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Sedation and General Anaesthesia for Colonoscopy in Childhood

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1. Introduction

Fiberoptic colonoscopy was successfully introduced into paediatric practice several decades ago and has improved the detection and management of gastrointestinal diseases in children worldwide (El Mouzan et al, 2005). Since the early 1970's colonoscopy has become more useful and more advanced method for diagnosis and treatment in many large-bowel diseases in paediatric population (Steiner et al, 2006). This expansive development has also been possible thanks to the rapid development of anaesthetic techniques and new drugs. There are many indications for colonoscopy in children: diarrhea, hematochezia, unexplained rectal bleeding, abdominal pain, inflammatory bowel disease, polyposis syndrome, polypectomy, vascular ablation, dilation of stricture, foreign body removal, decompression. All reports have shown that this procedure could be safe and useful tool in children of all age groups only if it is based on good practice standards and experienced management, provided by both paediatric gastroenterologist and paediatric anaesthesiologist (Dillon et al, 1998).

Children are often difficult and non-cooperative patients. Due to the anatomical differences, when compare with adults, they need diagnostic specificity and ability to be examined by the paediatric endoscopist. His opinion and comfort during the procedure is a key for effective and satisfactory diagnostic or therapeutic procedure. On the other hand children are completely different group of patients with the higher risk of unpredictable events during invasive procedures being associated with the younger child is. Therefore they need paediatric anaesthesiologist to provide deep sedation or general anaesthesia. In some cases, conscious sedation should be also provided by anaesthesiologist if the child is extremely ill. Although paediatric colonoscopy is performed routinely in hospitals still the most important thing to remember to perform this procedure at least safely, reasonably quickly, and comfortably for the children (Strauss & Giest, 2003). They feel pain and discomfort connected with the overinsuflation of the bowel and heavy-handed instrumental technique. They are more sensitive to dehydration as a consequence of preoperative and preanaesthetic management and this could be reflected in cardiovascular and respiratory complications.

Finally, they can present different responses to the administered drugs that could complicate procedural and post-procedural course (Groot & Mulder, 2010).
Thus, conscious sedation, deep sedation, and general anaesthesia have been widely adopted in paediatric gastroenterological practice because the number of noninvasive and minimally invasive procedures performed in pediatric population has grown exponentially.
Evidenced Base Medicine (EBM) does not allow to answer which method is the best and could be recommended as a standard. To optimize the choice one should be considered three main aspects:

1. Ideal and excellent conditions for instrumental technique
2. Short recovery time
3. High level of satisfaction

The first point is assessed by the endoscopist and his opinion is the most important. Reduced total time for sedation and recovery of patients undergoing colonoscopy plays a special role as large number of procedures are undertaken as day-cases. The last aspect, the patients' satisfaction, is the most difficult to assess because of the age of child and the child is sleeping during the procedure. Additionally discomfort and pain is more with instrumental procedure than sedation or anaesthesia. When child is not able to give an answer, parents' or relatives' opinion will be important but also somewhat subjective.

2. Preanaesthetic management

Children should be routinely assessed by anaesthesiologist in connection with the plan for anaesthesia at least one day before sedation or general anaesthesia. In childrens' hospitals there should be a special room – a preoperative assessment clinic - where children and parents can get answers and explanations to their questions and where good conditions exist for comfortable examination of the child (Cavill & Kerr, 2009a). Equally important is getting the consent for anesthesia during this visit signed by each patient (in Poland over 16 years old) and/or parents or the legal representatives (Steiner et al, 2006, Malviya S, 2011).
Babies and younger children are not very often interested in this visit. They don't understand what happens nor the purpose of this interest. They may be running around the room, not accepting the examination and sometimes crying upon seeing doctor or nurse wearing an white. The person responsible for this first contact (in different countries are different systems e.g. doctors, register nurses) should be strongly experienced in the paediatric field.

2.1 Assessment of child's state of health

Children differ significantly from adults depending on their anatomy, physiology and pathophysiology the greater the difference the smaller child is. Therefore the ratio of complications in the perioperative period is higher than in adults, especially the risk of cardiac arrest. In paediatric anaesthetic cases the incidence of cardiac arrest is assessed to be approximately 1,4 in 10,000. Moreover, an overall mortality of 26% was reported following cardiac arrest (from current database of Paediatric Perioperative Cardiac Arrest (POCA) Registry (Bharti et al, 2009). Compared to adults, two predictors of mortality are the same: ASA physical status 3–5 and emergency surgery. Despite this, 33% of paediatric patients who suffered a cardiac arrest were ASA physical status 1–2. The most important causes are cardiovascular (37%), medication related (32%), respiratory (20%), equipment related (7%) and other (4%).

2.1.1 American Society of Anesthesiologists (ASA) scoring system

The ASA scoring system is helpful in the description of physical status of a patient and is routinely used by the anaesthesiologists all over the world (Saklad, 1941). Even though there is a correlation between ASA score and perioperative mortality it was never intended for risk mortality prediction (Table 1).

Code - ASA	Description
I	A normal healthy patient
II	A patient with mild systemic disease
II	A patient with severe systemic disease
IV	A patient with severe systemic disease that is a constant threat to life
V	A moribund patient who is not expected to survive without the operation
VI	A declared brain-dead patient whose organs are being removed for donor purpose

Table 1. ASA classification (modified)

Neonates are classified as ASA III and infants as ASA II due to their immature organs and significantly unpredictable responses to the drugs. When the endoscopist desires to perform both the colonoscopy and the sedation only by himself he should remember the statistics about the high risk found for paediatric patients even though ASA physical status was assessed for I or II.

2.1.2 Airway associated problems in children

Inadequate ventilation and difficult intubation are everyday hazards in paediatric anaesthesia and can cause higher morbidity and mortality in this group of patients. During the preoperative visit the ability to recognize "difficult to ventilate patient" is essential. Neonates, and smaller children have a unique anatomy of the larynx with the shape of funnel. Other important differences are a large tongue, a long epiglottis, and short and narrow trachea and bronchi which result in increased resistance. Intercostal muscles are very poorly developed and ventilation is therefore diaphragmatic and rate dependent, abdominal distension may cause splinting of the diaphragm (Berg, 2006). Some congenital defects of upper airways disturb normal ventilation (e.g. Pierre-Robin syndrome, Marfan's syndrome, mucopolysaccharidosis) (Inal, 2010).

Assessment should be based on the search for predictors of the difficult airways. A number of useful tests are available for clinical practice. The modified Mallampati scoring system can be applied among older children, who are able to open the mouths and protrude the tongues (Table 2)

Class	Comment
Class 1	Faucial pillars, soft palate, visible uvula
Class 2	Faucial pillars and soft palate visible, uvula masked by base of tongue
Class 3	Only soft palate visible
Class 4	Soft palate not visible

Table 2. Mallampati Scoring Scale

When the child is classified as class 3 or 4 the child should be assessed further using laryngoscopy to obtain a better view of things capable of causing higher risk of respiratory disturbances during deep sedation or general anaesthesia. (Cormack & Lehane, 1984)

Grade	Comment
Grade 1	Whole of glottis visible
Grade 2	Glottis incompletely visible
Grade 3	Epiglottis but not glottis visible
Grade 4	Epiglottis not visible

Table 3. Laryngoscopy Scoring

The most important thing to remember is that combination of sedatives and opioid analgesics decrease the ability to sustain sufficient ventilation, as worse as concomitant defects.

Airway obstruction (another adverse event) should be distinguished from the respiratory depression. Upper airway obstruction in paediatric patients arises from both anatomical structures and laryngospasm. The latter one results from the closure or spasm of the glottic muscles including the false and true vocal cords. This state could be very dangerous during procedural and deep sedation in young children when secretions from upper airway and a impaired cough irritate the larynx and triggered the spasm (Becker & Haas, 2007).

2.2 Requirement laboratory tests

There are many different opinions about the necessity of the laboratory tests among the children before medical procedures. The range of these tests depends on the invasiveness of medical or diagnostic procedure on the one hand and comorbidity of chronic diseases on the other. Healthy children (ASA I and II) should be able to be sedated or receive anaesthesia without any lab tests if the gastroenterologist doesn't see any unusual risk factors from the bowel disease e.g. unexplained bowel bleeding, diarrhea or inflammation. If he does, it is necessary to collect venous blood and check at least blood type, CBC, electrolytes, coagulation parameters before the procedure. For those children with congenital defects or diseases and coexisting severe systemic diseases it is necessary to consider additional laboratory tests and/or to send the child to proper consultant.

2.3 Exclusion criteria

Contraindications for sedation or anaesthesia for elective procedures include the presence of or contact with patients with contagious diseases (postpone procedure for the intubation period, usually 2 to 3 weeks), abnormalities in the physical examination or laboratory tests e.g. productive cough, purulent chest or nasal secretions, pyrexia or signs of viraemia. Anaesthesia in the presence of upper respiratory tracts infection is associated with a higher risk of excess secretions, airway obstruction, laryngospasm and bronchospasm. Children just inoculated (before 3rd day after vaccination containing killed and 3rd week after vaccines with live, attenuated microorganisms) should not be electively sedated or anaesthetized. Vaccines often stimulate the immune system to react as if there were a real infection. A child found to be post viral infection, afebrile, and with no chest signs is probably fit for the procedure even if he has a runny nose (Berg, 2006).

2.4 Feeding before the procedure

Before having a colonoscopy, the bowel needs to be completely empty. This requirement is helpful for anaesthesia because every patient before sedation or general anaesthesia needs to be fasting to perform anaesthesia safely and comfortably. In the last decade the idea of a shorter fasting is preferred among the paediatric and adult anaesthesiologist. Prolong fasting doesn't decrease the risk of gastric aspiration even though it helps to minimize the volume of gastric fluid up to 0.4 ml/kg but there is no reduction in gastric pH which is closed to 2.5 (Royal College of Nursing, 2005). In small children the rate of gastric emptying after feeding breast milk is about 25 minutes while that after the administration of formula compound is 50 minutes. For this reason minimally safe time from the breast milk feeding is 4 hours and for artificial feeding mixtures and solid foods - 6 hours. If the child needs hydration, up to 2 hours before procedure is possible to give clear fluids including water, apple juice, weak tea. Children stratified to a high-risk group of regurgitation are not allowed to be fed 6 (or even 8 hours) regardless of the type of the food (Table 4).
Children with diagnosed chronic disease could continue the most of their medications as usual.

	No risk of gastric aspiration	High risk of gastric aspiration
Clear fluid	2 hours	6 (8) hours
Breast milk	4 hours	6 (8) hours
Formula/cow's milk, solid food	6 hours	6 (8) hours

Table 4. Restrictions of feeding before sedation or anaesthesia in children

2.5 Premedication

The aim of premedication is to achieve state of controlled perioperative emotions and behaviors among the child. For children, any medical procedure can be very distressing and may lead to a lack of cooperation and refusal (Machotta, 2010). Knowledge about the reasons of this behavior is important to develop strategies and techniques to minimize preoperative stress and fear. Another desired effect of premedication is to cause amnesia, especially in the group of patients undergoing colonoscopic procedure, often repeatedly. Additionally, premedication could be helpful in inhibiting unwanted vegetative reflexes and reduction of the secretion of saliva and mucus in the airways, so typical and characteristic for pediatric population under 5-7 years old. The last indication for specific premedication is the elimination of pain accompanying the disease to minimize child's discomfort. Considering all these aspects, adequate preparation and the use of anxiolytic premedication are important modalities. Non-pharmacological interventions are interesting and could be an alternative to the use of sedative drugs in the future (Vagnoli et al, 2010)
In many cases parental presence could be helpful, even during the initiation of sedation or the induction of general anesthesia. The enthusiasts of the use of psychological methods try to introduce completely modern methods including even the presence of a clown in the preoperative room (Vagnoli et al., 2010). They achieved a significantly better effect when compared to parental presence or the influence of midazolam. In many hospitals this practice is not common for not only medical but also organizational and administrative reasons.

The best-documented practice for premedication of children for minor procedures seems to be the pharmacological method with midazolam (Kentrup et al, 1994, Isik et al, 2010).

2.5.1 Midazolam

Midazolam (described in 3.1.1) is indicated for premedication because it produces amnesia, anxiolysis and sedation. Oral administration is a favorite choice for premedication in children with the dose of 0.5 – 0.75 mg/kg given 30 minutes before the procedure but the effect is not always predictable (Robinson, 2000). Recently for smaller children (up to 30 kg of body weight) a syrup can be prepared for use by the hospital pharmacy department to avoid the use of intravenous route. The total volume of this mixture is limited to the 6 ml. Older children willingly use tablets. Oral midazolam is useful prior to planned intravenous sedation and general anaesthesia but does not give the prolonged depression of consciousness (Baygin et al, 2010, Kazak et al, 2010, Kulikov et al, 2010)

2.5.2 Clonidine

Clonidine is a partial agonist of central and peripheral alfa-2 adrenoreceptors and is a central imidazole receptor agonist. It also effects alfa-1 receptors (alfa1:alfa2 > 200:1). It is a known antihypertensive agent but with its sedative and analgesic effects potentiates volatile anaesthetic agents and decreases intraoperative requiments for propofol, although recovery time may be prolonged. It has a synergistic analgesic effect with opioids (Thompson, 2007). Oral clonidine premedication in dose of 4 – 5 mcg/kg has been shown to reduce the incidence of sevoflurane induced emergence agitation. (Tazeroualti et al, 2007). It also attenuates reflex sympathetic responses and may improve cardiovascular stability during anaesthesia (Cao et al, 2011).

2.5.3 Dexmedetomidine

Dexmedetomidine, an imidazole compound, is the pharmacologically active dextroisomer of medetomidyne and is the most selective central alfa-2 adenoreceptor agonist available clinically. This agonist has eight times higher affinity for the alfa-2 adenoreceptor than clonidine. It offers beneficial pharmacological properties, provides dose-dependent sedation, analgesia, sympatholysis and anxiolysis without significant respiratory depression (Goksu et al., 2008). Like clonidine, dexmedetomidine reduces occurrence of sevoflurane emergence agitation in a dose of 2.5 mcg/kg (Ozcengis, 2011). Both agents also can be administered intranasally for premedication in doses of 0.5-1 mcg/kg for dexmedetomidine and 2-4 mcg/kg for clonidine(Yuen, 2008; Basker, 2009).
Clonidine and dexmedetomidine preoperatively have similar levels of anxiety and sedation postoperatively as midazolam. However, children given alpha-2 agonists had less perioperative sympathetic stimulation and less postoperative pain than those given midazolam (Ali & El Ghoneimy, 2010, Al-Zaben, 2010, Dere et al, 2010, Schmidt, 2007).

3. Procedural sedation

Procedural sedation and analgesia (PSA) is intended to result in a depressed level of consciousness that allows the patient to maintain oxygenation and airway control independently. It is divided into two types: minimal sedation and conscious sedation.

3.1 Minimal sedation (anxiolysis)

Minimal sedation could be accurate and sufficient type of sedation for gastrointestinal procedures performed in older children. They are able to respond to verbal stimulation normally, but cognitive function and coordination may be impaired. What is most important is that ventilatory and cardiovascular functions are unaffected.

3.2 Conscious sedation (moderate sedation)

This type of sedation is usually performed for smaller and for older children and the depression of consciousness is drug-induced. Conscious sedation also commonly known as "moderate sedation" means that patient retains the ability to respond to vocal and light touch commands at any time during the sedation. Usually the circulatory system is not disturbed. Additionally patients have to be able to breathe spontaneously and protect their own airway. This last condition is extremely difficult to achieve in babies and smaller children because of specific anatomy and unpredictable response to drugs. In this group of patients intravenous administration of hypnotic drugs could provoke depression of spontaneous breathing and result in the need for manual or automatic ventilation via facial mask. This type of sedation could very often change from "moderate" to "deep" without clear symptoms and therefore requires the presence and expertise of an experienced pediatric anesthesiologist.

Some authors suggest that intravenous procedural sedation can be administered by the endoscopist, who both administers the sedation drug and performs the procedure. Of course this can only be done when qualified nurse helps the doctor monitor the patient's state of consciousness and vital signs. This method seems to be safe in the endoscopist's hands when restricted to ASA I and ASA II patients. Children relegated to ASA III and more status should have anaesthesia performed by a pediatric anaesthesiologist even if only minimal procedural sedation is planned (Hansen et al, 2003, Heuss et al, 2003, Lee et al, 2003). Other authors, highly experienced in paediatric anaesthesiology are opposed to idea "sedationist-operator". They claim the best and the safest method of sedation for children is to have it performed by an anesthesiologist who is highly experienced and understands the differences of paediatric population.

3.3 Drug regimens

Pharmacologic regimens that ensure safe, effective and efficient sedation for all paediatric patients would be ideal but are not always achievable. Those used should act predictably and rapidly and allow the anaesthesiologist to induce the desired level of sedation necessary for the procedure being performed. After the procedure, the drugs should allow the child to awaken quickly and they should not prolong the recovery time.

Various drugs are available to provide procedural sedation. Midazolam either alone or in combination with an opioid analgesic is commonly selected for procedural sedation. Combining use of a benzodiazepine and an opiate may be preferable for longer procedures but increases the risk respiratory and circulatory depression. Specific reversal agents for opioids (naloxone) and benzodiazepines (flumazenil) must be available during the procedure.

3.3.1 Midazolam

The effect of midazolam as a short acting benzodiazepine (in children half-life 2.5-4 hours) is controlled, reversible and produces light sedation, anxiolysis, and amnesia. Midazolam is

characterized by a relatively high volume of distribution (V_d) compared with other benzodiazepines because of its lipophilicity. In obese patients the activity could be increased from 2.7 hours to 8.4 hours. Midazolam is cleared by hepatic hydroxylation to 1-hydroxymidazolam (which has about 10% of the pharmacologic activity as parent compound).

Age	Administration route			Comment
	Intravenous	Rectal	Oral	
Up to 6 month	0.04 – 0.1 mg/kg b.w.	-	-	-
6 month–5 year	0.05 – 0.1 mg/kg	0.35 – 0.45 mg/kg	0.5 mg/kg	Total dose 6 mg/kg/d
5 – 12 year	0.025 – 0.05 mg/kg	0.35 – 0.45 mg/kg	0.5 mg/kg	Total dose 0.4 mg/kg/d; max 10 mg/d
5 – 12 year	0.025 – 0.05 mg/kg	0.35 – 0.45 mg/kg	0.5 mg/kg	Total dose 0.4 mg/kg/d; max 10 mg/d
12 -18 year	2.5 mg	0.35 – 0.45 mg/kg	0.5 mg/kg	i.v. bolus 1 mg; Total dose 10 mg
	1 – 1.5 mg			i.v. bolus 1 mg; Total dose 3.5 mg

Table 5. Midazolam dosing for procedural sedation in children.

Intravenous administration is the best way in this group of patients but sometimes oral, rectal and possibly nasal method might be equally as good for colonoscopy as well as other procedures (Wood, 2011). The most important thing to consider is the route of the administration of the drug to the child. Dosing of midazolam depends very strictly on the age and body weight of patient.
Intravenous doses of midazolam should be titrated to effect, especially in neonates and small babies, to achieve a desirable level of sedation and prevent inadvertent and deeper sedation (Robinson, 2000).

3.3.2 Other benzodiazepines

Diazepam has an extremely long half-life (0.8-2.25 day) especially in neonates and babies but also in obese patients (3.9 day and 3.29 day). Additionally, its active metabolites have long half-lives (*N*–desmethyldiazepam, nordiazepam). Lorazepam is another benzodiazepine that may be used for mild-to-moderate sedation; its limitation is onset of action up to 15-20 minutes after administration. The duration of action of lorazepam is longer (6-8 hours) than that of midazolam (30-60 min).

3.3.3 Other sedative drugs

In the literature there are also proposals for the use of other sedatives (e.g. etomidate, propofol or ketamine) for procedural sedation. These drugs are registered as anaesthetic drugs, not sedative, so according to the strict recommendations of the Food and Drug Administration (FDA) and The Helsinki Declaration on Patient Safety in Anaesthesiology 2010 are not allowed for procedural "sedation". (Mellin-Olsen et al, 2010)

Given the above specific conditions midazolam is the only single drug that can be used by the non-anaesthesiologists for procedural sedation.

3.3.4 Analgesic opioids

Analgesic opioids (described in 4.1.4) should be added when more painful colonoscopy is planned. Reducing the dose of opioids of about 50% is recommended because of the accumulation of side effects, especially depression of spontaneous ventilation.

3.4 Indications and contraindications for procedural sedation in children

Children are sometimes a major challenge for doctors and nurses. On the other side is necessary to understand their immaturity and lack of experience to accept fear, pain or disconnection from parents.

3.4.1 Indications for conscious sedation in children

Indications in the paediatric population differ from those among adults. They could be divided into two groups depending on the side of interest: patient and doctor.

Indication of the patient	Indication of the doctor
Unexplained fear	Babies and small children
Unaccepted discomfort	Non-cooperative children
Claustrophobia	Diagnostic and therapeutic procedures
Prolonged and repeated procedures	associated with pain

Table 6. Indications for conscious sedation during colonoscopy in children

3.4.2 Contraindications for procedural sedation in children

Contraindications for procedural sedation, whether performed by an anaesthesiologist or by non-anaesthesiologist are following:

- Congenital defects of respiratory system
- Acute respiratory insufficiency
- Persistent respiratory insufficiency
- Congenital Central Hypoventilation Syndrome (CCHS)
- Important circulatory insufficiency
- Neuromuscular diseases
- Impaired or loss of consciousness in the history
- Child too excitable, even after the earlier application sedatives
- Child with behavioral disorders
- Lack of agreement of child and/or parents and/or legal representatives

Additionally special conditions for performing conscious sedation should be met in the following general situations:

- Neonates, particularly preterm birth neonates, especially with regard to individual susceptibility to depressive influence of sedatives on respiratory depression
- Children below 1 year and 5 year, with regard to higher risk complications and adverse events after overdosing of drugs and/or insufficient sedation
- Renal insufficiency
- Liver insufficiency

3.5 Complications of procedural sedation

Factors that increase the risk of complications during conscious sedation in children are: age below 12 months and coexisting congenital and/or chronic diseases.
The most important adverse events after conscious sedation among children are:

- Loss of protective reflexes of the upper respiratory tract
- Closure and upper airway obstruction
- Allergic reaction
- Breathing disturbances
- Cardiac arrest

3.6 Equipment and supplies

The place use to perform colonoscopy under procedural sedation should be equipped with an oxygen supply, a suction system, airway management equipment, resuscitation medications and equipment, intravenous accesses equipment, cardiac monitor equipment and a defibrillator.
Monitoring. All the time of performing procedure should be monitored ECG, pulse oximeter, respiratory rate, systemic blood pressure and other clinical sign such skin color.
The state of unconsciousness should be regularly assessed from the beginning to the end of sedation and this data be documented in the chart. In paediatric practice the most common used scale is Ramsay sedation scale.

Score	Response
1	Anxious or restless or both
2	Cooperative, orientated and tranquil
3	Responding to commands
4	Brisk response to stimulus
5	Sluggish response to stimulus
6	No response to stimulus

Table 7. Ramsay Sedation Scale

3.7 Recovery of the child after procedural sedation

Procedural sedation can be successfully performed for many interventional or diagnostic colonoscopy procedures in children. It should be provided by well-trained and credentialed professionals at all the times.
After successfully completing procedural sedation the child should breathe spontaneously, have throat reflexes present, be able to cough, and to adequately maintain an airway. Depending on the age of the child, child should sit and talk, and in this state may be given to parents.

4. Deep sedation

Deep sedation is a very good alternative for painful colonoscopy. Depression of consciousness is drug-induced but much deeper than in procedural sedation. The patient is not easily arousable but can respond following repeated or painful stimulation. Spontaneous ventilation may be inadequate and the patient may require assistance in

maintaining a patent airway. Independent ventilatory function is rather impaired while cardiovascular hemostasis is usually properly maintained.
Deep sedation is indicated for possibly painful colonoscopies, therapeutic examinations and those more invasive examinations, especially when it is essential to immobilize the patient. The most discussed dilemma is how to provide deep sedation. The first method is based rather on deeper sedation rather than analgesia and to limit adverse events by using high doses of opioid analgesic. The second method involves analgesia even at the expense of less hypnosis. The truth is that the compilation of sedative and analgesic agents varies slightly when these agents are used in children, especially younger than 1 year, but much existing data suggest more variability in choices when the child is older than 7 years (Patel et al, 2009).

4.1 Drug regimens

Drugs should be administered intravenously. It is important to use small loading doses and to titrate the dosage because of the narrow margin of their safety. For this reason they should not be used by the non-anaesthesiologist according to the restrictions imposed by the FDA and The Helsinki Declaration on Patient Safety. If they are, the provider should be skilled in airway management and resuscitation, and usage should depend upon regional statutes. The most important anaesthetic for this type of procedure such colonoscopy is propofol.

4.1.1 Propofol

Propofol (alkyl phenol) is a short-acting anaesthetic characterized by both rapid onset of action (within one arm-brain circulation time) and short recovery time. Propofol causes dose-dependent cortical depression within 30 seconds from the beginning of administration, mostly without epileptiform activity, although larger doses could provoke excitatory movements (Eer et al, 2009). The incidence of excitation, cough and hiccup are similar to those of thiopental. In contrast to barbiturates, propofol attenuates laryngeal reflexes, facilitating laryngeal mask insertion or intubation. By the way of decreased responsiveness to CO2, propofol is respiratory depressant, especially when used in conjunction with opioid analgesics (when more than 50-70% of children will need ventilatory support). Its influence on the vascular system and heart is variable but often there is a mild cardiodepressant effect. Propofol is metabolized by the pathway of glucuronidation in the liver and removed by the kidney (88%) and the digestive system (2%).
Te newest lipid formulations of this agent limit the pain sometimes experienced during intravenous administration making propofol closed to the “ideal drug” for paediatric sedation.
One important difference from other intravenous and inhaled anaesthetics is its antiemetic effect, a desired effect in gastroenterological group of patients (Leon et al, 2011).
Effective deep sedation could be achieved by a single dose method as well as continuous infusion with recovery time independent to the duration of sedation (10-20 minutes after discontinuation).
The disadvantage of propofol is its narrow therapeutic range (high rates of hypoxia and hypotension) and risk of inadvertent general anesthesia and that is the reason why it should be routinely administered by anesthesiologists. Only this strategy allow to properly control of the level of sedation and reduced recovery time (Lightdale, 2004).

The usual standard dose of propofol used for sedation for older children is 0,5-1,5 mg/kg while children younger than 8 years should be sedated with higher doses e.g. 1,5 – 3,0 mg/kg. The best effect is achieved when continuous infusion is planned, of course keeping in mind age differences in dosing.

4.1.2 Other anaesthetic drugs

The choice of anaesthetic drug is in the hands of anaesthesiologist based on the status of patient and predictive duration of and type of colonoscopy.

4.1.2.1 Benzodiazepines

Benzodiazepines are highly lipid-soluble agents and can cross the blood-brain barrier readily. When used intravenously the onset of their effect usually takes longer than one arm-brain circulation time. Depending on their lipophilicity they have long a long persistence. These characteristics limit the usage of this group of drugs for deep sedation.

4.1.2.2 Barbiturates

Sodium thiopental is the most commonly used thiobarbiturate that induces anaesthesia rapidly within one arm-brain circulation and maintain longer than propofol. Its main limitation is its cardiodepressant effect with decreased cardiac output and blood pressure. Respiratory depression as a result of reduced CO2 response is deteriorated by laryngeal spasm and bronchoconstriction. The other limitation is its prolonged half-life depending on the total dosage which influences recovery time.

4.1.2.3 Ketamine

Ketamine is a derivative of phencyclidine and cyclohexamine and as a non-competitive antagonist of the NMDA receptors it is responsible for dissociative anaesthesia and analgesia. This last advantage allows one to not have to use opioids and in thus decreases the risk of respiratory depression while maintaining analgesia.
Ketamine is slow-onset anaesthetic with an effect within 1 minute after intravenous administration and a duration of action much longer than other newer agents. In addition the dissociative influence of this agent on the brain possibly bringing about hallucinations, diplopia, and temporary blindness limits its usefulness in short procedures (less than 1 hour) such as colonoscopy even these symptoms are not that prevalent among children (Gilger et al., 2004)

4.1.2.4 Etomidate

Etomidate is an imidazole characterized by rapid induction with one arm-brain circulation time and simultaneously long duration of action. In children the main contraindication of this agent is excitatory phenomenon, epileptic activity, respiratory depression, a relatively higher risk of emesis and commonly, pain at the injection site (Evered, 2003).

4.1.3 Inhaled anesthetic

Sevoflurane halogenated ether has been available for clinical use since 1990. This volatile anaesthetic agent remains popular both for induction and maintenance of anaesthesia and sedation. It has low blood/gas and oil/gas solubility. This produces a more rapid response to changes in inhaled concentration, and speedier induction and recovery. Intracranial pressure is increased but minimally at less than 1 MAC (minimal alveolar concentration). Sevoflurane produces anaesthesia and sedation without analgesia and epileptogenic spikes,

decreases arterial pressure by reducing systemic vascular resistance with little effect on cardiac output until higher doses are used, and it lowers the heart rate and therefore helps to reduce myocardial oxygen consumption. This agent reduces tidal volume, respiratory rate and smooth muscle tone of the bronchi, and it is not irritant to the upper respiratory tract. Most sevoflurane is eliminated via the lungs, with 5% of the absorbed dose being metabolized by the liver. It can have toxic effect on the kidneys, liver and brain (Mushambi & Smith, 2007, Smith, 2008). The use of sevoflurane in paediatric patients which would enable rapid recovery is complicated by the frequent occurrence of emergence agitation, particularly with high concentration over 6 vol% with spontaneous breathing and over 5 vol% when ventilated mechanically (Ganzberg et al, 1999, Khattab, 2010)

4.1.4 Opiods

The following opioids (remifentanil, alfentanil and fentanil) are commonly used for induction and the maintenance of anaesthesia for endoscopic procedures (Colvin, 2007). Morphine is used additionally to maintain analgesia in the postoperative period.

4.1.4.1 Remifentanil

Remifentanil hydrochloride is a mu-receptor opioid agonist and is currently the shortest-acting opioid. The onset and peak effect is rapid and the duration of action is short (5 – 10 minutes). Therefore for longer action remifentanil should be administered continuously. There is a lack of drug accumulation even after prolonged infusions.

Remifentanil is indicated for intravenous administration during induction of anaesthesia with the infusion rate of 0.5 to 1 mcg/kg/min together with an intravenous or volatile agent. During the maintenance of anaesthesia the infusion rate may vary in accordance with the dosing guidelines. For paediatric patients aged 1 to 12 years continuous infusion of 0.25 mcg/kg/min (infusion dose range 0.05 – 1.3 mcg/kg/min) with sevoflurane (0.3 – 1.5 MAC) or isoflurane (0.4 – 1.5 MAC) is recommended.

Nonspecific blood and tissue esterase metabolizes remifentanil rapidly by hydrolysis.

Pseudocholinesterase plays no special role so if atypical plasma cholinesterase is present remifentanil's duration of action remains normal. The effects and side effects are dose dependent. After administration over 60 seconds a rapid and slower distribution half-life are 1 and 6 minutes respectively. A terminal elimination half-life lasts 10 - 20 minutes. Renal and liver insufficiencies do not affect remifentanil's pharmacokinetics (Toklu et al, 2009). Side effects, mostly dose-dependent are hypotension and bradycardia, respiratory depression, and skeletal muscle rigidity (including chest wall rigidity).

4.1.4.2 Alfentanil hydrochloride

Alfentanil hydrochloride is a an OP3 mu-opioid agonist which is ultra-short-acting (5 - 10 minutes). The onset of action is immediate (1 - 2 minutes). Administrated at doses of 8 - 40 mcg/kg it is excellent for procedures lasting up to 30 minutes e.g. colonoscopy. The recovery time is comparable to that observed with equipotent fentanil dosages. For children under 12 years of age it is not recommended.

Intravenous administration of a dose of 5 mcg/kg provides analgesia for the conscious but sedated patient; doses of 105 mcg/kg produce hypnosis; and induction of anesthesia requires doses 50-150 mcg/kg. Induction with alfentanil should be administered slowly (over 3 minutes) due to the danger of loss of vascular tone and hypotension. Fluid replacement prior to induction with this agent is important. Maintenance of anaesthesia (if

the procedure lasts up to 60 minutes) is carried out with a dose of 50 mcg/kg, but alternatively, continuous infusion 0.5 – 3 mcg/kg/min is acceptable. The infusion should be discontinued at least 10-15 minutes prior to the end of the procedure. In obese patients the dose of alfentanil should be determined on the basis of lean body weight.
After administration a rapid and slower distribution half-life are 1 and 14 minutes respectively. Terminal elimination half-life lasts 90 - 111 minutes. The volume of distribution is 0.4-1 L/kg, which is 4 – 10 times smaller than those for fentanil. The liver is responsible for major biotransformation. Metabolites are eliminated mostly by urinary excretion.
The important side effects consists of hypotension, secondary to vasodilation and bradycardia, respiratory depression, skeletal muscle rigidity (dose and speed dependent).

4.1.4.3 Fentanil

Fentanil is a strong mu-opioid agonist with a rapid onset (2 – 3 minutes) and short duration of action (20 – 60 minutes). Fentanil is 100 times more potent than morphine (100 mcg of fentanil approximately equals 10 mg of morphine). Because of its high lipophilicity it penetrates easily to the central nervous system causing the rapid onset of action. Due to its high lipophilicity there is a danger of possible redistribution of fentanil. Hemodynamics are stable after administration of fentanil, which makes this drug useful in cardiovascular diseases.
Fentanil could be administered orally, subcutaneously, or intravenously. For induction of anaesthesia doses of 0.5 – 1 mcg/kg (up to 5 mcg/kg) together with a intravenous or volatile agent are recommended and during maintenance of anaesthesia 1 – 4 mcg/kg according to a need.
The drug's large volume of distribution (3.5 – 5.9 L/kg) is responsible for relatively long half-life. The elimination half-life vary from 3.1 – 7.9 hours. There is a danger of possible redistribution of fentanil due to its lipophilicity (biphasic depression of ventilation). The liver is responsible for its metabolism. Side effects are as follows: respiratory depression, skeletal muscle rigidity (particularly if large doses are administered rapidly), and stimulation of parasympathetic system.

4.1.4.4. Morphine sulfate

Morphine sulfate is an important alkaloid of opium, a pure opioid agonist. It is mu-opioid agonist but at higher doses interacts with other opioid receptors. The onset of action after intravenous administration is 5 – 10 minutes, the duration of action 2 – 4 hours. The lipid solubility and degree of ionization are crucial in the onset and duration of analgesia as well as the effects of the central nervous system. The additional hydroxyl group on the molecule of morphine (pH 7.4) makes the molecule of morphine water soluble, more than other clinically used opioids. The most therapeutic action of morphine is analgesia but there are some others like euphoria and anxiolysis.
Administration intravenously requires average doses of 0.1 mg/kg and continuous infusion 20-25 mcg/kg/h, while intramusculary or subcutaneously doses of 0.15-0.2 mg/kg should be sufficient.
After intravenous administration the volume of distribution ranges from 1.0 to 4.7 L/kg. The terminal half-life vary from 1.5 – 4.5 hours. Morphine is metabolized to morphine glucuronide in the liver and eliminated by the kidneys.
Side effects are more extensive than others and include drowsiness, respiratory depression, peripheral vasodilation, decreased gastrointestinal motility, decreased biliary and pancreatic secretion, nausea, vomiting, alterations in the endocrine and autonomic nervous system, and release of histamine.

Analgesic opioid	Route of administration	Dosing
Morphine	i.v.	0.05-0.2 mg/kg b.w.
Fentanil	i.v.	0.5-1 mcg/kg b.w.
Alfentanil	i.v.	5-20 mcg/kg b.w.
Remifentanil	i.v.	0.25-1 mcg/kg b.w.

Table 8. Dosing of analgesic opioids during deep sedation in children

4.2 Advances in patient monitoring during deep sedation

Monitoring during colonoscopy in the paediatric population under deep sedation is essential for safety and effectiveness. The issue is controlling effects on the cardiovascular, respiratory and neurological systems particularly in younger children. Recent technologic advances include electronic vital-sign monitoring systems which should be useful to maintain physiologic condition in the perioperative time period. The most recent method is the proposal of advanced capnography as a method of providing early warning for preventing postoperative respiratory depression (American Society of Anesthesiologists, 1996, Hutchinson & Rodriguez, 2008). Only hospital and/or specially equipped endoscopy facilities are appropriate setting for colonoscopy under deep sedation among infants, babies and children.

5. General anesthesia

Colonoscopy under general anaesthesia in children allows endoscopist comfortably prepare the patient and perform painless procedure. These aspects are important because of the technical advantages during invasive colonoscopy and higher patient's satisfaction even the presence of reported symptoms.

The frequency of the episodes of perforation or bleeding is not described (Steiner et al, 2006). Similarly postprocedural pain is significantly lower after colonoscopy under general anesthesia probably because of mild and controlled insufflation resulted in lower gas excess and abdominal pain.

Complications connected with general anaesthesia are sometimes arguing by the oppositionists. They emphasize most often sore throat and hoarseness (after endotracheal intubation), postoperative nausea and vomiting (mainly after inhaled anesthetics) and rarely irritability and sleep disturbances. The serious adverse events such as respiratory complications and cardiodepressant effects are statistically comparable to others typical for paediatric anaesthesia (Samer Ammar et al, 2003, Stringer et al, 1999).

General anaesthesia is defined as reversible, controlled and temporary loss of consciousness, painless and/or muscle relaxation (anaesthesia & analgesia & muscle relaxation). It needs the usage of up to date anaesthesia machine and monitoring apparatus what increases indeed the cost of the colonoscopy and forces to organize the relevant endoscopy room.

5.1 Induction

General anaesthesia is induced by using one of the following techniques: inhalational or intravenous. Drugs used belong to the three classes according to the tenets of general anaesthesia: anaesthetics, analgesic opioids and muscle relaxants (the latter more for endotracheal intubation than colonoscopic technique).

5.1.1 Inhalational induction

The most common indication for inhalational induction of anaesthesia are following:

- young children
- no accessible veins
- fear of needles by the child
- upper airway obstructions e.g. epiglottis, asthma
- a predictably difficult endotracheal intubation
- acceptance of the use of a child's face mask

Contraindications include in fear of the child regarding the use of a face mask, a higher risk of aspiration of gastric content and the risk of malignant hyperthermia.

There are three main techniques of induction with inhaled anesthetics:

- single-breathe technique – for cooperative and older children
- normal breathing volumes – for children of all ages, especially infants and babies
- increasing doses of inhaled gases - for children of all ages

After consciousness is lost it is possible to introduce access into a peripheral vein and continue fluid and drug administration in this way. At the same time depending on the extent of colonoscopy and the child's ASA physical state is necessary to consider insertion of oropharyngeal airway, laryngeal mask airway or endotracheal tube. Laryngeal mask airway become a major advance in anesthetic airway management, particularly when children breathe spontaneously during colonoscopy. This method limits the adverse events that accompany endotracheal intubation.

The most important inhaled anaesthetic in paediatric anaesthesia is sevoflurane (described in 4.1.3).

5.1.2 Intravenous induction

Intravenously inducted anaesthesia is preferable for most routine procedures, including colonoscopy because of a less complicated technique used when applying inhaled anesthetics. Additionally it is very useful for rapid induction in patients with a higher risk of regurgitation of gastric contents. Many authors report higher comfort and tolerance for patients. After insertion of a cannula into the peripheral vein administration of the required drugs is started. In children cannulation is a painful procedure and local anaesthetics should be used on suitable veins in both forearms (EMLA [Eutectic Mixture of Local Anesthetic], 50% lidocaine and 50% prilocaine).

Currently the most commonly used intravenous hypnotic for colonoscopy is propofol (described in 4.1.1). Its disadvantage e.g. narrow therapeutic range and risk of hypoxia and hypotension applies to general anaesthesia as well as deep sedation.

5.2 Maintenance of anaesthesia

For complicated and prolonged colonoscopies in children the preferred method of maintenance could be Total Intravenous Anaesthesia (TIVA) conducted with a special infusion pump. After the loading dose continuous infusion is done. The profile of propofol allows the patient to recover quickly irrespectively of the time of anaesthesia (stop the infusion 10 minutes before the end of colonoscopy).

In the other cases the maintenance of anaesthesia can be combined with inhalation of oxygen, air, nitrous oxide, sevoflurane or isoflurane, depending on the available choices. For colonoscopy in children appropriate level of maintenance of anaesthesia could be achieved by the method of inhalational anaesthesia with spontaneous ventilation.

Other than the above described intravenous and inhaled anaesthetics there may be some additional agents which have a role in providing general anaesthesia, decision to use them belonging to the anaesthesiologist.

5.3 Recovery

After the completion of colonoscopy anaesthetic drugs should be withdrawn and 100% oxygen delivered. Removal of the endotracheal tube or laryngeal mask airway should be done when respiratory reflexes are fully returned. This maneuver is challenging in small children up to 4 year because half of them following laryngeal spasm. After the patient is ready he should be transported into the recovery area.

5.4 Drug regimens

Anaesthetic drugs (intravenous and inhaled) have to be combined with strong and short acting analgesic opioids. The introduction of these newer less-toxic, shorter-acting anaesthetic drugs has reduced the requirement for muscle relaxants not only for diagnostic procedures like colonoscopy but also for general surgery in the paediatric population. Moderate anaesthesia conducted with combination of sevoflurane–remifentanil or propofol–remifentanil can keep children immobile without producing hypotension and facilitate controlled ventilation once the effects of the intubating dose of a muscle relaxant have worn off (Meakin, 2007, Liao et al, 2010).

Neuromuscular blocking agents could be selected only for those indications like difficult airway, higher risk of gastric regurgitation, obesity, and difficulties with patient's position. The usage of these agents is limited by prolong muscle blocking and risk of postprocedural respiratory depression. Thus, only relatively short acting nondepolarizing blocking agents such mivacurium and rocuronium are recommended for colonoscopy in children (Eikermann, 2001).

Mivacurium produces onset of maximum block in 1–2 min and 25% recovery in 9–10 min. This type of action is faster and longer during anesthesia with sevoflurane than with propofol.

Rocuronium retains the characteristics of an intermediate-duration relaxant in the younger age group of children, longer in infants than in children (42 vs. 27 min).

The introduction of the newest selective relaxant binding agent (SRBA) – sugammadex (Bridion) - has been an important development in the last few years because of its ability to provide a rapid reversal from any depth of neuromuscular blockade. Sugammadex is a modified gamma-cyclodextrin, chemically water-soluble cyclic oligosaccharides with a lipophilic core, which encapsulates and inactivates rocuronium or vecuronium (Bom, 2007). Rapid reversal with this agent occurs respectively after less than 4 minutes from deep neuromuscular blockade (dose 4 mg/kg) and less than 3 minutes from moderate neuromuscular blockade (dose 2 mg/kg). Any effect on the cholinergic nervous system has not been observed. Currently there are no recommendations to use sugammadex in full-term neonates or young infants even though there have been good results off-label but for older children it is the most desirable (Meretoja, 2010).

6. Conclusion

Recently fiberoptic colonoscopy has become more useful and advanced method for treating a large number of large-bowel disorders in the paediatric population. All reports have

shown that this procedure can be a safe and useful tool in children of all age groups only if it is based on good practice standards and experienced management, provided by both: paediatric gastroenterologists and paediatric anaesthesiologists. The most important trend among paediatric gastroenterologists is acceptance of the anaesthesiologist's performance of intravenous sedation and/or general anaesthesia based on differences between children and adults as were presented in this chapter. The choice of sedation or general anaesthesia for those paediatric gastrointestinal procedures is in the hands of anaesthesiologists who are the most experienced in this area. Only this pattern of conduct may provide not only optimal routine sedation or anaesthesia but the most standardized and the safest care for all age groups of children.

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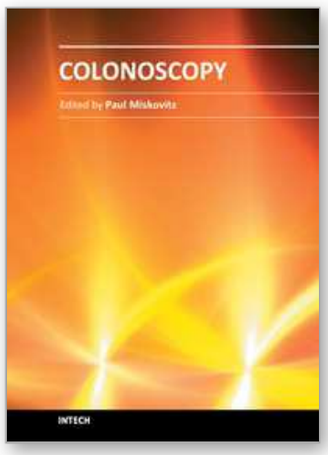

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To publish a book on colonoscopy suitable for an international medical audience, drawing upon the expertise and talents of many outstanding world-wide clinicians, is a daunting task. New developments in videocolonoscope instruments, procedural technique, patient selection and preparation, and moderate sedation and monitoring are being made and reported daily in both the medical and the lay press. Just as over the last several decades colonoscopy has largely supplanted the use of barium enema x-ray study of the colon, new developments in gastrointestinal imaging such as computerized tomographic colonography and video transmitted capsule study of the colonic lumen and new discoveries in cellular and molecular biology that may facilitate the early detection of colon cancer, colon polyps and other gastrointestinal pathology threaten to relegate the role of screening colonoscopy to the side lines of medical practice. This book draws on the talents of renowned physicians who convey a sense of the history, the present state-of-the art and ongoing confronting issues, and the predicted future of this discipline.

How to reference

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