American Society For Gastrointestinal Endoscopy

Guidelines for the use of deep sedation and anesthesia for GI endoscopy

This is one of a series of statements discussing the utilization of gastrointestinal endoscopy in common clinical situations. The Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy prepared this text. In preparing this guideline, a MEDLINE literature search was performed, and additional references were obtained from the bibliographies of the identified articles and from recommendations of expert consultants. When little or no data exist from well-designed prospective trials, emphasis is given to results from large series and reports from recognized experts.

Guidelines for appropriate utilization of endoscopy are based on a critical review of the available data and expert consensus. Further controlled clinical studies are needed to clarify aspects of this statement, and revision may be necessary as new data appear. Clinical consideration may justify a course of action at variance to these recommendations.

BACKGROUND

"Sedation and analgesia" represent a continuum from minimal sedation or anxiolysis through general anesthesia. Practice guidelines have been put forth by the American Society of Anesthesiologists Committee for Sedation and Analgesia by Non-Anesthesiologists, and approved by the American Society for Gastrointestinal Endoscopy.[1,2] In general, most endoscopic procedures are performed with the patient under moderate sedation and analgesia, which is also known as "conscious sedation." At this level of sedation, the patient is able to make a purposeful response to verbal or tactile stimulation, and both ventilatory and cardiovascular function are maintained. Patient responsiveness during "deep sedation" involves purposeful responses to painful stimuli. Airway support may be required. At the level of general anesthesia, the patient is unarousable, even to painful stimuli. Airway support is frequently required and cardiovascular function may be impaired. The endoscopy team must be able to recognize the various levels of sedation and analgesia and rescue a patient who exhibits loss of responsiveness, airway protection, spontaneous respiration, or cardiovascular function.

The level of sedation should be titrated to achieve a safe, comfortable and technically successful procedure. Different patients may require different levels of sedation for the same procedure and patients may attain varying levels of sedation during a single procedure. The purpose of sedation and analgesia is to relieve anxiety, discomfort, or pain, and diminish memory for the event. The level of sedation that is adequate to perform a procedure may range from minimal sedation through general anesthesia. In general, diagnostic and uncomplicated therapeutic upper endoscopy and colonoscopy are successfully performed with moderate (conscious) sedation. Outside of the United States, endoscopy without sedation has been the standard in many countries. Deeper levels of sedation may be considered for longer and more complex procedures, including, but not limited to, ERCP and EUS. Additionally, patients who have been or are anticipated to be intolerant of standard sedatives are also considered for deep sedation or anesthesia. These patients include chronic users of narcotics and benzodiazepines, alcoholics, drug addicts, and patients with neuropsychiatric disorders. Routine use of short-acting anesthetics (e.g., propofol) has been advocated by some authors as a means to improve patient comfort during standard endoscopic procedures.

USE OF ANESTHETIC AGENTS FOR ENDOSCOPY

The combination of a benzodiazepine and narcotic can be used to achieve deep sedation but requires higher doses than those used for moderate sedation. Adjuncts to the benzodiazepine/narcotic combination include diphenhydramine, promethazine, and droperidol. These potentiate the action of the benzodiazepine/narcotic achieving a deeper level of sedation. Droperidol is a neuroleptic agent in the same class as haloperidol and has sedative effects. Randomized trials have demonstrated droperidol's efficacy in patients undergoing therapeutic endoscopy, particularly those who are difficult to sedate.[3,4] Although rarely reported in the GI literature, droperidol has been associated with potentially life-threatening cardiac arrhythmia (Torsade de Pointes).[5] Guidelines for the use of droperidol are shown in Table 1.

Anesthetic agents that have been used for endoscopic procedures include propofol and the inhalational agents such as nitrous oxide, enflurane,

Table 1. Guidelines for the use of droperidol for endoscopic procedures

- Use only in select patients with:
  - Anticipated intolerance of standard sedatives
  - Anticipated long procedure time
- Obtain 12-lead ECG. Droperidol is contraindicated if the QTc is prolonged (>440 msec males, >450 msec females)
- Patients should remain on a cardiac monitor during the procedure and for 2-3 hours afterward
- Use with caution in patients at risk for development of prolonged QT syndrome: CHF, bradycardia, cardiac hypertrophy, hypokalemia/magnesemia, on other drugs known to prolong the QT interval
- Dosage: In adults the initial dosage should not exceed 2.5 mg. Additional doses should be in 1.25 mg aliquots to achieve the desired effect. Maximum dose: 5 mg

Table 2. Appropriate personnel and equipment for propofol use in an endoscopic procedure room

- At least one person who is qualified in both basic and advanced life support skills (i.e., tracheal intubation, defibrillation, use of resuscitation medications)
- Physiologic monitoring should include pulse oximetry, electrocardiography, and automated blood pressure measurement. Monitoring oxygenation by pulse oximetry is not a substitute for monitoring ventilatory function
- Equipment for airway management and resuscitation
- Trained personnel dedicated to the continuous and uninterrupted monitoring of the patient's physiologic parameters and administration of propofol
- Extended monitoring with capnography should be considered as it may decrease the risks during deep sedation

isoflurane, and sevoflurane. The inhalational agents will not be further considered.

Propofol is an anesthetic agent that is Food and Drug Administration–approved for the induction and maintenance of general anesthesia and for sedation in ventilated patients. It is classified as an ultrashort-acting hypnotic agent that provides amnesia, but minimal levels of analgesia. Propofol increases the likelihood of satisfactory deep sedation as well as the risk of rapid and profound decreases in the level of consciousness and cardiorespiratory function, which may culminate in general anesthesia. Propofol rapidly crosses the blood-brain barrier and causes a depression in consciousness that is thought to be related to potentiation of the γ-aminobutyric acid activity in the brain. Typically, the time from injection to the onset of sedation is 30 to 60 seconds. The plasma half-life ranges from 1.3 to 4.13 minutes. Dose reduction is required in patients with cardiac dysfunction and in the elderly because of decreased clearance of the drug. Propofol potentiates the effects of narcotic analgesics and sedatives such as benzodiazepines, barbiturates, and droperidol, and therefore, the dose requirements of these agents may be reduced. Pain at the injection site is the most frequent local complication, occurring in up to 5% of patients. The most serious risk of its use is respiratory depression. Episodes of severe respiratory depression necessitating temporary ventilatory support have occurred in large series using propofol for endoscopic procedures.[6] Personnel specifically trained in the administration of propofol with expertise in emergency airway management must be present during the procedure, constantly monitoring the patient's physiologic parameters (Table 2).

Specific contraindications to propofol administration include allergies to propofol or any of the emulsion components, pregnant or lactating females, and patients with an American Society of Anesthesiologists (ASA) IV or V physical status classification.

EFFICACY OF PROPOFOL FOR ENDOSCOPIC PROCEDURES

The use of propofol in short endoscopic procedures, such as upper and lower endoscopy, has been investigated in several studies with conflicting results. In a randomized study, 90 patients received a bolus administration of propofol or midazolam both before and during upper endoscopy. The propofol treatment arm was superior in terms of patient tolerance, maximum level of sedation achieved, and shorter recovery room times, although amnesia for the procedure and perceived patient discomfort were not different.[8]

A smaller series of 40 patients randomized to receive midazolam or propofol titrated to the same level of sedation before upper endoscopy found that although propofol provided for a shorter recovery room time, it was associated with pain at the injection site, reduced patient acceptance, and a shorter amnesia span.[9] Koshy et al.[10] compared the combination of propofol and fentanyl with midazolam and meperidine in a nonrandomized group of 274 patients undergoing upper endoscopy and colonoscopy. The group receiving propofol and fentanyl had better patient comfort and deeper sedation without an increase in untoward side effects. There was not, however, a significant difference in the recovery times between the two groups. Sipe et al.[11] randomized 80 patients undergoing colonoscopy to combination midazolam/meperidine versus propofol. The propofol group had a greater depth of sedation, modest improvement in satisfaction scores, and faster postprocedure recovery times, all of which were statistically significant. However, a prior randomized study of sedation for colonoscopy in 57 patients did not find a benefit for propofol/fentanyl over diazepam/meperidine or midazolam/fentanyl in

terms of sedation, analgesia, recovery rate, or incidence of side effects. Taken together, these studies have not shown a convincing benefit for propofol when used for standard upper and lower endoscopy. The published studies are heterogeneous with respect to propofol dose, use of a narcotic, and method of administration. Further randomized controlled trials are needed.

Propofol may have more clinically significant advantages when used for prolonged and therapeutic procedures. Two randomized, controlled trials in 80 and 196 patients compared propofol alone with midazolam for ERCP.[12,13] Both studies found improved levels of sedation and faster recovery room times with propofol. In one study, propofol was administered by an anesthesiologist; in the second study, propofol was administered by an assisting physician who was not involved in the endoscopic procedure. A study of propofol that included EUS in addition to ERCP found that patients receiving propofol exhibited significantly improved quality of sedation and shorter recovery times as compared with meperidine/midazolam.[14] In these studies untoward effects such as hypotension and hypoxemia occurred equally in both treatment groups. However, in both of the ERCP series, one patient in the propofol group developed prolonged apnea that necessitated discontinuation of the procedure and temporary ventilatory support.[12,13] The addition of midazolam to propofol in 239 patients undergoing therapeutic upper endoscopy or ERCP significantly lengthened mean recovery time without conferring other clinical benefits over propofol alone.[15]

ADMINISTRATION OF PROPOFOL BY NON-ANESTHESIOLOGISTS

Propofol has been administered by non-anesthesiologists in endoscopic series, including a dedicated gastroenterologist, registered nurses and patient-controlled systems. Vargo et al.[14] conducted a randomized, controlled trial of gastroenterologist-administered propofol versus meperidine and midazolam for elective ERCP and EUS. In this study, a separate gastroenterologist who was trained in propofol administration was used. Additionally, capnography was used to detect apnea or hypercapnea, in order to adjust the propofol dosing accordingly. Patients randomized to propofol exhibited a faster mean recovery time (18.6 vs. 70.5 min), could perform independent transfer after the procedure and were able to achieve a return to a baseline food intake and activity level (71% vs. 16%) more quickly.

The safety and experience with propofol administered by registered nurses has been reported in an abstract including over 1000 patients undergoing elective EGD and/or colonoscopy, and in a single published randomized study.[11,16] All patients were ASA class I or II, standard monitoring with automated blood pressure, EKG, and oximetry was used, and all patients received 3 to 4 L/min of nasal cannula oxygenation. The propofol dosage was an initial bolus of 20 to 40 mg, followed by 10 to 20 mg boluses to maintain sedation. In the randomized study,[11] propofol achieved faster time to sedation, greater depth of sedation, and faster recovery than midazolam/meperidine sedation. Complication rates were similar. Patient satisfaction was high in both groups but better in those receiving propofol. In a separate report, cost effectiveness modeling with a sensitivity analysis found nurse-administered propofol to be the dominant strategy when compared with standard sedation and analgesia.[14]

Patient-controlled sedation and analgesia (PCS) with propofol has recently been reported. Kulling et al.[17] randomized 150 patients to 3 sedation arms: PCS with propofol/alfentanil (Group I), continuous propofol/alfentanil infusion (Group II), and nurse-administered midazolam/meperidine (Group III). Group I exhibited a higher degree of patient satisfaction and more of a complete recovery at 45 minutes when compared with conventional sedation and analgesia. In a similar study, Ng et al.[18] randomized 88 patients undergoing colonoscopy to PCS with propofol alone or midazolam. Patients receiving propofol PCS exhibited significantly shorter recovery times (43.3 min vs. 61.0 min) and improved satisfaction with overall level of comfort. PCS for ERCP however, has not been as successful. In a pilot study using a software system designed to deliver a "ceiling" for the plasma propofol concentration, only 80% of patients received a safe and fully effective sedation.[19]

Electroencephalography has been used to derive a patient state index (a multivariate algorithm that varies as a function of the hypnotic state) and guide propofol use for general anesthesia in non-endoscopic procedures.[20] This may have a role in the future for propofol delivery during endoscopic procedures.

WHO SHOULD BE QUALIFIED TO GIVE PROPOFOL?

Although properly trained physicians can administer propofol, the regulations governing its administration by nursing personnel are variable on a state-by-state basis. The ASA Taskforce recommends that patients receiving propofol should receive care consistent with deep sedation and that personnel should be capable of rescuing the patient from general anesthesia. Appropriate personnel and equipment for propofol use in an endoscopic procedure room are listed in Table 2.

Table 3. Guideline for anesthesiology assistance during gastrointestinal endoscopy

Anesthesiologist assistance may be considered in the following situations:

- Prolonged or therapeutic endoscopic procedure requiring deep sedation
- Anticipated intolerance to standard sedatives
- Increased risk for complication because of severe comorbidity (ASA class III or greater)
- Increased risk for airway obstruction because of anatomic variant (see text)

EXTENDED MONITORING TECHNIQUES

Transcutaneous CO_2 and end tidal CO_2 monitoring are noninvasive methods for measuring respiratory activity. Capnography is based on the principle that carbon dioxide absorbs light in the infrared region of the electromagnetic spectrum. Quantification of the absorption leads to the generation of a curve, which represents a real-time display of the patient's respiratory activity. Capnography more readily identifies patients with apneic episodes and when used to guide sedation results in less CO_2 retention.[21,22] Capnography has also been used to allow the safe titration of propofol by a qualified gastroenterologist during ERCP and EUS.[23] Whether capnography improves outcome has not been demonstrated and would likely require a prohibitively large study.

USE OF ANESTHESIOLOGIST ASSISTANCE FOR ENDOSCOPIC PROCEDURES

Sedation-related risk factors, the depth of sedation, and the urgency of the endoscopic procedure all play important roles in determining whether the assistance of an anesthesiologist is needed. Sedation-related risk factors include significant medical conditions such as extremes of age, severe pulmonary, cardiac, renal or hepatic disease, pregnancy, the abuse of drugs or alcohol, uncooperative patients, or a potentially difficult airway for intubation. The ASA Task force states that airway management may be difficult in the following situations: (1) patients with previous problems with anesthesia or sedation; (2) patients with a history of stridor, snoring, or sleep apnea; (3) patients with dysmorphic facial features, such as Pierre-Robin syndrome or trisomy-21; (4) patients with oral abnormalities, such as a small opening (<3 cm in an adult), edentulous, protruding incisors, loose or capped teeth, high, arched palate, macroglossia, tonsillar hypertrophy, or a nonvisible uvula; (5) patients with neck abnormalities, such as obesity involving the neck and facial structures, short neck, limited neck extension, decreased hyoid-mental distance (<3 cm in an adult), neck mass, cervical spine disease or trauma, tracheal deviation or advanced rheumatoid arthritis; and (6) patients with jaw abnormalities such as micrognathia, retrognathia, trismus, or significant malocclusion.

The ASA Taskforce guidelines recommend that the presence of one or more of sedation-related risk factor, coupled with the potential for deep sedation, will increase the likelihood of adverse, sedation-related events. In this situation, if the practitioner is not trained in the rescue of patients from general anesthesia, then an anesthesiologist should be consulted (Table 3). The routine assistance of an anesthesiologist for average risk patients undergoing standard upper and lower endoscopic procedures is not warranted and is cost prohibitive.

SUMMARY

Anesthetic agents such as propofol and sedation adjuncts such as droperidol, promethazine, and diphenhydramine are useful in certain patients undergoing endoscopic procedures. Although propofol provides faster onset and deeper sedation than standard benzodiazepines and narcotics, as well as faster recovery, clinically important benefits have not been consistently demonstrated in average-risk patients undergoing standard upper and lower endoscopy.[A] The routine use of propofol in these patients cannot currently be endorsed. For prolonged therapeutic procedures, these agents have been demonstrated to be superior to standard benzodiazepine/narcotic sedation and their use should be considered.[A] Deep sedation requires more intensive monitoring by trained individuals.[B] The assistance of anesthesiologists should be considered in patients undergoing prolonged therapeutic procedures requiring deep sedation, anticipated intolerance of standard sedatives, and those at increased risk for sedation-related complications such as patients with severe comorbidities or with anatomic variants increasing the risk of airway obstruction.[C] The use of agents to achieve sedation for endoscopy must conform to individual institution's policies.

LEGEND

A. Randomized controlled trials
B. Nonrandomized controlled trials
C. Expert opinion

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