	37.1%(13)	86.0%(135)	97.1%(204)	
Minor improvement needed	26.7%(8)	37.1%(13)	11.5%(18)	1.9%(4)	
Significant adjustment needed	43.3%(13)	25.7%(9)	2.5%(4)	1.0%(2)	
Memory of Examination Initiation			[ab]	[ab]	0.000
Clear memory	33.3%(10)	11.4%(4)	1.9%(3)	0.5%(1)	
Fuzzy memory	26.7%(8)	28.6%(10)	1.3%(2)	0.0%(0)	
No memory	40.0%(12)	60.0%(21)	96.8%(152)	99.5%(209)	
Awareness During the Examination			[ab]	[ab]	0.000
Clear memory	50.0%(15)	28.6%(10)	1.9%(3)	0.5%(1)	
Fuzzy memory	26.7%(8)	57.1%(20)	0.0%(0)	0.0%(0)	
No memory	23.3%(7)	14.3%(5)	98.1%(154)	99.5%(209)	
Memory of Bronchoscope Removal			[ab]	[ab]	0.000
Clear memory	53.3%(16)	34.3%(12)	1.9%(3)	1.0%(2)	
Fuzzy memory	6.7%(2)	34.3%(12)	0.0%(0)	2.4%(5)	
No memory	40.0%(12)	31.4%(11)	98.1%(154)	96.6%(203)	
Memory of Leaving the Bronchoscopy Room			[ab]	[ab]	0.000
Clear memory	50.0%(15)	57.1%(20)	12.1%(19)	10.5%(22)	
Fuzzy memory	20.0%(6)	25.7%(9)	5.1%(8)	10.0%(21)	
No memory	30.0%(9)	17.1%(6)	82.8%(130)	79.5%(167)	
Discomfort Experienced During the Examination			[ab]	[ab]	0.000
Intolerable	36.7%(11)	22.9%(8)	1.9%(3)	0.5%(1)	
Moderate discomfort	13.3%(4)	5.7%(2)	0.0%(0)	0.0%(0)	
Mild discomfort	23.3%(7)	48.6%(17)	0.0%(0)	0.0%(0)	
None	26.7%(8)	22.9%(8)	98.1%(154)	99.5%(209)	
Impact of Sedation on Today		[a]	[a]	[ac]	0.000
No impact	23.3%(7)	82.9%(29)	73.2%(115)	91.0%(191)	
Mild impact	50.0%(15)	5.7%(2)	19.7%(31)	8.6%(18)	
Significant impact	26.7%(8)	11.4%(4)	7.0%(11)	0.5%(1)	

Notes: [a]Compared to M-S, the differences were significant; [b]Compared to R-S, the differences were significant; [c]Compared to M-S-P, the differences were significant (P < 0.05).

Sedation Completion Rate

The number of patients unable to complete the examination as per the original sedation plan is shown in Figure 1. The bronchoscopy completion rates for the M-S and R-S groups were significantly lower than those for the two BPS groups (Table 4).

Time Indicators

The induction time, recovery time, and discharge time for the M-S and M-S-P groups were significantly longer than those for the other two groups, with the R-S group exhibiting the shortest induction time (P < 0.01) (Figure 3a–c).

Table 4 Sedation Completion Rates

Completion %(n)	M-S Group (n = 30)	R-S Group (n = 35)	M-S-P Group (n = 157)	R-S-P Group (n = 210)	P
Completed	80.0%(24)	88.6%(31)	98.1%(154) [ab]	99.5%(209)[ab]	0.000
Not Completed	20.0%(6)	11.4%(4)	1.9%(3) [ab]	0.5%(1) [ab]	

Notes: [a]Compared to the M-S group, the difference was significant; [b]Compared to the R-S group, the difference was significant (P < 0.05).

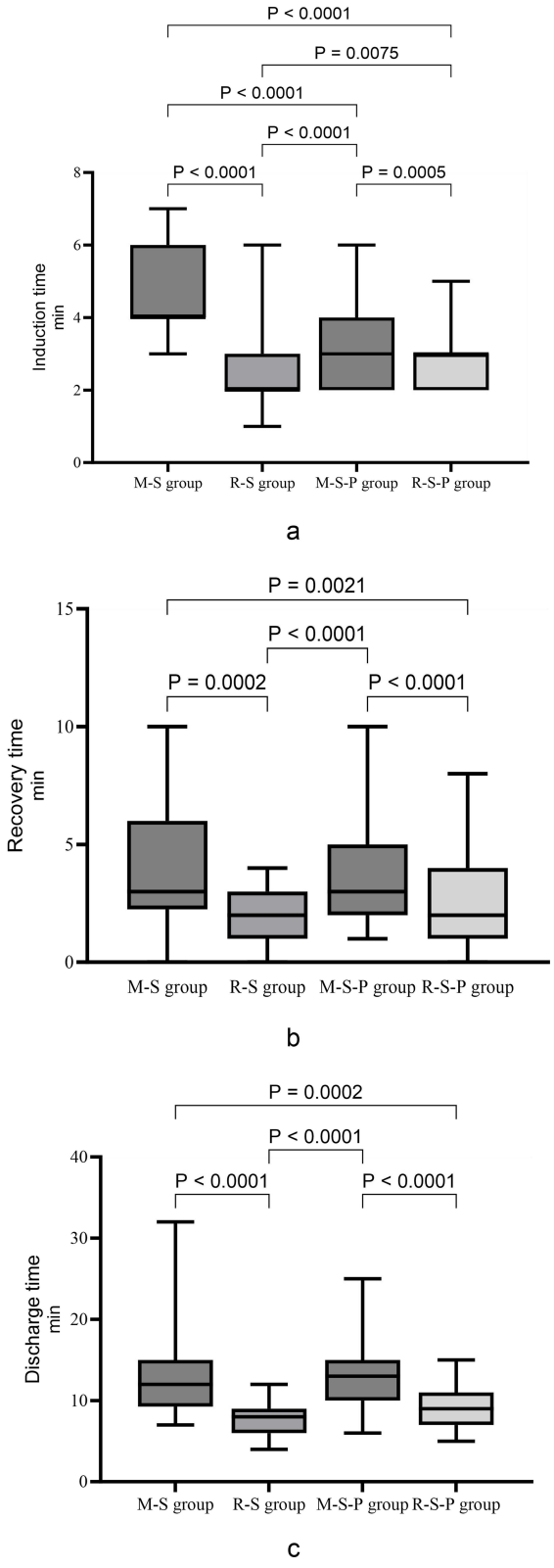

Figure 3 Box plots of time indicators. (**a**): Box plots of the induction time; (**b**): Box plots of the recovery time; (**c**): Box plots of the discharge time.

Dose Indicators

The dosage of benzodiazepines in the BPS groups was significantly lower than that in the traditional sedation groups (P < 0.001). The differences in the induction, maintenance, or supplementary doses of propofol between the M-S-P and R-S-P groups were not significant. However, the M-S-P group received slightly more addition frequency of propofol than the R-S-P group (1.0 vs 0.0, P = 0.025). The M-S and R-S groups had higher supplementary doses and frequencies of 2% lidocaine than the two BPS groups (P < 0.001) (Table 5).

Intraprocedural Adverse Reactions

Compared to the patients in the traditional sedation group, those in the BPS group experienced significantly fewer coughing and body movements during surgery (P = 0.003; P < 0.001). Compared to the patients in the BPS sedation group, those in the traditional sedation group also had a significantly greater incidence of hypertension and tachycardia during surgery (P < 0.001). The overall incidence of hypotension was 12.7% (53 patients), with the highest incidence in the M-S-P group (19.5%), which was significantly greater than that in the R-S-P group (9.1%, P = 0.005) but was not significantly different from that in the traditional sedation groups. None of the patients in any group experienced apnea during surgery, and although a few patients experienced transient hypoxemia, no significant differences among the groups were recorded for this condition (P =0.367) (Table 6).

Postprocedural Adverse Reactions

The incidence of postprocedural dizziness in the R-S-P group (17.2%) was significantly lower than that in the M-S and M-S-P groups (45.8% vs 31.8%, P = 0.001). The differences in the incidence of postprocedural nausea among the groups were not significant (P = 0.084) (Table 7).

Discussion

Sedation for bronchoscopy presents a significant challenge to anesthesiologists. This occurs primarily due to the shared airway with the operating physician, necessitating a greater focus on maintaining normal respiratory function. Compared to anesthesia for gastrointestinal endoscopy, anesthesia for bronchoscopy is considerably more complex. Propofol, widely used in painless diagnostic and therapeutic procedures, has a narrow safety margin and pronounced cardiopulmonary

Table 5 Dosage Indicators

Dosage M (QR)	M-S Group (n = 24)	R-S Group (n = 31)	M-S-P Group (n = 154)	R-S-P Group (n = 209)	P
Midazolam (mg)					
Induction dose	3.5 (1.4)*		2.5 (0.5)*		0.000
Total dose	4.5 (2.5)*		2.5 (0.5)*		0.000
Remimazolam (mg)					
Induction dose		6.0 (2.0)*		2.5 (0.5)*	0.000
Maintenance dose		4.0 (4.0)*		1.8 (1.7)*	0.000
Total dose		10.0 (6.0)*		4.6 (2.0)*	0.000
10 mg/mL propofol (mL)					
Induction dose			3.0 (1.5)	3.0 (1.0)	0.815
Maintenance dose			3.0 (3.1)	3.0 (2.7)	0.915
Supplemental frequency			1.0 (2.0)*	0.0 (2.0)*	0.025
Supplemental dosage			2.0 (4.0)	0.0 (4.0)	0.077
Total dose			8.1 (5.1)	7.4 (5.2)	0.186
2% lidocaine (mL)					
Supplemental frequency	4.0 (3.0)	3.0 (2.0)	2.0 (2.0)[ab]	2.0 (1.0)[ab]	0.000
Supplemental dosage	12.0 (9.0)	10.0 (9.0)	6.5 (6.0)[ab]	7.0 (5.0)[ab]	0.000

Notes: * P < 0.05; [a]Compared to the M-S group, the difference was significant; [b]Compared to the R-S group, the difference was significant (P < 0.05).

Table 6 Incidence of Adverse Reactions During the Procedure

Adverse Reactions During the Procedure	M-S Group (n = 24)	R-S Group (n = 31)	M-S-P Group (n = 154)	R-S-P Group (n = 209)	P
Coughing M (QR)/time	7.5(10.0)	7.0(4.0)	5.0(4.3)[b]	5.0(2.0)[ab]	0.003
Movement M (QR)/time	2.0(6.0)	3.0(3.0)	0.0(1.0)[ab]	0.0(1.0)[ab]	0.000
Hypertension %(n)	25.0%(6)	19.4%(6)	2.6%(4)[ab]	5.7%(12)[ab]	0.000
Hypotension %(n)	0.0%(0)	12.9%(4)	19.5%(30)	9.1%(19)[c]	0.007
Tachycardia %(n)	37.5%(9)	22.6%(7)	9.7%(15)[a]	8.1%(17)[a]	0.000
Hypoxemia %(n)	12.5%(3)	6.5%(2)	5.2%(8)	4.8%(10)	0.367

Notes: (1) Hypertension: During surgery, the patient's systolic blood pressure exceeds 180 mmHg, the diastolic pressure exceeds 110 mmHg, or it is more than 20% above the patient's baseline blood pressure. (2) Hypotension: During surgery, the patient's systolic blood pressure drops below 80 mmHg, the diastolic pressure drops below 40 mmHg, or it is more than 20% below the baseline blood pressure. (3) Tachycardia: a heart rate that exceeds 100 beats per minute or is more than 20% above the baseline heart rate. (4) Hypoxemia: The oxygen saturation level decreases below 90% and persists for more than 10s. (5) a: Compared to the M-S group, the difference was significant; b: Compared to the R-S group, the difference was significant; c: Compared to the M-S-P group, the difference was significant ($P < 0.05$).

Table 7 Incidence of Adverse Reactions After the Procedure

Adverse Reactions After the Procedure	M-S Group (n = 24)	R-S Group (n = 31)	M-S-P Group (n = 154)	R-S-P Group (n = 209)	P
Dizziness %(n)	45.8%(11)	19.4%(6)	31.8%(49)	17.2%(36)[ac]	0.001
Nausea %(n)	12.5%(3)	0.0%(0)	3.2%(5)	2.4%(5)	0.084

Notes: [a]Compared to the M-S group, the difference was significant; [c]Compared to the M-S-P group, the difference was significant ($P < 0.05$).

depression, both of which increase the difficulty of respiratory management and the risks associated with sedation. Thus, the safe application of propofol during bronchoscopy is a critical issue.

To increase the safety of propofol-induced sedation in non-operating settings, Dr. Lawrence B. Cohen et al introduced the concept of BPS in 2004. They demonstrated that BPS can better regulate the depth of sedation during painless gastroenteroscopy, effectively reducing the incidence of cardiopulmonary complications and achieving high levels of satisfaction among patients and physicians.[1] This concept was later validated in several studies.[2,15,16] This study was the first evaluation of the efficacy and safety of BPS in sedation for bronchoscopy. Compared to traditional sedation methods, the methods involving the application of BPS in bronchoscopy significantly improved patient comfort and cooperation, enhanced operator satisfaction, and did not increase the incidence of adverse reactions during or after the procedure.

Moderate sedation using midazolam combined with opioid medications is also widely used for bronchoscopy sedation.[17] However, midazolam has a slow onset and long duration of action, and patients under moderate sedation during bronchoscopy often experience significant discomfort. In this study, patient satisfaction in the M-S and R-S groups was significantly lower than that in the BPS group; additionally, follow-up questionnaires revealed that some patients had considerable negative memories of the procedure.

The core principle of BPS involves the use of low-dose propofol based on sedation and analgesia to precisely control the depth of sedation while maintaining normal respiratory and circulatory functions and facilitating rapid recovery after the procedure. With a deeper understanding of this concept, the range of sedative and analgesic drugs administered to patients has expanded beyond traditional midazolam and opioids. Compared to midazolam, remimazolam, a novel ultrashort-acting benzodiazepine, does not cause significant cardiopulmonary depression and has a rapid onset and short recovery time. Thus, it is a promising candidate for procedural sedation.[18,19] In this study, the induction and recovery times in the R-S-P group were shorter than those in the M-S-P group, with less intense effects on postprocedural daily activities. The faster onset of remimazolam also resulted in shorter induction times, leading to greater satisfaction among endoscopic physicians and nurses.

In this study, the group administered BPS achieved deep sedation, yet the induction and recovery times were similar to those of the traditional sedation groups. This finding was similar to those of previous studies,[20,21] indicating that BPS facilitates rapid induction and recovery. This high efficiency is attributed to the synergistic effects of propofol, benzodiazepines, and opioids, which enable BPS to reach the desired depth of sedation while significantly reducing the dosage of sedative and analgesic medications.

Research conducted by Qiuyue Wu and Sun-Hyung Kim et al has shown that, in comparison to midazolam, remimazolam requires a smaller dose of antidote for antagonism after surgery, has a shorter duration of action, and a lower incidence of additional postoperative sleep.[22,23] This is mainly because remimazolam can be rapidly metabolized by carboxylesterase-1α into a metabolite without pharmacological activity. In this study, the higher incidence of postprocedural dizziness in the M-S group and the M-S-P group may be related to the residual effects of midazolam. Moreover, sedation with a small dose of propofol combined with benzodiazepines does not increase the incidence of postprocedural dizziness and nausea, which is in line with the research findings of Fan Zhang et al.[24]

However, this study had several limitations: 1. This was a real-world, single-center study conducted with a few patients; thus, it lacked the rigor of randomized controlled trials (RCTs). 2. The assessment of sedation levels was based solely on the MOAA/S scale and did not incorporate brain electrical activity monitoring, such as the bispectral index (BIS), potentially compromising the accuracy of sedation depth evaluation. 3. A control group involving the administration of only propofol or a combination of propofol with opioids was not included, thus preventing a direct comparison of sedation effects between BPS and these alternatives.

Conclusion

This study indicates that, compared with traditional methods, when deep sedation by BPS is used in bronchoscopy, the satisfaction of patients and operators is relatively high. It can induce and recover quickly, significantly reduce the number of coughs and body movements during the operation, and does not increase the intraoperative or postoperative adverse events. Among the various combinations tested, the administration of remimazolam, sufentanil, and a small dose of propofol were the most effective sedation strategies.

Data Sharing Statement

The individual participant data will be available. The data specifically includes individual participant data that underlie the results reported in this article, after de-identification (text, tables, figures). No other documents will be available. Under reasonable requirements, the data of this study can be obtained from the corresponding author and the data will be available beginning 9 months and ending 36 months following article publication.

Disclosure

No conflict of interest exits in the submission of this manuscript, and manuscript is approved by all authors for publication. I would like to declare on behalf of my co-authors that the work described was original research that has not been published previously, and not under consideration for publication elsewhere, in whole or in part. All the authors listed have approved the manuscript that is enclosed.

References

1. Cohen LB, Hightower CD, Wood DA, Miller KM, Aisenberg J. Moderate level sedation during endoscopy: a prospective study using low-dose propofol, meperidine/fentanyl, and midazolam. *Gastrointest Endosc*. 2004;59(7):795–803. doi:10.1016/S0016-5107(04)00349-9
2. Levitzky BE, Lopez R, Dumot JA, Vargo JJ. Moderate sedation for elective upper endoscopy with balanced propofol versus fentanyl and midazolam alone: a randomized clinical trial. *Endoscopy*. 2012;44(1):13–20. doi:10.1055/s-0031-1291421
3. Lee CK, Lee SH, Chung IK, et al. Balanced propofol sedation for therapeutic GI endoscopic procedures: a prospective, randomized study. *Gastrointest Endosc*. 2011;73(2):206–214. doi:10.1016/j.gie.2010.09.035
4. Wahidi MM, Jain P, Jantz M, et al. American College of Chest Physicians consensus statement on the use of topical anesthesia, analgesia, and sedation during flexible bronchoscopy in adult patients. *Chest*. 2011;140(5):1342–1350. doi:10.1378/chest.10-3361
5. Du Rand IA, Blaikley J, Booton R, et al. Summary of the British Thoracic Society guideline for diagnostic flexible bronchoscopy in adults. *Thorax*. 2013;68(8):786–787. doi:10.1136/thoraxjnl-2013-203629

6. Xiaoming D, Yuelan W, Yi F, et al. Expert consensus on sedation and anesthesia for bronchoscopy(2020 version). *Int J Anesthesiol Resusc*. 2021;42(8):785–794.
7. Yuan Y, Jie Z, Hongli Y, et al. A preliminary study of different methods of anesthesia for painless bronchoscopy. *Chin J Tubercul Respir Dis*. 2019;42(2):106–113. doi:10.3760/cma.j.issn.1001-0939.2019.02.006
8. Announcement of the National Medical Products Administration, Ministry of Public Security, and National Health Commission on Adjusting the Catalogue of Psychotropic Drugs (No. 54 of 2024). May 7, 2024. Available from: https://www.nmpa.gov.cn/xxgk/ggtg/ypggtg/ypqtggtg/20240507084000186.html. Accessed December 10, 2024.
9. Clark G, Licker M, Younossian AB, et al. Titrated sedation with propofol or midazolam for flexible bronchoscopy: a randomised trial. *Europ resp J*. 2009;34(6):1277–1283. doi:10.1183/09031936.00142108
10. Han SJ, Lee TH, Park SH, et al. Efficacy of midazolam- versus propofol-based sedations by non-anesthesiologists during therapeutic endoscopic retrograde cholangiopancreatography in patients aged over 80 years. *Dig Endosc*. 2017;29(3):369–376. doi:10.1111/den.12841
11. Müller T, Thümmel K, Cornelissen CG, Krüger S, Dreher M. Analogosedation during flexible bronchoscopy using a combination of midazolam, propofol and fentanyl - A retrospective analysis. *PLoS One*. 2017;12(4):e0175394. doi:10.1371/journal.pone.0175394
12. Yamada J, Hazama D, Tachihara M, et al. The utility of bispectral index monitoring in flexible bronchoscopy: a single-center, retrospective observational study. *Thoracic Cancer*. 2022;13(21):3052–3057. doi:10.1111/1759-7714.14658
13. Chernik DA, Gillings D, Laine H, et al. Validity and reliability of the observer's assessment of alertness/sedation scale: study with intravenous midazolam. *J Clin Psychopharmacol*. 1990;10(4):244–251.
14. Suhre WM, Lang JD Jr, Madtes DK, Abdelmalak BB. Partnership with interventional pulmonologist: an anesthesiologist's perspective. *Otolaryngol Clin North Am*. 2019;52(6):1049–1063. doi:10.1016/j.otc.2019.08.006
15. VanNatta ME, Rex DK. Propofol alone titrated to deep sedation versus propofol in combination with opioids and/or benzodiazepines and titrated to moderate sedation for colonoscopy. *Am J Gastroenterol*. 2006;101(10):2209–2217. doi:10.1111/j.1572-0241.2006.00760.x
16. Sipe BW, Scheidler M, Baluyut A, Wright B. A prospective safety study of a low-dose propofol sedation protocol for colonoscopy. *Clin Gastroenterol Hepatol*. 2007;5(5):563–566. doi:10.1016/j.cgh.2007.01.013
17. Dreher M, Ekkernkamp E, Storre JH, Kabitz HJ, Windisch W. Sedation during flexible bronchoscopy in patients with pre-existing respiratory failure: midazolam versus Midazolam plus Alfentanil. *Respir Int Rev Thorac Dis*. 2010;79(4):307–314. doi:10.1159/000267227
18. Lee A, Shirley M. Remimazolam: a review in procedural sedation. *Drugs*. 2021;81(10):1193–1201. doi:10.1007/s40265-021-01544-8
19. Pastis NJ, Yarmus LB, Schippers F, et al. Safety and efficacy of remimazolam compared with placebo and midazolam for moderate sedation during bronchoscopy. *Chest*. 2019;155(1):137–146. doi:10.1016/j.chest.2018.09.015
20. Zhang K, Xu H, Li HT. Safety and efficacy of propofol alone or in combination with other agents for sedation of patients undergoing colonoscopy: an updated meta-analysis. *Eur Rev Med Pharmacol Sci*. 2020;24(8):4506–4518. doi:10.26355/eurrev_202004_21033
21. Hsu CD, Huang JM, Chuang YP, et al. Propofol target-controlled infusion for sedated gastrointestinal endoscopy: a comparison of propofol alone versus propofol-fentanyl-midazolam. *Kaohsiung J Med Sci*. 2015;31(11):580–584. doi:10.1016/j.kjms.2015.09.004
22. Kim SH, Cho JY, Kim M, et al. Safety and efficacy of remimazolam compared with midazolam during bronchoscopy: a single-center, randomized controlled study. *Sci Rep*. 2023;13(1):20498. doi:10.1038/s41598-023-47271-w
23. Wu Q, Xu R, Zhou X, et al. Bolus administration of remimazolam was superior to midazolam for deep sedation in elderly patients undergoing diagnostic bronchoscopy: a randomized, double-blind, controlled trial. *Medicine*. 2024;103(12):e37215. doi:10.1097/MD.0000000000037215
24. Zhang F, Chang H, Qing W, Yu R, Liao Q, Tong J. Remimazolam tosylate combined with low-dose propofol improves sedation and safety in hysteroscopy. *Drug Des Devel Ther*. 2022;16:4101–4108. doi:10.2147/DDDT.S390403