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New Drugs and New Modes of Administration in Pediatric Anesthesia

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Abstract **Original Research Article**

Pediatric anesthesia is a rapidly evolving field, driven by ongoing innovations in pharmacology and anesthetic techniques tailored to the unique needs of children. This review focuses on recent developments in anesthetic drug use in pediatric patients, highlighting newly introduced agents as well as novel administration routes and indications for established medications. The discussion includes the pharmacodynamic and pharmacokinetic profiles of these drugs in neonates, infants, and children, along with their clinical efficacy, safety, and applicability in various perioperative scenarios. By synthesizing current literature and evidence-based practices, the review aims to inform clinicians about the expanding therapeutic options in pediatric anesthesia and to support safer, more effective anesthetic care for the pediatric population.

Keywords: Pediatric anesthesia, new anesthetic drugs, alternative drug administration, drug repurposing, pediatric pharmacology.

INTRODUCTION

Recently, many new drugs have been introduced into use in pediatric anesthesia, and studies conducted on these newly introduced drugs have provided clearer insights into their side effect profiles and efficacy. As pediatric anesthesia becomes an increasingly important field, the safety profiles and effectiveness of the drugs used are significant. In this review, we will present current literature information about drugs recently introduced into pediatric anesthesia, specifically those containing the active substances remimazolam, intranasal dexmedetomidine, ciprofol, intranasal fentanyl, and ropivacaine.

METHODS

Publications from April 2020 to the present were included in our study through a search on PubMed.

Remimazolam

Remimazolam is an ultra-short-acting benzodiazepine approved for clinical use in 2020 by the United States Food & Drug Administration (FDA). Acting as a gamma-aminobutyric acid A (GABA-A) receptor agonist, it induces amnesia, anxiolysis, and sedation, similar to other benzodiazepines. In clinical practice, it is used in the pediatric population either as a primary agent in procedural anesthesia or as an adjunct to general anesthesia [1]. It does not have FDA approval for use in pediatric patients, which further increases interest in pediatric studies involving this drug [2].

Recently, its success in anesthesia induction and side effect profile were investigated. Fang et al. [3] examined the side effect profile of remimazolam in children undergoing elective surgery under general anesthesia with tracheal intubation, in comparison to propofol. In this study, children aged 3–6 years, with an American Society of Anesthesiologists (ASA) physical status score of 1 or 2, and a body mass index between 14 and 25 kg/m², were evaluated. Among 187 children, who met the inclusion criteria, 140 received remimazolam and 47 received propofol. Anesthesia induction was successfully and uneventfully achieved in all children. Adverse events occurred in 19% of the children in the remimazolam group and in 49% of the propofol group. The most common adverse reaction was pain at the injection site, which was observed in 7 children who received propofol but in none of the children who received remimazolam. Another adverse effect was intraoperative bradycardia, which was well-controlled and occurred in 12 children in the propofol group and 13 in the remimazolam group. Delayed awakening due to prolonged anesthetic effect was observed in only 3 children, all of whom were in the remimazolam group; no such effect was observed in those who received propofol. It was concluded that remimazolam was well tolerated for induction and maintenance of general

anesthesia in preschool-aged children. Additionally, it was associated with a lower incidence of adverse effects and greater hemodynamic stability [3].

In another clinical study on remimazolam, 48 participants under the age of 18 were included. The median age of the participants was 7 years. Their body mass index ranged from 16.7 to 26.8. Patients with an ASA score of 3 or lower were included. In this study, remimazolam was found to have promising potential as an efficient, effective, and safe intravenous sedative for procedural sedation in the pediatric population, especially when used in combination with other edatives and analgesics. It was commonly used in procedures lasting up to 60 minutes. However, more comprehensive studies are needed to evaluate its pharmacodynamic and pharmacokinetic responses both when used in combination with multiple sedatives and analgesics and when used alone [4]. The study by Shen et al. [5] compared the effects of remimazolam and propofol in individuals aged between 3 and 15 years, undergoing elective surgery under general anesthesia. 90 patients whose ASA physical status scores of 1 or 2, were divided into 9 subgroups of 10 patients each. Five groups received remimazolam and four received propofol. The results revealed that remimazolam was 5.8 times more effective than propofol in inducing loss of consciousness in pediatric patients. A dose of 0.34 mg/kg of remimazolam was found to be effective and safe for general anesthesia induction in children [5].

The efficacy of intranasal form of remimazolam was investigated in another clinical study with regards to reducing preoperative anxiety in children aged 2 to 5 years, with ASA scores of 1 or 2, and undergoing surgery in the field of general surgery under general anesthesia. The participants were randomly divided into three equal groups; one group received intranasal distilled water, second received intranasal remimazolam, and the third group received intranasal dexmedetomidine. The results showed that both intranasal dexmedetomidine and intranasal remimazolam were effective in reducing preoperative anxiety. Intranasal remimazolam slightly improved mask acceptance during inhalational anesthesia induction in young children. Intranasal dexmedetomidine provided deeper sedation, but it had a slower onset and longer duration of action. In contrast, intranasal remimazolam had a faster onset and produced milder sedation. However, significant nasal irritation was observed in patients who received intranasal remimazolam [6].

Summary of Studies on Remimazolam

Author and Citation	Study Method	Result
Fang *et al*. [2]	A clinical study conducted on 187 children aged 3 to 6 years, in which 140 received remimazolam and 47 received propofol	In preschool-aged children, remimazolam was well tolerated for the induction and maintenance of general anesthesia. Additionally, it was associated with a low incidence of adverse effects and hemodynamic stability.
Hirano *et al*. [4]	A clinical study conducted on 48 participants under the age of 18.	Remimazolam was found to have promising potential as an efficient, effective, and safe intravenous sedative in the pediatric population when used in combination with other sedatives and analgesics for procedural sedation.
Shen *et al*. [5]	A clinical study conducted on 90 participants aged between 3 and 15 years	A dose of 0.34 mg/kg of remimazolam was found to be effective and safe for the induction of general anesthesia in pediatric patients.
Cai *et al*. [6]	A clinical study conducted on 90 participants aged between 2 and 5 years, investigating the reduction of preoperative anxiety.	Intranasal remimazolam has a faster onset of action and produces a milder sedative effect. Additionally, significant nasal irritation was observed in individuals who received intranasal remimazolam.

Ropivacaine

Ropivacaine is a long-acting local anesthetic used for postoperative pain management [7]. It is a chemical homologue of bupivacaine and mepivacaine. Preclinical studies have shown that it has less central nervous system toxicity and cardiotoxicity compared to bupivacaine [8]. This information was later confirmed in human volunteer studies [9, 10].

In a clinical study on ropivacaine, a total of 100 individuals undergoing hypospadias surgery were divided into two groups. Both groups received general anesthesia, and in addition, one group received a sacral block with ropivacaine (group R), while the other group received a sacral block with both hydromorphone and ropivacaine (group HR). Postoperative sedation levels were higher in the HR group compared to the R group. The HR group also had lower postoperative pain and analgesia levels compared to the R group. No significant differences were found between the two groups in vital signs. Regarding postoperative adverse reactions, 5 individuals in the HR group experienced nausea and vomiting, 5 had hypoxemia, and 4 had respiratory depression. In the R group, 7 individuals experienced nausea and vomiting, 5 had hypoxemia, 5 had respiratory depression, and 3 experienced pruritus. However, no significant differences were found between the two groups in terms of these adverse effects. It was concluded

that ropivacaine was well tolerated and it could be a viable agent for pediatric use [11].

Another clinical study by Faramarzi et al. [12] investigated the effects of ropivacaine on pain and hospital stay after tonsillectomy. The study population comprised of three groups, one group received ropivacaine and normal saline injected into the peritonsillar region before surgery (group RB), second group received ropivacaine and normal saline after surgery (group RA), and the third group received only normal saline after surgery (control group). Postoperative pain was assessed at 4, 8, and 24 hours using the Wong-Baker pain scale. The study revealed that the RB group showed a significant reduction in postoperative pain and analgesic requirements. This suggests that ropivacaine administered through peritonsillar injection before tonsillectomy in pediatric patients is beneficial.

The effectiveness of ropivacaine during ultrasound-guided axillary brachial plexus block in preschool-aged children undergoing hand surgery was also evaluated. The results of the study indicated that the effective volume for 50% (EV50) and 95% (EV95) of the effect for the 0.2% ropivacaine formulation in ultrasound-guided axillary brachial plexus block in preschool-aged children were 0.185 ml/kg and 0.280 ml/kg, respectively. This suggests that ropivacaine can be safely used for nerve blocks in the pediatric population [13].

Another clinical study compared the effects of two block techniques on post-sternotomy pain in children with acyanotic heart disease [14]. Although this study did not directly focus on ropivacaine, it was demonstrated that ropivacaine is safe and effective for use in pediatric patients. Two participants were excluded from the study as they refused participation, and two others were excluded during the preoperative period due to the need for inotropic support. The study proceeded with 86 participants, who were divided into three groups. One group received ultrasound-guided erector spinae plane block (ESPB) with ropivacaine, the second group received multiple injection costotransverse block (MICB), and the third group did not receive any block and was considered the control group. Postoperative pain levels were significantly lower in the block groups during the first 12 hours, but no significant difference was found between the two block techniques. Additionally, after the 12th hour, no significant difference was found between the control group and the block groups. This study also demonstrated that ropivacaine can be safely used for nerve blocks in the pediatric population.

The Summary of Studies on Ropivacaine

Author and Citation	Study Method	Result
Cai *et al*. [11]	A total of 100 pediatric participants undergoing hypospadias surgery were divided into two groups of 50. One group received a caudal block with only ropivacaine, while the other group received a caudal block with both ropivacaine and hydromorphone.	Due to its good tolerance and its use in studies in the current literature, ropivacaine may be a suitable agent for use in the pediatric age group.
Faramarzi *et al*. [12]	In this study conducted on a total of 108 pediatric patients undergoing tonsillectomy, the patients were divided into three equal groups of 36. One group received ropivacaine injection in the peritonsillar region before the surgery, another group received the injection after the surgery, and the control group received only normal saline.	It was shown that the application of ropivacaine through peritonsillar injection before tonsillectomy in the pediatric age group is beneficial.
Chen *et al*. [13]	In 27 participants aged 3-6 years, who were scheduled for upper limb surgery, ultrasound-guided ropivacaine injection was administered for brachial plexus block.	It has been shown that ropivacaine can be safely used for nerve blocks in the pediatric age group.
Somani *et al*. [14]	In a study conducted with 86 pediatric participants undergoing sternotomy, various nerve blocks were performed using ropivacaine, and the superiority of these nerve block types was compared to each other.	This study has shown that ropivacaine can be safely used for nerve blocks in the pediatric age group.

Intranasal Dexmedetomidine

Dexmedetomidine has been approved by FDA for perioperative sedation in non-intubated patients and for sedation in intubated or mechanically ventilated patients in the intensive care unit. As an alpha agonist, it exhibits sympatholytic effects, which include sedative, hypnotic, analgesic, and anxiolytic effects. The most significant side effects include hypotension, bradycardia, and hypertension. The hypertensive side effect arises from the alpha agonist effect, which stimulates vascular smooth muscles, causing them to contract. The intravenous (IV) form was approved by the FDA in 1999 for adults and in 2013 for pediatric patients (ages 1 month to 16 years). However, the intranasal form has not yet received FDA approval, which has sparked interest in research on this form, particularly in the pediatric age group, where non-invasive methods have gained importance [15].

A single center, randomized, double-blind, and controlled clinical study was conducted to investigate the effects of intranasal dexmedetomidine and intranasal esketamine on the acceptance of face masks in the pediatric age group. The study involved 95 patients aged 1-6 years who were scheduled for elective surgery. After the exclusion of five patients for various reasons, 90 patients were divided into two groups. One group received intranasal dexmedetomidine and normal 0.9% saline, while the other group received both intranasal dexmedetomidine and intranasal esketamine. The participants were then assessed using various scoring methods. It was shown that preoperative sedation with intranasal dexmedetomidine combined with esketamine led to a higher mask acceptance rate and anxiolytic effect compared to intranasal dexmedetomidine alone. Pediatric anesthesia delirium was observed in 13 participants in the intranasal dexmedetomidine group and in 17 participants in the intranasal dexmedetomidine and esketamine group. However, there was no significant difference between the two groups. This demonstrated that intranasal dexmedetomidine is effective and safe for use in the pediatric age group [16].

Another clinical study was conducted to compare the procedural sedation and analgesic effects of intranasal dexmedetomidine and inhaled nitrous oxide in the pediatric age group, who had severe extremity fractures and dislocations in the emergency department. The importance of effective and rapid analgesic activity in such situations in this age group is quite evident. The study included 156 patients aged 3-15 years, with ASA levels 1 and 2. One group received intranasal dexmedetomidine, and the other received 50% inhaled nitrous oxide. The study revealed that intranasal dexmedetomidine was found to be equally effective as inhaled nitrous oxide in providing analgesia for painful procedures in pediatric patients [17].

The efficacy of intranasal dexmedetomidine in pediatric preanesthetic sedation was evaluated in another study [18]. The children in the study group received intranasal dexmedetomidine in doses ranging from 30 µg to 50 µg according to their body weight. It was shown that 94.4% of children in the study group reached a Ramsay score of 3 within 45 minutes, while only 32% in the placebo group achieved the same. As for side effects, 90.7% of the intranasal dexmedetomidine group and 84% of the placebo group experienced side effects. However, no life-threatening or significant adverse effects were observed. Bradycardia was seen in 26% of the placebo group and 38.3% of the dexmedetomidine group. A decrease in diastolic blood pressure was seen in 20% of the placebo group and 19.6% of the dexmedetomidine group. These and similar side effects in the dexmedetomidine group were observed within 45 minutes after treatment, and there were no significant differences in the observed values for these side effects on the second and third follow-up days in both groups. It was concluded that the use of intranasal dexmedetomidine in pediatric pre-anesthesia sped up the transition to anesthesia and the separation of parents and children without causing significant adverse effects.

In the study Azemati et al. [19] the efficacy of intranasal dexmedetomidine (D), midazolam (M), and ketamine (K) in surgical premedication before elective unilateral inguinal herniorrhaphy was compared. All intervention was administered 60 minutes before anesthesia induction. Anxiety and sedation levels of patients were assessed every 10 minutes until the 50th minute, both before and after the drug was administered. Preoperative nausea and vomiting were observed in 8 patients from Group K, 1 patient from Group M, and none from Group D. There was no significant difference in postoperative pain scores among the three groups within the first hour. Postoperative nausea and vomiting were observed in 2 patients from Group D, 2 patients from Group M, and 4 patients from Group K. Ketamine exhibited the strongest sedative effect at 10, 20, and 30 minutes, while dexmedetomidine exhibited the strongest sedative effect at 40 and 50 minutes. In terms of side effect profiles, ketamine had the most side effects, but none of the groups experienced any life-threatening adverse events. It was concluded that intranasal ketamine is appropriate for emergency situations due to its rapid onset, while intranasal dexmedetomidine, which has a stronger sedative effect but a delayed onset, is suitable for elective situations where there is no time constraint.

In another study, one group receiving intranasal dexmedetomidine (Group D) and the other receiving intranasal ketamine (Group K) 45 minutes before general anesthesia as a premedication. The patients' anxiety levels were measured using the FLACC (Faces, Legs, Activity, Cry, and Consolability) scale. Group D had a significantly higher FLACC score compared to Group K. The sedation level was also significantly higher in Group D compared to Group K. While 8% of the patients in Group K experienced side effects such as nausea and vomiting, no side effects were observed in any patients in Group D. It was seen that intranasal ketamine is more effective in anesthesia premedication compared to intranasal dexmedetomidine, but it has a higher incidence of adverse effects [20].

The Summary of Studies on Intranasal Dexmedetomidine		
Author and Citation	**Study Method**	**Result**
Zhang *et al*. [16]	Ninety patients aged 1-6 years were divided into two equal groups. One group was administered only intranasal dexmedetomidine, while the other group received intranasal dexmedetomidine along with esketamine.	It demonstrates that intranasal dexmedetomidine is effective and safe for use in the pediatric age group.
Nikula *et al*. [17]	A total of 148 patients aged 3-15 years were divided into two equal groups. One group received anesthesia with nitrous oxide, while the other group was administered anesthesia with intranasal dexmedetomidine.	It has been found that the analgesic effectiveness of intranasal dexmedetomidine for painful procedures in the pediatric age group is not inferior to inhaled nitrous oxide.
Gao *et al*. [18]	A total of 156 patients aged 2-6 years were divided into two groups of 106 and 50. The 106 patients received preanesthetic intranasal dexmedetomidine, while the other group, serving as the placebo group, received nothing.	The use of intranasal dexmedetomidine in pediatric premedication has expedited parent-child separation and the transition to the anesthesia level without causing significant side effects.
Azemati *et al*. [19]	A total of 90 patients aged 2-7 years were divided into three groups, each consisting of 30 patients. One group received intranasal ketamine for surgical premedication, another group received intranasal dexmedetomidine, and the third group received intranasal midazolam.	In emergency situations, intranasal ketamine is suitable due to its rapid onset of action, while in elective situations where time constraints are not a concern, intranasal dexmedetomidine, which has the strongest sedative effect but a slower onset, is more appropriate.
Kumari *et al*. [20]	A total of 100 participants aged 2-10 years were divided into two groups of 50. One group received intranasal ketamine for anesthesia premedication, while the other group received intranasal dexmedetomidine.	Intranasal ketamine is more effective than intranasal dexmedetomidine for anesthesia premedication, but the incidence of adverse effects is higher.

Intranasal Fentanyl

Fentanyl is an opioid agent discovered in 1960 and approved by the FDA in 1984 [21]. It is 50 to 100 times more potent than morphine, another opioid agent, at the same dose [22]. It is frequently used to provide sedation in intubated patients and manage severe pain in patients with severe renal failure due to its primary hepatic elimination feature [23]. Fentanyl specifically exerts an agonistic effect on mu-opioid receptors [24]. It can be administered intramuscularly, intravenously, transdermally via skin patches, intrathecally, and intranasally. It also comes in buccal and sublingual tablet forms that dissolve for application [25]. Although fentanyl is used in individuals over 65 years old, there is limited information in the literature about its use in the pediatric age group. Due to its high potency, the use of low doses via intranasal administration has gained interest in the pediatric population, where non-invasive methods are becoming increasingly important.

A clinical study was conducted to investigate the efficacy of intranasal fentanyl and nitrous oxide in procedural sedation in the pediatric population [26]. The participants had refrained from fluid intake and solid food for a minimum of 2 hours before the procedure. Early vomiting was observed in 62 individuals, and 100 participants out of 400 who could be contacted 24 hours after the procedure experienced vomiting. Early vomiting was found to be significantly associated with the dose of intranasal fentanyl. This suggested that intranasal fentanyl use in pediatrics may cause early vomiting, potentially leading to various complications. In another study, it was aimed to investigate the superiority of intranasal dexmedetomidine plus fentanyl combination over intranasal midazolam plus fentanyl combination [27]. After application of medications 20 minutes before general anesthesia, the pain levels of participants were observed using Oucher's Facial Pain Scale 2 hours after the surgery. More pain was reported in patients who received intranasal midazolam plus fentanyl combination. It was seen that intranasal dexmedetomidine and fentanyl provided better analgesia. This study demonstrated that intranasal fentanyl can also be used in premedication.

Alhaidari *et al*. [28] investigated the effects of intranasal fentanyl in uncooperative children during dental sedation. In this study, one group received oral midazolam plus intranasal placebo during the first visit and oral midazolam and intranasal fentanyl during the second visit. The other group received oral midazolam and intranasal fentanyl during the first visit and oral midazolam and intranasal placebo during the second visit. Both groups experienced side effects such as hiccups, hallucinations, and vomiting. Vomiting occurred only in two procedures where oral midazolam

was used, but it was minor, clear liquid vomiting triggered by crying. It was seen that combining oral midazolam with intranasal fentanyl improved the quality of sedation. Intranasal fentanyl extended the duration of oral midazolam's effects. However, intranasal fentanyl should be used with caution due to its rapid onset of action and the potential for severe adverse effects in cases of dosage errors or misuse.

The effectiveness of intranasal fentanyl was also evaluated for acute pain management in pediatric emergencies in children aged 3 to 17 years. Half of the children received intranasal ketamine, while the others received intranasal fentanyl. Pain levels were assessed at 10, 20, 30, and 60 minutes after administration. The results showed that intranasal ketamine and intranasal fentanyl demonstrated similar analgesic effects after 20 minutes, but fentanyl had a more significant analgesic effect at 10 minutes. The group receiving intranasal ketamine had a significantly higher incidence of side effects, with dizziness being the most notable. Dizziness was observed in 73% of the ketamine group, compared to 9% in the fentanyl group. Consequently, due to its rapid onset, effectiveness, and lower side effect profile, intranasal fentanyl may be preferred in pediatric patients [29].

Summary of Studies on Intranasal Fentanyl

Author and Citation	Study Method	Result
Fauteux-Lamarre *et al*. [26]	The study conducted on 436 participants investigates the effect of intranasal fentanyl used in procedural sedation on early vomiting.	It has shown that intranasal fentanyl in pediatric use can lead to early vomiting, causing various complications.
Kaur *et al*. [27]	100 participants were divided into 2 groups. One group received intranasal fentanyl and midazolam, while the other group received intranasal fentanyl and dexmedetomidine.	This study has shown that intranasal fentanyl can be used in premedication.
Alhaidari *et al*. [28]	Oral midazolam and intranasal placebo were administered to 32 participants aged 3-6 years, along with oral midazolam and intranasal fentanyl.	The combination of oral midazolam with intranasal fentanyl improved the quality of sedation. Intranasal fentanyl extended the duration of action of oral midazolam. However, intranasal fentanyl should be used cautiously due to its rapid onset of action, potential dosing errors, and the risk of serious adverse effects with improper use.
Quinn *et al*. [29]	Twenty-two participants aged 3-17 years were divided into two equal groups of 11 people, with one group receiving intranasal ketamine and the other receiving intranasal fentanyl, and their effects on pain management were observed.	Due to its rapid onset, effectiveness, and lower side effect profile, intranasal fentanyl may be preferred in the pediatric age group.

Ciprofol

Ciprofol is a GABA-A agonist and structurally resembles propofol, with the key difference being the presence of an additional cyclopropyl group in its structure [30]. This added cyclopropyl group increases its volume, making it more lipophilic, which allows it to cross the blood-brain barrier more efficiently than propofol, thereby enhancing its sedative effect. In similar doses, ciprofol is 4-5 times more sedative than propofol [30-33]. Clinically, it is used for anesthesia induction, maintenance of anesthesia, pain management, and sedation in intensive care. While its high lipophilicity and efficacy make it preferable for use in the elderly population, there is limited information in the literature regarding its use in pediatric populations, with only three published studies available. With more multicenter and effective publications in this area, ciprofol may become a widely used pediatric anesthetic agent in the future. Although there are many studies on the use of ciprofol in adults, a clinical study was conducted to evaluate the efficacy and safety of ciprofol for general anesthesia induction and maintenance in pediatric patients aged 2-17 years [34]. Fourteen participants aged 2-5, twelve participants aged 6-11, and twelve participants aged 12-17 were included. All patients were classified as ASA 1 and 2, and anesthesia induction and maintenance were performed using ciprofol without the need for any additional agents. During the study, adverse effects were observed in only four participants, none of which were life-threatening. One patient developed fever, two had muscle tremors, and one developed a local infection. The results showed that ciprofol can be safely used for general anesthesia induction and maintenance in pediatric patients aged 2 and above.

In another study, the authors investigated the ED50 value of ciprofol when combined with fentanyl and when administered without fentanyl using a

laryngeal mask airway in pediatric patients [35]. The participants were randomly divided into three groups; Group C0 received 1.6 mg/kg ciprofol and saline, group C1 received 0.6 mg/kg ciprofol and 1 µg/kg fentanyl, and group C2 received 0.6 mg/kg ciprofol and 2 µg/kg fentanyl. No serious adverse effects were observed during the study. The most common side effect was hypotension, which was observed in 23.3% of group C1 and 13.3% of group C2. All participants received oxygen for three minutes before anesthesia induction, and no hypoxia was observed in any of them. The results showed that the ED50 value of ciprofol decreased significantly when combined with fentanyl, suggesting that ciprofol can be used in pediatric anesthesia without causing major complications.

In the study by Pei et al. [37] it was aimed to find the appropriate dose of ciprofol when combined with low dose rocuronium in children undergoing adenotonsillectomy. Group C4 received 0.4 mg/kg ciprofol, group C6 received 0.6 mg/kg ciprofol, and group C8 received 0.8 mg/kg ciprofol. The only side effect observed was injection site pain in 5 patients, approximately 3.5% of participants, which is much lower than the 25-85% incidence rate seen in studies with propofol [36]. No other side effects were observed. The study concluded that 0.6 mg/kg ciprofol, when combined with low dose rocuronium, was well tolerated in the pediatric age group. This study also demonstrated that ciprofol can be safely used in pediatric patients without significant side effects.

Summary of Studies on Ciprofol

Author and Citation	Study Method	Result
Chen *et al*. [34]	The study included 38 individuals aged 2-17 years. Ciprofol was used for anesthesia induction and maintenance in these individuals undergoing elective surgery.	Ciprofol has demonstrated a safety profile that allows it to be used safely for anesthesia induction and maintenance in pediatric patients over the age of 2
Wang *et al*. [35]	Ciprofol was administered alone and in combination with fentanyl to 90 participants aged 3-6 years, and its effect on the ED50 value of ciprofol was evaluated.	The study has provided hope that ciprofol can be used in pediatric anesthesia without causing significant complications.
Pei *et al*. [37]	A total of 147 participants aged 3-12 years were divided into three groups, with 49 participants in each group, and ciprofol was administered in varying doses to the groups.	This study has shown that ciprofol can be safely used in the pediatric age group without significant side effects.

Thiamylal

Thiamylal is an ultra-short-acting barbiturate, like thiopental [38, 39]. There is only one study on thiamylal, which was conducted in 23 participants with febrile refractory status epilepticus lasting longer than 60 minutes. This study found thiamylal to be effective in reducing the frequency of seizure recurrence. However, in cases where a bolus was not administered, it frequently caused hemodynamic disturbances and infections. These side effects were observed at similar rates to other treatments without bolus administration, but the use of thiamylal without a bolus in such cases has raised concerns [40].

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