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

The Joint Commission on Accreditation for Hospitals bas 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 protocol (policy attached, this educational material, quiz and credentials paperwork comprise the credentialing packet for "sedation and analgesia" by non-anesthesiologists.

Intravenous (IV) sedation and analgesia (a.k.a. conscious sedation) is produced by the administration of pharmacological agents which alone, or in combination, produce a depressed level of consciousness but the ability to independently and continuously, maintain a "patent airway and respond appropriately to physical stimulation is retained. Our goal in providing "the practitioner with this educational module (containing the hospital's Policies and Procedures on Sedation and Analgesia by non-anesthesiologists for elective procedures, this overview of Perspectives on sedation and analgesia and the questions that follow) is to assure the same level of quality patient care by all individuals with delineated clinical privileges, within medical staff departments, and across all departments and services at the hospital. This perspective is a guideline for EDUCATIONAL PURPOSES ONLY. It is NOT designed to establish or reflect standards, nor is it intended to be used for legal purposes.

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 Degree 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 and Combativeness
- Hypoventilation
- Respiratory Depression
- Airway Obstruction
- Apnea

Sedation and Analgesia, as defined by the hospital's policy and procedures is a minimally depressed level of consciousness that retains the patient's protective reflexes and ability to maintain a patent airway independently and continuously. It must be distinguished from pre-medication which is defined as a single dose of medication, usually given either by mouth or intramuscularly, prior to a procedure and post-procedure or post-operative pain management including patient-controlled
analgesia. Refer to the hospital's Policy regarding Sedation and Analgesia for further information regarding pre-medications and post-procedure pain management. These items are not part of the policy regarding Sedation and Analgesia. Pre-medications are not usually titrated to effect as are medications given for sedation and analgesia. Examples of pre-medications include IM valium, IM Demerol / vistaril or choralhydate given to a child. The dosages and/or routes of administration of drugs used for pre-medications, or for post-procedure (post-operative) pain management or patient-controlled analgesia (PCA) are not considered to have a reasonable risk of causing loss of the patient’s protective airway reflexes and therefore similar medication(s) used for these purposes are not part of the policy on sedation and analgesia by non-anesthesiologists. Sedation and analgesia, or “conscious sedation” must also be distinguished from deep sedation. Deep sedation is a controlled state of depressed consciousness or unconsciousness from which the patient is not easily aroused and is unable to respond purposefully to physical stimulation or verbal command. This may be accompanied by a partial or complete loss of protective reflexes and an inability to maintain a patent airway independently. Deep sedation should only be administered by an anesthesiologist (except in circumstances where a patient is already mechanically ventilated for medical reasons. Sedation of mechanically ventilated patients is not considered in this policy).

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 include the benzodiazepines and the narcotics. Other intravenous anesthetic agents are sometimes used for conscious or deep sedation. These include pentothal, methohexital, ketamine and propofol. Due to the greater propensity for respiratory, depression and other reactions, they should not be routinely used by non-anesthesiologists for sedation and analgesia. While some practitioners have experience and are familiar with the use of these agents, they may be used provided specific protocols (to include procedure, route, dose and timing of administration) are submitted to, and approved by the anesthesiologist-in-chief regarding their use.

Benzodiazepines are widely used for sedation and analgesia. They are considered to be sedative-hypnotics or tranquilizers. They are used for 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 a 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 severe 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 midazolam, 0.01 mg/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 pre-medication, 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. The patient must be monitored by qualified personnel after administration of these agents.

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. When given intravenously, the dose 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 which is the goal. In addition, a local anesthetic injection or topical anesthetic may then be used to provide anesthesia for a specific indication such as catherization 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-synthetic opioids and synthetic opioids. The potency and duration of action between these different classes varies considerably.

For analgesia, a mu receptor agonist is ideal. It acts 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. Sufentanil 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 catabolic metabolism. This stress may also cause abrupt release of epinephrine, norepinephrine, glucagon, 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, methadone hydrochloride, meperidine hydrochloride, fentanyl citrate, sufentanil citrate and alfentanil hydrochloride. 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 nonselective. Naloxone 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. The duration of action of naloxone is about 2q to 30 minutes. Repeat boluses or a continuous infusion are used to maintain adequate blood levels until the opioid antagonist is eliminated. Also, it is important to recognize that the opioid-analgesia is antagonized like the respiratory depression. This antagonism can precipitate acute withdrawal in opioid-addicted patients. Rare, but potentially fatal reactions to naloxone 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.

Nitrous oxide is the first inhalational anesthetic to be used clinically. There are now over 150 years of clinical experience with this agent. Nitrous is a weak anesthetic agent but it maybe used in subanesthetic doses for analgesia or as a supplement to potent anesthetic agents to reduce the concentration required. Nitrous oxide is a myocardial depressant. However, it indirectly stimulates the sympathetic nervous system. Nitrous oxide is nonirritating to the upper airways. It lacks any direct bronchodilatory effects. The major toxic effects of nitrous oxide are associated with its inactivation of methionine synthase. This decreases the concentrations of methionine, a precursor to thymidine, which is incorporated into DNA. Nitrous oxide should be avoided in pregnant patients because of the potential effect on DNA. For sedation and analgesia, it should not exceed concentrations of 50% in oxygen.

Ketamine hydrochloride is a derivative of phencyclidine. It may be administered intravenously or intramuscularly to produce a pain-free cataleptic state. The patient may appear awake but is
dissociated from the environment. The cataleptic state produced by ketamine has been called "dissociative anesthesia". Ketamine can increase intracranial pressure as it is a potent cerebral dilator. It also increases heart rate, cardiac output and systemic and pulmonary vascular resistance. Although laryngeal reflexes are only moderately depressed, an endotracheal tube is still necessary if there are full stomach considerations. The major disadvantage of ketamine is the propensity for psychic disturbances on emergence from anesthesia. These may manifest as unpleasant dreams or hallucinations that may progress to delirium. The incidence of emergence delirium from ketamine reportedly ranges from 5 to 30%. The sympathomimetic effects of ketamine make it a poor choice for patients with severe hypertension, significant coronary artery disease or aortic or cerebral aneurysms. For sedation and analgesia, ketamine may be administered in doses of 0.2 to 0.3 mg/kg IV or 2 to 3 mg/kg IM.

Pre-Procedural Evaluation

A physician administering sedation and analgesia should be familiar with 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, history of alcohol, tobacco or substance abuse. The pre-procedural examination should include 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, retrognathia) 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.

Consultation for Sedation and Analgesia

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

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<thead>
<tr>
<th>ASA Physical Status</th>
<th>Description</th>
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<tbody>
<tr>
<td>1</td>
<td>No Systemic Disease</td>
</tr>
<tr>
<td>2</td>
<td>Mild, or Well Controlled Systemic Disease. No Functional Limitations</td>
</tr>
<tr>
<td>3</td>
<td>Severe Systemic Disease. Definite Functional Limitations</td>
</tr>
<tr>
<td>4</td>
<td>Severe Systemic Disease. Constant Threat to Life</td>
</tr>
<tr>
<td>5</td>
<td>Moribund. Not Expected to Survive for 24 Hours. Irrespective of Operation</td>
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The patient with a physical status rating of ASA 3 or higher should alert the practitioner that a higher level 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 appropriate pre-procedure consultation with appropriate specialists' including, but not limited to anesthesiologists, cardiologists, pulmonologists, nephrologists, obstetricians or pediatricians.

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. The Department of Anesthesiology may be contacted at xxx-xxxx (office) or in the operating room at xxx-xxxx and ask for the anesthesiology coordinator.

During the administration of sedation and analgesia, should a situation become unmanageable or life-threatening, the hospital operator should be instructed to page “Anesthesia, STAT to your location or phone number” or initiate a “CodeBlue” response by dialing the hospital’s “Code Blue” phone number if those criteria are fulfilled.

**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 administered:

- Oxygen
- Suction
- Bag and Mask (AMBU) in Appropriate Sizes (for Positive Pressure Ventilation)
- Airways (Oral/Nasopharyngeal) in Appropriate Sizes
- Intubation Equipment (ET Tubes, Laryngoscopes, Stylets)
- Pulse Oximeter
- Cardiac Monitor -EKG (when indicated)
- Non-Invasive Blood Pressure Monitor
- Code Cart/Defibrillator

The monitoring of the level of consciousness, respiratory function and hemodynamics reduces the risk of adverse outcomes. Patient's ventilatory status and level of oxygenation as well as hemodynamic variables 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: before the procedure, after administration of sedative or analgesic agents, upon completion of the procedure, during the initial recovery phase and at the time of discharge.

Documentation on the patient record during the administration of sedation and analgesia should include:

- Dose, Route, Time, Effects of Drugs Used
- Type/Amount of IV Fluids/Blood/Blood Products Used
- Physiological Data (i.e.; Recorded every 5 to 15 minutes)
- Level of Consciousness
- Untoward/Significant Reactions and Resolutions

A designated individual, other than the physician performing the procedure should be continuously present to monitor the patient throughout the procedure. This individual may assist with only minor interruptible tasks. This person should also have an understanding of the pharmacology of the agents administered as well as the role of antagonists. The person should also be able to recognize associated complications. This person should preferably be a registered nurse. At least one member of the care team should be capable of establishing a patent airway and providing positive pressure ventilation. There should also be a means for summoning additional assistance whenever sedation and analgesia is administered. Ideally, a person with advanced life-support skills is immediately available.

In addition to the drugs used for sedation, pharmacologic antagonists (flumazenil and naloxone) and emergency equipment should be immediately available. An example of the emergency equipment and drugs to be available during sedation and analgesia would include (this is a guide, which should 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, Breathing Bag-Valve Set (Ambu Bag)
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 needs for sedation and analgesia. Therefore, if a combination of agents is used, they should be 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 cardiorespiratory depression does not recur. 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 cardiorespiratory 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 or re-establishing IV access. In any event, an individual with the skill to establish intravenous access (especially if an emergency arises) should be immediately available.

The Pulse Oximeter and Electrocardiogram

The pulse oximeter is a non-invasive device which measures a pulse and oxygen-hemoglobin saturation ($S_O_2$). 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 mm (red light) and 940 mm (near-infrared light). The pulse oximeter is subject to signal artifacts which 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 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.

<table>
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<tr>
<th>Partial Pressure of Oxygen (PO$_2$ - Blood Gas)</th>
<th>Oxygen Saturation (SO$_2$ - Pulse Oximeter)</th>
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<tbody>
<tr>
<td>60 mmHg</td>
<td>90% Saturation</td>
</tr>
<tr>
<td>50 mmHg</td>
<td>80% Saturation</td>
</tr>
<tr>
<td>40 mmHg</td>
<td>70% Saturation</td>
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When used in conjunction with the other required monitors, the non-invasive pulse oximeter represents a significant advance in patient safety. It provides important information about oxygenation on a beat-to-beat basis and confirms EKG 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.

**Recovery and Discharge after Sedation and Analgesia (Conscious 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 contribute to cardiorespiratory depression. After administration of sedation and analgesia, the patient should be observed until they are no longer at an increased risk for cardiorespiratory depression. Vital signs and respiratory function should be monitored at regular intervals until a patient is ready for discharge. 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 cardiorespiratory depression.

The recovery area should be 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 should be immediately available. The vital signs, level of consciousness and respiratory function should be checked and recorded at regular intervals. The practitioner should be notified immediately if dramatic changes occur or if the parameters are not within the established limits for that patient.

The Aldrete Score has been used for almost 25 years in postanesthesia 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. Since the initial description by Aldrete 27 years ago, there have been some improvements in monitoring which have been incorporated into the modified Aldrete score. For intra-hospital transfers after receiving conscious 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 have satisfactory discharge criteria including dressing, pain, ambulation, fasting-feeding and urine output. For discharge the patient should achieve a Modified Aldrete score of 18 based upon all 10 criteria. 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 Altered Mental Status 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 Stable (pre-procedure range) and within Acceptable Limits
- Observation for 2 hours after the Last Administration of Antagonists (reversal agents)
- Discharged to the Care of A RESPONSIBLE ADULT who will accompany them home (i.e.; drive them) and be able to report any post-procedure complications
- Patient has received WRITTEN Instructions regarding diet, activity, medication and has an emergency phone number.
The Aldrete Score should be used for intra-hospital transfers, the Modified Aldrete Score for patients being Discharged Home after Sedation and Analgesia

We hope this educational module has been useful. Please refer to it as you consider the questions on the following pages.

Bibliography


