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Intravenous Sedation for Pediatric Gastrointestinal Endoscopy in a Developing Country

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1. Introduction

The field of pediatric sedation and analgesia has evolved over the past two decades. The growing number of pediatric gastrointestinal endoscopy procedures requiring sedation and analgesia are recognized even in developing countries. It is well accepted that children undergoing diagnostic and therapeutic gastrointestinal endoscopic procedures should receive sedation and/or anesthesia. Nevertheless, considerable practice variation prevails. The ability to provide safe and effective sedation and analgesia is an important skill for physicians involved in pediatric patients. Children are more prone to anxiety in the acute setting. 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.

Intravenous sedation for pediatric gastrointestinal endoscopic procedure is ubiquitous in any hospital that cares for children and depending on the institution and country. The developing countries have no their practice guidelines. The guidelines established by the American Academy of Pediatrics (AAP) (Cote et al., 2006), the American Society of Anesthesiologists (ASA, 2002) and the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) serve as the standard for institutional policy development in the area of pediatric intravenous sedation.

The guideline defines terms throughout and in particular:

Minimal sedation: a drug-induced state which patients respond normally to verbal commands.

Moderate sedation (conscious sedation): a drug-induced depression of consciousness which patients respond purposefully to verbal commands. Spontaneous ventilation is adequate. Cardiovascular function is usually maintained.

Deep sedation: a drug-induced depression of consciousness which patients can not be easily aroused but respond purposefully after repeated verbal or painful stimulation. Spontaneous ventilation may be inadequate. Cardiovascular function is usually maintained.

General anesthesia: a drug-induced loss of consciousness which patients are not arousable, even by painful stimulation. Patients often require assistance in maintaining a patent airway. Cardiovascular function may be impaired.

In this report, the author will seek to examine the role of anesthesiologists in determining the field of pediatric intravenous sedation, and the current status of intravenous sedation for pediatric gastrointestinal endoscopic procedures in Siriraj GI Endoscopy Center, Siriraj Hospital, Thailand. Additionally, this review is divided into three parts: 1. the pre-pediatric gastrointestinal endoscopic assessment period, 2. the intra-pediatric gastrointestinal endoscopic management period, and 3. the post-pediatric gastrointestinal endoscopy period.

2. Pre-pediatric gastrointestinal endoscopic assessment period

The general health status of each patient undergoing pediatric procedural intravenous sedation must be evaluated. A physical examination should focus primarily on the upper airway, lungs, cardiovascular system, and baseline neurological status. To aid in assessment risk, the American Society of Anesthesiologists (ASA) has developed a classification system for patients, which categorizes individuals on a general health basis. Several studies have documented the fact that sedation risk in children rises with increasing ASA physical status (Cote et al., 2006; Krauss & Green, 2006; Vespasiano et al., 2007). ASA physical status 1 and 2 are considered low risk patient populations. ASA physical status 3 and 4 are high risk patient populations. The specific high risk patient populations in which anesthesia consultation may be warranted including known respiratory or hemodynamic instability, obstructive sleep apnea, high risk airway management, ASA physical status ≥4, infants born <37 weeks and <60 weeks post conception, history of sedation related adverse events, and patients with neuromuscular disease affecting respiratory or brain stem function.

In this pre-assessment period, there are no differences in a routine practice between the developed countries and the developing countries. Additionally, the majority of intravenous sedation practices for pediatric gastrointestinal endoscopic procedures in the developing countries were sedated by anesthesiologists and/or anesthetic personnel in the operating room.

3. Intra-pediatric gastrointestinal endoscopic management period

Any time 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 intravenous sedation, there are some key pieces of equipment that must be in place. These equipments that should be in place before starting a sedation are suction, oxygen, airway, pharmacy, monitors, and extra equipment such as defibrillator (SOAPME) (Cote et al., 2006). In general, intravenous sedation for pediatric gastrointestinal endoscopic procedures is done by anesthesiologists or anesthetic personnel directly supervised by the anesthesiologist or anesthetic personnel.

In a developing country where pediatric endoscopy is performed at increasing rates, the majority of cases (as noted by anecdotal observation) are treated under general anesthesia in the operating room. At Siriraj Hospital, there is a dedicated endoscopy unit with dedicated anesthesia service. Over the last four years, 2006–2010, we performed most pediatric gastrointestinal endoscopic procedures with intravenous sedation technique. We followed the guidelines provided by the American Academy of Pediatrics (Cote et al., 2006) and American Society of Anesthesiologists standards (ASA, 2002). Our review of intravenous sedation practice in pediatric population showed that intravenous sedation can be done

safely with various sedative combinations with proper monitoring and anesthesiology service supervision.

Patient monitoring during the procedure should be included continuous monitoring of heart rate and oxygen saturation, and intermittent recording of respiratory rate and blood pressure. Additionally, capnography detects increasing levels of carbon dioxide before desaturation occurs and can detect early inadequately ventilation (Krauss & Green, 2000). However, the cost of capnometer is relatively high. The developing countries like Thailand have none or few capnometers, though this monitor is not routinely used. A sedative drug can only be considered safe after experience in hundreds or thousands of cases. Good protocols are important for the safety and success of the intravenous sedation technique. Depending on the procedure, pediatric intravenous sedation can involve monotherapy or combination therapy. Each regimen and administration of intravenous sedation must be carefully personalized for each patient. When administered, the drugs should be given as an appropriate initial dose with subsequent doses until titrated to effect. However, the most important factor is the judgement of the physician (ASA, 2002; Sury, 2004; Cote et al., 2006; Krauss & Green, 2006; Vespasiano et al., 2007; Meredith et al., 2008).

Common drug-receptor systems used by anesthesiologists in Thailand include the following:
1.   Opioid receptors: fentanyl, meperidine
2.   Gamma-aminobytyric acid (GABA) receptors: propofol
3.   Benzodiazepine receptors: midazolam
4.   N-methyl-D-aspartate (NMDA) receptors: ketamine

Sedation should be administered based on the patient's weight and titrated by response. Dosing requirements for individual patients may vary significantly based on the patient's psychosocial development and attention to the surrounding environment by the endoscopy team. Adequate time should be allowed between doses to assess sedation effects and determine the need for additional medication. For example, midazolam should be titrated to the effect with at least three minutes between doses, while fentanyl should have five minutes between doses. Higher doses of sedative/analgesic agents are frequently needed in preschool, school aged and preteen patients compared with those used in teenage children. The most common intravenous sedation regimen for pediatric gastrointestinal endoscopic procedure is the use of an opioid and a benzodiazepine combination to achieve analgesia and amnesia (Dar & Shah, 2010). Many safe regimens were reported. Consequently, anesthesiologist or the anesthetic personnel must exercise extreme caution while administering the intravenous sedation for pediatric gastrointestinal endoscopic procedure. The use of intravenous sedation drugs is reliability, efficacy and easy titration to achieve the end point. However, monitoring during the procedure is essential.

3.1 Analgesic drugs
3.1.1 Fentanyl
Fentanyl is a potent synthetic opioid with no intrinsic anxiolytic or amnestic properties. It has high lipid solubility allows for quick penetration of the blood-brain barrier, resulting in a very rapid onset of action (<1 minute) and short duration of action (30-45 minutes) (Nowicki & Vaughn, 2002; Dar & Shah, 2010). Fentanyl lacks of direct of myocardial depressant effects, and absence of histamine release, making it an excellent choice for intravenous sedation. Intravenous fentanyl can be easily and rapidly titrated for painful procedures (Kennedy et al., 1998; Pitetti et al., 2003). The combination of fentanyl and midazolam is a popular intravenous sedation regimen, with a safety profile when both

drugs are carefully titrated (Kennedy et al., 1998; Pena & Krauss, 1999; Pitetti et al., 2003). Fentanyl can cause respiratory depression and apnea, especially when combined with other sedatives or in infants less than 3 months of age (C.L. Algren & C.T. Algren, 1997). Fentanyl-induced bradycardia may need treatment with a vagolytic drug such as atropine. Chest wall and glottic rigidity has been observed with rapid administration of fentanyl. Safe intravenous administration therefore requires slow titration of 0.5-1.0 mcg/kg boluses, and may repeat every 3 minutes, but the maximum cumulative dose is 4 to 5 mcg/kg in one hour (Tolia et al., 2000).

3.1.2 Meperidine (Pethidine)

Meperidine is a synthetic opioid and has grown out of favor in past years. The metabolites of meperidine are toxic to the central nervous system at high doses and in patients with renal impairment. Meperidine has a long and favorable experience in intravenous sedation for pediatric gastrointestinal endoscopic procedure (Bahal-O'Mara et al., 1993). Meperidine 0.5-1.0 mg/kg i.v. combined with midazolam 0.05-0.1 mg/kg i.v. provides effective sedation for gastrointestinal endoscopy. However, meperidine is not recommended for intravenous sedation in the emergency department (Lewis & Stanley, 1999; Mace, 2004). Side effects of meperidine are respiratory depression, nausea, vomiting, and dysphoria (Goad & Webster, 1997). It causes less histamine release and urticaria than morphine (C.L. Algren & C.T. Algren, 1997). Fatal reactions have also occurred in patients taking monoamine oxidase inhibitors.

3.2 Sedative drugs
3.2.1 Propofol

Propofol is a phenol derivative with sedative, hypnotic and anesthetic properties. It has a rapid onset (< 1 minute), shorter duration of action, and rapid recovery. Its clinical effects are dose dependent. Propofol has antiemetic, anxiolytic, hypnotic, amnestic and anesthetic properties. However, it does not have analgesic effects. Propofol can be given to children in the settings of gastroenterology (Barbi et al., 2003; Amornyotin et al., 2009, 2010), emergency department (Bassett et al., 2003; Green & Krauss, 2003), and critical care series (Lowrie et al., 1998) with good efficacy, rapid recovery, and apparent safety. The most serious adverse effect of propofol is potent respiratory depression and apnea can occur suddenly. The respiratory depression rates vary extensively by the study (Green & Krauss, 2003). Propofol can also produce hypotension, although this effect is typically transient and of little clinical importance in healthy patients (Green & Krauss, 2003). Propofol is well known to be painful upon injection, the addition of lidocaine has been shown to decrease the incidence of pain during injection (Bassett et al., 2003).

Currently, most centers utilize an anesthesiologist or nurse anesthetist to administer propofol (Sury & Smith, 2008), although recently nurse administered and patient controlled dosing has been reported in adult patients. In our endoscopy center, propofol is also administered by an anesthesiologist or nurse anesthetist. Propofol provides equal or better control and more rapid recovery when compared with midazolam for sedation (O'Hare et al., 2001). 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. In my experience, I use the initial bolus dose of propofol and follow by the continuous intravenous technique. The continuous intravenous infusion of propofol dose is 100-150 mcg/kg/min. Majority of our patients received propofol in combination with other sedatives. Over the last decade, the use of propofol for endoscopic sedation has increased. It has gained wide acceptance among adult

gastroenterologist. The use of propofol in pediatric population has been shown to be safe, effective, and reliable (Balsells et al., 1997; Kaddu et al., 2002). The drug, now commonly used outside the operating room, has demonstrated an excellent safety profile, despite a narrow therapeutic window. Desirable properties of propofol for endoscopic procedures include ease of use, quick onset of action, and rapid metabolization leading to shorter recovery time (Aouad M.T. et al., 2008).

3.2.2 Midazolam

Midazolam is the drug most commonly used for sedation in children during procedures (Kennedy et al., 1998; Pena & Krauss, 1999). It is a shorting, water soluble benzodiazepine with anxiolytic, amnestic, sedative, muscle relaxant, and anticonvulsant properties. It is very widely used because of its more rapid onset of action and shorter duration of effect compared with diazepam (Tolia et al., 2000). Disadvantages of midazolam include transient hypotension and vomiting. Midazolam is approved for many routes, including intravenous, oral and nasal and is most useful for intravenous sedation. Because of greater clearance of midazolam in children, larger weight-adjusted dosages may be required in pediatric patients than in adult to achieve similar levels and duration of sedation (Gilger, 1993 & Tolia et al., 2000). The shorter clinical half-life of the drug necessitates additional boluses for longer or complicated procedures. Less midazolam is needed when fentanyl is administered than when meperidine is given with midazolam. 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. In our endoscopy center, we commonly use midazolam combined with low dose propofol and/or low dose fentanyl.

3.2.3 Ketamine

Ketamine is a phencyclidine derivative with dissociative sedative, analgesic and amnestic properties (Green & Krauss, 2000). It is one of the most sedative-analgesic agents and results in a number of desired clinical effects that are dose dependent (Krystal et al., 1994). Typically spontaneous respiration and airway reflexes are maintained although may not be totally normal. Neuropsychiatric effects of ketamine include visual hallucinations that may be accompanied by emergence phenomena and agitation. 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 single most severe adverse effect with ketamine sedation is laryngospasm. 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 minutes as needed. In Thailand, we commonly used low dose of ketamine, and combined with low dose of midazolam, opioid drug, and/or low dose of propofol (Amornyotin et al., 2009). This combination technique produces stable hemodynamic effects, and can reduce the sedation related adverse effects.

The ideal combination of sedative drugs for intravenous sedation in pediatric patients undergoing gastrointestinal endoscopic procedure is unknown. The drug combination provides synergistic action while lowering the doses of each agent. The combination regimen may be a superior sedation technique (Cohen et al., 2004; Van Natta & Rex, 2006). Our practice reflects this technique where many different combination regimens were used. Midazolam and fentanyl are the most common agents used in combination with propofol in this study. The next most common combination includes midazolam, fentanyl, ketamine, and propofol.

Cardiopulmonary complications account for more than half of the major complications during endoscopy (Lamireau et al., 1998) and are often related to hypoxia, especially in children less than 1-year old (Lamireau et al., 1998 & Lightdale et al., 2008). In a study by Barbi et al., using propofol in 811 children undergoing upper endoscopy, desaturation on supplemental oxygen is 3%, and major desaturation was noted in 0.7% of all the children. Additionally, a study by Yldzdas et al. demonstrated that the use propofol and midazolam/ fentanyl in 126 children who were randomly assigned to different sedation regimens had a 16.6% incidence of respiratory depression as shown by high end-tidal carbon dioxide (>50 mmHg). The higher incidence of respiratory depression reflected the better detection of respiratory depression by the use of end-tidal carbon dioxide. The adverse events in our clinical practice are comparable to those in the studies that did not use end-tidal carbon dioxide monitoring (Balsells et al., 1997; Malviya et al., 1997 & Barbi et al., 2006).

4. Post-pediatric gastrointestinal endoscopic period (Recovery and discharge)

Following sedation it is important that patient monitoring continue until the children are fully awake and ready for discharge. The recovery area should be equipped with oxygen, suction, and equipment for tracheal intubation. Monitoring equipment including non-invasive blood pressure, pulse oximetry, electrocardiography, and ventilation monitoring should be available as well. Patients should be discharged only when they have met specific criteria. The criteria for discharge should include:

1. stable vital signs
2. a return to the level of consciousness that is similar to the baseline for that patient
3. pain under control
4. adequate muscle strength to maintain a patent airway
5. speech and ambulation appropriate for age should return to pre-sedation level
6. nausea and/or vomiting should be controlled.

Patients who received reversal drugs such as naloxone or flumazenil may require longer periods of observation, because the half-life of the offending agent may exceed that of the reversal medication and lead to resedation. At the time of discharge, specific written and verbal instruction and information as well as the status of the child should be given to a parent, legal guardian or other responsible adult. Specific instructions should be given to the child's family instructing them what to do if the child should appear sedated or have any other medical problems. In the western countries, most of GIE procedures for children can be safely done with ambulatory setting. However, the majority of pediatric GIE procedures in eastern countries like Thailand are done with inpatient setting.

In summary, no method of intravenous sedation can be universally applied to all children requiring gastrointestinal endoscopic procedures. However, in a tertiary care teaching hospital in a developing country, intravenous sedation for pediatric gastrointestinal endoscopic procedures can be safely and effectively performed outside the operating room with a multi-drug sedation regimen utilizing anesthesiologists and anesthetic personnel with appropriate basic monitoring.

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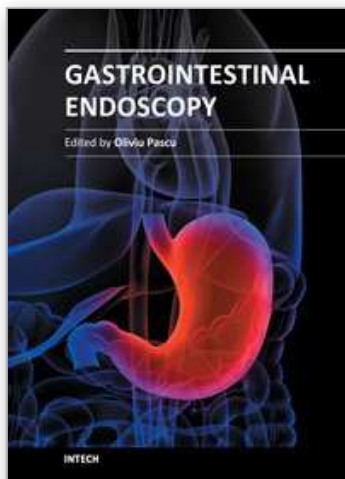
Gastrointestinal Endoscopy

Edited by Prof. Oliviu Pascu

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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