

Sedation for Colonoscopy in Children

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ABSTRACT

Colonoscopy has become an essential modality for evaluation and treatment of lower gastrointestinal tract. This endoscopic procedure is complex and may be unsafe if special concerns are not considered. It is well accepted that children undergoing colonoscopy should receive sedation for the procedure. Nevertheless, considerable practice variation prevails. The goal of procedural sedation is the safe and effective control of pain, anxiety and motion as well as to provide an appropriate degree of memory loss or decreased awareness. Regardless of regimen used, the safe administration of sedation to children requires an awareness of the particular needs of this population. Although colonoscopy is considered safe, the procedure has a potential for complications. Procedure and sedation-related complications can more easily occur in pediatric patients. Increased awareness of the complications associated with sedation during colonoscopy in children and involving the anesthesiologists in caring for these children may be optimal for safety. Proper patient preparation, endoscopic personnel and endoscopic unit are imperative to successful sedation and procedure. Additionally, postprocedural monitoring is important to insure that children have fully recovered from sedation.

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INTRODUCTION

The field of pediatric sedation and analgesia has evolved over the past two decades. The growing number of pediatric procedures requiring sedation and analgesia are recognized even in developing countries^[1-3]. Procedural sedation and analgesia is the use of sedative, analgesic and dissociate drugs to provide anxiolysis, analgesia, sedation and motor control during painful and unpleasant procedures. The purpose of sedation is to reduce a patient's anxiety and discomfort, minimize patient's risk for injury during the procedure, to improve tolerance and performance of endoscopy as well as to provide patient satisfaction. However, the negative outcomes of sedation are increased overall costs, delayed recovery from the procedure and increased risk of cardiopulmonary complications.

Pediatric colonoscopy differs significantly from its adult parallels in nearly every aspect including patient and parent management, preprocedural assessment, selection criteria for sedation and general anesthetic, bowel preparation and others. It is generally considered to be the preferred method of screening, evaluation and treatment of gastrointestinal abnormalities such as gastrointestinal bleeding, unexplained iron deficiency anemia, clinically significant chronic diarrhea, failure to thrive/weight loss, polyposis syndrome, clinically significant abdominal pain, rejection of intestinal transplant, foreign body removal, decompression of acute nontoxic megacolon or sigmoid volvulus, and balloon dilation of stenotic lesions. The contraindications for colonoscopy are the absence of signed consent or competent medical personnel, coagulopathy, suspected bowel perforation, neutropenia and suspected bowel ischemia^[4].

The level of sedation targeted and the sedative agents chosen depend on the characteristics of the endoscopic procedure including type and length of procedure, degree of invasiveness and the endoscopist experience. Additionally, the patient factors involved in the choice of sedation regimen include age, patients' physical status and existing medical conditions, patient anxiety, prior experience with endoscopic procedures, current use of opiates or other sedatives, need for patient cooperation, patient satisfaction and patient preferences.

PRE-PROCEDURAL ASSESSMENT

Prior to administration of intravenous sedation a patient history and physical examination designed to identify aspects that could

adversely affect the outcome of endoscopic sedation. Children should be routinely assessed by anesthesiologist in connection with the plan for sedation or general anesthesia before the procedure. The general health status of each patient must be evaluated. Physical examination should focus primarily on the upper airway, lungs, cardiovascular system and neurological status. Pre-sedation assessment appears to reduce the complications of deep sedation in children. Informed consent should be obtained from the appropriately designated parent or children.

The American Society of Anesthesiologist (ASA) scoring system is helpful in the description of physical status of a patient and is routinely used by the anesthesiologists. Many studies have documented the fact that sedation risk in children rises with increasing ASA physical status^[5,6]. Children relegated to ASA III and more status should have sedation/anesthesia performed by anesthesiologist even if only minimal sedation is planned. Specific high risk patient populations in which anesthesia consultation may be warranted including known respiratory or hemodynamic instability, obstructive sleep apnea, patients with anticipated difficult airway management, ASA physical status ≥ 4 , infants born <37 weeks and <60 weeks post-conception, history of sedation related adverse events, inadequate response to moderate sedation, and when sedation to the point of unresponsiveness is necessary for optimal effect as well as children with neuromuscular disease affecting respiratory or brain stem function.

The recommendations of the ASA advise the pediatric patients should be fasted for a minimum of 2 h after ingested clear liquids, fasting from breast milk for 4 h and from nonhuman milk and solids for 6 h before elective sedation^[7]. Fasting in emergency cases must be weighed against the necessity for the procedure and the risks of sedation.

PREPARING FOR COLONOSCOPY

Colonoscopy requires thorough cleansing of the large intestine for full visualization as well as the safe and effective completion of the procedure. Inadequate bowel preparation is responsible for up to one third of all incomplete colonoscopy procedures^[8]. Consequently, poor bowel preparation raises costs due to repeated procedures. Colonoscopy in pediatric population is relatively uncommon. There are no uniform protocols or national guidelines for colonoscopy preparation. Several regimens are available that are based either on lavage or cathartics. Both methods are subject to failure because they usually rely upon the cooperation of the children. Polyethylene glycol (PEG) is the most common bowel cleansing agent used in children. PEG 3350 solution was studied with a dose of 1.5 g/kg for 4 days before the procedure, with clear liquid diet on day 4^[9]. Other regimens are fleet phosphosoda 22.5 mL (<30 kg) or 45 mL (≥ 30 kg) in morning and evening and a clear liquid diet on the day before the procedure+, and senna syrup (8 mg/5 mL) 15 mL (5-12 years) or 30 mL (≥ 12 years) in morning and evening with a full liquid diet 2 days before and a clear liquid diet 1 day before procedure and one fleet enema on the morning of procedure^[11].

REQUIREMENT OF LABORATORY TESTS

There are controversial issues about the necessity of the laboratory tests among the children before the endoscopic procedures. The need of these tests depends on the invasiveness of procedure and comorbidity of chronic diseases of pediatric patients. Healthy children (ASA physical status I and II) should be able to be sedated without any laboratory tests before the procedure. For those children

with congenital defects or diseases and patients with coexisting severe systemic diseases, it is necessary to consider laboratory tests such as blood type, complete blood count, electrolytes and coagulation parameters.

SEDATION FOR COLONOSCOPY

The use of sedation for colonoscopy in pediatric population is undergoing changes both in the developed countries and in the developing countries like Thailand^[1,2,12,13]. The majority of gastrointestinal endoscopy in children is performed by using deep sedation or general anesthesia. Physiologically differences between pediatric and adult patients alter the risks for potentially serious complications during sedation. Routine oxygen administration has been advised because previous data suggest that a significant proportion of children develop oxygen desaturation during sedation for endoscopy^[14]. Administration of sedative drugs should be weight based and titrated by response, allowing adequate time between doses to assess effects and the need for additional medication. Increasingly, propofol, which can be given alone or in combination with other sedatives, administered by a dedicated anesthesiologist, is being used^[15].

PREMEDICATION

The aim of premedication is to achieve state of controlled peri-procedural emotions and behaviors among the child. Another effect of premedication is to cause amnesia, inhibiting unwanted reflexes, reduction of secretion in the airways, and elimination of pain to minimize the child's discomfort. Adequate preparation and the use of anxiolytic premedication are important issues. Additionally, non-pharmacological interventions could be an alternative to the use of sedative agents^[16]. However, the use of premedication for pediatric patients depends on the child's physical status and the anesthesiologist's preference.

PROCEDURAL SEDATION

Procedural sedation and analgesia (PSA) must provide a safe environment for the patient and the result must be effective control of pain, anxiety and movement. It also is intended to result in a depressed level of consciousness that allows the patient to maintain oxygenation and airway control independently. PSA encompasses a continuum of altered state of consciousness, varying from minimal sedation to deep sedation^[17].

Minimal sedation (anxiolysis)

Minimal sedation is a drug-induced state during which patients respond normally to verbal commands. Although cognitive function and physical coordination may be impaired, airway reflexes, ventilatory and cardiovascular functions are unaffected. Minimal sedation could be accurate and sufficient type of sedation for gastrointestinal endoscopic procedures performed in older children.

Moderate sedation (conscious sedation)

Moderate sedation is a drug-induced depression of consciousness during which patients respond purposefully to verbal commands, either alone or accompanied by light tactile stimulation. No interventions are required to maintain a patent airway, and spontaneous ventilation is adequate. Cardiovascular function is usually maintained. This type of sedation is usually performed for smaller and for older children.

Deep sedation

Deep sedation is a drug-induced depression of consciousness during which patients cannot be easily aroused but respond purposefully following repeated or painful stimulation. The ability to independently maintain ventilatory function may be impaired. Patients may require assistance in maintaining a patent airway, and spontaneous ventilation may be inadequate. Cardiovascular function is usually maintained.

MONITORING DURING COLONOSCOPY

The endoscopy room should be equipped with an oxygen supply, suction system, airway management equipment, resuscitation drugs and equipment, as well as cardiac monitor equipment including defibrillator. During colonoscopy, blood pressure and heart rate, electrocardiography, pulse oximeter, respiratory rate, consciousness and other clinical signs should be monitored. In addition, capnography also should be monitored during colonoscopy in pediatric patients under deep sedation. The capnography is a method of providing early warning for preventing postoperative respiratory depression^[18]. However, the cost of capnometer is relatively high. The developing countries have none or few capnometers, though this monitor is not routinely used. The presence of an anesthetic personnel or a qualified registered nurse to monitor the patient during the procedure is essential.

INTRA-PROCEDURAL MANAGEMENT

When sedative and analgesic medications are to be given to a pediatric patient, a clearly worded informed consent should be obtained. This consent should include a listing of the possible consequences of adverse drug reactions, allergic reactions and airway difficulties. Prior to undertaking sedation, the equipments that should be in place before starting a sedation are suction, oxygen, airway, pharmacy, monitors, and extra equipment such as defibrillator (SOAPME)^[5].

Midazolam

Midazolam is a shorting, water soluble benzodiazepine with anxiolytic, amnestic, sedative, muscle relaxant, and anticonvulsant properties. It is approved for many routes, including intravenous, oral and nasal. When administered in combination with other sedative drugs, midazolam is likely to result the loss of upper airway muscle tone with airway obstruction. Paradoxical agitation, ataxia, dystonia and diplopia are possible adverse effects associated with midazolam use. Initial intravenous dose of midazolam is 0.025-0.1 mg/kg and may repeat another dose, but the maximum recommended dose is 0.4-0.6 mg/kg.

Fentanyl

Fentanyl is a potent synthetic opioid with no intrinsic amnestic properties. It has a rapid onset, short duration of action, lack of direct of myocardial depressant effects, and absence of histamine release. Intravenous fentanyl can be easily and rapidly titrated for painful procedures^[19]. The combination of fentanyl and midazolam is a popular sedation regimen. Initial intravenous dose is 0.5-1.0 mcg/kg and may repeat every three minutes, but the maximum recommended dose is 2 mcg/kg.

Meperidine (pethidine)

Meperidine is a synthetic opioid and is metabolized in the liver by hydrolysis and N-demethylation. The metabolites of meperidine

are toxic to the central nervous system at high doses and in patients with renal impairment. Meperidine 0.5-1.0 mg/kg IV combined with midazolam 0.05-0.1 mg/kg IV provides effective sedation for gastrointestinal endoscopy. However, meperidine is not recommended for sedation in the emergency department^[20].

Propofol

Propofol is a phenol derivative with sedative, hypnotic and anesthetic properties. It has antiemetic, anxiolytic, hypnotic, amnestic and anesthetic properties, but it does not have analgesic effects. The disadvantage of propofol is its narrow therapeutic range and risk of inadvertent general anesthesia and that is the reason why it should be routinely administered by anesthesiologists. The most serious adverse effect of propofol is potent respiratory depression and apnea can occur suddenly. Propofol can also produce hypotension, although this effect is typically transient and of little clinical importance in healthy patients^[21]. Initial intravenous bolus dose of propofol is 1.0 mg/kg and is followed by 0.5 mg/kg, and the repeated dose is needed. Continuous intravenous infusion of propofol dose is 100-150 mcg/kg/min.

Today, physicians feel that propofol is the agent of choice for sedation for colonoscopy^[22,23]. Propofol guarantees an excellent level of procedural success, optimal timing and maximal patient comfort. Increasing demand for sedating and properly monitoring patients may not be met by anesthesiology departments. Currently, the use of propofol in this setting by non-anesthesiologists is controversial^[24,25]. Propofol-based sedation is safe and highly effective. Mild respiratory adverse events occur frequently and major complications may happen rarely, but adverse events do not occur more frequently compared to other sedation regimens^[26]. Kaddu *et al.*^[27] showed that deep sedation with propofol is an equivalent alternative for general anesthesia.

Ketamine

Ketamine is a phencyclidine derivative with dissociative sedative, analgesic and amnestic properties^[5]. Typically spontaneous respiration and airway reflexes are maintained although may not be totally normal. Ketamine generally causes an increase in heart rate, blood pressure, cardiac output, intracranial pressure, and intraocular pressure. Ketamine can induce salivation, and cholinergics have traditionally been coadministered. The emergence delirium associated with ketamine is less common in children, and of a much smaller magnitude than in adults. The single most severe adverse effect with ketamine sedation is laryngospasm. Ketamine, as a single agent, can be used at subhypnotic dose to achieve an analgesic effect. However, the addition of ketamine, midazolam or fentanyl to propofol-based sedation may have beneficial effects on sedative quality. Ketamine is clinically effective by a number of different routes. Intravenous dose of ketamine is 1-1.5 mg/kg, and may repeat dose every 10 min as needed.

Ketofol

Ketofol is a combination of ketamine and propofol. There is a synergistic effect between propofol and ketamine, and combination therapy allows the use of lower dose of both drugs, thereby decreasing the likelihood of side effects^[28]. If ketofol is used alone, it is adequate for minor procedures. The author commonly uses low dose ketamine in combination with low dose midazolam, opioid drug, and/or low dose of propofol^[29,30]. This combination technique produces stable hemodynamic effects, and can reduce the sedation-related adverse effects. The recommended preparation of ketofol for pediatric use is a 50 mg of ketamine and a 90 mg of propofol diluted

to 10 mL. This result in a concentration of 5 mg/mL ketamine and 9 mg/mL propofol and, of this solution, 0.005 mg/kg is recommended.

POST-PROCEDURAL MANAGEMENT

The recovery unit should be equipped with oxygen, suction, and equipment for tracheal intubation. Monitoring equipment including non-invasive blood pressure, pulse oximetry, electrocardiography and ventilation monitoring as well as resuscitation drugs and defibrillator should be available as well. If the patient is sleeping, the patient is placed in the lateral position. Drinks are allowed 1 hour after the end of the procedure^[31]. Standardized discharge criteria should be used to assess recovery from sedation. This practice is designed to facilitate safe and efficient discharge. Many recovery scales have been developed. One example is the Aldrete scoring system, which evaluates five parameters including respiration, oxygen saturation, blood pressure, consciousness, and activity. The status of the child should be documented at the time of discharge. All patients being discharged will receive verbal and written instructions outlining diet, activity, medication, and follow-up evaluation and receive contact information.

There has been a great deal of debate as to which drugs should be used in pediatric sedation, who should be administering drugs, and what type of setting is most appropriate. According to the demands for the provision of high quality pediatric sedation services have increased in the face of limited resources, nonanesthesiologist professionals have assumed an increasing responsibility for the provision of sedation to children. Many specialists including pediatricians, emergency medicine physicians and intensivists represent the majority of specialists providing sedation and analgesia to the children. Moderate sedation requires nonanesthesiologists to be credentialed. Further training and education are necessary to provide deep sedation. Strict adherence to published guidelines is essential to reducing the incidence of sedation-related adverse events. However, nonanesthesiologist personnel should be administered only for ASA I and II patients.

Several studies demonstrated that pediatric sedation for colonoscopy procedures by well-trained personnel were relatively safe and effective. The protocol of procedural sedation by nonanesthesiologists allowed a significant increase in the number of procedures performed with sedation and saved anesthesiology resources^[32,33]. No differences exist in the rates of major complications among different specialists were occurred. However, colonoscopy is an invasive procedure. It is associated with a variety of complications. The most important adverse events after sedation among children are loss of protective reflexes, upper airway obstruction, breathing disturbances, allergic reaction and cardiac arrest. Importantly, the credentialed individual must be able to rescue the patient from the next deeper level of sedation. Generally, the sedation provider should be able to provide basic life support.

In summary, sedation for colonoscopy in children is considered safe and effective. Several sedation regimens can be used for this procedure. Criteria such as risk factors, age, yield, potential complications, and the most effective sedation protocol must be discussed among the anesthesiologist and endoscopist. Increased awareness of the complications associated with sedation during procedure and involving the anesthesiologists in caring for these children may be optimal for safety. Proper patient preparation, endoscopic personnel and endoscopic unit, adequate monitoring as well as postprocedure management are imperative to successful sedation and colonoscopy.

REFERENCES

- 1 Amornyotin S, Aanpreung P, Prakanrattana U, Chalayonnavin W, Chatchawankitkul S, Srikureja W. Experience of intravenous sedation for pediatric gastrointestinal endoscopy in a large tertiary referral center in a developing country. *Pediatr Anesth* 2009; **19**: 784-791
- 2 Amornyotin S, Aanpreung P. Clinical effectiveness of an anesthesiologist-administered intravenous sedation outside of the main operating room for pediatric upper gastrointestinal endoscopy in Thailand. *Intern J Pediatr* 2010
- 3 Amornyotin S, Kongphlay S. Esophagogastroduodenoscopy procedure in sick pediatric patients: a comparison between deep sedation and general anesthesia technique. *J Anesth Clin Res* 2012; **3**: 185
- 4 American Society for Gastrointestinal Endoscopy. Modifications in endoscopic practice for pediatric patients. *Gastrointest Endosc* 2008; **67**: 1-9
- 5 Cote CJ, Wilson S, and Work Group on Sedation. Guidelines for monitoring and management of pediatric patients during and after sedation for diagnostic and therapeutic procedures: an update. *Pediatrics* 2006; **118**: 2587-2602
- 6 Krauss B, Green SM. Procedural sedation and analgesia in children. *Lancet* 2006; **367**: 766-780
- 7 American Society of Anesthesiologists. Practice Guidelines for Sedation and Analgesia by Non-anesthesiologists. *Anesthesiology* 2002; **96**: 1004-1017
- 8 Henry PO, Jenkins JT, Diamant RH. The impact of poor bowel preparation on colonoscopy: a prospective single center study of 10571 colonoscopies. *Colorectal Dis* 2007; **9**: 745-748
- 9 Pashankar DS, Uc A, Bishop WP. Polyethylene glycol 3350 without electrolytes: a new safe, effective, and palatable bowel preparation for colonoscopy in children. *J Pediatr* 2004; **144**: 358-362
- 10 El-Baba MF, Padilla M, Houston C, Madani S, Lin CH, Thomas R, Tolia V. A prospective study comparing oral sodium phosphate solution to a bowel cleansing preparation with nutrition food package in children. *J Pediatr Gastroenterol Nutr* 2006; **42**: 174-177
- 11 Trautwein AL, Vinitiski LA, Peck SN. Bowel preparation before colonoscopy in the pediatric patient: a randomized study. *Gastroenterol Nurs* 1996; **19**: 137-139
- 12 Chuang E, Zimmerman A, Neiswender KM, Liacouras CA. Sedation in pediatric endoscopy. *Gastrointest Endosc Clin N Am* 2001; **11**: 569-584
- 13 Meredith JR, Keefe KPO, Galwankar S. Pediatric procedural sedation and analgesia. *J Emerg Trauma Shock* 2008; **1**: 88-96
- 14 Thakkar K, El-Serag HB, Mattek N, Gilger MA. Complications of pediatric EGD: a 4-year experience in PEDS-CORI. *Gastrointest Endosc* 2007; **65**: 213-221
- 15 Elitsur Y, Blankenship P, Lawrence Z. Propofol sedation for endoscopic procedures in children. *Endoscopy* 2000; **32**: 788-791
- 16 Vagnoli L, Caprilli S, Messeri A. Parental presence, clowns or sedative premedication to treat preoperative anxiety in children: what could be the most promising option? *Pediatr Anesth* 2010; **20**: 937-943
- 17 Cohen LB, DeLegge MH, Aisenberg J, Brill JV, Inadomi JM, Kochman ML, Piorkowski JD Jr; AGA Institute. AGA Institute Review of Endoscopic Sedation. *Gastroenterology* 2007; **133**: 675-701
- 18 Hutchinson R, Rodriguez L. Capnography and respiratory depression. *Am J Nurs* 2008; **108**: 35-39
- 19 Pitetti RD, Singh S, Pierce MC. Safe and efficacious use of procedural sedation and analgesia by nonanesthesiologists in a pediatric emergency department. *Arch Pediatr Adolesc Med*

- 2003; **157**: 1090-1096
- 20 Bassett KE, Anderson JL, Pribble CG, Guenther E. Propofol for procedural sedation in children in the emergency department. *Ann Emerg Med* 2003; **42**: 773-782
- 21 Green SM, Krauss B. Propofol in emergency medicine: pushing the sedation frontier. *Ann Emerg Med* 2003; **42**: 792-797
- 22 Amornyotin S, Srikureja W, Pausawasdi N, Prakanrattana U, Kachintorn U. Intravenous sedation for gastrointestinal endoscopy in very elderly patients of Thailand. *Asian Biomed* 2011; **5**: 485-491
- 23 Luginbuhl M, Vuilleumier P, Schumacher P, Stuber F. Anesthesia or sedation for gastroenterologic endoscopies. *Curr Opin Anaesthesiol* 2009; **22**: 524-531
- 24 Tan G, Irwin MG. Recent advances in using propofol by non-anesthesiologists. *F 1000 Med Reports* 2010; **2**: 79
- 25 American Society for Gastrointestinal Endoscopy. Position statement: nonanesthesiologist administration propofol for GI endoscopy. *Gastrointest Endosc* 2009; **70**: 1053-1059
- 26 Larsen R, Galloway D, Wadera S, Kjar D, Hardy D, Mirkes C, Wick L, Pohl JF. Safety of propofol sedation for pediatric outpatient procedures. *Clin Pediatr (Phila)* 2009; **48**: 819-823
- 27 Kaddu R, Bhattacharya D, Metriyakool K, Thomas R, Tolia V. Propofol compared with general anesthesia for pediatric GI endoscopy: is propofol better? *Gastrointest Endosc* 2002; **55**: 27-32
- 28 Amornyotin S, Chalayonnawin W, Kongphlay S. Clinical efficacy of the combination of propofol and ketamine versus propofol alone for deep sedation for colonoscopy. *Gastrointest Endosc* 2011; **73**: AB 422
- 29 Amornyotin S, Chalayonnawin W, Kongphlay S. Assisted sedation for percutaneous endoscopic gastrostomy in sick patients in a developing country. *Gastroenterol Insights* 2010; **2**: 17-20
- 30 Amornyotin S, Chalayonnawin W, Kongphlay S. Propofol-based sedation does not increase rate of complication during percutaneous endoscopic gastrostomy procedure. *Gastroenterol Res Pract* 2011
- 31 Kim YJ. General considerations and updates in pediatric gastrointestinal diagnostic endoscopy. *Korean J Pediatr* 2010; **53**: 817-823
- 32 Barbi E, Gerarduzzi T, Marchetti F, Neri E, Verucci E, Bruno I, Martelossi S, Zanazzo G, Sarti A, Ventura A. Deep sedation with propofol by nonanesthesiologists. A prospective pediatric experience. *Arch Pediatr Adolesc Med* 2003; **157**: 1097-1103
- 33 van Beek EJA, Leroy PLJM. Safe and effective procedural sedation for gastrointestinal endoscopy in children. *J Pediatr Gastroenterol Nutr* 2012; **54**: 171-185

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