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CLINICAL TRIAL REPORT

Efficacy and Safety of Dexmedetomidine Nasal Spray as a Premedication in Patients Undergoing Fiberoptic Bronchoscopy Under Sedation: A Randomized Controlled Trial

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Background: Fiberoptic bronchoscopy (FB) under sedation can provoke patient discomfort, cough, and hemodynamic fluctuations. This study evaluated the efficacy and safety of dexmedetomidine nasal spray as a premedication compared to intranasal normal saline and lidocaine.

Methods: A total of 90 patients scheduled for FB under sedation were randomly assigned to three groups. Group D (dexmedetomidine), Group C (control, normal saline), and Group L (lidocaine) received pre-induction nasal sprays via the same metered-dose aerosolization device. At 10 min post-spray, all patients received standard monitored anesthesia care (MAC) with preserved spontaneous ventilation (respiratory rate, RR ≥10 breaths/min; peripheral oxygen saturation, SpO_2 ≥95%). Outcomes included hemodynamic parameters (heart rate, HR; mean arterial pressure, MAP) measured at specific time points (T_1-T_8), Modified Observer's Assessment of Alertness/Sedation (MOAA/S) scores, cough severity and adverse events.

Results: Group D demonstrated better overall performance. Hemodynamically, HR in Group D was lower than Group C at T_3 and T_5, and lower than Group L at T_5. MAP in Group D was lower than both control groups from T_3-T_6. Recovery time in Group D was shorter than in both Group C and Group L. Group D also exhibited superior MOAA/S scores (lower at T_1, but higher at T_6-T_8), higher bronchoscopist satisfaction, and a lower incidence of both moderate-to-severe cough and postoperative nausea and vomiting (PONV) compared to the other groups. Respiratory rates were comparable, with Group D showing a higher RR than Group C at T_6.

Conclusion: Premedication with dexmedetomidine nasal spray in patients undergoing FB under sedation was associated with more effective suppression of procedure-induced cough, better hemodynamic stability, a lower incidence of PONV, and a faster recovery profile compared to both intranasal saline and lidocaine, without increasing respiratory depression. Consequently, dexmedetomidine nasal spray can effectively and safely enhance patient comfort and safety, and optimize the procedural conditions for the bronchoscopists.

Keywords: dexmedetomidine nasal spray, normal saline, lidocaine, fiberoptic bronchoscopy, sedation

Introduction

Fiberoptic bronchoscopy (FB) is the gold standard for diagnosing and treating airway and pulmonary diseases.[1] Anesthetic management complexities always make this procedure challenging. Effective anesthesia for FB necessitates adequate anesthetic depth to prevent coughing and involuntary movements, maintain hemodynamic stability, and facilitate rapid postprocedural recovery. The combination of propofol and opioids, as the most commonly used IV regimen, can effectively achieve these goals but brings dose-dependent risks of respiratory and circulatory depression. Supplementing this IV approach with local anesthesia can improve patients' tolerance and satisfaction.[2]

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Lidocaine, a widely administered topical airway anesthetic for FB, offers rapid onset, short duration, and low toxicity.[3] By topically inhibiting airway sensory nerves, it effectively suppresses procedure-induced cough.[4] Intranasal administration of local anesthetics offers distinct advantages: it is a simple, non-invasive approach with high patient compliance and facilitates a rapid onset of action. This rapid efficiency is attributable to two main mechanisms. Firstly, intranasal administration evades hepatic first-pass metabolism, enhancing bioavailability and rapid systemic absorption.[5] Secondly, there is a vascular plexus in the nasal cavity, which can establish a direct connection with the subarachnoid space via the olfactory pathway. This provides a route for the rapid delivery of therapeutic agents to the central nervous system (CNS), thereby shortening the onset time.[6] Studies have shown that intranasally administered lidocaine can provide local anesthesia during invasive procedures. Nebulized lidocaine provides sufficient laryngopharyngeal anesthesia for diagnostic transnasal tracheoscopy.[7] In addition, nebulized lidocaine was shown to provide adequate airway anesthesia, optimal intubation conditions, and stable hemodynamics for awake fiber-optic intubation.[8] However, lidocaine is characterized by inherent limitations, particularly short duration of action and limited block area.

In contrast, dexmedetomidine used for intranasal administration demonstrates unique advantages and considerable potential. It is a safe and effective sedative for minor pediatric procedures.[9] Moreover, it has become one of the most common non-intravenous modalities of inducing anesthesia in clinical practice, which can be widely used for preoperative sedation and analgesia in invasive procedures.[10,11] It can be administered via traditional intranasal instillation and the mucosal atomization device (MAD), with equivalent efficacy.[12] When dexmedetomidine is administered via traditional intranasal instillation, it can reduce the incidence of laryngospasm, breath-holding, and coughing during FB in children.[13] However, it still brings inherent risks. Particularly, dosage variations may result in inadequate sedation, respiratory depression, or pulmonary aspiration due to regurgitation.

To overcome these limitations, the dexmedetomidine nasal spray utilizes the Mucosal Atomization Device (MAD) technology to achieve optimized and precise dosing. This approach has been shown to provide effective sedation and analgesia with a favorable safety profile, including a minimized risk of respiratory depression.[9,14] This combination of efficacy and safety provides a distinct advantage in procedures such as FB that necessitate spontaneous respiration and is particularly beneficial for stimulus-sensitive patients.

Nevertheless, high-quality randomized controlled trials (RCTs) evaluating the efficacy and safety of dexmedetomidine nasal spray as a premedication in patients undergoing FB under sedation remain scarce. Therefore, we designed this double-blind RCT. All participants will receive standard monitored anesthesia care (MAC) preserving spontaneous respiration and will be randomized to one of three preprocedural intranasal regimens via MAD: dexmedetomidine nasal spray, normal saline, or lidocaine. This study aimed to compare the efficacy of the three interventions in attenuating bronchoscopy-induced cough response, maintaining hemodynamic stability, and optimizing procedural conditions for operators, with the ultimate goal of evaluating the efficacy and safety of dexmedetomidine nasal spray as a premedication in patients undergoing FB under sedation.

Methods

Study Design and Patient Enrollment

This prospective, randomized, double-blind, controlled study evaluated the efficacy and safety of dexmedetomidine nasal spray in patients undergoing FB under sedation. This trial was approved by the ethics committee of the Second Affiliated Hospital of Guangxi Medical University (2024-KY0508) and was registered in the China clinical trial registry (ChiCTR2400092233). The research protocol complied with the Consolidated Standards of Reporting Trials (CONSORT) statement and the Helsinki Declaration, Good Clinical Practice (GCP) guidelines for Drug Clinical Trials outlined by the State Drug Administration (SDA), and other relevant regulations. Before participation, written informed consent was obtained from the patients and their legal representatives.

A total of 90 patients who were scheduled to undergo FB under sedation at the Second Affiliated Hospital of Guangxi Medical University from November 2024 to June 2025 were selected. Patients regardless of gender, aged 18–75 years, with a body mass index (BMI) of 18–28 kg/m^2 and classified as American Society of Anesthesiologists (ASA) physical status I–III were enrolled. The exclusion criteria were as follows: 1) allergy to fentanyl, etomidate, propofol, dexmedetomidine nasal

spray, lidocaine injection, or sodium chloride injection; 2) any mental diseases; 3) patients with concurrent conditions, such as acute myocardial infarction or hemodynamic instability, etc.; 4) patients with concurrent severe hepatic or renal diseases; 5) patients with concurrent severe obesity or obstructive sleep apnea. The withdrawal criterion was intraoperative conversion to laryngeal mask insertion requiring general anesthesia. Based on this criteria, 90 patients were enrolled and randomly divided into three groups: the dexmedetomidine nasal spray group (Group D, n = 30), the normal saline nasal spray group (Group C, n = 30), and the lidocaine nasal spray group (Group L, n = 30).

Randomization and Blinding

Before trial initiation, an independent data manager produced a computer-generated random list using IBM SPSS Statistics version 26.0 (IBM Corp, Armonk, NY, USA), with a block size of six and a 1:1:1 allocation ratio for 90 participants. Patients were assigned to three groups based on the generated sequences.

The intranasal solutions were prepared and loaded by the hospital pharmacy department. Commercially available dexmedetomidine nasal spray (25 μg/spray; Shanghai Hengrui Pharmaceutical Co., Ltd) was used for Group D. For Groups C and L, the respective solutions were loaded into new, identical, pre-sterilized, and empty metered-dose spray devices of the same type and brand as those used in Group D; these were 0.9% sodium chloride injection (250 mL: 2.25 g; Guangdong Otsuka Pharmaceutical Co., Ltd) for Group C and 2% lidocaine injection (5 mL: 0.1 g; China Otsuka Pharmaceutical Co., Ltd) for Group L. This ensured that all devices were physically indistinguishable and prevented any risk of cross-contamination or residual drug. The total delivered volume was standardized at 0.4 mL per administration (equivalent to 4 sprays). All devices were calibrated to deliver 0.1 mL per spray (validated by gravimetric measurement; <5% variance across 10 sprays). External labels displayed only group codes (D/C/L), and allocation was concealed in sequentially numbered opaque envelopes secured by non-study personnel.

Upon enrollment, coded devices were dispensed by the Pharmacy Department to a trained research nurse for standardized administration. The administering nurse was the only individual with access to the group codes and was strictly prohibited from communicating this information or participating in any subsequent patient assessment, data collection, or anesthesia management. The anesthesiologists performing the procedure and all outcome assessors were completely blinded to the group assignments. Seated patients were instructed to tilt their head forward 15° and receive one spray per nostril (total 2 sprays). Before receiving a second pair of sprays (one per nostril), the patients were instructed to tilt their head backward 20–30° while gently inhaling for 30 seconds. This resulted in a total of 4 sprays (cumulative dose per administration: Group D: dexmedetomidine 100 μg; Group C: sodium chloride 0.4 mL; and Group L: lidocaine 8 mg).

A double-blind design was thus maintained for patients, anesthesiologists, and all outcome assessors using indistinguishable devices containing colorless solutions. Outcome assessment (hemodynamics/sedation scores) was conducted by researchers who were masked to group assignment. Statisticians analyzed blinded data coded as A/B/C groups. To mitigate the bias caused by local anesthetic effects of lidocaine: (1) cough response was assessed by physicians who completed standardized training but were independent of the intervention team, with inter-observer agreement ≥0.8 (Cohen's Kappa) on video-based assessments; (2) patients were prohibited from disclosing subjective sensations to assessors; (3) post-trial unblinding guess rates were quantified to assess the success of blinding and the risk of bias.

Anesthesia Management

All patients fasted from solids for 8 hours and abstained from fluids for 2 hours preoperatively, with bilateral nasal cavities cleared. Upon entering the procedure room, the patients laid down in the supine position and underwent continuous electrocardiographic monitoring for heart rate (HR), mean arterial pressure (MAP), respiratory rate (RR), and peripheral oxygen saturation (SpO_2). An upper limb peripheral intravenous channel was established, and supplemental oxygen was administered via a nasal catheter at a rate of 6 L/min.

Before anesthesia induction, Group D received 100 μg dexmedetomidine nasal spray, Group C received 0.4 mL of 0.9% normal saline nasal spray, and Group L received 0.4 mL of 2% lidocaine (8 mg) nasal spray. All nasal sprays were administered before anesthesia induction using identical metered-dose spray devices. At 10 min after nasal spray administration, all patients received IV fentanyl 2.0–3.0 μg/kg and etomidate 0.2–0.3 mg/kg. Each drug was infused

over 30 seconds to achieve standard MAC, preserving spontaneous ventilation (RR ≥10 breaths/min, SpO_2 ≥95%). FB was performed when the MOAA/S score reached ≤1. For patients maintaining MOAA/S >1 in 3 minutes with any triggering event (persistent cough ≥2 episodes/minute; purposeful limb movement >5 seconds; hypertension: SBP >20% above baseline; sustained tachycardia: HR >100 beats/min for >120 seconds), a rescue bolus of propofol (one-third to one-quarter of the initial dose) was administered IV over 30 seconds. During the procedure, certified bronchoscopists applied a standardized protocol of 10 mL 1% lidocaine via a spray catheter to the vocal cords, tracheobronchial tree, and main carina to achieve topical anesthesia, which suppressed sensory nerve transmission to reduce coughing, thereby ensuring patient comfort and procedural feasibility.[15] It is important to note that the study interventions (intranasal dexmedetomidine, lidocaine, or saline) were administered pre-procedurally to evaluate and compare their systemic effects as premedications, rather than for providing local anesthesia for the procedure itself.

All procedures were performed by experienced anesthesiologists and certified bronchoscopists. Standard intraoperative contingency measures comprised oxygen supplementation with jaw thrust for SpO_2 <90%. When sustained >60 seconds, the bronchoscope was removed and manual ventilation was conducted using a simple breathing bag. The patients received IV atropine 0.5 mg when HR <50 beats/min, esmolol 10–20 mg when HR >100 beats/min, ephedrine 5 mg when SBP <90 mmHg and/or >20% decline from baseline, urapidil 10–20 mg when SBP elevation >20% above baseline. Following the procedure, patients were transferred to the post-anesthesia care unit (PACU) for continuous observation until the MOAA/S score reached ≥9. Patients were discharged only when accompanied by a family member.

Data Collection and Result Evaluation

The baseline characteristics of patients, such as gender, age, BMI, ASA classification, operation time, anesthesia time, induction time (time from drug administration to MOAA/S ≤1), and recovery time (time from discontinuation of anesthetics to MOAA/S =5) were recorded. HR, MAP, RR, SpO_2, and MOAA/S scores were recorded at the following time points: upon room entry (T_0), 10 minutes after nasal spray administration (T_1), immediately after induction (T_2), immediately after the bronchoscope entered the glottis (T_3), immediately after the bronchoscope reached carina (T_4), immediately after the bronchoscope reached the target bronchopulmonary segments (T_5), and at the time of bronchoscope withdrawal (T_6). Intraoperative consumption of fentanyl, etomidate, and propofol was measured. The incidence of bradycardia (HR <50 bpm), tachycardia (HR >100 bpm), hypertension (MAP >20% baseline), hypotension (MAP <20% baseline or <90 mmHg), respiratory depression (SpO_2 <95% or RR <10 breaths/min), and the number requiring rescue were recorded. Cough severity was assessed by independent, trained physicians continuously throughout the bronchoscopic procedure (from scope insertion to withdrawal, corresponding to time points T_3-T_6) using a validated 4-point scale: 0 = none; 1 = mild (<2 coughs); 2 = moderate (3–5 coughs); 3 = severe (>5 coughs).[16] The worst cough score observed during this period was recorded for each patient. The incidence of postoperative nausea and vomiting (PONV), drowsiness, dizziness, headache, and agitation during recovery was recorded. MOAA/S scores were reassessed at 15 min (T_7) and 30 min (T_8) after the procedure. Doctor-patient satisfaction score was recorded and measured using a 10-point scale (0= extremely dissatisfied; 10= extremely satisfied). Patients' satisfaction scores were evaluated based on recall accuracy, procedure-related pain, and postprocedural adverse events. Bronchoscopists' satisfaction scores were comprehensively assessed based on temporal precision (time deviation within ±15% of the planned duration), target completion rate (100% successful sampling of imaging-confirmed lesions), and procedural fluency (absence of unplanned rescue maneuvers including >2 instrument repositioning attempts or unscheduled administration of medications).

Assessment of Primary and Secondary Outcomes

The primary outcome was the severity of cough during the bronchoscopic procedure, defined as the worst cough score observed from scope insertion (T_3) to withdrawal (T_6) using the 4-point scale mentioned above.

Secondary outcomes included perioperative vital signs (HR, MAP, RR, SpO_2) at all time points, the incidence of adverse events (bradycardia, tachycardia, hypotension, hypertension, respiratory depression, postoperative nausea and vomiting, drowsiness, dizziness, headache, and agitation), anesthesia induction time, recovery time, the consumption of fentanyl, etomidate, and propofol, as well as satisfaction levels of both patients and bronchoscopists.

Sample Size Calculation

The sample size was calculated based on the primary outcome of cough severity. Using PASS 2021 (NCSS, LLC), a one-way ANOVA power calculation was performed. Based on preliminary data with mean cough scores of 1.2±0.7 in Group D, 2.0±0.8 in Group C, and 1.5±0.7 in Group L, a one-way ANOVA power calculation ($\alpha = 0.05$, $1-\beta = 0.80$, and effect size $f = 0.35$) yielded a minimum sample size of 78 subjects. Accounting for a projected 10% attrition rate, 90 participants were screened as eligible subjects.

Statistical Analysis

Statistical analyses were conducted using IBM SPSS Statistics v26.0 (IBM Corp, Armonk, NY, USA). The normality of data was assessed using the Shapiro–Wilk test. Normally distributed data with homogeneous variance (Levene's test, $P > 0.05$) are presented as mean ± standard deviation and were compared using one-way ANOVA. Significant between-group differences (ANOVA, $P<0.05$) were analyzed using Tukey's honestly significant difference (HSD) test. The Games-Howell test was used for data with variance heterogeneity (Levene's, $P \leq 0.05$). Non-normally distributed data are expressed as median (interquartile range) and were analyzed using the Kruskal–Wallis test. Significant results (Kruskal–Wallis, $P < 0.05$) underwent pairwise comparisons using Dunn's test with Bonferroni-adjusted α ($\alpha = 0.05/k$, k=number of comparisons). Categorical data are presented as numbers (%) and were compared using Chi-square or Fisher's exact test (when >20% of cells had expected counts <5), applying the Bonferroni correction method for multiple comparisons. Two-tailed tests were conducted at $\alpha=0.05$, with $P < 0.05$ considered statistically significant.

Results

Patient Enrollment and Baseline Characteristics

There were no excluded cases in this study, and 90 patients (Group D, n=30; Group C, n=30; Group L, n=30) completed the test, as shown in Figure 1.

There was no significant difference in gender, age, BMI, ASA classification, operation time and anesthesia time among the three groups ($P > 0.05$), as shown in Table 1.

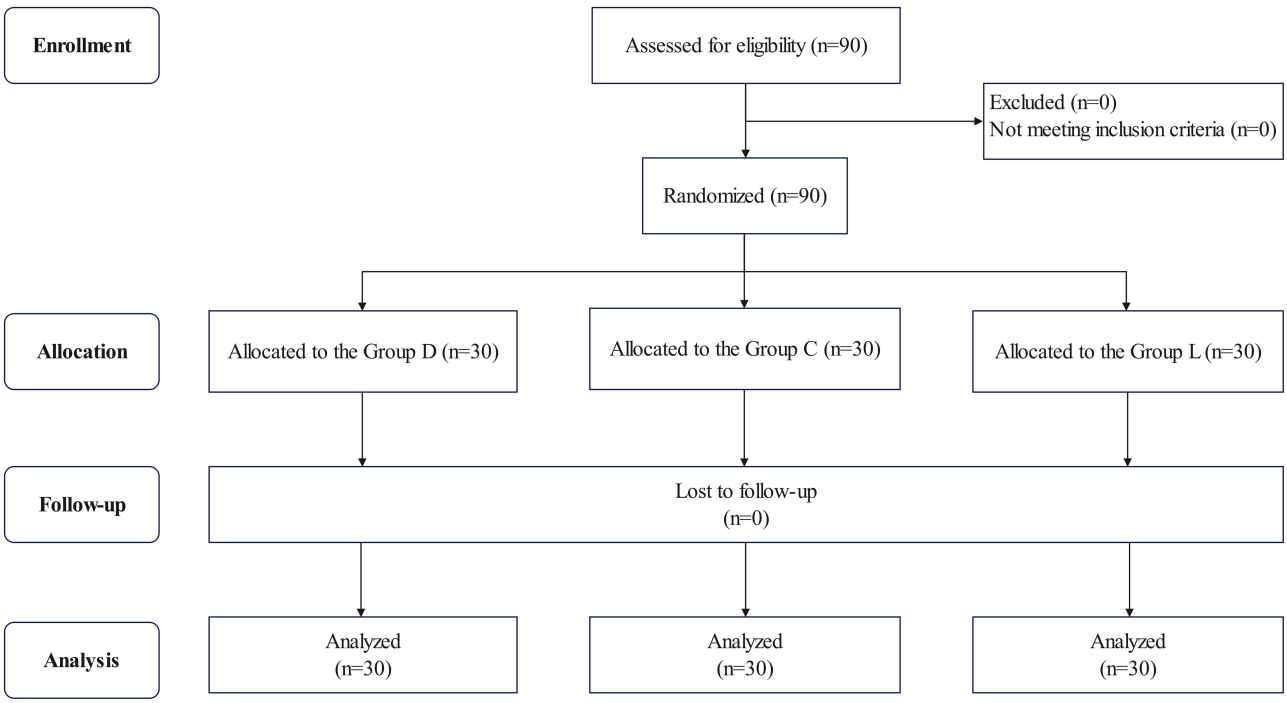

Figure 1 Flow diagram of the study.

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Table 1 Comparison of Baseline Characteristics Among Three Groups of Patients

Variable	Group D (n=30)	Group C (n=30)	Group L (n=30)	χ^2/F	P
Gender (male/female, n)	16/14	16/14	17/13	0.090	0.956
Age (years)	56.13±10.37	58.07±11.86	56.97±16.56	0.074	0.929
BMI (kg/m^2)	21.99±1.95	21.16±3.03	22.70±2.42	2.568	0.083
ASA (I/II/III, n)	8/15 /7	3/21/6	7/20/3	5.065	0.281
Operation time (min)	17.50 (9.75, 28.50)	16.00 (10.75, 20.50)	13.50 (9.75, 20.00)	1.570	0.456
Anesthesia time (min)	20.77 (13.89, 32.34)	18.73 (14.99, 25.39)	16.26 (13.07, 22.82)	4.010	0.135

Notes: Variables presented as numbers, mean±standard deviation, and median (interquartile range). Chi-square test or Fisher' s exact test, one-way ANOVA, and Kruskal–Wallis test were used for data analysis.
Abbreviations: BMI, body mass index; ASA, American Society of Anesthesiology; Group D, the dexmedetomidine nasal spray group; Group C, the normal saline nasal spray group; Group L, the lidocaine nasal spray group.

Hemodynamic Parameters

HR in Group D was lower than that in Group C at T_3 (P=0.029), however, compare to Group L, there was no significant difference between the two groups (P>0.05). HR in Group D was lower than that in Group C (P=0.033) and Group L (P=0.019) at T_5. There was no significant difference in HR among the three groups at T_0-T_2,T_4,T_6 (P>0.05), as shown in Figure 2.

MAP in Group D was lower than that in Group C ($P \leq 0.025$) and Group L ($P \leq 0.048$) at T_3-T_6. There was no significant difference in MAP among the three groups at T_0-T_2 (P >0.05), as shown in Figure 3.

RR in Group D was higher than that in Group C at T_6 (P =0.001). RR in Group L was higher than that in Group C at T_6 (P =0.001), however, there was no significant difference in RR between Group D and Group L (P >0.05). There was no significant difference in RR among the three groups at T_0-T_5 (P >0.05), as shown in Figure 4.

There was no significant difference in SpO_2 among the three groups at T_0-T_6 (P >0.05), as shown in Figure 5.

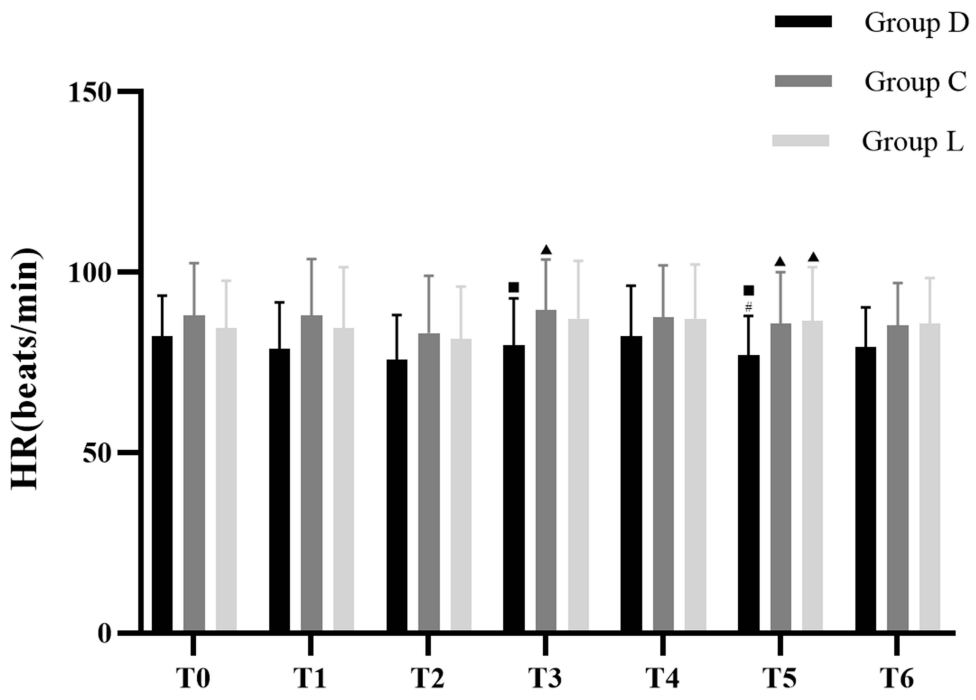

Figure 2 Comparison of HR among three group at each time.
Notes: Data expressed as mean±standard deviation. "▲" represents the group had significant difference with Group D (P <0.05); "■" represents the group that had significant differences with Group C (P <0.05); "#" represents the group that had significant differences with Group L (P <0.05).
Abbreviation: HR, heart rate.

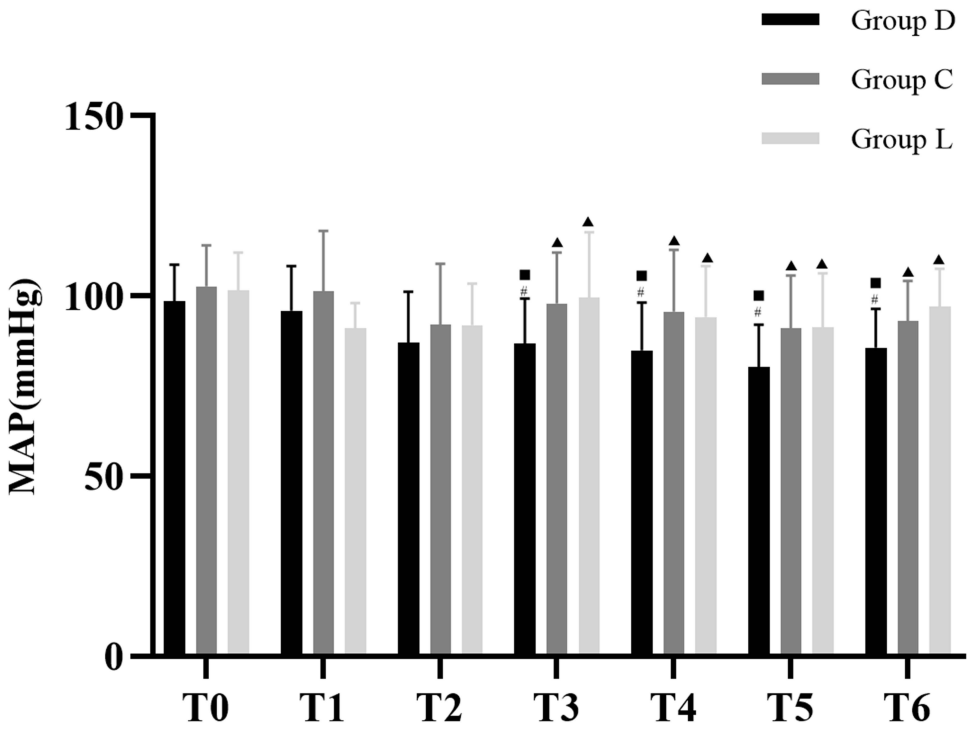

Figure 3 Comparison of MAP among three group at each time.
Notes: Data expressed as mean±standard deviation. "▲" represents the group had significant difference with Group D (P <0.05); "■" represents the group that had significant differences with Group C (P <0.05); "#" represents the group that had significant differences with Group L (P <0.05).
Abbreviation: MAP, mean arterial pressure.

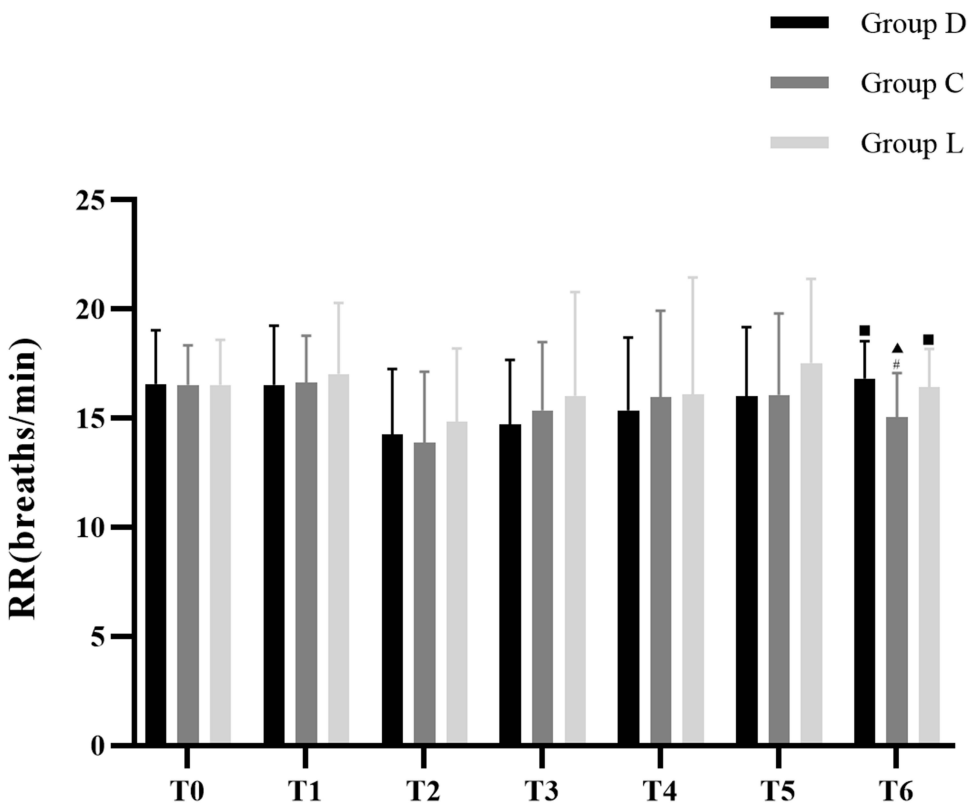

Figure 4 Comparison of RR among three group at each time.
Notes: Data expressed as mean±standard deviation. "▲" represents the group had significant difference with Group D (P <0.05); "■" represents the group that had significant differences with Group C (P <0.05); "#" represents the group that had significant differences with Group L (P <0.05).
Abbreviation: RR, respiratory rate.

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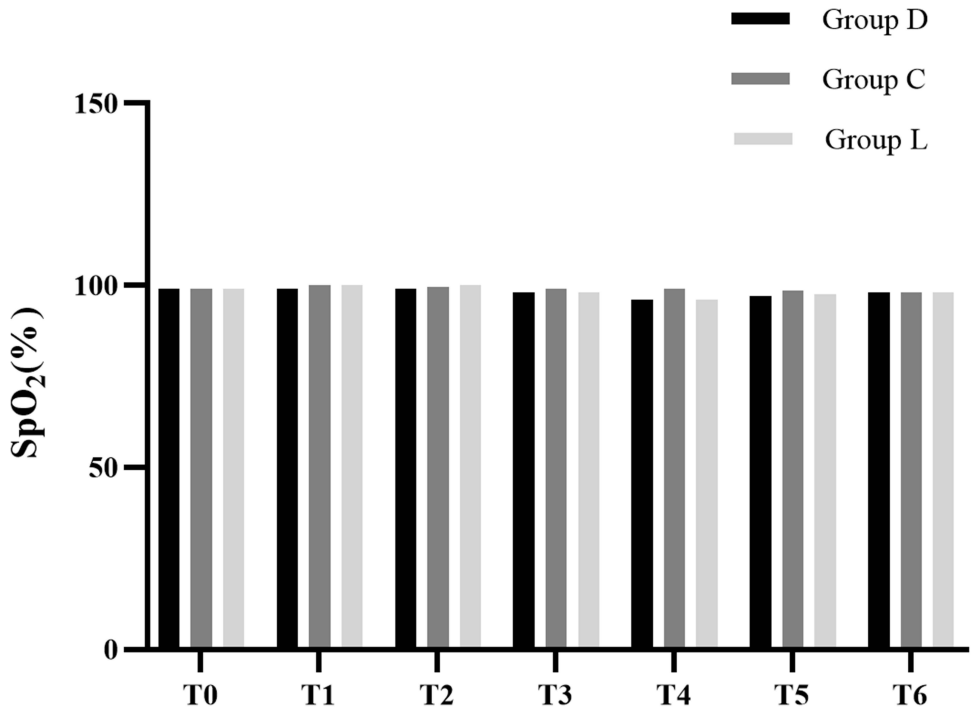

Figure 5 Comparison of SpO_2 among three group at each time.
Note: Data expressed as median (interquartile range).
Abbreviation: SpO_2, peripheral oxygen saturation.

Sedation and Recover

The induction time of Group D was shorter than that of Group C (P <0.001), however, compare to Group L, there was no significant difference between the two groups (P >0.05). The recovery time of Group D was shorter than that of Group C (P =0.001) and Group L (P =0.017), as shown in Table 2.

The MOAA/S score of Group D was lower than that of Group C (P =0.003) and Group L (P =0.001) at T_1. The MOAA/S score of Group D was higher than that of Group C (P =0.007) at T_6. The MOAA/S score of Group D was higher than that of Group C (P <0.001) and Group L (P <0.001) at T_7-T_8. There was no significant difference in MOAA/S score among the three groups at T_0, T_2-T_5 (P >0.05), as shown in Figure 6.

Drug Consumption, Satisfaction Scores, and Adverse Events

The bronchoscopists' satisfaction scores in Group D were higher than that in Group C (P <0.001) and Group L (P <0.001); There was no significant difference in the dosage of fentanyl, etomidate, propofol and patients' satisfaction scores among the three groups (P >0.05), as shown in Table 3.

Table 2 Comparison of Sedative Effects Among the Three Groups

Variable	Group D (n=30)	Group C (n=30)	Group L (n=30)	χ^2/F	P
Induction time (min)	2.02 (1.89, 2.09)■	2.75 (2.05, 3.08)▲	2.05 (1.97, 2.37)	14.653	0.001*
Recovery time (min)	9.06±4.06■#	13.55±4.96▲	12.40±4.82▲	7.632	0.001*

Notes: Variables presented as mean±standard deviation, or median (interquartile range). For normally distributed data (presented as mean±standard deviation), significant differences determined by one-way ANOVA were further analyzed with Tukey's HSD or Games-Howell post-hoc tests. For non-normally distributed data (presented as median [interquartile range]), significant differences determined by the Kruskal–Wallis test were further analyzed with Dunn's test, incorporating Bonferroni correction. "*" indicated statistically significant differences among three groups. "▲" represents the group had significant difference with Group D (P <0.05); "■" represents the group that had significant differences with Group C (P <0.05); "#" represents the group that had significant differences with Group L (P <0.05).
Abbreviations: Group D, the dexmedetomidine nasal spray group; Group C, the normal saline nasal spray group; Group L, the lidocaine nasal spray group.

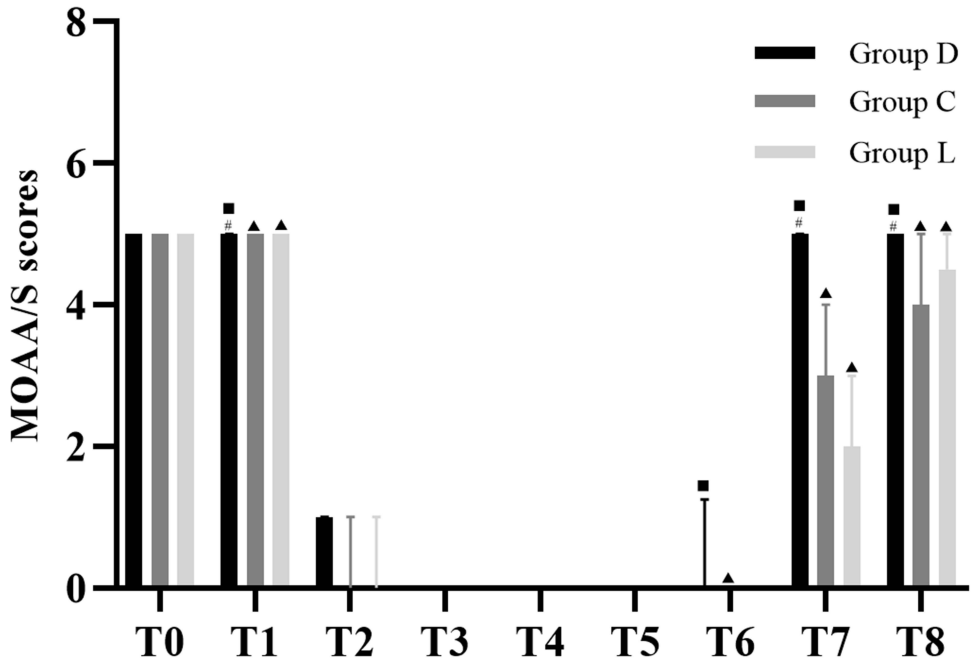

Figure 6 Comparison of MOAA/S scores among three group at each time.
Notes: Data expressed as median (interquartile range). "▲" represents the group had significant difference with Group D (P <0.05); "■" represents the group that had significant differences with Group C (P <0.05); "#" represents the group that had significant differences with Group L (P <0.05).
Abbreviation: MOAA/S, Modified Observer's Assessment of Alertness/Sedation.

The incidence of moderate-to-severe cough in Group D was lower than that in the Group C (P =0.005) and Group L (P =0.003). The incidence of PONV in Group D was lower than that in Group C (P =0.048), however, compare to Group L, there was no significant difference between the two groups (P >0.05). There was no significant difference in the incidence of hypotension, hypertension, bradycardia, tachycardia, respiratory depression, drowsiness, dizziness and headache, agitation during recovery and the number of cases requiring remedial drugs among the three groups (P >0.05), as shown in Table 4.

Table 3 Comparison of Anesthetic Drug Consumption and Doctor-Patient Satisfaction Among the Three Groups

Variable	Group D (n=30)	Group C (n=30)	Group L (n=30)	χ^2	P
Fentanyl (μg)	100.00 (100.00, 120.00)	115.00 (100.00, 135.00)	120.00 (100.00, 130.00)	5.753	0.056
Etomidate (mg)	15.50 (14.00, 18.00)	15.00 (13.00, 16.25)	16.00 (12.00, 18.00)	0.667	0.716
Propofol (mg)	50.00 (37.50, 65.00)	80.00 (50.00, 120.00)	72.50 (50.00, 112.50)	4.939	0.085
Patients' satisfaction scores	6.00 (5.00, 7.50)	6.00 (5.00, 7.00)	6.00 (5.00, 7.00)	1.092	0.579
Bronchoscopists' satisfaction scores	7.00 (6.00, 7.00)■#	5.00 (4.00, 6.00)▲	5.00 (4.00, 6.00)▲	29.045	<0.001*

Notes: Variables presented as median (interquartile range). Kruskal–Wallis test was used for data analysis, and which were further analyzed with Dunn's test, incorporating Bonferroni correction. "*" indicated statistically significant differences among three groups. "▲" represents the group had significant difference with Group D (P <0.05); "■" represents the group that had significant differences with Group C (P <0.05); "#" represents the group that had significant differences with Group L (P <0.05).
Abbreviations: Group D, the dexmedetomidine nasal spray group; Group C, the normal saline nasal spray group; Group L, the lidocaine nasal spray group.

Table 4 Comparison of Comparison of Intraoperative and Postoperative Adverse Events Among Three Groups

Variable	Group D (n=30)	Group C (n=30)	Group L (n=30)	χ^2	P
Hypotension	1 (3.0)	0	0	1.840	1.000
Hypertension	0	1 (3.0)	0	1.840	1.000
Bradycardia	0	0	1 (3.0)	1.840	1.000
Tachycardia	0	1 (3.0)	0	1.840	1.000
Respiratory depression	1 (3.0)	5 (16.7)	3 (10.0)	2.848	0.284

(*Continued*)

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Table 4 (Continued).

Variable	Group D (n=30)	Group C (n=30)	Group L (n=30)	χ^2	P
Number requiring rescue	3 (10.0)	7 (23.3)	5 (16.7)	1.890	0.450
Cough severity (none/mild/moderate/severe)	14/9/5/2■#	7/5/6/12▲	3/9/9/9▲	17.311	0.008*
PONV	2 (6.7)■	9 (30.0)▲	4 (13.3)	6.240	0.044*
Drowsiness	1 (3.0)	0	0	1.840	1.000
Dizziness and headache	0	0	0	/	/
Agitation during recovery	0	0	1 (3.0)	1.840	1.000

Notes: Variables presented as number (%) or numbers. Chi-square test or Fisher' s exact test were used for data analysis, and the Bonferroni method was used to correct for multiple comparisons. "*" indicated statistically significant differences among three groups. "▲" represents the group had significant difference with Group D (P <0.05); "■" represents the group that had significant differences with Group C (P <0.05); "#" represents the group that had significant differences with Group L (P <0.05).

Abbreviations: PONV, Postoperative nausea and vomiting; Group D, the dexmedetomidine nasal spray group; Group C, the normal saline nasal spray group; Group L, the lidocaine nasal spray group.

Discussion

This study systematically evaluated the efficacy and safety of dexmedetomidine nasal spray in patients undergoing FB under sedation. The results indicated that compared to the normal saline nasal spray group (Group C) and the lidocaine nasal spray group (Group L), the dexmedetomidine nasal spray group (Group D) demonstrated superior performance in several key areas. Specifically, Group D showed more effective attenuation of procedure-induced cough, more stable hemodynamic (evidenced by lower HR T_5 and MAP at T_3-T_6), shorter recovery time, and lower incidence of specific adverse events, notably moderate-to-severe cough and PONV. While the induction time in Group D was shorter than in Group C, it was comparable to that in Group L. Furthermore, bronchoscopists' satisfaction was significantly higher in Group D compared to both control groups.

Suppression of airway adverse reactions represents a critical indicator for a drug's efficacy and safety. The primary safety concerns during FB include excessive coughing and respiratory depression. Under light anesthesia, repeated bronchoscopic stimulation and airway suctioning may elicit cough and reflex-mediated bronchoconstriction.[17] Topical dexmedetomidine decreased cough and improved patient tolerance and intubation scores during FB.[18] In this study, the incidence of moderate-to-severe cough in Group D was lower than that in Group C and Group L. This effect may be attributed to two mechanisms. Firstly, the α_2 adrenoceptor agonist dexmedetomidine reduced cholinergic electrical field stimulation (EFS)-induced contractions and acetylcholine release, consistent with the presence of inhibitory α_2 adrenoceptors on the prejunctional side of the postganglionic cholinergic nerve-smooth muscle junction. Dexmedetomidine also attenuated both exogenous acetylcholine-induced contraction and C-fiber-mediated contraction, suggesting its direct effect on airway smooth muscle and revealing an underlying mechanism for cough suppression, respectively.[19] Secondly, dexmedetomidine may decrease airway sensitivity by downregulating the plasma concentrations of inflammatory mediators, such as interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α).[20] In contrast, deep anesthesia may cause respiratory depression. In this study, compared to Groups C and L, Group D exhibited faster recovery of RR at the time of bronchoscope withdrawal (T_6). Meanwhile, there were no significant differences between the three groups in terms of SpO_2 or the incidence of intraoperative respiratory depression, although Group D showed a trend toward a lower incidence of intraoperative respiratory depression. These findings align with the minimal respiratory depression caused by dexmedetomidine nasal spray.[21]

In addition to airway safety, hemodynamic stability is a crucial safety and efficacy indicator in FB. Previous studies have indicated that premedication with dexmedetomidine nebulization can attenuate sympathetic stimulation associated with laryngoscopy and endotracheal intubation (ETI), thereby reducing the risk of adverse cardiovascular/cerebrovascular events in susceptible patients.[22] Our results align with these findings. Compared to Groups C and L, Group D exhibited significantly lower MAP throughout key stages of bronchoscopy from bronchoscope enter the glottis (T_3) until its withdrawal (T_6). Additionally, although a statistically significant differences in HR was only confirmed at the bronchoscope reached target bronchopulmonary segments (T_5), a consistent numerical trend toward lower HR was

observed in Group D throughout the procedure (T_3-T_6) compared to both control groups. Notably, despite the absence of significant differences in the incidence of discrete circulatory adverse events (eg, hypotension, hypertension, bradycardia, tachycardia), the overall hemodynamic profile was markedly more stable in Group D. This enhanced stability can be attributed to the pharmacological profile of dexmedetomidine. It binds to presynaptic α_2-adrenergic receptors in the brainstem, inhibiting the release of norepinephrine (NE), reducing central sympathetic activity, and relatively enhancing vagal tone, thereby reducing MAP and HR.[23] Furthermore, intranasal dexmedetomidine can maintain a relatively stable drug concentration, avoiding transient hypertension and bradycardia caused by the initial peak concentration of IV loading doses, thereby suppressing cardiovascular stress responses during FB.[24] Consequently, dexmedetomidine nasal spray reduces the risk of hemodynamic abnormalities during FB with a great safety margin, which is particularly critical for patients with cardiovascular comorbidities.[25] This protective effect is especially beneficial for high-risk patients prone to cardiovascular stress, as it may reduce myocardial oxygen consumption in those with hypertension or coronary artery disease, help maintain stable cardiac output in patients with dysfunction, and minimize the risk of physiological reserve depletion in the elderly or debilitated.[26]

Under the premise of hemodynamic stability, rapid-onset sedation and high-quality recovery are essential for optimizing the experience of patients undergoing FB under sedation. In this study, the induction time in Group D was shorter than that in Group C but comparable to that in Group L. The rapid-onset sedation of dexmedetomidine observed in our study is likely attributable to its advanced intranasal delivery system. Specifically, the dexmedetomidine nasal spray utilized here employs a Mucosal Atomization Device (MAD). This technology overcomes the limitations of traditional instillation and enables optimized and precise dosing. Compared to traditional methods, dexmedetomidine nasal spray provides greater sedation for pediatric patients and minimizes stress responses to peripheral intravenous catheter insertion.[14] In adult patients undergoing total hip arthroplasty, this nasal spray improved sedation and analgesia, reduced postoperative opioid consumption, and shortened hospital stay.[27,28] Furthermore, this nasal spray reduced opioid consumption without causing respiratory depression and may be used to treat postoperative restlessness, agitation, and pain in geriatric patients.[29] This finding appears inconsistent with that of Li et al, who reported that in healthy adult volunteers, intranasal dexmedetomidine delivered by drops from a syringe or by nasal mucosal atomization had a slower onset of action compared to IV dexmedetomidine administration.[30] This discrepancy primarily originates from the significant advantages of the drug delivery system of the novel dexmedetomidine nasal spray used in this study. Its unique nasal MAD significantly enhances the efficiency and extent of intranasal absorption. The absolute bioavailability of this formulation reaches 85%,[31] which is substantially higher than the 30–65% reported for conventional intranasal formulations.[32] Furthermore, this formulation achieved a considerably shorter time to peak concentration (T_{max}), approximately 0.25–0.5 hours.[31] In comparison, conventional intranasal formulations exhibited slower absorption kinetics with T_{max} typically ranging from 0.75 hours to 1.5 hours,[32] underscoring the superior absorption kinetics of the investigational agent. This significant increase in bioavailability and absorption efficiency provides a solid pharmacokinetic basis for the rapid onset of action of this formulation. Li et al compared a specific intranasal formulation to traditional IV administration, whereas we observed that the optimized novel intranasal formulation had a faster onset of action compared to placebo and was comparable to lidocaine after intranasal administration. This difference aligns with the inherent pharmacological characteristics of dexmedetomidine and reflects the improved performance of the new formulation. In summary, compared to conventional intranasal formulations, this technically optimized, high-bioavailability dexmedetomidine nasal spray demonstrated rapid action in achieving target sedation depth (MOAA/S≤1). It not only achieved a faster onset of action compared to the intranasal formulation reported by Li et al,[30] but also suggests a pharmacokinetic profile approaching that expected after IV administration, though such extrapolations require future validation. Furthermore, this study suggests that dexmedetomidine nasal spray has a faster recovery profile for patients. Firstly, compared to Groups C and L, the recovery time in Group D was shorter. It is consistent with the findings that nebulized dexmedetomidine shortens bronchoscopy recovery time.[33] This finding suggests that intranasal administration may optimize recovery through rapid nasal absorption and high-efficiency activation of central α_2-adrenoceptor. Secondly, at 15 min (T_7) and 30 min (T_8) after the procedure, compared to Groups C and L, MOAA/S scores were higher in Group D. In addition, the study confirmed that the individual variability was significantly reduced by standardizing the details of head angle and inspiration maneuver in intranasal administration, and the relative standard

deviation was nearly 20%.[30] Crucially, the novel formulation used in this study exhibited a bioavailability of up to 85% and low between-individual variability.[31] This efficient and consistent delivery system ensures faster and more stable activation of central α_2-adrenoceptors, allowing high-quality recovery of consciousness.

This study suggests that the rapid onset, high-quality recovery of consciousness, and favorable adverse event profile of this high-bioavailability formulation collectively optimized the perioperative experience for patients. These advantages were reflected in the satisfaction scores. In terms of patient satisfaction, which predominantly relies on postprocedural experiences due to limited intraprocedural recall, the incidence of PONV in Group D was significantly lower than that in Group C. Although there was no significant difference in the incidence of drowsiness, dizziness, headache, and agitation during recovery among three groups, the reduction in PONV likely contributed to a more comfortable recovery experience. This finding suggests that dexmedetomidine can reduce the incidence of PONV in adult patients under general anesthesia and promote postoperative recovery.[34] Dexmedetomidine can reduce the dosage of opioids.[35] Opioid dosage directly affects the frequency and severity of PONV.[36] Although there was no significant difference in the dosage of fentanyl among the three groups, the dosage of fentanyl in Group D showed a decreasing trend, suggesting that dexmedetomidine may indirectly lower the risk of PONV by reducing opioid dosage, which requires further validation. Secondly, dexmedetomidine inhibits the release of NE by activating α_2-adrenergic receptors in the locus coeruleus (LC).[23] Sugino et al reported that elevated NE release and adrenergic receptor hyperactivity in the nucleus tractus solitarius (NTS) constitute the core pathological mechanism underlying PONV.[37] Preclinical and clinical evidence demonstrates that dexmedetomidine, a selective α_2-agonist, attenuates this dysregulation by inhibiting presynaptic NE release and suppressing catecholaminergic activity, which may reduce PONV incidence. On the contrary, in terms of anesthesia-related aspects, bronchoscopists' satisfaction mostly focuses on procedural fluency. Procedural interruptions caused by excessive coughing, respiratory depression, or apnea significantly correlate with lower bronchoscopists' satisfaction scores.[38] Group D exhibited a lower incidence of respiratory depression, milder cough severity, and greater respiratory stability. Consequently, bronchoscopists' satisfaction scores were significantly higher than in Groups C and L.

Limitations

This study suffers from several limitations. First, only participants with ASA physical status I–III were included, potentially restricting the generalizability of our findings and conclusions to high-risk populations, such as ASA IV or obese patients (BMI >30 kg/m^2). Further studies are needed to validate these results. Second, variability among bronchoscopists may have introduced technical bias affecting the duration and quality of the procedure. Third, as a single-center clinical study with a small sample size, our findings warrant confirmation through large-scale, multi-center clinical trials.

This study demonstrated that dexmedetomidine nasal spray as an adjunct can effectively suppress coughing, improves hemodynamic stability, and reduces the incidence of PONV in patients undergoing FB under sedation. Its respiratory depression-sparing effects also establish the value of dexmedetomidine in optimizing the safety and efficacy profile of FB under sedation.

Conclusion

Premedication with dexmedetomidine nasal spray in patients undergoing FB under sedation was associated with more effective suppression of procedure-induced cough, better hemodynamic stability, a lower incidence of PONV, and a faster recovery profile compared to both intranasal saline and lidocaine, without increasing respiratory depression. Consequently, dexmedetomidine nasal spray can effectively and safely enhance patient comfort and safety, and optimize the procedural conditions for the bronchoscopists.

Data Sharing Statement

The datasets generated during and/or analyzed during the current study are available from the corresponding authors on reasonable request. Requests should be directed to Dr. Lini Chen.

Ethical Approval and Consent Participation

This trial was approved by the ethics committee of the Second Affiliated Hospital of Guangxi Medical University (2024-KY0508) and was registered in the China clinical trial registry (ChiCTR2400092233). The research protocol complied with the Consolidated Standards of Reporting Trials (CONSORT) statement and the Helsinki Declaration, Good Clinical Practice (GCP) guidelines for Drug Clinical Trials outlined by the State Drug Administration (SDA), and other relevant regulations. Before participation, written informed consent was obtained from the patients and their legal representatives.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is 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 to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no competing financial interests or personal relationships that could influence this work.

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