CROUSE HEALTH
Affiliate of Northwell Health

Perspectives on Sedation and Analgesia: Pharmacology, Monitoring and Educational Materials To Supplement the Moderate Sedation Policy

The Joint Commission on Accreditation for Hospitals has Guidelines for the use of drugs that trigger the use of anesthesia standards. The pharmacological classification of the drug is not the sole determinant; the dose and route of administration are also factors because this combination determines the risk for loss of the patient's protective airway reflexes. Because sedation is a continuum, it is not always possible to predict how an individual patient receiving sedation will respond. Therefore, each institution has been asked to develop specific protocols for the care of patients receiving sedation which carries a reasonable risk of loss of protective reflexes.

The objectives for the patient include:

- Alteration of level of consciousness/mood
- Maintenance of consciousness
- Cooperation
- Elevation of the pain threshold
- Minimal variation of vital signs
- Rapid onset of amnesia
- Safe return to ambulation

The desired effects include:

- Relaxation
- Cooperation
- Purposeful responses to verbal communication and tactile stimulation
- Easy arousal from sleep

Undesirable effects of sedation and analgesia are:

- Deep unarousable sleep
- Hypotension
- Bradycardia
- Agitation **or** combativeness
- Hypoventilation
- Respiratory depression
- Airway obstruction
- Apnea

Moderate sedation as defined by JCAHO and the Crouse Hospital's Policy and Procedures, is 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 patient airway, and spontaneous ventilation is adequate. Cardiovascular function is usually maintained. It must be distinguished from pre-medication and pain management which are not governed by the Moderate Sedation Policy. Although the drugs may be the same as some of those used

for moderate sedation, the circumstances surrounding their use and the dosages used for pre-medication or for pain management are considered to pose a risk of impairing the patient's protective airway reflexes.

Moderate sedation must also be distinguished from deep sedation. Deep sedation is a drug-induced depression of consciousness during which patients cannot be easily aroused but respond purposefully following repeated or painful stimulation. The ability to independently maintain ventilatory function may be impaired. Patients may require assistance in maintaining a patient airway and spontaneous ventilation may be inadequate. Cardiovascular function is usually maintained. Deep sedation should only be administered by an anesthesiologist or other specially credentialed providers (see Deep Sedation Policy). Sedation of mechanically ventilated patients is not considered in this policy.

Ketamine, etomidate, pentothal, methohexital and propofol are only to be administered by providers who are separately credentialed to provide deep sedation. These drugs are not to be given by credentialed moderate sedation providers.

This perspective will consider the pharmacology of some of the drugs which may be used for sedation and analgesia, as defined above, as well as the personnel, monitoring and patient evaluation necessary for procedures requiring sedation and analgesia.

Pharmacological Principles of Sedation and Analgesia

Sedation and analgesia may be provided by a variety of drugs which differ significantly in their pharmacological classification and effects. The most widely used drugs include the benzodiazepines and the narcotics. Other intravenous anesthetic agents are sometimes used for deep sedation. These include pentothal, methohexital, ketamine and propofol. Due to the grater propensity for respiratory depression and other reactions, they may only be administered by anesthesiologist and ATTENDING PROVIDERS or Emergency Medicine residents working the Emergency room who are separately credentialed to provide deep sedation.

Benzodiazepines are widely used for sedation and analgesia. They are considered to be sedative-hypnotics or tranquilizers. They are used to anxiolysis, sedation and amnesia. The most widely used include diazepam (Valium), midazolam (Versed) and lorazepam (Ativan). Midazolam use has overtaken that of diazepam due to its shorter duration of action and water solubility which helps to decrease the pain associated with injection.

The benzodiazepines produce a spectrum of effects. Depending upon the dose, they range from tranquility and drowsiness to sedation, and ultimately, unconsciousness. Anterograde amnesia is associated with all of the benzodiazepines. The most significant side effect of any of the benzodiazepines is severs respiratory depression, particularly when used in combination with other CNS depressants. Benzodiazepines cause minimal cardiac depression when used alone. However, when combined with other anesthetic agents, including narcotics, (which, by themselves are cardiostable drugs) cardiovascular depression and even hemodynamic collapse may occur.

A sedating dose of diazepam is 0.05 to 0.1 mg/kg IV. For mid**a**zolam, 0.01 m**g**/kg IV as an initial dose may be used*. Lorazepam has a much longer clinical duration than either diazepam or midazolam. It is most useful as a premedication, given intramuscularly at a dose of 0.05 mg/kg. These agents should be administered slowly due to the widely varied response from patient to patient. The dose should be lowered in the elderly or debilitated patient. Qualified personnel must monitor the patient after administration of these agents.

***For Pediatric doses, refer to the Harriet Lane Handbook.**

Flumazenil (Romazicon), a **benzodiazepine antagonist** can reverse the effects of the agents above. It should be used cautiously because it can precipitate acute withdrawal in patients who are chronically dependent on benzodiazepines. It can also cause seizures. When given intravenously, the does is 0.2 mg repeated at 1-minute intervals to a maximum of 1 mg. the onset of action **is** usually within 2 minutes. While flumazenil reliably antagonizes the sedative effects of benzodiazepines, its antagonism of respiratory depression is not as reliable and should not be depended upon. Respiratory depression should be initially treated with supplemental oxygen, and if needed, positive pressure ventilation by a bag/valve/mask (Ambu) system. Furthermore, the duration of action of the benzodiazepine used may exceed that of flumazenil. Continued monitoring is essential even after flumazenil use.

Narcotics, which are routinely used for sedation and analgesia, act at a variety of different receptor sites. The use of narcotics serves to produce analgesia. In combination with a benzodiazepine, this provides sedation, anxiolysis and analgesia achieving the goal of moderate sedation. In addition, a local anesthetic injection or topical anesthetic may then be used to provide anesthesia for a specific indication such as catheterization of an artery, excision of skin lesion or introduction of an endoscope.

The **narcotics** can be divided into several classes. They include naturally occurring opioids, semi-synthetics opioids and synthetic opioids. The potency and duration of action between these different classes varies considerably.

For analgesia, a mu receptor agonist is ideal. They act centrally in pain-suppressing areas of the brain and spinal cord. These areas include the periaqueductal gray, medial thalamus, substantia gelatinosa and laminae I and II of the spinal cord. Sufetanil (which should not be used for moderate sedation) is the clinical standard for mu efficacy. While it can render a patient apneic, and completely unresponsive to noxious stimulation, the patient may retain enough residual awareness to later recall the procedural events. For this reason, a narcotic is rarely given alone. A combination with a benzodiazepine produces more reliable amnesia.

Anxiety and discomfort from a procedure can produce stress, which causes large swings in hemodynamic variables, as well as increased catabolism. This stress may also cause abrupt release of epinephrine, norepinephrine, glucagons, cortisol, growth hormone and antidiuretic hormone which increases the cardiovascular stress. These considerations are of major importance to patients with marginal hemodynamic and metabolic reserves, such as neonates or those with advanced cardiac, vascular or renal disease.

Widely recognized mu agonists include morphine sulfate, meth**a**done hydrochloride, meperidine hydrochloride, fentanyl citrate, sufentanil citrate and alfentanil hydrochloride. Of these, fentanyl, morphine and meperidine are usually chosen for moderate sedation. Agonist-antagonist opioids are also used. They have different actions at different receptor sites, resulting in diverse pharmacologic effects. They may also precipitate withdrawal in narcotic addicted patients. Agents in this class include butorphanol tartrate (Stadol) and nalbuphine (Nubain).

The **narcotic antagonists** include naloxone hydrochloride and naltrexone. Both are non-selective. Nal**o**xone is a pure antagonist of all opioid effects except those mediated by the sigma receptor. It is used primarily to antagonize respiratory depression and acute opioid overdose. Naloxone is administered in doses of 0.04 mg – 0.08 mg IV at 2 minute intervals until the desired effect is reached. The duration of action of naloxone is about 20 to 30 minutes. Repeat boluses or a continuous infusion are used to maintain adequate blood levels until the opioid agonist is eliminated. Also, it is important to recognize that both the opioid-analgesia and respiratory depression are antagonized. This antagonism can precipitate acute withdrawal in opioid-addicted patients. Rare, but potentially fatal reactions to naloxon**e** include pulmonary edema, seizures, hypertension, arrhythmias, and

cardiovascular collapse. Careful titration and close monitoring are essential. Naltrexone is also a pure antagonist. Clinically it is used for antagonism of opioids with long elimination half-lives such as **normeperidine** or methadone. It has no use in the antagonism of medications used for sedation and analgesia.

Pre-Procedural Evaluation

The practitioner administering sedation and analgesia must review and document relevant aspects of the patient's medical history including major organ system abnormalities, previous experiences with sedation, regional and general anesthesia, current medication and drug allergies, the time and nature of the last oral intake, and history of alcohol, tobacco or substance abuse.

The pre-procedural examination includes a focused evaluation of the airway, the heart and lungs. The practitioner should be alerted to the possibility of difficult tracheal intubation in patients with significant obesity, especially involving the neck and facial structures. Individuals with a short neck, a small jaw or a receding chin (micrognathia) may be difficult to intubate in an emergency.

Medical conditions such as rheumatoid arthritis or other conditions which limit the range of motion of the neck or jaw, or significant maxillary/mandibular malocclusion may also present a challenge to tracheal intubation.

Laboratory tests should be guided by the patient's medical condition and how the results will affect the management of sedation. The provider will determine the appropriateness of electrocardiograph monitoring during the procedure.

Consultation for Sedation and Analgesia

The American Society of Anesthesiologists has established criteria by which a patient's physical status is evaluated pre-operatively (pre procedurally). It is a scale ranging from 1 to 5 and use**s** the additional designation of "E" for an emergency procedure. The description is as follows:

ASA Physical Status	Description
1	No Systemic Disease
2	Mild, or Well Controlled Systemic Disease, No Functional Limitations
3	Severe Systemic Disease, Definite Functional Limitation
4	Severe Systemic Disease, Constant Threat to Life
5	Moribound, Not Expected to Survive for 24 Hours, Irrespective of Operation.
E	Emergency – a modifier to ASA Status

The patient with a physical status rating of ASA 3 or higher should alert the practitioner that a higher leve**l** of vigilance is required. In patients of ASA physical status 3, 4, or 5 (e.g., severe cardiac, pulmonary, hepatic, renal, CNS disease, morbid obesity, sleep apnea, others) or in certain selected classes of patients such as uncooperative patients, extremes of age (under 1 year or over 70 years of

age), the pregnant patient, those with sleep apnea or drug/alcohol abusers there is an increased risk of developing complications related to sedation and analgesia unless special precautions are taken. This risk may be reduced by pre-procedure consultation with appropriate specialist including, but not limited to anesthesiologist, cardiologists, pulmonologists, nephrologists, obstetricians or pediatricians. **The provider must assign an ASA physiologic status classification based on the patient's history and physical examination.**

Whenever possible, appropriate medical specialists should be consulted before the administration of sedation and analgesia to a patient with significant underlying conditions. If it appears likely that sedation to the point of unresponsiveness or even general anesthesia may be necessary to obtain adequate conditions, an anesthesiologist should be consulted prior to planning the procedure. At Crouse Hospital, the Department of Anesthesiology may be contacted at 470-7828; or in the operating room at 470-7885.

During the administration of sedation and analgesia, should a situation become unmanageable or life-threatening, the hospital operator should be instructed to **call a code blue** to your location.

Monitoring and Equipment for Sedation and Analgesia

The following equipment must be present and ready for use in any area where sedation and analgesia is administrated:

- Oxygen
- Oxygen delivery devices (flow meters, nasal cannulae, face masks, etc.)
- Suction
- Ambu bag and masks in appropriate sizes **for** positive pressure ventilation
- One-way valve mask
- Airways (oral/nasopharyngeal) in appropriate sizes
- Intubation equipment (ET tubes, laryngoscopes, stylets)
- Pulse oximeter
- Capnography measuring and monitoring device
- Cardiac monitor – EKG (when indicated)
- Non-invasive blood pressure monitor
- Code cart/defibrillator

Monitoring level of consciousness, respiratory function and hemodynamics reduces the risk of adverse outcomes. The patient's ventilatory status and level of oxygenation as well as hemodynamic variables should be recorded at a frequency determined by the type and amount of medication administered, duration of the procedure, and patient's general medical condition. At a minimum, this should be done immediately prior to the administration of sedative medication, after administration of sedative or analgesic agents, every 10 minutes during the procedure, upon completion of the procedure, during the initial recovery phase and at the time of discharge.

Documentation in the patient record during the administration of sedation and analgesia will include:

- Dose, route, administration time, effects of drugs used.
- Type/amount of IV fluids/blood/blood products used
- Physiological data (recorded at least every 10 minutes) including end tidal CO2.
- Level of consciousness
- Untoward/significant reactions and resolutions

A designated individual, other than the provider performing the procedure, will be continuously present to monitor the patient throughout the procedure. The monitor will have an understanding of the pharmacology of the agents administered as well as the role of antagonists. The monitor will also be able to recognize associated complications. According to Crouse Hospital policy the monitor can be a credentialed RN or Respiratory Therapist (see definition of Credentialed Monitor). At least one member of the care team must be capable of establishing a patent airway and providing positive pressure ventilation. There will also be a means for summoning additional assistance whenever sedation and analgesia is administered.

In addition to the drugs used for sedation, pharmacologic antagonists (flumazenil and naloxone) and emergency equipment will be immediately available in the procedural area. An example of the emergency equipment and drugs to be available during sedation and analgesia would include: (this is a guide, which may be modified depending upon the individual practice circumstances):

Intravenous Equipment

- Gloves, tourniquets, alcohol wipes, gauze pads
- IV catheters (20, 22, 24 gauge) and IV tubing, IV fluids
- Three-way stopcocks, assorted needles, syringes, tape

Airway Management Equipment

- Oxygen source (with regulator/flowmeter, i.e., positive pressure)
- Suction, suction catheters (soft and Yankauer type)
- Face masks (appropriate sizes)
- Self-inflating breather bag-valve set (Ambu bag)
- One way valve mask
- Oral/nasal airways (appropriate sizes) and lubricant
- Laryngoscope handles/blades (pretested)
- Endotracheal tubes (sizes 6.0, 7.0, 8.0 for adults) and/or
- Pediatric endotracheal tubes (sizes 2.5 to 6.0) as indicated
- Endotracheal tube stylets (appropriate sizes)

Pharmacological antagonists of Narcotics/Benzodiazepines

- Naloxone
- Flumazenil

Emergency Medications

- Epinephrine
- Ephedrine
- Atropine
- Lidocaine
- Glucose, 50%
- Diphenhydramine
- Hydrocortisone, methylprednisolone or dexamethasone
- Diazepam or midazolam (for treatment of local anesthetic toxicity)
- Ammonia spirits

The use of a combination of drugs (i.e. a benzodiazepine and a narcotic) may be more effective in providing the desired sedation. However, literature also suggests that the combination of sedatives and opioids may increase the likelihood of adverse outcomes such as ventilatory depression and

hypoxemia. Fixed combinations of sedatives and analgesic agents may not meet the individual patient's need for sedation and analgesia. Therefore, if a combination of agents is used, they are administered separately and titrated to effect. Sufficient time must elapse between doses to observe the effect before subsequent drug administration. The propensity for combinations to produce respiratory depression emphasizes the need to reduce the dose of each drug accordingly and to continually monitor vital signs. If patients have received antagonists (flumazenil and/or naloxone) they should be encouraged or stimulated to breathe deeply, receive positive pressure ventilation and receive supplemental oxygen. These patients must be monitored long enough after the administration of antagonists to ensure that cardio respiratory depression does not occur. Generally, this should be considered to be 2 hours.

All patients receiving sedation and analgesia should have intravenous access maintained throughout the procedure and until such time that the patient is no longer at risk for cardio respiratory depression. If a patient has received sedation by a non-intravenous route or if the IV has become dislodged or blocked, the practitioner should determine the advisability of establishing IV access. In any event, an individual with the skill to establish intravenous access (especially if an emergency arises) will be immediately available.

The Pulse Oximeter and Electrocardiogram

The pulse oximeter is a non-invasive device that measures a pulse and oxygen-hemoglobin saturation (SO_2). The operating principle of a pulse oximeter involves absorption of different wavelengths of red and infrared light by oxygenated and deoxygenated hemoglobin as it is transmitted through, and reflected by a tissue bed. Pulse oximeters use the pulse to distinguish between blood and tissue absorptions (only arterial blood pulsates). The pulse oximeter uses two specific wavelengths of light: 660 nm (red light) and 940 nm (near-infrared light). The pulse oximeter is subject to signal artifacts that are usually related to ambient light, low perfusion and patient motion. It can also be affected by injected dyes like methylene blue, which have absorbances similar to deoxygenated hemoglobin and can cause brief artifactual oxygen desaturation when administered by intravenous injection.

Oxygen saturation is not the same as oxygen partial pressure, which is measured by blood gas analysis. Oxygen saturation will be 100% when the oxygen partial pressure is 100 mmHg or greater. While partial pressures of oxygen can be several hundred mm Hg, the oxygen saturation remains at 100% and oxygen is dissolved in the blood. Despite the differences, saturation is very useful because it is an early warning indicator of low-oxygen states. The partial pressure of oxygen and oxygen saturation can be approximated at lower oxygen levels.

Partial Pressure of Oxygen (PO2-Blood Gas)	Oxygen Saturation (SO2 – Pulse Oximeter)
60 mmHg	90% Saturation
50 mmHg	80% Saturation
40 mmHg	70% Saturation

When used in conjunction with other required monitors, the noninvasive pulse oximeter represents a significant advance in patient safety. It provides important information about oxygenation on a beat-to-beat basis and confirms ECG pulse tracings. The pulse oximeter must be used routinely. Electrocardiographic monitoring should be used in those patients with a significant cardiovascular disease, as well as during procedures in which dysrhythmias are anticipated. If ECG monitoring is necessary, the credentialed monitor should have an established competency in dysrhythmia recognition and interpretation.

Capnography

- Capnography is the measurement of exhaled CO2
- Some monitors display a number in millimeters of Mercury(mm Hg)
- Capnography also provides the clinician with a waveform showing exhaled CO2 over time.
- Is used to confirm, monitor, and document ET tube intubation
- Is used to monitor the ventilatory status of a non-intubated patient
- The measurement of end-tidal CO2 (ET CO2) currently is the optimal method of continuously monitoring the adequacy of ventilation and circulation in the adult, child, and infant.
- Changes in ETCO2 can be a reliable indicator in metabolic changes
    - Metabolic Increased ETCO2 (Fever, sepsis, shivering, convulsions, malignant hyperthermia)
    - Metabolic Decreased ETCO2 (Hypothermia, paralytics, sedation)
- ETCO2 transport to the lungs is dependent on adequate cardiovascular function
- With ventilation constant, changes in ETCO2 can indicate circulation changes
    - Circulatory Increased ETCO2 (Return of Spontaneous Circulation)
    - Circulatory Decreased ETCO2 (Low cardiac output, hypovolemia, hypotension)
- Normal = 35 mmHg – 45 mmHg
- ETCO2 measurements exhibit significant change immediately
- Respiratory Rate versus CO2
    - Hypoventilation = CO2 > 45 mmHg (COPD possible chronic hypercapnea/ hypercarbia)
    - Hyperventilation = CO2 < 35 mmHg
    - CO2 >55 mmHg think Ventilatory Failure
- Adequacy of CPR is also easily assessed through capnography
    - The measurement helps in assessing the effectiveness of CPR
- ETCO2 levels have a strong correlation with cardiac output
    - As cardiac output decreases during cardiopulmonary arrest, pulmonary blood flow diminishes, CO2 available for exhalation is decreased, and ETCO2 levels drop
    - Attempt to maintain a minimum of 10 mmHg during CPR
- ETCO2 can also help predict survival.
    - Levine and colleagues reported 100% mortality in out of hospital cardiac arrests where ETCO2 did not return to 10 mmHg after 20 minutes of CPR
- Return of Spontaneous Circulation

At Crouse Hospital the presence or absence of a wave form generated by capnography monitoring is documented. A plus (+) sign indicates the wave form is adequate and shows a normal pattern. A minus sign (-) indicates that the wave form was not adequate and the patient must be assessed.

Recovery and Discharge after Moderate Sedation

Patients may continue to be at significant risk for complications after completion of a procedure. A lack of stimulation, prolonged drug absorption or post-procedural hemorrhage may continue to cardio respiratory depression. After administration of sedation and analgesia, patients are observed until they are no longer at an increased risk for cardio respiratory depression. Vital signs and respiratory function are monitored every 15 minutes until the vital signs and pulse oximetry are consistent with the range of pre-procedural norms and LOC is no more than 2 on the Ramsey scale or less than 8 on the Aldrete scale. A patient should not be discharged until specific discharge criteria are met which are designed to minimize the risk of complications from central nervous system and/or cardio respiratory depression.

The recovery area is equipped in a similar fashion to the procedure room. It should have appropriate monitoring and resuscitation equipment. An R.N. or other trained individual should be in attendance until discharge criteria are fulfilled. An individual capable of providing or maintaining the airway and administering positive pressure ventilations must be immediately available. The practitioner is notified immediately if dramatic changes occur of if the parameters are not within the established limits for that patient.

The Aldrete score has been used for more than 25 years in post-anesthesia care units to clinically assess the physical status of patients recovering from an anesthetic and follow their awakening process. This method of assessment has been adopted as the suggested criteria for discharge from the post-anesthesia care unit by the Joint Commission of Accreditation of Health Care Organizations. For intra-hospital transfers after receiving moderate sedation, the patient should achieve an Aldrete score of 8 based upon criteria including activity, respiration, circulation, consciousness and oxygen saturation. For discharge home, in addition to these criteria, patients must meet satisfactory discharge criteria including a dry dressing, pain control, ability to ambulate, ability to take nutrition and adequate urine output. The Aldrete scoring system is shown in the table (attached).

Guidelines for discharge (many are incorporated into the Aldrete score**)** may include:

- Patient is alert and oriented (infants or patients with altered mental status have returned to baseline)
- Patient has eaten a light snack (i.e., crackers and juice), voided and ambulated without difficulty (i.e., dizziness, nausea or vomiting)
- Patient has no or minimal pain from the procedure
- Vital signs and respiratory function are stable (pre-procedure range) and within acceptable limits
- Observation for 2 hours after the **LAST ADMINISTRATION OF ANTAGONISTS** (reversal agents)
- Patient is discharged to the care of a <u>RESPONSIBLE ADULT</u> who will accompany them home (i.e., drive them) and be able to report any post-procedure complications
- Patient has received <u>WRITTEN</u> instructions regarding diet, activity, medication and has an emergency phone number.

Sedation and Analgesia – Medication Guidelines

Medication	Adult Dose (Initial)	Adult Dose (Incremental)	Pediatric Dose	Pediatric Dose (Incremental)	Comments
Chloral Hydrate			Oral 50 – 100 Mg/kg		Respiratory Depression, Prolonged Sedation, vomiting
Diazapam (Valium)	2 to 3 mg	up to 10 mg (slow IV push)	Oral 0. 15-0.3 mg/kg max 10 mg IV 0.05 to 0.08 Mg/kg		Respiratory Depression,
Fentanyl (Sublimazae)	25 – 75 mcg	25 mcg every 2 to 3 minutes	1-1.5 mcg/kg IV	1-2 mcg/kg/hr	Respiratory Depression Especially with Benzodiazepine
Meperidine (Demoral)	50 to 75 mg IV	25 mg if needed	1 mg/kg IV, Max 75 mg		Dilute to 10 mg/**ml** Avoid use with MOAI's
Midazolam (Versed)	1 to 2 mg IV	0.5 mg every 2 to 3 minutes If needed	0.08 mg/kg IV over 5 minutes Max 5 mg	May repeat dose after 5 minutes if needed	More than 5 mg is rarely needed
Morphine	5 to 10 mg IV (slow push over 5 minutes)	0.05 to 0.08 mg/kg IV over 5 minutes. Max 10mg	0.05 to 0.08 mg/kg IV over 5 minutes max 8mg		

Antagonists

Flumazenil (Romazicon)	0.2 mg IV over 15 Seconds	May repeat 0.2 mg every minute up to 1 mg max	0.01 mg/kg (Max 0.2 mg)	0.005 mg/kg (Max 0.2mg) Every minute to 1 mg max	Short half-life may need to repeat dose in 20 minutes
Naloxone (Narcan)	0.04 to 0.08mg	Every 2 minutes to desired effect	0.01 mg/kg IV	0.01 mg/kg every 2 minutes to desired effect	Short half-life may need to repeat dose in 20 minutes

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