CHAPTER 4

PROCEDURAL SEDATION AND ANALGESIA

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PERSPECTIVE

The performance of painful diagnostic and therapeutic procedures is common in emergency care. Many of these are associated with significant anxiety, especially in children.1,2 Procedural sedation and analgesia (PSA) has therefore become a fundamental and required skill for emergency physicians and an integral part of the core training of emergency medicine residents.4-8

PSA improves the quality of patient care and satisfaction through relief of pain and anxiety and by facilitating the timeliness and success of therapeutic or diagnostic procedures.7,8-14 These include fracture or joint reduction, incision and drainage of abscesses, cardioversion, tube thoracostomy, lumbar puncture, complex wound repair, and imaging studies in young or uncooperative patients.

Many of the agents used for PSA have the potential to cause significant respiratory, cardiovascular, or central nervous system (CNS) depression.15-25 The Joint Commission (TJC), the Centers for Medicare and Medicaid Services (CMS), the American College of Emergency Physicians (ACEP), and the American Society of Anesthesiologists (ASA) have produced expert consensus or evidence-based documents concerning its use26-28 (Box 4-1). Although significant controversy continues with respect to credentialing and oversight of PSA outside the operating room, the advent of these guidelines has led to PSA becoming a safe, common, and practical emergency department (ED) procedure.9,29 It has been further improved by the development of shorter-acting, more effective drugs and the use of noninvasive monitoring devices.

With the wide variety of procedures and patient populations, the ability to individualize PSA and maximize the risk-benefit ratio for each unique situation is a necessary skill. This can be best achieved through a detailed understanding of: the preprocedural patient assessment, the protocols delineating the required personnel and their roles, the supplies and equipment required, the specific drugs used (including their routes of administration, dosages, effects, interactions, and complications), consideration for special populations and patient monitoring, recovery, and discharge criteria.

Terminology

Anxiolysis is a state of decreased apprehension concerning a particular situation in which the patient’s level of awareness does not change. Analgesia refers to the relief of pain without the intentional alteration of mental status, such as occurs in sedation. An altered mental state may be a secondary effect of the medications administered for this purpose.

Dissociation is a trancelike cataleptic state induced by an agent such as ketamine and characterized by a profound analgesia and amnesia. Protective reflexes, spontaneous respirations, and cardiopulmonary stability are retained.

Sedation is a controlled reduction of environmental awareness. Procedural sedation and analgesia is a technique of administering a sedative or dissociative agent, usually along with an analgesic, to induce a state that allows the patient to tolerate unpleasant procedures while maintaining adequate spontaneous cardiorespiratory function. It is intended to result in a depressed level of consciousness that allows the patient to maintain oxygenation and airway control independently and continuously. The drugs, doses, and techniques used are not likely to produce a loss of the protective airway reflexes.28

Prior terminology defined three levels of sedation: conscious sedation, deep sedation, and general anesthesia. The term conscious sedation was often misinterpreted, confusing, and imprecise. It was coined in 1985 to describe lightly sedated dental patients. It was then further incorporated into pediatric sedation guidelines to distinguish a level of sedation from which the patient is easily arousable from the more advanced techniques of deep sedation, in which patients are difficult to arouse, and general anesthesia, in which patients are not arousable.30-32 Despite the focused intent of these definitions, practitioners quickly labeled all levels of procedural sedation taking place outside the operating room as “conscious sedation.”

In 2001 TJC adopted the ASA definition of sedation and analgesia that was created to better describe the continuum of sedation and analgesia33 (Fig. 4-1). Although this truly is a continuum, the ASA divided PSA into four distinct subgroups: minimal sedation, moderate sedation, deep sedation, and general anesthesia. A fifth category, dissociative sedation, has since been added34 (Table 4-1). This new nomenclature is more intuitive, clear, and logical.

Minimal sedation (anxiolysis) is a drug-induced state during which patients respond normally to verbal commands. Although cognitive functions and coordination may be impaired, ventilatory and cardiovascular functions are unaffected. Moderate sedation/analgesia (formerly called “conscious sedation”) refers to a drug-induced depression of consciousness during which patients respond purposefully to verbal commands, either alone or accompanied by light tactile stimulation. Reflex withdrawal from the painful stimulus is not considered a purposeful response. No interventions are required to maintain a patent airway, and spontaneous ventilation is adequate. Cardiovascular function is always maintained.
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General anesthesia is a drug-induced loss of consciousness and an increased risk of adverse respiratory and cardiovascular events. If medication administration continues, the patient will ultimately reach a state of general anesthesia with loss of protective airway reflexes and ventilatory drive. The transition from one level of sedation to the next is often difficult to predict and varies from patient to patient.

The progression from minimal sedation to general anesthesia truly is a dynamic continuum that lacks distinct separation between stages. The transition from one level of sedation to the next is often difficult to predict and varies from patient to patient. The sedation continuum is not drug-specific, and levels from mild sedation to general anesthesia can be achieved with virtually all of the PSA agents. Because of this, it is recommended that clinicians administering PSA be competent in the skills required to treat patients in at least one level greater than the intended level of sedation.

**Approach to Procedural Sedation and Analgesia for Procedures**

**Patient Assessment**

To date, no outcome-based studies have demonstrated clear benefit from extensive evaluation beyond vital signs, mental status, and airway and cardiopulmonary assessment before PSA. Despite this, consensus guidelines suggest that an increased risk of adverse events may exist in select subsets of patients. These include patients at the extremes of age, patients with difficult facial or neck anatomy or any other reason for potential intubation or bag-valve-mask ventilation difficulty, and patients with underlying significant disease states. A patient’s general physical status is conventionally categorized according to the ASA’s classification system (Table 4-2). Most practice guidelines require that a history and focused physical examination be performed and documented before PSA. There is no literature to support the need for routine diagnostic testing other than diagnostic testing driven by the patient’s current status, including comorbidities.

The patient’s age; current illness or injury for which the PSA is intended; underlying medical problems (comorbidities); previous experiences or problems with PSA or general anesthesia; drug allergies and current medications; and tobacco, drug, and alcohol use are reviewed and recorded. A directed physical examination focuses on the vital signs, the heart and lungs, and evaluation of the airway for potential difficulty providing bag-valve-mask ventilation or intubation.

A discussion including the risks, benefits, and potential side effects of PSA should take place with patients or their families before the procedure. Written consent is obtained, unless this is not possible. Patient selection is important to the safety of the sedation. Not every patient is an appropriate candidate for PSA in the ED. Depending on the clinical circumstances, a patient with an anticipated difficult airway or an ASA classification of III or IV may require consultation with an anesthesiologist. It may be advisable in some cases to have the anesthesiologist perform the

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**American College of Emergency Physicians**

**Policy Statement on Sedation in the Emergency Department (January 2011)**

The American College of Emergency Physicians recommends the following:

- Emergency physicians who have received the appropriate training and skills necessary to safely provide procedural sedation should be eligible for credentialing in all levels of procedural sedation.
- The decision to provide sedation and the selection of the specific pharmacologic agents should be individualized for each patient by the emergency physician and should not be otherwise restricted.
- Emergency physicians and staff are expected to be familiar with the pharmaceutical agents they use and be prepared to manage their potential complications.
- To minimize complications, the appropriate drugs and dosages must be chosen and administered in an appropriately monitored setting, and a patient evaluation should be performed before, during, and after their use.
- Institutional and departmental guidelines related to the sedation of patients should include credentialing and verification of competency of providers, selection and preparation of patients, informed consent, equipment and monitoring requirements, staff training and competency verification, criteria for discharge, and continuous quality improvement.

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**Dissociative sedation** is a trancelike cataleptic state induced by the dissociative agent ketamine and characterized by profound analgesia and amnesia, while protective airway reflexes, spontaneous respirations, and cardiopulmonary stability are maintained.

**Deep sedation/analgesia** describes a drug-induced depression of consciousness during which patients cannot be easily aroused but respond purposefully after repeated or painful stimulation. The ability to independently maintain ventilatory function may be impaired. Patients may require assistance in maintaining a patent airway, and spontaneous ventilation may be inadequate. Cardiovascular function is usually maintained.

**General anesthesia** is a drug-induced loss of consciousness during which patients are not arousable even with painful stimulation. The ability to independently maintain ventilatory 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 or drug-induced depression of neuromuscular function. Cardiovascular function may be impaired.

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**Box 4-1**

**Schematic representation of the sedation continuum.** As increasing doses of nondissociative agents are given, patients move along the sedation continuum, experiencing a progressive decline in their level of consciousness and an increased risk of adverse respiratory and cardiovascular events. If medication administration continues, the patient will ultimately reach a state of general anesthesia with loss of protective airway reflexes and ventilatory drive. The transition from one level of sedation to the next is often difficult to predict and varies from patient to patient.
sedation or to undertake the procedure in the operating room under more controlled circumstances.

Preprocedural Fasting

The need for preprocedural fasting in PSA remains controversial. Currently the ASA recommends a period of 2 hours after ingestion of clear liquids, a period of 4 hours after ingestion of breast milk, and a period of 6 hours after ingestion of other liquids (infant formula, nonhuman milk) or solids before PSA, but there are no outcome studies to support these recommendations. These guidelines are based on expert consensus and extrapolated from data describing circumstances in which patients received sedation to the level of general anesthesia followed by the manipulation of the airway during intubation and extubation. PSA in the ED attempts to avoid both of these specific situations.

Many studies fail to support the notion that gastric emptying has any effect on the incidence of complications or outcome with PSA. There have been no published studies demonstrating an increased risk of aspiration after a liquid or solid meal and no studies showing a benefit of fasting before PSA. In one large study of nearly 5000 children and 18,000 adults, no clinically significant differences with airway complications, emesis, or other adverse effects were observed between various groups of patients classified by their preprocedural fasting status. During PSA, the combination of vomiting and the loss of the airway protective reflexes is an extremely rare occurrence. Furthermore, most episodes of vomiting and aspiration occur during airway manipulation, which is also very unlikely to occur during PSA.

Although recent food intake is not a contraindication for administering PSA, risks of pulmonary aspiration and the benefits of providing PSA are weighed in accordance with the needs of each individual patient. Some procedures, such as reduction of a dislocated joint, should not be delayed for consideration of fasting status, whereas others, such as abscess drainage, are not as time-sensitive, and the sedation plan can be adapted accordingly.

Personnel

TJC and most institutional policies suggest that PSA providers should have adequate training to administer the agents effectively and safely, the skills to monitor the patient’s response to the medications given, and the expertise needed to manage all potential complications. This generally implies that PSA in the ED should be supervised by an emergency physician or other appropriately trained and credentialed physician. It is also recommended that a qualified support person (nurse, respiratory therapist) be present for the continuous monitoring of the patient. Such support persons should focus on the patient’s status and not take part in the procedure. They should also be able to recognize and respond to the complications of PSA. They may assist with minor, interruptible tasks; however, they should have no other responsibilities that would interfere with the level of monitoring and documentation appropriate for the planned level of sedation. They should be free to monitor the patient from the start of the procedure through the completion of the recovery phase.

Supplies and Equipment

PSA may result in an allergic reaction, oversedation, respiratory depression, or, rarely, cardiopulmonary arrest. The incidence of these complications depends on patient selection, the drugs used, the rate and dosage of administration, and specific patient sensitivities. Consequently, appropriate equipment to monitor the patient’s condition at all times; to manage airway complications, allergic reactions, and drug overdoses; and to treat respiratory or cardiopulmonary arrest should be readily available. Supportive equipment includes oxygen, suction, patient-monitoring devices, basic and advanced airway management equipment, a monitor/defibrillator, advanced life-support medications, reversal or rescue agents, and vascular access equipment (Box 4-2).

In most situations, the agents used for PSA in adult patients should be administered intravenously (IV). Nearly all adults undergoing PSA in the ED should therefore have an intravenous line placed before the procedure. This need in children is less clear and depends on the presence of comorbid conditions and the choice and route of drug to be administered. If the procedure is likely to be lengthy, or if multiple doses of drugs will be needed, an intravenous line should be considered.
The requirement for supplemental oxygen, and its benefits during PSA, have not been well studied and remain somewhat controversial. 56-62 Supplemental oxygen may prevent hypoxemia in many patients; however, significant respiratory depression in these patients may not be detected because of their normal oxygen saturation. This may delay the recognition of respiratory compromise and hypercarbia when capnography is not used. On the other hand, transient hypercarbia is not harmful, and maintenance of adequate oxygen saturation is much more important. The use of capnography eliminates this issue, because ventilatory status is displayed continuously. We recommend the use of supplemental oxygen in administering PSA to a patient in the ED.

Monitoring

The most important aspect of monitoring during PSA is the visual observation and assessment of the patient. The patient’s ability to follow commands in response to varied levels of stimulation is useful in quantifying the level of consciousness. Furthermore, the patient’s ventilatory rate may be readily assessed by direct observation, although depth of respiration (tidal volume) is much harder to estimate clinically. Other components of monitoring, which should be documented, include respiratory rate, heart rate, blood pressure, oxygen saturation, and perhaps cardiac rhythm and capnometry. 63-67 Pulse oximetry is a reliable and important monitoring modality, used in conjunction with close and continuous observation of the patient and the response to medications and procedures.

There is no evidence that cardiac monitoring during PSA is of any benefit, but it certainly is not harmful, is readily available, and is inexpensive to use. 68-70 We recommend continuous electrocardiographic monitoring in older patients and in patients with a history of cardiovascular disease, hypertension, or dysrhythmia. In young healthy patients without underlying significant disease, this may be safely replaced by continuous pulse oximetry, which also displays the heart rate, but, in most circumstances, monitors capable of showing heart rate, blood pressure, and pulse oximetry will also easily facilitate cardiac rhythm monitoring.

Capnometry or capnography measures end-tidal carbon dioxide (CO₂) partial pressure and has been shown to detect cases of inadequate ventilation earlier than clinical assessment or detection of hypoxemia by oximetry. 60,62,71-80 Several studies have demonstrated this, but none have shown an effect on clinical outcome to date. In July 2011, the ASA updated its procedural sedation standards to include capnography during moderate or deep sedation to evaluate the adequacy of ventilation in addition to continual observation of qualitative clinical signs. 31,82 Capnography should be used when deep sedation is planned, as respiratory depression is common in patients undergoing deep sedation. It is optional when only light sedation is planned, but even in such cases, it will help the observer recognize unintended oversedation with respiratory depression.

The Bispectral Index (BIS) is monitored via a noninvasive device attached to the patient’s forehead and derives a depth of sedation level via frontal lobe electroencephalographic measurements. It has been used in the operating room as an objective measure of sedation depth. 83-85 Studies have shown that it may be beneficial in preventing oversedation in PSA and reducing the time to discharge. 86 These investigations have also suggested that its use may better guide the depth of sedation endpoint than traditional sedation scales have, and it may have further benefit for PSA in children, as they frequently require deeper levels of sedation for prevention of movement. 87-90 Early ED studies for its use in PSA to discriminate between mild-to-moderate and moderate-to-deep levels of sedation have not been reliable, nor has it been shown to be predictive of patients sedated to the point of general anesthesia from those with lesser degrees of sedation. BIS monitoring may have a beneficial role for emergency medicine use and PSA in the future but requires more investigation before its possible uses and benefits can be completely defined.

If it is necessary to perform sedation outside the ED for a diagnostic procedure, every attempt should be made to provide the same level of monitoring during the transport and the procedure as would be used within the department.

The highest risk of serious adverse events generally occurs within 5 to 20 minutes of receiving the last dose of intravenous medication and at the completion of procedures, when the patient remains sedated but is no longer receiving the painful stimulus. Similarly, patients undergoing prolonged procedures in which deeper sedation is desired to reduce motion (e.g., magnetic resonance imaging [MRI]) are also at an increased risk. 96-19,23,36,91 Patients should continue to be monitored closely at these times, and this should continue until clinical recovery has occurred.

Recovery

Monitoring as part of the PSA routine should continue until patients are spontaneously awake and able to function independently, even though they may not be completely back to baseline function or ready for discharge. Drowsy patients should not be left unattended.

Discharge Criteria and Instructions

Before discharge, baseline cognitive and motor function should be achieved. The patient should be able to follow commands, speak clearly, and ambulate or sit unassisted (infants). Vital signs and respiratory status should be back to baseline and within normal limits. Residual pain should be addressed. Nausea should be minimal, and vomiting should be resolved. It is preferable that all patients, including adults, be sent home with a responsible adult, but if this is not possible, the patient remains in the ED until normal baseline has been achieved. 4,92-96

Patients should be advised not to drive or participate in other dangerous activities for 12 to 24 hours. Despite the short clinical duration of most of the agents used, many people may exhibit subtle signs of cognitive deficits and mild drowsiness. 38,97 It is therefore preferable that they remain in the company of a responsible adult at home for 4 to 8 hours. For children, light play at home should be the extent of activities, with no bicycle riding, swimming, or other complex motor activity until the next day. An antinauseant and progressive diet is helpful if nausea or vomiting is experienced. Standard discharge instructions should also be provided for the presenting complaint, and all patients should be...
instructed to immediately return if any confusion or respiratory symptoms arise.

**Pharmacology**

In selecting agents, consideration is given to the effects desired, the risks and benefits, and the logistics of administration for each situation. The ideal agent would provide analgesia, amnestic effects, and sedation. However, ketamine has been shown to provide consistent and predictable results when given intramuscularly (IM). Nitrous oxide has predictable behavior when used as a sole inhalational PSA agent in children but is also frequently used as an analgesic adjunct to a sedating agent. In pediatric patients, the benefits of intravenous drug administration may be outweighed by the difficulty and distress to the patient in obtaining intravenous access. In this situation, drugs given by the alternative routes may be preferred.

Drugs should be administered by titrated slow intravenous bolus to minimize hypotension or respiratory depression in many situations. It is important to allow adequate time between doses to achieve and assess peak effect before an additional dose is given. Lower initial doses should be chosen in sensitive patients or when drugs from multiple classes are being administered. One exception is ketamine. Unlike the other agents described, it possesses a threshold response rather than an additive dose-response continuum. Smaller doses of ketamine cause analgesia and disorientation. Dissociation occurs when a dosage threshold of 1 to 1.5 mg/kg IV in adult patients or 2 to 2.5 mg/kg in younger pediatric patients is reached. Higher doses do not enhance or deepen the sedation.

**Opioids**

Parenteral opioids are commonly used as analgesics before painful procedures are performed. For PSA, an opioid is rarely optimal as a single agent, and most clinicians combine an opioid with a sedative-amnestic agent to balance sedation-amnesia and analgesia with the least likelihood of respiratory depression. The most commonly used opioids in the ED for PSA are fentanyl and morphine. These are often combined with benzodiazepines such as midazolam for moderate sedation and used in smaller doses to provide analgesia during deep sedation with etomidate or propofol. Meperidine historically was used for PSA but is no longer recommended because seizures are commonly associated with the accumulation of its long-lasting metabolite normeperidine.

**Fentanyl**

Fentanyl has many advantages as an analgesic agent for PSA, given its rapid onset of action, short duration of activity, lack of

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**Table 4-3 Procedural Sedation and Analgesia Agents—Recommended Adult Starting Doses**

<table>
<thead>
<tr>
<th>AGENT</th>
<th>CLASS</th>
<th>MAIN EFFECT</th>
<th>ROUTE</th>
<th>USUAL STARTING DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl</td>
<td>Opioid</td>
<td>Analgesia</td>
<td>Intravenous</td>
<td>1 µg/kg</td>
</tr>
<tr>
<td>Morphine</td>
<td>Opioid</td>
<td>Analgesia</td>
<td>Intravenous</td>
<td>0.1 mg/kg</td>
</tr>
<tr>
<td>Midazolam</td>
<td>Benzodiazepine</td>
<td></td>
<td>Sedation Amnesia</td>
<td>Intravenous</td>
</tr>
<tr>
<td>Methohexital</td>
<td>Barbiturate</td>
<td>Sedation Amnesia</td>
<td>Intravenous</td>
<td>1 mg/kg</td>
</tr>
<tr>
<td>Pentobarbital</td>
<td>Barbiturate</td>
<td>Sedation Amnesia</td>
<td>Intravenous</td>
<td>2 mg/kg</td>
</tr>
<tr>
<td>Ketamine</td>
<td>Phencyclidine derivative</td>
<td>Dissociation Analgesia Sedation Amnesia</td>
<td>Intravenous</td>
<td>1-2 mg/kg</td>
</tr>
<tr>
<td>Etomidate</td>
<td>Imidazole derivative</td>
<td>Sedation Amnesia</td>
<td>Intravenous</td>
<td>0.1 mg/kg</td>
</tr>
<tr>
<td>Propofol</td>
<td>Alkylphenol derivative</td>
<td>Sedation Amnesia Antiemetic</td>
<td>Intravenous</td>
<td>0.5 mg/kg</td>
</tr>
<tr>
<td>Nitrous oxide</td>
<td>Anesthetic gas</td>
<td>Analgesia</td>
<td>Inhaled</td>
<td>30-70%</td>
</tr>
</tbody>
</table>
### Table 4-4  Procedural Sedation and Analgesia Agents—Recommended Pediatric Starting Doses

<table>
<thead>
<tr>
<th>AGENT</th>
<th>CLASS</th>
<th>EFFECT</th>
<th>ROUTE</th>
<th>USUAL STARTING DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl</td>
<td>Opioid</td>
<td>Analgesia</td>
<td>Intravenous</td>
<td>1 µg/kg</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Transmucosal</td>
<td>10 µg/kg</td>
</tr>
<tr>
<td>Morphine</td>
<td>Opioid</td>
<td>Analgesia</td>
<td>Intravenous</td>
<td>0.1 mg/kg</td>
</tr>
<tr>
<td>Midazolam</td>
<td>Benzodiazepine</td>
<td>Sedation</td>
<td>Intravenous</td>
<td>0.1 mg/kg</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Oral</td>
<td>0.5 mg/kg</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Rectal</td>
<td>0.5 mg/kg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Amnesia</td>
<td>Transmucosal</td>
<td>0.2 mg/kg</td>
</tr>
<tr>
<td>Methohexital</td>
<td>Barbiturate</td>
<td>Sedation</td>
<td>Intravenous</td>
<td>1 mg/kg</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Rectal</td>
<td>25 mg/kg</td>
</tr>
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<td>Pentobarbital</td>
<td>Barbiturate</td>
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<td>Intravenous</td>
<td>2 mg/kg</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Intramuscular</td>
<td>4 mg/kg</td>
</tr>
<tr>
<td>Ketamine</td>
<td>Phencyclidine derivative</td>
<td>Dissociation</td>
<td>Intravenous</td>
<td>1-2 mg/kg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Analgesia</td>
<td>Intramuscular</td>
<td>4-5 mg/kg</td>
</tr>
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<td></td>
<td></td>
<td>Sedation</td>
<td>Oral</td>
<td>10 mg/kg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Amnesia</td>
<td>Rectal</td>
<td>10 mg/kg</td>
</tr>
<tr>
<td>Etomidate</td>
<td>Imidazole derivative</td>
<td>Sedation</td>
<td>Intravenous</td>
<td>0.1 mg/kg</td>
</tr>
<tr>
<td>Propofol</td>
<td>Alkylphenol derivative</td>
<td>Sedation</td>
<td>Intravenous</td>
<td>0.5 mg/kg</td>
</tr>
<tr>
<td>Nitrous oxide</td>
<td>Anesthetic gas</td>
<td>Analgesia</td>
<td>Inhaled</td>
<td>30-70%</td>
</tr>
</tbody>
</table>

Table 4-5  Procedural Sedation and Analgesia Agents—Benefits and Adverse Effects

<table>
<thead>
<tr>
<th>AGENT</th>
<th>ROUTE</th>
<th>ONSET (min)</th>
<th>DURATION (min)</th>
<th>ADVANTAGES</th>
<th>ADVERSE EFFECTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl</td>
<td>Intravenous</td>
<td>1-2</td>
<td>30-40</td>
<td>Rapid onset</td>
<td>Respiratory depression</td>
</tr>
<tr>
<td></td>
<td>Transmucosal</td>
<td>10-30</td>
<td>60-120</td>
<td>Short duration</td>
<td>Rigid chest syndrome</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>†Histamine release</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Minimal CV effects</td>
<td></td>
</tr>
<tr>
<td>Morphine</td>
<td>Intravenous</td>
<td>10</td>
<td>240-360</td>
<td>Longer lasting</td>
<td>Hypotension</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Respiratory depression</td>
</tr>
<tr>
<td>Midazolam</td>
<td>Intramuscular</td>
<td>1-2</td>
<td>30-60</td>
<td>Rapid onset</td>
<td>Respiratory depression</td>
</tr>
<tr>
<td></td>
<td>Oral</td>
<td>10-15</td>
<td>60-120</td>
<td>Short duration</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rectal</td>
<td>10-30</td>
<td>60-90</td>
<td>Easy to titrate</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Intranasal</td>
<td>10-15</td>
<td>45-60</td>
<td>Multiple routes</td>
<td></td>
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<tr>
<td>Methohexital</td>
<td>Intravenous</td>
<td>&lt;1</td>
<td>4-7</td>
<td>Rapid onset</td>
<td>Respiratory depression</td>
</tr>
<tr>
<td></td>
<td>Rectal</td>
<td>5-10</td>
<td>20-60</td>
<td>Short duration</td>
<td>Apnea</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Airways reflexes maintained</td>
<td>Hypotension</td>
</tr>
<tr>
<td>Pentobarbital</td>
<td>Intravenous</td>
<td>1-2</td>
<td>30-60</td>
<td>Rapid onset</td>
<td>Respiratory depression</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Airways reflexes maintained</td>
<td>Apnea</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Hypotension</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Prolonged recovery</td>
</tr>
<tr>
<td>Ketamine</td>
<td>Intravenous</td>
<td>1</td>
<td>15</td>
<td>Airway reflexes maintained</td>
<td>Emergence phenomena</td>
</tr>
<tr>
<td></td>
<td>Intramuscular</td>
<td>5</td>
<td>15-30</td>
<td></td>
<td>Emesis</td>
</tr>
<tr>
<td></td>
<td>Oral</td>
<td>30-45</td>
<td>120-240</td>
<td>No respiratory depression</td>
<td>Laryngospasm</td>
</tr>
<tr>
<td></td>
<td>Rectal</td>
<td>5-10</td>
<td>15-30</td>
<td>Predictable</td>
<td>†ICP and †IOP</td>
</tr>
<tr>
<td>Etomidate</td>
<td>Intravenous</td>
<td>&lt;1</td>
<td>5-10</td>
<td>Rapid onset</td>
<td>Respiratory depression</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Short duration</td>
<td>Myoclonus</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Minimal CV effects</td>
<td>Adrenal suppression</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Cerebral protective</td>
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<tr>
<td>Propofol</td>
<td>Intravenous</td>
<td>&lt;1</td>
<td>8-10</td>
<td>Rapid onset</td>
<td>Respiratory depression</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Short duration</td>
<td>Hypotension</td>
</tr>
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<td></td>
<td></td>
<td>Antiemetic</td>
<td>Injection pain</td>
</tr>
<tr>
<td>Nitrous oxide</td>
<td>Inhaled</td>
<td>1-2</td>
<td>3-5</td>
<td>Rapid onset</td>
<td>Expansion of gas-filled structures</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Short duration</td>
<td>Emesis</td>
</tr>
</tbody>
</table>

CV, cardiovascular; ICP, intracranial pressure; IOP, intraocular pressure.
Because fentanyl readily creates a reservoir in the adipose tissue, these properties permit the administration of multiple small doses that can be easily titrated to the desired clinical effect. Because fentanyl readily creates a reservoir in the adipose tissue, accumulated large doses may result in a progressively increasing duration of effect. This does not generally occur in doses less than 10 µg/kg.

For deep sedation, a single dose of 1 to 2 µg/kg of fentanyl is often given before the sedating agent. After adequate pain relief has been achieved, a smaller dose of a sedative agent may then be added and titrated to effect. For moderate sedation, fentanyl can be titrated, along with a sedative agent, often midazolam, depending on whether the clinician feels that more sedative effect (midazolam) or analgesic effect (fentanyl) is required. Dosage should begin at 1 µg/kg and be slowly titrated upward every 1 to 2 minutes until the desired level of analgesia has been achieved. Sufficient analgesia for painful procedures under moderate sedation usually is accomplished with doses of 2 to 3 µg/kg and under deep sedation with 1 to 2 µg/kg. Lower doses should be used in elderly patients or when other CNS depressants have been previously administered (e.g., ethanol).

Respiratory depression is more likely at higher doses, when the drug is given rapidly, or when it is combined with other CNS depressants such as benzodiazepines or alcohol. Other side effects may include vomiting and pruritus, although these are less common than with other opioids. Hypotension and bradycardia are rare but may occur with high doses. Chest wall rigidity and glottic spasm, which may make ventilation difficult, are unique complications seen with high doses (anesthetic) of fentanyl given rapidly (generally more than 7 µg/kg). Many of these adverse effects may be readily reversed by naloxone. The exception to this is chest wall rigidity, which may not reliably be antagonized and may necessitate neuromuscular blockade and intubation to enable adequate ventilation. This complication is extremely rarely reported with the doses of fentanyl used for PSA.

In children, oral or transmucosal fentanyl has been used widely as a premedication for anesthesia and intravenous placement. It has also been used for PSA when intravenous access is not feasible. This is generally in the form of a fentanyl-impregnated, sweetened matrix in lozenge form on a holder—the “fentanyl lollipop.” Transmucosal delivery allows rapid onset of action by avoiding first-pass metabolism in the liver. It has been shown to decrease activity and relieve pain in 10 to 30 minutes, resulting in scores similar to those after comparable intravenous doses of fentanyl. Despite this fairly rapid onset, transmucosal delivery does not allow for easy titration. The general dose is 10 to 15 µg/kg. Larger doses have been shown to cause more nausea and vomiting without improving analgesia or activity scores. The combination of transmucosal fentanyl and transmucosal midazolam has not been shown to have additional benefit over either agent used singularly for laceration repair in the ED and has been shown to increase adverse events. Its use before other agents such as propofol has not been studied well. The use of transmucosal fentanyl for PSA has largely been limited by unacceptable levels of nausea and vomiting, which approach 20 to 40% of patients.

Morphine

Morphine is poorly lipid soluble and penetrates the blood-brain barrier more slowly after small bolus injections. A period of 10 to 30 minutes is required before its peak effects are seen, although when used for PSA, morphine performs in similar fashion to fentanyl, with comparable recovery times. A general starting dosage of 0.1 mg/kg is commonly used and then titrated to desired effect as with fentanyl. Morphine has much more histamine release and therefore is more likely to produce hypotension, especially in preload dependent patients. It has similar potential to other opioids for producing respiratory depression, especially when used with other CNS depressants such as benzodiazepines. Morphine undergoes hepatic metabolism to an active metabolite, followed by renal excretion. Insufficiency of either organ system may lead to increased serum half-life.

Benzodiazepines

Benzodiazepines are potent amnestic, hypnotic, and anxiolytic medications. They also have anticonvulsant and purported muscle relaxant properties but do not have analgesic effects. Because of this, they are commonly coadministered with an analgesic agent such as fentanyl or morphine. They may be given IV, IM, orally (PO), intranasally (IN), or per rectum (PR) but are virtually always used IV for PSA in adults. Midazolam is the most commonly used agent because of its favorable pharmacokinetics.

Midazolam

Midazolam has many advantages for PSA, given its rapid onset of action and short duration of activity compared with other benzodiazepines. Its amnestic properties also appear to be superior to many of the others. The starting intravenous dose is 0.05 mg/kg. Children may need slightly higher doses. Onset of sedation is generally within 1 to 2 minutes, and the duration of action is 30 to 60 minutes. Alternatives to the intravenous route are often used in children, particularly when sedation alone, without analgesia, is desired as for performance of a radiologic study. With intramuscular administration the same doses may be used, but the onset of action is delayed and the duration of effect is increased. Oral doses are often used in children, with a recommended starting dose of 0.5 mg/kg. Sedation is generally achieved within 30 minutes. Rectal administration may also be useful with doses of 0.5 mg/kg. The response when the drug is given by this route may be less predictable, and the rectal route is generally not accepted by older children. Intranasal administration may be useful but is irritating and often difficult in older children as well. The starting dose for this route is 0.2 mg/kg and results in sedation in 10 to 15 minutes. Of note, 1% of children younger than 5 years may experience a paradoxical reaction and become excited and agitated when given midazolam. If necessary, the agitated state is reversible by flumazenil. Midazolam has been shown to be an extremely safe and effective agent for PSA, both alone and when used in combination with fentanyl.

Side effects include dose-dependent hypoventilation and hypoxemia. Apnea and hypotension are uncommon but occur more often at high doses or when other CNS depressants such as opioids are used. Headache, nausea, emesis, coughing, and hiccups have been shown to occur, although rarely. Lower doses should be used when other agents such as analgesics are given concomitantly and in the elderly. Prolonged effects may be seen in elderly patients or those with liver dysfunction owing to decreased hepatic or first-pass metabolism. Midazolam is highly lipophilic, and its effects may be greatly amplified in obese patients, resulting in an increased plasma half-life of up to 8 hours with high or repetitive doses. Chronic alcohol users who do not have liver dysfunction may require relatively high doses of midazolam to achieve the same clinical effects as a result of cross-tolerance.
Barbiturates

Barbiturates are also potent hypnotics, with amnestic and anticonvulsant effects. They do not have analgesic properties. Before the widespread use of midazolam and the advent of propofol for deep sedation, barbiturates were commonly used for brief painless procedures, but they are rarely used now. They are not commonly combined with other agents owing to their narrower therapeutic window. We do not recommend the use of barbiturates for procedural sedation in adults, but these agents are still used in children, particularly for radiology procedures.

Methohexital

Methohexital is a highly lipophilic ultra-short-acting barbiturate with a rapid onset of amnesia and deep sedation in 30 to 60 seconds. It does not provide analgesia, and an opioid, such as fentanyl, is required for painful procedures. The concomitant use of fentanyl or another opioid increases the risk of apnea. Intravenous doses of 1 mg/kg produce unconsciousness for approximately 5 minutes. Methohexital may also be administered PR in children at a dose of 25 mg/kg but has a more variable effect and longer onset and duration of action.

Depressed respiratory drive and apnea are more common than with other agents but are generally transient and mild. Most patients respond to supplemental oxygen and repositioning of the airway. Its use in the ED appears to be safe and effective, particularly for brief orthopedic joint reductions, cardioversions, and radiologic imaging procedures. Only a small percentage of patients require brief periods of assisted ventilation. In several studies, no ED patients required intubation or change in disposition after having received methohexital for PSA.126-129 Methohexital does have the potential to cause significant hypotension as well and should be used with caution in patients with hemodynamic instability or occult blood loss. It also may cause activation of the respiratory reflexes, inducing coughing, hiccups, and, rarely, laryngospasm. In contrast to the other barbiturates, methohexital may worsen or precipitate seizures, and it is prudent to avoid it in patients with a known seizure disorder.128,130,131 Propofol has largely supplanted methohexital for PSA because it has more reliable, consistent effects, is easily titrated, and can be administered as an infusion for longer procedures.

Pentobarbital

Pentobarbital is also a barbiturate sedative agent, best used IV for nonpainful diagnostic studies in children. Its onset of action is generally within 1 to 2 minutes, with a duration of 30 minutes. It is usual to start with an initial dose of 2 mg/kg and titrate to effect, with subsequent doses of 1 to 2 mg/kg every 30 seconds as needed. The predominant complications with pentobarbital are respiratory depression, hypotension, and prolonged recovery.

Ketamine

Ketamine is a well-studied, safe, and predictable agent for use in the pediatric population for PSA.124,126,132,135 It continues to gain popularity for use in adults as well.126,129-131 It is a derivative of the street drug phencyclidine and is classified as a dissociative agent. It causes disruption between the thalamocortical and limbic systems, preventing the higher centers from perceiving visual, auditory, or painful stimuli. Because of this, its use leads to profound analgesia, amnesia, and catalepsy. It does not produce unconsciousness, but rather a trancelike state. Patients often experience nystagmus, roving eye movements, and random movements of the extremities unrelated to painful stimuli. Parents observing procedures in which ketamine is used may be disturbed at seeing this and should be forewarned.

Ketamine has several advantages over other PSA agents.124,128,132-135 The most notable are its profound analgesic effect and the lack of significant respiratory depression. The protective airway reflexes, such as coughing, swallowing, and muscular tone of the tongue and pharynx, are well maintained or slightly enhanced. This is particularly useful in the ED setting where preprocedural fasting might not be assured. Its use further leads to blockade of catecholamine reuptake, and blood pressure is generally well supported. It also induces bronchial smooth muscle relaxation and is well tolerated in patients with reactive airway disease. It has a fast onset and offset and is predictable when given by the intravenous or intramuscular route. After administration, it is rapidly distributed and taken up by the cerebral tissues. The effects are maintained until the drug redistributes into the peripheral tissues and is metabolized by the liver. Because of this mechanism, repeat doses are well tolerated in longer procedures with predictable results but may lead to longer recovery times and increased incidence of emesis.

Ketamine may be given by multiple routes but is administered almost exclusively by the intravenous route in adults. After an intravenous dose of 1 to 2 mg/kg, a dissociative state results in approximately 1 minute, with duration of action of approximately 15 minutes. Complete recovery generally requires 1 to 2 hours. Similar cataleptic results may be seen with an intramuscular administration of 4 to 5 mg/kg in approximately 5 minutes, with effects lasting 15 to 30 minutes. For pediatric sedation, ketamine is generally administered by the intravenous or intramuscular route but may also be given PO (10 mg/kg), PR (10 mg/kg), or IN (6 mg/kg). These other routes are infrequently used because of variable onset of action, slow offset, and less predictable results.

The most common side effect seen with ketamine is the emergence phenomenon.19,136-140 This occurs in approximately 15% of patients and is mild in almost all. They may wake up with unpleasant, vivid dreams or hallucinations or report nighttime awakenings as a result of unpleasant dreams for several days after the administration of ketamine. Less than 1 to 2% of patients have significant emergence agitation. This is more commonly seen in female patients, adolescents or adults, and in those with underlying psychiatric disorders. Its rare occurrence, especially in children, should not limit ketamine’s use when indicated. Some studies have suggested that proprocedural or concurrent administration of midazolam may mitigate this reaction, but others have disputed the utility of this strategy. The most recent clinical practice guideline update does not recommend this practice in children.53,106,141-144 We do not recommend the routine concomitant use of a benzodiazepine when administering ketamine sedation, unless it is judged to be of benefit for preprocedural anxiety. Benzodiazepines are useful for treating emergence phenomena, however, if such phenomena occur during recovery. Other side effects seen with ketamine use are transient apnea, laryngospasm, and emesis.135-137 These are also rare but more common with rapid intravenous administration or with larger doses. Doses given slowly, at a rate of 0.5 mg/kg/min, may limit much of this. Ketamine also stimulates tracheobronchial and salivary secretions. In young children and in any patient undergoing airway examination (e.g., fiberoptic laryngoscopy), pretreatment with glycopyrrolate, 0.01 mg/kg given 10 minutes before the ketamine, may be beneficial. Because airway reflexes are maintained, this generally is not a concern in other patients. Propylactic pretreatment with anticholinergics is unnecessary, and we no longer recommend this practice.53,132-136 Postrecovery nausea and vomiting are also frequently seen but generally short lived and respond well to typical antiemetics such as ondansetron.149

Significant laryngospasm has been seen in infants younger than 3 months and in children with upper respiratory tract infections.
It is recommended that ketamine be avoided in these patients. Because of catecholamine-mediated hypertension and tachycardia, ketamine should also be avoided in those with significant cardiovascular or coronary artery disease. Ketamine also increases intraocular pressure and should be avoided in those with open globe injuries. Ketamine is contraindicated in patients with psychosis (even when well controlled).

**Etomidate**

Etomidate is a short-acting sedative-hypnotic agent that is structurally unrelated to the other PSA agents and has no analgesic properties. Its use leads to the very rapid onset of profound sedation and hypnosis by enhancing neurotransmission at γ-aminobutyric acid (GABA) receptors. Etomidate has been used for deep sedation because of its rapid onset, short duration of action, and, most important, minimal effects on respiratory and cardiovascular function.157-165

After intravenous administration, sedation occurs in approximately 1 minute, and patients recover in 5 to 10 minutes. Etomidate induces deep sedation that borders on general anesthesia with higher doses and may be more difficult to titrate than the other sedative hypnotic agents. It is generally administered IV, with an initial dose of 0.1 mg/kg given slowly over 1 to 2 minutes. Additional doses of 0.05 to 0.1 mg/kg may be administered every 2 to 3 minutes until the desired level of sedation has been achieved. Smaller initial doses should be considered when etomidate is combined with analgesics agents or in the elderly. Because it has little effect on the cardiovascular system and is cerebral protective, it is an excellent choice for patients who have the potential for hemodynamic instability or increased intracranial pressure.

Adverse effects that may limit its usefulness include apnea, respiratory depression, myoclonus, nausea, vomiting, and adrenal suppression.163,164,166-170 These side effects are more common with rapid intravenous administration, when higher doses are used, and in older patients. Although respiratory depression is rare and generally transient, few patients may require brief periods of assisted ventilation. Myoclonus is also typically described as mild and brief but at times may interfere with the procedure. Vomiting is unlikely with doses administered in the ED. Etomidate suppresses adrenal function by inhibiting 11β-hydroxylase activity. This is generally not clinically relevant when a single sedating dose is used (see Chapter 1).171-178

**Propofol**

Propofol is another ultra-short-acting sedative-hypnotic agent that is structurally unrelated to the other PSA drugs and has no analgesic properties. It has an extremely rapid onset, a short duration of action, and predictable efficacy for inducing deep sedation.191-192 Sedation quickly clears completely, permitting a predictable and rapid onset in 1 to 2 minutes and rapid elimination in 3 to 5 minutes.

Propofol also possesses potent antientmetic properties and decreases intracranial pressure. Because of its properties, propofol is a highly desirable and widely used agent for deep sedation in the ED. It does not provide analgesia, however, and should be preceded by an opioid for painful procedures. As with all sedative agents, the addition of an opioid may increase the risk of deeper than anticipated sedation, respiratory depression, apnea, and hypotension, and smaller starting doses are recommended.

Propofol is administered with an initial intravenous bolus dose of 0.5 to 1 mg/kg that is then titrated every 1 to 3 minutes by 0.25– to 0.5-mg/kg aliquots to the desired sedation level. Children may require slightly higher doses than adults. The onset of sedation occurs in less than 1 minute, and patient recovery is in 10 minutes. For procedures lasting longer than this, additional boluses of 0.5 mg/kg may be administered, or a continuous infusion of 3 to 6 mg/kg/hr may be titrated to the desired level of sedation. Smaller doses should be used when sedating elderly patients or when administering propofol in patients pretreated with analgesics.

Adverse effects include dose-dependent respiratory depression, apnea, hypotension, and pain on injection. Other agents, such as opioids, may intensify these effects. In most cases apnea is transient, and patients will not experience significant falls in oxyhemoglobin levels before recovering their respiratory function. This underscores the values of supplemental oxygen administration during sedation. If the oxygen saturation falls into the low 90s, the patient may require a brief period of assisted ventilation. Propofol commonly results in a transient drop in systolic and diastolic blood pressure, which rarely necessitates fluid administration and is well tolerated by healthy patients. The hypotensive effect is exaggerated in the elderly and in patients with hypovolemia, and the initial dose of propofol should be reduced to 0.25 to 0.5 mg/kg in such patients. Pain associated with propofol injection occurs in the majority of patients and can be reduced with small infusions of intravenous lidocaine under tourniquet before its administration. Despite these concerns, propofol has been shown to be reliable and safe when used with proper monitoring in the ED setting. In a series of more than 25,000 pediatric patients in whom propofol was administered by emergency physicians, serious adverse effects were rare and there were no adverse outcomes.180

**Ketamine Plus Propofol (“Ketofol”)**

Ketamine is commonly combined with propofol for PSA, especially in children. The two completely different agents are felt to have synergistic effects that balance each other’s deficits while decreasing the overall dose of propofol. Ketamine provides the analgesic effects that propofol lacks, and the respiratory depression and hypotension caused by propofol are balanced by the cardiorespiratory stimulating effects of ketamine. Furthermore, vomiting and recovery hallucinations from ketamine are mitigated by the antientmetic and hypnotic effects of propofol.106,141,142,144,193-197

In several recent studies, ketofol was not shown to be clinically superior to either agent used alone with regard to respiratory depression or airway complications.106,141,142,144 There was statistically significant benefit in provider satisfaction, sedation quality, and decreased emesis and clinically insignificant improvement in recovery time. Although the use of this combination is extremely popular, it cannot be currently recommended as superior to propofol, propofol plus fentanyl, or ketamine with or without ondansetron.

**Nitrous Oxide**

Nitrous oxide is a gas that, when used in combination with oxygen, provides excellent analgesia to supplement procedural sedation. It defuses rapidly across the alveoli in the lungs, providing a predictable and rapid onset in 1 to 2 minutes and rapid elimination in 3 to 5 minutes.

Nitrous oxide is administered as a 30 to 70% mixture with oxygen by a demand-valve mask or mouthpiece held by the patient. It is administered with at least 30% oxygen to avoid hypoxemia. A 30% concentration may be less than effective for PSA, especially in children, whereas a 70% mix may result in the loss of protective airway reflexes.

The need for a scavenger device and proper ventilation exhaust has limited the use of nitrous oxide in the ED. Because nitrous oxide rapidly defuses into gas-filled pockets, it can potentially worsen conditions such as pneumothoraces, small-bowel obstructions, decompression sickness, chronic obstructive pulmonary disease, and middle ear effusions. High concentrations may lead
to nausea and vomiting, respiratory depression, and general anesthesia.

**Reversal and Rescue Agents**

Careful titration of PSA drugs to the desired level of sedation is the goal. At times, unanticipated deeper levels of sedation may be reached, and respiratory depression or apnea may be experienced. Airway repositioning, supplemental oxygen, and bag-valve-mask ventilation may be required. If these periods are prolonged, partial or complete reversal of agents such as opioids or benzodiazepines may be necessary. Elective reversal of PSA after the completion of the procedure is not recommended.108,199

**Naloxone**

Naloxone is a competitive antagonist of opioids and has been effectively used for the reversal of opioid-induced respiratory depression during PSA. It has a rapid onset of action and a mean plasma half-life of approximately 45 minutes, although its clinical effects last only 15 to 30 minutes. Resedation is generally not a problem for patients who have been given fentanyl or morphine in doses recommended for PSA. Nevertheless, these patients should be observed for a minimum of 1 hour after the administration of naloxone. It is especially important for patients who have received large doses of fentanyl to ensure that redistribution of fentanyl within the body does not result in the recurrence of sedation.

Naloxone may be administered IV, IM, subcutaneously, or via endotracheal routes, but it is almost universally given IV. The smallest dose necessary to restore respiratory effort should be used, because reversal of the opioid’s respiratory depressive effect is matched by reversal of the analgesia. Initial dosage depends on the patient and the specific goals desired. For partial reversal, titrated doses of 0.1 to 0.2 mg may be used every 1 to 2 minutes to desired effect. Complete reversal is almost never desirable and requires doses of 1 to 2 mg. Similar doses may be used in children. In patients who are opioid dependent, these doses may precipitate an acute withdrawal state. Smaller initial doses should be considered. Large doses of naloxone may also make it more difficult to control postprocedure pain. Naloxone use has little risk, but pulmonary edema, seizure, and dysrhythmia rarely have been reported.

**Flumazenil**

Flumazenil is a competitive antagonist of benzodiazepines. Although it reverses the sedation effect of benzodiazepines, it is not as effective for reversing respiratory depression. In general, when oversedation occurs, brief support of ventilation permits the patient to recover sufficient spontaneous respiration without the need for reversal. Flumazenil has a rapid onset of action in 1 to 2 minutes, a peak effect in 5 to 10 minutes, and an individually variable clinical duration of 30 to 90 minutes. Continuous patient monitoring must be ensured when flumazenil is used to reverse respiratory depression associated with longer-lasting benzodiazepines because resedation is likely. Flumazenil has also been shown to be effective in reversing paradoxical excitement in children.

It is generally titrated in doses of 0.1 to 0.2 mg IV every 1 to 2 minutes to the desired effect. A maximum dose of 1 mg is generally sufficient. Common pediatric doses of 0.02 mg/kg are generally used, with a maximum of 0.2 mg. It should be used with extreme caution in patients with benzodiazepine dependence or a history of seizures, as it may precipitate life-threatening status epilepticus refractory to common treatment. Routine reversal is not recommended.

**Drug Selection and Administration**

When choosing a strategy for PSA, it is important to consider the type of procedure being performed (painful or not), the length of the procedure, specific procedural requirements (anxiolysis vs. immobility), and whether sedation may need to be prolonged. The need for intravenous access generally is an issue only in small children. Planned adjuncts, such as topical, local, or regional anesthesia, are also considered. Patient factors, including age, medications, alcohol and drug use, and comorbid conditions, are considered when selecting both the agent and the initial dose. Procedures necessitating sedation may be broadly divided into three categories: nonpainful procedures requiring immobilization (e.g., computed tomography [CT], MRI); low-pain, high-anxiety procedures (e.g., laceration repair, lumbar puncture); and highly painful, high-anxiety procedures (e.g., fracture or joint reduction, tube thoracostomy, abscess drainage, cardioversion). These are summarized in Table 4-6 for adult patients and Table 4-7 for pediatric patients.

For brief nonpainful procedures requiring complete immobilization, intravenous midazolam and propofol are excellent choices, and etomidate is a reasonable alternative. For longer procedures, oral or rectal midazolam or propofol infusion is reasonable.

For briefly painful procedures requiring minimal to moderate sedation and when topical or local anesthetics may be used (e.g., for reduction of a glenohumeral dislocation for which intra-articular lidocaine will be used), midazolam is a reliable and safe choice. Intravenous propofol (preceded by a modest dose of fentanyl) is an excellent choice for brief painful procedures requiring deep sedation (e.g., cardioversion, joint reduction, and other highly painful procedures). Ketamine by both the intravenous and intramuscular routes has been extensively studied in children and is highly effective with a large margin of safety. The same may be said for intravenous midazolam plus fentanyl in both the adult and pediatric populations.

### Table 4-6 Adult Drug Selection Strategies

<table>
<thead>
<tr>
<th>PROCEDURE TYPE</th>
<th>EXAMPLES</th>
<th>RECOMMENDATION</th>
<th>ALTERNATIVES</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonpainful</td>
<td>Radiologic imaging</td>
<td>Midazolam (intravenous)</td>
<td>Propofol (intravenous)</td>
<td>Midazolam has considerable support and safety.</td>
</tr>
<tr>
<td>Low pain, high anxiety</td>
<td>Central line placement</td>
<td>Midazolam (intravenous)</td>
<td>Propofol (intravenous)</td>
<td>Analgesia may be accomplished with local or topical agents frequently.</td>
</tr>
<tr>
<td></td>
<td>Lumbar puncture</td>
<td></td>
<td>Ketamine (intravenous)</td>
<td></td>
</tr>
<tr>
<td>High pain, high anxiety</td>
<td>Fracture or joint reduction</td>
<td>Midazolam + fentanyl (intravenous)</td>
<td>Etomidate + fentanyl (intravenous)</td>
<td>There are far more data supporting the safety of fentanyl and midazolam, although the other choices have significant support.</td>
</tr>
<tr>
<td></td>
<td>Abscess drainage</td>
<td></td>
<td>Propofol + fentanyl (intravenous)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Burn debridement</td>
<td></td>
<td>Ketamine (intravenous, intramuscular)</td>
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<tr>
<td></td>
<td>Cardioversion</td>
<td></td>
<td>Propofol + ketamine (intravenous)</td>
<td></td>
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<tr>
<td></td>
<td>Chest tube placement</td>
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Table 4-7 Pediatric Drug Selection Strategies

<table>
<thead>
<tr>
<th>PROCEDURE TYPE</th>
<th>EXAMPLES</th>
<th>RECOMMENDATION</th>
<th>ALTERNATIVES</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonpainful</td>
<td>Radiologic imaging</td>
<td>Midazolam (oral, intravenous) Propofol (intravenous) Ketamine (intravenous, intramuscular) Methohexital (intravenous, rectal)</td>
<td>Methohexital (intravenous) Ketamine (intravenous, intramuscular) Propofol (intravenous)</td>
<td>Intravenous access is often not required for brief procedures.</td>
</tr>
<tr>
<td>Low pain, high anxiety</td>
<td>Laceration repair Lumbar puncture Foreign body removal Sexual assault examination</td>
<td>Midazolam (oral, intravenous) Propofol (intravenous) Ketamine (intravenous, intramuscular)</td>
<td>Ketamine (intravenous, intramuscular)</td>
<td>Analgesia may be accomplished with local or topical agents frequently.</td>
</tr>
<tr>
<td>High pain, high anxiety</td>
<td>Fracture or joint reduction Abscess drainage Burn débridement</td>
<td>Ketamine (intravenous, intramuscular) Fentanyl + midazolam (intravenous) Propofol + fentanyl (intravenous)</td>
<td>Propofol + ketamine (intravenous)</td>
<td>There are far more data supporting the safety of ketamine or fentanyl and midazolam, although propofol and fentanyl have significant support.</td>
</tr>
</tbody>
</table>

Special Considerations for Pediatric Populations

Performing painful procedures on children in the ED is often distressing for the parent and the provider as well as the child. This often includes obtaining intravenous access as well as performing more traditional procedures. In many cases, a calm and reassuring bedside manner, combined with distraction techniques, may be highly successful. Child life practitioners, coloring books, toys, video games, and television may be helpful.

The advent of ultrafast spiral CT scanners has nearly eliminated the need for sedation for this procedure. For prolonged CT studies or MRI, deep sedation is generally required in young children to ensure immobility. The need and desire for intravenous access in children should also be considered when planning PSA. Agents such as midazolam may be very effective in infants, but they do not reliably ensure immobility in young children except at high doses.200-203 Methohexital and pentobarbital have demonstrated efficacy for sedating children for these longer imaging procedures.202,204-211 Ketamine has been the most extensively studied and has been shown to be highly effective with a large margin of safety.212-214 Many of these drugs have been largely supplanted by propofol as studies continue to show its efficacy and safety in pediatric PSA.

For mildly painful procedures such as laceration repair or lumbar puncture, topical agents such as cream eutectic mixture of local anesthetics (EMLA) or lidocaine, epinephrine, tetracaine (LET) gels in combination with transmucosal or oral midazolam may preclude the need for placement of an intravenous line.

Brief painful procedures or those requiring deeper sedation may be accomplished with a single intramuscular injection of ketamine. Longer procedures or those requiring intravenous PSA agents require venous access. This should be considered a mildly painful procedure in itself, and distraction techniques, oral midazolam, and topical agents such as EMLA should be considered if time and the situation permit. Guidelines for patient preparation, personnel requirements, monitoring, drug administration, recovery care, and discharge criteria for children receiving intravenous PSA are similar to those outlined for adults.

With PSA in children, it is essential that drug dosages be calculated precisely using the child’s current weight and not a parent’s estimate. Equipment to manage the airway and resuscitation supplies must be size appropriate, and the physician must be skilled in pediatric airway management and resuscitation.

Chloral hydrate, a pure sedative-hypnotic agent, has been historically popular for sedating children for a wide variety of procedures. It offers no advantage over currently available agents.209,210,220,221 It has a poor safety record, delayed onset of 45 minutes, prolonged recovery time of hours, and residual sedation of nearly a day. Its use should be discontinued. Likewise, the combination of meperidine (Demerol), promethazine (Phenergan), and chlorpromazine (Thorazine), also known as DPT, is not recommended. It has an unacceptable rate of sedation failure, prolonged sedation times, high risk of respiratory depression, and frequent dystonic reactions.222

KEY CONCEPTS

- Safe, effective PSA requires high-level skills and knowledge and sound protocols, including patient monitoring.
- Propofol is the agent of choice for deep sedation in the ED but requires supplementation with an opioid analgesic when a painful procedure is planned.
- Preprocedural fasting guidelines are not evidence based but represent a best consensus for minimizing risk. Absence of a preprocedure fasting period is not, however, a contraindication to procedural sedation for an emergent, time-sensitive condition.
- Pulse oximetry is mandatory during sedation, and end-tidal CO₂ should be monitored if moderate or deep sedation is the goal. Oxygen should be administered to patients undergoing procedural sedation.

The references for this chapter can be found online by accessing the accompanying Expert Consult website.
References


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