Fundamental of Endoscopic Surgery: Online Study Guide
Module 3 – Sedation & Analgesia

Learning Objectives

The purpose of sedation and analgesia is to relieve patient anxiety and discomfort, improve the outcome of the examination, and diminish the patient's memory of the event.

Four stages of sedation have been described, ranging from minimal to moderate, deep, and general anesthesia.

After finishing this module, you will be able to:

- Describe the types of sedation used in endoscopic procedures
- Understand the guidelines for sedation and analgesia for non-anesthesiologists
- Describe the levels of consciousness
- Describe how to monitor levels of consciousness
- Describe the medications used for sedation and analgesia in endoscopy

Types of Sedation

While it is possible to perform endoscopic procedures without the use of consciousness altering drugs, in the United States, patients and doctors both have come to expect the convenience and comfort procedural sedation provides.

Moderate sedation with analgesia, commonly referred to as conscious sedation, is characterized by:

- Depressed level of consciousness
- Patient responds to verbal commands
- Patient maintains their own airway
- Airway reflexes remain intact
- Hemodynamic equilibrium maintained

Deep sedation is characterized by:

- Painful stimulus is necessary to evoke a withdrawal response
- Airway protective reflexes cannot be relied upon
- Hemodynamics are usually preserved although instability can occur

Beginning with anxiolysis, and progressing to moderate sedation, deep sedation, and the state of general anesthesia, the level of sedation represents a point on a continuum without clear beginning and endpoints.

Therefore, the clinician endeavoring to provide a comfortable, amnestic endoscopic service must be familiar with the progressive states of sedation, how to induce them, in whom, and how to rescue sedated patients whose vital functions are compromised.

Monitoring

Practice Guidelines

Updated Practice Guidelines for Sedation and Analgesia for Non-Anesthesiologists set forth by the American Society of Anesthesiology Task Force in 2002 recommend that all patients undergoing moderate sedation and analgesia be monitored with:

- Pulse oximetry
- Verbal stimulation to track level of consciousness
- Observation and auscultation of pulmonary ventilation
- Exhaled carbon dioxide monitoring when patient cannot be directly observed
- Blood pressure and heart rate at five-minute intervals during the procedure
- Continuous electrocardiography (ECG) for patients with significant cardiovascular disease.

Monitoring end tidal CO_2 (capnography) and an ECG should be routine for patients who undergo deep sedation or sedation with propofol.

Anesthesia Monitoring

During the endoscopic procedure, a designated person other than the endoscopist should be dedicated to monitoring the patient. This is usually a nurse, physician assistant, or another physician.

The assistant's primary role must be to attend to the patient at all times. The assistant should be certified in basic life support (BLS) and have a working knowledge of the pharmacology of hypnotics and sedatives.

In addition to immediate availability of BLS, the following should be available for all procedures to be performed under sedation:

- Advanced life support should be available within 5 minutes
- A resuscitation cart with appropriate equipment, medications, and instructions must be nearby if a patient with significant medical disease is to undergo sedation

Morbidity/Mortality

While the morbidity and mortality associated with endoscopic procedures is low, there is room for improvement.

In 1997 Schauer et al reported complications of surgical endoscopy performed by residents in 9,201 cases.

- Overall complication rate was
    - 1.4% for upper endoscopy
    - 0.42% for lower endoscopy
- The mortality rate was
    - 0.76% for upper endoscopy
    - 0.6% for lower endoscopy

No deaths could be directly attributed to the endoscopic procedure.

Morbidity and mortality rates for conscious sedation are higher than for general anesthesia. Inadequate monitoring has been cited as one factor that may lead to increased complications.

Oxygenation

Oxygenation is measured using continuous pulse oximetry. The oximeter should have an audible indicator to facilitate early recognition of desaturation.

Muller et al's study of 186 patients undergoing ERCP found the following risk factors associated with desaturation:

- Age greater than 60 years
- ASA 3 or higher
- Lengthy, more complex procedures were more likely to show hypoxemia

Several studies show that supplemental oxygen delivery reduces the risk of hypoxia as well as its duration and degree. The ASA Task Force recommended that supplemental oxygen should be considered for moderate sedation and should be administered during deep sedation unless specifically contraindicated.

Care must be taken to avoid respiratory depression by eliminating the hypoxic drive in those patients who have COPD.

The ASA task force warns specifically against using pulse oximeters to monitor hypoventilation since they give no information regarding ventilatory function. Instead, the task force recommends capnography if the procedure is anticipated to be prolonged or if it is warranted by the clinical situation.

Level of Consciousness

MOAA/S

Interval prompting for verbal responsiveness to commands or light physical stimulation indicates the level of consciousness and helps guide drug administration. Verbal responsiveness is a reliable indicator of a moderately sedated patient and verifies the patient is breathing.

During a procedure where verbal response is impossible, such as upper endoscopy, the patient is asked to give “thumbs up” or a similar purposeful gesture to indicate alertness.

While most procedures are intended to be performed under moderate sedation/analgesia, Patel et al showed that deep sedation occurs more frequently than anticipated. They employed the Modified Observer’s Assessment of Alertness/Sedation Score (MOAA/S) to measure sedation. Fortunately, deeply sedated patients were not more likely to suffer adverse effects. At least in relatively healthy subjects, deep sedation appears to be well tolerated for brief periods.

In deep sedation, only painful stimulation or repeated physical stimulation elicits a purposeful withdrawal response.

Bispectral Index

Employing Bispectral (BIS) index monitoring to help guide conscious sedation has become common in many facilities. This technology uses selective continuous electroencephalographic (EEG) monitoring to give an objective assessment of the sedation level.

The monitor uses a complex mathematical algorithm to calculate the level of sedation and assigns a score from 0 to 100. Zero represents no brainwave activity (coma) and 100 is fully awake.

Using BIS monitoring, Bower et al demonstrated a temporal correlation with sedation levels measured by the Observers Assessment of Alertness/Sedation (OAA/S) scoring system. In their preliminary, observational study, they were able to correlate a BIS level near 82 as sufficient to perform routine endoscopy.

Unfortunately, BIS levels become less precise as patients became more deeply sedated.

A recent study demonstrated that BIS had a low accuracy for detecting deep sedation as a result of a considerable overlap of MOAA/S scores across the sedation levels.

Further refinements in BIS are needed to differentiate deep from moderate sedation for future studies on conscious sedation.

Pulmonary Ventilation

According to the ASA Task Force, the primary causes of morbidity in patients undergoing endoscopy stem from drug-induced respiratory depression (hypoventilation) and airway obstruction.

Pulmonary ventilation has traditionally been monitored using auscultation and visual assessment of respiratory excursion. In most cases, these methods are adequate provided that the thorax remains undraped and readily visible.

Two more effective methods of identifying hypoventilation have been proposed:

- Side channel end tidal CO_2 ($PetCO_2$) capnography
- Transcutaneous ($PtcCO_2$) capnography
    - Based on the same principle as pulse oximetry

Both of these methods give real-time, graphical information regarding respiratory/ventilatory function and are non-invasive.

Two studies have demonstrated the superiority of capnography over clinical assessment in the detection of apnea.

Hemodynamics

As sedation deepens, undesirable hemodynamic effects may emerge.

Hemodynamic complications include hypotension, hypertension, and arrhythmia.

Blood pressure and heart rate should be checked before administration of any sedatives to establish a baseline.

The ASA Task Force recommends monitoring patients with underlying cardiovascular disease or a history of arrhythmia with continuous electrocardiogram.

Routine cases should be monitored with:

- Automated blood pressure cuffs
- ECG tracings
- Pulse oximetry

Conscious Sedation

Endoscopist Delivered Sedation

For the purposes of routine screening endoscopy and limited-duration therapeutic procedures, conscious sedation generally suffices and can be delivered safely and cost-effectively by the endoscopy team.

Traditionally, endoscopists have relied upon benzodiazepines combined with narcotics to deliver sedation and analgesia to their patients undergoing endoscopy. The usual combination is Sublimaze® (fentanyl) and Versed® (midazolam).

Anesthesiologist Assistance

Anesthesiologists have increasingly become involved with providing conscious sedation, especially in more advanced endoscopic procedures. According to Medicare records, the services billed by anesthesiologists for sedation for endoscopy more than doubled between 2001 and 2003.

Guidelines published by the ASGE endorse the assistance of an anesthesiologist when there are significant airway abnormalities that may interfere with emergent intubation. These include:

- Prolonged or therapeutic endoscopic procedures requiring deep sedation
- Anticipated intolerance to standard sedatives
- Increased risk of complication because of severe comorbidities (ASA class 3 or greater)
- Increased risk of airway obstruction because of anatomic variant

The ASA Task Force guidelines further caution that the presence of serious comorbidities may lead to more sedation-related adverse events, especially when there is the potential for deep sedation.

Medications

Benzodiazepines

Short-acting benzodiazepines commonly used to provide relaxation and enhance cooperation during endoscopy include Versed® (midazolam) and Valium® (diazepam).

The benefits of Versed® (midazolam) compared to Valium® (diazepam) include:

- Shorter duration of action
- Less venous irritation
- Water solubility
- More pronounced anterograde amnesia

The dosage of Versed® (midazolam) depends on the clinical status of the patient, comorbidities, complexity and duration of the procedure, and concomitant usage of narcotics. The usual starting dose is 0.5 mg to 2 mg IV or 0.05 to 0.1 mg/kg given slowly as an initial bolus dose.

Onset of action is between 3 and 5 minutes and even more rapid when combined with a narcotic. Dosages can be titrated to effect during the procedure in 0.5 mg increments at 2 to 5 minute intervals. Allow at least two minutes before re-dosing to evaluate the full sedative effect.

The usual dose for routine upper and lower endoscopy ranges from 2.5 mg to 5 mg.

Dosages should be reduced in the following instances:

- Elderly, debilitated, or chronically ill patients (50% reduction)
- Liver disease (50% reduction)
- Renal failure (50% reduction)
- When used in combination with narcotics (30 to 50% reduction).

Administration

There is evidence that giving a single large bolus of Versed® (midazolam) is efficacious and safer than titrating slowly throughout the procedure.

Yi et al randomized three groups undergoing upper endoscopy to receive varying doses of Versed® (midazolam) as a single pre-procedure bolus. With a single bolus dose of 0.06 mg/kg Versed® (midazolam):

- Patient satisfaction was good
- Time to discharge was shortened
- There were fewer paradoxical reactions

Romazicon® (flumazenil) was not found to be helpful in shortening the time to discharge except in patients receiving 0.09 mg/kg Versed® (midazolam).

Complications

In addition to providing relaxation and amnesia, benzodiazepines can cause serious, at times life threatening, side effects, most notably:

- Hypoventilation
- Hypotension
- Paradoxical agitation

The antagonist, Romazicon® (flumazenil)**,** counteracts the respiratory depressant effects of Versed® (midazolam) and should be readily accessible. The starting dose of Romazicon® (flumazenil) is 1 mg IV titrating to effect in 0.2 mg increments. Peak effect occurs 10 minutes after administration.

Exercise caution in patients who are on chronic benzodiazepines as seizures can occur.

Opioids

Fentanyl

Opioids, such as Demerol® (meperidine) and Sublimaze® (fentanyl) administered intravenously, provide both analgesia and sedation. Fentanyl has a more rapid onset of action and clearance and has a lower incidence of nausea compared with meperidine.

Because opioids and benzodiazepines have synergistic effects when combined, their doses must be reduced to prevent oversedation.

Sublimaze® (fentanyl) is a synthetic opioid. If given alone, dosage should begin at 1 to 2 µg/kg, which is about 75 to 150 µg for an average size adult. Use less if combining with benzodiazepine. The average patient usually requires 50 to l00 µg.

Sublimaze® (fentanyl) has an immediate response and provides excellent analgesia. The half-life is 2 to 4 hours, but patients should not do any activities that require fine motor or cognition skills (such as driving or cooking) on the day of administration.

Remifentanil

Ultiva® (remifentanil), an ultra-short-acting opioid, has advantages over other opioids, because of its rapid onset and offset times, making it suitable for control of pain during colonoscopy.

Clinical studies have demonstrated that low-dose remifentanil has the following advantages compared to propofol:

- Better hemodynamic stability
- Excellent patient satisfaction
- Faster recovery
- No significant difference in respiratory depression

However, discharge times were similar for remifentanil and propofol.

A recent study showed that remifentanil during colonoscopy compared to moderate sedation with midazolam and meperidine provides:

- Sufficient pain relief
- Better hemodynamic stability
- Less respiratory depression
- Faster recovery

Reversal

Whenever opioids are used for analgesia, Narcan® (naloxone) should be immediately available. Narcan® (naloxone) is a high affinity, competitive inhibitor of the opioid receptor.

It dramatically reverses the central nervous system depressive effects and analgesia within 2 minutes. It has a half-life of 1 to 1.5 hours.

The usual dose is 0.4 mg IV, repeating as necessary up to 2 mg. Repeat dosing may be necessary as many opioids have longer duration of action compared with Narcan® (naloxone). Therefore, after reversal, close monitoring of the patient for re-sedation is necessary.

Rapid IV administration can lead to a rigid chest wall and difficulty breathing. Emergent intubation may be necessary if Narcan® (naloxone) fails to reverse the effects completely.

Propofol

Propofol is classified as an ultra-short-acting hypnotic agent that provides sedative, amnestic, and hypnotic effects with no analgesic properties. Propofol potentiates the central nervous system effects of narcotic analgesics and sedatives such as benzodiazepines, barbiturates, and droperidol.

Typically, the time from injection to the onset of sedation is 30 to 60 seconds. Its duration of effect is 4 to 8 minutes.

The cardiovascular effects of propofol include:

- Decrease in cardiac output
- Decrease in systemic vascular resistance
- Decrease in arterial pressure
- Negative cardiac inotropy
- Respiratory depression

These effects reverse rapidly with dose reduction or interruption of drug infusion and rarely require temporary ventilatory support.

There is no reversal agent for propofol.

Because of synergistic effects, propofol doses can be reduced significantly when used in combination with midazolam and narcotics, possibly improving safety.

Propofol is contraindicated in patients with:

- Propofol allergy
- Hypersensitivity to eggs or soybeans

Studies have demonstrated an advantage of sedation with propofol for endoscopy over sedation with an opioid/benzodiazepine combination for:

- Recovery time
- Patient satisfaction

However, none of the trials is adequately powered to demonstrate superior safety of propofol compared to traditional sedative regimens.

Recovery

Observation

After the procedure, the patient should be transferred to the recovery area and directly observed by staff until discharge.

While in recovery, patients are still at high risk for complications related to sedation. Delayed presentation of undesirable side effects can be produced by:

- Lack of procedural stimulation
- Variable drug absorption
- Slow drug elimination

Monitoring patients post-procedure should be tailored according to the patient's comorbidities, drugs used, type, and duration of procedure performed.

Rescue equipment and medications (such as resuscitation/code cart) should be readily available as well as a clinician trained in advanced cardiac life support and airway management. Vital signs should be checked frequently (q 5 min) initially, then less so after the patient shows signs of stabilization.

If reversal agents were administered, the patient should remain under observation until the sedating drugs have worn off. Vigilance protects against resedation that may need reversal.

Discharge Criteria

Discharge criteria are usually standardized and include:

- The ability to stand unassisted
- The ability to tolerate clear fluids
- A return to baseline alertness

The discharge criteria and practice recommendations by the American Society of Anesthesiologists Task Force include:

- Alert and oriented or back to baseline mental status
- Stable vital signs that are within acceptable limits: documentation of patient's vital signs are kept
- Use of scoring system (for example, the OAA/S or the MOAA/s) may help assist in documentation of fitness for discharge
- Sufficient time (up to 2 h) should have elapsed after the last administration of reversal agents (naloxone, flumazenil) to ensure that patients do not become re-sedated after reversal effects have worn off.
- Outpatients should be discharged to care of adult who can transport the patient home and report complications
- Provide written instruction regarding diet, medications, and activities
- An emergency phone number should be provided

Reduce Time/Cost

A large part of the cost of outpatient endoscopy is made up of the staff time needed to recover patients after conscious sedation. Some have proposed using Romazicon® (flumazenil) routinely post-benzodiazepine administration to reduce recovery time and charges.

Wille et al, in a study of 100 patients undergoing routine EGD, randomized half to get Romazicon® (flumazenil) post Versed® (midazolam) and Demerol® (meperidine). The remaining patients received a placebo. Using discharge criteria based on the OAA/S, they showed that the Romazicon® (flumazenil) group had shorter recovery times. However, when they factored in the cost of the drug, overall charges were not reduced by a statistically significant amount.

Alternative Sedation

Distraction

Controlling patient anxiety may decrease the dose of sedative medication required for endoscopic procedures.

Lee et al conducted a prospective randomized controlled trial to evaluate the efficacy of visual and audio distraction during colonoscopy.

They showed when both audio and visual distractions were introduced together, the dose of sedative medication required and the patients' pain scores decreased significantly.

Nitrous Oxide

Nitrous oxide has been tried as a sedative for colonoscopy but results have been poor.

Forbes et al randomized patients to undergo either routine sedation (midazolam/meperidine) or Entonox® (50%/50% oxygen, nitrous oxide gas) for colonoscopy. Results showed that Entonox® patients:

- Reported more pain (p less than 0.0001)
- Tolerated colonoscopy less well (p less than 0.0001)
- Were less satisfied (p = 0.01)
- Were less willing to undergo colonoscopy again under the same circumstances (p = 0.04)

Dexmedetomidine

The α2 adrenergic receptor analog, Precedex® (dexmedetomidine), proved to be inferior to the combination of meperidine and midazolam or fentanyl in spite of its success as an ICU sedative.

Dexmedetomidine's problems include:

- Significant hemodynamic instability
- Frequently required the addition of fentanyl to complete the procedure
- Produced prolonged recovery
- Was complicated to administer

Small Caliber Endoscopy

Characteristics/Benefits

With the advent of small caliber endoscopy (SCE), it is now feasible to perform an ever-expanding range of endoscopic procedures without the inherent risks and costs of procedural sedation.

- The characteristics of the small caliber endoscope are:
- Diameter of 3 to 6 mm
- Lengths varying from 65 to 110 cm
- Working port
    - Allows biopsy specimens of the mucosal surface to be obtained

Provides full examination of the oropharynx, hypopharynx, esophagus, stomach, and the duodenum.

Studies show that SCE is comparable to conventional endoscopy in diagnostic yield and is generally well tolerated. Most patients would undergo the procedure again.

Using SCE in procedures has several advantages including:

- Reduced risks from procedural sedation
- Cost savings by eliminating a staff of trained nurses
- Cost savings from eliminating monitoring equipment
- Patients do not have to miss an entire day of work
- Patients do not require an escort home

Application

Complete anesthesia of the nasopharynx, oropharynx, and hypopharynx is critical for the comfortable passage of the endoscope.

Position the patient upright in a sitting position and anesthetize as follows, instilling to the most patent naris:

- 7 ml aerosolized 4% lidocaine and 0.05% oxymetazoline hydrochloride 50% by volume over a 5-minute period by atomizer
- Single 3-second aerosolized 14% benzocaine to the hypopharynx
- 5 ml of 2% lidocaine jelly by syringe

The total amount of lidocaine administered should not exceed 200 mg.

Adverse effects of these topical anesthetics include:

- Aspiration
- Anaphylactoid reactions
- Methemoglobinemia

Complications

Despite its multitude of benefits, close monitoring of the patient during the procedure remains critical. SCE is not without its complications.

Side effects associated with SCE include:

- Profound vagal stimulation with possible hypotension and hypoxia
- Epistaxis

Loss of the normal sensory input of air traversing the hypopharynx may cause the patient some anxiety. A globus sensation is often reported. Trouble swallowing and a sensation of not getting enough air are common reports. Reassurance often settles the patient until they become accustomed to the lack of sensation.

Contraindications include:

- Coagulopathy
- Prior trauma or surgery to the nasopharynx, oropharynx, or hypopharynx

Because so few SCE procedures have been undertaken to date, the absolute complication rate is unknown.