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ORIGINAL RESEARCH

Effects of Ciprofol Combined with Varying Doses of Alfentanil on Anesthetic Efficacy and Safety in Pediatric Bronchoscopy: A Randomized Controlled Trial

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Objective: This study aims to evaluate the anesthetic safety of the ciprofol and alfentanil regimen for pediatric bronchoscopy and to determine the effective concentration of alfentanil.

Methods: In this single-center, prospective, double-blind, randomized controlled trial, pediatric patients scheduled for fiberoptic bronchoscopy were randomly divided into three groups: ciprofol combined with 5 μg/kg alfentanil group (Group A), ciprofol combined with 10 μg/kg alfentanil group (Group B) and ciprofol-only group (Group C). Firstly, the anesthesia nurse intravenously administered analgesic medication: 5 μg/kg alfentanil, 10 μg/kg alfentanil or 2 mL of normal saline intravenously. And then administered 0.4 mg/kg of ciprofol. After induction, supplemental ciprofol (0.1 mg/kg) was given as needed according to cough score and vital signs. The primary outcome was the coughing score during bronchoscope passage through the glottis (T3) and carina (T4). Secondary outcomes included anesthesia induction cooperation scores, intraoperative anesthesia effect ratings, operator satisfaction levels, occurrence of adverse reactions, as well as hemodynamics and oxygen saturation at T1–T5.

Results: Between February 2025 and October 2025, 97 patients were included (Group A: n=32, Group B: n=33, Group C: n=32). Group B has better anesthesia quality, as assessed by several measures. For example, Compared with the ciprofol-only group, Group B exhibited lower cough scores during passage through the glottis and carina (median (IQR): T3, 2 (1.5–2) vs. 2.5 (2–4), $p = 0.015$; T4, 2 (1–2) vs. 2 (2–3), $p = 0.02$). Additionally, this group significantly improved operator satisfaction ($p = 0.04$), and higher rates of excellent or good anesthesia outcomes ($p = 0.026$). Finally, there was no significant difference in adverse reactions and safety indicators among the three groups ($p > 0.05$).

Conclusion: The combination of ciprofol with 10 μg/kg alfentanil may be more appropriate for clinical anesthesia during pediatric bronchoscopy without increasing the incidence of side effects.

Trial Registration: ChiCTR.org.cn (ChiCTR2500097084). Date of registration: February 12, 2025.

Plain Language Summary: Our team's research has demonstrated that the combined use of ciprofol and alfentanil in pediatric painless bronchoscopy yields a "1+1>2" comfort effect: ciprofol induces loss of consciousness and quiet sleep in children, while alfentanil provides profound analgesia and suppresses the cough reflex. Both drugs can be administered at lower doses than when used individually, yet achieve superior results.

Therefore, the combination of ciprofol and alfentanil for pediatric painless bronchoscopy is akin to a tailored solution for children, significantly enhancing patient cooperation during anesthesia induction and the overall anesthetic effect without increasing adverse reactions such as respiratory depression.

Keywords: pediatric anesthesia, ciprofol, bronchoscopy, alfentanil, cough score

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Introduction

Pediatric bronchoscopy serves as a crucial diagnostic and therapeutic tool, widely utilized in the management of pediatric respiratory diseases.[1] Studies[2,3] indicate that the increasing annual incidence of conditions such as childhood asthma and bronchial foreign bodies imposes significant economic burdens on families and society, highlighting the necessity for effective treatment methods to enhance patients' quality of life. Previous epidemiological data reveal that the prevalence of childhood asthma has consistently risen over the past decades, a phenomenon that has attracted extensive attention from both academic and clinical medical communities.[4]

Currently, the primary treatment approaches for pediatric respiratory diseases encompass drug therapy, mechanical ventilation, and bronchoscopy.[5–7] However, these methods often encounter challenges in clinical application, including suboptimal efficacy and significant side effects. While drug therapy can alleviate symptoms, prolonged use may result in drug dependence and other adverse effects.[8] Although mechanical ventilation can rapidly enhance oxygenation status, it may also lead to ventilation-associated injuries, necessitating particularly cautious use in pediatric patients.[9] Bronchoscopy serves as both a diagnostic and therapeutic tool, rendering it an indispensable and powerful instrument in managing pediatric respiratory diseases. It provides definitive diagnoses and effective treatments for numerous children with complex or severe respiratory conditions.[10,11] However, most pediatric bronchoscopies are conducted under intravenous general anesthesia, which carries risks such as respiratory depression, hypotension, and emergence agitation. Consequently, identifying a safe, effective, and minimally adverse anesthesia protocol has become an urgent issue in current pediatric bronchoscopy practice.

Although several studies[12–14] have explored the application of anesthesia in pediatric bronchoscopy, comparative research on various anesthetic drug combinations remains insufficient. Ciprofol, a novel GABA-A receptor agonist, shares a similar molecular structure with propofol but features a cyclopropyl group and exists as R- and S-enantiomers. This agent can rapidly induce general anesthesia while enhancing both the depth and stability of the anesthetic state.[15] In the existing literature, ciprofol, a novel anesthetic agent, has garnered attention due to its favorable sedative effects and fewer side effects, while alfentanil, a potent opioid, is widely recognized for enhancing anesthetic efficacy.[16,17] Furthermore, during outpatient transesophageal echocardiography examinations, the combination of ciprofol and low-dose alfentanil demonstrated higher safety compared to propofol, with significantly lower incidences of adverse reactions and injection pain.[18] In gynecological day surgery anesthesia, the efficacy of ciprofol combined with alfentanil was found to be superior to that of propofol combined with alfentanil, providing more stable hemodynamics while reducing adverse events.[19] However, systematic research on the efficacy and safety of combining ciprofol with alfentanil for pediatric bronchoscopy remains insufficient. Although relevant studies[20] suggest that dexmedetomidine combined with 10μg/kg alfentanil appears to be more suitable than other dosage combinations, significantly reducing the incidence of emergence agitation and postoperative nausea and vomiting, the optimal dose of alfentanil in the context of this study has not been clearly defined. This presents an opportunity for our research. We hypothesize that the combination of 10μg/kg alfentanil with ciprofol can effectively suppress the cough reflex during bronchoscopy, thereby achieving safe and satisfactory anesthesia. Furthermore, we aim to explore the inhibitory effect of a lower dose of 5μg/kg alfentanil combined with ciprofol on the cough reflex in pediatric patients at this safe dosage level.

In summary, this study aims to investigate the synergistic effects of ciprofol and varying doses of alfentanil in pediatric bronchoscopy. Through comprehensive research on the combined administration of ciprofol and alfentanil, we aspire to establish a safer and more effective anesthesia protocol for pediatric bronchoscopy.

Materials and Methods

Study Design

This study is a prospective, single-center, double-blind, randomized controlled trial that has received approval from the hospital's medical ethics committee (Ethics Approval No.: (2024) Lun Shen Lin Di (58)) and has completed clinical trial registration (Registration No.: ChiCTR2500097084). Prior to the trial, the study protocol was thoroughly explained to patients and their families, relevant treatment measures were clarified, and written informed consent was obtained from all participants. We adhered to the Consolidated Standards of Reporting Trials (CONSORT) reporting guidelines.

Participants

Eligible patients scheduled for fiberoptic bronchoscopy under total intravenous anesthesia at Ganzhou Maternal and Child Health Hospital from February 2025 to October 2025 were enrolled. Inclusion criteria included being scheduled for fiberoptic bronchoscopy under total intravenous anesthesia, being under 18 years of age regardless of gender, having an ASA physical status of I–II, and having no history of allergy to opioids or amide local anesthetics. Exclusion criteria consisted of children or their guardians refusing to participate in the study, contraindications to general anesthesia, known or suspected hypersensitivity or contraindications to ciprofol excipients or opioids, a history of allergy to amide-type local anesthetics, severe major diseases affecting the heart, lungs, liver, kidneys, brain, or other vital organs, as well as neurological or psychiatric disorders and long-term use of sedatives or antidepressants. Children whose surgical methods were altered or who experienced specific adverse events during surgery (such as requiring emergency intubation, massive hemorrhage, severe arrhythmia, drug allergy, or cardiac arrest) were excluded from the study. If patients refused to continue participating in the study during its implementation, they were considered withdrawn.

Randomization and Blinding

Participants were randomly assigned in a 1:1:1 ratio to three groups using computer-generated randomization tables under blinded conditions: the ciprofol combined with 5 µg/kg alfentanil group (Group A), the ciprofol combined with 10 µg/kg alfentanil group (Group B), and the ciprofol-only group (Group C) (Figure 1). The study numbers and group allocations were maintained in sealed envelopes by the same operating room nurse who was not involved in the study. Prior to the administration of anesthesia, the sealed opaque envelopes were opened by the operating room nurse, and the corresponding drugs were prepared according to the random sequence before being provided to the anesthesiologist

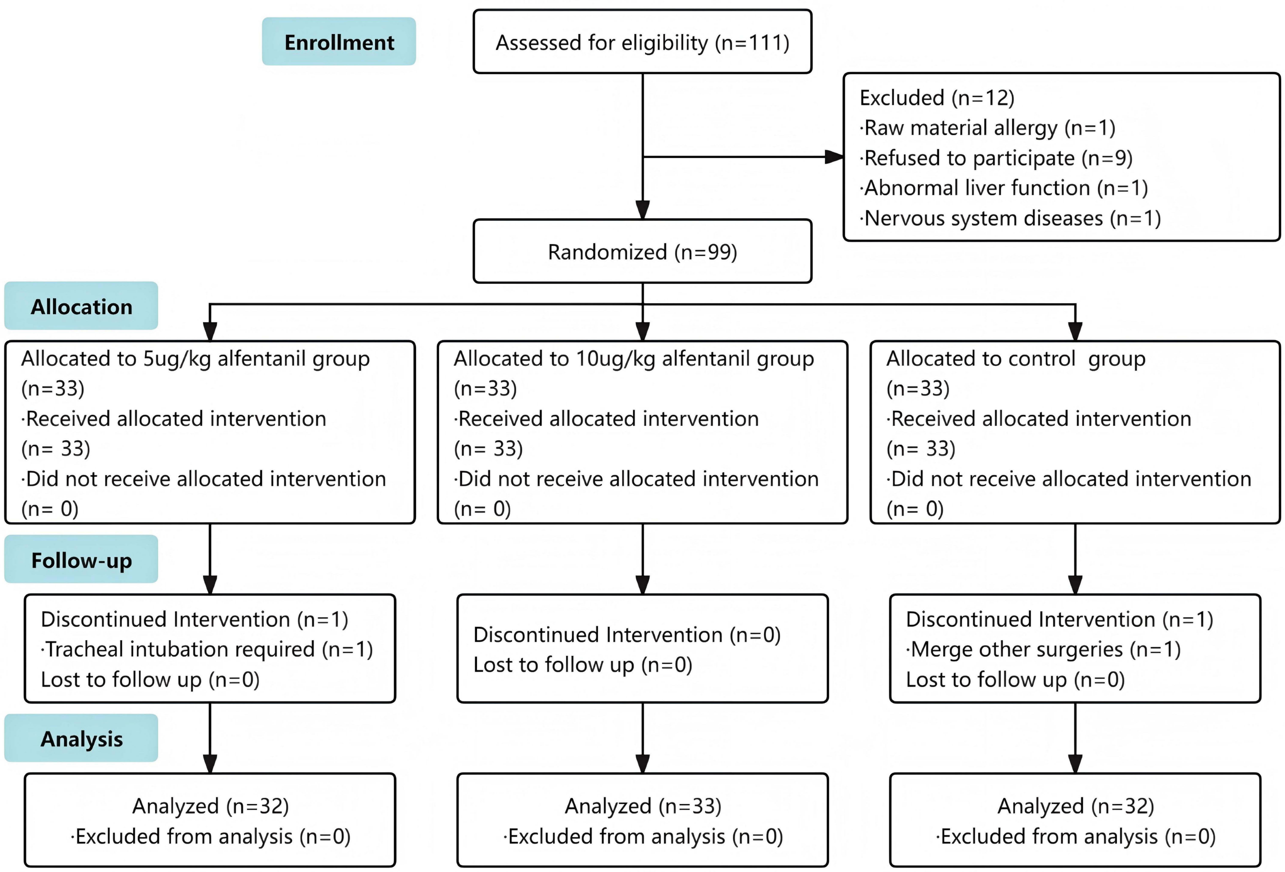

Figure 1 Study Flow Diagram. Group A: ciprofol combined with 5 ug/kg alfentanil group, group B: ciprofol combined with 10 ug/kg alfentanil group, group C: ciprofol-only group.

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(Qiao Yang) responsible for implementing the anesthesia. The pediatric patients were unaware of their group assignments, operative doctor and the anesthesiologists (Qiao Yang, Fan Li) involved in anesthesia management and postoperative follow-up were blinded to the group allocations until the conclusion of the experiment, when the group assignments were disclosed. Anesthesiologists who evaluated all primary and secondary outcomes were blinded to ensure the objectivity of the data.

The Preparation of Items

Alfentanil Hydrochloride Injection (Humanwell pharmaceutical, Yichang City, Hubei Province, China, 2 mL: 1 mg), Ciprofol Injection (Liaoning HISCO Pharmaceutical Co., Ltd., Xingcheng City, Liaoning Province, China, 20 mL: 50 mg), 0.9% Sodium Chloride Injection (10 mL: 0.09 g), 100 mL of 0.9% Sodium Chloride Injection, disposable sterile syringes in sizes of 2.5 mL, 5 mL, and 10 mL, Atropine (1 mL: 0.5 mg), and Lidocaine Hydrochloride Injection (5 mL: 100 mg), along with sterile gloves.

Preoperative Preparation and Monitoring

Prior to the procedure, a preoperative assessment was conducted for each patient, including medical history, physical examination, and laboratory findings. Following detailed communication about the examination process, anesthesia risks, and study objectives, written informed consent for both anesthesia and research participation was obtained from the parents or guardians. All pediatric patients were fasted according to standard guidelines: 8 hours for solid food, 6 hours for infant formula, 4 hours for breast milk, and 2 hours for clear fluids.Upon arrival in the endoscopy suite, standard monitoring was established, including continuous electrocardiography, pulse oximetry, non-invasive blood pressure, and respiratory rate. Intravenous access was secured in an upper limb. To facilitate scope insertion and reduce mucosal trauma, lidocaine gel was applied to both nostrils for lubrication and local anesthesia.Hemodynamic and respiratory parameters, specifically oxygen saturation, heart rate, and mean arterial pressure, were recorded at the following time points: before anesthesia induction (T1), after anesthesia induction (T2), during glottis passage (T3), during carina passage (T4), and at the end of the procedure (T5).

Anesthesia Process

Prior to bronchoscopy, patients inhaled pure oxygen for 3 minutes at a flow rate of 4–6 L/min. After ensuring that both the patient and the operating physician were adequately prepared, an anesthesia nurse, who was not involved in the observation, administered intravenous analgesic medication. In Group A, alfentanil was administered intravenously at a dosage of 5 µg/kg; in Group B, the dosage was increased to 10 µg/kg; and in Group C, 2 mL of normal saline was administered intravenously. All injections were delivered over a period of 30 seconds.

Following the completion of Alfentanil Hydrochloride Injection administration, a blinded anesthesiologist administered 0.4 mg/kg of Ciprofol via a micro-infusion pump over one minute. The entire anesthesia induction process was conducted by the same experienced senior anesthesiologist, and the intraoperative anesthesia induction cooperation score was assessed by observing the child's behavior post-induction. The examination was performed when the patient's Modified Observer's Assessment of Alertness/Sedation (MOAA/S)[21] score was ≤1. All patient groups received nasal oxygen inhalation at a rate of 4–6 L/min during the examination. The procedure was conducted nasally, and following endoscope insertion, 1% lidocaine (2–6 mL, prepared by diluting 5 mL of 2% lidocaine with 5 mL of 0.9% sodium chloride injection to a total volume of 10 mL) was applied for local anesthesia at the glottis and bilateral bronchi. Cough scores were recorded upon passing through the glottis (T3) and carina (T4). In instances of sinus bradycardia during the procedure, atropine 0.03 mg/kg could be administered intravenously, with a maximum single dose not exceeding 0.5 mg. Additional Ciprofol was administered as necessary based on patient movement and vital signs during the procedure, such as the operation cannot continue due to severe cough (cough score ≥ 3) or body movement, with each supplemental dose being 0.1 mg/kg. If the patient requires tracheal intubation for assisted breathing due to changes in the surgical approach or serious adverse events during the operation, anesthesia should be immediately deepened, tracheal intubation performed or a laryngeal mask inserted, and the patient excluded from the trial, with no further trial intervention. This patient will not be included in the final intention-to-treat analysis. Respiratory depression is defined as SPO2 (oxygen saturation) < 90%. If intraoperative SPO2 falls below 90%, support the mandible; if SPO2 remains below 85% for 15 seconds without improvement, pause the endoscopic procedure, withdraw the bronchoscope, and administer oxygen via mask. Bronchoscopy may resume once oxygen saturation returns to normal. In cases of severe refractory hypoxemia, endotracheal intubation should be performed as necessary.

At the conclusion of the procedure (T5), the anesthetic effect was evaluated, and a satisfaction questionnaire was administered to the operating physician. Subsequently, the child was transferred to the recovery room, where they were promptly provided with pure oxygen at a flow rate of 4–6 L/min and closely monitored for respiration, heart rate, oxygen saturation, non-invasive blood pressure, and electrocardiogram readings. The child's level of consciousness was assessed every two minutes, with orientation and wakefulness determined by the child's ability to respond to commands. If the child did not open their eyes or grasp hands upon being called, or exhibited no significant response to painful stimuli after 30 minutes post-operation, delayed recovery was indicated. The child was returned to the ward after achieving a modified Aldrete score of 9 in three consecutive assessments. Additionally, the operation time, recovery time, and discharge time from the recovery room were meticulously recorded.

Main Indicators

General Information

Demographic data, including age, gender, height, weight, and ASA grading, alongside baseline data such as platelet count, hemoglobin, white blood cell count, surgery duration, and basic vital signs, will be collected.

Main Outcome

The coughing score during bronchoscope passage through the glottis (T3) and carina (T4) is categorized as follows: 1 point indicates no coughing and smooth scope insertion; 2 points denote mild cough with occasional coughing and acceptable scope insertion; 3 points represent moderate cough with frequent coughing and resistance during scope insertion; and 4 points signifies severe cough with persistent coughing and difficult scope insertion.[13]

Secondary Outcomes

1. Heart Rate (HR), Mean Arterial Pressure (MAP), and Oxygen Saturation (SpO2) will be recorded before anesthesia induction (T1), after induction (T2), during glottis passage (T3), during carina passage (T4), and at the end of the procedure (T5).
2. Occurrence of adverse reactions such as intraoperative injection pain, intraoperative respiratory depression, postoperative respiratory depression, postoperative coughing, and delayed recovery.
3. The total dosage of lidocaine hydrochloride administered and the total number of additional Ciprofol injections used during bronchoscopy procedures in each group of pediatric patients were recorded.
4. The operation duration (from start to end), wake-up time (from the end of the surgery to the patient's recovery of orientation), and checkout time (from the end of the surgery to the patient meeting the discharge criteria).
5. Anesthesia induction cooperation scores, intraoperative anesthesia effect ratings, and operator satisfaction levels.

At T2, the Induction Compliance Checklist (ICC) was utilized by observers to evaluate the degree of cooperation during intraoperative anesthesia induction by assessing the child's behavior. The scoring criteria are as follows: (1 point) Excellent, actively cooperative: the child voluntarily accepts the mask, appears happy or smiling, and interacts positively with medical staff; (2 points) Good, slight hesitation: the child does not voluntarily accept the mask but shows no resistance, can be comforted (eg., through verbal reassurance or parental hugs), does not resist the mask, may ask questions, and follows instructions; (3 points) Fair, moderate resistance: the child refuses the mask, requires physical restraint, and exhibits signs of distress such as crying, turning their head, or pushing hands away; (4 points) Poor, severe resistance: the child struggles intensely and requires multiple personnel to enforce restraint; (5 points) Very poor, difficult induction: the child displays severe panic, struggles, anger, strong resistance, and is completely uncooperative, resulting in an extremely challenging induction process. In clinical practice, a score of 1 or 2 is generally considered indicative of successful cooperation, whereas a score of 3 or higher indicates poor cooperation. The level of cooperation during anesthesia induction is calculated using the following formula: Cooperation level during anesthesia induction = (Number of cases with scores 1 or 2 / Total number of cases) × 100%.

At the conclusion of procedure T5, a satisfaction survey was administered to the respiratory physicians conducting the examination, utilizing a structured questionnaire. The satisfaction ratings were evaluated on a 5-point Likert scale,[22] categorized as follows: very satisfied (5 points), satisfied (4 points), neutral (3 points), somewhat dissatisfied (2 points), and very dissatisfied (1 point). The overall satisfaction rate was computed using the formula: Overall satisfaction rate = (Number of cases rated 4 or 5 / Total number of cases) × 100%.

Intraoperative anesthesia efficacy is rated as follows: Excellent: characterized by a good glottal opening with no coughing or only occasional coughing during bronchoscopy insertion; Good: marked by a well-opened glottis that allows smooth entry of the bronchoscope, although accompanied by 3–5 episodes of paroxysmal coughing; Fair: indicated by a poorly opened glottis, persistent nausea reflex, difficulty in bronchoscope entry, and 7–8 or more episodes of obvious paroxysmal coughing, along with restlessness, but without significant cyanosis or asphyxia; Poor: defined by a severely compromised glottal opening, reflux, obstruction of the bronchoscope, and severe paroxysmal coughing and agitation, accompanied by cyanosis and asphyxia. To calculate the overall rate of excellent and good outcomes, use the following formula: Total excellent and good rate = (number of excellent cases / total cases) × 100%.

Sample Size and Statistical Analysis

Preliminary pre-experimental results indicated that the mean ± standard deviation of cough scores for pediatric patients in groups A, B, and C were as follows. With a Type I error rate set at 0.05 and a statistical power of 0.90, the calculated minimum sample size required was 93 subjects. To account for potential attrition due to changes in clinical conditions, 111 pediatric patients were initially recruited for the study. No interim analyses were planned or conducted. The normal distribution of variables was checked by Kolmogorov Smirnov test. Continuous data is expressed as mean (SD), and if it is normally distributed, ANOVA/repeated measurement ANOVA is used for comparison. The non normal distribution data were reported as the median (IQR) and analyzed by Kruskal Wallis test. Categorical variables were reported as quantities (%), Fisher's exact test were employed to analyze categorical data. A p-value of less than 0.05 was established as the threshold for statistical significance. All data analyses were conducted using the Statistical Package for the Social Sciences version 26.0 (SPSS).

Results

Among the 111 eligible pediatric cases selected, 12 (9 refusals, 1 allergic reaction to the excipients of ciprofol injection, 1 abnormal liver function, and 1 neurological disorder) were excluded based on the exclusion criteria. Additionally, 1 was excluded due to a modification in the surgical method, and 1 was excluded for requiring intraoperative endotracheal intubation. Consequently, a total of 97 patients were included in the final analysis, the participant flow is detailed in the CONSORT diagram (Figure 1). The 97 pediatric patients were randomly divided into three groups: the ciprofol combined with 5μg/kg alfentanil group (Group A, n=32; median (IQR) age, 15 (9.25–49.75) months), the ciprofol combined with 10μg/kg alfentanil group (Group B, n=33; median (IQR) age, 15 (7–39.5) months), and the control group (Group C, n=32; median (IQR) age, 14.5 (7–65) months) (Table 1).

Comparison of General Characteristics Among the Three Groups of Pediatric Patients

The patient characteristics including age, gender, weight, height, WBC, HGB, PLT, operation time, recovery time, discharge time from Postanesthesia care unit (PACU), type of surgery, and preoperative oxygen saturation are presented below, showing no statistically significant differences between the two groups (Table 1).

Primary Outcome: Cough Score

Kruskal–Wallis test was used to analyze cough scores, and the results showed that compared with the ciprofol-only group (Group C), Group B exhibited lower cough scores during passage through the glottis and carina (median (IQR): T3, 2

Table 1 Demographic and Perioperative Characteristics

Characteristic	Patients, Median (IQR)				P
	Group A (n=32)	Group B (n=33)	Group C (n=32)	H/F/χ2	
Age [range], months	15 (9.25–49.75) [3–180]	15 (7–39.5) [2–132]	14.5 (7–65) [4–120]	0.746	0.689
Height, cm	77.5 (68.5–100)	75 (65–98)	75 (69.25–110.25)	0.236	0.888
Weight, kg	10.85 (7.25–17.13)	9 (7–15)	10 (8–17.48)	1.145	0.564
WBC, 10^9/L	10.26 (6.98–12.46)	10.08 (7.36–14.17)	10.08 (7.53–11.92)	0.186	0.911
HGB, g/L	124 (116.75–133.75)	122 (112–128)	124.5 (118–129.75)	1.617	0.445
PLT, 10^9/L	356.5 (300.75–453.5)	393 (289–462)	337.5 (267.5–421.5)	0.964	0.618
Respiratory Rate, breaths per minute	32.5 (28–40.5)	36 (27–38)	36 (28–39.5)	0.290	0.865
SPO_2, %	96 (95–97)	96 (95–97)	96 (95–98)	1.572	0.456
Surgical duration, min	25 (20–25)	25 (15–25)	25 (20.5–25)	1.620	0.445
Amount of lidocaine, mg	20 (20–40)	20 (20–30)	20 (20–40)	1.880	0.391
Preoperative diagnosis					
Tracheal foreign body, No. (%)	5 (15.6)	7 (21.2)	7 (21.9)	0.481	0.786
Pneumonia, No. (%)	20 (62.5)	22 (66.7)	20 (62.5)	0.164	0.921
Other, No. (%)	7 (21.9)	4 (12.1)	5 (15.6)	1.148	0.563
Preoperative blood oxygen saturation					
≥95, No. (%)	28 (87.5)	29 (87.9)	27 (84.4)	0.289	0.934
<95, No. (%)	4 (12.5)	4 (12.1)	5 (15.6)		
Gender					
Male, No. (%)	23 (71.9)	22 (66.7)	22 (68.7)	0.209	0.901
Female, No. (%)	9 (28.1)	11 (33.3)	10 (31.3)		

Notes: Group A: ciprofol combined with 5 ug/kg alfentanil group, group B: ciprofol combined with 10 ug/kg alfentanil group, group C: ciprofol-only group.
Abbreviations: IQR, Interquartile range; PLT, Platelet; HGB, Hemoglobin; WBC: White blood cells; SPO2: Pulse Oxygen Saturation.

(1.5–2) vs. 2.5 (2–4), $p = 0.015$; T4, 2 (1–2) vs. 2 (2–3), $p = 0.02$). However, there was no significant difference between group A and group C (T3: $p = 0.636$; T4: $p = 0.932$). These results confirmed that Group B had superior intraoperative cough suppression efficacy, indicating that Group B could provide better sedation for pediatric bronchoscopy (Table 2 and Figure 2).

Table 2 Comparison of Bronchoscopy Cough Scores Among Three Groups

Variable	Group A (n=32)	Group B (n=33)	Group C (n=32)	H/χ2	P
Bronchoscopy Cough Scores at T3, median (IQR)					
Score value	2 (2–3)	2 (1.5–2)	2.5 (2–4)	7.934	0.019
$P_{C\text{-}A}$ $P_{C\text{-}B}$ $P_{A\text{-}B}$	0.362 0.015 0.636				
Bronchoscopy Cough Scores at T4, median (IQR)					
Score value	2 (1–2)	2 (1–2)	2 (2–3)	7.513	0.023
$P_{C\text{-}A}$ $P_{C\text{-}B}$ $P_{A\text{-}B}$	0.274 0.020 0.932				

Notes: Group A: ciprofol combined with 5 ug/kg alfentanil group, group B: ciprofol combined with 10 ug/kg alfentanil group, group C: ciprofol-only group. T3, when passing through glottis; T4, when passing through carina.
Abbreviation: IQR, Interquartile range.

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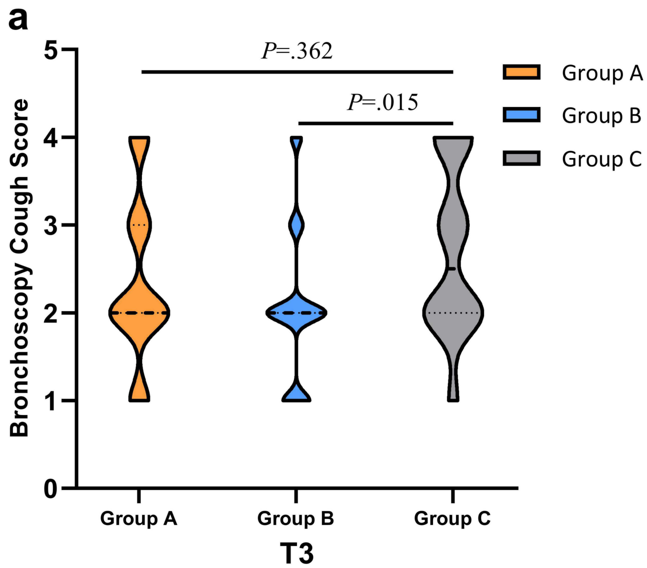

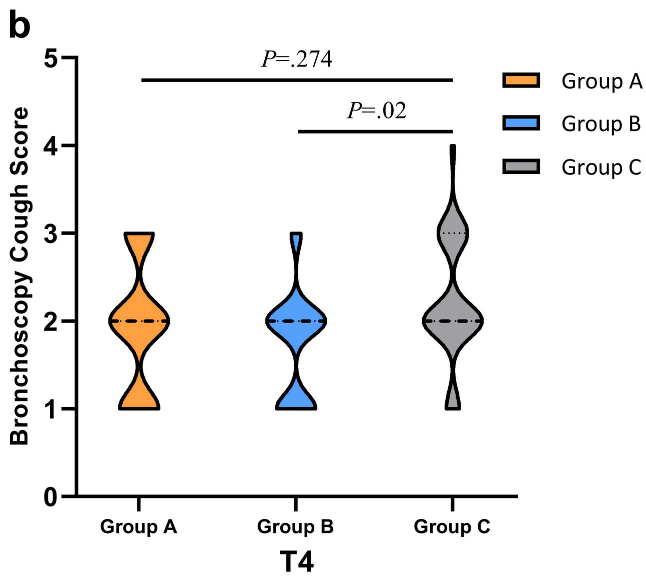

Figure 2 Comparison of Bronchoscopy Cough Scores among three groups of children. (**a**) Bronchoscopy Cough Scores at T3. (**b**) Bronchoscopy Cough Scores at T4. Group A: ciprofol combined with 5 ug/kg alfentanil group, group B: ciprofol combined with 10 ug/kg alfentanil group, group C: ciprofol-only group. T3, during glottis passage; T4, during protuberance passage.

Secondary Outcomes

Comparison of Adverse Reactions Among the Three Groups of Pediatric Patients

Fisher's exact test was used to analyze the incidence of adverse reactions. All three groups exhibited low levels of injection pain ($P > 0.05$), with rates of 6.3%, 6.1%, and 12.5%, respectively. The incidence rates of intraoperative respiratory depression, postoperative respiratory depression, postoperative nausea and vomiting (PONV), postoperative coughing, and delayed recovery were comparable ($P > 0.05$). This finding indicates that compared with Group C, Group A and Group B did not increase the occurrence of related adverse reactions, thereby demonstrating favorable safety profiles (Table 3 and Figure 3).

Table 3 Comparison of Adverse Reactions Among Three Groups of Children

Variable	Patients, No. (%)			$H/\chi 2$	*P*
	Group A (n=32)	Group B (n=33)	Group C (n=32)		
Injection pain	2 (6.3)	2 (6.1)	4 (12.5)	1.095	0.655
Intraoperative respiratory depression	4 (12.5)	7 (21.2)	5 (15.6)	0.921	0.631
Postoperative respiratory depression	0 (0)	1 (3.0)	1 (3.1)	1.243	1
Postoperative cough	10 (31.3)	9 (27.3)	13 (40.6)	1.376	0.503
Delayed recovery	1 (3.1)	2 (6.1)	3 (9.4)	1.099	0.693

Notes: Group A: ciprofol combined with 5 ug/kg alfentanil group, group B: ciprofol combined with 10 ug/kg alfentanil group, group C: ciprofol-only group.
Abbreviation: IQR, Interquartile range.

Comparison of Excellent Anesthesia Rate, Ciprofol Supplementation Frequency, Recovery Status, Induction Cooperation Degree, and Operator Satisfaction Among the Three Groups of Pediatric Patients

Fisher's exact test were employed to analyze categorical data. The operator satisfaction and excellent anesthesia rate in Group B were significantly higher than those in Group C (90.9% [30/33] vs. 65.6% [21/32], P = 0.04; 87.9% [28/33] vs. 59.4% [17/32], P = 0.026). Analysis of anesthesia induction cooperation revealed that Group B also demonstrated significant superiority (P = 0.003). Although Group A showed improvements in all aspects, the differences were not statistically significant (P > 0.05). Additionally, the Kruskal–Wallis test revealed that the number of ciprofol supplemental doses decreased significantly with increasing doses of alfentanil (P < 0.001). This indicates that Group B can improve the intraoperative anesthetic efficacy and cooperation in pediatric patients, further enhancing their surgical safety without prolonging the recovery time (P = 0.672) or discharge time (P = 0.347) (Table 4 and Figure 3).

Comparison of Hemodynamics and Oxygen Saturation Among Three Groups of Pediatric Patients

Repeated-measures analysis of variance (RMANOVA) revealed a significant group-by-time interaction for heart rate (F = 13.471, P < 0.001) and for mean arterial pressure (F = 7.873, P < 0.001). Post-hoc pairwise comparisons with Bonferroni correction showed that the MAP in group B was significantly lower than that in group C at T3 (P = 0.009), with no significant differences observed among the three groups at all other time points (P > 0.05). Regarding perioperative HR: At the T2 and T5 time point, Group B exhibited a lower heart rate level compared to Group C (P =0.014, P =0.032). At the T3 time point, Group B showed a significantly lower heart rate than Group C (P =0.001), while Group A also demonstrated a lower heart rate level than Group C (P =0.042), though no significant difference was observed between Group A and Group B (P =0.228). At the T4 time point, both Group A and Group B had lower heart rate levels compared to Group C (P =0.046, P =0.005), but the difference between Group A and Group B was not statistically significant (P =0.414). At the T1 time points, there were no significant differences in heart rate among the three groups of children (P > 0.05). Additionally, the Kruskal–Wallis test revealed that the three groups of children exhibited high consistency in intraoperative oxygen saturation levels at various time points, with no statistically significant differences (P > 0.05), further confirming the safety of ciprofol combined with alfentanil (Table 5 and Figure 3).

Discussion

This study employed a randomized controlled trial design to systematically evaluate the anesthetic effects of ciprofol in combination with varying doses of alfentanil during pediatric bronchoscopy. The results indicated that the ciprofol-alfentanil combination significantly alleviated discomfort in children undergoing bronchoscopic procedures. Notably, as the concentration of alfentanil increased, the high-dose alfentanil group exhibited significantly lower cough scores during glottic and carinal stimulation compared to the propofol-only group (P < 0.05). Furthermore, heart rates at time points T2, T3, T4 and T5 were significantly reduced (P < 0.05), and blood pressure at T3 also showed a significant decrease (P = 0.009), suggesting a reduction in stress responses. These findings further corroborate the anesthetic efficacy of the propofol-alfentanil combination, potentially demonstrating its capacity to create a more favorable operative environment for bronchoscopy. In comparison to ciprofol alone, the addition of high-dose alfentanil enhanced operator satisfaction

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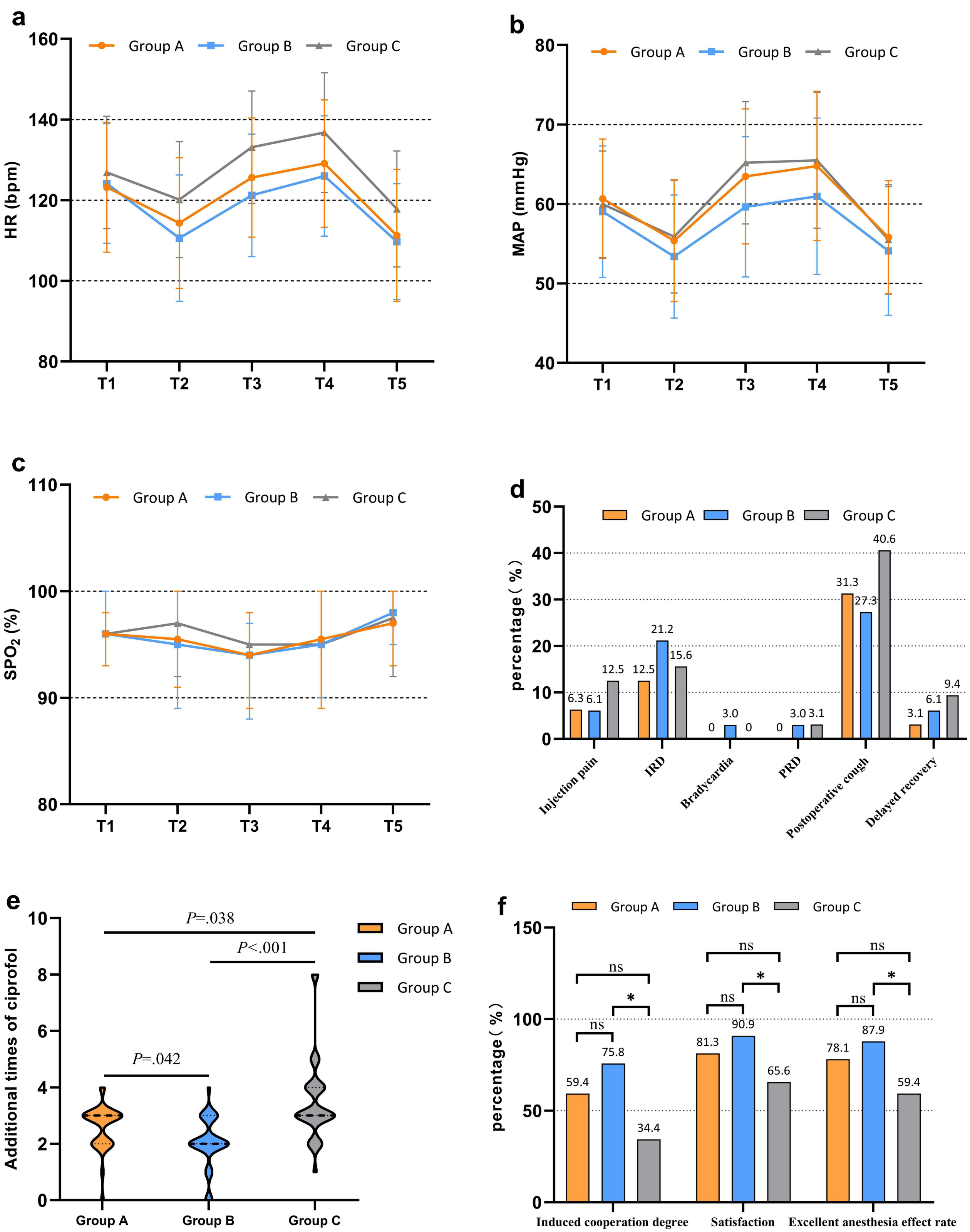

Figure 3 Comparison of secondary indicators among three groups. (**a**) Comparison of HR among three groups. (**b**) Comparison of MAP among three groups. (**c**) Comparison of blood oxygen saturation among three groups. (**d**) Comparison of adverse reactions among three groups of children. (**e**) Comparison of Additional times of ciprofol among three groups of children. (**f**) Comparison of anesthesia related indicators among three groups of children. Group A: ciprofol combined with 5 ug/kg alfentanil group, group B: ciprofol combined with 10 ug/kg alfentanil group, group C: ciprofol-only group. T1-T5, T1, before anesthesia induction; T2, after induction; T3, during glottis passage; T4, during carina passage; T5, at the end of the procedure. $^{*}P < 0.05$.

Table 4 Comparison of Perioperative Data of Three Groups of Children

Variable	Patients, Median (IQR)			H/χ2	P
	Group A (n=32)	Group B (n=33)	Group C (n=32)		
Additional times of ciprofol	3 (2–3)[bc]	2 (2–3)[ac]	3 (3–4)[ab]	24.753	<0.001
Recovery time	18 (15–19.5)	15 (15–21)	17.5 (15–25)	0.796	0.672
Time out of OR	30 (30–30)	30 (30–32.5)	30 (30–30)	2.118	0.347
Induced cooperation degree, No. (%)	19 (59.4)	25 (75.8)[c]	11 (34.4)[b]	11.471	0.003
Doctors' satisfaction, No. (%)	26 (81.3)	30 (90.9)[c]	21 (65.6)[b]	6.447	0.040
Excellent anesthesia effect rate, No. (%)	25 (78.1)	29 (87.9)[c]	19 (59.4)[b]	7.300	0.026

Notes: Group A: ciprofol combined with 5 ug/kg alfentanil group, group B: ciprofol combined with 10 ug/kg alfentanil group, group C: ciprofol-only group. Compared with group A, $^{a}P < 0.05$; Compared with group B, $^{b}P < 0.05$; Compared with group C, $^{c}P < 0.05$.
Abbreviations: IQR, Interquartile range; OR, Operating Room.

Table 5 Comparison of Hemodynamics and Blood Oxygen Saturation

Variable	T1	T2	T3	T4	T5
HR of children at various time points, mean (SD), mmHg					
Group A (n=32)	123.19 (16.10)	114.34 (16.19)	125.63 (14.77)[c]	129.09 (15.79)[c]	111.25 (16.36)
Group B (n=33)	124.15 (14.82)	110.58 (15.65)[c]	121.21 (15.18)[c]	126.00 (14.93)[c]	109.70 (14.37)[c]
Group C (n=32)	126.91 (13.93)	120.13 (14.37)[b]	133.16 (13.94)[ab]	136.78 (14.84)[ab]	117.84 (14.38)[b]
F	0.532	3.153	5.512	4.320	2.663
P	0.589	0.047	0.005	0.016	0.075
$P_{C\text{-}A}$	0.323	0.137	0.042	0.046	0.083
$P_{C\text{-}B}$	0.460	0.014	0.001	0.005	0.032
$P_{A\text{-}B}$	0.796	0.327	0.228	0.414	0.679
P-group	*F*=2.920	*P*=0.059			
P-time	*F*=706.209	*P*<0.001			
P-group×time	*F*=13.471	*P*<0.001			
MAP of children at various time points, mean (SD), bpm					
Group A (n=32)	60.66 (7.52)	55.38 (7.66)	63.47 (8.50)	64.78 (9.39)	55.81 (7.12)
Group B (n=33)	59.03 (8.28)	53.39 (7.73)	59.64 (8.83)[c]	60.97 (9.84)	54.09 (8.09)
Group C (n=32)	59.97 (6.70)	55.88 (7.09)	65.19 (7.69)[b]	65.50(8.55)	55.53 (6.89)
F	0.382	0.999	3.767	2.247	0.509
P	0.684	0.372	0.027	0.111	0.602
$P_{C\text{-}A}$	0.716	0.790	0.413	0.757	0.879
$P_{C\text{-}B}$	0.617	0.186	0.009	0.052	0.434
$P_{A\text{-}B}$	0.387	0.290	0.068	0.101	0.350
P-group	*F*=1.402	*P*=0.251			
P-time	*F*=398.222	*P*<0.001			
P-group×time	*F*=7.873	*P*<0.001			
SPO_2 of children at various time points, median (IQR), %					
Group A (n=32)	96 (95–97)	95.5 (94–98)	94 (93–95)	95.5 (94.25–96.75)	97 (96–99)
Group B (n=33)	96 (95–97)	95 (92.5–97)	94 (91.5–95)	95 (94–97)	98 (97–99)
Group C (n=32)	96 (95–98)	97 (94.25–98)	95 (93.25–96)	95 (93.25–96.75)	97.5 (96–99)
H	1.572	4.888	4.801	0.677	1.796
P	0.456	0.087	0.091	0.713	0.407

Notes: Group A: ciprofol combined with 5 ug/kg alfentanil group, group B: ciprofol combined with 10 ug/kg alfentanil group, group C: ciprofol-only group. T1-T5, T1, before anesthesia induction; T2, after induction; T3, during glottis passage; T4, during carina passage; T5, at the end of the procedure. Compared with group A, $^{a}P < 0.05$; Compared with group B, $^{b}P < 0.05$; Compared with group C, $^{c}P < 0.05$.
Abbreviations: IQR, Interquartile range; MAP, Mean arterial pressure; HR, heart rate; SPO_2, Pulse Oxygen Saturation; mmHg, millimeter of mercury; bpm, beat per minute.

($P = 0.04$), improved patient cooperation during anesthesia ($P = 0.03$), and increased the incidence of excellent anesthetic outcomes ($P = 0.026$). These results may provide valuable insights for optimizing the anesthetic protocol for pediatric bronchoscopy through the combined use of ciprofol and alfentanil.

This study demonstrated that the combination of ciprofol with varying doses of alfentanil significantly enhances the efficacy of pediatric anesthesia ($P = 0.026$). As the concentration of alfentanil increased, the frequency of intraoperative ciprofol supplementation gradually decreased ($P < 0.001$). As an ultra-selective μ-opioid receptor agonist, alfentanil may partially account for its anesthetic-enhancing properties by potentiating inhibitory neurotransmission within the GABAergic system of the central nervous system.[23] Additionally, this drug may suppress airway reflex responses, aligning with the findings of Chen et al[24] As a novel option for pediatric general anesthesia, ciprofol demonstrates more stable hemodynamic performance compared to propofol in adenoidectomy and adenotonsillectomy procedures. Additionally, it offers advantages such as a relatively lower incidence of postoperative delirium and a lack of significant anesthesia-related complications.[25] Compared to single-drug administration, the combined administration strategy demonstrates synergistic effects, significantly improving anesthesia efficiency while maintaining safety. These findings align with clinically reported results of ciprofol combined with varying doses of alfentanil.[26]

Further analysis of the effects of different doses of alfentanil revealed that, compared to the groups receiving ciprofol alone or ciprofol in combination with low-dose alfentanil, the high-dose alfentanil group did not exhibit increased side effects but demonstrated significantly enhanced anesthetic efficacy. This phenomenon may be attributed to the dose-dependent pharmacodynamic characteristics of alfentanil, whereby higher doses effectively suppress the stimulation induced by bronchoscopy, thereby improving anesthetic outcomes and providing greater patient satisfaction.[27] However, significant differences exist in the tolerance and pharmacokinetic characteristics of alfentanil between pediatric and adult patients, which may result in varied clinical responses. Therefore, careful dose adjustments are essential in pediatric anesthesia. Research[28] indicates that children's responses to alfentanil may be influenced by factors such as body weight. These factors were well controlled in the sample selection of this study, thereby ensuring the reliability of the results.

This study also found that in evaluating anesthetic side effects, the combined use of ciprofol and alfentanil did not increase the incidence of complications, such as respiratory depression, compared to the ciprofol-alone group. This phenomenon may be attributed to ciprofol's lower respiratory impact on patients, which has been validated in multiple studies[29,30] and is of significant importance for prolonged and complex bronchoscopy procedures.[31] Furthermore, we observed that the incidence of injection pain during anesthesia induction was relatively low across all three patient groups. Although the combination of ciprofol and alfentanil resulted in even lower injection pain, there was no statistically significant difference compared to the ciprofol-alone group. This may be due to the inherently low injection pain associated with ciprofol,[32,33] which is particularly beneficial for anxious and uncooperative pediatric patients, effectively improving their compliance.[34] Therefore, this combination regimen demonstrates substantial potential for clinical application.

Limitations

This study presents certain limitations. Firstly, the alfentanil dosing regimen for children was derived from doses reported in previous studies,[20] considering safety factors and the standard dosages utilized in the department. Consequently, the dose selection was relatively conservative, and higher concentration groups were not investigated, leading to insufficient data to establish the upper limit of the effective dose range. Secondly, the assessment of injection pain was based solely on observations made by anesthesiologists, lacking precise Visual Analog Scale (VAS) pain evaluation, which may compromise reliability. The evaluation of surgeon satisfaction primarily relied on patients' subjective feedback, potentially introducing bias, as it was not further corroborated through objective physiological indicators. These limitations may affect clinicians' decision-making in practical applications, particularly regarding the evaluation of effectiveness across different age groups or patients with comorbidities. Additionally, because all enrolled patients were undergoing bronchoscopy, only short-acting Ciprofol and alfentanil were used intraoperatively, with a focus on cough score and anesthetic effect, no follow-up was conducted for long-term outcomes. Finally, this study did not perform more detailed age stratification for children. Future research should consider conducting stratified studies by specific age groups to enhance applicability.

In conclusion, this study demonstrates the efficacy and safety of combining ciprofol with varying doses of alfentanil during pediatric bronchoscopy, significantly enhancing anesthetic effectiveness and improving surgeon satisfaction. Future research should consider expanding sample sizes and extending follow-up periods to investigate the long-term outcomes of this drug combination.

Conclusions

In this single-center randomized trial, the combination of Ciprofol and 10 μg/kg Alfentanil effectively reduced the cough reflex during pediatric painless fiberoptic bronchoscopy without increasing adverse effects. These findings necessitate validation through multicenter studies that involve diverse pediatric populations to ensure the generalizability of the conclusions.

Abbreviations

ASA, American Society of Anaesthesiologists; BMI, Body Mass Index; MAP, Mean arterial pressure; MOAA/S, Modified Observer's Assessment of Alertness/Sedation; HR, Heart rate; PLT, Platelet; PACU, Postanesthesia care unit; SpO2, Pulse Oxygen Saturation; Hb, Hemoglobin; WBC, White blood cells; VAS, Visual Analog Scale; M, Median; IQR, Interquartile range; SD, Standard deviation; ICC, Induction Compliance Checklist; IRD, Intraoperative respiratory depression; PRD, Postoperative respiratory depression; SPSS, Statistical Product and Service Solutions.

Data Sharing Statement

The data sets used and/or analyzed during the present study are available from the corresponding author on reasonable request. The Email of corresponding author is jiangqiong@mail.gzsrmyy.com.

Ethics Approval and Consent to Participate

This Randomized controlled trial was approved by the Ethics Committee of Ganzhou Maternal and Child Health Care Hospital, with the consent letter No. (2024) Lun Shen Lin Di (58). Following the principles of the Declaration of Helsinki, Clinical trial registration (Registration No.: ChiCTR2500097084) was completed. All patients voluntarily signed the informed consent.

Consent for Publication

All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

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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 that the research was conducted in the absence of any commercial or financial relationships. All authors declare no conflicts of interest.

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