Sedation and Analgesia in the Performance of Interventional Procedures

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ABSTRACT

Interventional procedures can produce pain, anxiety, and physical and mental distress. Analgesia and sedation in the interventional radiology suite are given routinely during interventional procedures and allow a safe, comfortable, and technically successful procedure to be performed. Appropriate sedation decreases patient movement, patient anxiety, pain perception, and is crucial to successfully perform percutaneous interventions. A thorough understanding of the preoperative patient assessment, intraprocedural monitoring, pharmacologic characteristics of medications, postoperative care, and treatment of complications is required for the practicing interventionalist. Complications related to sedation and analgesia can occur secondary to preexisting medical conditions, incorrect drug administration, and/or inadequate patient monitoring.^{1,2}

KEYWORDS: Sedation, analgesia, amnesia, Mallampati scoring

Objectives: Upon completion of this article, the reader should be able to recall the preoperative assessment, intraprocedural management, and the pharmacologic agents utilized in sedation and analgesia for interventional procedures.

Accreditation: Tufts University School of Medicine (TUSM) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

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The requirements for sedation and analgesia need to be individualized for each patient. The factors to consider include the patient's anxiety level, pain tolerance level, history of narcotic and benzodiazepine use, and the anticipated pain that will be produced by a particular procedure.³ The estimated length of time the procedure will take to complete also should be taken into account. A thorough discussion of the procedure with the patient will help to alleviate many preprocedural concerns and will help the clinician estimate the sedation requirements for a particular patient. There is a need for a more patient-oriented approach to intravenous (IV)

sedation and analgesia. Lang and colleagues have illustrated that habits and philosophies of individual institutions, rather than physician guidance or patients' needs, tend to determine the amount and utilization of IV sedatives and analgesics.⁴ The goals of sedation and analgesia should include patient comfort, providing a safe and controlled environment, pain relief, and minimizing negative psychological responses through relief of anxiety and fear. It is important to formulate an efficient, patient-oriented approach to sedation and analgesia. The patient should be able to maintain protective reflexes and a patent airway with the ability to

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Pharmacology in Interventional Radiology; Guest Editors, Kimi L. Kondo, D.O. and Charles E. Ray, Jr., M.D.

Semin Intervent Radiol 2010;27:368–373. Copyright © 2010 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA. Tel: +1(212) 584-4662.

DOI: <http://dx.doi.org/10.1055/s-0030-1267851>.

ISSN 0739-9529.

Table 1 Definitions and Characteristics of Levels of Sedation/Analgesia

	Minimum Sedation (anxiolysis)	Moderate Sedation "Conscious Sedation"	Deep Sedation	General Anesthesia
Responsiveness	Normal response to verbal stimulation	Purposeful response to verbal/tactile stimulation	Purposeful response to repeated/painful stimuli	Unarousable even to painful stimuli
Airway	Unaffected	No intervention required	Intervention may be required	Intervention usually required
Spontaneous ventilation	Unaffected	Adequate	May be impaired; assistance may be required	Frequently impaired; assistance may be required
Cardiovascular function	Unaffected	Usually maintained	Usually maintained	May be impaired

respond appropriately to verbal and physical stimuli. Deep sedation with its associated cardiovascular and respiratory risks is to be avoided whenever possible. The patient should return to baseline consciousness relatively rapidly and the risks of complications from sedation should be minimized.

DEFINITIONS OF LEVELS OF SEDATION/ANALGESIA/ ANESTHESIA CONTINUUM

The American Society of Anesthesiologists (ASA) and Joint Commission on Accreditation of Healthcare Organizations (JCAHO) recognize four levels of sedation/analgesia that occur on a dose-dependent continuum from minimal sedation to general anesthesia (Table 1). This continuum is described as follows²:

Minimal sedation: a drug-induced state during which patients respond normally to verbal commands. Although cognitive function and coordination may be impaired, cardiovascular and respiratory functions are unaffected.

Moderate sedation/analgesia: a drug-induced depression of consciousness during which patients respond purposefully to verbal commands either alone or accompanied by light tactile stimulation. No intervention is required to maintain a patent airway, spontaneous ventilation is adequate, and cardiovascular function is maintained.

Deep sedation/analgesia: a drug-induced depression of consciousness during which patients cannot be easily aroused but respond purposefully following repeated stimulation. Patients may require assistance in maintaining a patent airway, spontaneous ventilation may be inadequate, but cardiovascular function is usually maintained.

Anesthesia: consists of general, spinal, or regional anesthesia. General anesthesia is a drug-induced loss of consciousness during which patients are not arousable even by painful stimulation. The ability to independently maintain respiratory function is often impaired. Patients often require assistance in maintaining a patent airway

and positive pressure ventilation may be required because of depressed spontaneous ventilation and neuromuscular function. Cardiovascular function may be impaired.

PREPROCEDURAL PATIENT ASSESSMENT

The interventionalist should follow their institutional sedation policy guidelines with respect to preprocedural patient assessment requirements. This usually requires the completion and documentation of a focused history and physical, ASA assessment and classification (Table 2), an airway assessment with Mallampati scoring, and oral intake restrictions according to institutional guidelines. The preprocedural consent process needs to include a discussion of the risks, benefits, and alternatives for sedation and analgesia. The signed informed

Table 2 American Society of Anesthesiologists (ASA) Classification

ASA 1	A normal healthy patient
ASA 2	A patient with systemic disease either caused by the condition to be treated or other pathophysiologic process but does not result in limitation of activity. Example: well-controlled diabetes, hypertension, asthma
ASA 3	Patient with moderate or severe systemic disease that does limit activity. Example: poorly controlled asthma that limits activity; diabetes with systemic sequelae (renal insufficiency, etc.)
ASA 4	Patient with severe systemic disease that is a constant threat to life. Example: renal failure requiring dialysis
ASA 5	Patient who is at substantial risk of death within the next 24 hours and who is undergoing the procedure in desperation. Example: patient with fixed/dilated pupils and head injury
E	Emergency status: this is added to ASA classification when undergoing emergency procedure; healthy patient undergoing emergent appendectomy

Figure 1 Mallampati airway classification.

consent for the procedure needs to include documentation of this sedation discussion. The ASA recommends 6 to 8 hours of no oral intake for solids and nonclear liquids, and 3 hours for clear liquids in adults and children over 36 months of age. In children 6 to 36 months of age, the recommendation is 6 hours for solids/nonclear liquids and 2 hours for clear liquids. For infants (<6 months old), they must have nothing per oral (NPO) 4 hours for solids/nonclear liquids and 2 hours for clear liquids. In emergent cases in which the recommended preprocedure fasting has not occurred, care should be taken to protect against aspiration by limiting the depth of sedation, delaying the procedure, or arranging an anesthesia consult with consideration for endotracheal intubation.^{1,2} The focused history and physical examination should include an assessment of the adequacy of the patient's airway. Patients who have an abnormal airway should be considered a higher risk for airway obstruction during sedation; they also potentially have a difficult airway to manage if ventilatory support becomes necessary. The Mallampati airway classification is used to determine airway adequacy (Fig. 1). A class 3 or 4 airway is considered abnormal. A normal examination of the airway confirms the mouth opens normally, the ability to visualize at least part of the uvula and tonsils with mouth open, normal chin length, and normal flexion/extension of the neck. Abnormal findings include a recessed or small chin, inability to open the mouth normally, high arched palate, inability to visualize part of the uvula or tonsils, tonsillar hypertrophy, a limited range of motion of the neck, low set ears, and significant obesity.^{1,2,6}

SEDATION/ANALGESIA PHARMACOLOGY

There has been a migration away from the use of morphine and diazepam to the use of fentanyl and midazolam because of their rapid onset, short duration of action, and ability to be successfully titrated. Sedative and analgesic medications should be given in small, incremental doses that are titrated to the desired effect of sedation and analgesia. Sufficient time must be allowed for the first medication to exert its full effect prior to administering additional doses or another medication; at least 2 minutes should pass before additional doses are administered. Vascular access needs to be maintained during and after the procedure

until the risk of cardiopulmonary complications has subsided. When using opioids and benzodiazepines in combination, it is important to remember that they are synergistic in producing desired effects as well as undesired effects such as cardiopulmonary compromise. When used in combination, smaller doses of each medication produce the desired sedation or cardiopulmonary depression than if the medications are used alone. Opioids should be administered first to ensure that analgesia occurs before the initial painful stimulus.^{1,2,6,8,9} It is not uncommon for resedation and cardiopulmonary depression to become more apparent after the stimulation from the procedure has ceased. Therefore, an appropriate monitored recovery period needs to occur, the duration of which is patient-, procedure-, and dose-dependent.^{1,6,8,9,12,14} Patients with high anxiety states and chronic narcotic use usually require higher medication dosages. Reducing the anxiety state through nonpharmacologic adjunctive measures can be very helpful in lowering anxiety levels. Measures that can be easily implemented include allowing the patient to bring their own music or select the music played during the procedure. The use of empathic attention, relaxation training, guided imagery, and hypnosis has been increasingly utilized prior to and during interventional procedures. These techniques have been effective in decreasing anxiety levels and decreasing the amount of sedation required for a procedure.^{4,5,7}

LOCAL ANESTHETIC DRUGS

Administration of local anesthesia significantly decreases the dose requirements for sedation and analgesia, but rarely eliminates the need for these medications. However, a common mistake of physicians-in-training is to use an insufficient amount of local anesthesia. Initial patient discomfort is greatly decreased when the practitioner raises a subcutaneous wheal using a small (30-gauge) needle. Pain is increased with rapid injection so slow administration can also greatly decrease patient discomfort. Additionally, icing the area to be anesthetized for 1 minute minimizes the initial pain associated with needle placement. Because lidocaine and bupivacaine are acidic, buffering the medication with 1 to 2 cc 8.4% sodium bicarbonate solution for every 8 to 9 cc of anesthetic reduces the initial burning sensation associated with these medications.^{1,6} Although bupivacaine can precipitate when buffered with sodium bicarbonate, this is rarely clinically significant.

Lidocaine is available in 0.5 to 5% injectable solutions, as well as topical solutions. It is an amide local anesthetic with onset of action in 2 to 3 minutes, and its effects last approximately one hour. The duration of action is longer if the solution contains epinephrine. Central nervous system (CNS) toxicity can occur with

excessive doses; the maximum safe dose is 300 mg without epinephrine and 500 mg with epinephrine.¹⁵

Not infrequently, the patient may report an allergy to lidocaine; however, most patients who claim to have had an allergy actually have had a vasovagal response. Rarely, a patient may have reacted to the preservatives in the lidocaine, and in these patients utilization of preservative-free lidocaine is recommended.^{1,2}

Bupivacaine is also an amide local anesthetic, but with a slower onset of action (5–10 minutes) and a longer duration of action (3–4 hours). It is available in 0.25 to 0.75% injectable solutions. The maximum safe dose is 150 mg without epinephrine and 225 mg with epinephrine.^{1,2,15} It can have significant cardiac toxicity so intravascular injection must be avoided. It is ideal for procedures such as biliary drainage procedures when pain (or the procedure) is expected to persist for hours.

A mixture of 1 to 2% lidocaine with 0.25% bupivacaine combines the rapid onset of lidocaine with the long-term anesthesia of bupivacaine and can be ideal for interventional procedures expected to have significant postoperative discomfort or for those procedures that are expected to be lengthy.^{1,6}

Eutectic Mixture of Local Anesthetics (EMLA)

EMLA is a mixture of 2.5% lidocaine and 2.5% prilocaine in an oil and water emulsion. The lotion should be applied to the desired area under an occlusive dressing for ~1 hour prior to procedures. It provides effective analgesia and can be useful in children, venipunctures, and in patients who have severe needle phobias. Care should be taken to not place EMLA cream over compromised skin, as this may lead to systemic absorption and toxicity.

Bacteriostatic Saline

Bacteriostatic saline can be utilized as an alternative local anesthetic because it contains benzyl alcohol, which acts as a painless anesthetic. The volume of saline required is 2 to 3 times the volume normally administered with lidocaine. Also, the effect rapidly dissipates when administered subcutaneously. The addition of 1 to 3 cc of 1 mg/cc (1:100,000) epinephrine to 20 to 30 cc normal saline (NS) will prolong the local anesthetic effect.

BENZODIAZEPINES

Benzodiazepines occupy the receptor that modulates GABA, the major inhibitory neurotransmitter in the brain, producing sedation and amnesia. These drugs can relieve muscle spasms but do not provide analgesia. The lipid solubility of each benzodiazepine determines its onset and duration of activity. Midazolam (Versed[®],

Roche Laboratories, Nutley, NJ) and diazepam (Valium[®], Roche Laboratories, Nutley, NJ) have a more rapid onset than lorazepam (Ativan[®], Biovail Pharmaceuticals, Inc., Bridgewater, NJ). The short duration of action of a single, small dose of midazolam is due to rapid distribution to the CNS. The duration of action is also related to the drug blood level, and the administration of repeated or large doses will prolong its action. The beneficial effects of benzodiazepines include anxiolysis, amnesia, anticonvulsant therapy, and muscle relaxation. Side effects of benzodiazepines are dose dependent and can include CNS depression and apnea. Apnea is more likely to occur following a rapid bolus administration of midazolam. The risk of respiratory depression and apnea are increased when administered with opioids. Hypotension and tachycardia can also occur and are more likely in elderly patients or in patients with unstable cardiovascular status. Paradoxical agitation has been reported, particularly in elderly patients. Benzodiazepines are contraindicated in patients with acute narrow-angle glaucoma. Midazolam is 2 to 4 times more potent than diazepam (10 mg diazepam = 3–4 mg midazolam). The initial dose of midazolam for sedation in adults is usually 1mg, but lower doses are indicated in elderly or debilitated patients. Midazolam should not be administered by rapid injection in neonates because severe hypotension and seizures have been reported, particularly when used concomitantly with fentanyl. Lorazepam is ~5 times more potent than diazepam (10 mg diazepam = 2 mg of lorazepam). Diazepam and lorazepam have significantly longer half-lives than midazolam and should be used with caution for outpatient procedures. Most benzodiazepines undergo hepatic metabolism. Diazepam and midazolam have active metabolites that require renal excretion. Therefore, dose reduction should be considered in patients with renal and hepatic dysfunction.^{1,2,6,12}

PROPOFOL

Propofol is an intravenous sedative-hypnotic agent that is administered by continuous infusion or by a 10 to 20 mg bolus for the induction or maintenance of anesthesia or sedation. It is recommended that anesthesiologists administer propofol. Onset of action is 40 seconds and its effects last 3 to 5 minutes (half-life is 1–3 minutes). Discontinuation of the infusion results in rapid awakening of the patient. Some practitioners have advocated the use of propofol for interventional procedures because propofol has a favorable side-effect profile and has equivalent or improved sedative effects when compared with the use of IV midazolam and opioids. However, extreme caution is in order because even in relatively low doses, propofol can unpredictably cause a loss of airway reflexes. Propofol can also rapidly cause apnea and hypotension in large doses. In excessive doses, dystonic

reactions have been reported with painful stimuli. Undesirable side effects are likely to occur after bolus dosing or after rapid increases in infusion rates.^{2,6,10}

KETAMINE

Ketamine is a rapid acting, nonnarcotic, nonbarbiturate agent characterized by its profound analgesia, maintenance normal airway reflexes, mild cardiac stimulation, and mild respiratory depression. It produces a state of unconsciousness that has been defined as "dissociative," and it appears to selectively interrupt association pathways to the brain before producing sensory blockade. It has been particularly helpful in patients chronically dependent on narcotics and in pediatric patients. It is not commonly utilized in interventional radiology (IR) suites and an anesthesia consult is usually recommended prior to its use. It has a rapid onset of action with effects seen in 1 to 2 minutes that last 45 to 60 minutes after a 5 to 10 mg IV bolus. It can cause vivid hallucinations and dissociative symptoms, which are dose dependent. Another side effect is involuntary muscle movements, potentially limiting its use during IR procedures.^{1,2,11,14}

DRUGS FOR REVERSING THE EFFECTS OF OPIOIDS AND BENZODIAZEPINES

Naloxone (Narcan®)

Naloxone (Narcan®, ENDO Pharmaceuticals, Newark, DE) is an opioid-receptor antagonist used to counteract overdoses of opioids like morphine and fentanyl. Naloxone blocks the action of opioids on the opioid receptor and reverses respiratory depression. It is important to remember that naloxone also reverses the pain-relieving effects of the opioids. Patients can experience significant pain, anxiety, and agitation with rapid administration of naloxone. Therefore, incremental dosing is recommended with full-dose administration reserved for life-threatening respiratory arrest. Other reported side effects with abrupt reversal of opioids include tachycardia, nausea, vomiting, hypertension, ventricular tachycardia, seizures, and pulmonary edema. Narcan® is available in three concentrations: 0.02 mg, 0.4 mg, and 1 mg of naloxone hydrochloride per mL. For postoperative opioid respiratory depression, 0.1 to 0.2 mg should be given IV every 2 to 3 minutes until the desired effect (respiratory rate >10 breaths/minute) has been achieved. Drug administration should be titrated in increments to the desired effect to minimize the reversal of the analgesia and withdrawal effect. When the patient is awake and responsive, the reversal effect has been achieved. If no IV access is available, then the entire ampule (0.4 mg) should be administered by intramuscular (IM) or subcutaneous (SQ) injection. For known or suspected opioid overdose, an initial dose of 0.4 mg to 2 mg of

Narcan® may be administered IV, and can be repeated at 2 to 3 minute intervals. The half-life of naloxone is <90 minutes; therefore, if Dilaudid (Purdue Pharma, Stamford, CT) or morphine has been administered, repeat doses of naloxone may be necessary. If short-acting fentanyl is the offending agent, repeat dosing might not be needed. Because the sedative effect of the longer-acting opioids may outlast the reversal effect of naloxone, the patient must be monitored for a long enough period (usually 2 to 4 hours) to ensure resedation does not return.^{1,2,6,7}

FLUMAZENIL (ROMAZICON®)

Flumazenil (Romazicon®, Roche Laboratories, Nutley, NJ) is a benzodiazepine receptor antagonist that binds to the benzodiazepine receptor GABA, thus blocking the CNS effect of the benzodiazepine. This results in reversal of sedation with cessation of amnesia and reversal of respiratory depression. Flumazenil does not reverse the effects of opioids, alcohol, or barbiturates. Adverse effects such as anxiety, tremors, and agitation can occur. In the high-risk patient who has an underlying seizure disorder or who is benzodiazepine dependent, reversal with flumazenil has been associated with seizures. The reversal and associated side effects occur 1 to 2 minutes after IV administration. The dose for reversal is 0.01 mg/kg and should be given in increments of 0.1 to 0.2 mg in adults. Generally, doses of 0.1 to 0.2 mg produce partial antagonism and higher doses of 0.4 mg to 1 mg produce complete reversal. Similar to naloxone, flumazenil has a shorter duration of action than most benzodiazepines and resedation requiring readministration of flumazenil is possible. Resedation has been reported in 3 to 9% of patients and is more common in patients who have received higher doses of benzodiazepines. Such patients need to be monitored for a longer period.^{1,2,6,7}

MONITORING DURING SEDATION AND ANALGESIA

An independent trained observer needs to be present to monitor patients during procedures in which sedation and analgesia is being provided. Oxygen saturation, heart rate and rhythm, respiratory rate, and responsiveness are monitored continuously and should be recorded at least every 15 minutes or when there are significant or symptomatic changes. Blood pressure should be recorded at least every 15 minutes or when there are significant or symptomatic changes. Pain level is also monitored before, during, and after the procedure. Capnography is the continuous analysis and recording of end-tidal CO₂ monitoring. Capnography may be able to detect hypoventilation before pulse oximetry detects oxygen saturation. CO₂ monitoring during moderate sedation has been advocated by some, but there are

currently no guidelines requiring it. Capnography should be strongly considered in cases of deep sedation. Oxygen, suction equipment, nasal cannulae, oral airways, and a bag-valve mask should be in the interventional suite. The procedure room should be equipped with a cardiac monitor, an automatic blood pressure cuff, and a pulse oximeter. A core cart with emergency resuscitation equipment and advanced cardiac life support (ACLS) medications must be immediately available. Obese patients, patients with chronic obstructive pulmonary disease, septic patients, elderly patients, patients with recent myocardial infarction or unstable angina, and pediatric patients are all at a higher risk for complications. An anesthesia consult in these subgroups of patients may be helpful depending on the level of anesthesia required and the experience of the interventionalist.^{1,2,6,7,13}

CONCLUSION

Knowledge of sedative and analgesic agents, experience and training with the administration of such medications, preoperative assessment and planning, and careful independent monitoring of sedated patients during and after interventional procedures will allow safe performance of interventional procedures. Appropriate use of sedation and analgesia is key to improving outcomes and patient satisfaction.

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