Primary Care

Sedation and Analgesia for Procedures in Children

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The management of acute pain and anxiety in children undergoing therapeutic and diagnostic procedures outside the operating room has developed substantially in the past 15 years. The widespread availability of noninvasive monitoring, short-acting opioids and sedatives, and specific opioid and benzodiazepine antagonists has enabled clinicians to administer sedation safely for procedures in diverse settings. The goal of procedural sedation is the safe and effective control of pain, anxiety, and motion so as to allow a necessary procedure to be performed and to provide an appropriate degree of memory loss or decreased awareness. This article reviews the current status of sedation and analgesia for procedures in children.

Terminology and Guidelines

The Continuum of Sedation

The progression from mild sedation or analgesia to general anesthesia is not easily divided into discrete stages. Low doses of opioids and sedative-hypnotic agents induce mild analgesia and sedation, respectively, with little danger of adverse events. As the dose increases and the level of drug in the central nervous system rises, consciousness decreases and the risk of cardiorespiratory depression increases. As the dose increases further, the patient continues to advance along the sedation continuum until protective airway reflexes are lost and general anesthesia is reached. This continuum is not drug-specific, since various states, from mild sedation to general anesthesia, can be achieved with essentially all sedative agents.

Guidelines for Sedation

Specialty societies and government agencies have published 12 conflicting sets of guidelines for sedation. Most of the guidelines are based on the degree of sedation induced rather than the specific pharmacologic agent administered. The definitions of states of sedation in the guidelines most applicable to children are shown in Table 1.

If the child is cooperative, many procedures that are minimally invasive can be performed with the child in a primary sedation state, as defined in Table 1. In this state cardiorespiratory depression is unlikely, and therefore there is little risk of complications when appropriate monitoring is used and the personnel are trained. Most health care providers will confine their sedation practice to this level.

However, when the procedure is painful (e.g., complex repair of facial lacerations, bone marrow aspiration, or fracture reduction) or when there is considerable emotion and anxiety (e.g., in young children), successful and humane practice may require either intentional deep sedation or a close approach to the upper limits of a primary sedation state, in which intermittent brief periods of deep sedation may occur. Such intermediate sedation can be performed by physicians, such as anesthesiologists, intensivists, and emergency physicians, who are trained in advanced life-support interventions (including airway management and resuscitation) and have experience with the administration of deep sedation.

Patient Care Before and After the Procedure

Skills and Training of Personnel

Sedation must be administered by personnel capable of rapidly identifying and treating cardiorespiratory complications, including respiratory depression, apnea, partial airway obstruction, emesis, and hyper-salivation. They must understand the pharmacology of the sedatives they use and be proficient at maintaining airway patency and assisting ventilation if needed. At least two experienced persons are required, usually a physician and an assistant, such as a nurse or respiratory therapist. The physician typically oversees drug administration and then performs the procedure, while the assistant continuously monitors the patient for complications and documents the medications administered, the response to sedation, and periodic vital signs. The assistant may perform minor, interruptible tasks, but the assistant’s ability to remain focused while the physician continues to advance along the sedation continuum until protective airway reflexes are lost and general anesthesia is reached. This continuum is not drug-specific, since various states, from mild sedation to general anesthesia, can be achieved with essentially all sedative agents.

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**Evaluation and Preparation of the Patient before Sedation**

A directed history taking and physical examination should precede sedation.\textsuperscript{12-14} Underlying medical problems should be assessed (Table 2), and information about medication use, allergies, previous adverse experiences with sedation or general anesthesia, and the time and nature of the last oral intake should be obtained. Auscultation of the heart and lungs should be performed, and the airway must be evaluated for conditions that might impair endotracheal intubation and cardiopulmonary resuscitation, such as a short neck, small mandible, large tongue, or trismus.

According to the guidelines of the American Society of Anesthesiologists, children should not consume clear liquids for two to three hours or solids and nonclear liquids for four to eight hours before undergoing sedation for an elective procedure; the recommended duration of fasting varies with age. However, the guidelines acknowledge that “the literature...
provides insufficient data to test the hypothesis that preprocedure fasting results in a decreased incidence of adverse outcomes" of procedural sedation.12 When the patient has not fasted, especially during nonelective or emergency procedures when the guidelines are virtually impossible to follow, the risks and benefits must be assessed for each patient by balancing the potential for vomiting and aspiration with the timing and urgency of the procedure and the required depth of sedation.

Monitoring

The most important element of monitoring during sedation is close, continuous observation of the patient. The designated person must continuously observe the child's face and mouth and the motion of the chest wall; this observation must never be blocked by equipment or sterile drapes unless blocking is completely unavoidable, as during MRI scanning.

The sedation area must include all necessary age-appropriate equipment for airway management and resuscitation; at a minimum, an appropriately sized bag-valve mask, oxygen, and suction and endotracheal tubes should be present. Continuous pulse oximetry with an audible and visual signal is mandatory for all procedural sedation. Although there is no evidence that continuous electrocardiographic monitoring in the absence of cardiovascular disease has an effect on patients' outcomes in these types of procedures, such monitoring provides a simple, inexpensive, and readily available backup to pulse oximetry and should be considered routine.

At a minimum, the vital signs should be measured at base line, after the administration of the drug, on completion of the procedure, during early recovery, and at the completion of recovery. If an increased depth of sedation is anticipated or the child has an underlying illness, the frequency of measurement of vital signs should be increased (e.g., every five minutes with deep sedation).1 Patients are at highest risk for complications during the 5 to 10 minutes after the intravenous administration of medication and during the period immediately after the end of the procedure when procedural stimuli are discontinued.

When sedation is administered by the oral, nasal, rectal, or intramuscular route, intravenous access is not mandatory. However, the intravenous route may be preferred for deeper levels of sedation or anticipated administration of multiple doses. When sedation is performed without intravenous access, equipment for vascular access and a person skilled in initiating vascular access in children must be immediately available.

The need for supplemental oxygen during procedural sedation and its benefits have not been formally studied. Although this intervention will decrease the incidence and severity of hypoxemia due to airway complications,12 it will also delay the detection of apnea with pulse oximetry.12 Given the lack of supporting evidence, supplemental oxygen cannot be considered mandatory and remains an option best left to the physician's preference. If oxygen is administered, continual visual inspection of chest-wall motion and air movement is especially important.

Discharge

All patients must be monitored until they are no longer at risk for cardiorespiratory depression. Before discharge, children should be alert and oriented (or have returned to an age-appropriate base line), and their vital signs should be stable and at base-line levels.12 14 Many hospitals use recovery-scoring systems similar to those used in their surgical postanesthesia recovery areas.13 If the child is an outpatient, a responsible adult must be present to observe the child for complications after discharge. This adult should be given written instructions on appropriate diet, medications, and level of activity.

PHARMACOPEIA

The pharmacopeia of procedural sedation, described in Table 3, has evolved from a small number of long-acting agents (meperidine, morphine, diazepam, and chloral hydrate) with limited routes of administration to a wide range of shorter-acting agents with multiple routes of administration (topical, local, transmucosal, oral, intranasal, rectal, intramuscular, intravenous, and inhalational).54 55 Drug-selection strategies and indications for procedural sedation are shown in Table 4.

Sedative–Hypnotic Agents

Chloral Hydrate

One of the oldest drugs, oral chloral hydrate has a well-established safety profile.15–18 Chloral hydrate has no analgesic properties, and its use is now mainly restricted to diagnostic imaging, particularly in children under three years of age.

Benzodiazepines

Midazolam is the drug most commonly used for sedation in children and adults during procedures.19–28 This short-acting benzodiazepine can be administered by multiple routes. It provides potent sedation, loss of memory, and anxiolysis and is preferred over the longer-acting diazepam and lorazepam. Benzodiazepines provide no analgesia, and for painful procedures midazolam is commonly administered with an opioid. Caution must be exercised when using benzodiazepines and opioids together, since the risks of hypoxia and apnea are significantly greater than when either is used alone.38 39 The effects of midazolam can be reversed with the antagonist flumazenil.

Barbiturates

Barbiturates have been used for preinduction of anesthesia for over 30 years and have an extensive safe-
ty profile. They are widely regarded as the drugs of choice to facilitate diagnostic imaging in children three years of age or older. Though lacking analgesic properties, they provide effective immobilization and can be delivered by multiple routes. Intravenous pentobarbital and rectal methohexital and thiopental are the most extensively studied barbiturates used for procedural sedation.\textsuperscript{16-19,29-37}

**Analgesic Agents**

**Topical Agents**

Topical analgesia has substantially reduced the discomfort associated with laceration repair, intravenous cannulation, and lumbar puncture in children by providing a noninvasive means of delivering local anesthesia. The first available topical anesthetic for nonintact (lacerated) skin was a combination of tetracaine, epinephrine, and cocaine referred to as TAC.\textsuperscript{50} Recently, this combination has been widely replaced by lidocaine, epinephrine, and tetracaine (LET), which is safer, less expensive, and equally effective, and has an onset time of approximately 20 minutes.\textsuperscript{51,52}

Intact skin can be treated with sprays that numb by cooling (ethyl chloride or fluoromethane) for procedures lasting less than one minute, such as intravenous cannulation, or with a eutectic mixture of local anesthetics, or EMLA (2.5 percent lidocaine and 2.5 percent prilocaine in a cream base) to provide one to two hours of anesthesia for intravenous cannulation or lumbar puncture.\textsuperscript{53-56} The chief disadvantage of the eutectic mixture is the relatively long time to peak effect (60 minutes), a delay that cannot be circumvented, since 30 to 40 minutes produces inadequate analgesia. Recent reports describe success in delivering lidocaine transdermally by electrical current (iontophoresis). This noninvasive technique shows promise for reducing the discomfort of intravenous cannulation.\textsuperscript{52,53}

**Transmucosal Agents**

The use of fentanyl lozenges initially appeared promising as a method of delivering opioids by a noninvasive route through the oral mucosa, but unacceptably high rates of emesis (31 to 45 percent) have limited the popularity of this method.\textsuperscript{65,66}

**Systemic Agents**

The short-acting opioid fentanyl is preferred to the traditional long-acting meperidine and morphine for procedural analgesia because its action has faster onset and shorter duration and involves no histamine release.\textsuperscript{19,20,40} Concomitant administration of an antihistimetic is not required with fentanyl. This opioid causes pruritus in the nasal area that may interfere with procedures. Morphine and meperidine remain the preferred agents for analgesia of longer duration. The effects of opioids can be reversed with the antagonist naloxone.

**Ketamine**

When given parenterally (intramuscularly or intravenously), ketamine rapidly induces a trancelike cataleptic condition characterized by profound analgesia, sedation, amnesia, and immobilization.\textsuperscript{19,20,41-46} This unique state of cortical dissociation permits painful procedures to be performed more consistently and effectively than with other procedural-sedation agents. Ketamine preserves upper-airway muscular tone and protective airway reflexes. Spontaneous respiration is maintained, although when administered intravenously ketamine must be given slowly (over a period of one to two minutes) to prevent respiratory depression. Although unpleasant hallucinations and dreams during the recovery period have substantially limited the use of ketamine in adults, such dysphoric emergence reactions are rarely noted in children.\textsuperscript{42}

The safety of ketamine has been extensively documented in a variety of settings throughout the world since its introduction in 1970. Ketamine is used widely in outpatients for brief, painful procedures such as fracture reduction and to provide immobility for repair of facial lacerations in young children. Because of its unique preservation of protective airway reflexes, ketamine may be preferred over other agents for emergency procedures when fasting is not assured. In 30 years of regular use, there have been no documented reports of clinically significant ketamine-associated aspiration in patients without established contraindications. Clinicians administering ketamine must be especially knowledgeable about the unique actions of this drug and the numerous contraindications to its use (Table 3).

**Nitrous Oxide**

Nitrous oxide gas is dispensed in a preset mixture with a minimum of 40 percent oxygen, or it can be blended with oxygen in a flow meter. It is self-administered by a demand-valve mask that requires negative inspiratory pressure to initiate gas flow and thus can be used only for a cooperative child (usually one over four years of age). Although nitrous oxide is easy to use and noninvasive and provides rapid onset of sedation and recovery, in the concentrations used for procedural sedation it is a weak analgesic, sedative, and anxiolytic.\textsuperscript{47-50}

**Antagonists**

The availability of specific benzodiazepine and opioid antagonists (reversal agents) has greatly increased the safety of procedural sedation, since oversedation leading to respiratory depression can often be rapidly reversed if necessary. Naloxone is a short-acting opioid antagonist with a well-established safety profile.\textsuperscript{51,52} Flumazenil, the benzodiazepine antagonist, appears to be safe in the absence of contraindications (Table 3).\textsuperscript{53}
### Table 3. Recommendations for Dosages in Pediatric Procedural Sedation and Analgesia. *

<table>
<thead>
<tr>
<th>Drug</th>
<th>Clinical Effects</th>
<th>Indications</th>
<th>Dose†</th>
<th>Time to Onset</th>
<th>Duration of Action</th>
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</thead>
<tbody>
<tr>
<td><strong>Sedative–hypnotic agents</strong></td>
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<tr>
<td>Cilorlurate</td>
<td>Sedation, motion control, anxiolysis. No analgesia. Not reversible.</td>
<td>Diagnostic imaging (age &lt; 3 yr)</td>
<td>PO: 25–100 mg/kg of body weight; after 30 min may repeat 25–50 mg/kg. Maximal total dose: 2 g or 100 mg/kg (whichever is less). Only single use in neonates.</td>
<td>15–30</td>
<td>60–120</td>
</tr>
<tr>
<td>Midazolam‡</td>
<td>Sedation, motion control, anxiolysis. No analgesia. Reversible with flumazenil.</td>
<td>Procedures requiring sedation or anxiolysis</td>
<td>IV (age of child, 0.5–5 yr): initially 0.05–0.1 mg/kg, then adjusted to a maximum of 0.6 mg/kg. IV (6–12 yr): initially 0.025–0.05 mg/kg, then adjusted to a maximum of 0.4 mg/kg</td>
<td>2–3</td>
<td>45–60</td>
</tr>
<tr>
<td>Pentobarbital</td>
<td>Sedation, motion control, anxiolysis. No analgesia. Not reversible.</td>
<td>Diagnostic imaging</td>
<td>IV: 1–6 mg/kg, adjusted in increments of 1–2 mg/kg to desired effect. IM: 2–6 mg/kg, to a maximum of 100 mg. PO or PR (≥4 yr): 3–6 mg/kg, to a maximum of 100 mg. PO or PR (≥4 yr): 1.5–3 mg/kg, to a maximum of 100 mg</td>
<td>3–5</td>
<td>15–45</td>
</tr>
<tr>
<td>Methohexital</td>
<td>Sedation, motion control, anxiolysis. No analgesia. Not reversible.</td>
<td>Diagnostic imaging</td>
<td>PR: 25 mg/kg</td>
<td>10–15</td>
<td>60–120</td>
</tr>
<tr>
<td>Thiopental</td>
<td>Sedation, motion control, anxiolysis. No analgesia. Not reversible.</td>
<td>Diagnostic imaging</td>
<td>PR: 25 mg/kg</td>
<td>10–15</td>
<td>60–120</td>
</tr>
<tr>
<td><strong>Analgesic agents</strong></td>
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<tr>
<td>Fentanyl§</td>
<td>Analgesia. Reversible with naloxone.</td>
<td>Procedures with moderate-to-severe pain</td>
<td>IV: 1.0 µg/kg/dose, may repeat every 3 min, adjust to desired effect</td>
<td>2–3</td>
<td>30–60</td>
</tr>
<tr>
<td>Ketamine</td>
<td>Analgesia, dissociation, amnesia, motion control. Not reversible.</td>
<td>Procedures with moderate-to-severe pain or requiring immobilization</td>
<td>IV: 1–1.5 mg/kg slow over period of 1–2 min, may repeat ½ dose every 10 min as required. IM: 4–5 mg/kg, may repeat after 10 min</td>
<td>1 Dissociation: 15; recovery: 60</td>
<td>Dissociation: 15–30; recovery: 90–150</td>
</tr>
<tr>
<td>Nitrous oxide</td>
<td>Analgesia, sedation, amnesia (all mild)</td>
<td>Procedures requiring mild sedation.</td>
<td>Preset mixture with minimum of 40% oxygen self-administered by demand valve mask (requires cooperative child)</td>
<td>&lt;5</td>
<td>&lt;5 min after discontinuation</td>
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<tr>
<td><strong>Reversal agents (antagonists)</strong></td>
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<tr>
<td>Naloxone</td>
<td>Opioid reversal</td>
<td>Overdose of opioids</td>
<td>IV or IM: 0.1 mg/kg/dose, to a maximum of 2 mg/dose; may be repeated every 2 min as required</td>
<td>IV: 2</td>
<td>IV: 20–40</td>
</tr>
<tr>
<td>Flumazenil</td>
<td>Benzodiazepine reversal</td>
<td>Overdose of benzodiazepines</td>
<td>IV: 0.02 mg/kg/dose, may be repeated every 1 min to a maximum of 1 mg</td>
<td>1–2</td>
<td>30–60</td>
</tr>
</tbody>
</table>

*The dose of intravenous agents should be carefully adjusted to achieve the desired effect. Alterations in dosing may be indicated on the basis of the clinical situation and the practitioner’s experience with these agents. Individual dosages may vary when these drugs are used in combination with other agents, especially when benzodiazepines are combined with opioids.

†PO denotes oral, IV intravenous, IM intramuscular, IN intranasal, and PR rectal.

‡Midazolam is preferred to other benzodiazepines (e.g., diazepam and lorazepam) because of its shorter duration of action and multiple routes of administration.

§Fentanyl is preferred to other opioids (e.g., morphine and meperidine) because it has a faster onset of action and shorter recovery period and does not induce histamine release. Not enough data have been published on intranasal sufentanil for procedural sedation and analgesia to recommend its use.

¶The generally accepted contraindications to ketamine therapy are an age of <3 months; a history of airway instability, tracheal surgery, or tracheal stenosis; procedures involving stimulation of the posterior pharynx; active pulmonary infection or disease (including active upper respiratory tract infection); cardiovascular disease, including angina, heart failure, or hypertension; substantial head injury, central nervous system masses, or hydrocephalus; glaucoma or acute globe injury; psychosis; porphyria; and thyroid disorder or use of thyroid medication.

||The generally accepted contraindications to nitrous oxide are pregnancy (of the patient or personnel), preexisting nausea or vomiting, and trapped gas pockets (e.g., in middle-ear infection, pneumothorax, or bowel obstruction).
Intravenous ultra-short-acting agents (etomidate, methohexital, propofol, remifentanil, and thiopental) have theoretical promise for procedural sedation, since the dose of these drugs can be rapidly titrated to produce a desired depth of sedation, and recovery is very rapid. However, there appears to be a higher likelihood of inadvertent oversedation and rapid swings in consciousness with ultra-short-acting agents than with other agents, especially when they are administered by clinicians with limited training and experience in their use. Further research is required to clarify the safety profile of these drugs and to determine the settings in which nonanesthesiologists may administer them.
FUTURE DIRECTIONS

Future directions in procedural-sedation research and clinical practice will focus on ways to make sedation safer and more efficient with respect to time. These initiatives include studies in pharmacogenomics (matching the drug to the genetic disposition of the patient in order to minimize side effects), studies that match the drug and route of administration to the specific procedure and age of the patient, expanded use of regional anesthesia as an adjunct to systemic sedation and analgesia, and research into the safety of intravenous ultra-short-acting agents.

REFERENCES

11. The role of the registered nurse in the management of patients receiv-

### Table 4. Indications and Strategies for Procedural Sedation and Analgesia.*

<table>
<thead>
<tr>
<th>Clinical Situation</th>
<th>Indications</th>
<th>Procedural Requirements</th>
<th>Suggested Sedation Strategies†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Noninvasive procedures</td>
<td>Computed tomography, Echocardiography, Electrocencephalography, Magnetic resonance imaging, Ultrasonography</td>
<td>Motion control</td>
<td>Comforting alone, Chloral hydrate PO (in patients &lt;3 yr of age), Pentobarbital IV or IM, Midazolam IV</td>
</tr>
<tr>
<td>Procedures associated with low level of pain and high anxiety</td>
<td>Dental procedures, Flexible fiberoptic laryngoscopy, Foreign-body removal, simple intravenous cannulation, Laceration repair, simple, Lumbar puncture, Ocular irritation, Phlebotomy, Slt-lamp examination</td>
<td>Sedation, Anxiolysis, Motion control</td>
<td>Comforting and topical or local analgesia, Midazolam PO, IN, PR, or IV, Nitrous oxide</td>
</tr>
<tr>
<td>Procedures associated with high level of pain, high anxiety, or both</td>
<td>Abscess incision and drainage, Arthrocentesis, Bone marrow aspiration, Burn débridement, Cardiac catheterization, Cardioversion, Central catheter placement, Endoscopy, Foreign-body removal, complicated fracture or dislocation reduction, Hernia reduction, Interventional-radiology procedures, Laceration repair, complex, Paracentesis, Paraphimosis reduction, Sexual-assault examination, Thoracentesis, Thoracostomy-tube placement</td>
<td>Sedation, Anxiolysis, Analgesia, Amnesia, Motion control</td>
<td>Midazolam and fentanyl IV, Ketamine IM or IV</td>
</tr>
</tbody>
</table>

*This table is intended as a general overview. Sedation strategies should be individualized. Although the pharmacopeia is large, clinicians should familiarize themselves with a few agents that are flexible enough to be used in the majority of procedures. In all cases it is assumed that practitioners are fully trained in the technique, appropriate personnel and monitoring are used as detailed in this article, and specific drug contraindications are absent.
†PO denotes oral, IV intravenous, IM intramuscular, PR rectal, and IN intranasal.


