Techniques for Pediatric Procedural Sedation for gastrointestinal endoscopy

Nahla Mohamed Amin, Zeinab Hamid Sawan, Salih Salim Salih Bahri *, Woud Mohyeldin Mohamed Abdelfattah

Department of Anesthesiology, Intensive care and Pain management, Faculty of Medicine, Zagazig University, Egypt

Email: salihbahri86@gmail.com

Abstract

In the field of pediatric gastroenterology, upper gastrointestinal endoscopy has established itself as a diagnostic and therapeutic tool. In order to increase patient tolerance during this procedure, deep sedation is essential. Children are at a higher risk of serious adverse effects from procedural sedation; thus, their safety is a primary issue throughout this procedure. The agent of choice for procedural sedation should be safe, provide adequate analgesia and sedation with quick onset and short duration to allow the performance of a procedure with quick recovery and discharge. Benzodiazepines, ketamine, propofol, ketamine with propofol, nitrous oxide, and etomidate are all well-studied agents in pediatric procedural sedation. Multiple studies have been done to find the ideal method for procedural sedation in terms of ease of administration, quality, safety of sedation and recovery profile, but the consensus seems lacking

Keywords: Pediatric Procedural Sedation, gastrointestinal endoscopy

INTRODUCTION

Children find discomfort and emotional disturbance during pediatric gastrointestinal procedures including esophagogastroduodenoscopy (EGD) and colonoscopy, which need significant immobility for successful performance **(1).**

Goals of sedation in upper GI endoscopy: ensure the patient's safety, minimize physical discomfort and pain, control anxiety and minimize psychological trauma in the child and parents, control behavior and/ or movement to allow the safe completion of the procedure and return the patient to a state in which safe discharge from medical supervision is possible**(2).**

There are four levels of sedation defined by the American Society of Anesthesiologists (ASA) and these may be thought of as a continuum: minimal sedation (anxiolysis), moderate sedation and analgesia (conscious sedation), deep sedation (unconscious), and general anesthesia**(3)**.

Table 1: Levels of sedation and anesthesia **(4)**

Level	Minimal sedation	Moderate sedation (conscious sedation)	Deep sedation	General anesthesia
Response	Normal response to verbal stimulation	Purposeful response to verbal or tactile stimulation	Purposeful response after repeated or painful stimulation	Unarousable even with painful stimulus
Airway	Unaffected	No intervention required	Intervention may be required	Intervention often required
Spontaneous ventilation	Unaffected	Adequate	May be inadequate	Frequently inadequate
Cardiovascular function	Unaffected	Usually maintained	Usually maintained	May be impaired

Children younger than 6 or 7 years often require deep level of sedation in order to safely complete an uncomfortable procedure, where respiratory drive, airway patency and protective reflexes may be disturbed **(2).**

- **Pre-procedure Preparation and Patient Assessment:**

Preparation for gastrointestinal endoscopy in children should respect the special physiology as well as the psychosocial and emotional needs of pediatric patients and their parents. Prior to elective procedures, informed consent of the parents or guardians has to be obtained**(5).**

➢ History and physical examination:

A history and focused physical examination are necessary. Elements of the history that may impact sedation include:

(1) History of snoring, stridor or sleep apnea.

(2) History of drug allergies, use of current medications, and potential for drug interactions.

(3) History of an adverse reaction to sedation or anesthesia.

(4) History of any chronic illness **(4).**

(5) History of recent onset of fever or cough: In pediatrics, URI is a common occurrence. The choice to postpone a surgery due to an upper respiratory infection can have an effect on patient care and cause logistical issues for parents and medical staff. Numerous studies indicate that

airway events like coughing or laryngo/bronchospasm occur more frequently when anesthesia is given to a patient who has an active or recent URI**(2).**

A focused physical examination includes vital sign measurements, auscultation of the heart and lungs, and assessment of the patient's baseline level of consciousness and airway anatomy **(4)**

Particular attention must be paid to the oropharynx for findings such as micrognathia, craniofacial dysmorphism like down syndrome, tonsillar hypertrophy, or any other condition which could affect the airway. Heart examination should focus on the presence of murmurs or gallops which could indicate anatomical or functional issues. The airway exam should focus on the presence of stridor or wheezing**(2).**

- Risk stratification:

ASA classification is used to risk-stratify patients for sedation. General anesthesia with endotracheal intubation is mandatory in patients graded III or higher according to the ASA physical status classification. In emergent procedures such as gastrointestinal bleeding or foreign body removal or more complex procedures such as endoscopic gastrostomy insertions or stenosis dilations. a tracheal tube provides some airway protection against aspiration. **(2).**

- Airway examination:

The Mallampati classification (Class 1–4) is based on the structures visualized with maximal mouth opening and tongue protrusion in the sitting position (Figure 1). Tonsil size should be evaluated since the tonsils of pediatric patients are frequently enlarged and may be the source of upper airway obstruction (Figure 2). A standardized system for evaluation of tonsils exists and is based on the percentage of pharyngeal area that is occupied by hypertrophied tonsils**(6).**

- Pre-procedural fasting:

The guideline of the American Academy of Pediatrics (AAP) on sedation follows the fasting recommendations of the American Society of Anesthesiologists (ASA) **(7)** (table 1).

- Checklist Prior to Sedation:

Using a systematic approach is a crucial component of the safety net of sedation because it prevents you from forgetting to have a crucial drug, piece of equipment, or monitor on hand in case of an impending emergency. The acronym **SOAPME**, which stands for the following, is frequently used and is helpful while planning and preparing for an procedure.

S = Size-appropriate suction catheters and a functioning suction apparatus.

O = an adequate Oxygen supply and functioning flow meters or other devices to allow its delivery.

A = size-appropriate Airway equipment (eg, bag-valve-mask or equivalent device [functioning]), nasopharyngeal and oropharyngeal airways, LMA, laryngoscope blades (checked and functioning), endotracheal tubes, stylets, face mask.

P = Pharmacy: all the basic drugs needed to support life during an emergency, including antagonists as indicated.

M = Monitors: functioning pulse oximeter with size-appropriate oximeter probes, end-tidal carbon dioxide monitor, and other monitors as appropriate for the procedure (e.g., noninvasive blood pressure, ECG, stethoscope).

E = special Equipment or drugs for a particular case (e.g., defibrillator) **(7).**

Table 2: Appropriate Intake of Food and Liquids Before Elective Sedation**(7).**

Ingested Material	**Minimum Fasting Period**
Clear liquids: water, fruit juices without pulp, carbonated beverages, clear tea, black coffee	**2**
Human milk	**4**
Infant formula	**6**
Nonhuman milk: because nonhuman milk is similar to solids in gastric emptying time, the amount ingested must be considered when determining an appropriate fasting period.	**6**
Light meal: a light meal typically consists of toast and clear liquids. Meals that include fried or fatty foods or meat may prolong gastric emptying time. Both the amount and type of foods ingested must be considered when determining an appropriate fasting period.	**6**

- Monitoring:

For deep sedation, continuous electrocardiogram (ECG) heart rate, respiratory rate, pulse oximetry, and noninvasive blood pressure monitoring are strongly recommended. End-tidal carbon dioxide (CO_2) capnography monitoring has become the standard of care for deeply sedated children. Intravenous access for patients receiving deep sedation is also recommended. Monitoring is needed throughout the sedation and recovery. In addition to electrophysiological monitoring, the child's color, airway patency, and rate and depth of respiration should be monitored by direct observation **(8).**

End-tidal capnography is a noninvasive way to monitor a patient's ventilatory status. Respiratory gases are sampled either from a chamber attached in-line to an endotracheal tube or at the nares via nasal cannula. Increases in end-tidal carbon dioxide ($ETCO_2$) with respiratory depression are detected before hypoxemia particularly in those who are receiving supplemental oxygen**(9).**

Another non-invasive method for monitoring a patient's state of sedation is by Bispectral (BIS) index monitoring. BIS index is in the range of 0 to 100. Coma has a BIS index of 0, deep hypnotic state from 0 to 40, general anesthesia from 40 to 60, deep sedation from 60 to 70, light to moderate sedation from 70 to 90, and 100 is awake (**9).**

- Personnel:

To provide sedation, two providers are ideal. The planned procedure will be carried out by one provider, while the other will supervise the sedation and patient monitoring**(10)**

- Sedation scoring scales:

There are several scoring systems used to document the patient's mental status and depth of sedation, such as the Ramsay Sedation Scale**,** the Observer's Assessment of Alertness/Sedation Scale, the comfort Scale and the Sedation-Agitation Scale**(11).**

The Ramsay Sedation Scale (RSS) was described by Ramsay and colleagues in 1974 for the purpose of monitoring sedation with alphaxalone/alphadolone. The Ramsay Scale was one of the earliest sedation scales, and although not strictly validated in children, it is one of the most widely used scales for assessing and monitoring pediatric sedation in daily practice, as well as in clinical research. A later modification of the Ramsey Scale more clearly coincides with the AAP and Joint Commission guidelines (table 2). A score of 2–3 is anxiolysis, 4–5 is moderate sedation, 6 is deep sedation, and 7–8 is general anesthesia.**(11).**

Table 3: Modified Ramsy Score**(12)**

SCORE	DEFINITION
1	Awake and alert, minimal or no cognitive impairment.
2	Awake but tranquil, purposeful responses to verbal commands at conversation level.
3	Appears asleep, purposeful responses to verbal commands at conversation level.
4	Appears asleep, purposeful responses to verbal commands but at louder than usual conversation level or requiring light glabellar tap.
5	Asleep, sluggish purposeful responses only to loud verbal commands or strong glabellar tap.
6	Asleep, sluggish purposeful responses only to painful stimuli.
7	Asleep, reflex withdrawal to painful stimuli only (no purposeful responses).
8	Unresponsive to external stimuli, including pain.

- Patient Positioning:

All patients undergoing diagnostic upper and lower endoscopic procedures with sedation should be placed in the left lateral decubitus position. This is because patients who are placed in the supine position are more susceptible to pooling of secretions in oral pharynx and risk upper airway obstruction or laryngospasm**(6).**

- Postsedation Recovery:

Patients should be monitored until they return to baseline mental status and are no longer at risk for cardiorespiratory depression (**13).**

1. Techniques for Pediatric Procedural Sedation

Pediatric procedural sedation (PPS) refers to techniques and medications used to minimize anxiety and pain associated with unpleasant or painful procedures **(14).**

➢ Choice of PPS techniques:

The most appropriate PPS technique depends on the following factors:

- Type of procedure.
- Length of procedure.
- Target level of sedation.
- Contraindications for specific drugs.
- Known side effects of diagnostic or therapeutic procedures.
- Child or parent preference based on full information of risks, benefits, and alternatives.
- Age and level of understanding of the child **(15).**

➢ Drug techniques:

The agent of choice should provide adequate analgesia, sedation, and anesthesia with quick onset and short duration to allow the performance of a procedure with quick recovery and discharge. PPS can vary from anxiolysis for nonpainful procedures to sedation for painful procedures, and the agent of choice should reflect the goals of sedation. Benzodiazepines, ketamine, propofol, ketamine with propofol, nitrous oxide, and etomidate are all well-studied agents used in PPS **(14).**

1. For nonpainful Procedures:

Midazolam:

Dose: PO/PR 0.5 mg/kg. IV/IM 0.05 to 0.1 mg/kg (maximum 6 mg/dose). Intranasal 0.3 to 0.5 mg/kg (maximum 10 mg/dose); **Onset**: PO/PR 20 to 30 min. IV 3 to 5 min. IM 10 to 20 min. Intranasal 5 to 10 min. Note: oral/rectal administration has a slow onset and is less predictable; **Duration**: 0.5 to 2 hours.

Comments: It functions as an anxiolytic. Midazolam solutions are acidic and intranasal administration is associated with stinging pain and can cause increased secretions. Midazolam should be prepared in 1mg/ml solution for children less than 15 kg in body weight, where solutions that greater than 1 mg/mL are not recommended **(16)**

Pentobarbital:

Dose: PO 3 to 5 mg/kg; **Onset**: 30 minutes; **Duration**: variable.

Comments: Works as a sedative. No analgesia. Variable efficacy. Long recovery times**(17).**

Nitrous Oxide:

Dose: Inhaled starting at 100% O2 and increasing concentration nitrous oxide to effect. Maximum 70% nitrous oxide/30% O2 ratio; **Onset**: 30 seconds (peak effect 3 to 5 minutes); **Duration**: Effects decrease 70% 3 minutes after discontinuation

Comments: Works as a sedative. No analgesia. Variable efficacy. Long recovery times**(14)**.

2. Minor Painful Procedures:

Fentanyl:

Dose: Intranasal 1.5 mcg/kg (maximum 0.5 mL per nare); **Onset**: 10 minutes; **Duration**: 20 minutes.

Comments: Works as an analgesic. Equivalent to IV morphine. Little to no adverse effects. Advantage of being short-lived **(18).**

Sub dissociative dose ketamine:

Dose: IV 0.3 mg/kg IV. Intranasal 1 mg/kg, **Onset**: Variable, **Duration**: 60 minutes.

Comments: Analgesic and amnestic without full dissociation at the above dose. Sub dissociative doses are sufficient for minor procedures such as laceration repair or abscess drainage but not sufficient for major painful **(19).**

Dexmedetomidine:

Dose: Intranasal 0.5 to 2 mcg/kg; **Onset**: 25 minutes; **Duration**: 85 minutes.

Comments: Hypnotic and sedative. Longer time to onset and longer duration than other agents. No respiratory or hemodynamic compromise **(20).**

3. Major Painful Procedures:

Propofol:

Dose: IV 1 to 2 mg /kg, followed by repeat doses of 0.5 mg /kg as needed; **Onset**: Seconds ; **Duration**: 6 minutes.

Comments: Hypnotic, sedative. No analgesia. Rapid onset with short duration of action producing motionless anesthesia. Causes respiratory and cardiovascular depression. Increased dosing requirement for younger patients. Causes burning pain at the injection site **(21).**

Etomidate:

Dose: IV 0.2 to 0.3 mg/kg; **Onset**: Seconds; **Duration**: 5 to 15 minutes.

Comments: Hypnotic, sedative. No analgesia Causes cardiovascular and respiratory depression. Avoid in patients with increased muscle tone (e.g., cerebral palsy) due to the risk of myoclonic jerks **(22).**

Ketamine:

Dose: IV 1 to 1.5 mg/kg. IM 4 to 5 mg/kg ; **Onset**: IV 1 to 2 min. IM 3 to 5 min; **Duration**: IV 15 minutes. IM 30 to 45 minutes.

Comments: Works as a dissociative analgesic agent. Respiratory and cardiovascular stimulant. Acts as a bronchodilator. Can cause increased intraocular pressure, intracranial pressure, salivation, and laryngospasm. The risk of airway obstruction, apnea, and laryngospasm is higher in infants <3 months, so patient age under 3 months is an absolute contraindication to ketamine use. It is emetogenic. Consider pretreatment with ondansetron. Midazolam coadministration does not reduce the risk of emergence agitation**(23).**

Propofol + Ketamine:

Dose: IV Propofol 1 milligram/kg, Ketamine 0.5 milligram/kg ;**Onset**: 1 minute; **Duration**: Propofol minutes; Ketamine 15 to 45 minutes.

Comments: Decreased dosing requirement of both agents. Lessens respiratory and cardiovascular depression, vomiting. Increased risk of oxygen desaturation compared to ketamine as a single agent **(24).**

- Reversal Agents:

Naloxone:

Dose: Infants and children <5 years old or <20 kg: IV 0.1 mg/kg/dose, IM 0.1 mg/kg/dose; Children >5 years old or >20 kg: IV 2 mg/dose, IM 2 mg/dose. Infants, children, and adolescents: intranasal 4 mg, endotracheal 2 to 3 times the IV dose; **Onset**: One minute; **Duration**: 15 to 30 minutes**(14).**

Comments: Opiate reversal. The dose can be repeated every two to three minutes to effect. May need to repeat doses every 20 to 60 minutes if the duration of action of opioid used is longer than naloxone. The onset of action is slightly delayed in intranasal administration.

Flumazenil:

Dose: IV 0.01 mg/kg (maximum dose 0.2 mg) given over 15 seconds. May repeat dose after 45 seconds, then every minute to a maximum total cumulative dose of 0.05 milligrams/kg or 1 mg; Onset: One minute; **Duration**: 45 minutes**.**

Comments: Benzodiazepine reversal. Avoid use in chronic benzodiazepine users as it can induce seizures. After the procedure, the patient should be monitored until recovery is complete and they resume the pre-sedation level of consciousness**(14).**

2. Adverse events & their management

Many of the complications related to procedural sedation can be prevented by:

- ✓ Appropriate monitoring and recognition of respiratory depression.
- ✓ Adequate monitoring.
- ✓ Ensuring the correct dose of medications (avoid drug calculation error).
- ✓ Careful titration of medications.
- ✓ Appropriate patient assessment.
- ✓ Avoiding drug–drug interactions.
- ✓ Staff members who have received resuscitation and airway management training **(25).**

.1. Oxygenation & ventilation:

Some of the potentially life-threatening adverse events associated with oxygenation and ventilation include oxygen desaturation, central apnea, airway obstruction (partial or complete), laryngospasm**(26).**

Loss of muscular tone in the airway lowers patency and reduces the entire upper airway in sedated infants. The majority of obstruction, however, occurs at the level of the soft palate and epiglottis. Resistance during inspiration causes negative airway pressure and increases airway collapse **(27).**

Because of the child's sensitive and reactive airway, laryngospasm occurs more commonly in children than in adults. Laryngospasm is triggered by secretions or airway instrumentation stimulating the glottic and supraglottic mucosa. It is typically simple to diagnose and treat, but if not properly controlled, it has the potential to bring the child to a bradycardic hypoxic arrest, may cause negative pressure pulmonary edema. Deep anesthesia reduces the likelihood of laryngospasm**(27)**

The management of respiratory/airway adverse events includes one or more of the following interventions:

• Supplemental or increased inspired oxygen delivery.

• Vigorous tactile stimulation.

• Careful titration of reversal agents; naloxone and flumazenil if respiratory depression is noted and positive pressure ventilation.

• Airway intervention, including shoulder roll, chin lift, jaw thrust and neck extension.

• Oral and pharyngeal suctioning.

• Placement of an oral or nasal airway.

• If laryngospasm is noted, initial treatment includes continuous positive airway pressure (CPAP) with 100% oxygen and airway manipulation (jaw thrust and chin lift). If the initial interventions were unsuccessful, increase the depth of anesthesia with additional doses of sedative agents, and if necessary, administer small doses of succinylcholine to relax the vocal cords. Tracheal intubation should be considered if the laryngospasm remains refractory.

• Placement of a laryngeal mask airway or endotracheal tube if other airway management is unsuccessful.

• If the patient has pulmonary aspiration, the child's head should be placed on a lower level, and rapid suction of the airway and placement of an endotracheal tube should be carried out. Before the first ventilation, if the saturation is adequate, endotracheal suction should be performed to remove the stomach contents from the trachea and lower airway**(26).**

2. Cardiovascular adverse events:

One of the most crucial signs to watch for is bradycardia and hypotension. The management of adverse cardiovascular events includes maintaining oxygenation of the lungs and one or more of the following interventions: administration of intravenous fluids; chest compressions; and administration of medications, including atropine and epinephrine(**26).**

3. Emergence agitation:

Emergence agitation is a drug-induced disorientation in which the child cries or screams, is uncooperative, inconsolable, and thrashes around. Treatment begins with removing other reasons, such as hypoxia (though precise oximeter readings on a thrashing child might be difficult) and pain. Reassure the parents, and make sure the child does not get injured. Most children require just observation, but some seek treatment. Agitation normally lasts no more than 30 minutes. If the condition does not improve spontaneously, consider small doses of propofol 0.5-2 mg/kg (ensuring equipment is accessible in case of apnea), IV clonidine (0.5-1 mcg/kg), or fentanyl 0.5-1 mcg/kg. Ketamine or dexmedetomidine may also be effective, but midazolam is not **(28).**

4. Other rare complications during sedation are permanent neurological injury and death.

References

1. *Khalila, A., I. Shavit and R. Shaoul (2019). "Propofol Sedation by Pediatric Gastroenterologists for*

Endoscopic Procedures: A Retrospective Analysis." Frontiers in Pediatrics 7.

2. *Kallay, T., R. Orel and J. Brecelj (2021). Pediatric procedural sedation and general anesthesia for gastrointestinal endoscopy. Practical Pediatric Gastrointestinal Endoscopy: 15-22.*
3. *Barnes, S., M. Yaster and S. R. Kudchadkar (2016). "Pediatric Sedation Management." Pediatr Rev 37(5): 203-212.*
4. *Early, D. S., J. R. Lightdale, J. J. Vargo, R. D. Acosta, V. Chandrasekhara, K. V. Chathadi, J. A. Evans, D. A. Fisher, L. Fonkalsrud and J. H. Hwang (2018). "Guidelines for sedation and anesthesia in GI endoscopy." Gastrointestinal endoscopy 87(2): 327-337.*
5. *Friedt, M. and S. Welsch (2013). "An update on pediatric endoscopy." European Journal of Medical Research 18(1): 24.*
6. *Lightdale, J. R. (2021). Sedation for Pediatric Gastrointestinal Procedures. Pediatric Sedation Outside of the Operating Room: A Multispecialty International Collaboration. M. D. K. P. Mason. Cham, Springer International Publishing: 397-412.*
7. *Coté, C. J., S. Wilson, A. A. o. Pediatrics and A. A. o. P. Dentistry (2019). "Guidelines for monitoring and management of pediatric patients before, during, and after sedation for diagnostic and therapeutic procedures." Pediatrics 143(6).*
8. *Carlson, D. W. and S. S. Mendez (2021). The Pediatric Hospital Medicine Service: Models, Protocols, and Challenges. Pediatric Sedation Outside of the Operating Room: A Multispecialty International Collaboration. M. D. K. P. Mason. Cham, Springer International Publishing: 285-303.*
9. *Sahyoun, C., A. Cantais, A. Gervaix, S. Bressan, R. Löllgen and B. Krauss (2021). "Pediatric procedural sedation and analgesia in the emergency department: surveying the current European practice." European Journal of Pediatrics 180(6): 1799-1813.*
10. *Krmpotic, K., M. J. Rieder and D. Rosen (2021). "Recommendations for procedural sedation in infants, children, and adolescents." Paediatr Child Health 26(2): 128-129.*
11. *Andropoulos, D. B. (2021). Sedation Scales and Discharge Criteria: How Do They Differ? Which One to Choose? Do They Really Apply to Sedation? Pediatric Sedation Outside of the Operating Room: A Multispecialty International Collaboration. M. D. K. P. Mason. Cham, Springer International Publishing: 83-94.*
12. *Agrawal, D., H. A. Feldman, B. Krauss and M. L. Waltzman (2004). "Bispectral index monitoring quantifies depth of sedation during emergency department procedural sedation and analgesia in children." Ann Emerg Med 43(2): 247-255.*
13. *Stefan , A. and R. Valani (2012). Procedural Sedation and Recovery. ESSENTIAL EMERGENCYPROCEDURAL SEDATION AND PAIN MANAGEMENT . edited by Valani and K. H. Shah. Philadelphia LIPPINCOTT WILLIAMS & WILKINS 31-38.*
14. *Stern, J. and A. Pozun (2022). Pediatric Procedural Sedation. StatPearls. Treasure Island (FL), StatPearls Publishing Copyright © 2022, StatPearls Publishing LLC.*
15. *Zielinska, M., A. Bartkowska-Sniatkowska, K. Becke, C. Höhne, N. Najafi, E. Schaffrath, D. Simic, M. Vittinghoff, F. Veyckemans and N. Morton (2019). "Safe pediatric procedural sedation and analgesia by anesthesiologists for elective procedures: A clinical practice statement from the European Society for Paediatric Anaesthesiology." Pediatric Anesthesia 29(6): 583-590.*
16. *Mehdi, I., S. Parveen, S. Choubey, A. Rasheed, P. Singh and M. Ghayas (2019). "Comparative Study of Oral Midazolam Syrup and Intranasal Midazolam Spray for Sedative Premedication in Pediatric*

Surgeries." Anesth Essays Res 13(2): 370-375.

17. *Burger, R. K., J. Figueroa, C. McCracken, M. D. Mallory and P. P. Kamat (2021). "Sedatives used in children to obtain head CT in the emergency department." Am J Emerg Med 44: 198-202.*

18. *Pansini, V., A. Curatola, A. Gatto, I. Lazzareschi, A. Ruggiero and A. Chiaretti (2021). "Intranasal drugs for analgesia and sedation in children admitted to pediatric emergency department: a narrative review." Ann Transl Med 9(2): 189.*

19. *Reynolds, S. L., K. K. Bryant, J. R. Studnek, M. Hogg, C. Dunn, M. A. Templin, C. G. Moore, J. R. Young, K. R. Walker and M. S. Runyon (2017). "Randomized Controlled Feasibility Trial of Intranasal Ketamine Compared to Intranasal Fentanyl for Analgesia in Children with Suspected Extremity Fractures." Acad Emerg Med 24(12): 1430-1440.*

20. *Azizkhani, R., F. Heydari, M. Ghazavi, M. Riahinezhad, M. Habibzadeh, A. Bigdeli, K. Golshani, S. Majidinejad and A. Mohammadbeigi (2020). "Comparing Sedative Effect of Dexmedetomidine versus Midazolam for Sedation of Children While Undergoing Computerized Tomography Imaging." J Pediatr Neurosci 15(3): 245-251.*

21. *Min, J. Y., J. R. Lee, Y. S. Kang, J. H. Ho and H. J. Byon (2021). "Pediatric characteristics and the dose of propofol for sedation during radiological examinations: a retrospective analysis." J Int Med Res 49(2): 300060521990992.*

22. *Moningi, S., G. P. Reddy, S. A. Nikhar, R. Chikkala, D. K. Kulkarni and G. Ramachandran (2022). "Comparison of the influence of low dose etomidate and propofol as priming dose on the incidence of etomidate induced myoclonus: a randomised, double-blind clinical trial." Braz J Anesthesiol 72(2): 261-266.*

23. *Bellolio, M. F., H. A. Puls, J. L. Anderson, W. I. Gilani, M. H. Murad, P. Barrionuevo, P. J. Erwin, Z. Wang and E. P. Hess (2016). "Incidence of adverse events in paediatric procedural sedation in the emergency department: a systematic review and meta-analysis." BMJ Open 6(6): e011384.*

24. *Foo, T. Y., N. Mohd Noor, M. B. Yazid, M. H. Fauzi, S. F. Abdull Wahab and M. Z. Ahmad (2020). "Ketamine-propofol (Ketofol) for procedural sedation and analgesia in children: a systematic review and meta-analysis." BMC Emerg Med 20(1): 81.*

25. *Stone , A. and M. Freedman (2012). ''Adverse Events and Complications of Procedural Sedation''. ESSENTIAL EMERGENCYPROCEDURAL SEDATION AND PAIN MANAGEMENT. R. edited by Valani and K. H. Shah. Philadelphia, by LIPPINCOTT WILLIAMS & WILKINS: 45-51.*

26. *Ramaiah, R. and S. Bhananker (2011). "Pediatric procedural sedation and analgesia outside the operating room: anticipating, avoiding and managing complications." Expert Review of Neurotherapeutics 11(5): 755-763.*

27. *von Ungern-Sternberg, B. and C. Sims (2020). Airway Managementairway management in Children. A Guide to Pediatric Anesthesia. C. Sims, D. Weber and C. Johnson. Cham, Springer International Publishing: 77-114.*

28. *Sims, C. and T. Farrell (2020). An Overview of Pediatric Anesthesia. A Guide to Pediatric Anesthesia. C. Sims, D. Weber and C. Johnson. Cham, Springer International Publishing: 1-26.*