

Effect of Esketamine on Postoperative Pain in Children Undergoing Plasma Tonsillectomy: A Double-Blind, Randomized Controlled Trial

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Purpose: To investigate the effects of esketamine compared with fentanyl on postoperative pain, sedation, and hemodynamics in children undergoing tonsillectomy under general anesthesia with endotracheal intubation.

Methods: This randomized, double-blind, controlled trial included 54 children scheduled for plasma tonsillectomy, randomly allocated into group E (esketamine 0.5 mg·kg⁻¹) and group C (fentanyl 4 µg·kg⁻¹) at anesthesia induction, with identical anesthesia protocols otherwise. Primary outcome was FLACC pain score at 2 hours postoperatively. Secondary outcomes included FLACC scores at 8 and 24 hours, Ramsay Sedation Scale scores at 5, 10, 15 minutes after extubation, hemodynamic variables, anesthesia and surgery duration, emergence and extubation time. Safety outcomes were adverse events within 48 hours postoperatively.

Results: FLACC scores at 2, 8, and 24 hours were comparable between groups ($P > 0.05$). Mean arterial pressure and heart rate were significantly higher in group E after induction and at the beginning of surgery ($P < 0.05$). Sedation scores, anesthesia and surgery duration, emergence and extubation time, anesthetic consumption, and adverse events within 48 hours showed no significant differences between groups (all $P > 0.05$).

Conclusion: Esketamine showed no significant difference in pain scores but more stable intraoperative hemodynamics compared with fentanyl in pediatric tonsillectomy using plasma energy.

Keywords: esketamine, pediatric, plasma tonsillectomy, postoperative pain

Introduction

Tonsillar hypertrophy represents a prevalent condition among children in China, particularly within the 2–6 years age group.¹ Enlarged tonsils frequently lead to obstructive sleep apnea syndrome (OSAS), upper airway obstruction, and associated symptoms such as snoring and chronic mouth breathing.² Plasma tonsillectomy has emerged as an effective surgical intervention for this condition. This technique, conducted at relatively low temperatures, aims to minimize thermal damage to adjacent tissues, thereby mitigating postoperative swallowing pain and promoting mucosal healing.^{3,4}

Despite these procedural advantages, managing postoperative pain remains a significant and common clinical challenge, especially within the critical first two weeks following surgery. This issue is of paramount importance given the increasing adoption of plasma tonsillectomy as a day-surgery procedure, which necessitates effective and rapid recovery. In the pediatric population, the consequences of poorly controlled post-tonsillectomy pain extend far beyond general discomfort and carry distinct, severe implications. Children may manifest their pain and distress through refusal of oral intake, which directly elevates the risk of dehydration and delays nutritional recovery. Sleep architecture, crucial for healing and development, can be profoundly disrupted. Furthermore, the experience of acute pain in young children is intrinsically linked to significant anxiety, distress, and behavioral regression, which can impede cooperation with postoperative care, negatively affect the child–caregiver dynamic, and potentially contribute to longer-term negative psychological associations with medical care.⁵ These child-specific sequelae, spanning physiological compromise, behavioral disturbance, and psychological distress, collectively

contribute to delayed recovery, an increased likelihood of unplanned healthcare visits or hospital readmission, and a diminished postoperative quality of life for both the child and the family.⁶

Plasma tonsillectomy, as a contemporary alternative to traditional cold dissection, differs substantially in its mechanism, characterized by reduced tissue trauma and concurrent hemostasis during dissection. These technical distinctions are not merely procedural but may translate into a distinct postoperative pain trajectory, potentially altering inflammatory mediators and neural sensitization patterns.⁷ Consequently, a nuanced, procedure-specific analgesic approach is warranted. In current multimodal analgesic regimens, non-opioid agents such as dexmedetomidine and non-steroidal anti-inflammatory drugs (NSAIDs) are frequently employed. Dexmedetomidine, an α_2 -adrenoceptor agonist, provides sedation and analgesia while reducing opioid requirements; however, its use in children can be limited by dose-dependent bradycardia and hypotension, which may necessitate careful hemodynamic monitoring and dose titration.⁸ NSAIDs, though effective for inflammatory pain, carry concerns regarding potential bleeding risk in tonsillectomy patients, as well as gastrointestinal and renal side effects, particularly with prolonged use or in vulnerable pediatric populations.⁹ Opioids, such as fentanyl, remain a cornerstone for induction and intraoperative analgesia. Nevertheless, their use in children is constrained by well-documented adverse effects, including postoperative nausea and vomiting (PONV), respiratory depression, pruritus, and potential prolongation of hospital stay,^{10,11} underscoring the ongoing need for effective analgesic adjuncts with a more favorable side-effect profile.

Ketamine is a commonly used agent in pediatric anesthesia. Esketamine, the S(+) enantiomer of ketamine, acts as an N-methyl-D-aspartate (NMDA) receptor antagonist with additional activity at opioid receptors, producing potent sedative and analgesic effects. It possesses 3 to 4 times greater affinity for the NMDA receptor compared to the R(-) enantiomer.¹² Importantly, esketamine is associated with a lower incidence of adverse effects such as nausea, vomiting, respiratory depression, and psychomimetic reactions compared to racemic ketamine. Furthermore, esketamine stimulates the sympathetic nervous system, which helps maintain hemodynamic stability and perfusion of vital organs.¹² Several studies suggest that the adjunctive use of esketamine in pediatric surgery can accelerate recovery, reduce opioid consumption, shorten hospital stays, and improve the overall perioperative experience.^{13,14}

However, the specific effects of esketamine on postoperative pain outcomes in children undergoing tonsillectomy have not been extensively reported. Based on relevant studies and clinical practice, an induction dose of 0.5 mg/kg was selected for this investigation, as it provides effective sedation and analgesia while minimizing the risk of serious adverse events.^{15,16} We hypothesize that esketamine provides comparable postoperative analgesia to fentanyl in pediatric plasma tonsillectomy, while reducing the incidence of opioid-related adverse events. Therefore, this study aims to evaluate and compare the effects of esketamine and fentanyl on postoperative pain intensity, sedation levels, hemodynamic stability, and the profile of adverse reactions in children undergoing this procedure. The goal is to contribute further evidence for the selection of safe, effective, and child-centric anesthetic protocols.

Methods and Materials

Study Design and Ethical Statements

This prospective, double-blind, randomized, controlled trial was conducted to evaluate the effect of esketamine on postoperative pain in pediatric patients undergoing plasma tonsillectomy. The study protocol received approval from the Ethics Committee of Anqing Municipal Hospital (Medical Ethics Approval No. 2025009) and was implemented in accordance with the principles of the Declaration of Helsinki. The trial was registered at ClinicalTrials.gov (identifier: NCT07062601) on July 10, 2025, and participant recruitment and data collection took place between June 2025 and October 2025. Written informed consent was obtained from the parents or legal guardians of all enrolled children one day prior to surgery.

Study Participants

Fifty-four pediatric patients scheduled for tonsillectomy using plasma technology at Anqing Municipal Hospital from June 2025 to October 2025 were selected. Inclusion Criteria included aged 2–10 years, ASA grades I–II, voluntarily participated and signed informed consent after a thorough explanation of the clinical trial content. Exclusion Criteria: (1) Children whose parents did not sign informed consent; (2) Liver or kidney dysfunction; (3) Those with increased intracranial or intraocular pressure; (4) Schizophrenia, mania, or any other mental disorders; (5) With a history of chronic pain; (6) Children with preoperative

sinus bradycardia or atrioventricular block; (7) Use of analgesics or sedatives within 48 hours prior to surgery; (8) Children allergic to the drugs used in the study; (9) Children who took steroids or long-term glucocorticoids before surgery; (10) Children who participated in other treatments within the last 6 months (at the time of consent); (11) Others deemed unsuitable by the attending clinician or clinical director. Termination Criteria: (1) Occurrence of severe adverse events, judged by the physician to warrant trial cessation; (2) Temporary changes in surgical or anesthetic methods, or cases requiring reoperation; (3) Post-randomization discovery of serious violations of inclusion or exclusion criteria.

Randomisation and Blinding

Participants were randomly allocated in a 1:1 ratio to either the esketamine group (Group E) or the fentanyl group (Group C). The randomization sequence was computer-generated by an independent statistician using a stratified block design. To ensure balance across groups for key prognostic factors, randomization was stratified by age (2–5 years, 6–10 years), and tonsil size (Grade 1–2, Grade 3–4). Within each stratum, a block size of 4 was used, with the block sequence itself being randomized to enhance concealment. Allocation concealment was strictly maintained using sequentially numbered, opaque, sealed envelopes. Each envelope was opened only by a pharmacist who did not involve in the research for drug preparation immediately prior to induction of anesthesia, ensuring that the treatment assignment remained concealed from all other study personnel. During anesthetic induction, patients in Group C received $4 \mu\text{g}\cdot\text{kg}^{-1}$ of fentanyl, while those in Group E received $0.5 \text{ mg}\cdot\text{kg}^{-1}$ of esketamine. Both study drugs were prepared in identical syringes by the dedicated pharmacists not involved in further patient management or outcome assessment. To maintain blinding, all syringes were visually indistinguishable and labeled only with the participant's study identification number. All participants, anesthesiologists, surgeons, operating room nurses, and outcome assessors were blinded to group assignment throughout the trial. Postoperative pain assessments were conducted by trained staff unaware of the intraoperative medication regimen. Any emergency unblinding procedures were predefined and documented but were not required during the study.

Anesthesia Protocol

All children were routinely required to preoperatively fast 8 hours for solids and 2 hours for clear liquids. Upon entering the operating room, pediatric patients were continuously monitored using the Philips MIX500 monitor for non-invasive arterial blood pressure (NIBP), mean arterial pressure (MAP), heart rate (HR), electrocardiogram (ECG), and peripheral pulse oxygen saturation (SPO₂). The anesthesiologist recorded baseline values during routine monitoring. Non-dominant arm intravenous line was established for lactated Ringer's solution infusion at a rate of $3\text{--}5 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$. Anesthesia Induction: Both groups received 3–5 minutes of pure oxygen inhalation ($4\text{--}6 \text{ L}\cdot\text{min}^{-1}$) via face mask before induction, followed by intravenous administration of penthyclidine $0.01 \text{ mg}\cdot\text{kg}^{-1}$, midazolam $0.05 \text{ mg}\cdot\text{kg}^{-1}$, etomidate $0.3 \text{ mg}\cdot\text{kg}^{-1}$, and cisatracurium $0.1 \text{ mg}\cdot\text{kg}^{-1}$. The group C additionally received fentanyl $4 \mu\text{g}\cdot\text{kg}^{-1}$, while the group E received esketamine $0.5 \text{ mg}\cdot\text{kg}^{-1}$. After achieving sufficient muscle relaxation, tracheal intubation was performed using a portable video laryngoscope. The tracheal tube size is determined by dividing the age by four and adding four. The intubation depth is determined by dividing the age by two and adding twelve. Following successful intubation, the tube was connected to the Fabius anesthesia machine set to volume-controlled ventilation (VCV) mode with an oxygen flow rate of $1 \text{ L}\cdot\text{min}^{-1}$, tidal volume (VT) of $10 \text{ mL}\cdot\text{kg}^{-1}$, respiratory rate (RR) of $14\text{--}16 \text{ breaths}\cdot\text{min}^{-1}$, and inspiratory-to-expiratory ratio (I:E) of 1:1.5. The respiratory rate was adjusted based on end-tidal carbon dioxide partial pressure (P_{et}CO₂) maintained at 35–45 mmHg. The inspired oxygen fraction was set at 50–60%. Anesthesia was maintained with continuous intravenous infusions of propofol and remifentanyl. To ensure reproducibility and address the clinically necessary individualization within the specified ranges (propofol $4\text{--}12 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$, remifentanyl $3\text{--}6 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$), a standardized titration protocol was employed. Following induction, infusions were initiated at $8 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ for propofol and $4.5 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ for remifentanyl. These doses were then titrated in real-time with the primary goal of maintaining hemodynamic parameters (mean arterial pressure and heart rate) within $\pm 20\%$ of pre-induction baseline values and ensuring no somatic response to surgical stimulus. Specifically, the remifentanyl infusion was increased by increments of $0.5 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ in response to hypertension, tachycardia, or movement, while the propofol infusion was increased by $1 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ if such responses persisted after remifentanyl adjustment. Conversely, reductions were made first to the remifentanyl infusion (by $0.5 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$) for hypotension or bradycardia, followed by propofol if needed. All titration decisions were confined to the stated ranges and made by the attending anesthesiologist, who was blinded

to the patient's group allocation. Ephedrine and metaraminol were administered as needed if these thresholds were exceeded. Infusions of propofol and remifentanyl were discontinued at the end of surgery. Intravenous ondansetron $0.1\text{mg}\cdot\text{kg}^{-1}$ was administered to prevent postoperative nausea and vomiting before the end of the operation. After extubation, pediatric patients were transferred to the post-anesthesia care unit (PACU) for continuous observation until discharge.

Outcome Measures

The primary outcome was the level of postoperative pain, assessed using the Face, Legs, Activity, Cry, Consolability (FLACC) scale at 2 hours following surgery. This scale evaluates five behavioral domains with a total score ranging from 0 to 10, where higher scores indicate greater pain severity.¹⁴ To ensure consistency and minimize observer bias in this subjective assessment, all research personnel responsible for scoring underwent standardized training prior to the study. This training included a review of official scoring criteria, instructional videos, and practice sessions with standardized scenarios to calibrate interpretations. Throughout the data collection period, FLACC assessments were performed by a dedicated research nurses who were blinded to patient group allocation, thereby promoting inter-rater reliability and uniformity in measurement.

Secondary outcomes included postoperative FLACC scores at 8 and 24 hours, and sedation levels evaluated with the Ramsay Sedation Scale at 5, 10, and 15 minutes after tracheal extubation, using the same rater-consistency protocol described for the primary outcome. Additionally, we recorded mean arterial pressure (MAP) and heart rate (HR) at predefined perioperative time points: before induction (T_0), after induction (T_1), at surgical incision (T_2), 10 minutes post-incision (T_3), and at surgery end (T_4). Other recorded parameters were the total intraoperative dosage of propofol and remifentanyl, anesthesia time, surgical time, recovery time (from end of surgery to eye-opening), extubation time, post-anesthesia care unit (PACU) stay, and postoperative hospitalization duration. Furthermore, adverse events were monitored for 48 hours post-operatively using explicit, objective criteria to prevent measurement bias: postoperative nausea and vomiting (PONV) was defined as either verbally reported nausea or vomiting episodes by the child; agitation was defined by a Pediatric Anesthesia Emergence Delirium (PAED) scale score ≥ 10 ; Tachycardia was defined as a heart rate sustained above the age-specific reference value (>130 beats per minute for children aged 2–3 years; >120 bpm for 3–5 years; >110 bpm for 5–10 years) for more than 5 minutes.

Sample Size Calculation

The sample size was calculated using PASS 11.0 according to the primary endpoint of the present study. The results of our pilot study showed that the mean values and standard deviations (SD) of the total FLACC score in both two groups were 125.3, 129.0, 3.7, and 3.6, respectively. Therefore, 22 patients in each group were required with an α of 0.05, and $\beta=0.1$. Allowing for a 20% dropout rate, we selected 54 patients for the present study.

Statistical Analysis

Statistical analyses were performed using SPSS (version 22.0; IBM Corp, Armonk, NY, USA). The normality of continuous variables was assessed using the Shapiro–Wilk test. Normally distributed data are presented as mean $\pm$ standard deviation and were compared between groups using independent samples *t*-tests. Non-normally distributed continuous variables are summarized as median (interquartile range) and compared using the Mann–Whitney *U*-test. Categorical variables are expressed as number (percentage) and were compared using the Chi-square test, with Fisher's exact test employed when expected cell counts were less than 5. A two-sided *P*-value <0.05 was considered statistically significant. A modified intention-to-treat (mITT) analysis was pre-specified for the primary outcome. For handling missing data, a complete-case analysis was planned for the primary outcome; secondary outcomes were analyzed using available data without imputation.

Results

Demographic Data

A total of 60 children were assessed for eligibility. Six children were excluded (three did not meet the inclusion criteria and three declined to participate), resulting in 54 participants who were randomized, received the intervention, and completed the trial protocol (Figure 1). Consequently, complete follow-up data for all primary and secondary outcome

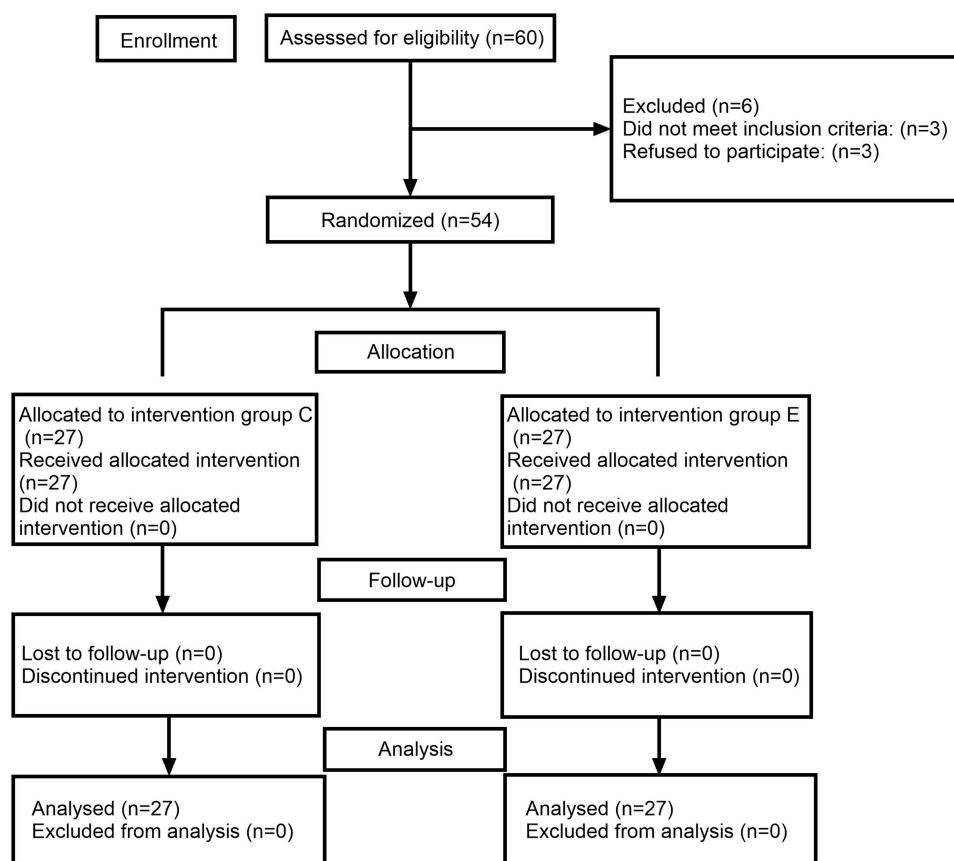


Figure 1 CONSORT flow diagram for the study.

assessments were obtained for the entire analyzed cohort. No post-randomization dropouts or missing data points occurred, thus the pre-specified plan for handling missing data did not require implementation.

The Comparison of The General Information in Two Groups

No significant differences were observed between the two groups in terms of gender, age, ASA classification, anesthesia duration, operation time, recovery time, or extubation time ($P > 0.05$), as shown in [Table 1](#).

The Comparison of The FLACC Scale Scores in Two Groups

The FLACC pain scores for both groups of patients post- surgery are presented in [Table 2](#). There were no significant differences in pain scores between the group C and the group E at 2 hours, 8 hours, and 24 hours post-surgery ($P > 0.05$).

The Comparison of The Ramsay Sedation Scores in Two Groups

The Ramsay sedation scores during the recovery period for both groups are presented in [Table 3](#). No significant differences were found between group C and group E at 5 minutes, 10 minutes, or 15 minutes after extubation ($P > 0.05$).

The Comparison of The MAP and HR in Two Groups

Compared to group C, group E had significantly higher MAP at T1 and T2 ($P < 0.05$), as shown in [Figure 2](#). Additionally, the group E exhibited significantly higher HR at T1, T2 and T3 compared to the group C ($P < 0.05$), as shown in [Figure 3](#).

Table 1 General Characteristics

Parameter	Group C (n=27)	Group E (n=27)	P-value
Age (years)	7.3±1.9	7.5±2.5	0.089
BMI (kg/m ²)	15.5±3.0	16.9±2.3	0.053
Operation time (min)	35.7±15.5	38.0±13.2	0.181
Anesthesia time (min)	47.0±15.0	51.5±13.5	0.455
Postoperative hospital stay (day)	4.5±1.0	4.8±1.2	0.806
Recovery time (min)	18.5±9.5	17.4±12.4	0.457
Extubation time (min)	18.5±9.5	17.4±12.4	0.457
PACU stay duration (min)	43.3±12.2	45.4±13.0	0.453

Notes: Data are present as mean ± standard deviation or number.

Abbreviations: Group C, fentanyl group; Group E, esketmine group; BMI, Body mass index; PACU, post-anesthesia care unit.

Table 2 FLACC Scores of the Two Groups Postoperatively

Parameter	Group C (n=27)	Group E (n=27)	P-value
FLACC at postoperative 2 h	2.2±0.4	2.1±0.3	0.427
FLACC at postoperative 8 h	3.0±0.3	3.0±0.2	0.299
FLACC at postoperative 24 h	3.2±0.4	3.1±0.3	0.085

Notes: Data are present as mean ± standard deviation or number.

Abbreviations: Group C, fentanyl group; Group E, esketmine group; FLACC, Face, Legs, Activity, Cry, Consolability score.

Table 3 Ramsay Scores After Extubation in the Two Groups

Parameter	Group C (n=27)	Group E (n=27)	P-value
Ramsay at postoperative 5 min	1.8±0.4	1.9±0.3	0.085
Ramsay at postoperative 10 min	1.9±0.4	1.9±0.3	0.085
Ramsay at postoperative 15 min	2.0±0.2	2.0±0.2	1.000

Notes: Data are present as mean ± standard deviation or number.

Abbreviations: Group C, fentanyl group; Group E, esketmine group; Ramsay, Ramsay Sedation Scale.

The Comparison of The Adverse Reactions in Two Groups

All the adverse reactions during the recovery period for both groups are shown in Table 4. In the group C, 2 cases of nausea and vomiting, 5 cases of postoperative agitation and 3 cases of tachycardia occurred, with an adverse reaction rate of 37.0% (10/27).

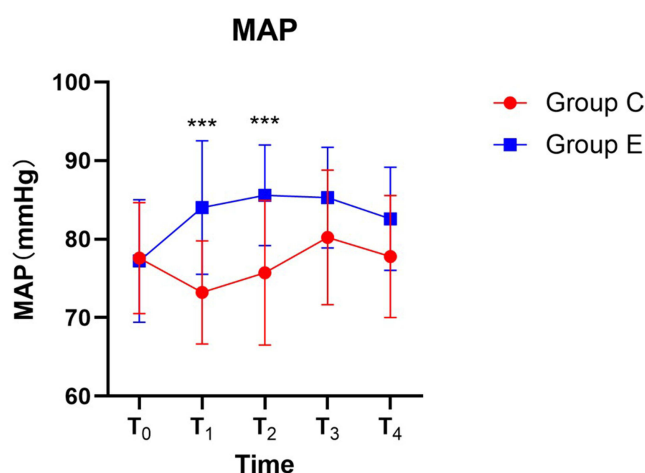


Figure 2 Data are present as median (interquartile range). Group (C) fentanyl group; Group (E) esketmine group; T₀: before anesthesia induction; T₁: after anesthesia induction; T₂: at the start of surgery; T₃: 10 minutes after surgery start; T₄: at the end of surgery; ***p<0.001.

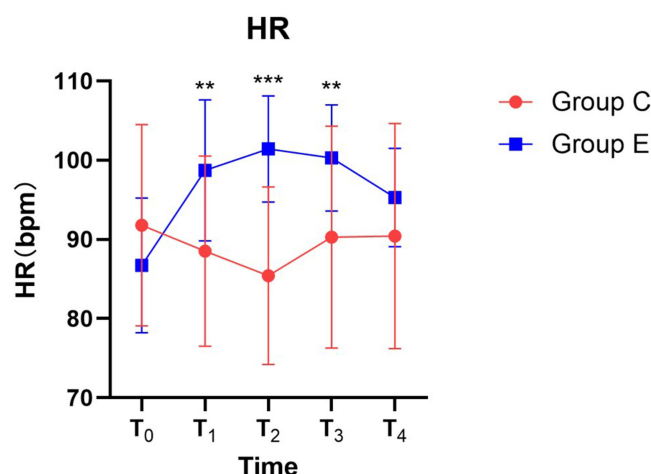


Figure 3 Data are present as median (interquartile range). Group (C) fentanyl group; Group (E) esketamine group; T₀: before anesthesia induction; T₁: after anesthesia induction; T₂: at the start of surgery; T₃: 10 minutes after surgery start; T₄: at the end of surgery; ** $p < 0.01$; *** $p < 0.001$.

In the group E, 3 cases of nausea and vomiting, 4 cases of postoperative agitation and 5 cases of tachycardia occurred, with an adverse reaction rate of 44.4% (12/27). No adverse reactions such as nystagmus were observed in either group. There was no significant difference in the incidence of adverse reactions between the group C and the group E (all $P > 0.05$). All adverse reactions were mild and improved after symptomatic treatment.

Discussion

The findings of this randomized controlled trial demonstrate that, compared with fentanyl, esketamine induction showed no significant differences in postoperative pain scores, sedation scores in pediatric tonsillectomy. While induction with esketamine increases blood pressure and heart rate after anesthesia induction and maintains more stable hemodynamics, there was no increase in postoperative adverse reactions.

The comparable postoperative pain scores between the esketamine and fentanyl groups, both of which were relatively low, indicate that esketamine represents a viable alternative to a conventional opioid for providing effective early analgesia in this surgical context. Relevant studies have demonstrated that esketamine can provide satisfactory sedation and analgesia for nerve block anesthesia in pediatric orthopedic surgery, and its combined use with nerve block is superior to administration alone.¹⁷ Numerous studies have demonstrated that esketamine exerts favorable sedative and analgesic effects in pediatric orthopedic and other surgeries.^{18,19} The underlying pharmacological rationale is multifaceted. Primarily, as a non-competitive antagonist of the N-methyl-D-aspartate (NMDA) receptor, esketamine modulates central sensitization and pain perception.^{20,21} Furthermore, its action extends to the inhibition of thalamo-neocortical projections and interaction with opioid receptor systems,^{22–24} contributing to a synergistic sedative-analgesic effect suitable for multimodal pain management strategies. This finding supports that esketamine exerts a favorable analgesic effect on postoperative pain following plasma tonsillectomy.

A key observation from this study was the more favorable hemodynamic profile associated with esketamine induction. By stimulating the sympathetic nerve centers, esketamine further activates the cardiovascular system, leading to increased HR and

Table 4 Adverse Reactions Postoperatively

Parameter	Group C (n=27)	Group E (n=27)	P-value
Nausea and vomiting, n (%)	2(7.4%)	3(11.1%)	0.999
Emergence agitation, n (%)	5(18.5%)	4(14.8%)	0.702
Tachycardia, n (%)	3(11.1%)	5(18.5%)	0.999
Nystagmus, n (%)	0	0	0.999

Notes: Data are present as mean $\pm$ standard deviation or number (%).

Abbreviations: Group C, fentanyl group; Group E, esketamine group.

elevated MAP, thereby compensating for the circulatory caused by drugs like etomidate and propofol during anesthesia induction and maintenance, and help maintain cardiac output and organ perfusion pressure.^{8,25–28} This finding suggest that the administration of esketamine in pediatric anesthesia not only contributes to favorable hemodynamic stability but also mitigates the risk of organ hypoperfusion during airway procedures. While this study specifically enrolled ASA I–II patients, the clinical relevance of stable hemodynamics warrants emphasis, particularly when considering potential translation to more vulnerable populations. In children with comorbidities, such as those with cardiovascular compromise or reduced physiological reserve, even transient hypotension carries a heightened risk of end-organ hypoperfusion. On the other hand, in the specific context of tonsillectomy, elevated heart rate and blood pressure may raise concerns regarding postoperative bleeding risk. Increased arterial pressure could theoretically translate to greater vascular engorgement and less effective intraoperative hemostasis, potentially predisposing patients to higher rates of secondary hemorrhage. While this trial was not powered to detect differences in bleeding outcomes, this physiological possibility warrants acknowledgment and cautious consideration. Therefore, while the favorable hemodynamic profile of esketamine may support its use in scenarios where stability is paramount, its application in surgeries where hypertension constitutes a material risk, such as tonsillectomy, should be individualized. Future studies should aim to correlate intraoperative hemodynamic parameters with clinically relevant endpoints, including postoperative bleeding incidence, to better delineate the risk–benefit balance of esketamine in different surgical settings.

The incidence of specific adverse events, including PONV, emergence agitation, and tachycardia, was numerically lower in the esketamine group than fentanyl group. This may be attributed to esketamine's dual action of antagonizing NMDA receptors and opioid receptors, providing both analgesic and sedative effects.^{13,29–31} Moreover, esketamine can counteract the respiratory depression caused by opioids, improving prognosis. Similarly, metrics for recovery, such as time to extubation and emergence, trended earlier with esketamine. This may be related to esketamine's high bioavailability and short elimination half-life.^{32–35} According to studies investigating esketamine for pediatric upper gastrointestinal endoscopy, both 0.5 mg·kg⁻¹ and 1 mg·kg⁻¹ esketamine provide adequate sedation for the procedure. However, 1 mg·kg⁻¹ esketamine is associated with a higher incidence of adverse events related to vomiting and visual disturbances.³⁶ Although esketamine may induce hypertension and tachycardia as cardiovascular adverse reactions, investigations have demonstrated that the ED₅₀ of preoperative esketamine in pediatric patients with congenital heart disease is 0.7 mg·kg⁻¹, with a 95% confidence interval of 0.54–0.86 mg·kg⁻¹, and no significant adverse reactions were observed throughout the study period.³⁷ Collectively, these findings indicate that 0.5 mg/kg esketamine achieves sufficient sedation while yielding a lower incidence of adverse reactions. However, in this study, as none of these differences reached statistical significance, caution is required in their interpretation. From a statistical perspective, these are negative findings within the confines of our sample size and study power. Nevertheless, from a clinical relevance standpoint, these consistent trends are noteworthy.

While this study provides valuable insights, several limitations warrant acknowledgment. First, our exclusive inclusion of ASA physical status I–II patients, while ensuring a homogeneous and low-risk cohort for initial safety and efficacy evaluation, inherently limits the generalizability of our findings. The results may not be directly applicable to the broader pediatric population undergoing tonsillectomy who present with greater comorbidities, in whom physiological reserve and medication responses may differ. Second, the investigation was mechanistic in scope; we did not perform laboratory analyses of inflammatory or stress mediators. Consequently, the precise biological mechanisms through which esketamine exerts its analgesic effects in this specific surgical context remain to be fully elucidated. Third, our pain assessment was confined to the immediate 24-hour postoperative period. The absence of longer-term follow-up precludes any conclusions regarding the durability of analgesia, late recovery milestones, or the potential impact on chronic pain development. Fourth, the primary outcome measures, including the FLACC scale, Ramsay sedation score, and BARS nausea/vomiting scores, though validated and standard in pediatric research, are inherently susceptible to some degree of subjective interpretation by caregivers and observers, introducing potential measurement bias. Finally, the sample size, though calculated a priori, remains modest. A larger, multicenter trial would be required to confirm our findings, enhance statistical power for subgroup analyses, and more robustly characterize the incidence of rarer adverse events. Future research should aim to address these limitations by including a more diverse patient population with varying comorbidities, incorporating objective biomarkers, extending the follow-up period, and employing larger sample sizes to strengthen the evidence base for esketamine's role in pediatric multimodal analgesia.

Conclusion

This study is the first to investigate the differences in efficacy between esketamine and fentanyl during pediatric tonsillectomy using plasma technology, compared with fentanyl, the use of esketamine for induction in pediatric tonsillectomy procedures showed no significant difference in postoperative analgesia and sedation levels. Furthermore, esketamine induction resulted in more stable intraoperative hemodynamics, which helped reduce the risk of intraoperative organ hypoperfusion without increasing the incidence of postoperative adverse reactions.

Data Sharing Statement

The datasets used and analyzed during the current study are available from corresponding author Siqi Xu (Email: errtg555@163.com) upon reasonable request.

Acknowledgments

We extend our profound gratitude to all involved parties. Foremost, we are deeply indebted to the pediatric patients and their families for their invaluable participation and cooperation, which served as the foundational pillar of this research. Our sincere appreciation is also directed towards our colleagues, Dr. Fanfan Gao and Dr. Shenghong Hu, for their indispensable and meticulous contributions throughout the research process. We further acknowledge the exceptional professionalism and seamless collaboration of the entire operating room team, anesthesia staff, and ward nurses at Anqing Municipal Hospital during the clinical phase of this project. Moreover, we are grateful to the anonymous reviewers for their insightful comments and constructive suggestions, which substantially enhanced the manuscript's rigor and clarity. Finally, we extend our thanks to the institutional ethics committee for their approval and steadfast support throughout this investigation.

Disclosure

The authors reported no conflicts of interest in this work.

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