Sedation, Analgesia, and Monitoring

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ABSTRACT

Endoscopic procedures are common and sedation is frequently used to minimize anxiety and discomfort, reduce the potential for physical injury during the procedure, and improve overall patient tolerability and satisfaction. In this article, the authors review the variety of options for sedation and analgesia available to the gastroenterologist or surgical endoscopist.

KEYWORDS: Sedation, analgesia, endoscopy, monitoring

Objectives: Upon completion of this article, the reader should be able to describe methods of sedation and analgesia for endoscopy and be familiar with monitoring methods.

Modern day colonoscopy was first described by Wolff and Shinya four decades ago.¹ Using a flexible fiberoptic scope and general anesthesia, retrograde visualization of the entire colon was accomplished. Initially, the indications for colonoscopy were few; mostly limited to diagnostic procedures and for evaluation of abnormal radiographic studies. Over the years the techniques and applications of colonoscopy have grown tremendously. Today millions of colonoscopies are performed annually in the United States. Colonoscopy has now become the modality of choice for diagnosis and therapy of numerous diseases processes affecting the large intestine.²

As colonoscopic technique evolved, so have the methods used to achieve patient sedation and analgesia. The purpose of sedation during endoscopy is to minimize anxiety and discomfort, reduce the potential for physical injury during the procedure, and improve overall patient tolerability and satisfaction.³ In the United States, 98% of endoscopists administer some form of sedation during upper and lower endoscopy.⁴ A wide variety of options for accomplishing this are available to the gastroenterologist or surgical endoscopist. The focus of this article is to provide an overview of the common

applications of sedation, analgesia and monitoring used during colonoscopy.

SEDATION

Preprocedure Patient Assessment

Evaluation of the patient by the individual performing the procedure should occur prior to administration of any sedation. The purpose is to identify those with preexisting medical conditions or factors on physical examination that may adversely affect the outcome of endoscopic sedation.³ The American Society of Anesthesiologists (ASA) recommends that the following key points of the patient's history be identified: (1) abnormalities of the major organ systems; (2) previous adverse reaction to sedation or anesthesia; (3) current medications, drug, and food allergies, and potential drug interactions; (4) time and nature of last oral intake; (5) history of tobacco, alcohol, or substance use or abuse.⁵ Patients should fast for at least 2 hours following clear liquids and 6 hours after light meals prior to undergoing sedation.⁶ A focused physical examination should also be performed including

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Table 1 American Society of Anesthesiologists (ASA) Classification

Class	Description
I	The patient is normal and healthy.
II	The patient has mild systemic disease that does not limit their activities (e.g., controlled hypertension or controlled diabetes without systemic sequelae).
III	The patient has mild systemic disease that does limit their activities (e.g., stable angina or diabetes with systemic sequelae).
IV	The patient has severe systemic disease that is a constant potential threat to life (e.g., severe congestive heart failure, end stage renal failure).
V	The patient is morbid and is at substantial risk of death within 24 hours (with or without a procedure).
E	Emergency status: In addition to indicating underlying ASA status (1–5), any patient undergoing an emergency procedure is indicated by the suffix “E.”

patient vital signs, heart and lung auscultation, and upper airway assessment.⁷

Patients should undergo risk stratification according to any comorbid medical conditions elucidated during the initial assessment (see ASA classification, Table 1). Sedation administered by the endoscopist is appropriate for ASA class I–III patients. ASA class IV–V patients are at a higher risk of adverse events related to sedation; consultation of an anesthesia specialist should be considered for this group.³ Pregnancy testing for women of childbearing age may be considered unless they have previously undergone a hysterectomy, tubal ligation, or are menopausal.⁷ Endoscopy during pregnancy is generally not recommended unless there is a strong indication, and if possible, should be postponed until the second trimester.⁸

Sedation is generally defined as a drug-induced state of reduced excitement or anxiety. It represents a continuum of varying levels of consciousness that range from simple anxiolysis to general anesthesia. The ASA describes four stages of sedation, as depicted in Table 2.⁵ Moderate sedation is the stage targeted during most colonoscopies. At this level, the patient is able to purposefully respond to verbal and tactile stimulation while maintaining ventilation and cardiovascular function. Patients with a prior poor response to moderate sedation or those who may be physiologically resistant to

sedatives (i.e., chronic narcotic, alcohol, or benzodiazepine use) may be considered for deep sedation.⁷

Agents Used for Sedation and Analgesia

Ideal drugs for endoscopic sedation have a rapid onset and short duration of action, maintain hemodynamic stability, and do not cause major side effects. Commonly used agents include opiates, such as meperidine or fentanyl, benzodiazepines, such as midazolam or diazepam, or a hypnotic, such as propofol. The choice among these agents is a matter of personal preference, but typically consists of a benzodiazepine administered alone or in combination with an opiate (Table 3).

Benzodiazepines induce central nervous system (CNS) depression resulting in anxiolysis, sedation, muscle relaxation, and anterograde amnesia.⁹ The principle class side effect is respiratory depression. This effect is intensified when coadministered with opiates and dose reduction of the benzodiazepine, opiate, or both is often required. Diazepam is also notorious for injection site pain and phlebitis.¹⁰ Midazolam and diazepam are the most commonly used benzodiazepines. In a nationwide survey, midazolam was preferred over diazepam for endoscopic sedation.⁴ Both drugs demonstrate similar efficacy with regards to sedation.¹¹ Midazolam, however, is associated with greater potency, better amnesic effects,

Table 2 Levels of Sedation and Anesthesia

	Responsiveness	Airway	Spontaneous Ventilation	Cardiovascular Function
Minimal sedation (anxiolysis)	Normal response to verbal stimulation	Unaffected	Unaffected	Unaffected
Moderate sedation (conscious sedation)	Purposeful response to verbal or tactile stimulation	No intervention required	Adequate	Usually maintained
Deep sedation	Purposeful response after repeated or painful stimulation	Intervention may be required	May be inadequate	Usually maintained
General anesthesia	Unarousable even with painful stimulus	Intervention often required	Frequently inadequate	May be impaired

Adapted from Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy, Lichtenstein DR, Jagannath S, Baron TH, et al. Sedation and analgesia in GI endoscopy. *Gastrointest Endosc* 2008;68:815–826.

Table 3 Sedation and Analgesia Medications

Drug	Dosing		Onset	Duration	Comments
	Pediatric	Adult			
Midazolam (Versed [®] , Hoffman LaRoche, Nutley, NJ)	Initial: 0.05–0.1 mg/kg Titrate: 0.025 mg/kg every 5 min	Initial: 0.5–2.5 mg/kg slowly over 2 min Titrate: 0.5 mg/kg	1–5 min	1–2.5 hrs	Major side effect is respiratory depression.
Diazepam (Valium [®] , Roche Pharmaceuticals, Nutley, NJ)	0.1–0.3 mg/kg	Initial: 2.5–10 mg slowly Titrate: 2–5 mg every 5–10 min Max: 20 mg/kg	30 sec–5 min	2–6 hrs	Painful on injection
Meperidine hydrochloride (Demerol [®] , Sanofi-Aventis Pharmaceuticals, Paris, France)	Initial: 1–1.5 mg/kg Titrate: 1 mg/kg increments	Initial: 10 mg Titrate: 10 mg increments	1–5 min	1–3 hrs	
Fentanyl (Sublimaze [®] , Akorn, Inc., Buffalo Grove, IL)	Not recommended	Initial: 0.005–2 µg/kg slowly Titrate: 1 µg/kg every 30 min Max: 4 µg/kg	30–60 sec	30–60 min	
Propofol (Diprivan [®] , Astra Zeneca Corporation, Wilmington, DE)		Initial: 20–60 mg Titrate: 10–30 mg every 30–60 sec	30–45 sec	4–8 min	Deep sedation possible

reduced respiratory depression, and superior patient satisfaction when compared with diazepam.^{12–14}

Midazolam has a rapid onset (1–2 minutes), short duration of action (15–60 minutes), and favorable amnesic properties.¹⁵ The initial dose is 1mg, followed by repeat doses (if needed) of 1 mg in 2-minute intervals until the desired effect is achieved.³ When given in combination with an opiate or other sedatives, the dose of midazolam should be reduced by 30%.¹⁶ Because it is lipophilic, midazolam can be sequestered in adipose tissue resulting in a prolonged sedative effect.¹⁰ Patients who are obese, elderly, or those with impaired hepatic or renal function are at increased risk for delayed drug clearance. In this population, utilization of lower doses and longer intervals of administration should be considered.¹⁶ By comparison, diazepam has less amnesic capabilities, a slower onset of action (2–3 minutes), and prolonged duration of effect (360 minutes).¹⁵ The dose for colonoscopy is 2.5 to 5 mg initially. Additional doses of 2.5 mg every 3 to 5 minutes can be given as needed.

The benzodiazepine receptor antagonist flumazenil should be immediately available for administration in all endoscopy suites. The primary effect of flumazenil is reversal of benzodiazepine-induced sedation and psychomotor impairment. It has minimal effect on reversal of respiratory depression.¹⁷ For this reason, opioid reversing agents (i.e., naloxone) are given prior to flumazenil in situations of benzodiazepine/opioid-induced respiratory depression. The typical flumazenil dose is a 0.2 mg intravenous (IV) bolus and can be repeated three times.¹⁶

Similar to benzodiazepines, opioids are efficacious for induction of moderate sedation.⁷ However, unlike benzodiazepines they provide analgesia as well. This

favorable characteristic enhances the overall sedative effect when opioids are adjunctively used with benzodiazepines. Fentanyl and meperidine are two short-acting opioids used for sedation during colonoscopy. Many endoscopists prefer fentanyl due to its pharmacologic profile and reduced incidence of nausea as compared with meperidine.⁷ Additionally, fentanyl was associated with a shorter procedure time in a recent study comparing meperidine and fentanyl use during upper endoscopy and colonoscopy.¹⁸

Fentanyl is a lipid soluble, synthetic opioid narcotic with a rapid onset (1–2 minutes) and short duration of action (30–70 minutes).¹⁰ For endoscopic procedures, an initial bolus of 50 µg is given. Subsequent doses of 25 µg in 2–5 minute intervals can be administered if necessary. Meperidine has a longer onset (3–6 minutes) and duration of effect (3–5 hours) as compared with fentanyl.^{3,10} The starting dose of meperidine is usually 25 to 50 mg, followed by 25 mg every 2 to 5 minutes if required.

Opioids cause synergistic central nervous system (CNS) and respiratory depression when used in patients taking other centrally acting medications such as antihistamines, benzodiazepines, narcotics, monoamine oxidase inhibitors, and phenothiazines.¹⁶ All opioids reduce seizure thresholds, and narcotic dose reduction or avoidance should be considered in patients with epilepsy. Chest wall rigidity due to increased skeletal muscle tonicity has been reported with high doses of fentanyl.¹⁹ This may result in difficulty with assisted ventilation. Meperidine is metabolized in the liver to normeperidine, an active metabolite with a half-life of 15 to 20 hours.¹⁰ Patients with renal and hepatic insufficiency are at risk for normeperidine accumulation, which

can cause tremors, myoclonus, and seizures.¹⁶ Naloxone does not reverse normeperidine-induced seizures.²⁰ Unlike meperidine, fentanyl does not cause accumulation of active metabolites.²¹

Naloxone is an opioid receptor antagonist used for reversal of narcotic induced CNS effects including respiratory depression, sedation, and analgesia. The typical dose is 0.4 mg every 2 to 4 minutes until adequate clinical response has occurred. The duration of effect of naloxone is shorter than that of fentanyl and meperidine, so all patients receiving rescue doses should be closely monitored for relapse of sedation. In such circumstances, repeat administration of naloxone may be required.

Propofol is an ultra-short acting hypnotic used for induction and maintenance of anesthesia, conscious sedation in minor procedures, and sedation in intensive care unit patients.¹⁰ At doses used during colonoscopy, it provides sedation and mild amnesia but has no analgesic properties.²² It is usually administered in combination with a short-acting benzodiazepine or opioid to enhance each individual drug's desired effect, a method referred to as "balanced propofol sedation" or "multidrug propofol."²³ Given the lack of analgesic effects, when used alone during endoscopy higher propofol doses may be required to maintain patient comfort. This may result in more profound levels of sedation (i.e., deep sedation) than originally targeted for colonoscopy. Indeed, several studies have demonstrated that utilization of balanced propofol for achieving moderate sedation is associated with fewer instances of deep sedation than when opioids and benzodiazepines are used alone.^{24,25}

Propofol is usually given as an initial 20 to 60 mg bolus, followed by repeat doses of 10 to 30 mg in 30- to 60-second intervals as needed.³ As with benzodiazepines and opioids, use of propofol with other sedatives results in synergistic respiratory depression and dose reduction of all medications used may be required.²⁶ It has a rapid onset of action (30–45 seconds) and short duration of effect (4–8 minutes). The primary side effects of propofol are respiratory depression and hemodynamic disturbance, including hypotension, decreased cardiac output, and systemic vascular resistance.¹⁰ Unlike benzodiazepines and opioids, there is no medication available to reverse the effects of propofol.⁷ Instances of propofol oversedation are treated supportively with intravenous fluids and vasopressors as needed for hypotension and maintenance of ventilation until drug effect wears off. Injection site pain during bolus infusion is reported in ~30% of patient's and can be minimized by using a large vein and avoiding veins in the dorsum of the hand.^{7,26} Propofol is formulated in a soybean, egg phosphatide, and glycerol emulsion and is contraindicated in patients who are allergic to soy, egg, or sulfite.¹⁵ Propofol, however, is not contraindicated in patients with sulfonamide allergy.²⁷

Propofol is the most frequently used intravenous anesthetic today.²⁶ It was originally described in 1977

and subsequently approved for "induction and maintenance of general anesthesia" by the Food and Drug Administration (FDA). For this reason, administration of propofol has traditionally been limited to anesthesiologists. However, its utilization and experience by non-anesthesiologists has expanded over the years and now includes a variety of outpatient procedures. A recent survey of gastroenterologists in the United States found that propofol is used in up to 25% of endoscopies; however, 68% of physicians indicated they were reluctant to give propofol due to perceived increased risk of complications.⁴

There is a well-established and growing body of literature to support the safety and efficacy of propofol administration by the endoscopist (termed GI-directed propofol) or nurse administration of propofol under the direction of the endoscopist for sedation during colonoscopy.^{28–32} Greater than 220,000 cases of GI-directed propofol have been reported, with only one reported instance of intubation and no instances of death.²⁸ A recent meta-analysis comparing the effectiveness of propofol to other sedation regimens for colonoscopy found that propofol sedation was associated with faster recovery and discharge times, and increased patient satisfaction without increased side-effects.³³ Given the amount of supporting data, the American College of Gastroenterology (ACG), the American Gastroenterological Association (AGA), and the American Society for Gastrointestinal Endoscopy (ASGE) jointly conclude that "Compared to standard doses of benzodiazepines and narcotics, propofol may provide faster onset and deeper sedation" and that "with adequate training physician-supervised nurse administration of propofol can be done safely and effectively."³⁴

COLONOSCOPY IN THE UNSEDATED PATIENT

Advantages to unsedated colonoscopies include reduced risk of medication-related adverse events such as hypoxemia and hypotension, decreased overall cost, increased recovery time, and ability for the patient to drive and return to work after the procedure. Traditionally, endoscopic evaluation of the colon without administration of pharmacologic sedation has been limited to the flexible sigmoidoscopy. However, there is increasing evidence to support performance of complete colonoscopy without sedation or with on-demand sedation in select cases. Rex et al³⁵ randomized volunteers to undergo colonoscopy with routine sedation or as-needed sedation. In that study, patients of male gender, increasing age, and patients without abdominal pain were more likely to agree to randomization. In the group that received sedation only as needed, colonoscopy was achieved without sedation in 94% of cases. A more recent study from Taiwan found that male gender, high body mass index,

no previous history of gynecological surgery, and previous colonic resection were factors associated with successful completion of colonoscopy without sedation.³⁶ According to the ASGE, characteristics that favor tolerance of colonoscopy with little or no sedation include male gender, patients who are not anxious, older patients, or patients without a history of abdominal pain.⁷ The decision to perform sedation-free colonoscopy should be individualized and take into account the patient's relationship with the performing endoscopist and personal preferences.

PATIENT MONITORING

Conscious sedation is practiced commonly for endoscopic procedures. It is associated with a small but definitive risk. To minimize this risk, patient monitoring is performed in a variety of ways. Some of these modalities are established; others are evolving and more data are needed prior to their incorporation in everyday endoscopy practice. The term monitoring includes the use of both visual as well as physiologic measurement of these parameters. Standard monitoring includes measurement of blood pressure, pulse rate, oxygen saturation, and electrocardiogram (ECG) monitoring. This is usually accomplished by the use of a pulse oximeter, a portable ECG monitor, and automatic sphygmomanometers.

Electrocardiogram

Continuous ECG monitoring is recommended per ASA guidelines for patients with a significant history of cardiovascular disease and arrhythmias.⁵ Other groups benefiting from this are patients with pulmonary disorders, the elderly, and when prolonged procedures are anticipated. The use of continuous ECG monitoring in low-risk patients is not required.

Oxygen Saturation

Arterial hemoglobin oxygen saturation can be monitored in a noninvasive manner with pulse oximetry. Measurement of oxygen saturation is relatively insensitive to early desaturation and as such it is recommended that monitoring of ventilatory function should also include close patient observation. Baseline oxygen saturation of <95%, a procedure of long duration, difficulty with esophageal intubation, comorbid illnesses, and emergency indication for endoscopic procedure are risk factors for hypoxemia. Both ASA and ASGE recommend that pulse oximetry be used during all endoscopic procedures.^{5,7}

Hemodynamics

Monitoring heart rate and blood pressure is important to assess the circulatory status and properly monitor the

effect of sedation. Tachycardia and hypertension may indicate that the patient is sedated inadequately, whereas bradycardia and hypotension may be an indication of oversedation. After baseline measurement of blood pressure and pulse rate, it should be monitored at every 3- to 5-minute interval. Automated noninvasive blood pressure devices are now widely used for this purpose. A recent study advocated using continuous blood pressure monitoring as conventional intermittent blood pressure monitoring of patients receiving sedating agents failed to detect fast changes in BP. The new technique, continuous noninvasive arterial pressure (CNAP) improved the detection of rapid blood pressure changes, and may contribute to better patient safety for those undergoing interventional procedures.³⁷

Capnography

Capnography is a noninvasive technique used to quantify carbon dioxide in expired gases, providing a measure of ventilatory function. It can detect hypoventilation before pulse oximetry can detect oxygen desaturation.³⁸ Data also suggests that capnography is more sensitive in detected alveolar hypoventilation than visual observation.^{39,40}

The principal risk factor for adverse respiratory events during sedation is hypoxia from depressed respiratory activity. Thus, it has been suggested that integrating this modality into patient monitoring protocols may improve patient safety.⁴⁰ Currently, there is insufficient data in support of its use during routine sedation for colonoscopy.^{7,41} The ASA concludes that carbon dioxide monitoring "should be considered for all patients whose ventilation cannot be observed directly during moderate sedation."⁵

Bispectral Index Monitoring

Bispectral index monitoring (BIS) is a noninvasive method of assessment of a patient's level of consciousness. It utilizes an electroencephalographic- (EEG-) based method of measuring a patient's level of consciousness by using a complex algorithm to generate a weighted index.⁴² A BIS index between 70 and 90 corresponds to moderate sedation, between 60 and 69 is deep sedation, between 40 and 59 is general anesthesia, and less than 40 denotes deep hypnosis.⁴³ Several studies have shown a correlation of BIS with validated sedation scales.^{44,45} Compared with clinical assessment of sedation, BIS monitoring values exhibit a significant lag time. Titration of BIS also was not associated with any improvement in clinical outcomes nor was it found to be useful alone in sedation with benzodiazepine/opioid sedation.⁴⁶ The use of EEG monitoring may have a role in the future, but at the current time remains uncertain.⁴⁷

Computer-Assisted Personalized Sedation

CAPS utilizes multiple physiologic feedback parameters, which include electrocardiography, capnography, and automated response monitoring. Patient response to otic and vibratory stimuli is assessed. In a recent study involving 24 patients, oxygen desaturation was noted in only 6% with no device related adverse events.⁴⁸ CAPS is currently not FDA approved.

SUMMARY

Today's colonoscopist is well positioned to play a major role in the management of diseases affecting the large intestine. Thorough knowledge and understanding of techniques available for sedation, analgesia, and monitoring during endoscopic examination of the colon are integral to maximizing patient safety and outcomes.

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