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CLINICAL TRIAL REPORT

Comparison of the ED50 of Ciprofol Combined With or Without Fentanyl for Laryngeal Mask Airway Insertion in Children: A Prospective, Randomized, Open-Label, Dose-Response Trial

Sicong Wang, Yan Li, Fang Chen, Hua-Cheng Liu, Lezhou Pan, Wangning Shangguan

Department of Anesthesiology and Perioperative Medicine, The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Key Laboratory of Pediatric Anesthesiology of Ministry of Education, Wenzhou, Zhejiang Province, People's Republic of China

Correspondence: Wangning Shangguan, Email sgwning@163.com

Purpose: This study aimed to estimate the effect of different doses of fentanyl on the median effective dose (ED50) of ciprofol for attenuating the airway and motor response to laryngeal mask airway (LMA) insertion response in healthy children.

Patients and Methods: 90 healthy preschool patients undergoing inguinal hernia repair surgery were randomly assigned to one of three groups: C0 (ciprofol+saline), C1 (ciprofol + fentanyl 1μg/kg), C2 (ciprofol + fentanyl 2μg/kg). Anesthesia was induced with either prepared fentanyl or saline, followed by ciprofol. The dose of ciprofol for each patient was determined using the up-and-down sequential study design. The primary outcome was the ED50 of ciprofol required for smooth LMA insertion in the three groups. Additionally, the time to loss of consciousness and any perioperative adverse events were recorded.

Results: Compared with the C0 group, the ED50 (95% confidence interval) of ciprofol in the C1 and C2 groups were significantly lower (1.81 [1.73–1.90]mg/kg versus 0.67 [0.64–0.71]mg/kg and 0.48 [0.42–0.54] mg/kg, respectively; $P<0.05$). Additionally, the ED50 of ciprofol in the C2 group was lower than that in the C1 group (0.42 [0.42–0.54] mg/kg vs 0.67 [0.64–0.71]mg/kg; $P<0.05$). Furthermore, the time to loss of consciousness in the C1 and C2 groups decreased by 60% and 53%, respectively, compared to the C0 group. There were no significant differences in the incidence of drug-related hypotension after anesthesia induction among the three groups. No adverse events of hypoxia, bradycardia, or injection pain were observed in any groups.

Conclusion: In healthy, non-obese Chinese children undergoing elective inguinal hernia repair surgery, fentanyl 1 μg/kg and 2 μg/kg before ciprofol injection significantly reduced the ED50 of ciprofol for attenuating LMA response, with minimal occurrence of severe side effects.

Keywords: ciprofol, laryngeal mask airway, pediatric anesthesia, 50% effective dose

Introduction

Inguinal hernia is a common condition among children, and day surgery mode for pediatric inguinal hernia repair is becoming increasingly popular.[1] The ideal anesthetic for pediatric day surgery should allow rapid onset, potent efficacy, predictable clearance, and minimal side effects. Propofol is commonly employed for general anesthesia in pediatric patients due to its advantageous properties. Nonetheless, propofol is associated with the following limitations, including a narrow therapeutic window, a high prevalence of cardiovascular and respiratory depression, and pain on injection. Ciprofol, also known as HSK3486, is a recently developed sedative with a chemical structure of (R)-2-(1-cyclopropyl ethyl)-6-isopropylphenol. It is an agonist at the gamma-aminobutyric acid-A (GABAA) receptor, similar to propofol, but with superior target selectivity.[2] Previous research indicates that ciprofol exhibits cardiovascular depressant properties comparable to propofol, with reduced respiratory suppression and minimal injection pain.[3–7] These advantages render ciprofol a potentially suitable option for pediatric daytime surgery anesthesia. Despite its recognized benefits in sedation

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and anesthesia for adult patients, the appropriate dosage for pediatric patients has yet to be extensively studied and validated.

The use of laryngeal mask airway (LMA) has been deemed appropriate and safe for airway management during inguinal hernia day surgery.[8] The smooth insertion of LMA requires a sufficient depth of anesthesia to attenuate unwanted airway reflexes and body movement, which is often achieved by a combination of propofol and fentanyl.[9,10] While ciprofol has been shown to be about 4–5 times more potent than propofol for procedural sedation in adults, its anesthetic dose in pediatric patients when combined or not with fentanyl is still unknown. We choose the insertion of a LMA as a model to determine the effective dose of ciprofol needed to prevent traumatic LMA insertion and observe drug-related adverse events.

Therefore, the present prospective, randomized, open-label study was designed to explore the median effective dose (ED50) of ciprofol combined with 1 μg/kg fentanyl, or 2 μg/kg fentanyl, or without fentanyl for attenuating LMA insertion response in healthy preschool children undergoing inguinal hernia repair surgery using an up-down sequential allocation method. The primary objective was to determine and compare the ED50 values to estimate the effects of fentanyl or another opioid on the requirement of ciprofol for smooth LMA insertion, which can contribute as a reference for clinical use.

Material and Methods

Study Design and Patient Enrollment

A prospective, randomized, open-label, up-down sequential allocation study was conducted to estimate the ED50 of ciprofol when combined with or without fentanyl for attenuating laryngeal mask insertion response in children undergoing inguinal hernia repair surgery. This research received approval from the Ethics Committee of the Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University and was registered in the Chinese Clinical Trial Registry (registry number ChiCTR2200058954). The clinical trial followed the Declaration of Helsinki, Good Clinical Practice (GCP) guidelines for Drug Clinical Trials as outlined by the State Drug Administration (SDA) and other relevant regulations. Prior to participation, written informed consent was obtained from parents or guardians. Study subjects who met the following inclusion criteria were considered: patients classified as American Society of Anesthesiologists Physical Status class I and II, aged between 3–6 years, body mass index (BMI) ≤20, and undergoing elective inguinal hernia repair surgery under general anesthesia. The Exclusion criteria included children with anticipated difficult airway, acute upper respiratory tract infection, uncontrolled asthma, and major coexisting diseases (eg cardiomyopathy, hepatic disease, and renal insufficiency), preoperative administration of sedative-hypnotics (including benzodiazepines such as midazolam and barbiturates such as phenobarbital) within 7 days prior to surgery; and allergies to the ingredients or components of drugs such as ciprofol and opioids.

Randomization and Blinding

The randomization scheme was generated by an independent research assistant using Microsoft Excel (Microsoft Corporation, Redmond, WA, USA) with a block size of three prior to the commencement of participant enrollment. Group allocation codes were concealed in opaque envelopes and revealed at the time of randomization. Participants were then assigned randomly to one of three doses of fentanyl (Fentanyl Citrate Injection, 2 mL:100 μg, Hubei Yichang Renfu Pharmaceutical Co., Ltd).: 0 μg/kg, 1 μg/kg, or 2 μg/kg. The anesthesiologist responsible for medication and administration, along with the investigator conducting outcome assessments, were aware of the group allocation. Patients were blinded to their group assignment, as well as the data analysts.

Interventions

The participants were randomly allocated into three groups: the C0, C1 group, and C2 groups. Anesthesia was induced with varying doses of fentanyl (0 μg/kg, 1 μg/kg, or 2 μg/kg) and ciprofol was administrated 60 ±10s prior to the LMA insertion. In our preliminary study, we included 10 unpremedicated children and 5 children premedicated with 1 μg/kg fentanyl. We determined that a ciprofol dosage of 1.6 mg/kg for the C0 group and 0.6 mg/kg for the C1 and C2 groups

served as a common turning point, defined as the dosage at which responses in subsequent subjects transitioned from negative to positive, or vice versa. Additionally, step sizes of 0.05 mg/kg were deemed appropriate for the study. Based on our preliminary findings, the initial ciprofol dosage was set at 1.6 mg/kg for the C0 group and 0.6 mg/kg for the C1 and C2 groups. Subsequent adjustments of 0.05 mg/kg were made based on the previous patient's response to the first attempt of LMA insertion.

Anesthesia Management

Patients were fasted for at least 8 hours and were not allowed to drink water at least 2 hours before the operation. Upon arrival in the operating room, they had placement of a peripheral venous catheter and started an infusion of Ringer's lactate at a rate of 2 mL/kg/h. Patients were administered mask oxygen inhalation at a rate of 5 L/min for 3 min before induction. Continuous monitoring of noninvasive blood pressure (BP), electrocardiogram, and peripheral pulse oxygen saturation (SpO2) was conducted with vital signs recorded every minute during induction and every 5 min during the maintenance phase. The baseline of BP and heart rate (HR) was defined as the average of three consecutive measurements upon the patient's arrival in the operating room while in a supine position. Anesthesia induction was conducted with the administration of saline, 1 or 2 μg/kg fentanyl over a period of 10s. 120s later, ciprofol (Ciprofol Injection, 20 mL:50 mg, Liaoning Chengdu Haisco Pharmaceutical Co., Ltd.) administered within 25 ± 5s. After the administration of ciprofol, the pain was evaluated by a four-point behavioral rating scale ((no pain = 0; mild pain (grimace) = 1; moderate pain (grimace+cry) = 2; severe pain (cry+withdraw limb) = 3),[11] and the Modified Observer's Assessment of Alertness/Sedation (MOAA/S) and the eyelash reflex were measured at 30-second intervals. No controlled ventilation was instituted during the induction phase. 60 ± 10 seconds following cipropol injection and attainment of a MOAA/S ≤ 1 (no response to mild prodding or shaking), a size of 2.0 or 2.5 Ambu AuraOnce LMA (Ambu Inc.) was inserted by the same anesthesiologist with extensive experience, having performed over 200 cases using the 90° rotation technique. This technique, consistent with previous reports,[12] after insertion of the entire cuff inside the mouth, the AuraOnce LMA was rotated anticlockwise through 90° and advanced through the right side of the tongue until resistance was felt, and was then turned back in the hypopharynx. Successful insertion was confirmed by bilateral chest wall movement, adequate end-tidal carbon dioxide trace, and auscultation. A second anesthesiologist evaluated the patient's response and collected the data. The conditions of LMA insertion were assessed using a 3-point, 6-category scale.[13,14] The score for insertion conditions was determined by summing the grades for swallowing, gagging, movement, and laryngospasm (Table 1), while excluding mouth opening and ease of insertion due to their dependence on anatomical upper airway features.[13] A score of 4 was considered to represent the optimal conditions for LMA insertion. If the LMA insertion conditions score exceeded 4, the LMA was removed and an additional dose of ciprofol 0.2 mg/kg was administered, followed by another attempt of LMA insertion after 60 seconds. A maximum of three insertion attempts were allowed, beyond which the trachea intubation was performed. According to the up-and-down sequential allocation method, a decrease of 0.05 mg/kg in ciprofol dosage was implemented for the subsequent patient if the previous patient exhibited an effective response. Conversely, an increase of 0.05 mg/kg in ciprofol dosage was administered for the next patient if the response was deemed ineffective. The effective response was defined as achieving an LMA insertion conditions score of 4 on the first attempt within 60 ±10s following the administration of ciprofol, without the need for supplementary anesthetic or muscle

Table 1 The Score of LMA Insertion

Behavior	Score
Swallowing	nil=1, slight=3, gross=3
Coughing and gagging	nil=1, slight=3, gross=3
Head or body movement	nil=1, slight=3, gross=3
Laryngospasm	nil=1, slight=3, gross=3

Note: A score of 4 was defined as "effective" and a score of ≥5 was defined as "ineffective.

relaxant. Conversely, if a score ≥ 5 was obtained, indicating an ineffective dose. After successful insertion of the LMA, patients were administered 0.1mg/kg of cisatracurium and ventilated with a mixture of sevoflurane at 3% and 60% oxygen, delivered at a flow rate of 2.0 L/min. If LMA insertion failed three times, the patient's data were excluded from the study analysis, and the subsequent patient received the same dosage of ciprofol. Hypotension was defined as a reduction in mean arterial pressure (MAP) exceeding 30% of the baseline levels. If hypotension persisted for 2 minutes, phenylephrine 0.5 μg/kg was injected intravenously. Bradycardia, defined as HR < 60 beats per minute, was treated with 0.2 mg/kg of atropine intravenously. Hypoxemia, defined as SpO2 < 92%, was treated with assisted ventilation via a face mask.

Data Collection and Result Evaluation

The baseline characteristics of the patients, such as age, gender, BMI, MAP, and HR, were documented. The MOAA/S was used to assess the level of anesthesia. The primary outcome was to determine the ED50 of ciprofol in attenuating the LMA insertion response. Secondary outcomes included the time to achieve the loss of consciousness (defined as MOAA/S ≤ 1 following initial dose administration), awakening time in the post anesthetic care unit (PACU) after surgery, and the incidence of hypoxia, hypotension, bradycardia, laryngospasm and injection pain. Patient follow-up was conducted 24 hours post-surgery, during which any complications such as awareness during general anesthesia or sore throat were recorded.

Sample Size

The non-independence and unknown distribution of data from an up-and-down sequential methodology study prevents the formulation of theoretically strict rules for calculating sample size. The sample size is decided according to the stop rule. Dixon's up-and-down method requires a minimum of six crossover points in each group to estimate the ED50.[15] Simulation studies have indicated that including at least 20–40 patients could provide stable estimates of the target dose for most scenarios.[16] Therefore, a sample size of 30 study subjects per group was deemed necessary to observe more than six pairs of sequence reversals.

Statistical Analysis

IBM SPSS Statistics for Windows version 26.0 (IBM Corp, Armonk, NY, USA), and R software (R Foundation for Statistical Computing, Vienna, Austria) were used for data analysis. The Shapiro–Wilk test was applied to assess the normal distribution of the data. Continuous variables that were normally distributed were presented as mean ± standard deviation, and group comparisons were made using one-way ANOVA. Non-normally distributed data were presented as median (interquartile range), and group comparisons were conducted using the Wilcoxon rank-sum test and Kruskal Wallis *H*-tests. Categorical data were represented as n (%) and analyzed using chi-square testing. The ED50 (95% CI) of ciprofol was determined as the average of midpoints of ineffective-effective crossovers.[15,17] Probit regression analysis was employed as a backup and sensitivity analysis using the Generalized Linear Model function in R software for each group. The comparison of ED50 values between groups was conducted using overlapping confidence intervals.[15] For all analyses, P< 0.05 was considered a statistically significant difference.

Results

A total of 94 participants were initially screened for eligibility in the clinical trial between July 2022 and December 2023, with 90 participants ultimately meeting the criteria and being randomly allocated into three groups for inclusion in the final analysis. (see Figure 1). The demographic characteristics and baseline hemodynamic data are shown in Table 2. There was no significant difference in demographic variables, baseline MAP, or HR across the three groups.

The results of the up-down sequential allocation method are depicted in Figure 2, while the ED50 values with 95% confidence intervals are presented in Table 3. Using the post-Bonferroni test and methodology of overlapping confidence intervals as a sensitivity analysis, it was determined that compared to the C0 group, the ED50 of ciprofol in the C1 and C2 groups was significantly lower (1.81 [1.73–1.90]mg/kg vs 0.67 [0.64–0.71]mg/kg; 0.48 [0.42–0.54]mg/kg, P<0.05). Furthermore, the ED50 of ciprofol in the C2 group was found to be lower than that of the C1 groups (0.48 [0.42–0.54] mg/kg vs 0.67 [0.64–0.71]mg/kg, P<0.05). While using the probit regression, the ED50 values of ciprofol were

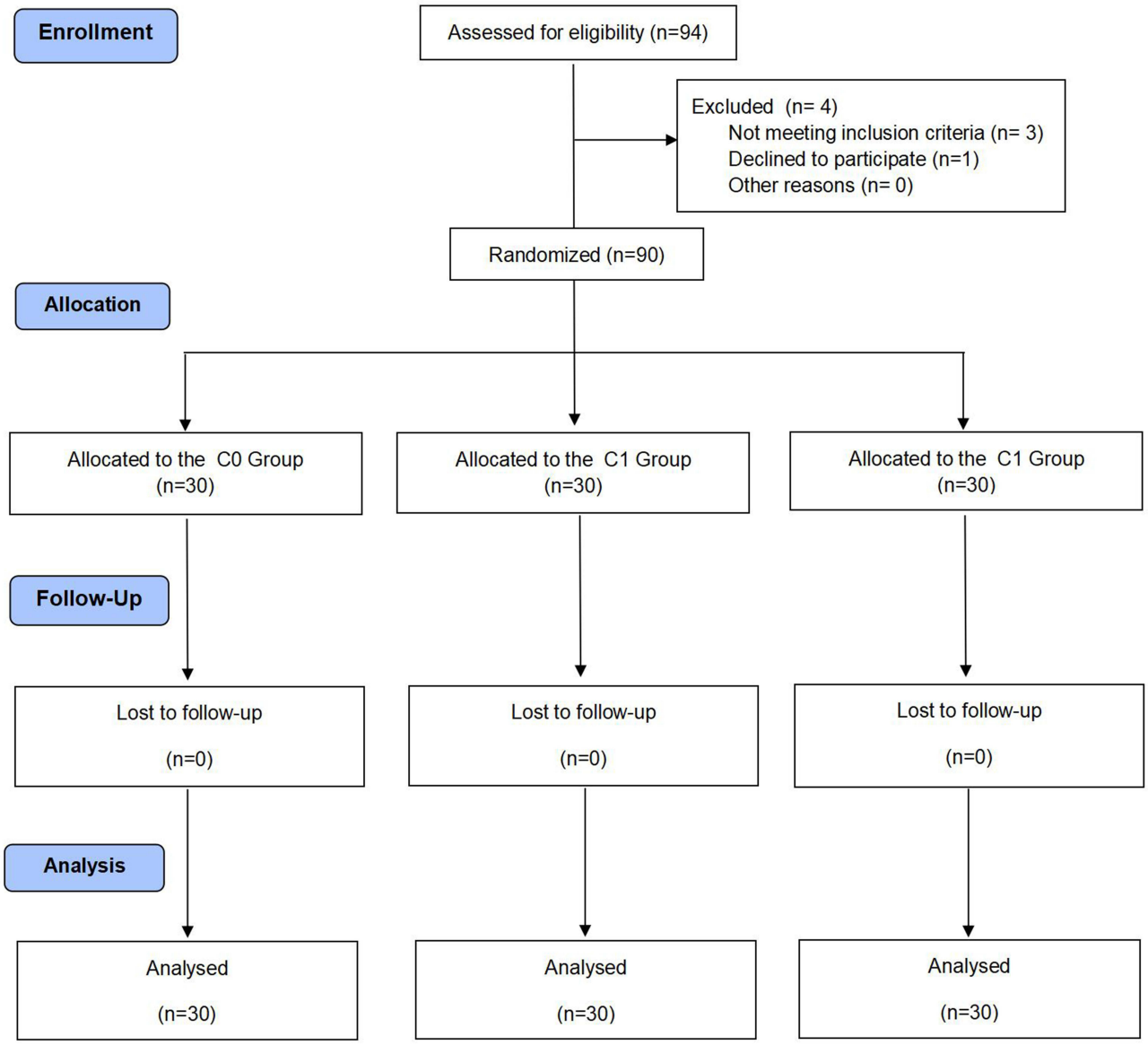

Figure 1 CONSORT Diagram.

determined to be 1.89 [1.75–2.17] mg/kg in the C0 group, 0.70 [0.57–0.86] mg/kg in the C1 group, and 0.46 [0.30–0.89] mg/kg in the C2 group. The dose-effect analysis of fentanyl and ciprofol on patients' responses within the three groups is shown in Figure 3.

Table 2 Demographic and Baseline of Vital Signs Data

	C0 Group (n=30)	C1 Group (n=30)	C2 Group (n=30)	P value
Age (years)	4.5±1.1	4.1±1.1	4.3±1.0	0.491
BMI (kg/m^2)	15.5±1.5	15.9±1.6	15.6±1.8	0.671
Gender (male/female)	22/8	24/6	23/7	0.830
Baseline HR (beat per minute)	98.8±14.0	97.9±17.5	96.3±17.3	0.833
Baseline MAP (mmHg)	84.0±10.9	81.1±12.4	80.9±10.9	0.519

Notes: Data are mean ± SD or n (%). A value of $p<0.05$ was considered to indicate statistical significance.

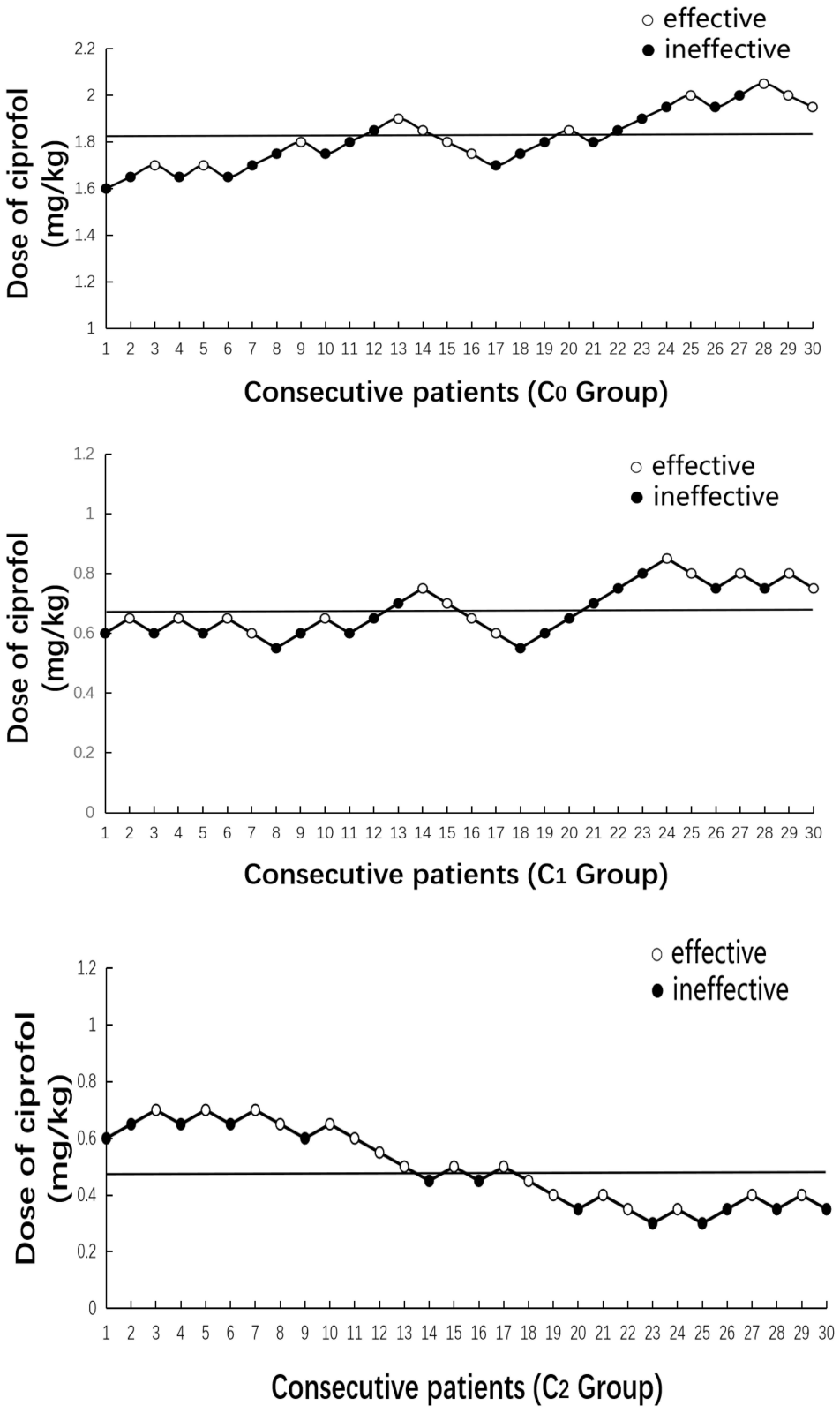

Figure 2 Dixon Up-and-Down Plots for Three Groups.
Note: The solid line represents the ED50 of ciprofol for LMA insertion.

Table 3 ED50 of Ciprofol (with 95% Confidence Intervals) in Three Groups, Based on the Dixon–Massey Up-and-Down Sequential Allocation Method and Probit Regression, Respectively

	C0 Group	C1 Group	C2 Group
ED50 (Dixon–Massey) (mg/kg)	1.81 (1.73, 1.90)■#	0.67 (0.64, 0.71)▲#	0.48 (0.42, 0.54)▲■
ED50 (Probit Regression) (mg/kg)	1.89 (1.75, 2.17)■#	0.70 (0.57, 0.86)▲	0.46 (0.3, 0.89)▲

Notes: ED50, effective dose in 50% of the population; "▲" represents the group had significant difference with group C0 (P<0.05). "■" represents the group that had significant differences with group C1 (P<0.05). "#" represents the group that had significant differences with group C2 (P<0.05).

According to the data presented in Table 4, the C1 and C2 groups exhibited a reduction of 60% and 53%, respectively, in the time taken to lose consciousness compared to the C0 group. The awakening time in PACU and the occurrence of other perioperative adverse events, including hypotension, laryngospasm, hypoxia, bradycardia, injection pain, and sore throat were not different across the three groups. Furthermore, none of the patients reported any recall of events during LMA insertion or the surgical procedure.

Discussion

The insertion of LMA in children requires a sufficient depth of anesthesia, which may increase the risk of hemodynamic complications. This study explored the ED50 of ciprofol when combined or not with fentanyl needed to attenuate motor responses to the insertion of a LMA using up-down sequential allocation methodology, corroborated by probit analysis. It demonstrated that the ED50 of ciprofol significantly decreased when combined with an increasing dose of fentanyl from 1 to 2 μg/kg.

As a new anesthetic sedative, the findings that ED50 of ciprofol combined with or without fentanyl for attenuating LMA insertion responses in children could be important. LMA is a widely utilized supraglottic airway device in pediatric anesthesia, but its insertion in children is more complicated than in adults due to two primary factors that hinder easy insertion in non-paralyzed pediatric patients. Firstly, children's distinctive anatomical airway characteristics, such as a larger tongue, larger epiglottis, and hypertrophic tonsils, present challenges for the smooth insertion of aLMA.[18] Secondly, it requires an adequate depth of anesthesia to attenuate airway reflexes and minimize body movement. Propofol is recommended as the drug for creating optimal conditions for LMA insertion.[19] In unpremeditated children, the ED50 of propofol is reported to be 3.8 mg/kg.[20] The results of this study show that, when used alone, a dose of 1.81 mg/kg ciprofol is necessary to achieve satisfactory conditions for LMA insertion in 50% of the population studied (Chinese preschool children). Our data suggest that ciprofol is two times more potent than propofol in facilitating anesthesia for

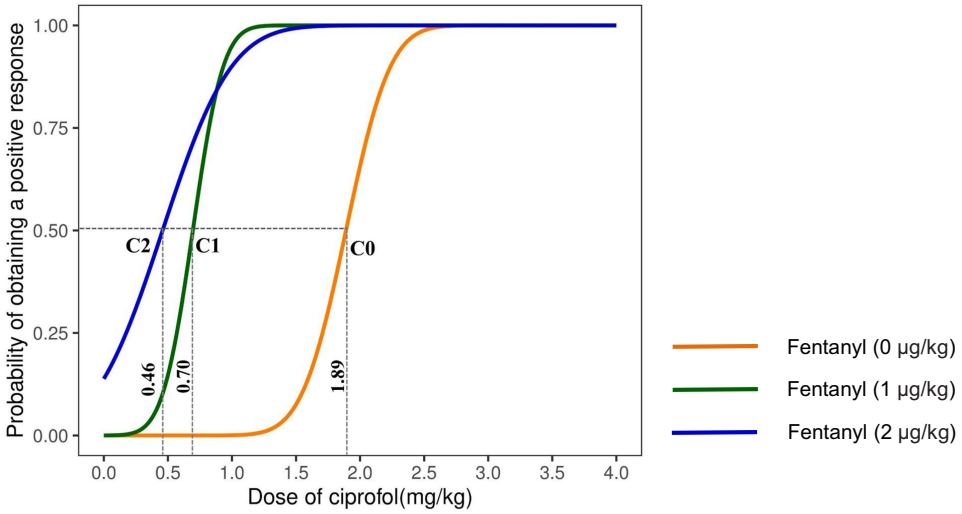

Figure 3 Dose-Effect Analysis of Fentanyl and Ciprofol on Patients' Response in Three Groups.

Table 4 Exploratory Outcomes

	C0 Group (n=30)	C1 Group (n=30)	C2 Group (n=30)	P value
Consciousness loss time (MOAA/S ≤ 1,Second)	31.8±2.5	12.6±1.9	14.9±2.1	<0.001
Awakening time in PACU (min)	15.3±5.3	12.2±7.5	12.4±6.2	0.114
Hypotension (n, %)	3 (10.0%)	7 (23.3%)	4 (13.3%)	0.439
Laryngospam (n, %)	0 (0%)	0 (0%)	0 (0%)	–
Hypoxia (n, %)	0 (0%)	0 (0%)	0 (0%)	–
Bradycardia (n, %)	0 (0%)	0 (0%)	0 (0%)	–
Injection pain (n, %)	0 (0%)	0 (0%)	0 (0%)	–
Sore throat (n, %)	5 (16.7%)	4 (13.4%)	8 (26.7%)	0.493

Notes: Data are mean ± SD or n (%). A value of $p<0.05$ was considered to indicate statistical significance.

LMA insertion in children, which is consistent with previous pharmacokinetic and pharmacodynamic investigations of ciprofol.[21] The higher selective binding ability of ciprofol for GABAA receptors allows for equivalent anesthetic efficacy to propofol at a reduced dosage.

Opioids are often utilized in conjunction with different intravenous anesthetic agents to facilitate the insertion of LMA. Fentanyl, a highly lipid-soluble opioid, is approximately 80 to 100 times more potent than morphine. The onset of fentanyl occurs in less than 60 seconds, with peak effects typically observed within 2 to 5 minutes. The analgesic and sedative effects of fentanyl are typically achieved at a dosage of 1 to 2 μg/kg.[22] Based on the above, the study incorporated two distinct fentanyl pre-treatment dosage groups along with fentanyl injection at least 120 seconds prior to the insertion of LMA. The results indicated that the combination of 1.0 μg/kg fentanyl led to a 63% decrease in the ED50 of ciprofol, while 2.0 μg/kg fentanyl resulted in a 73% reduction. These discrepancies are likely attributable to a possible ceiling effect of fentanyl in this indication and interindividual variability in response to the drug.[23,24] Similarly, Wu X et al[25] observed a reduction in the required ciprofol dosage when combined with 7 μg/kg alfentanil for suppressing responses to gastroscope insertion. This result may be best explained by the typical properties of fentanyl, which is known to suppress airway reflex responses.[26]

Of note, the consciousness loss times were significantly different among the three groups ($P<0.001$). In a Phase III clinical trial involving adult gastroscopy,[7] the induction time for the ciprofol group (0.4 mg/kg) was recorded as 1.1 ± 0.5 minutes. In another multicenter study focusing on elective surgery in adults,[27] it was found that the loss of consciousness occurred after 0.91 ± 0.03 minutes following ciprofol 0.4 mg/kg injection. The time of loss of consciousness in the ciprofol group in this trial was measured at 31.8±2.5 seconds, which was a shorter interval compared to the findings of a previous study. This discrepancy may be attributed to variations in drug dosage, injection speed, and characteristics of the study population with increased cardiac output, all of which could impact the rate at which ciprofol penetrates the blood-brain barrier.

There were no severe adverse events during the study period. No hypoxia event was detected among the three groups, which was partly due to the preoxygenation strategy. In the present study, pediatric patients received oxygen for 3 minutes before anesthesia induction, with LMA insertion occurring once an appropriate depth of anesthesia was achieved within 60 ± 10 seconds. Therefore, we did not observe any hypoxia event. Similar to propofol, ciprofol is known to induce hypotension following anesthesia induction. The study revealed a higher incidence of hypotension events in the 1 μg/kg fentanyl group (23.3%) compared to the fentanyl 2 μg/kg group (13.3%). Given the higher dose of ciprofol administered to the patients in the 1 μg/kg fentanyl group, a more pronounced decrease in blood pressure was anticipated. Nevertheless, the transient hypotension observed in our study was reversible through the pressure response of the LMA. Besides, no instances of bradycardia were identified. Previous studies have reported that ciprofol induces a comparable level of bradycardia to propofol in adult patients, with rates of 12.5% and 13.6%, respectively.[27] This disparity may be attributed to variations in patient demographics, drug combinations, and monitoring periods. Last but not least, no injection pain occurred even when ciprofol was used exclusively in the study. The results were nearly

identical to those observed by Zhong J et al[28] Additionally, several studies have revealed that the incidence of ciprofol-related injection pain was extremely low.[6,27] The mechanism may be that ciprofol is formulated as an oil-in-water emulsion.[25] Furthermore, when ciprofol is combined with fentanyl, its higher potency and lower plasma concentration may contribute to a reduction in injection pain. The reduction of injection pain is advantageous in alleviating perioperative anxiety and distress in children, while also enhancing the comfort level during pediatric day surgery.

This study has some limitations. First, the study only included subjects classified as ASA physical status I or II without respiratory or cardiovascular disease, thus potentially limiting the generalizability of the results and conclusions to high-risk patient populations. Second, it should be noted that the participants included in this study fell within the normal weight range for children aged 3 to 6 years. It is important to consider that the outcome may vary when applied to children who are either overweight or underweight. Finally, it is worth mentioning that Dixon's up-and-down method does not yield a reliable estimation of ED95,[29] which is a more relevant parameter in clinical application. Given these limitations, there is a need for a multi-center, large-scale trial to evaluate the clinical application of ciprofol combined with or without fentanyl in a diverse pediatric population.

Conclusion

The present study provides valuable preliminary findings on the dose-response relationships related to the effectiveness and safety of ciprofol in combination with or without fentanyl in children. Specifically, in healthy, non-obese Chinese children undergoing elective inguinal hernia repair surgery, the administration of fentanyl at a dose of 1μg/kg and 2μg/kg before ciprofol injection has been shown to significantly reduce the ED50 of ciprofol for attenuating LMA response without increasing the incidence of adverse perioperative events, thus offering potential benefits for the management of day surgery. Future studies are warranted to explore the use of ciprofol in a broader range of pediatric populations, as well as to assess the effects of ciprofol on premature brain development.

Data Sharing Statement

The data generated during the study are available from the corresponding author (Wangning Shangguan) by request.

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Disclosure

The authors report no conflicts of interest in this work.

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