Managing Pain in Children

May 11, 2023

Navid Dehghani

Nothing to Declare

Disclosures

- Nothing to disclose

Objectives

- Discuss pain in children
- Discuss means of managing pain in acute pediatric care settings
- Apply pharmacological means of controlling pain to alleviate pain

Pain in Children

- One of the most common reasons for children to seek emergency healthcare
- Children are less likely than adults to have pain treated adequately.
- Pain treatment does not confuse diagnostic evaluation or mask important symptoms.
- Pain exposure can alter pain processing, development, and behavior in infants and neonates.
- Untreated pain in children is known to cause harm, and the effects extend into adulthood.

Reporting pain

- The expression of pain is highly subjective and is modulated, in part, by emotional state, developmental age, cultural influences, context of disease, and prior pain experience.
- A child's pain experience is influenced by their developmental abilities to report pain, especially in times of severe pain or stress.
- Children should be encouraged to self-report their pain whenever possible.
- Utilizing an appropriate pain measure for a child's age and developmental abilities is necessary to guide effective treatment.

Non-pharmacological Intervention in Children

- Use of physical, behavioral, cognitive measures
- When analgesia provided, these measures may prevent the need for procedural sedation
- When used complementary to pharmacological interventions can

  -reduce pre-procedural agitation

  -allow for easier transition to sedation

  -may reduce amount of meds required for effective sedation

  -may decrease the freq. of adverse events, e.g. emergence rxn
- Child life specialists are particularly helpful in facilitating these techniques

Case 1

- 10-year-old girl is brought in via wheelchair by her mother.
- The girl is developmentally delayed, nonverbal, writhing and moaning, and keeps batting your hands away when you try to examine her.
- Her temperature is 39.2°C, and her heart rate 150 beats/min.
- Her mother is tearful, saying that she has never seen her daughter in so much pain.
- How would you manage her pain?

(1) IV Ketamine
(2) IN Midazolam +/- IN Fentanyl
(3) IV Dexmedetomidine
(4) Inhaled Nitrous Oxide
(5) IV Morphine and IV Ketorolac

Case 1 Progression

- You provide
  - 1.5 mcg/kg of IN fentanyl
  - 15 mg/kg dose of acetaminophen through her g-tube
- Her writhing settles.
- On exam, you find RLQ tenderness.
- Topical anesthetic cream is applied to her hand. IV is established.
- You administer
  - morphine 0.05 mg/kg dose IV
  - ketorolac 0.5 mg/kg dose IV
- The diagnosis of appendicitis is confirmed on US.
- The girl heads safely to the operating room.

TREKK Recommendations for Analgesic Medication Dosing for Children Aged ≥1 Year

Drug	Dose	Comments/Cautions
Mild Pain (e.g., 1-3 out of 10)		
ibuprofen PO	10 mg/kg/dose q6h PRN (MAX 600 mg/dose)	For children ≥6 months, first-line option for musculoskeletal injuries and most other painful inflammatory conditions.
acetaminophen PO	15 mg/kg/dose q4h PRN (MAX 1000 mg/dose)	Do not exceed 75 mg/kg/day or 4 g/day (whichever is less).
Moderate Pain (e.g., 4-6 out of 10) Always start with non-opioid medications above, layer on opioid medications below as needed.		
morphine PO	0.2-0.5 mg/kg/dose q3-4h PRN (MAX 15 mg/dose)	Most common pediatric opioid. Lack of demonstrated efficacy for musculoskeletal pain. For initial pain management, second dose may be given sooner than 3 hrs.
HYDROmorphone PO	0.03-0.06 mg/kg/dose q3-4h PRN (MAX 1-2 mg/dose)	Higher risk of dosing errors. Do not use if <6 months or <10 kg.
oxyCODONE PO	0.1-0.2 mg/kg/dose q4-6h PRN (MAX 5-10 mg/dose)	Risk of QT interval prolongation. Tablets must be swallowed whole.
If not responding to PO opioid, consider lower dose IV/Intranasal opioid (see Severe Pain below).		
Severe Pain (e.g., 7-10 out of 10)		
fentaNYL Intranasal	1.5 mcg/kg/dose (MAX 100 mcg/dose). May repeat 0.5-1 mcg/kg/dose (MAX 50 mcg/dose) 10 min after 1st dose if needed. Divide dose between nostrils (MAX 1 mL/nostril)	Provides rapid pain reduction. Provides early pain relief if IV access is not yet established. Give via mucosal atomization device for enhanced absorption. Monitor level of consciousness, vital signs, and pain score prior to therapy and at 10 min post administration.
fentaNYL IV	1 mcg/kg/dose q1-2h PRN (MAX 50 mcg/dose)	Monitoring as per Morphine IV below. For initial pain management, second dose may be given sooner than 1 hr. Monitor level of consciousness, vital signs, and pain score prior to therapy and q10 min post administration (for MIN 30 min). Some institutions recommend continuous O_2 sat monitoring for 30 min post administration.
morphine IV	0.05-0.1 mg/kg/dose q2-4h PRN (MAX 4-8 mg/dose)	For initial pain management, second dose may be given sooner than 2 hrs. DO NOT push medication to avoid rigid chest. Monitoring as per fentaNYL IV above.
ALWAYS ADD PO OR IV NSAID FOR OPIOID-SPARING EFFECT if the pain is expected to require multiple opioid doses.		
ibuprofen PO	Dosing as for Mild Pain section above	
ketorolac IV	0.5 mg/kg/dose q6h PRN (MAX 30 mg/dose, 15 mg/dose for subsequent)	Avoid IV ketorlac if ibuprofen or NSAIDs were given less than 6 hours before.

Case 2

A 10-year-old falls off a monkey bar and sustains an angulated fracture of distal radius. You would like to proceed with a reduction. Which of the following is most appropriate agent for the procedure?

(1) IV Ketamine

(2) IN Midazolam +/- IN Fentanyl

(3) IV Dexmedetomidine

(4) Inhaled Nitrous Oxide

(5) IV Morphine and IV Ketorolac

Ketamine Effects

- Phencyclidine derivative
- Dissociative state through binding of NMDA receptor
- Provides sedation and analgesia
- Preserves airway protective reflexes and spontaneous breathing
- Short onset of action (1-2 minutes)
- Ideal for brief, painful procedures such as fracture reduction or complex laceration repair
- Ketamine’s dissociative effects occur at a certain threshold rather than on a dose-response continuum; once the state is reached, additional meds don’t enhance the effect

Ketamine Adverse Effects

- The adverse events are not heightened by increased dosing so long as one stays withing the standard dosing range
- Fasting times are not associated with adverse events
- IV dose is 1-2 mg/kg over 30-60 seconds to avoid transient respiratory depression
- IM dose is 4-5 mg/kg and a repeat dose 2-4 mg/kg could be given 10 minutes following the first dose, if required
- IM dose associated with higher rates of apnea and vomiting
- Laryngospasm occurs more commonly in children 0.39% vs. 0.11% and is potentiated by rapid infusion

Bhatt M, *et al.* JAMA 2017

Bhatt M, *et al.* Acad Emerg Med 2020

Case 3

- You are performing a procedural sedation. After administration of medication(s), you note a drop in SpO2 and the ETCO2 drops to 0. The chest is not moving. You suspect laryngospasm. Which of the following is the likeliest culprit?

(1) IV Ketamine
(2) IN Midazolam +/- IN Fentanyl
(3) IV Dexmedetomidine
(4) Inhaled Nitrous Oxide
(5) IV Morphine and IV Ketorolac

Laryngospasm

BMJ Open

Incidence of adverse events in paediatric procedural sedation in the emergency department: a systematic review and meta-analysis

M Fernanda Bellolio,[1,2] Henrique A Puls,[3] Jana L Anderson,[1] Waqas I Gilani,[1] M Hassan Murad,[2,4,5] Patricia Barrionuevo,[2,5] Patricia J Erwin,[6] Zhen Wang,[2,5] Erik P Hess[1,2]

To cite: Bellolio MF, Puls HA, Anderson JL, *et al*. Incidence of adverse events in paediatric procedural sedation in the emergency department: a systematic review and meta-analysis. *BMJ Open* 2016;**6**:e011384. doi:10.1136/bmjopen-2016-011384

► Prepublication history and additional material is available. To view please visit the journal (http://dx.doi.org/10.1136/bmjopen-2016-011384).

Received 4 February 2016
Revised 6 May 2016
Accepted 23 May 2016

For numbered affiliations see end of article.

Correspondence to
Dr M Fernanda Bellolio;
Bellolio.fernanda@mayo.edu

ABSTRACT

Objective and design: We conducted a systematic review and meta-analysis to evaluate the incidence of adverse events in the emergency department (ED) during procedural sedation in the paediatric population. Randomised controlled trials and observational studies from the past 10 years were included. We adhere to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

Setting: ED.

Participants: Children.

Interventions: Procedural sedation.

Outcomes: Adverse events like vomiting, agitation, hypoxia and apnoea. Meta-analysis was performed with random-effects model and reported as incidence rates with 95% CIs.

Results: A total of 1177 studies were retrieved for screening and 258 were selected for full-text review. 41 studies reporting on 13 883 procedural sedations in 13 876 children (≤18 years) were included. The most common adverse events (all reported per 1000 sedations) were: vomiting 55.5 (CI 45.2 to 65.8), agitation 17.9 (CI 12.2 to 23.7), hypoxia 14.8 (CI 10.2 to 19.3) and apnoea 7.1 (CI 3.2 to 11.0). The need to intervene with either bag valve mask, oral airway or positive pressure ventilation occurred in 5.0 per 1000 sedations (CI 2.3 to 7.6). The incidences of severe respiratory events were: 34 cases of laryngospasm among 8687 sedations (2.9 per 1000 sedations, CI 1.1 to 4.7; absolute rate 3.9 per 1000 sedations), 4 intubations among 9136 sedations and 0 cases of aspiration among 3326 sedations. 33 of the 34 cases of laryngospasm occurred in patients who received ketamine.

Conclusions: Serious adverse respiratory events are very rare in paediatric procedural sedation in the ED. Emesis and agitation are the most frequent adverse events. Hypoxia, a late indicator of respiratory depression, occurs in 1.5% of sedations. Laryngospasm, though rare, happens most frequently with ketamine. The results of this study provide quantitative risk estimates to facilitate shared decision-making, risk communication, informed consent and resource allocation in children undergoing procedural sedation in the ED.

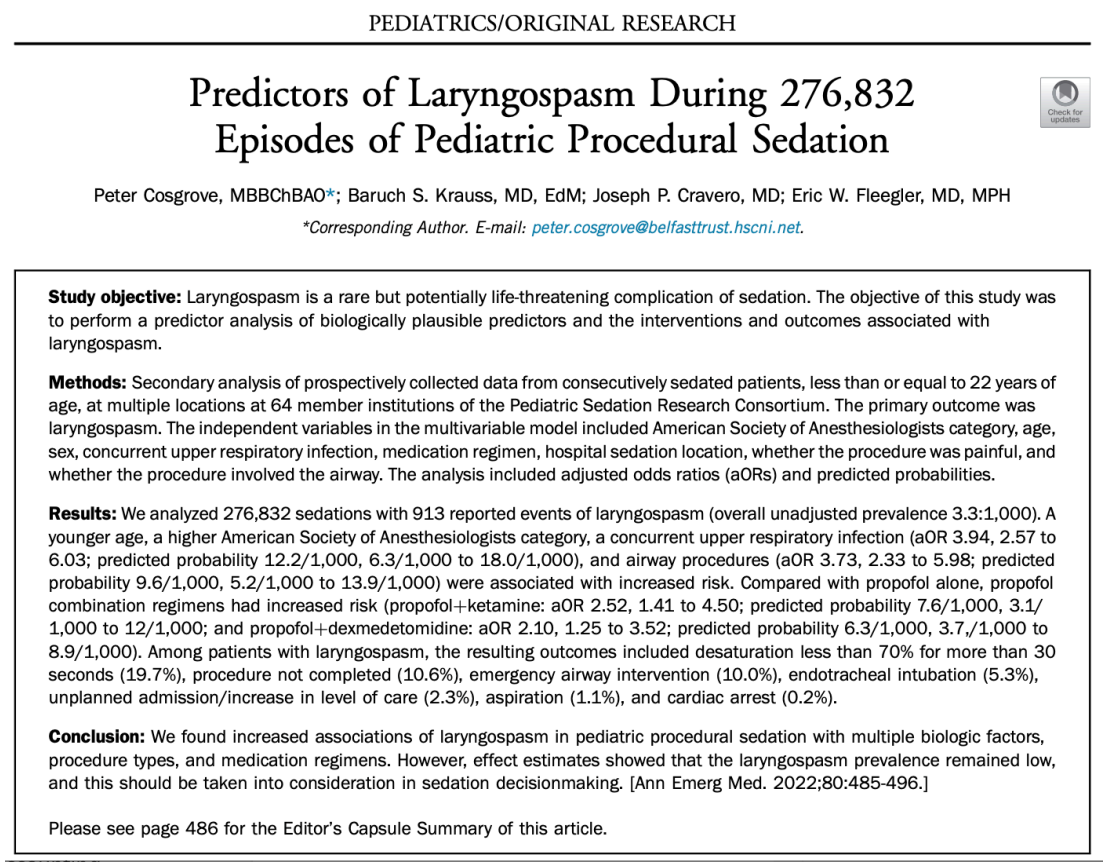
Strengths and limitations of this study

- This is a large systematic review and meta-analysis of current data on procedural sedation in children and adheres to recommendations made in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.
- We searched MEDLINE, EMBASE, EBSCO, CINAHL, CENTRAL, the Cochrane Database of Systematic Reviews, Web of Science and Scopus from inception through June 2014 without language restrictions.
- Randomised controlled trials and observational studies of procedural sedations in the emergency department were included. We did not search for unpublished literature or ongoing trials.
- Restriction to paediatric population (younger than 18 years of age).
- There was lack of standardisation and variation in the definition of the outcomes.

INTRODUCTION

Procedural sedation and analgesia (PSA) in the emergency department (ED) is frequently performed for painful or potentially agitating procedures performed on children.[1] Several large paediatric studies have investigated the use of PSA in a variety of settings outside of the operating room.[2–4] PSA performed in the ED is distinctive from other settings in that the procedures performed are likely to be more painful and urgent in nature.[5] Over the past decade, PSA in the ED has been in a relative steady state regarding the guidelines set forth and the

This study in 2016 showed the incidence is highest with Ketamine.



PEDIATRICS/ORIGINAL RESEARCH

Predictors of Laryngospasm During 276,832 Episodes of Pediatric Procedural Sedation

Peter Cosgrove, MBBChBAO*; Baruch S. Krauss, MD, EdM; Joseph P. Cravero, MD; Eric W. Fleegler, MD, MPH

*Corresponding Author. E-mail: peter.cosgrove@belfasttrust.hscni.net.

Study objective: Laryngospasm is a rare but potentially life-threatening complication of sedation. The objective of this study was to perform a predictor analysis of biologically plausible predictors and the interventions and outcomes associated with laryngospasm.

Methods: Secondary analysis of prospectively collected data from consecutively sedated patients, less than or equal to 22 years of age, at multiple locations at 64 member institutions of the Pediatric Sedation Research Consortium. The primary outcome was laryngospasm. The independent variables in the multivariable model included American Society of Anesthesiologists category, age, sex, concurrent upper respiratory infection, medication regimen, hospital sedation location, whether the procedure was painful, and whether the procedure involved the airway. The analysis included adjusted odds ratios (aORs) and predicted probabilities.

Results: We analyzed 276,832 sedations with 913 reported events of laryngospasm (overall unadjusted prevalence 3.3:1,000). A younger age, a higher American Society of Anesthesiologists category, a concurrent upper respiratory infection (aOR 3.94, 2.57 to 6.03; predicted probability 12.2/1,000, 6.3/1,000 to 18.0/1,000), and airway procedures (aOR 3.73, 2.33 to 5.98; predicted probability 9.6/1,000, 5.2/1,000 to 13.9/1,000) were associated with increased risk. Compared with propofol alone, propofol combination regimens had increased risk (propofol+ketamine: aOR 2.52, 1.41 to 4.50; predicted probability 7.6/1,000, 3.1/1,000 to 12/1,000; and propofol+dexmedetomidine: aOR 2.10, 1.25 to 3.52; predicted probability 6.3/1,000, 3.7,/1,000 to 8.9/1,000). Among patients with laryngospasm, the resulting outcomes included desaturation less than 70% for more than 30 seconds (19.7%), procedure not completed (10.6%), emergency airway intervention (10.0%), endotracheal intubation (5.3%), unplanned admission/increase in level of care (2.3%), aspiration (1.1%), and cardiac arrest (0.2%).

Conclusion: We found increased associations of laryngospasm in pediatric procedural sedation with multiple biologic factors, procedure types, and medication regimens. However, effect estimates showed that the laryngospasm prevalence remained low, and this should be taken into consideration in sedation decisionmaking. [Ann Emerg Med. 2022;80:485-496.]

Please see page 486 for the Editor's Capsule Summary of this article.

This Study in 2022 showed the incidence is lowest with Ketamine.

Ketamine-induced laryngospasm

- A rare potentially life-threatening complication of a common procedure. Overall incidence is 0.3-0.4%.
- Spasmotic closure of the glottic aperture
- Associated with lack of chest wall excursion, decrease in oximetry, a sudden drop of $EtCO_2$ to 0 with flatlining of capnography
- More likely to occur with age < 1 yr, comorbid URTI, and airway procedures
- Usually occurs shortly after administration of ketamine; typically transient and self-limited
- Idiosyncratic reaction: no association with dose
- When it occurs, first perform a jaw-thrust maneuver followed by PPV with 100% oxygen using BMV
- If this fails, administer succinylcholine to relax vocal cord musculature then BMV or intubate until paralytic is worn off
- Larson maneuver: firm pressure applied to the ‘laryngospasm notch’ bilaterally while lifting the mandible and providing PPV using 100% oxygen could relieve laryngospasm within a few breaths.

Case 4

A 13 year old twists her knee at soccer and comes in with a lateral patellar displacement.

On exam the patella is displaced laterally and the patient is screaming in pain.

What sedation modality is most appropriate when you attempt a reduction?

(1) IV Ketamine

(2) IN Midazolam +/- IN Fentanyl

(3) IV Dexmedetomidine

(4) Inhaled Nitrous Oxide

(5) IV Morphine and IV Ketorolac

Inhaled Nitrous Oxide (N2O) - Entenox

- Anesthetic gas
- Nitrous oxide with 30-50% oxygen
- Requires cooperation through a demand valve
- Minimal age of use 4 years
- Provides mild analgesia, sedation, amnesia, and anxiolysis
- Preserves airway protective reflexes, and hemodynamic status
- Rapid onset
- Excellent safety profile
- Minor side effects include nausea, vomiting (7%), and dysphoria

Case 5

- A 2-year-old boy is not tolerating his BiPAP for severe bronchiolitis. What sedation modality would be most appropriate?

(1) IV Ketamine
(2) IN Midazolam +/- IN Fentanyl
(3) IV Dexmedetomidine
(4) Inhaled Nitrous Oxide
(5) IV Morphine and IV Ketorolac

Dexmedetomidine (precedex)

- Selective alpha-2 adrenergic agonist
- Relatively longer onset of action (8-16 minutes) but longer duration of action (30 minutes)
- Can be given IN – an area of emerging interest
- Minimal respiratory depression in children
- Maintains ventilation and preserves upper airway tone
- Is often used for children requiring neuroimaging or for compliance during NIV
- Laryngospasm is an uncommon side effect occurring in 0.3%
- IV dose is 1.5 mcg/kg in < 2 year-olds and 2 mcg/kg in 2-18 year-olds
- For continuous sedation, the dose 1.5 mcg/kg could be given followed by 2 mcg/kg/hr thereafter
- IN dose is 2.5-3 mcg/kg

Case 6

- A 6 year-old runs into a pole and sustains a laceration to his forehead. He is agitated and anxious. Which sedation modality is best to consider in this setting?

(1) IV Ketamine

(2) IN Midazolam +/- IN Fentanyl

(3) IV Dexmedetomidine

(4) Inhaled Nitrous Oxide

(5) IV Morphine and IV Ketorolac

IN Midazolam

- Benzodiazepine
- Anxiolytic and amnestic
- Rapid onset of action
- IN associated with most rapid onset of sedation but shorter duration of sedation
- May result in paradoxical agitation if lower doses are used e.g. 0.3 mg/kg IN vs. 0.4-0.5 mg/kg IN
- May opt to use Fentanyl if painful procedure

Agents not commonly used

- Chloral hydrate
  - Delayed onset of action
  - Prolonged and unpredictable effect
  - High frequency of adverse effects

- Propofol
  - No analgesic properties
  - Require combination with an analgesic agent
  - Can impair hemodynamic stability
  - Maybe used in combination with other agents such as ketamine

Sedation in the Neurodivergent Patient

- Make environmental adaptation changes
  - Reduce stimuli
  - Dark quiet rooms
- Consider sedation for non-painful procedures e.g. physical examination
- Opt to use non-intravenous routes e.g. IN
- Dosing required is similar
- More likely to have paradoxical agitation
- Use full dose of medications (low doses associated with disinhibition)

Comparative Analysis

	Routes	Dose	Min. Age	Onset	Effects	Side Effects	Procedures
Ketamine	IV IM	1-2 mg/kg 2-4 mg/kg	3 mo.	Rapid	Sedation Analgesia	Vomiting Laryngospasm	Fracture reduction Complex laceration
Dexmedetomidine	IV IN	1-2 mcg/kg		6-18 m	Sedation Limited Analgesia		Ventilation Neuroimaging
Midazolam + Fentanyl	IN IN	1.5 mcg/kg			Sedation Analgesia		Laceration Repair Burn Dressing FB removals EUA
Nitrous Oxide	Inhaled		4 yr	Rapid	Sedation Limited Analgesia		dislocation reduction IV Starts
Morphine	IV				Analgesia	Respiratory Depression Vomiting	Abdominal Pain Trauma
Ketorolac	IV		6 mo.		Opioid-sparing Analgesia		Migraine Abdominal/Pelvic Pain

Summary

- Appreciate pitfall of inadequate pain control in children
- Use non-pharmacological measures to enhance response to medication
- Use opioids and opioid-sparing medications to treat pain
- Ketamine provides strong analgesia and sedation and is the ideal agent for severe pain control, such as in orthopedic reductions.
- Ketamine as a single agent has the safest medication profile.
- Dexmedetomidine is a sedative with limited analgesia effects used for sedation in children requiring NIV.
- Inhaled NO is ideal for short procedures requiring sedation and limited analgesia, such as patellar relocation.
- IN midazolam +/- IN fentanyl can be used for anxiety-provoking procedures such as laceration repair.
- When using procedural sedation, be prepared for laryngospasm…

References/Resources

- Samina Ali and Amy Drendel. Responsible and Safe Use of Opioids in Children and Adolescents in the Emergency Department. Evidence-based Pediatric Emergency Medicine. 20 (1). 2023 (Jan)

- Inna Elikashvili and Adam Vella. An Evidence-Based Approach To Pediatric Procedural Sedation. Evidence-based Pediatric Emergency Medicine. 9 (8). 2012 (August)

- TREKK. Bottom-line Recommendations. Procedural Sedation. 2018

- CPS. Recommendations for procedural sedation in infants, children, and adolescents. 2021