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ANESTHESIA FOR BRONCHOSCOPY

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INTRODUCTION

Instrumentation of the airway is among the most noxious procedures physicians perform. Laryngoscopy and tracheal intubation require 1.3–2.8 times more inhalation anesthesia than does surgical incision. Physiologic responses to bronchoscopy include hypertension, tachycardia, increased cardiac output, laryngospasm, bronchospasm, retching, and vomiting. These hemodynamic and respiratory changes may be well tolerated by healthy individuals, but can lead to myocardial ischemia or respiratory compromise in others. To safely and effectively perform bronchoscopy and other airway procedures, pulmonary specialists must be able to adequately anesthetize the upper airway with local anesthetics, and safely administer moderate (conscious) sedation. This chapter will describe the methods used to anesthetize the oropharynx and upper airway, and the safe use of sedative hypnotics to minimize the frequency and severity of these complications.

AIRWAY ANESTHESIA

Neuroanatomy of the Airway

Branches of the Vth, IXth, and Xth cranial nerves provide sensation to the airway. The nasal mucosa is innervated by the sphenopalatine plexus, composed of branches of the maxillary branch of the trigeminal nerve. These fibers lie just below the mucosa along the lateral wall of the nares, posterior to the middle turbinate. Sensation to the anterior 2/3 of the tongue is provided by fibers of the mandibular branch of cranial nerve V. The posterior 1/3 of the tongue and the pharyngeal mucosa to the vocal cords are innervated by the glossopharyngeal nerve through the pharyngeal plexus. The superior laryngeal and recurrent laryngeal branches of the vagus innervate the vocal cords, trachea, and bronchi.

Local Anesthetic Techniques

Many of the nerves of the airway can be directly anesthetized by injection or topical application of local anesthetics. Direct injection of the sphenopalatine plexus nerves can be accomplished by injecting 2–3 mL of local anesthetic below the nasal mucosa just posterior to the middle turbinate. However, this technique is impractical and runs the risk of intravascular injection. It also can lead to blood in the airway, obscuring fiber-optic visualization. More commonly, local anesthesia-soaked pledgets or cotton packing is pressed against the mucosa, anesthetizing the underlying nerves. A cotton swab is introduced into the nares and advanced along the turbinate all the way to the posterior wall of the nasal passage. A second swab is then advanced angled slightly more cephalad to the first along the middle turbinate. This swab is more likely to block

the sphenopalatine plexus. These pledgets should be kept in place for 2–3 minutes to allow submucosal penetration of the local anesthetic. A 4% cocaine solution has traditionally been used for this procedure because of its vasoconstrictive properties, but lidocaine works as well.

The glossopharyngeal nerve can be similarly blocked by either injection or topical administration of local anesthetic at the base of the posterior tonsillar pillar (palatopharyngeal fold). After careful aspiration to prevent injection into the nearby carotid artery, approximately 5 mL of local anesthetic are injected into the submucosa. A 22-gauge, 9-cm needle is used, and the last 1 cm is bent to facilitate injection behind the pillar. Alternatively, cotton pledgets soaked in local anesthetics can be placed at the base of the posterior tonsillar pillar. Care must be taken not to inject too anteriorly, or the hypoglossal nerve can be blocked and motor function of the tongue impaired.

The internal branch of the superior laryngeal nerve can be blocked where it pierces the thyrohyoid membrane, halfway between the hyoid bone and the superior border of the thyroid cartilage. With the patient's neck extended, the hyoid bone is moved laterally. The overlying skin is prepped with an alcohol wipe. A 25-gauge, 2.5-cm needle is advanced until it contacts the superior cornu of the hyoid bone, and is then walked off the cornu inferiorly. It is then advanced another 2–3 mm. As the needle passes through the thyrohyoid membrane, a loss of resistance or "pop" is felt. At that point, approximately 3 mL of local anesthetic are injected deep and superficial to the membrane. Alternatively, the needle can be advanced until air is aspirated and then withdrawn to the submucosal space and the medication injected. The procedure is then repeated on the contralateral side. Care must be taken to avoid intravascular injection into the carotid artery.

Finally, the trachea can be anesthetized by injection of lidocaine through the cricothyroid membrane. With the patient supine, the skin over the membrane is sanitized with an alcohol wipe, and a 22- or 20-gauge needle is used to puncture the membrane. Approximately 4 mL of 2% lidocaine is then quickly injected during maximal exhalation. Although this technique is simple and very effective, hemorrhage and even death have been reported because of laceration of small arteries in the cricothyroid membrane.

Although the nerve blocks and injections described above are all effective, they require multiple steps and can be unpleasant for the patient. Therefore, techniques that simply deliver the local anesthetics topically to the mucosa of the airway are more common. Several such techniques exist. First, the patient can be asked to gargle and "swish" a 2% viscous lidocaine solution. This technique can effectively anesthetize the tongue, mouth, and posterior pharynx. Alternatively, a nebulizer can be used to deliver aerosolized local anesthetic from the mouth to the lungs. Approximately 10 mL of 4% lidocaine are administered through a standard nebulizer. This technique is well tolerated, effective as the sole technique in 50% of patients, and may be associated with lower plasma levels compared with direct endobronchial administration; however, nebulized lidocaine may not decrease the amount of supplemental lidocaine needed by direct, endobronchial injection, and high serum levels have been described with this technique. Various sprays and atomizers can be used to directly spray the posterior pharynx. After the tongue has been sprayed, it can be grasped with gauze and the spray device inserted into the posterior pharynx. The patient is asked to take deep breaths, and local anesthetic is sprayed during inspiration. Commercially available products can be used to administer benzocaine, or a standard atomizer can be filled with lidocaine for this technique.

Finally, the bronchoscopist can simply use the "spray-as-you-go" method, administering the local anesthetic through the working port of the scope. Lidocaine (4%) is used most frequently above the vocal cords with this method, whereas 2% lidocaine is generally used below the cords. One report found this technique superior to nebulized lidocaine. All of the techniques described

Table 5.1. *Local anesthetics*

Drug	Maximum dose	Concerns
Lidocaine	• 4–9 mg/kg (37,40) • 200–400 mg max dose (25,87) • <175 mg/m^2 (20)	• Seizures • Ventricular tachydysrhythmias • Sedation
Benzocaine	1–2 s spray of Cetacaine or Hurricaine (9)	• Methemoglobinemia
Cocaine	1 mg/kg (4)	• Hypertension • Tachycardia • Myocardial ischemia and infarction

above for anesthetizing the airway are effective and safe when properly employed. Comparisons between them have not demonstrated that one is clearly superior to another.

Local Anesthetic Drugs and Their Complications

Several local anesthetics have been described for airway anesthesia, including lidocaine, tetracaine, benzocaine, and cocaine (see Table 5.1). Of these, 2% and 4% lidocaine are the most common. Irrespective of the technique used for airway anesthesia, the bronchoscopist must be vigilant in watching for signs and symptoms of local anesthetics toxicity. During a nerve block technique, the intra-arterial injection of even a small amount of local anesthetic into the carotid artery can cause seizures and other central nervous system (CNS) toxicity. Topical techniques can lead to the absorption of large quantities of the local anesthetic and to systemic toxicity. The signs and symptoms of local anesthetic toxicity are described in Table 5.2. When doses of 300–400 mg of lidocaine are used, serum lidocaine levels are generally well below toxic levels. The serum concentration is directly related to the dose of local anesthetic administered , and symptoms generally occur when the serum level is >5 mg/L. However, clinicians frequently administer more than the recommended doses without apparent complications, with doses exceeding 600 mg being described. The apparent relative safety of these larger doses is probably due to the fact that 88%–92% of the drug administered by a nebulizer is wasted. Nonetheless, high serum lidocaine levels, seizures, and even death from local anesthetic toxicity have been described.

Table 5.2. *Signs and symptoms of local anesthetic toxicity*

Early signs and symptoms	Late signs and symptoms
Metallic taste	Somnolence
Tinnitus	Sedation
Anxiety	Seizure
Light-headedness	Ventricular arrhythmia (V. Tach and V. Fib)
	Cardiovascular collapse

The use of benzocaine spray or cocaine solution raises other specific concerns. Benzocaine metabolism in the blood can lead to the formation of methemoglobinemia. Although this is a relatively rare complication, severe cyanosis, arterial desaturation to levels below 40%, and death have been reported. Methemoglobin levels above 30% are common. Use of a benzocaine spray (compared with other gel or solution applications) increases the likelihood of methemoglobinemia, and it has been described after only a single spray. Treatment includes supplemental oxygen and intravenous (IV) methylene blue (1 mg/kg). Cocaine is frequently used for topical anesthesia of the nose. Its effects on the cardiovascular system are well known. Myocardial ischemia and infarction have been described after topical cocaine administration to the airway.

The administration of anticholinergic agents, such as atropine or glycopyrrolate, is frequently

recommended to decrease secretions, improve visibility, and enhance the efficacy of topical local anesthetics. Although this practice is not recommended prior to bronchoscopy, it remains common. Randomized trials have demonstrated that these medications do not improve the quality of airway anesthesia or bronchoscopic view. Higher serum lidocaine concentrations have been reported after the use of atropine. Clinicians should be wary of the potential complications from the tachycardia caused by these medications.

MODERATE SEDATION

Introduction

Adequate local anesthesia allows the clinician to perform flexible, fiber-optic bronchoscopy without the addition of sedatives or anxiolytics, and the concomitant administration of moderate (conscious) sedation during this procedure is controversial. Conflicting data exist as to whether sedation improves patient tolerance of the procedure. In addition, many of the complications associated with bronchoscopy, and up to 1/2 of the life-threatening events can be attributed to the sedation. Others have suggested that sedation should be routine for bronchoscopy. Irrespective of this controversy, a large majority of physicians routinely administer sedation during bronchoscopy. Thus, it is incumbent on the bronchoscopist to understand the regulatory requirements, risks, benefits, medication dosages, monitoring requirements, and impact of patient disease states to safely administer moderate sedation.

Definition and Oversight

Many local, state, and national agencies have published recommendations, guidelines, and standards for the administration of sedation. The clinician must become familiar with these regulations and any local hospital policies regulating the practice of sedation. The American Society of Anesthesiologists (ASA) has published guidelines for the administration of sedation and analgesia by nonanesthesiologists. These guidelines define a continuum of sedation depth, ranging from minimal sedation (anxiolysis) to general anesthesia, as described below.

- **Anxiolysis:** A drug-induced state during which patients respond normally to verbal commands. Although cognitive function and coordination may be impaired, ventilator and cardiovascular functions are unaffected.
- **Moderate sedation/analgesia (previously called conscious sedation):** A drug-induced depression of consciousness during which patients respond purposefully to verbal commands, either alone or accompanied by light tactile stimulation. No interventions are required to maintain a patent airway, and spontaneous ventilation is adequate. Cardiovascular function is usually maintained (withdrawal from a noxious stimulus is not purposeful movement).
- **Deep sedation:** A drug-induced depression of consciousness during which patients cannot be easily aroused but respond purposefully following repeated painful stimulation. The ability to independently maintain ventilatory function may be impaired. Patients may require assistance in maintaining a patent airway, and spontaneous ventilation may be inadequate. Cardiovascular function is usually maintained (withdrawal from a noxious stimulus is not purposeful movement).
- **General anesthesia**: A drug-induced loss of consciousness during which patients are not awakened, even by painful stimuli.

The ASA guideline outlines recommendations for preprocedure patient evaluation, patient monitoring, equipment availability, training of personnel, drug administration, and the recovery and discharge of patients during moderate or deep sedation. A full review of these guidelines is beyond the scope of this chapter, but the pulmonary physician should be familiar with its contents. In addition, The Joint Commission has adopted many of the recommendations of

the ASA guideline and uses the same definitions for moderate and deep sedation. Furthermore, nine Joint Commission standards apply directly to the administration of sedation. All clinicians who administer sedation for interventional pulmonary procedures in the United States must comply with these standards:

- **Moderate or deep sedation is provided by qualified personnel.** This indicates that all personnel who administer sedation must be trained in and have privileges for the safe administration of the sedative medications. In addition, they must be trained to rescue the patient from a deeper than expected level of sedation. Advanced Cardiac Life Support (ACLS) training generally fulfills this requirement.
- **Sedation risks and options are discussed prior to administration.** Clinicians frequently include informed consent for sedation on the form for the procedure.
- **A presedation assessment is performed.** This includes a history and physical examination, evidence that the patient is NPO (*nil per os*, i.e., nothing by mouth) in accordance with guidelines, and specific comorbidities that might impact the safe conduct of the sedation are identified. It also includes a determination that the patient is an appropriate candidate for the procedure and sedation and an immediate preinduction reassessment.
- **Moderate or deep sedation is planned.** Many clinicians create a set of sedation orders that they can complete prior to the procedure.
- **Each patient's physiologic status is monitored during sedation**. See section on monitoring.
- **Each patient's postprocedure status is assessed on admission to and before discharge from the postsedation recovery area.**
- **Patients are discharged from the postsedation recovery area by a licensed, independent practitioner (LIP) or according to criteria approved by the medical staff.** Most institutions create specific, objective criteria for discharge home or to an inpatient unit for patients who receive sedation. These criteria should include an adult escort home and postsedation instructions (including 24-hour contact information). The clinician must be aware that he or she is still responsible for the safe discharge of the patient, even if the patient has been sent home by a nurse in accordance with hospital criteria.
- **Each patient's physiologic status while undergoing moderate or deep sedation is collected and analyzed.** Many institutions have created a form, much like an anesthesia record, for documenting the conduct of moderate or deep sedation.
- **Outcomes of patients undergoing moderate or deep sedation are collected and analyzed.**

Many other organizations, including the American Association of Respiratory Care, the Association of Operating Room Nurses, the American College of Emergency Physicians, and others, have published guidelines and standards regarding sedation to which the pulmonary physician may be held.

Preprocedure Assessment

The ASA moderate sedation guidelines and The Joint Commission standards require that all patients undergoing moderate or deep sedation have a presedation medical assessment. In addition to a standard history and physical examination, this assessment should include information specific to the safe conduct of moderate sedation:

- Evidence that the patient is NPO in accordance with recommended guidelines
- Assessment of the airway (see below)
- Determination of the ASA Physical Status score (see below)
- Evaluation for abnormalities of any major organ system that could negatively impact the safe conduct of sedation
- Determination that the patient has an adult escort home (for those undergoing an outpatient procedure)

Table 5.3. *ASA physical status*

ASA class	Definition	Examples
Class I	No organic, physiologic, biochemical, or physical disturbances. Process for which the procedure is being performed is localized	Healthy patient
Class II	Mild to moderate systemic disturbance caused either by the condition to be treated or other process	Controlled hypertension, mild asthma, AODM, stable (mild) CAD
Class III	Severe systemic disturbance from whatever cause. Impacts daily function	CAD, COPD, compensated CHF, SLE
Class IV	Life-threatening systemic disturbance	Unstable CAD, end-stage renal failure, severe CHF/COPD, long-standing IDDM with end-organ involvement
Class V	Moribund. Not expected to survive 24 h with or without therapy	Ruptured AAA, gunshot wound, severe sepsis

Note: AODM, adult-onset diabetes mellitus; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CHF, congestive heart failure; SLE, systemic lupus erythematosus; IDDM, insulin-dependent diabetes mellitus; AAA, abdominal aortic aneurysm.

- History of adverse experience with sedation
- Consent for sedation (this may be included in the procedural consent)

Assessment of the airway is important because it helps identify those patients in whom endotracheal intubation may be difficult or impossible if they were to become oversedated. The Mallampati classification is one way to identify patients who might be difficult to intubate. To perform this evaluation, ask the patient to open his or her mouth fully and extend the tongue without phonating. The classification is as follows:

- Class I: The entire tonsillar pillars are visible, as is the posterior pharynx
- Class II: The top half of the tonsillar pillars can be seen
- Class III: The tonsillar pillars cannot be seen, but the base of the uvula is visible
- Class IV: Only the hard palate can be seen

Other physical markers of a potentially difficult intubation include a receding mandible, limited mouth opening (<3.5 cm between upper and lower incisors), pronounced overbite of the maxillary incisors, a decreased thyromental distance, and a history of a difficult or failed intubation. Patients deemed to be at significantly increased risk for difficult intubation may benefit from having an anesthesiologist perform the procedural sedation.

The physician who administers moderate or deep sedation must also understand the impact that comorbid diseases may have on the safe conduct of the sedation. Although fiber-optic bronchoscopy with sedation has been performed on patients with significant comorbidities, including obesity, pregnancy, brain lesions, and coronary disease, having such concurrent medical conditions increases the likelihood of complications from the sedation. A full review of the impact of coexisting disease on sedation is beyond the scope of this chapter, but several points can be made. First, the ASA Physical Status should be determined for each patient receiving moderate or deep sedation (see Table 5.3). Perioperative and anesthesia-related mortality correlates well with increasing ASA class. Many institutions restrict the administration of

Table 5.4. *Risk for complications from sedation*

Comorbidity	Sedation risk
Obesity/sleep apnea	• Central sensitivity to sedatives • Rapid arterial desaturation • Difficulty with mask ventilation or intubation
Hypertension	• Increased rate of hypertension • Exaggerated hypotension from vasodilating effect of medications
Systolic cardiac dysfunction	• Slow circulatory time. Delayed effects of sedatives • Prone to pulmonary edema with IV fluids or hemodynamic consequences of bronchoscopy
Ischemic heart disease	• Myocardial ischemia or infarction • Less when supplemental oxygen is used
Aortic valve stenosis	• Limited ability in increase cardiac output in response to hypotension from medications • Increased myocardial oxygen demand from left ventricular hypertrophy. Demand ischemia from hypotension or tachycardia
Dementia	• Increased sensitivity to sedatives • Delayed recovery • Paradoxical agitation is common (reversal agents may help) • Dose slowly and small
Pregnancy	• Aortocaval compression at 20 wk. 15° left uterine displacement • Benzodiazepines were once thought to cause cleft lip/palate. Probably not true. • Uteroplacental circulation and fetal well-being
Chronic pain	• Tolerance. May require very high narcotic dose • Naloxone contraindicated for oversedation

sedation by nonanesthesiologists to patients who are ASA class III or below. Furthermore, the Joint Commission may deem this an indication that the patient was assessed and found to be an appropriate candidate for the procedure and sedation. Second, those patients with significant comorbidities should have their disease processes maximally controlled prior to the administration of sedation. When appropriate, a multidisciplinary team approach should be employed, and consultation with an anesthesiologist should be considered. Finally, several disease processes place the patient at significant risk for complications from sedation (see Table 5.4). The pulmonary physician should use extreme caution when administering sedation to these patients.

Equipment and Monitoring

Bronchoscopy and other interventional pulmonary procedures are highly technical and require advanced equipment. In addition, the safe conduct of moderate or deep sedation requires that specific equipment be readily available, irrespective of the degree of complexity of the medical procedure. Table 5.5 describes the recommended equipment needed specifically for sedation.

Although the equipment outlined is important, the vigilance of a clinician monitoring the patient while under sedation is the most important factor influencing patient safety during moderate sedation. Inadequate monitoring of patients has been cited as both too common and a frequent cause of adverse events during bronchoscopy. The monitor, generally a nurse, should have no other significant clinical duties and must have the same training and privileging in the safe administration of sedation and rescue techniques as does the physician performing the procedure. The monitor should continuously evaluate the patient's respiratory rate, cardiac

Table 5.5. *Recommended equipment*

Category	Specific equipment
Airway	• Laryngoscopes: Multiple sizes • Endotracheal tubes: Multiple sizes with stylettes • Laryngeal airway mask • Oxygen source and appropriate tubing, masks, or nasal cannulae • Bag/mask ventilation device • Suction with appropriate suction device (Yankauer) • Oral and nasal airways: Multiple sizes
Monitoring	• Noninvasive blood pressure device • Electrocardiograph • Pulse oximeter • Capnograph (required for intubated patients)
Emergency	• Cardiac defibrillator • ACLS medications • Reversal agents (naloxone, flumazenil)
Intravenous access	• Gloves • Tourniquets • Alcohol wipes • IV catheters: Multiple sizes • IV tubing with needleless access ports • Tape • Appropriate IV fluids

Note: Adapted from Godwin SA, Caro DA, Wolf SJ, et al.

rate and rhythm, blood pressure, oxygen saturation, level of consciousness, and skin condition. These parameters should be documented every 5 minutes on a flow sheet designed specifically for moderate sedation (this document can be incorporated into the procedural documentation). In addition, the monitor should document the timing, dose, and indication for all medications administered and the amount of IV fluid administered. Recent literature has suggested the use of expiratory CO_2 monitoring as a way to objectively measure respiration.

Most of the physiologic parameters monitored during sedation are objective and relatively easy to measure. However, both the adequacy of respiration and the level of sedation can be more subjective and prone to error. Simply observing the rise and fall of the chest as a measure of respiration may be misleading as upper airway obstruction caused by oversedation does not prevent chest wall movement. Thus, a patient may have no alveolar ventilation despite apparently normal chest wall movement. Even observing the presence of condensation on the oxygen mask during exhalation does not adequately assess minute ventilation or the presence of oversedation. Furthermore, the use of a full face mask is impractical during bronchoscopy. Given these limitations, the use of expired CO_2 monitors during moderate sedation has been recommended. This monitor identifies hypoventilation and patients at risk for hypoxemia before other clinical markers and with nearly 100% sensitivity. In one series, clinicians identified poor ventilation in only 3% of cases, whereas CO_2 monitoring found that 56% of patients were hypoventilated. More important, active intervention based on early detection of mild hypoventilation as indicated by expiratory CO_2 can effectively prevent subsequent hypoxia. Although measuring true end-tidal CO_2 may be impossible during bronchoscopy in a

nonintubated patient, nasal cannula devices with side-port CO_2 detection may be used.

Monitoring the level of consciousness is fraught with subjectivity and inaccuracy. The definition of moderate sedation is that patients should respond to verbal commands, perhaps in conjunction with light touch. Furthermore, their protective reflexes should be intact. This standard is highly subjective, and is made more difficult when the protective airway reflexes are blunted by local anesthetics as is the case in bronchoscopy. Semiobjective scoring systems that monitor the patient's response to reproducible stimuli are often advocated, including the Ramsay score, the Continuum of Depth of Sedation Scale (CDSS), and the Observers Assessment of Alertness/Sedation Scale (OAAS). Each of these is based on a point scale, ranging from alert/anxious to unconscious. More recently, some authors have advocated the use of electroencephalogram- (EEG-) based physiologic monitoring to obtain more objective sedation data. This monitoring appears to correlate well with the Ramsay scale, OAAS, and CDSS. More importantly, it may allow clinicians to administer less medication and improve patient cooperation. More work needs to be done in this area before EEG-based monitors become standard sedation monitors.

Monitoring of the patient who has received moderate or deep sedation should continue in the postprocedure recovery area. Vital signs should be continually assessed and documented at regular intervals (generally every 1–30 minutes) while the patient is in the recovery area. Patients who received reversal agents (flumazenil or naloxone) should remain in the recovery area for at least 2 hours after the reversal is administered. For other patients, no predetermined recovery time should be required, but the patient should demonstrate objective evidence of recovery from the sedative medications prior to discharge to an in-patient unit or to home. Aldrete and Kroulik developed the postanesthesia recovery (PAR) scoring system, similar to the Apgar score for newborns, which helps to determine readiness for discharge. This includes assigning 0–2 points for activity level, respiration, circulation consciousness, and oxygen saturation. (The original scoring system evaluated skin color, but this was modified when pulse oximetry became readily available.) When the patients reach a PAR score of 9 or 10, they are ready for discharge to the in-patient unit. Patients with a PAR score of 10 may still demonstrate significant impairment from the sedative medications, and thus a second level of assessment has been added to the PAR score to determine readiness for discharge home. This postanesthesia discharge (PAD) score includes assigning 0–2 points for the dressing, the level of pain, the ability to ambulate, the ability to drink liquids, and urine output. When the sum of the PAR and PAD scores is 18 or greater, the patient is ready for discharge. These scoring systems are used in dozens of countries and are accepted by The Joint Commission.

The medical center should develop specific discharge criteria based on the PAR and PAD score or other objective criteria. Independent licensed practitioners can then discharge patients in accordance with these criteria. Prior to final discharge home, patients and their families should be given verbal and written instructions regarding diet, level of activity and medications, and a 24-hour contact number in case of emergencies. All patients should be discharged in the presence of a responsible adult who will escort them home.

MEDICATIONS

Introduction

Moderate sedation represents a middle ground between the responsive and cooperative conditions of the lightly sedated patient and the unconscious, anesthetized condition of the patient under general anesthesia. Light sedation can always be augmented by the effective use of topical local anesthesia to numb the oropharynx and blunt the airway reflexes. During optimal situations, moderate sedation allows the patient to be

Table 5.6. *Common medications used in sedation and adult dosing schedules.*

Drug	Dose	Onset	Duration
Bolus type			
Midazolam	.5–2 mg	2 min	30 min
Fentanyl	25–100 μg	5 min	30 min
Ketorolac	15–30 mg	30 min	4–6 h
Infusion type			
Remifentanil	.1–.3 μg/kg/min	1–2 min	
Propofol	25–100 μg/kg/min	1–2 min	

comfortable, sleepy, amnestic, and stable hemodynamically with a modicum of medications. During difficult times, the patient is agitated, semiconscious, uncooperative, and tachycardic. Choosing the anesthetic medications to achieve optimal results requires an understanding of the kinetics and effects of each agent with its potential side effects and the patience to deliver divided doses and to titrate to effect. This section will review some of the commonly used medications in the delivery of moderate sedation to patients who are to undergo airway procedures. (See Table 5.6.)

Benzodiazepines

Midazolam is the most appropriate and commonly used benzodiazepine medication for moderate sedation. The combination of amnesia, anxiolysis, and sedation make midazolam an ideal drug either alone or in combination for moderate sedation during procedures that are of short duration and without significant painful stimulation. Midazolam may be administered IV, orally, intramuscularly, or rectally. Unlike the more lipid-soluble benzodiazepines lorazepam and diazepam, midazolam is not diluted in propylene glycol. This additive is associated with pain on injection and thrombophlebitis. In sedative doses, midazolam reaches peak effect in 2 minutes and produces sedation for 30 minutes. The rapid onset and short duration make midazolam a useful drug for moderate sedation by bolus injection or infusion.

All benzodiazepines act on the γ-aminobutyric acid (GABA) receptors by enhancing their affinity for GABA. The actions of GABA are to produce both sedation and anxiolysis [73]. Other drugs that act on GABA, such as barbiturates, etomidate, and propofol, can act synergistically to enhance the effects of the benzodiazepines. Other CNS depressants, such as opioids, anesthetic vapors, and α-2 agonists, also have synergistic effects when combined with a benzodiazepine.

Anterograde amnesia is an important component of all benzodiazepines. These agents produce amnestic effects that are out of proportion to the sedative effects. For example, patients may appear alert and conversant, but may remain amnestic for postoperative conversations and instructions. The condition is anterograde (not retrograde) amnesia, and this distinction is frequently misstated. Although the event that is forgotten has occurred in the past, the storage of that event in a patient's memory happens after the administration of midazolam, and thus is properly termed anterograde amnesia. Benzodiazepine cannot reliably cause patients to forget events that occurred before the medication was administered.

Midazolam should be used with caution in elderly patients or in patients with impaired liver function. Midazolam is highly protein bound and is cleared by the liver; therefore, patients with decreased concentrations of serum albumin or with decreased cytochrome P-450 enzymatic

activity will have exaggerated effects and duration of activity. Agents that either raise or lower the cytochrome P-450 activity will also affect the action of midazolam. Sedative doses should be administered in a divided fashion, leaving sufficient time to assess the clinical effect of each interval dose. Midazolam does have a reversal agent, flumazenil, which will be discussed later.

Opioids

Although the opioid class of drugs includes dozens of medications with natural and synthetic origins, the major differences consist of their potencies and their rates of equilibration. All opioids are μ-receptor agonists, and this action accounts for their analgesic properties. In addition to the desired analgesic and antitussive effects, all μ-agonists share the side effects of nausea, vomiting, itching, muscle rigidity, and respiratory depression. The use of preemptive antiemetics has been shown to prevent the nausea and vomiting caused by opioids. Fentanyl has been shown to cause chest wall muscular rigidity more often than other synthetic opioids. In some cases, the chest wall rigidity is so severe that it can compromise ventilation and can only be successfully treated with the administration of neuromuscular blocking agents (paralytics). To be effective for moderate sedation, opioids should have high potency and rapidly reach equilibration. Fentanyl and remifentanil possess these properties.

Fentanyl is highly protein bound, lipid soluble, and metabolized by the liver. The time to peak analgesic effect following a single IV bolus is 5 minutes. The lipid solubility facilitates the movement of fentanyl across the blood–brain barrier. A single dose will last 30 minutes. Much of the initial bolus is taken up by inactive tissue sites in the lung, fat, and skeletal muscle. As these tissue sites become saturated by either repeated doses or by a continuous infusion, the context-sensitive half-life becomes longer. With continued administration of fentanyl, the half-life approaches the elimination half-life of 3–4 hours. Therefore, the advantage of fentanyl as a short-acting agent is lessened as the duration of the procedure requires multiple repeated boluses or a continuous infusion. Specific opioid antagonists do exist and will be discussed later.

An alternative opioid to fentanyl that can be used for both brief procedures and those with varying duration is remifentanil. This opioid is used for general anesthesia only, as remifentanil will cause apnea. Remifentanil is a synthetic opioid with equivalent potency to fentanyl; both are about 100 times more potent than morphine. A rapid onset of analgesic effect occurs after an IV bolus of remifentanil, with peak effect within 1–1.5 minutes. Unlike the other synthetic opioids, remifentanil has a unique degradation, being metabolized by plasma esterases. The elimination half-life is 8–20 minutes and is independent of liver or kidney function. Repeated dosing or continuous infusions do not prolong the elimination half-life. For example, a 5-hour infusion of remifentanil produced return of breathing within 3–5 minutes following discontinuation. Rapid elimination of remifentanil means that it does not provide any residual analgesia in the postoperative period. Other analgesics need to be started in the recovery area.

It is important to realize that all opioids have the unique property of providing intense pain relief without loss of proprioception or consciousness. Although this property has brought comfort to millions, it also brings the possibility of awareness. Intraoperative awareness under general anesthesia is a recognized complication and one that is more common when opioids are used. Awareness during moderate sedation should be an expected condition, but often patients will complain of hearing and feeling portions of their procedure. It is essential that anyone who is planning to administer moderate sedation advise the patient that some degree of recall is to be expected.

Propofol

Under the general heading of sedatives/hypnotics, propofol emerges as a versatile and

effective agent to use when administering moderate sedation. Currently the most commonly used parenteral anesthetic agent in the United States, propofol is a substituted isopropylphenol that is insoluble in water and usually prepared in a lipid vehicle for IV administration. The emulsion consists of soybean oil, egg lecithin, and glycerol. Disodium ethylene diamine tetraacetic acid (EDTA) or sodium metabisulfite is added as a preservative and to inhibit bacterial growth, but the propofol mixture does support bacterial proliferation and serious infections have been reported.

As with the benzodiazepines and other sedatives/hypnotics, propofol acts on the GABA receptors and decreases the dissociation rate of GABA from the receptor. Metabolized in the liver by cytochrome P-450, there is also extensive nonhepatic metabolism as well as inactive tissue uptake. As a result of these elimination pathways, the context-sensitive half-life is not prolonged in such conditions as a propofol infusion lasting 8 hours. Propofol concentrations are not elevated in cirrhotic or alcoholic patients (suggesting the ability of the extrahepatic pathways to metabolize propofol) nor in patients with renal failure, but concentrations are higher in elderly patients.

Propofol produces rapid sedation without associated nausea or vomiting and a rapid return of cognitive function. Either an infusion or incremental boluses every 5 minutes can create levels of moderate sedation. The potential side effects of propofol include hypotension, apnea, and airway obstruction, so the patient needs to have close hemodynamic monitoring and immediate access to emergency airway interventions. Propofol does not seem to provoke bronchospasm. It often produces pain at the injection site, but this pain incidence can be reduced to $<10\%$ with the administration into a large vein (e.g., antecubital) or pretreatment with 1% lidocaine or opioids. The use of propofol by health care providers other than anesthetists is controversial. Many states require that the providers be certified in sedation techniques and competent in managing the airway.

Severe lactic acidosis as a consequence of prolonged propofol administration has been described in both adults and children. Although initially described with propofol infusions lasting more than 24 hours, there have been a number of reports of acidosis developing in shorter durations. Any patient on a propofol infusion with an unexplained tachycardia should be suspected of having "propofol infusion syndrome." The arterial blood gas and serum lactate levels should indicate a metabolic acidosis. Other causes of metabolic acidosis – such as tourniquet release, diabetic ketoacidosis, sepsis, and hyperchloremic metabolic acidosis from extensive infusions of normal saline – should be excluded. Treatment includes discontinuation of the propofol and supportive care, which has included extracorporeal membrane oxygenation in at least one report. The mechanism for propofol infusion syndrome appears to be interruption of the electron transport chain and impairment of the long-chain fatty acid metabolism.

Nonsteroidal Antiinflammatory Drugs (NSAIDs)

The NSAIDs share the three properties of acting as analgesics, antiinflammatories, and antipyretics. Although a larger, heterogeneous group of medications exists in this category, ketorolac is the only applicable drug to the administration of moderate sedation. As one of the few NSAIDs approved for parenteral use, ketorolac has greater analgesic activity than antiinflammatory activity. As a traditional NSAID, ketorolac does block cyclooxygenase-1 and therefore does promote gastric ulceration and platelet inhibition.

Administered as a sole analgesic or in combination with opioids to potentiate the analgesic effect, ketorolac provides rapid pain relief. Ketorolac does not induce tolerance nor does it cause respiratory depression. In patients with an aspirin allergy, nasal polyposis, or asthma, ketorolac has been reported to trigger life-threatening bronchospasm. Patients with congestive heart failure, hypovolemia, or hepatorenal syndrome may be susceptible to

ketorolac-induced renal failure because of their dependence on local renal prostaglandin production to maintain renal blood flow.

Antiemetics

The sensation of nausea and act of emesis are a coordinated set of muscular, autonomic, behavioral, and emotional responses that exist to rid the stomach of toxins. In clinical practice, nausea and vomiting are unpleasant and unintended consequences to anesthesia, inflammation, or motion that can add morbidity to and complicate the recovery from any procedure. The coordination of the vomiting response occurs in the central emesis center in the lateral reticular formation of the mid brainstem in the area adjacent to both the chemoreceptor trigger zone (CTZ), found in the area postrema at the base of the fourth ventricle, and the nucleus solitarius of the vagal nerve. The CTZ monitors the cerebrospinal fluid for toxins and receives information from the gut. The emesis center also receives information from the cerebral cortex regarding anticipatory nausea and vestibular input with respect to motion sickness.

This complex neural connection has a variety of neurotransmitter influences. Serotonin, histamine, acetylcholine, dopamine, and prostaglandins have key roles in the neural modulation of the emesis center. The antiemetic strategy, therefore, can be targeted at one or several of these neural modulators. For example, ondansetron can block the specific 5-hydroxytryptamine−3 receptors in the CTZ, and the antihistamine cyclizine or the antimuscarinic scopolamine can block the vestibular input from motion sickness. A steroid such as dexamethasone can block the emetogenic influence from inflammation, and benzodiazepines can suppress anticipatory nausea. Therefore, the cause of the nausea may differ in different patients, and the effective treatment may address the particular etiology. Often, however, multiple medications that use a variety of mechanisms of action are required to reduce the symptoms of nausea and prevent vomiting.

Ondansetron is structurally similar to serotonin, and an IV dose reaches peak effect within 30–60 minutes. Interestingly, the drug conveys antiemetic action long after it has disappeared from the plasma circulation, suggesting a continued interaction at the serotonin receptor. For this reason, all the serotonin antagonists may be given once daily. Metabolized in the liver by cytochrome P-450 enzymes, ondansetron should be reduced in patients with liver failure, although no such reduction is needed in elderly patients. Ondansetron is effective for nausea from chemotherapy and postoperative sources but is ineffective in treating motion sickness. Side effects from ondansetron are usually headache and diarrhea. The usual dose of ondansetron in the postoperative setting is 4 mg IV. Higher doses do not show greater reduction of postoperative nausea and vomiting.

Reversal Agents

All medication antagonists have their own chemical properties, kinetics, binding characteristics, and elimination pathways. The constellation of characteristics will determine how well the antagonist can reverse the action of the agonist, but also will determine what other concerns the practitioner should have in the process of using a reversal agent.

An imidazolebenzodiazepine, flumazenil binds with high affinity to sites on the GABA-A receptor. Flumazenil, when combined with a benzodiazepine, does not produce water. In other words, all drugs have side effects, and using one to reverse the effects of another does not come without some risk. Flumazenil competitively inhibits the binding of both agonists and reverse agonists to the GABA-A receptor. Slight activity, which resembles a reverse agonist at low concentrations and an agonist at high concentrations, has been reported. The agonist activity of flumazenil, however, does not prevent the withdrawal symptoms that have been reported. Just as withdrawal from chronic benzodiazepine use can cause a variety of effects, flumazenil can cause dysphoria, irritability,

anorexia, sweating tremors, unpleasant dreams, dizziness, exacerbation of insomnia or anxiety, and frank seizures. Flumazenil is not recommended in patients who are taking antiseizure medication.

Usually, 1–5 mg of flumazenil is given in divided doses between 1 and 10 minutes until the desired reversal of sedation is achieved. The clinical effects last from 30 to 60 minutes and, therefore, the potential for resedation is possible and the flumazenil may need to be rebolused or an infusion started. If 5 mg of flumazenil does not reverse sedation, the sedation was probably not caused by benzodiazepine overdose. In practice, benzodiazepine overdose rarely causes respiratory depression, and, therefore, the urgent need for reversal using flumazenil is exceedingly uncommon.

As with flumazenil, the administration of naloxone to reverse the effects of opioids does not produce water. A nonselective competitive antagonist, naloxone binds with high affinity to all three opioid receptors (μ, Δ, κ). Used to treat narcotic-induced depression of ventilation, the side effect of naloxone is to also reverse narcotic-induced analgesia. Postsurgical patients can develop hyperacute, severe pain. The activation of the sympathetic nervous system in response to naloxone-induced pain can include tachycardia, hypertension, pulmonary edema, and cardiac arrhythmias, including ventricular fibrillation. Plasma cortisol and catecholamine levels rise following naloxone administration. Less obvious side effects from naloxone are decreased performance on memory tests and dysphoria.

Given in divided doses of 1–4 μg/kg, naloxone quickly reverses opioid-induced respiratory depression and has a short duration of action (30–45 minutes). Thus, the effects of naloxone may be shorter than the half-life of the opioid that is causing the respiratory depression. A continuous infusion of naloxone may be necessary and is usually started at 5 (μg/kg)/h.

In clinical practice, careful titration of the opioid medications with understanding of the time to peak activity and the potential for respiratory depression should make the use of opioid antagonists uncommon. Opioid doses should be adjusted in elderly patients and in patients with limited hepatic function or poor pulmonary reserve. Opioid doses should be adjusted downward whenever other sedative agents are used in combination. Finally, the narcotic effect should be reserved with naloxone as a rescue strategy when respiratory depression occurs and when mechanical or supplemental breathing measures are not practical or beneficial in improving the situation.

COMPLICATIONS OF SEDATION

Complications from moderate sedation can occur, from undersedation, oversedation, and idiosyncratic responses to "therapeutic levels" of sedation. Too little sedation can lead to excessive movement, delirium, and pain. Too much sedation can produce hemodynamic collapse and respiratory depression. Even those patients receiving "optimal" therapeutic concentrations of sedation can demonstrate allergic reactions, rigidity, or laryngospasm. Even therapeutic levels of sedatives can worsen such conditions as acute intermittent porphyria, malignant hyperthermia, or carcinoid crisis. Specific complications can occur with specific pharmacologic agents, such as adrenal suppression from etomidate and rhabdomyolysis from propofol. This section will focus on the general complications that occur from oversedation.

Most sedatives are myocardial depressants and/or vasodilators that can act to profoundly lower blood pressure. The degree of cardiovascular depression will depend on the patient's cardiovascular and volume status, any medications that have additive effects on the blood pressure, and any surgical conditions that may affect the patient. For example, the reverse Trendelenburg position can lower the preload and cause an exaggerated hypotensive response to sedatives. Effects on the blood pressure from sedation can be

greater in patients with cardiomyopathy, valvular heart disease, or pericardial conditions, such as acute tamponade. Resuscitative drugs should always be immediately available to administer when a sedative is given.

Many sedatives are respiratory depressants and, in large enough doses, can cause apnea. Most sedatives blunt the ventilatory response to both high levels of carbon dioxide and low levels of oxygen. For this reason, all patients who receive sedation need to be monitored for both ventilation and oxygenation. Respiratory rates can be misleading, however, as they may not reflect minute ventilation. For this reason, either minute ventilation or end-tidal CO_2 should be used for deeper sedation techniques, to better detect hypoventilation. For oxygenation status, the pulse oximeter provides a reliable and sensitive predictor of desaturation in most settings. Evidence of hypoxemia may not occur until the patient has been hypoventilating or apneic for several minutes. To rescue patients from conditions of hypoventilation or hypoxemia, advanced airway equipment needs to be immediately available, along with a source of enriched oxygen, continuous suction, and the trained personnel to use them.

In conclusion, the use of moderate sedation to allow the accomplishment of airway procedures requires a balance of anesthetic drugs with their relaxant, sedative, and analgesic effects with the unwanted and potentially dangerous side effects. The conduct of the anesthetic and the recognition of these side effects require planning and monitoring. Every patient needs a history and physical examination, including an examination of the airway. All patients need standard monitoring and a person designated as the monitor. Each bronchoscopic procedure requires the proper equipment, medications, and training to administer the medications and to deal with side effects. Finally, all patients need a safe environment in which to recover from sedation. With careful preparation, proper supplies, and protocols, bronchoscopy can be performed under excellent surgical conditions and with minimal adverse events.

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