

Pediatric Sedation for intubated patients: Perspectives from a PICU doctor

Amit Mehta, MD

Associate Professor, Pediatrics

Oregon Health and Sciences University

Medical Director, Pediatric and Neonatal
ECLS

November 13, 2023



DOERNBECHER
CHILDREN'S
Hospital



Financial Disclosures

- None

Goals:

- By the end of this presentation, the audience will:
 - Be able to describe general categories of medications used for intubated pediatric patients
 - Recognize common side effects of sedative medications

Caveats

- While I want this to all be "evidence based", most of this is evidence informed and a general discussion of my personal experiences
- Most data we have does not come from randomized trials, and most guidelines in this area are based on "expert consensus"
- Most of the specific medication data comes from Lexicomp. Most medications are listed per kg, as is common in pediatrics. As always, please max out the drug doses at adult doses.

Thank you!

- For taking the time to listen
- For taking care of the critically ill children of Oregon

Clinical case

- 22 mo vaccinated girl presents to ER with five days of fever, poor po intake, cough, runny nose, becoming more "lethargic" per family
- VS: 39.2 170 60 85/50 72% (RA)
- Awake, alert, appears quite tired, focused on breathing
- + significant tachypnea, + retractions throughout, no wheezing, decreased BS in right base
- Strong pulses, brisk CR, though mucous membranes are dry

Case continued

- Immediately placed on HFNC
- IV established, treated with 20 mL/kg IVF bolus
- Glucose 85
- CXR with large right sided infiltrate
- Blood culture drawn, labs sent; Ceftriaxone and vancomycin ordered
- Saturations improve to 85% on HFNC, still working quite hard to breathe
- You decide to intubate her

The nurses ask:

- What medications should I draw up for intubation???

Primary adverse events associated with intubation

- Inadequate sedation, intubation trauma
- Inability to secure airway, cardiac arrest, death

REVIEW ARTICLE

Endotracheal intubation in the pediatric emergency department

Elliot Long^{1,2,3}, Stefan Sabato^{2,4} & Franz E. Babl^{1,2,3}

1 Department of Emergency Medicine, Royal Children's Hospital, Parkville, Vic., Australia

2 Murdoch Children's Research Institute, Parkville, Vic., Australia

3 Department of Paediatrics, Faculty of Medicine, Dentistry, and Health Sciences, University of Melbourne, Melbourne, Vic., Australia

4 Department of Anaesthesia and Pain Management, The Royal Children's Hospital, Parkville, Vic., Australia

- Pediatric Anesthesia 2014
- 66 intubations in Australia 2013

Table 5 Adverse events during tracheal intubation

Adverse event	<i>n</i> (%)
Hypotension	15 (21)
Desaturation	10 (14)
Bradycardia	5 (7)
Second dose paralytic	3 (4)
Esophageal intubation	1 (1)
Endobronchial intubation	1 (1)
Equipment failure	1 (1)
Medication error	1 (1)
Vomit with aspiration	1 (1)

(easy ones)... some kids don't need sedation

- All medications have side effects, so sometimes the risks outweigh the benefits
- Absolutely obtunded patients

Received: 9 June 2021

Revised: 23 October 2021

Accepted: 22 November 2021

DOI: 10.1111/acem.14431

ORIGINAL CONTRIBUTION



Intubation practice and outcomes among pediatric emergency departments: A report from National Emergency Airway Registry for Children (NEAR4KIDS)

2015-2018

TABLE 2 Provider and practice characteristics

Characteristics	ED (n = 756)	PICU/CICU (n = 12,512)
Medications		
Lidocaine	11 (1.5)	227 (1.8)
Vagolytic ^d	110 (14.6)	3,767 (30.1)
Atropine	104 (13.8)	2,996 (24.0)
Glycopyrrolate	6 (0.8)	783 (6.3)
Fentanyl	164 (21.7)	7,290 (58.3)
Midazolam	118 (15.6)	5,373 (42.9)
Etomidate	179 (23.7)	267 (2.1)
Ketamine	241 (31.9)	4,385 (35.1)
Propofol	53 (7.0)	1,875 (15.0)
Rocuronium	489 (64.7)	9,578 (76.6)
Vecuronium	12 (1.6)	1,171 (9.4)
Succinylcholine	132 (17.5)	291 (2.3)
Cisatracurium	0 (0.0)	89 (0.7)

Commonly used

-
- PICU: Fentanyl and midazolam
 - ER: etomidate
 - Both use ketamine
 - Propofol PICU > ER
 - Succinylcholine ER > PICU

Opioids

- Fentanyl
- Morphine
- Hydromorphone

Fentanyl

- Binds to opioid receptors
- Highly lipophilic, crosses blood brain barrier quickly
- Usual dosing: 1-4 mcg/kg IV (lower per kg doses in older children)
- [For all drugs mentioned, max out at standard adult doses]
- Onset: "almost immediate" half life: 2-5 hours, depending on age
- Side effects include: Respiratory depression, addiction/abuse, withdrawal syndromes, constipation, additive effect when given with benzodiazepines, hypotension
- Chest wall rigidity (less common if given over 1 to 2 minutes)
- Gtts: usual starting dose 0.5 mcg/kg/hr; bolus as needed if blood pressure stable

Fentanyl

- Standard PICU "go-to" drug
- Less hypotension than other drugs like morphine
- Great for pain control
- Works quickly
- The profound respiratory depression is not really a concern in intubated patients
- Likely does not have amnestic properties, so usually used in combination with another drug for induction

Morphine

- Many of the same side effects as fentanyl
- Chest wall rigidity more specific to fentanyl, though
- Usual dose: 0.05-0.1 mg/kg
- Onset of action: 5 minutes
- Half life: 1 –6 hours; longer in younger children
- Usual starting gtt dose: 0.05 mg/kg/hour

Morphine

- With several minute onset, not a usual induction of anesthesia medication
- compared to fentanyl, slightly more hypotension due to histamine release
- Lasts longer
- Has more "sedative" property than fentanyl
- We tend to use it in gtt form because of that

Hydromorphone

- Again, not for induction of anesthesia
- We tend to use it in gtt form when switching because of tachyphylaxis to fentanyl

Midazolam

- Side effects include: Respiratory depression, additive effect with opioids, abuse, withdrawal, hypotension, paradoxical reactions, anterograde amnesia, hypotension, delirium; (also treats seizures)
- From lexicomp:
 - Pediatric neurotoxicity: In pediatric and neonatal patients <3 years of age and patients in third trimester of pregnancy (ie, times of rapid brain growth and synaptogenesis), the repeated or lengthy exposure to sedatives or anesthetics during surgery/procedures may have detrimental effects on child or fetal brain development and may contribute to various cognitive and behavioral problems. Epidemiological studies in humans have reported various cognitive and behavioral problems, including neurodevelopmental delay (and related diagnoses), learning disabilities, and attention-deficit hyperactivity disorder. Human clinical data suggest that single, relatively short exposures are not likely to have similar negative effects. No specific anesthetic/sedative has been found to be safer. For elective procedures, risk versus benefits should be evaluated and discussed with parents/caregivers/patients; critical surgeries should not be delayed (US FDA Safety Communication 2017 Update).
- In this presentation, this is only listed under midazolam, but the warning applies to most other sedatives as well.

Benzodiazepines

- Midazolam
- Lorazepam

Midazolam

- HYPOTENSION!
- Myocardial depression, hypotension
- Mechanism: binds to GABA receptors
- Onset: 1 – 5 minutes (dose dependent)
- Half life elimination: 3-6 hours (longer in younger children)
- Usual dose: 0.05 - 0.1 mg/kg IV
- From personal experience, 0.1 mg/kg is rarely enough to get good intubating conditions. I usually repeat doses if blood pressure stable
- Gtt dose: starting 0.05 mg/kg/hr

Midazolam

- Another PICU workhorse
- Great for intubating patients with seizures
- Be careful with hypotensive patients or in shock
- DCH PICU has tended to move away from midazolam gtts because of delirium risk

Lorazepam

- Anti-epileptic properties
 - Similar side effects as midazolam
 - Onset within 10 minutes for IV dosing
 - Longer elimination half life
-
- We tend to use it as an adjunct or for breakthrough agitation in intubated patients

Dexmedetomidine

7) *We suggest* the use of alpha₂-agonists as the primary sedative class in critically ill pediatric patients requiring MV.

Conditional

Low

2022 Society of Critical Care Medicine Clinical Practice Guidelines on Prevention and Management of Pain, Agitation, Neuromuscular Blockade, and Delirium in Critically Ill Pediatric Patients With Consideration of the ICU Environment and Early Mobility

Pediatric Critical Care Medicine [23\(2\):p e74-e110, February 2022.](#)

Dexmedetomidine

- Centrally acting alpha₂ agonist
- Inhibits release of norepinephrine
- Same class as clonidine
- Side effects include: Bradycardia, hypotension, withdrawal syndrome, respiratory depression
- Can give a bolus dose over 10 minutes (bolus doses associated with hypertension)
- Usual dose: 0.2 - 1.5 mcg/kg/hour

Dexmedetomidine

- Not used for induction of anesthesia
- Most common sedative gtt at DCH PICU
- Less association with delirium
- Use with caution in patients with shock – causes hypotension and blunts appropriate tachycardic response
- Doesn't induce a "deep" state of anesthesia like propofol
- Less respiratory depression than fentanyl or midazolam
- Although respiratory depression listed as a side effect, we tend to use it in babies with bronchiolitis who need BiPAP

Propofol

- Mechanism of action: unknown, ? Related to GABA
- Onset: ~ 30 seconds; Duration: 3 – 10 minutes
- Neonates: many get hypotensive; avoid use in neonates
- Side effects include: prolonged QT, bradycardia, hypotension, respiratory depression, hypertriglyceridemia, burning at injection site, green urine, propofol related infusion syndrome

Propofol related infusion syndrome

- Rare, but high mortality rate
- Hypotension, arrhythmias, metabolic acidosis, rhabdomyolysis, AKI
- Mechanism unclear but potentially related to mitochondrial inhibition
- Risk factors include young age, critical illness, higher doses (≥ 4 mg/kg/hr for two days), inborn error of metabolism
- Reports have occurred with lower doses and shorter duration

Guidelines

- From 2022 SCCM guidelines:

10) <i>We suggest</i> that continuous propofol sedation at doses less than 4 mg/kg/hr (67 µg/kg/min) and administered for less than 48 hr may be a safe sedation alternative to minimize the risk of propofol-related infusion syndrome development.	Conditional	Low
11) Short term (< 48 hr) continuous propofol sedation may be a useful adjunct during the periextubation period to facilitate weaning of other analgo-sedative agents prior to extubation.	Good practice	
12) <i>We suggest</i> consideration of adjunct sedation with ketamine in patients who are not otherwise at an optimal sedation depth.	Conditional	Low

Propofol use has evolved

- Adult ICUs use lots of propofol
- DCH PICU uses much less propofol. No guarantees with propofol
- Pediatric anesthesiologists use this routinely for short procedural sedation (ie. MRI in a toddler)
- Avoid use in patients with shock... hypotension is a high risk
- Works quickly, gets patients "deep"; wears off quickly
- We have used it in the first 12 hours for TBI patients where turning off the drug quickly to get a neurologic assessment is important

Propofol

- Bridge to extubation
- Short duration of intubation
- We have used it in difficult to sedate patients where we have tried almost everything else or there are contraindications
- Small doses and for short periods are associated with less risk of propofol infusion syndrome, but need to watch carefully for hypotension

Ketamine

From 2022 SCCM guidelines:

- | | | |
|--|---------------|-----|
| 10) <i>We suggest</i> that continuous propofol sedation at doses less than 4 mg/kg/hr (67 µg/kg/min) and administered for less than 48 hr may be a safe sedation alternative to minimize the risk of propofol-related infusion syndrome development. | Conditional | Low |
| 11) Short term (< 48 hr) continuous propofol sedation may be a useful adjunct during the periextubation period to facilitate weaning of other analgosedative agents prior to extubation. | Good practice | |
| 12) <i>We suggest</i> consideration of adjunct sedation with ketamine in patients who are not otherwise at an optimal sedation depth. | Conditional | Low |

Ketamine

- NMDA receptor antagonist
- Dissociative anesthetic
- Analgesic properties
- Onset: within 30 seconds
- Recovery: 1 to 2 hours
- ACEP says not to use in children less than 3 months
- Usual dose: 1 –2 mg/kg IV

Ketamine

- Side effects include: CNS depression, intracranial hypertension** (newer studies show no effect on ICP), increased intraocular pressure, laryngospasm, sialorrhea, withdrawal, emergence delirium, respiratory depression *
- Tachycardia, hypertension (endogenous release of catecholamines)
- Myocardial depressant – can cause hypotension as well (especially if pre-existing depressed cardiac function)

Ketamine

- 2020 septic shock guidelines:
 - "Unfortunately, there is no conclusive evidence to recommend an optimal alternative induction agent to etomidate, although ketamine and fentanyl are routinely available and can offer favorable hemodynamic profiles in the setting of shock"
- (Weiss et al. "Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children" Pediatric Critical Care Medicine 2020)

Registry Data

- Tarquino et al. "Current medication practice and tracheal intubation safety outcomes from a prospective multicenter observational cohort study" *Pediatric Critical Care Medicine* 2015
- 3366 intubations in PICUs from 2010-2013
- "Ketamine was used in 27% of tracheal intubations but more often for tracheal intubations in patients with unstable hemodynamics (39% vs 25%; $p < 0.001$). However, ketamine use was not associated with lower prevalence of new hypotension (ketamine 8% vs no ketamine 14%; $p = 0.08$)"

Ketamine

- Ketamine is my "go-to" drug – asthma, septic shock
- Larger therapeutic window
- Outside of cardiogenic shock patients, tends to preserve blood pressure
- For asthmatics, tends to cause bronchodilation
- Works quickly; patients become "deep" quickly
- Tends to preserve respiratory rate

Etomidate

- Short acting nonbarbiturate general anesthetic
- Onset: 30 – 60 seconds
- Duration: 2 – 5 minutes, depending on dose
- Usual dose: 0.2-0.4 mg/kg IV
- Side effects include: myoclonus; adrenal suppression (inhibits 11-beta hydroxylase, leading to decreased cortisol production), transient skeletal movements
- Tends to be hemodynamically well tolerated acutely

Etomidate

- **Lexicomp:** "Adrenal suppression has been documented with etomidate use, even after a single dose. Cortisol concentrations decrease quickly after the induction dose, lasting up to 8 hours in healthy adults and up to 24 hours in pediatric surgical patients; however, 2 prospective pediatric studies have reported no adverse clinical outcomes due to the adrenal suppression (Du 2015; Gu 2015). However, a retrospective study of pediatric patients admitted for meningococcal sepsis found patients receiving a single etomidate dose for rapid sequence intubation (n=23) had significantly decreased cortisol concentrations for at least 24 hours, and higher ACTH and 11-deoxycortisol concentrations compared to those who did not receive etomidate. In this study, 8 patients died due to hemodynamic failure, 7 of whom had received etomidate."

Etomidate

- 2020 pediatric septic shock guidelines: "We suggest not to use etomidate when intubating children with septic shock or other sepsis-associated organ dysfunction (weak recommendation, low quality of evidence)"
- Personally, I have only used etomidate once in 15 years

Lidocaine

- Sodium channel blocker with anesthetic properties
- Historically used to blunt the ICP response when intubating children with suspected intracranial hypertension
- Some people still use it. Lexicomp does not give dosing recommendations for intubation. I can find no mention of it in TBI guidelines (Kochanek et al. "Guidelines for the Management of Pediatric Severe Traumatic Brain Injury, Third Edition: Update of the Brain Trauma Foundation Guidelines" Pediatric Critical Care Medicine 2019).

Neuromuscular blockade

- No sedative properties!
- Avoid muscle relaxant if a difficult airway is anticipated
- Rocuronium
- Vecuronium
- Succinylcholine
- (Suggamadex) - reversal agent

Systematic review

- Vanlithout et al. "Neuromuscular-blocking agents for tracheal intubation in pediatric patients (0-12 years): A systematic review and meta-analysis"; 2019 Pediatric Anesthesia
- Conclusion: "The use of a neuromuscular-blocking agent during light-to-moderate depth of anesthesia can improve the quality as well as the success rate of tracheal intubation and is associated with better hemodynamic stability during induction of anesthesia."

Rocuronium

- Nondepolarizing
- Onset: 30 seconds to 1 minute, longer in adults
- Duration: 20-70 minutes, depending on dose and age
- Usual dose: 0.6-1.2 mg/kg IV

Vecuronium

- Nondepolarizing
- Onset: 2 to 3 minutes
- Duration: 25 to 65 minutes, depending on dose
- Usual dose: 0.1 mg/kg IV

Succinylcholine

- Depolarizing neuromuscular blockade
- Onset: 30 seconds to 1 minute, depending on age
- Duration: 4 to 10 minutes, depending on dose
- Usual dose: 1-3 mg/kg IV depending on age

Why do PICU doctors use such little succinylcholine???

- US Box Warning:
- **Ventricular dysrhythmias, cardiac arrest, and death from hyperkalemic rhabdomyolysis in pediatric patients:**
- Acute rhabdomyolysis with hyperkalemia followed by ventricular dysrhythmias, cardiac arrest, and death has occurred after the administration of succinylcholine to apparently healthy pediatric patients who were subsequently found to have undiagnosed skeletal muscle myopathy, most frequently Duchenne muscular dystrophy.
- When a healthy appearing pediatric patient develops cardiac arrest within minutes after administration of succinylcholine, not felt to be due to inadequate ventilation, oxygenation, or anesthetic overdose, immediate treatment for hyperkalemia should be instituted. In the presence of signs of malignant hyperthermia, appropriate treatment should be instituted concurrently.
- Reserve the use of succinylcholine in pediatric patients for emergency intubation or instances where immediate securing of the airway is necessary (eg, laryngospasm, difficult airway, full stomach) or for IM use when a suitable vein is inaccessible. [Copied from Lexicomp]

Why do PICU doctors use such little succinylcholine???

- Other adverse events include:
 - Bradycardia, hyperkalemia, rhabdomyolysis, increased intraocular, intracranial, intragastric pressures, Malignant hyperthermia

Suggamadex

- Mechanism: Binds to rocuronium and vecuronium
- Onset: < 3 minutes
- Side effects include: bradycardia (potentially severe), hypotension, nausea, increased PT/PTT; recurrence of neuromuscular blockade
- Usual dose: 2 – 4 mg/kg IV slow push; depending on how many twitches are present
- If using, may not be able to muscle relax again using rocuronium or vecuronium for 24 hours.

Atropine

- Historically used as a pre-treatment to prevent bradycardia
- Starting in 2015, PALS guidelines changed to:
 - "It may be reasonable for practitioners to use atropine as a premedication in specific emergency intubations when there is higher risk of bradycardia," specifically giving example to when succinylcholine is used as a paralytic agent."

Atropine

The Effect of Atropine on Rhythm and Conduction Disturbances During 322 Critical Care Intubations*

- Jones et al, PCCM 2013
- Children in France < 8 years old
- 322 intubations
- 152 intubations got atropine
- "New arrhythmias during intubation were related to bradycardia and were less common with atropine use (odds ratio, 0.14 [95% CI, 0.06–0.35], $p < 0.001$). "

Atropine

Atropine does not prevent hypoxemia and bradycardia in tracheal intubation in the pediatric emergency department: observational study

- Carvalho et al. Rev Paul Pediatrics 2023
- 126 intubations in Portugal
- 43 got atropine
- "Critical bradycardia" was defined as HR < 60 bpm
- "Critical bradycardia occurred in only three patients, being two in the atropine group (p=0.26). Bradycardia was analyzed in only 42 procedures. Atropine use was associated with higher odds of bradycardia in multivariable analysis (OR: 11.00; 95%CI 1.3–92.8; p=0.028)"

Atropine

- Personally, I rarely if ever use it prophylactically (I also have never used succinylcholine)
- Caveats: in the setting of succinylcholine or neonates < 1 mo, I may be more likely to use it.

"Dwindle epi"

- I don't think you will find this in a textbook
- This is our PICU's practice
- For high risk intubations or unstable patients, we use code dose epinephrine 10 mcg/kg IV for arresting patients
- Also usually have "dwindle epinephrine" available (1 mcg/kg IV) for "peri-arrest" severely hypotensive patients pre-arrest to get blood pressure up quickly.
- Some people like phenylephrine (5-10 mcg/kg IV) - pure alpha effect, without chronotropy

Specific situations

- Septic shock... avoid propofol; I like Ketamine
- Asthma... ketamine
- Seizures... benzodiazepines

Thank you!

- Questions?