CURRENT DRUG THERAPY

Clinical implications of developments in pharmacology



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KEY POINTS:

Conscious sedation demands skills in airway management, since the line between sedation and general anesthesia is easy to cross.

Conscious sedation requires secure intravenous access. Equipment for intubation and ventilation, drugs for resuscitation, and someone skilled in using these items should be readily available.

Oxygenation, ventilation, cardiac function, and level of sedation must be continuously monitored. The person supervising the sedation must not be involved in performing the procedure.

Restlessness and agitation in a sedated patient should always be considered hypoxemia until proven otherwise.

Combinations of agents can be used to provide the desired blend of anxiolysis and analgesia, but tend to produce greater amounts of circulatory or respiratory depression than when the drugs are used alone.

Conscious sedation: what an internist needs to know

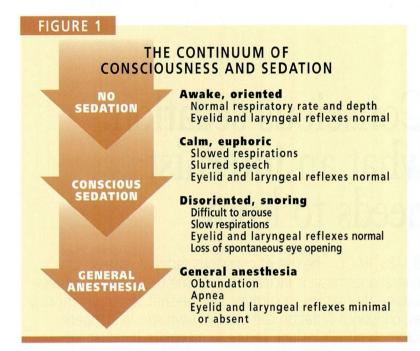
ABSTRACT: The use of conscious sedation instead of general anesthesia is increasing with the development of less-invasive alternatives to surgery and the shift to outpatient care. Yet, conscious sedation can pose its own special dangers. Common pitfalls include failure to recognize hypoxemia, inadequate analgesia, inappropriate dosing with respect to individual variability, and lack of appropriate backup support.

onscious sedation occupies a point in the continuum between full wakefulness and general anesthesia, the dividing line being loss of protective airway reflexes (FIGURE 1). As surgical techniques become less invasive, and more procedures are performed in outpatient settings, the use of local anesthesia with conscious sedation is becoming more common.

Some degree of sedation has always been used for procedures such as endoscopy and cardiac catheterization. As the use of conscious sedation with intravenous (IV) agents increases in these and other areas, many nonanesthesiologists will require some specific knowledge and skill in anesthesia. Yet, as use of the technique increases, there is concern about the use of sedation outside the operating room, especially when it may result in loss of the patient's protective reflexes. This problem is compounded when analgesia is required in addition to sedation. Because the line between conscious sedation and general anesthesia is easily crossed, it is essential that anyone conducting conscious sedation be aware of the potential to sedate too deeply, with attendant respiratory and hemodynamic effects.

This article reviews the methods of conscious sedation and the current pharmacologic options, emphasizing the importance of proper patient preparation and monitoring. The benefits of conscious sedation for both patient and operator are presented in light of the dangers. This review is not a substitute for formal training in anesthesia. We do hope, however, to communicate an appreciation of the risk involved in the use of rapid-acting IV agents, which are far more likely than oral





sedatives to cause insidious cardiac or respiratory depression.

RISKS AND BENEFITS OF CONSCIOUS SEDATION

Conscious sedation is desirable during invasive procedures for several reasons. Anxiety and discomfort may arise from fear, from the procedure itself, and from having to lie immobile on a treatment table. The proper combination of analgesia and anxiolysis can alleviate pain and anxiety and forestall agitation during a procedure. Adequate sedation helps attenuate tachycardia and hypertension, which can be detrimental in patients with coronary artery disease and valvular heart disease. 1 Analgesic drugs with long half-lives will continue to work after the procedure is over, further limiting pain and stress. Amnesia may be desirable for events such as cardiac defibrillation. Finally, proper sedation allows the operator to focus on the procedure without undue distraction from patient movement.

Yet, conscious sedation does present risks. The introduction of potent, rapid-acting IV drugs such as midazolam has been associated with an increase in adverse events such as res-

piratory depression and hypoxemia,² recognized in both the medical literature and the general press.³ Patients with coronary artery disease are at particular risk of myocardial ischemia due to sedation-induced hypotension and hypoxemia.

BEFORE THE PROCEDURE

Because conscious sedation is not without risk, internists should always ask several questions before proceeding.

Does the patient really need sedation? Some patients may be adept in self-relaxation techniques or stoic enough to tolerate brief discomfort without pharmacologic intervention. Education before the procedure, constant reassurance, and local anesthetics may suffice for some brief procedures and may reduce the total dose needed in most patients.⁴

Why is sedation needed, to treat pain or anxiety? Pain responds best to analgesics and anxiety to anxiolytics, although there is a certain amount of overlap between these classes. Although a combination of these two types of agents may provide better comfort than a single agent, these classes of drugs can interact synergistically to increase the risk of respiratory depression.

What is the patient's risk? Healthy patients, who have acceptable physiologic reserve, allow considerable latitude in sedation, because they can easily compensate for reductions in cardiac output, airway resistance, or carbon dioxide responsiveness. In addition, they can metabolize sedative agents normally. The risks of losing protective airway reflexes and respiratory drive and of adverse hemodynamic changes are higher in elderly patients and patients with organ dysfunction, particularly if they are already receiving medications that interfere with protein binding, metabolism, or elimination of sedative agents.⁵ In our experience, these higher-risk patients tend to be less anxious and reactive to stimuli than younger, low-risk patients. Often, a "wait, then sedate" attitude makes more sense than empiric, prophylactic sedation in high-risk patients.

Is there any personal or family history of

anesthetic complications? Before the procedure, the functional equivalent of a preanesthetic interview should be performed, specifically addressing the medical history, family history, drug allergies, adverse drug reactions, previous anesthetic complications, and pregnancy status. A family history of malignant hyperthermia should raise concern, even though the agents commonly used for conscious sedation are not known triggers of malignant hyperthermia. The work-up and preparation for a patient at risk for malignant hyperthermia are beyond the scope of this review and should, in any case, be discussed with an experienced anesthesiologist. The history should be followed by a brief physical examination to evaluate the heart, lungs, and airway. Informed consent should be obtained before giving any medications.

Expect the worst: planning for emergency intubation

Conscious sedation, in which spontaneous respiration is maintained, avoids some of the disadvantages of general anesthesia, but the need for monitoring and airway protection does not change. In fact, because there is no secure airway (endotracheal tube, laryngeal mask, or full-face mask), the need to monitor ventilation is even more imperative.

The need for intubation and mechanical ventilation must always be assumed and anticipated, even though the aim is to avoid invasive airway support. Therefore, a back-up plan must be developed for providing respiratory support, should it be required during the procedure.

A difficult airway must be appreciated before starting the procedure. The scoring system of Mallampati and colleagues⁶ is widely used to determine the likelihood of difficult intubation. Common conditions that make visualization of the larvnx and subsequent intubation extremely difficult include limited neck flexion (as in rheumatoid arthritis), limited mouth opening, a short mandible, and loose teeth. If the patient has undergone anesthesia at the same facility previously, a review of old anesthesia records often reveals if intubation was difficult.

Patients should receive no solid foods for at least 6 hours, although access to clear liquids might be possible up to 2 to 3 hours before the procedure.⁷ Recent oral intake of more than a few mL of clear liquid (ie, with premedications) should prompt delay or cancellation of the procedure because of risk of aspiration.

Equipment and personnel needed

The practitioner who uses sedation must have access to equipment (TABLE 1) and back-up personnel to help manage emergencies. Resuscitation equipment, including that necessary to intubate and ventilate, must always be readily available.

The clinician should prepare the room before the patient arrives, planning for additional time and effort when procedures are performed in multiple locations. Some advance planning is needed to assemble the equipment when sedation is planned in

immediate

TABLE 1

EQUIPMENT NECESSARY FOR CONSCIOUS SEDATION

Oxygen (wall source or portable tanks)

Suction source (wall source or portable)

Emergency cardiac medications Phenylephrine 0.1 mg Epinephrine 0.1 mg Nitroglycerin 0.08 mg Atropine 1 mg

Nasal cannula, simple and nonrebreathing masks

Ambu bag and assorted masks

Oral and nasal airways

Endotracheal tubes and stylet

Laryngoscopes (at least two)

Continuous pulse oximeter

Continuous electrocardiograph

Blood pressure monitor (noninvasive or invasive)

Temperature monitor

Intravenous access

Method to summon additional help

remote locations. If there is no organized clinical engineering team that can respond to requests for additional needs, the sedating clinician must expect to be responsible for securing this equipment. Suction (for clearing airways), oxygen, airway appliances (masks, connecting tubing, laryngoscopes, endotracheal tubes, oral airways), and emergency drugs should be assured. "SOAP" is a useful mnemonic for suction, oxygen, airway, and pharmacy. Specific reversal agents (ie, flumazenil and naloxone) should be available to counteract unexpected reactions.

It is of paramount importance that someone other than the operator be designated to monitor the patient during the procedure. It is often difficult to find someone experienced in airway management and resuscitation and to have them immediately available, especially when procedures are performed in remote locations or during hours of minimal staffing.

DURING THE PROCEDURE

A reliable IV access should be established in all patients receiving IV sedation. (Exceptions could probably be made in selected pediatric cases, in which physicians are familiar with using chloral hydrate without IV access.)



TABLE 2			
AGENTS USED IN CONSCIOUS SEDATION			
GENERIC AND TRADE NAMES	INTRAVENOUS DOSAGE	COMMENTS	
Benzodiazepines			
Diazepam (Valium)	0.02-0.05 mg/kg	Affected by age, liver function Usual duration of action 2–4 hours Intramuscular use not recommended Elimination half-life 20–70 hours	
Lorazepam (Ativan)	0.01–0.04 mg/kg	No active metabolites Slow onset, highly amnestic Elimination half-life 10–20 hours	
Midazolam (Versed)	0.01–0.04 mg/kg	May be given by infusion load 2–5 mg, infused at 1–4 mg/minute Elimination half-life 1–4 hours	
Reversal agent for	Reversal agent for benzodiazepines		
Flumazenil (Romazicon)	0.2-0.5 mg	Repeat dose to 1 mg maximum Elimination half-life 0.6–1.3 hours	
Opiates			
Fentanyl (Sublimaze)	0.8–1.2 µg/kg	Hemodynamic stability Muscle rigidity if given rapidly Less nausea and itching than morphine Typical dose 50–100 µg in adults	
Meperidine (Demerol)	0.5–1 mg/kg	May cause tachycardia Avoid with monoamine oxidase inhibitors, renal failure	
Morphine	0.01-0.02 mg/kg	Vasodilation Bradycardia, hypotension (histamine release)	
Reversal agents for opiates			
Naloxone (Narcan)	0.1-0.4 mg	Can precipitate tachycardia, hypertension	
Nalmefene (Revex)	0.5–1.5 mg	Elimination half-life 10 times that of naloxone Side effects similar to those of naloxone	
Anesthetic agent			
Propofol (Diprivan)	0.5 mg/kg over 3–5 minutes 25–75 μg/kg/min maintenance	Dose for monitored anesthesia care Easy to titrate Rapid recovery	

Before giving sedative medications, the baseline vital signs must be documented. The standards of care call for frequent blood pressure measurements and continuous monitoring of the heart rate and rhythm (by electrocardiography) and oxygen saturation (by pulse oximetry).⁸ Temperature monitoring must also be available.⁹ Real-time physiologic monitoring has been shown to identify adverse reactions promptly and prevent morbidity during endoscopy.¹⁰

Most, if not all, patients should receive supplemental oxygen before the onset of sedation to prevent hemoglobin oxygen desaturation. The supine position decreases the tidal volume, leading to a ventilation-perfusion mismatch and predisposing to hypoxemia, which becomes more pronounced as sedatives are given. Sedation depresses respiratory depth and frequency, resulting in progressive atelectasis.

Choice of drugs

The choice of agent involves consideration of pharmacologic effects, side effects, and duration of action. Space does not permit a detailed discussion of the various classes of drugs, but a summary of commonly used agents is presented in **TABLE 2**.

Slow, careful titration

The degree of sedation should be tailored to the individual patient and planned procedure. Individual patient sensitivity, fluid status, coexisting disease, and advanced age all affect the response to sedative drugs. However, the unpredictability of the response to sedatives and

opiates requires that doses be titrated until the desired effect is achieved. Although one can estimate the dose on the basis of clinical crite-

ria (TABLE 3), giving the drugs slowly and observing the response carefully will produce the best results. It is not unusual for $50~\mu g$ of IV fentanyl citrate to cause respiratory depression in some patients, and several times that dose to be insufficient for analgesia in others.

Although slow titration helps one recognize and manage respiratory and cardiovascular depression as they occur, some drugs produce respiratory depression even if given slowly. Giving two or more agents together is likely to produce synergistic effects, which may be pronounced.

As the sedative medication is given, the patient's response can be monitored by observing changes in heart rate, blood pressure, respiratory rate and depth, and oxygen saturation. Talking with the patient as he or she is sedated allows for assessment of slurred speech, loss of spontaneous eye opening, and depressed consciousness, corresponding with deepening levels of anesthesia. The Ramsay sedation scale¹² is useful for measuring and documenting the level of sedation. Under this system, a sedated patient is classified on a six-point scale: level 1 (anxious, agitated, or restless), level 2 (cooperative, oriented, and tranguil), level 3 (drowsy but responds to commands), level 4 (asleep but exhibits a brisk response to a stimulus), level 5 (asleep and exhibits a sluggish response to a stimulus), and level 6 (asleep with no response to a stimulus). Generally, a patient at Ramsay level 2 or 3 is ready for the procedure to begin. Levels 5 and 6 constitute the onset of general anesthesia, which goes beyond the desirable limits of conscious sedation.

PITFALLS AND PRECAUTIONS DURING THE PROCEDURE

Common pitfalls in conscious sedation include failure to recognize hypoxemia, inadequate analgesia, inappropriate dosing with respect to individual variability, and lack of appropriate backup support.

Failure to recognize hypoxemia

Restlessness and agitation in a patient who has received sedation should always be considered hypoxemia until proven otherwise. To give more sedatives to an agitated patient with hypoxemia can lead to a deadly scenario of deepening cardiorespiratory depression resulting in cardiac or respiratory arrest. Inexperienced practitioners frequently do not realize they are entering this vicious cycle,

focusing instead on performing the procedure to the exclusion of monitoring the patient's respiratory and cardiac status. As the patient becomes more restless. procedure becomes more difficult; the practitioner becomes increasingly frustrated and gives larger doses of sedatives (FIGURE 2). This sort of "tunnel vision" or fixation error is largely prevented by insisting that the observer of the patient's status not be involved in the procedure itself.

TABLE 3

FACTORS AFFECTING THE SEDATIVE DOSE

Higher doses required with:
Young, muscular patients
Extremely anxious patients
Chronic alcohol use
Long-term medication use
(eg, benzodiazepines, other drugs
that act on the central nervous system)
Chronic drug abuse
Cigarette smoking
Naltrexone use

Lesser doses required with:
Elderly patients
Chronic illness
Impaired hepatic or renal function
Adequate patient education before procedure
Patients with good stress-coping ability
Administration of other sedating drugs

Respiratory depression may occur both as a direct effect of the drug on the brain stem respiratory center and also indirectly as a result of increases in airway resistance. In healthy subjects, midazolam, at a dose of 0.1 mg/kg, reduces the response to carbon dioxide by 50% and also increases pulmonary and supraglottic airway resistance. Relaxation of the pharyngeal muscles may produce a partial airway obstruction, further increasing the work of breathing.

Ideally, conscious sedation should not be deep enough to cause airway compromise, but should this happen, desaturation and hypoventilation can sometimes be avoided by simply lifting the jaw or repositioning the head. The sedation practitioner must constantly listen to the patient's respiratory pattern and be alert to the onset of snoring or airway obstruction. Learning, with an anesthesia colleague, how to use a precordial stethoscope, position the airway, and ventilate with a mask is time well spent.

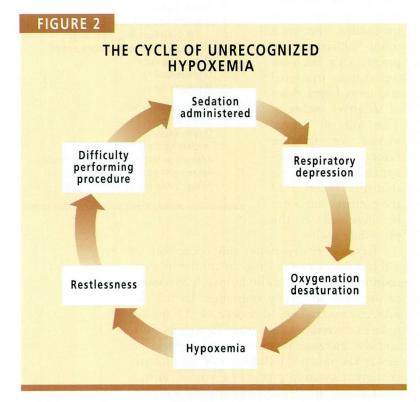
Giving inadequate analgesia

Another common error is failure to give adequate analgesia for an invasive procedure. Local anesthesia should be given carefully and doses repeated as appropriate for the half-life and toxic potential of the drug. Systemic analgesics should be supplemental, not primary, for most invasive procedures.

Dosing for individual variability

Similar sedative doses may result in dissimilar





Giving more sedatives to an agitated patient with hypoxemia can lead to a deadly scenario of deepening cardiorespiratory depression resulting in cardiac or respiratory arrest. As the patient becomes more restless, the procedure becomes more difficult; the practitioner becomes increasingly frustrated and gives larger doses of sedatives.

clinical results. Because of individual variability, any use of sedatives must involve slow titration until the desired clinical response occurs.

Lack of appropriate backup support

As noted earlier, it is of paramount importance that someone be designated to monitor the patient during the procedure, so as to recognize the signs of hypoxemia secondary to oversedation.

Monitoring must continue after the procedure for the expected duration of the sedative drug effect. Where and how this monitoring is done can be a problem. In some institutions, it may be possible to use the postanesthesia recovery unit so that patients requiring prolonged observation do not monopolize procedure room time. Hospitalized patients can generally return to a regular ward once they demonstrate normal mentation, stable

oxygenation, adequate cough and gag reflexes (particularly if the pharynx has been anesthetized), and stable hemodynamics after assuming the upright position. They will need frequent nursing assessments during the first hour after returning to the regular ward.

Using reversal agents

Although naloxone and flumazenil can reverse the action of opioids and benzodiazepines, respectively, they should be used with caution. Naloxone can trigger hypertension (from catecholamine release), 14 ventricular arrhythmias,15 pulmonary edema,16 and sudden death¹⁷ as the result of acute narcotic withdrawal. Doses of naloxone typically used in the emergency room (0.8 mg or more) are generally too high in the anesthetic setting. We usually dilute 0.4 mg of naloxone in 10 mL of saline and give increments of 0.04 mg (1 mL) to gently titrate reversal. Also of importance, both naloxone and flumazenil have shorter half-lives than their agonists do. The possibility of late resedation mandates extended monitoring (more than an hour) after antagonist administration.

Sending ambulatory patients home

Ambulatory patients must have a responsible person accompany them and drive them home. Both this person and the patient should receive detailed instructions, outlining possible late complications and steps to take, including a phone number to call, should questions arise or a complication occur.

FORMULATING GUIDELINES

Nonanesthesiologists must work with the anesthesia staff to develop mutually-acceptable practice guidelines and standards of care to be in compliance with Joint Commission on the Accreditation of Health Care Organization guidelines. ¹⁸ In the past, guidelines, such as those of the Harvard Anesthesia Group¹⁹ and the American Academy of Pediatrics²⁰ were adapted in formulating local hospital guidelines for conscious sedation. A task force on analgesia

and sedation by nonanesthesiologists has been commissioned by the American Society of Anesthesiologists, and final guidelines were published in February 1996.²¹

Proper monitoring and safety procedures should reduce the possibility of patient injury during conscious sedation. The anesthesia literature has focused extensively on the role of human factors in critical incidents.²² Facilitating the comfort of patients is a part of every physician's practice, not just the anesthesiologist's, but internists and other physician operators can take advantage of the anesthesiologist's knowledge and skills when setting up protocols for sedation outside the operating room.

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