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A Comprehensive Review of Drugs Used During Anesthesia in Pediatric Patients: Pharmacology, Safety and Clinical Considerations

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ABSTRACT :

Pediatric anesthesia presents unique challenges due to the anatomical, physiological, and developmental differences between children and adults. This review systematically evaluates pharmacologic agents used during the four crucial stages of pediatric anesthesia: premedication, induction, maintenance, and recovery. Intravenous anesthetics such as propofol, ketamine, and thiopental are examined with emphasis on their rapid onset and hemodynamic characteristics. Inhalational agents, particularly sevoflurane and isoflurane, are highlighted for their non-irritating properties and adjustable depth of anesthesia, making them preferable for mask induction in children. The role of opioid analgesics, including fentanyl, morphine, and remifentanil, is reviewed with attention to their efficacy in pain management and the risks of respiratory depression and tolerance in pediatric patients.

Neuromuscular blocking agents such as succinylcholine, rocuronium, and vecuronium are evaluated for their ability to facilitate intubation and improve surgical conditions. The use of local anesthetics, including lidocaine, bupivacaine, and ropivacaine, is explored in the context of regional anesthesia and postoperative pain management, with consideration of age-specific dosing and toxicity thresholds. Pharmacokinetics, pharmacodynamics, and safety profiles of each drug class are discussed in detail.

Given the physiological vulnerability of pediatric patients, the selection and administration of anesthetic agents require careful judgment. This study underscores the importance of a multidisciplinary approach, vigilant monitoring, and continuous education to ensure safe and effective anesthesia in children.

Keywords: pediatric, pediatric pharmacology, pediatric anaesthesia

Introduction

Neonates, infants, children, and adolescents are the focus of pediatric anesthesia, which differs from adult anesthesia in several key ways. Infants have a higher risk of anesthesia-related morbidity and mortality compared to adults (1,2). Thus, anesthesiologists must clearly understand the unique requirements of pediatric patients.

One challenge is the limited clinical research on anesthetic dosing in children, leaving anesthesiologists with little evidence-based guidance (3). Within the pediatric age range, there is marked variability in physiology, age, and weight, making it difficult to define a “standard” dose. This variability increases the risk of potentially serious medication errors in children compared to adults (4).

Anesthesia is also a stressful experience for both pediatric patients and their parents. Preoperative anxiety about anesthesia duration and recovery can elevate stress hormones, which may impair wound healing (5,6). In pediatrics, informed consent for anesthesia is obtained through parental approval following consent for surgery (7,8).

This review aims to provide a clear overview of medications commonly used in pediatric anesthesia, including mechanisms of action, age-appropriate dosing, routes of administration, duration, metabolism, side effects, interactions, and contraindications. Quick-reference tables are included to improve clarity and clinical relevance. Overall, this review highlights the importance of individualized, evidence-based, and developmentally appropriate anesthesia care in children. It underscores the need for interdisciplinary collaboration, continuous education, vigilant monitoring, and the integration of new evidence into routine practice to ensure maximum safety and effectiveness.

Classification of Anesthesia Drugs in Pediatrics

There are 5 major groups of drugs commonly used in anesthesia:

Intravenous Anesthetics in Pediatric Anesthesia

For rapid induction and maintenance, pediatric anesthesia commonly relies on intravenous (IV) anesthetic drugs. When using these agents, age-related pharmacokinetics, organ immaturity, and safety profiles must be carefully considered [9]. This section reviews the mechanisms, pharmacology, and safety of commonly used IV agents: propofol, ketamine, thiopental, etomidate, and dexmedetomidine.

1. Propofol

- Class: Hypnotic-sedative
- Mechanism of Action: Enhances GABA-A receptor activation, producing central nervous system depression [10].
- Onset: 30–60 seconds
- Duration: 5–10 minutes
- Applications: Procedural sedation; induction and maintenance of anesthesia

Pharmacology in Children:

- Suitable for short procedures due to rapid onset and recovery
- Children require higher doses than adults (2.5–3.5 mg/kg) due to larger volume of distribution and clearance [11]

Safety:

- Advantages: Smooth induction, rapid recovery, antiemetic properties
- Risks: Hypotension, bradycardia, respiratory depression, injection pain
- Note: Prolonged infusions may rarely cause propofol infusion syndrome (PRIS), especially in ICU settings [12]

2. Ketamine

- Class: NMDA receptor antagonist
- Mechanism of Action: Produces dissociative anesthesia with analgesia and amnesia by blocking NMDA receptors [13]
- Dosage: 1–2 mg/kg IV or 4–6 mg/kg IM

Pharmacology in Children:

- Useful in emergencies, uncooperative children, and patients with hemodynamic instability

Safety:

- Advantages: Preserves airway reflexes, increases blood pressure and heart rate (beneficial in hypovolemia), provides analgesia
- Risks: Laryngospasm, increased salivation, emergence reactions (e.g., hallucinations) [14]

3. Thiopental Sodium

- Class: Barbiturate
- Mechanism of Action: Enhances GABA-A receptor activity, leading to CNS depression
- Dosage: 3–5 mg/kg IV
- Onset: <30 seconds
- Duration: Longer context-sensitive half-life compared to propofol [15]

Safety:

- Advantages: Reduces cerebral metabolic rate (useful in brain injuries); effective for rapid induction
- Risks: Hypotension, respiratory depression, slower recovery than with propofol [16]
- Note: Use has declined due to safer alternatives such as propofol

4. Etomidate

- Class: Imidazole derivative
- Mechanism of Action: Produces hypnosis via GABA-A receptor modulation with minimal cardiovascular effects [17]
- Dosage: 0.2–0.3 mg/kg IV

Pharmacology in Children:

- Beneficial in patients with unstable or compromised cardiovascular function

Safety:

- Advantages: Minimal effect on heart rate and blood pressure
- Risks: Myoclonus, nausea, adrenal suppression, injection pain [18]
- Note: Reserved for high-risk patients requiring cardiac stability

5. Dexmedetomidine

- Class: Selective α2-adrenergic agonist
- Mechanism of Action: Inhibits norepinephrine release by stimulating central α2 receptors, resulting in sedation, analgesia, and anxiolysis with minimal respiratory depression

Pharmacology:

- Route: IV infusion
- Onset: 5–10 minutes
- Peak Effect: 15–30 minutes
- Half-life: ~2 hours
- Metabolism: Hepatic (CYP450)
- Elimination: Primarily renal

Applications in Children:

- Used for sedation in the OR and ICU, adjunct to general anesthesia, and in children with airway risk (low respiratory depression)

Safety:

- Common Adverse Effects: Dry mouth, nausea, hypotension, bradycardia
- Rare: Hypertension during loading dose (due to peripheral α2B stimulation)
- Precautions: Avoid rapid boluses; use cautiously in patients with heart block or hypovolemia; monitor blood pressure and heart rate closely

Other Agents (Less Common in Pediatrics)

- Methohexital: Short-acting barbiturate used in brief procedures (e.g., electroconvulsive therapy); may increase seizure risk
- Fospropofol: Prodrug of propofol with delayed onset; limited pediatric data

Inhalational Anaesthetics in Paediatric Patients

Inhalational anaesthetics are widely used in paediatric practice, especially for induction in young children who may resist intravenous (IV) access. These agents allow smooth and rapid induction with easy titration of anaesthetic depth. However, due to immature hepatic and renal systems, higher minute ventilation, and increased cardiac output, children demonstrate different pharmacodynamic responses and side-effect profiles compared with adults [9].

1. Sevoflurane (Volatile Halogenated Ether)

- MAC (children): ~2.5–3.0% (higher than adults)
- Blood: Gas Partition Coefficient: ~0.65 (rapid onset/offset)

Pharmacology:

Sevoflurane is the most commonly used agent for mask induction in children due to its rapid onset, non-pungent odour, and minimal airway irritation [19].

Safety:

- Advantages: Fast emergence, minimal airway irritation, ideal for inhalational induction.
- Risks: Emergence delirium (agitation, restlessness) [20], dose-dependent hypotension and respiratory depression [21]. Rare cases of nephrotoxicity have been reported with prolonged low-flow anaesthesia [22].

2. Desflurane (Halogenated Ether Volatile)

- MAC (children): ~6–9%
- Blood: Gas Partition Coefficient: ~0.42 (very rapid onset/recovery)

Pharmacology:

Due to its pungent odour and airway irritability, desflurane is usually reserved for maintenance rather than induction. It provides the fastest recovery of all volatile anaesthetics [23].

Safety:

- Advantages: Excellent for outpatient surgery due to rapid recovery.
- Risks: Airway irritation (cough, breath-holding, laryngospasm) if used for induction [24]; sympathetic stimulation with increased heart rate and blood pressure. Not recommended for induction in children.

3. Isoflurane (Volatile Anaesthetic)

- MAC (children): ~1.6%
- Blood: Gas Partition Coefficient: ~1.4

Pharmacology:

Isoflurane has a slower onset and is pungent, limiting its use for induction. It remains useful for maintenance during long procedures [25].

Safety:

- Advantages: Potent anaesthetic, muscle relaxation, cost-effective.
- Risks: Slower recovery, dose-dependent vasodilation and hypotension, and potential to increase intracranial pressure in patients with neurological conditions.

4. Nitrous Oxide (N_2O) – Inorganic Gas

- MAC: ~104% (not sufficient for general anaesthesia alone)
- Blood: Gas Partition Coefficient: 0.47

Pharmacology:

Used primarily as an adjunct to provide analgesia and reduce the MAC of volatile or IV agents [26].

Safety:

- Advantages: Rapid onset, minimal cardiovascular and respiratory depression.
- Risks: Diffusion hypoxia after discontinuation (prevented by 100% oxygen postoperatively) [27]; inhibition of methionine synthase, which may cause neurotoxicity or vitamin B12 deficiency with prolonged use, particularly in infants [28]. Contraindicated in patients with air-filled cavity disorders (e.g., bowel obstruction, pneumothorax).

Comparison Table of Common Inhalational Agents in Pediatrics

Agent	MAC (Child)	Smell	Induction Use	Recovery	Airway Irritation	Notes
Sevoflurane	2.5–3.0%	Pleasant	Yes	Fast	Minimal	Most commonly used
Desflurane	6–9%	Pungent	No	Very Fast	High	Not suitable for inhalational induction
Isoflurane	1.6%	Pungent	No	Slow	Moderate	Used in long surgeries
Nitrous Oxide	N/A	Sweet	Adjunct	Fast	None	Used with other agents, not alone

3. Opioids

Opioids are essential components of pediatric anesthesia, mainly for analgesia during and after surgery. Their use requires careful dosing and monitoring because infants and children are more sensitive and at higher risk of respiratory depression [9]. This section reviews the commonly used opioids in pediatric anesthesia—fentanyl, remifentanil, morphine, and hydromorphone—along with their pharmacology and safety considerations.

1. Fentanyl

- Class: Synthetic opioid
- Mechanism of Action: μ-opioid receptor agonist; provides analgesia by inhibiting nociceptive pathways in the CNS [29].
- Dose: 1–2 mcg/kg IV for intraoperative use

Pharmacology:

- Rapid onset (1–2 minutes), short duration (~30–60 minutes)
- Highly lipophilic → rapid CNS penetration
- Commonly used during both induction and maintenance of anesthesia

Safety:

- Advantages:
  - Hemodynamically stable
  - Effective analgesic even in neonates
- Risks:
  - Respiratory depression, bradycardia
  - Chest wall rigidity with rapid infusion [30]
  - Requires continuous monitoring

2. Remifentanil

- Class: Ultra-short acting synthetic opioid
- Mechanism of Action: μ-opioid receptor agonist; rapidly hydrolysed by nonspecific blood and tissue esterases [31]
- Dose: 0.05–2 mcg/kg/min IV infusion

Pharmacology:

- Ultra-short context-sensitive half-life (~3–10 minutes), independent of infusion duration
- Ideal for procedures requiring rapid wake-up or neuromonitoring

Safety:

- Advantages:
  - Predictable pharmacokinetics
  - Rapid recovery after infusion
- Risks:
  - Profound respiratory depression if not titrated properly
  - No residual analgesia—postoperative pain control must be provided [19]
  - Can cause hypotension and bradycardia

3. Morphine

- Class: Natural opioid
- Mechanism of Action: μ-opioid receptor agonist; provides long-lasting analgesia [32]
- Dose: 0.05–0.1 mg/kg IV in children (reduced in neonates due to immature metabolism)

Pharmacology:

- Slower onset (5–10 minutes)
- Long duration (3–5 hours)
- Metabolized in the liver → active metabolite (morphine-6-glucuronide), which may accumulate in neonates

Safety:

- Advantages:
  - Long-lasting postoperative pain control
- Risks:
  - Histamine release → vasodilation, hypotension, pruritus
  - Respiratory depression, especially in neonates with immature renal/hepatic function [33]

4. Hydromorphone

- Class: Semi-synthetic opioid
- Mechanism of Action: Strong μ-opioid receptor agonist; 5–7 times more potent than morphine [34]
- Dose: 0.01–0.015 mg/kg IV in children

Pharmacology:

- Onset: 10–15 minutes
- Duration: 2–4 hours
- Preferred for moderate-to-severe pain when longer action is needed or if morphine is not tolerated

Safety:

- Advantages:
  - Less histamine release compared to morphine
- Risks:
  - Respiratory depression, nausea, sedation (general opioid-related side effects)

5. Other Opioids (Less Common in Pediatrics)

- Sufentanil: 5–10× more potent than fentanyl; used in cardiac anesthesia
- Naloxone (opioid antagonist): Used to reverse opioid-induced respiratory depression (0.01 mg/kg IV) [35]

Drug	Potency vs Morphine	Onset	Duration	Key Use	Major Risk
Fentanyl	100×	1–2 min	30–60 min	Induction, maintenance	Chest wall rigidity, apnea
Remifentanil	~100×	1–2 min	5–10 min	TIVA, neurosurgery	No post-op analgesia
Morphine	1×	5–10 min	3–5 hrs	Post-op pain management	Histamine release, apnea
Hydromorphone	5–7×	10–15 min	2–4 hrs	Moderate-severe pain	Sedation, respiratory depression

4.MUSCLE RELAXANTS:

Muscle relaxants (neuromuscular blocking agents) are crucial in pediatric anesthesia for facilitating tracheal intubation, providing muscle relaxation during surgery, and improving surgical conditions. They are classified into depolarizing and non-depolarizing agents. Dosing must be carefully titrated, especially in neonates and infants, due to immature neuromuscular junctions and variable responses [9].

Classification of Muscle Relaxants

Type	Examples	Mechanism of Action
Depolarizing	Succinylcholine (Suxamethonium)	Mimics acetylcholine → sustained depolarization
Non-depolarizing	Rocuronium, Vecuronium, Atracurium, Cisatracurium, Pancuronium	Competitively block ACh at nicotinic receptors

1. Succinylcholine (Suxamethonium)

- Class: Depolarizing neuromuscular blocker
- Dose: 1–2 mg/kg IV or 3–4 mg/kg IM
- Onset: 30–60 sec | Duration: 5–10 min

Pharmacology:

Succinylcholine binds to nicotinic receptors, causing persistent depolarization and temporary paralysis [36].

Safety:

- Advantages:
  - Fastest onset → excellent for rapid sequence intubation.
- Risks:
  - Hyperkalaemia — especially in patients with undiagnosed neuromuscular disorders (e.g., Duchenne muscular dystrophy) [37].
  - Bradycardia, especially with repeated doses in infants.
  - Malignant hyperthermia (MH) trigger.
  - Increased intraocular and intracranial pressure.
- Note: Routine use in children is discouraged unless absolutely indicated [38].

2. Rocuronium

- Class: Non-depolarizing, amino steroid
- Dose: 0.6–1.2 mg/kg IV
- Onset: 60–90 sec | Duration: 30–60 min

Pharmacology:

Used as an alternative to succinylcholine for rapid sequence induction due to its fast onset [39].

Safety:

- Advantages:
  - Rapid onset at higher doses.
  - Fewer cardiovascular effects.
- Risks:
  - Prolonged paralysis if not properly reversed.
  - Requires sugammadex for rapid reversal (not always available or affordable) [40].

3. Vecuronium

- Class: Non-depolarizing, amino steroid
- Dose: 0.1 mg/kg IV
- Onset: 2–3 min | Duration: 30–45 min

Pharmacology:

Intermediate-acting; metabolized hepatically and excreted renally.

Safety:

- Advantages:
  - Stable hemodynamic profile.
- Risks:
  - Accumulation in neonates with liver/kidney dysfunction.
  - Slower recovery compared to rocuronium [41].

4. Atracurium

- Class: Non-depolarizing, benzylisoquinolinium
- Dose: 0.5 mg/kg IV
- Onset: 2–3 min | Duration: 20–35 min

Pharmacology:

Undergoes Hofmann elimination (organ-independent breakdown) — useful in patients with liver/kidney dysfunction [42].

Safety:

- Advantages:
  - Predictable recovery.
- Risks:
  - Histamine release → hypotension, flushing, bronchospasm.

5. Cisatracurium

- Class: Non-depolarizing, benzylisoquinolinium (isomer of atracurium)
- Dose: 0.1–0.2 mg/kg IV(43)
- Onset: 2–3 min | Duration: 40–60 min

Pharmacology:

More potent and cleaner alternative to atracurium with minimal histamine release.

Safety:

- Advantages:
  - Safe in neonates and organ dysfunction.
- Risks:
  - Expensive.
  - Slower onset compared to rocuronium.

6. Pancuronium

- Class: Long-acting, amino steroid
- Dose: 0.1 mg/kg IV
- Onset: 2–3 min | Duration: 60–100 min

Pharmacology:

Rarely used now due to long duration and tachycardia.

Safety:

- Advantages:

- Useful in cardiac surgeries (increases HR).
- Risks:
  - Prolonged paralysis.
  - Not preferred for short surgeries or neonates.

Neuromuscular Block Reversal Agents in Pediatrics

Agent	Mechanism	Pediatric Notes
Neostigmine	Inhibits acetylcholinesterase → ↑ACh	Used with atropine/glycopyrrolate to prevent bradycardia [47]
Sugammadex	Encapsulates rocuronium/vecuronium	Rapid reversal; dose: 2–4 mg/kg; expensive

5.LOCAL ANESTHETIC AGENTS

Local anesthetics are used to provide regional analgesia or anesthesia in pediatric patients by inhibiting nerve conduction. Their applications include caudal epidurals, peripheral nerve blocks, and topical administration.

Commonly Used Local Anesthetics

- Lidocaine: One of the most commonly used agents in pediatrics. It has a rapid onset (1–2 minutes) with a duration of ~1–2 hours. Frequently used for infiltration anesthesia, IV cannulation, and minor surgical procedures [44].
- Bupivacaine: Longer duration of action (4–8 hours), making it suitable for prolonged surgical procedures and postoperative analgesia. However, it must be used cautiously because of its potential cardiotoxicity, especially in neonates [32].
- Ropivacaine: A newer amide local anesthetic with less cardiotoxicity than bupivacaine. Commonly used for epidural and peripheral nerve blocks in children [45].

Administration Routes

- Topical: EMLA cream (a eutectic mixture of lidocaine and prilocaine) for minor procedures [46].
- Infiltration: Direct injection into tissues for localized effect.
- Peripheral nerve blocks: Used for limb surgeries, such as brachial plexus, sciatic, or femoral blocks [47].
- Caudal and epidural blocks: Frequently applied in infraumbilical procedures for infants and young children [48].

Safety and Toxicological Considerations

- Systemic toxicity: Overdose or accidental intravascular injection may cause CNS excitation (tinnitus, perioral numbness, agitation, convulsions) followed by CNS depression and cardiovascular collapse [37].
- Dose limitations: Maximum recommended doses vary by agent and must account for age and weight:
  - Lidocaine (without epinephrine): 3–5 mg/kg
  - Bupivacaine: 2–2.5 mg/kg
  - Ropivacaine: 2–3 mg/kg [49]
- Ultrasound guidance: Improves visualization of needle placement, reducing the risk of intravascular injection and increasing block efficacy [50].
- Adjuvants: Agents such as clonidine or dexmedetomidine may be added to prolong analgesia, but careful monitoring of dose and safety is required [51].

Summary

Because children's anatomy and physiology differ from those of adults, pediatric anesthesia requires specialized knowledge. This review examined the main drug classes used in the premedication, induction, maintenance, and recovery stages of pediatric anesthesia.

- Intravenous anesthetics such as propofol, ketamine, and thiopental are frequently used for rapid induction, with dosing adjusted to pediatric pharmacokinetics and administered under close observation.
- Inhalational agents such as sevoflurane and isoflurane are recommended for induction and maintenance in younger children because of their ease of use and non-invasive administration.
- Opioids including morphine, remifentanil, and fentanyl are essential for analgesia but must be dosed cautiously to minimize the risk of respiratory depression.
- Muscle relaxants such as rocuronium and succinylcholine facilitate intubation and surgical procedures, although they require reversal agents and careful monitoring.
- Local anesthetics such as lidocaine and bupivacaine are widely used for regional blocks and infiltration, providing effective postoperative pain control when dosed appropriately to avoid toxicity.

Each drug class was reviewed with emphasis on its pharmacological profile, safety considerations, and clinical applications in pediatric patients.

Conclusion:

The safe and effective use of anesthetic drugs in pediatric populations demands age-specific understanding of pharmacology, physiology, and clinical judgment. Anesthetic management should always consider the child's developmental stage, weight-based dosing, organ function, and potential adverse

effects. Continued research, updated guidelines, and vigilance in monitoring are essential to minimize risks and ensure positive surgical outcomes in pediatric patients.

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