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Sedation for Pediatric Endoscopies

Vidyut Bhatia[1] and Narendra Kumar Arora[2]
[1]*Apollo Centre for Advanced Pediatrics, Indraprastha Apollo Hospital, New Delhi*
[2]*The INCLEN (International Clinical Epidemiology Network) Trust International India*

1. Introduction

Endoscopy can be a very traumatic event for a child and it is essential that the procedure be smooth, painless and anxiety-free. Hence, endoscopy in children normally requires the simultaneous administration of sedation to warrant the patient's well-being, comfort, and cooperation throughout the procedure. The endoscopist has to balance the benefits with the possible adverse events because sedation related complications are reported to be much more than procedure related events like perforation and bleeding (Thakkar, Elserag et al. 2007). Although there is little agreement amongst pediatric endoscopists on best sedation practices everyone does agree that ensuring the child's safety is paramount (Lightdale, Mahoney et al. 2007).

2. Goals

The goal is always to optimize patient safety and minimize complications. The goals of sedation can be divided into two main categories. These are patient specific and physician/ endoscopist specific. The patient specific goals are anxiolysis, analgesia and amnesia for the procedure. From an endoscopists' perspective, the goals of sedation are cooperation from the patient, completion of the procedure, and no complications.

3. Patient assessment and risk stratification

Patient assessment and risk stratification is the most important initial step in planning for endoscopy in a child. This should be done at two stages. The first time is when the decision to perform an endoscopy has been made (i.e. in the outpatient clinic etc.) and once just before commencing the procedure. It is just like doing a pre-anesthetic check-up before any surgery.

4. ASA classification for pre anesthetic status

The ASA classification is used to identify at risk patients and plan sedation accordingly (Table. 1). This classification system although in vogue for nearly 5 decades does not specifically address issues related to children. Healthy neonates and infants do not tolerate similar anesthetics well in comparison to older children and young adults. For these reasons, in further discussions, sedation for endoscopy infants and neonates has been taken up separately.

ASA class	Status
1	A normal healthy patient
2	A patient with mild systemic disease
3	A patient with severe systemic disease
4	A patient with severe systemic disease that is a constant threat to life
5	A moribund patient who is not expected to survive without the operation
6	A declared brain-dead patient whose organs are being removed for donor purposes

Table 1. ASA (American Society of Anesthesiologist) classification of physical status

5. Sedation levels

Depending on the type of endoscopic procedure, children may require no sedation (e.g., flexible sigmoidoscopy in an infant), intravenous sedation, or general anesthesia. Levels of sedation range from a continuum of mild sedation to deep sedation (Mahoney and Lightdale 2007). Therefore it is important to keep in mind that the child can pass on from light sedation to a deep sedation easily with the same combination of drugs and dosage. The endoscopist has to remain prepared for such eventualities.

5.1 No sedation

Unsedated upper endoscopy has been routinely performed in very young and adolescent patients at several institutions without any difference in outcomes (Bishop, Nowicki et al. 2002). In particular, flexible sigmoidoscopy, changes or removals of percutaneous endoscopically placed gastrostomy tubes and placement of pH or impedance probes can be performed without sedation (Mahoney and Lightdale 2007). The advantages of not getting sedation include minimal complications, earlier recovery and lower cost of the procedure.

5.2 Light to moderate sedation

This is an another name for conscious sedation and defined as a medically controlled state of depressed consciousness that allows protected reflexes to be maintained, retains the ability to maintain a patent airway independently and continuously, and permits appropriate responses by the patient to physical stimulation or verbal commands; for example, "open your eyes.''

5.3 Deep sedation/analgesia

Deep sedation is defined as a medically controlled state of depressed consciousness or unconsciousness from which the patient is not easily aroused. It may be accompanied by a partial or complete loss of protective reflexes, and includes the inability to maintain a patent airway independently and respond purposefully to physical stimulation or verbal command.

5.4 General anesthesia

General anesthesia is defined as a medically controlled state of unconsciousness accompanied by a loss of protective reflexes, including the inability to maintain an airway independently and no purposeful response to physical stimulation or verbal command.

Children with the American Society of Anesthesiologists (ASA) physical status 3 and 4 and patients who are going to have procedures such as achalasia dilation, foreign body removal,

and percutaneous endoscopic gastrostomy placement are typically selected for general anesthesia and should be assessed by an anesthesiologist.

6. Method of sedation

Sedatives should not be administered in a facility unsupervised by medically trained personnel or where appropriate monitoring equipment and manpower are not available, since unrecognized complications may lead to disaster. The method of sedation is determined by the endoscopist and the needs of the patient. Many factors must be considered, including the patient's condition, ASA classification, patients age, the type of procedure (i.e., diagnostic versus therapeutic), the anticipated level of cooperation from the patient, the parents' and patient's preference after being provided these choices and explanation of their risks, as well as the endoscopist's experiences.

There is a wide variation in the method of practice of sedation. Within city of Delhi, India five pediatric gastroenterology setups practice different approaches ranging from no sedation at all to moderate sedation and a mix of deep sedation and general anaesthesia. From other published literature as well, the message is not consistent (Lightdale, Mahoney, et al. 2007). This probably reflects an uncertainty in the optimal method of sedation and the lack of proper guidelines according to the authors. Comfort of pediatric endoscopist for particular types of sedation is equally important.

A conscious sedation protocol is followed at the pediatric gastroenterology division of All India Institute of Medical Sciences, New Delhi, India. For infants below 6 months no sedation is given, while all other children including those under going procedures receive moderate IV sedation.

All children are given the following drugs according to the following protocol prior to endoscopy (Table 2).

Drug	Concentration (mg/ml)	Preparation	Concentration after dilution (mg/ml)	Dose (mg/kg)	Dose after dilution (ml/kg)
Atropine	0.6	Dilute 1 ampoule in 5ml of saline	0.1	0.1	0.15
Diazepam	5.0	2ml diazepam + 2ml 2% lignocaine* + 6ml saline	1.0	0.1	0.1
Ketamine	5.0	2ml of drug + 8 ml of saline	10.0	2.0	0.2

* Lignocaine is added for its cardiac stability

Table 2. Concentration, method of preparation and dosage of drugs used for pediatric sedation at the Pediatric Gastroenterology division, Department of Pediatrics, All India Institute of Medical Sciences, New Delhi, India

7. Preparation for the procedure

7.1 Fasting

Conventionally, fasting for solids for 6 hours and liquids for 2 to 4 hours is recommended (Tolia, Peters et al. 2000). Longer periods of fasting may be required for conditions such as

achalasia and gastric outlet obstruction, because retained food in the esophagus or stomach may increase the risk of aspiration. Infants and neonates are not fasted for long and often require to be put on IV fluids during fasting.

7.2 Antibiotic prophylaxis

Children with congenital heart diseases or a compromised immune system are candidates for endocarditis prophylaxis. We administer single injection of amoxicillin and gentamicin just before start of the procedure. In children sensitive to amoxicillin, vancomicin is given. For ERCP, a flouroquinolone is also added.

7.3 Time out

"Time-out" is an important component before any procedure on the patient. It is done immediately prior to starting the procedure and is performed to prevent any medical error by conducting a final verification of correct patient, procedure, and site. The timeout should also ensure that correct equipment, drugs and personnel to perform sedation are available. It is an active communication among all procedural team members that should be consistently performed prior to all procedures.

On-site equipment of appropriate sizes should be available prior to the procedure and include the following: (i) pulse oximetry (ii) suction and catheters; (iii) noninvasive blood pressure measurement equipment (iv) positive pressure O_2 delivery system (v) emergency kit with age and size appropriate drugs and resuscitation equipment.

7.4 Documentation before sedation

Although endoscopy has a relatively low risk as compared to other surgical procedures, it is important that all pediatric endoscopists be prepared for complications associated with either the procedure or the sedation. In turn, all patients and their families must be well informed prior to the endoscopy and the initiation of sedation about the possible risks of the procedure and of the sedation. It is extremely important to find a delicate balance between the full disclosure of the invasive nature of the procedure and related complications and anticipated parental and patient responses to the disclosed information.

Documentation before sedation must include the following:

1. Informed consent: Informed consent must involve disclosure by the endoscopist and deliberation by the parents or legal guardians. If the patient is an adolescent, it is appropriate to obtain informed assent. A separate consent form for sedation may be required.
2. Verbal instructions
3. Dietary precautions
4. Health evaluation

7.5 Topical anesthetic spray and premedication

For upper gastrointestinal endoscopy, pre-medication with topical sprays and oral sedatives prior to IV line insertion are used at many centers. Topical lidocaine applications (gel, sprays, inhalers or lollipops) have been used as an addition to sedation with varying results. Some formulations are associated with nausea, vomiting and gagging and might increase the need for sedation. Ayoub et al. performed a single-blind, randomized, prospective study (Ayoub, Skoury et al. 2007) to compare topical lidocaine application by means of a lollipop with the spray group and found that, gag reflexes in the lollipop group were significantly

weaker and patients were better able to tolerate scope introduction and manipulation during the procedure. Sedation was needed by 96% of patients given spray, but by only 32% of patients in the lollipop group (P <0.001). All these were adults and its extrapolation to pediatric population may be difficult.

Topical application is only effective when the anesthetic is delivered to the posterior pharynx. This system requires depression of the tongue and elicitation of a gag reflex with a tongue blade during spraying, which may be highly unpleasant for children. Opponents of the pharyngeal anesthesia postulate that this increases the distress in children (Ament, Berquist et al. 1988), whereas the proponents have propagated the more generally held view that it is the pharyngeal stimulation from the endoscope that causes more patient agitation (Evans, Saberi et al. 2006). We have in our setup never used topical anesthetics prior to endoscopy and after giving IV sedation, children of all ages tolerate endoscope well.

8. Post procedure instructions

After the procedure, children are retained in the hospital for 2 hours (conscious sedation) – 8 hours (general anaesthesia) depending upon the types of anaesthesia and the procedures. If any intervention has been done, child is advised to stay longer till they are stable. Approximately 2 hours after the procedure, if the child is conscious and awake, he / she can be offered something to drink. Most children sleep after leaving the hospital. When child wakes, he or she may be drowsy. Some children are sleepy for the remainder of the day. After child wakes up, do not allow him or her to walk alone for at least 4 hours. Child may feel suddenly dizzy and fall without warning. The sedative can affect the child's coordination ability and balance. For the first 12 hours after waking up the child should not do anything that requires alertness, coordination, or balance. The care providers are told that the sedative sometimes causes the child to behave in unexpected ways. However, by the next day child's behavior should return to normal. For infants it is okay to give "clear liquids" (water, apple juice, tea) after getting home. Wait approximately 30 minutes to make sure child does not choke or vomit. Then milk, formula or other foods may be given. If child can drink without vomiting or choking, he or she can have the foods he or she usually eats. The patient is instructed to return/seek medical help for recurrent vomiting and if any of the common effects listed above last more than 12 hours, or if child's pain increases. We also advise the patient not to travel if he/she has had sclerotherapy in the past 24 hours.

9. Sedation related complications and their management

There are no good published studies that have documented adverse events following pediatric sedation. Cote et al reported on the adverse sedation events in children in a study published in 2000 (Cote, Notterman et al. 2000). This study was a critical incident analysis of contributory factors. The primary event in both the hospital-based and non-hospital-based patients was respiratory, the secondary event was cardiac arrest, and the third was inadequate resuscitation. Drug–drug interactions, inadequate monitoring, inadequate medical evaluation, lack of an independent observer, and inadequate management of resuscitation were also some of the other causes of adverse sedation events. Successful outcome was related to the use of pulse oximetry in patients compared to those without any monitoring. At pediatric gastroenterology division of All India Institute of Medical Sciences, New Delhi, India, 4874 endoscopies were done over the past two and a half years. Following adverse events were observed amongst them (Table 3). Most complications from sedation

are avoidable. Children below one year are at the highest risk and need special attention. Desaturation and apnea are the most frequently encountered adverse effects which can be quickly reversed with administration of 0_2/ increasing flow. Uniform guidelines for both in hospital and out of hospital sedation must include appropriate personnel skilled in airway management and resuscitation. Health care personnel who sedate children for procedures must have advanced airway and resuscitation skills.

Adverse event	**N=4874**
Ineffective sedation	351 (7.2%)
Respiratory depression (Hypoxemia)	975 (20%)
Bronchospasm/ laryngospasm	101 (0.21%)
Combativeness/delirium	238 (0.49%)
Allergic reaction to drugs	118 (0.24%)

Table 3. Incidence of various adverse events observed over a period of two and a half years following endoscopies at the pediatric gastroenterology division of All India Institute of Medical Sciences, New Delhi, India

10. Pharmacological options

The main classes of drugs used for sedation analgesia for diagnostic and therapeutic procedures are narcotics, benzodiazepines, systemic anesthetics and reversal agents. They are described briefly in the following paragraphs.

10.1 Narcotics

10.1.1 Fentanyl

Fentanyl is a fat-soluble drug that rapidly enters the blood–brain barrier. It is more potent and fast acting than both morphine and meperidine. Fentanyl should be administered to children as a slow IV push since rapid administration has been associated with chest wall and glottic rigidity. Fentanyl's onset of action is approximately 30 seconds, and its opioid effects last approximately 30 to 45 minutes. Fentanyl should be administered in small doses to slowly titrate to effect, with several minutes allowed between each dose. Because its termination of action occurs with redistribution rather than from metabolism, the respiratory depressive effects of fentanyl outlast its analgesic effects.

10.1.2 Meperidine and the lytic cocktail

Until recently, meperidine was a favorite in longer procedures since its clinical duration of action is 2–4 hours. It may be given intravenously in dosage of 0.5–1.0 mg/kg, with maximum being 4 mg/kg. The time of peak effect for meperidine is 1–3 minutes after intravenous administration. In addition to respiratory depression, the active metabolite meperidine (nor-meperidine) may cause seizures. Meperidine should not be used long-term or in patients with poor renal clearance. Special consideration includes avoidance in patients taking monoamine oxidase inhibitors and in patients with cardiovascular instability. The other adverse reactions following meperidine include delirium, nausea, vomiting, urinary retention, pruritis, smooth muscle spasm, and hypotension. Central nervous system toxicity may occur in patients taking tricyclic antidepressants and phenothiazines. Meperidine in the past was commonly used as a cocktail mixed with promethazine and chlorpromazine. The cocktail is still, on occasion, used by some but it has very long sedation duration, anywhere

from 7 to 19 hours. It can also be associated with hypotension seizures, extra pyramidal reactions, and severe prolonged life-threatening respiratory depression.

10.2 Benzodiazepines

10.2.1 Midazolam

Midazolam has now become the preferred drug in many pediatric endoscopy suites. It is a benzodiazepine with three to six times greater potency than diazepam. It is given in the dose of 0.1-0.3 mg/kg/dose intravenously. Midazolam provides three advantages over diazepam. It provides patients better anterograde and retrograde amnesia for the procedure. It has a shorter half life and there appears to be no resedation as seen with diazepam. The onset of action for a dose of midazolam is within 1 to 5 minutes, and it achieves its peak effect in approximately 30 minutes to 1 hour. Unlike other benzodiazepines, the clearance of midazolam is dose related (i.e., increased clearance with increased dosage).

10.3 Systemic anesthetics

10.3.1 Ketamine

Ketamine in low doses can cause intense analgesia with minimal respiratory and cardiovascular depression. Typical doses are 1–2 mg/kg intravenous. The onset occurs in less than 1 minute, with a peak effect in several minutes and duration of action in approximately 15 minutes. Higher doses (2mg/kg) or supplementation with other sedatives or narcotics may produce deep sedation or general anesthesia. Ketamine should always be administered with an atropine (0.1 mg/kg) or glycopyrrolate (0.01 mg/kg) since profuse secretions from ketamine alone may induce laryngospasm.

Cardiovascular stability and blood pressure are usually maintained. Typically, ketamine has been associated with hallucinations during emergence in up to 12% of patients. It may be reduced by administration of benzodiazepam. It is contraindicated in patients with head injury, open globe injury, hypertension, and psychosis. It is recognized that ketamine can induce apnea in neonates as well as a decrease response to hypocarbia, laryngospasm, and coughing. There is no antagonist available.

10.3.2 Propofol

Propofol is a short-acting sedative hypnotic. It is available in an Intralipid formulation. It has no analgesic properties, but it does have antiemetic and antipruritic properties. Although small doses of propofol (25–50 μg/(kg min) can provide "conscious sedation'' in adults with deep sedation, airway obstruction quickly occurs in pediatric patients. It is titrated with an infusion pump and should be administered by individuals with advanced airway skills. There has been a lot of enthusiasm in using this agent in pediatric intensive care units and in Endoscopy suites. Cases of fatal metabolic acidosis, mild cardiac failure, and lipemic serum have been reported in children which limits its use for prolonged periods of time. Short-term sedation with propofol has been associated with no such problems. Propofol should be administered in large veins since it can cause pain on injection. Respiratory depression/apnea and hypotension are related to the dose, rate and co-adminstration with other CNS depressants. Hypotension occurs from using the medication, especially when it is given rapidly. Anaphylactic reactions and bacterial contaminations have been described and have been attributed to the lipid formulation in which it is dispensed. Strict aseptic technique must be used when one uses propofol because it may

support the growth of microorganisms. The dosage of this drug should be lowered if the patients are hemodynamically unstable. There is no antagonist available for this drug.

10.4 Antagonists/reversal agents

Flumazenil is a specific benzodiazepam antagonist and will rapidly reverse the sedative and respiratory effects of benzodiazepines. In patients who are taking benzodiazepines for seizures or drug dependency, seizures may recur if flumazenil is given. The recommended dose of flumazenil is 10 µg/kg up to 1 mg intravenously. Antagonism begins within 1–2 minutes and lasts approximately 1 hour. Since resedation after 1 hour is known to occur with diazepam, the patient must be carefully monitored for at least 2 hours. Flumazenil should not be administered for the routine reversal of the sedative effects of benzodiazepam, but reserved for reversal of respiratory depression only.

Naloxone reversal of meperidine due to respiratory depression may precipitate seizures caused by normeperidine. The initial dose for respiratory depression is 1–2 µg/kg titrated to affect every 2–3 minutes. A dose of 10–100 µg/kg up to 2 mg may be required for respiratory arrest.

11. Conclusions

Sedation for pediatric endoscopy is generally given to have a smooth and comfortable procedure. With proper safety precautions and adopting uniform guidelines, adverse events can be reduced to very low levels. However, pediatric endoscopy team must always be prepared for severe respiratory adverse events.

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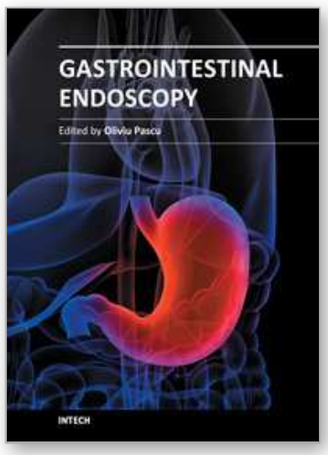

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Endoscopy has had a major impact in the development of modern gastroenterology. By using different data it provided a better understanding of pathogenic mechanisms, described new entities and changed diagnostic and therapeutic strategies. Meanwhile, taking advantage of many technical advances, endoscopy has had a developed spectacularly. Video-endoscopes, magnification, confocal and narrow-band imaging endoscopes, endoscopic ultrasounds and enteroscopes emerged. Moreover, endoscopy has surpassed its function as an examination tool and it became a rapid and efficient therapeutic tool of low invasiveness. InTech Open Access Publisher selected several known names from all continents and countries with different levels of development. Multiple specific points of view, with respect to different origins of the authors were presented together with various topics regarding diagnostic or therapeutic endoscopy. This book represents a valuable tool for formation and continuous medical education in endoscopy considering the performances or technical possibilities in different parts of the world.

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InTech Europe
University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China
Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

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