Özefagogastroduedonal Endoskopi için Sedasyon

Sedation for Esophagogastroduodenal Endoscopy

Esophagogastrodeudonal Endoscopy / Özefagogastroduedonal Endoskopi

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Özet

Özefagogastroduedonal endoskopi sırasında pek çok anestetik yöntem ve ilaç kullanılabilir. Özefagogastroduedonal endoskopi için uygulanacak sedasyon ilaç ve yöntemleri hakkında araştırmalar sürmektedir. Bu derlemenin amacı sedasyon ve özefagogastroduedonal endoskopi ve sedasyonla ilişkili konuları literature bilgileri ışığında tartışmaktır. Tanısal özefagogastroduedonal endoskopi için günümüzde kullanılan standart yöntem genellikle yüzeyel farengeal anestezi minimal sedasyon ya da anksiyolizdir. Gerekli olursa sonradan analjezi eklenebilir. Uzun süreli, karmaşık ya da sorunlu ve ağrılı işlemler için uzman denetiminde yapılan daha derin sedasyon yöntemleri gerekebilir.

Anahtar Kelimeler

Endoskopi; Gastrointestinal Endoskopi; Sedasyon

Abstract

Different anesthetic techniques and drugs can be used for esophagogastroduedonal endoscopy. However, the scientists are still searching for appropriate drugs and protocols for sedation during esophagogastroduedonal endoscopy. The aim of this review is to discuss the topics related with sedation and esophagogastroduedonal endoscopy in the light of literature. Today standard procedure for diagnostic esophagogastroduedonal endoscopy usually consists of topical pharyngeal anesthesia, minimal sedation or anxiolysis, which may be complemented with analgesia when needed. When a prolonged, complex, or particularly troublesome or painful examination is foreseen, deeper sedation with multiple drugs and in closed observation of a staff may be required.

Keywords

Endoscopy; Gastrointestinal Endoscopy; Sedation

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Introduction

Esophagogastroduodenal Endoscopy EGDE is a disturbing procedure. Even sedation is not required to perform a technically adequate EGDE; it has been accepted as a standard practice for decades. The primary aim of using sedation is to increase the comfort both for the patient and endoscopist and decrease the duration of the procedure by easing the endoscopy course and increasing patient cooperation and willingness for future EGDE's by diminishing the memory of the event. However, the use of sedation for endoscopic procedures varies widely throughout the world and there is still no consensus on sedation types for EGDE [1].

It is important to examine current practice for increasing the quality of EGDE and sedation techniques. We have much experienced in rigid EGDE than colonoscopy. So the purpose of this review is to summarize the characteristics of drugs used for rigid EGDE and to present an outline for endoscopist. There is also a controversy on the specialty of staff that performs sedation we did not criticize any suggestions on this issue.

Background

Sedation is a continuum of progressive impairment in consciousness that has been roughly divided into four different levels, ranging from anxiolysis or minimal sedation to general anesthesia [2].Sedation levels according to the American Society of Anesthesiology (ASA) were shown in table 1.

Preprocedural Preparation and Assessment

Table 1.Sedation levels according to the American Society of Anesthesiology (ASA)

	Minimal Sedation (anxiolysis)	**Moderate Sedation/analgesia (conscious sedation)**	**Deep Sedation/analgesia**	General Anesthesia
Responsiveness	Normal response to verbal stimulation	Purposeful* response to verbal or tactile stimulation	Purposeful* response after repeated or painful stimulation	Unarousabl, even with painful stimulus
Airway	Unaffected	No intervention required	Intervention may be required	Intervention often require
Spontaneous ventilation	Unaffected	Adequate	May be inadequate	Frequently inadequate
Cardiovascular function	Unaffected	Usually maintained	Usually maintained	May be impaired

***Reflex withdrawal from painful stimulus is not considered a purposeful response. Practice guidelines for sedation and analgesia by non-anesthesiologists. Anesthesiology 2002; 96:1004-17.**

Endoscopist will have to assess patient and procedural-related factors before reaching a decision on what specific type of endoscopic sedation and drug (if any) to use. These factors should include medical history of the patient, review of drug and food (egg, soy) allergies, current medications (history of antidepressant, neuroleptic or cardiologic agent), potential drug interactions, history of adverse reaction to sedation or anesthesia, preoperative fasting (time and nature of last oral intake). History of tobacco, alcohol, or substance usage should also be evaluated. In addition, all women of childbearing age should be queried about the possibility of pregnancy.

The preprocedural airway assessment is the most critical aspect of safe sedation practice [3]. In order to predict which patients may be more likely to show difficulties regarding airway, the following should be considered: History of problems with previous anesthesia, presence of sleep apnea, snoring; facial dimorphism; oral cavity abnormalities (mouth opening smaller than 3 cm, protruding incisors, high-arched palate, macroglossia, tonsillar hypertrophy or nonvisible uvula (Mallapati III-V), inability to bite upper lip by lower incisors, neck abnormalities (morbid obesity, short neck, limited neck extension, endothoracic goiter, neck mass, reduced hyoid-mental distance (< 3 cm)]; patients with mandibular abnormalities (micro-retrognatia,).

Patients who were not in good health (ASA>3-4) or had risk factors for the development of airway complications or possible airway management problems should be excluded.

How to Perform an Unsedated Endoscopy?

Selected older patients, male gender, patients who are not anxious, may have better tolerance of upper endoscopy patients may be able to undergo EGDE without sedation by use of topical pharyngeal anesthesia (TPA) [4]. However, first time examinees with high scores for trait anxiety poorly tolerate insertion of the endoscope. In order to perform an unsedated endoscopy the traditional techniques consist following steps.

1. Asking to patient whether he or she prefer spray or gargling before application of TPA.
2. Observing pharyngeal sensitivity during application of TPA. (Encouraging patient to say "aah" is not recommended because this might expose the larynx to the anesthetic agent and inhibits the cough reflex.)
3. Observing patient after first puff for any adverse events. (Patients may swallow the anesthetic after a while.)

Maximum dose of lidocaine (1-1.5 mg/kg) (7-10pufs) should be kept in mind. A high trait-anxiety score during local anesthesia application usually points out a difficult EGDE.

Topical Pharyngeal Anesthesia (TPA)

Main indication for TPA is to suppress vomiting reflex. Vomiting reflex during insertion of the endoscope and its operation in the upper gastrointestinal tract may cause

changes in hemodynamics, oxygen saturation and autonomic nervous activities, and even induce lethal disrhythmia or sudden death [5, 6, 7].

In clinical practice, topical anesthesia is used during unsedated EGDE. It is more beneficial for younger patients who are anxious or undergoing EGDE for the first time without sedation [8].

TPA can be applied either by spraying or gargling. Even patient's preferences among TPA is favored on gargling, spray application may be more feasible for the procedure because the anesthetic agent can be applied to the posterior pharyngeal wall visually. During administration of TPA, observing the presence of a strong gag reflex strongly correlates with pharyngeal sensitivity as a "real-life" clinical practice [9].

Some patients may dislike its taste, the burning sensation that accompanies anesthesia and the anesthetic feeling itself [10]. Lidocaine, benzocaine, and tetracaine are the most commonly used topical local anesthetics in the endoscopy suites [11]. Traditionally spraying posterior pharyngeal wall with 1-1.5 mg/kg lidocaine provides sufficient TPA. Commercial lidocaine sprays contains 10 mg lidocaine per puff. Lidocaine is relatively poorly absorbed (much is swallowed) from the nasopharynx. It is well tolerated in the elderly patients with co morbidities. However, lidocaine is irritant and can cause complete airway obstruction due to laryngospasm [12]. Lidocaine lollipops are promising form of local oropharyngeal anesthesia for EGDE.

Risks of TPA: The potential complications of TPA are mainly laryngospasm, anaphylactic reactions, systemic toxicity (methemoglobinemia) to topical anesthetics, and aspiration pneumonia [13].

Because up to 25% of patients receiving pharyngeal anesthesia showed radiologic evidence of aspiration, TPA should not be used in cases with predisposing factor for aspiration [14,15]. It should be kept in mind that the anesthetic effect of TPA can last for more than 30 to 40 minutes after the procedure. Patients should be strictly advised not to take any oral food and/or beverage (fast for about an hour) after EGDE.

Methemoglobinemia should be considered in patient who develops cyanosis after TPA especially with benzocaine [16]. Supplemental oxygen and Methylene blue, 1–2 mg/kg should be administered over 5 min after, arterial blood gases analyses with co-oximetry. Patients with a glucose-6 phosphodiesterase deficiency require transfusion or dialysis for treatment [17].

Intraprocedural Monitoring

During EGDE, patients routinely positioned on side lying or prone and a mouth adaptor and an endoscope in the mouth that narrows airway and restricts air flow. Because hypoxemia and hypoten¬sion are the major reasons of major complications during EGDE, patients should be monitored for hemodynamic and respiratory status. Baseline readings should be obtained at least four times; prior to sedation, during procedure, during recovery and before discharge.

Patients should be monitored with continuous electrocardiogram (ECG) during moderate sedation and blood pressure should be chequed by intervals.

The respiratory cycle of oxygenation and ventilation are related, but completely separate, physiologic processes. Human body has reserves that hold on and provides oxygen for several minutes. If sedation is deep enough to compromise breathing, body begins to consume these reserves while chest continues to move up and down and breathing efforts of patient moves dead space air only. SpO2 begins to drop after body oxygen reserves consumed.

From this point of view, it is not logical to expect the accurate level of ventilation and oxygenation breath to breath by pulseoximeters. To date the most pertinent information about frequency and adequacy of breathing during sedation is provided by capnography [18, 19, 20]. During endoscope introduction waveforms diminishes due to gag reflex. The waveform should return once the scope has advanced. However, a fall in SpO2 does not occur during introduction of endoscope.

Supplemental Oxygen

The ASA Task Force recommends supplemental oxygen for moderate and deep sedation unless specifically contraindicated. However, giving supplemental oxygen may cause long apnea periods in heavily sedated patients. and may result in higher rates of cardiopulmonary unplanned events [21]. An average 6 minutes of apnea is required before a healthy adult desaturates to less than 90% [22], and 2 to 4 minutes for healthy children [23, 24, 25].

Sedation and Analgesic Agents Used for Endoscopy

Before deciding the appropriate agent and application way of sedation, it is of paramount importance to decide the type of endoscopic procedure (diagnostic, therapeutic), the degree of pain associated with it, and the length of total procedure time. Diagnostic and uncomplicated therapeutic upper endoscopy can be performed under moderate sedation. More complicated, lengthy procedures and patients with special conditions may require deep levels of sedation. Sedation monitoring and rescue equipment should be available in the room.

Benzodiazepins

The most commonly used benzodiazepines are midazolam and diazepam. The efficacy of sedation with these 2 benzodiazepines is comparable [26]. However, there is a known favor on midazolam due to minimal risk of venous irritation and phlebitis resulting in painless İ.V. injection, strong anterograde amnesia and an existing

antidote flumazenil [27].

Midazolam has a longer interval to peak effect (8–12 min versus 2–5 min) and almost 3.5 times more potent than diazepam. The anti-anxiety and sleep effects are generally manifested 1–2 min after intravenous injection of 5 mg dose and anterograde amnesia effect becomes evident after 4 min, continuing up to 30 min after injection.

Standard i.v. dose for sedation induction is 0.06-0.07 mg/kg. Esophageal intubation could successfully be performed after 30 seconds and patients will not remember the procedure [28]. When the sedative state 30 s after i.v. midazolam is insufficient, appropriate additional doses should be administered [28]. It should be kept in mind that benzodiazepines are lipid-soluble (particularly midazolam) and repeated doses may accumulate into the adipose tissue and after subsequently releasing, prolongs recovery.

Benzodiazepine combinations: Because midazolam does not exhibit any analgesic effects, sole use for conscious sedation does not suppress sympathic stimulation due to esophageal intubation [29]. In order to reduce the harmful effects of sympathic stimulation benzodiazepines are usually combined with opioids. The obvious disadvantage of benzodiazepine-opioid combination is respiratory depression due to synergistic effect by flattening the carbon dioxide (CO2) response curve of the respiratory center. When given with fentanyl, only about 25% of the ED50 dose of midazolam and 25% of the ED50 dose of fentanyl were necessary to produce unresponsiveness. In past midazolam usually combined with pethidine. However, it has a slower onset of action that delays the start of endoscopy, longer duration of action that prolongs the recovery and produces more postprandial nausea and fatigue when compared with newer opioids. Nowadays, it is not realistic to use it while more suitable drugs like fentanyl were still exists.

Propofol

Propofol is the most studied sedative agent for gastrointestinal endoscopy. It is pure sedative/hypnotic without analgesic properties. It has a rapid onset and offset effect time. When used for GI endoscopy, 40 to 60 mg bolus doses are typically produce sedation in normal adults within 40 seconds ie, "1 arm-brain circulation". Subsequent doses should be administered after assessment of responses to the initial dose, but typically given in 10- to 20-mg increments every 1 to 2 minutes. Dose reduction is necessary in patients with cardiac dysfunction and in the elderly as a result of decreased clearance.

Therapeutic index (the difference between the doses for moderate and deep sedation) of propofol is very narrow. This means that patients may quickly slip from moderate to deep sedation or to general anesthesia. Therefore, vigilant monitoring is necessary.

It is a pregnancy category B drug and should be used with caution during lactation [30]. Vials are labeled for single-use only; unused portions should be discarded within 6 hours to decrease the risk of contamination.

Two preparations exist; one is prepared as an oil/water emulsion consisting of 1% propofol, 10% soybean oil, 2.25% glycerol, and 1.2% egg lecithin. It is contraindicated in patients with propofol allergy or hypersensitivity to eggs or soybean. The other preparation has bisulfates; and it is contraindicated in patients with, allergies/reactions to bisulfates.

Propofol is superior to other sedatives in terms of recovery time, physician and patient satisfaction and psychomotor testing during discharge [31]. However, a benefit in this regard over traditional benzodiazepine/narcotic combinations has not been uniformly demonstrated [32].

The total dosage needed to perform EGDE is slightly higher than for colonoscopies with an accompanying increased risk of apnea [33, 34]. Nevertheless, the short procedure time corresponds very well with the action of the drug. After an adequate level of sedation has been reached, most EGDE's could be performed without further additional doses.

It is concluded that propofol concentration which suppresses the somatic response to EGDE was higher than the concentration that suppresses a response to verbal command [35]. However, dose-related side effects such as hypotension, hypoventilation, or bradycardia are relatively frequent, when large doses are administered [36].

Propofol combinations

Due to the mentioned lack of analgesic effect of propofol it is logical to use it in conjunction with a pain-relieving drug (balanced anesthetic technique) [37]. In accordance with this data, nowadays propofol-opioid combination became an alternative to the traditional benzodiazepine-opioid combination. More precise dose titration is possible with smaller bolus doses of propofol (5-15 mg) and the potential for partial pharmacologic reversibility by naloxone [38,39].

Propofol-Pethidine Combination: Pethidine prolongs the recovery time compared with alfentanil [40].

Propofol Benzodiazepine Combination: This regimen was not superior in terms of sedation and was associated with longer recovery times [41]. In fact it eliminates the advantage of using propofol because both drugs are sedative and combining two same class drugs does not produce an effect that each one has.

Propofol-ketamine Combination: The combination of propofol with subhypnotic, analgesic dosages of ketamine improves patient comfort, suppress the need for supplemental opioids, reduces total propofol dose, and (in contrast to benzodiazepines) do not have cardiorespiratory depressant actions [42]. Guit et al. [43] reported that propofol-fentanyl combination depressed hemodynamics, but propofol-ketamine combination resulted in stable hemodynamics. Therefore Propofol-Ketamine may be an effective combination during EDGE's of patients with limited cardiac reserves.

Propofol-Ketamine combination was associated with more patient satisfaction and amnesia and a reduced need for restraint during fiberoptic bronchoscopy [43]. This suggests that the level of sedation was deeper with the PK combination.

Propofol-remifentanil Combination: Remifentanil is an ultra-short acting mu-opioid receptor agonist with zero-order kinetics and provides dense analgesia. However, it has no hypnotic or amnestic properties and it is not suitable for patients with high anxiety levels. It should be used under closed supervision of anesthetist [44].

There are now two different strategies in using propofol for EGDE. First one is to use propofol as a routine sedative for all EGDE's in outpatient settings due to its rapid re-awakening and metabolism even without an anesthesia staff [33, 34, 45]. However, propofol use by nonanesthesiologists remains a contraindication in the package insert of propofol in most countries. In fact there are some economic aspects of this tradition. These are the costs of anesthesia staffs and rather expensive cost of propofol.

The supporters of second strategy thought that propofol is primarily an anesthetic agent and should be reserved for prolonged and difficult endoscopic procedures [46, 47, 48]. Sedation guidelines produced by the American Society of Gastroenterology partially contradict those produced by the American Society of Anesthesiologists for sedation by non-anesthesiologists, whereas the German guidelines were developed with anesthesiologists involved. In accordance with ASA, it's our belief that propofol is an ideal agent for short diagnostic EDGE's. However, it should be used with closed observation of an anesthetist during long lasting therapeutic EDGE'S while this enables gastroenterologists to get pleasure of performing endoscopy without concerning of what is happening to the patient.

Pediatric Endoscopy

Diagnostic and therapeutic pediatric upper gastrointestinal endoscopy procedures have dramatically increased during last decades. Gastrointestinal endoscopy in an uncooperative child is very risky and may be associated with perforation of the gastrointestinal tract. Effective and safe sedation is crucial for this procedure.

The goals of anesthetic sedation regimens for pediatric gastrointestinal endoscopy are to ensure patient safety, immobility, comfort, successful completion, and amnesia of the procedure. Other goals are to maximize efficiency and contain costs [49]. The method of sedation is a matter of choice after careful consideration of a number of factors including the patient's condition, ASA classification, the type of procedure, the parents' and patient's preference, and the level of cooperation of the patientWith proper patient selection, intravenous sedation is a safe and effective method for sedation in pediatric endoscopy [50,51]. General anesthesia should be considered necessary for highly complicated procedures and for patients at high risk for cardiovascular complications.

Airway of infants and children requires a sound understanding and knowledge of the variations in anatomy, physiology, and pathology in a wide age range of patients. Each case, depending on the presenting problem, may require a different approach to anesthesia.

The Infant Airway

The larynx is anatomically higher. Tongue is closer to the roof of the mouth and can easily obstruct the airway. Larynx is more superior so visualization of laryngeal structures in infants is more difficult. The epiglottis is omega shaped, stiffer and tilted posteriorly, resulting in more difficulty in visualization of the vocal cords. Additionally, the trachea is more compliant than adults and more sensitive to dynamic compression. The cricoid cartilage is the narrowest part of the airway. It is nonexpendable and airway edema owing to instrumentation may easily obstruct the airway. Oxygen reserves in the infant are low and oxygen consumption is high. Hypoxemia occurs very rapidly and many times worsens by gastric distention.

Unlike adult patients who can receive minimal or moderate sedation, the pediatric patient requires deep sedation or general anesthesia [52]. Administration of sedative medications should be weight based and titrated by response after allowing adequate time to assess the effects of each dose. However, there is no standard practice for anesthesia in children undergoing gastrointestinal endoscopy. Communication between the endoscopist and the anesthesiologist is the cornerstone of successful endoscopy.

Propofol in conjunction with a short acting benzodiazepine such as midazolam and a narcotic such as fentanyl or remifentanyl may be titrated in small increments for intravenous sedation.

Ketamine with propofol and midazolam provides effective sedation in pediatric patients. However this regimen has more side effects such as cough, dizziness, vomiting, and diplopia. Small doses of ketamine largely spares the upper airway muscle tone and laryngeal reflexes

Non-per-OS Guidelines for pediatric patients: Non-per-OS guidelines are set forth by the ASA as well as the American Academy of Pediatrics in 1992, which require fasting for solids and breast milk 4 hours for infants younger than 6 months, 6 hours for those 6 to 36 months, and 8 hours for those older than 36 months.

Endoscopy in Pregnancy

Endoscopy is rarely required during pregnancy. If necessary the procedure should be performed with the lowest possible dose of category B and C drugs or if possible, without any sedation [53]. Category D drugs may be used

when the benefit clearly outweighs the risks safely.

Benzodiezepines (category D)

Prolonged use of diazepam during early pregnancy has been associated with cleft palate and other congenital abnormalities. Although there are no data on the use of intravenous diazepam for sedation for endoscopy, it is best avoided. Midazolam is a category D drug, but there are no reports of congenital abnormalities.

Pethidine (category B): There is no reported evidence of teratogenicity [54].

Topical lidocaine: Topical lidocaine is appears to be safe during pregnancy [55].

The potential risks associated with endoscopy during pregnancy:

1. Oversedation may cause maternal hypotension and hypoxia, which in turn may lead to fetal hypoxia, with potentially fatal consequences.
2. The fetus may be exposed to potentially teratogenic drugs and radiation.
3. Care must be taken with maternal positioning to avoid inferior vena caval compression by the pregnant uterus, which can lead to decreased uterine blood flow and fetal hypoxia.

Because of these known risk factors the following factors should be chequed.

(1) A strong indication, particularly in high-risk pregnancies.
(2) Defer endoscopy to the second trimester whenever possible.
(3) Try to use the lowest dose of sedative medication.
(4) Wherever possible, use category A or B drugs.
(5) Minimize procedure time.
(6) Pregnant patients should be positioned in left pelvic tilt or left lateral position to avoid vena caval or aortic compression.
(7) Fetal heart sounds should be confirmed before during and after sedation.
(8) Obstetric support should be available in the event of a pregnancy-related complication.
(9) Endoscopy should be avoided during obstetric complications such as placental abruption, imminent delivery, ruptured membranes or pre-eclampsia.

Nurse-Administered Sedation

The propofol dose must be carefully titrated according to the individual patient's response. Factors influencing dosage include age, ASA class, patient's height and procedure duration. Propofol's primary risk is its narrow therapeutic range which necessitates careful patient monitoring. The endoscopy team should take the responsibility of recussitation of the patient when necessary.

Patient-Controlled Sedation (PCS)

The combination of propofol with an anesthetic agent has likewise been repeatedly shown as practical for PCS during colonoscopy [56]. The typical self-administered bolus consists of 4.8 mg propofol and 125 μg alfentanil [40]. However there is lack of data for PCS during EDGE. Furthermore the concept of PCS depends on patient reaction to an unpleasant sensation necessitating patients to be sedated at levels that first permit to experiences pain than control the pain. This technique provides an individually tailored sedation and may only be applicable to convenient patients who can take responsibility for their own sedation.

Complications of Esophagogastroduedonal Endoscopy

The complication rate of EGDE is about 0.1% with cardiopulmonary events predominating [57].The majority of complications are due to oversedation, hypoventilation, vasovagal episodes, airway obstruction and aspiration [58]. Ascending ASA physiologic classification, age >60 years, inpatient status, the use of supplemental oxygen, and the involvement of a trainee in the procedure are the independent risk factors for CPC's [4].

Aspiration: The risk of aspiration is minimal during diagnostic endoscopy. Aspiration is particularly likely when protective reflexes are blunted by excessive sedation or coexisting diseases of patients like encephalopathy, diabetic gastroparesis sleep apnea syndrome, severe chronic obstructive pulmonary disease, or coronary heart disease and in the setting of emergency treatment of upper gastrointestinal hemorrhage, and during long-lasting procedures. Satisfactory oral suction and airway control are mandatory issues [59]. TPA should be avoided [15]. In order to prevent aspiration, patients should be fasted far enough time before sedation (2 hours for clear liquids and 6 hours for light meals) [2].

Conclusion

Today standard procedure for diagnostic EGDE usually consists of topical pharyngeal anesthesia (TPA), minimal sedation or anxiolysis, which may be complemented with analgesia when needed. When a prolonged, complex, or particularly troublesome or painful examination is foreseen, deeper sedation with multiple drugs may be required.

It is of paramount importance to use standart monitoring and recussitation equipment during procedure. Start with a low dose, assessing the response of the patient's sedation level, ventilatory and cardiovascular status; and proceeding gradually with titration along with topical pharyngeal anesthesia is the most common technique used for EDGE. Patients may require different levels of sedation for the same procedure and may attain varying levels of sedation during a single procedure due to interindividual variability of response to drugs used for sedation.

References

1. Rex DK, Khalfan HK. Sedation and the technical performance of colonoscopy. Gastrointest Endoscopy Clin North Am. 2005; 15: 661-72.
2. Practice guidelines for sedation and analgesia by non-anesthesiologists. Anesthesiology. 2002; 96:1004-1017.
3. Graber RG. Propofol in the endoscopy suite: an anesthesiologist's perspective [editorial]. Gastrointest Endosc. 1999; 49: 803-6.
4. Standards of Practice Committee, Lichtenstein DR, Jagannath S, Baron TH, Anderson MA, Banerjee S, Dominitz Ja. Sedation and anesthesia in GI endoscopy. Gastrointest Endosc. 2008; 68: 815-26.
5. Palmer ED. The abnormal upper gastrointestinal vagovagal reflexes that affect the heart. Am J Gastroenterol. 1976; 66: 513-22.
6. Rostkus PS, McDonald GB, Albert RK. Upper intestinal endoscopy induces hypoxemia in patients with obstructive pulmonary disease. Gastroenterology. 1980; 78: 488-91.
7. Hayashi T, Nomura M, Honda H, Teszuka K, Torisu R, Takeuchi Y, et. al. Evaluation of autonomic nervous function during upper gastrointestinal endoscopy using heart rate variability. J Gastroenterol. 2000; 35: 815-23.
8. Soma Yi, Saito H, Kishibe T, Takahashi T, Tanaka H, Munakata A. Evaluation of topical pharyngeal anesthesia for upper endoscopy including factors associated with patient tolerance. Gastrointest Endosc. 2001; 53: 14-8.
9. Smith JL, Opekun A, Graham DY. Controlled comparison of topical anesthetic agents in flexible upper gastrointestinal endoscopy. Gastrointest Endosc. 1985; 31: 255-258.
10. Isenberg G. Topical anesthesia: To use or not to use-that is the question. Gastrointest Endosc. 2001; 53: 130-133.
11. Waring JP, Baron TH, Hirota WK, Goldstein JL, Jacobson BC, Leighton JA., et al. Guidelines for conscious sedation and monitoring during gastrointestinal endoscopy. Gastrointestinal Endoscopy. 2003; 58: 317-322.
12. McGuire G, El-Beheiry H. Complete upper airway obstruction during awake fibreoptic intubation in patients with unstable cervical spine fractures. Can J Anaesth. 1999; 46: 176–8.
13. Stoelting, R. K. (1999). Local anesthetics. Pharmacology and physiology in anesthesia practice. 172-173.
14. Prout BJ, Metreweli C. Pulmonary aspiration after fibre-endoscopy of the upper gastrointestinal tract. Br Med J. 1972; 4: 269-71.
15. Quine MA, Bell GD, McCloy RF, Charlton JE, Devlin HB, Hopkins A. Prospective audit of upper gastrointestinal endoscopy in two regions of England: safety, staffing, and sedation methods. Gut. 1995; 36: 462-7.
16. Paparella S. Topical anesthetic sprays directly associated with a serious, sometimes fatal adverse reaction: methemoglobinemia. Journal of Emergency Nursing. 2005; 31, 468–469.
17. Srikanth MS, Kahlstrom R, Oh KH, Fox Sri Fox ERi Fox KM. Topical benzocaine (Hurricaine®) induced methemoglobinemia during endoscopic procedures in gastric bypass patients. Obesity Surgery. 2005; 15: 584-590.
18. Soto RG, Fu ES, Vila H Jr, Miguel RV. Capnography accurately detects apnea during monitored anesthesia care. Anesth Analg. 2004; 99: 379–382.
19. Capnography: The ventilation vital sign. RT Magazine. Retrieved September 26, 2004, from http://www.rtmagazine.com.
20. American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologists Paractice: Guidelines for sedation and analgesia by non-anesthesiologists. Anesthesiology. 2002; 96: 1004-17.
21. Sharma VK, NguyenCC, Cowell MD, Lieberman DA, de Garmo P, Flesicher DE. A national study of cardiopulmonary unplanned events after GI endoscopy. Gastrointest Endosc. 2007; 66: 27-34.
22. Patel R, Lenczyk M, Hannallah RS, McGill WA. Age and the onset of desaturation in apnoeic children. Can J Anesth. 1994; 41: 771-774.
23. Jense HG, Dubin SA, Silverstein PI, O'Leary-Escolas U. Effect of obesity on safe duration of apnea in anesthetized humans. Anesth Anal. 1991; 72:89-93.
24. Xue FS, Tong SY, Wang XL, Deng XM, An G. Study of the optimal duration of preoxygenation in children. J Clin Anesth. 1995; 7: 93-96.
25. Xue FS, Luo LK, Tong SY, Liao X, Deng XM, An G. A study of the safe threshold of apneic period in children during anesthesia induction. J Clin Anesth. 1996; 8: 568-574.
26. Zakko SF, Seifert HA, Gross JB. A comparison of midazolam and diazepam for conscious sedation during colonoscopy in a prospective double-blind study. Gastrointest. Endosc. 1999; 49: 684-9.
27. McCloy RF, Pearson RC. Which agent and how to deliver it? A review of benzodiazepine sedation and its reversal in endoscopy. Scand J Gastroenterol Suppl. 1990; 179: 7-11.
28. Yi SY, Shin JE. Midazolam for patients undergoing upper gastrointestinal endoscopy: a prospective, single-blind and randomized study to determine the appropriate amount and time of initiation of endoscopy. J Gastroenterol Hepatol. 2005; 2: 1873-9.
29. Yazawa K, Adachi W, Owa M, Koide N, Hanazaki K, Kajikawa S, et. al. Can sedation reduce the cardiac stress during gastrointestinal endoscopy? A study with non-invasive automated cardiac flow measurement by color Doppler echocardiography. Scand J Gastroenterol. 2002; 37: 602-7.
30. Qureshi WA, Rajan E, Adler DG, Davila RE, Hirota WK, Jacobson BC. ASGE guideline: guidelines for endoscopy in pregnant and lactating women. Gastrointest Endosc. 2005; 61: 357-62.
31. McQuaid KR, Laine L. A systematic review and meta-analysis of randomized, controlled trials of moderate sedation for routine endoscopic procedures. Gastrointest Endosc. 2008; 67: 910-23.
32. Van Natta ME, Rex DK. Propofol alone titrated to deep sedation versus propofol in combination with opioids and/or benzodiazepines and titrated to moderate sedation for colonoscopy. Am J Gastroenterol. 2006; 101: 2209-17.
33. Rex DK, Overley C, Walker J. Registered nurse-administered propofol sedation for upper endoscopy and colonoscopy: Why? When? How? Rev Gastroenterol Disord. 2003; 3: 70-80.
34. Heuss LT, Schnieper P, Drewe J, Pflimlin E, Beglinger C. Risk stratification and safe administration of propofol by registered nurses supervised by the gastroenterologist: A prospective observational study of more than 2,000 cases. Gastrointest Endosc. 2003; 57: 664-671.
35. Kazama T, Takeuchi K, Ikeda K, Ikeda T, Kikura M, Iida T. Optimal propofol plasma concentration during upper gastrointestinal endoscopy in young, middle-aged, and elderly patients. Anesthesiology. 2000; 93: 662-9.
36. Rex DK, Heuss LT, Walker JA, Qi R. Trained registered nurses/endoscopy teams can administer propofol safely for endoscopy. Gastroenterology. 2005; 129: 1384-91.
37. Short TG, Plummer JL, Chui PT. Hypnotic and anaesthetic interactions between midazolam, propofol and alfentanil. Br J Anaesth. 1992; 69: 162-7.
38. Kern SE, Xie G, White JL, Egan TD. A response surface analysis of propofol remifentanil pharmacıdynamic interaction in volunteers. Anesthesiology. 2004; 100: 1373-81.
39. Külling D, Fantin AC, Biro P, Bauerfeind P, Fried M. Safer colonoscopy with patient-controlled analgesia and sedation with propofol and alfentanil. Gastrointest Endosc. 2001; 54: 1-7.
40. Short TG, Chui PT. Propofol and midazolam act synergistically in combination. Br J Anaesth. 1991; 67: 539-45.
41. Gozal D, Valery Y, Cohen M, Wengrover D. Propofol/midazolam vs propofol/ketamine in patients undergoing gastrointestinal endoscopies. Gastrointest Endosc. 2006; 63: AB189.
42. Guit JBM, Koning HM, Coster ML, Niemeijer RPE. Mackie DP. Ketamine as analgesic for total intravenous anaesthesia with propofol. Anaesthesia. 1991; 46: 24-27.
43. Hwang J, Jeon Y, Park HP, Lim YJ, Oh YS. Comparison of alfentanil and ketamine in combination with propofol for patient-controlled sedation during fiberoptic bronchoscopy. Acta Anaesthesiol Scand. 2005; 49: 1334-1338.
44. Nieuwenhuijs DJ, Olofsen E, Romberg RR, Sarton E, Ward D, Englbers F. Response surface modeling of remifentanil-propofol interaction on cardiorespiratory control and bispectral index. Anesthesiology. 2003; 98: 312-22.
45. Walker JA, McIntyre RD, Schleinitz PF, Jacobson KN, Haulk AA, Adesman P. Nurse-administered propofol sedation without anesthesia specialists in 9,152 endoscopic cases in an ambulatory surgery center. Am J Gastroenterol. 2003; 98: 1744-1750.
46. Wehrmann T, Kokabpick S, Lembcke B, Caspary WF, Seifert H. Efficacy and safety of intravenous propofol sedation during routine ERCP: A prospective, controlled study. Gastrointest Endosc. 1999; 49: 677-683.
47. Vargo JJ, Zuccaro G Jr, Dumot JA, Shermock KM, Morrow JB, Conwell DL. Gastroenterologist-administered propofol versus meperidine and midazolam for advanced upper endoscopy: A prospective, randomized trial. Gastroenterology. 2002; 123: 8-16.
48. Jung M, Hofmann C, Kiesslich R, Brackertz A. Improved sedation in diagnostic and therapeutic ERCP: Propofol is an alternative to midazolam. Endoscopy. 2000; 32: 233-238.
49. Lightdale JR. Sedation and analgesia in the pediatric patient. Gastrointest Endosc Clin N Am. 2004; 14: 385-399.
50. Gilger MA. Editorial: sedation for pediatric GI endoscopy. Gastrointest Endosc. 2007; 65: 211-212.
51. Elitsur Y, Blankenship P, Lawrence Z. Propofol sedation for endoscopic procedures in children. Endoscopy. 2000; 32: 788-791.
52. Tosun Z, Aksu R, Guler G, Esmaoglu A, Akin A, Aslan D, Boyaci A. Propofol-ketamine versus propofol-fentanyl sedation during pediatric upper gastrointestinal endoscopy. Pediatr Anesth. 2007; 17: 983-988.
53. Cappell MS, Colon V, Sidhom O. A study at eight medical centers of the safety and clinical efficacy of esophagogastroduodenoscopy in 83 pregnant females with follow-up of fetal outcome and with comparison to control groups. Am J Gastroenterol. 1996; 91: 348-354.
54. ASGE Guideline: guidelines for endoscopy in pregnant and lactating women. Gastrointest Endosc. 2005; 61: 357-362.
55. Heinonen OP, Stone D, Shapiro S. Birth defects and drugs in pregnancy. Boston: John Wright, 1982.
56. Lee DW, Chan AC, Sze TS, Ko CW, Poon CM, Chan KC et.al. Patient-controlled sedation versus intravenous sedation for colonoscopy in elderly patients: A prospective randomized controlled trial. Gastrointest Endosc. 2002; 56: 629-632.
57. Carey WD. Indications, contraindications and complications of gastrointestinal endoscopy. In: Sivak MV, (edi). Gastroenterologic endoscopy, Philadelphia: WB Saunders, 1987: 868-80.
58. Hart R, Classen M. Complications of diagnostic gastrointestinal endoscopy. Endoscopy 1990; 22: 229-33.
59. Chon Y, Sub X. Mask adaptor-a novel method of positive pressure ventilation during propofol deep sedation for upper GI endoscopy. Gastrointest Endosc. 2008; 68: 127-31.