Procedural Sedation and Analgesia in Children

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5.1 Introduction

Invasive and noninvasive procedures have become an essential component of modern diagnostics and therapy in children. Often, the procedures are uncomfortable and anxiety-producing for both patients and their parents. Subsequently, in the last two decades, the management of acute pain and anxiety in children undergoing brief therapeutic and diagnostic procedures outside the operating room has developed substantially. Traditionally, these were performed by anesthesiologists. Increasingly, other specialists, such as emergency room physicians, pediatricians, and radiologists, are involved in the management of procedural sedation under elective or emergency situations.

Consequently, both anesthesiologists and nonanesthesiologists are striving to provide safe and effective sedation and analgesia to these children. The availability of noninvasive monitoring, and short-acting opioids and sedatives, has broadened the possibilities of sedation and analgesia in children in diverse settings. While most of these procedures themselves pose little risk to the child, the administration of sedation or analgesia may add substantial risk to the patient. Professional organizations such as the American Society of Anesthesiologists (ASA), the American Academy of Pediatrics (AAP), the Joint Commission on Accreditation of Healthcare Organizations, and other organizations are working continuously to make procedural sedation for children safe, economical, and tailored to the needs of the child and the diagnostic/therapeutic procedure being performed. In response to published recommendations and guidelines [1–5], many institutional systems for the provision of safe procedural sedation and analgesia for children have been developed. These system models range from the use of special teams, led by anesthesiologists, intensivists, emergency physicians, or nurses that serve the entire hospital, to reliance on individual practitioners who follow sedation guidelines in their own way.

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Therefore, it is important to review the current status of sedation and analgesia for invasive and noninvasive procedures in children, providing an evidence-based approach to several topics of importance, including safety factors, patient assessment, personnel requirements, equipment, monitoring, and drugs.

5.2 Initial Considerations

When planning sedation and/or pain management for a child, knowing what level of responsiveness needs to be achieved during the procedure or test is essential for choosing the appropriate medication regimen. Painful procedures that require relative immobility generally mandate a deeper level of sedation than noninvasive radiological tests. Each sedation plan should take into account the age, developmental level, and personality of the child. A 7-year-old child, for example, may require deep sedation for the incision and drainage of an abscess; local analgesia alone may be sufficient for another child of the same age undergoing such a procedure.

One of the most important aspects of pediatric sedation and analgesia is to optimize patient safety by minimizing complications. Adverse events during sedation in children can occur owing to a variety of reasons, such as drug overdose, inadequate monitoring, drug errors, inadequate skills of the personnel administering the drugs, and premature discharge [6]. In total, 80% of the complications during sedation and analgesia are secondary to adverse airway/respiratory events [7,8]. The majority of these complications can be managed with simple maneuvers, such as providing supplemental oxygen, opening the airway, suctioning, and using bag-mask-valve ventilation. Occasionally, more advanced airway management, such as endotracheal intubation or the use of a laryngeal mask airway, is required for ventilatory assistance.

5.3 The Concept of the Continuum of the Sedation Spectrum

In an effort to clarify sedation goals, ASA defined a continuum for the levels of sedation. Minimally sedated children may have an impaired level of cognitive functioning but maintain their airway-protective reflexes and cardiorespiratory status [9,10]. For example, for children undergoing voiding cystourethrograms (VCUGs), this level of sedation is often achieved through the use of inhaled nitrous oxide. Moderate sedation is associated with blunted-but-purposeful responses to verbal or tactile stimulation. There may be subtle alterations in ventilation, but airway reflexes and cardiovascular function are generally unchanged. Infants who receive chloral hydrate often reach a moderate level of sedation. In contrast, deeply sedated children may have inadequate spontaneous ventilatory drive and/or significant upper airway obstruction and may require airway intervention. During deep sedation (as opposed to general anesthesia), purposeful responses to painful stimulation remain intact. The combination of an opioid and a benzodiazepine often results in deep sedation.

These original guidelines defined three levels of depth of sedation: conscious sedation, deep sedation, and general anesthesia. Conscious sedation was defined as a minimally depressed level of consciousness that retains the patient's ability to maintain a patent airway independently and continuously, and respond appropriately to physical stimulation and/or verbal command, for example, "open your eyes." The choice of this terminology led to confusion, as conscious sedation is rarely attained in children. In 1992, the AAP Committee on Drugs revised the 1985 guidelines [11]. They stated that regardless of the intended level of sedation or route of administration, a patient could progress from one level of sedation to another and that the provider must have the skills and equipment necessary to safely manage patients who have progressed to a deeper level of sedation. Pulse oximetry was recommended for all patients undergoing sedation.

This new guideline also discouraged the practice of parents administering sedation at home. An amendment to this guideline was published by the AAP Committee on Drugs in 2002 [5]. It eliminated the use of the term "conscious sedation." The current guidelines use the terminology of minimal sedation, moderate sedation, deep sedation, and general anesthesia to describe the continuum of the sedation spectrum (see Table 5.1).

It is vital to remember that the patient may rapidly move from one level of sedation to another (e.g., a child can move from deep sedation to either moderate sedation or to a state of general anesthesia) and, hence, personnel should have the training, in addition to the equipment, to rescue the child from deeper levels of sedation at all times when procedural sedation is provided. There are some questions raised about the concept of the sedation continuum, as it relies on subjectivity in identifying and quantifying a patient's response to verbal or tactile stimulation. This subjectivity may vary among observers and it is not logical to apply this to patients who may be unable to respond appropriately, for example, patients with hearing impairments, developmental delay, neurological compromise, or at extremes of age. In the future, it may be possible to reformulate the sedation continuum by shifting away from subjective assessment to more objective vital signs monitoring, through focused research and the development of a multidisciplinary sedation community to help define the stages of sedation.

Table 5.1 The continuum of the sedation spectrum

	Minimal sedation axiolysis	Moderate sedation (conscious sedation)	Deep sedation	General anesthesia
Response	Responds normally to verbal commands	Responds purposefully to verbal commands or light touch	Responds to pain	No response
Airway	Maintained	Maintained	May require support	May be necessary
Cardiovascular support	Not needed	Not needed	May be needed	May be necessary

Perhaps the most important factor for ensuring safety during pediatric procedural sedation is the immediate availability of skilled rescue resources. Adverse pediatric sedation events are most common in facilities that lack adequately trained personnel and reliable emergency response support. Physicians should carefully consider the following questions before embarking on a sedation plan:

1. What is the skill set of the team that will be with the child at all times?
2. If the primary team needs help, who will respond?
3. How long will it take the rescue team to arrive?
4. Is a member of the rescue team an anesthesia specialist who is capable of providing reliable advanced airway support to children?

Satisfactory answers to these questions are critical to ensuring safety.

Following the implementation of the 2001 Joint Commission on Accreditation of Healthcare Organizations guidelines, the incidence of adverse events during procedural sedation has been markedly reduced [12]. Adherence to AAP/ASA guidelines for pediatric procedural sedation may reduce the adverse events, and there is direct evidence that elements of the AAP/ASA structural model for procedural sedation could be adopted by nonanesthesiologists with an apparent risk reduction [13].

5.4 Patient Evaluation

What "red flags" should providers look for when evaluating a child who would benefit from sedation for a painful or anxiety-provoking procedure? Although identifying every possible risk factor can be challenging even for the most seasoned pediatric anesthesiologist, there are specific patient characteristics that have been associated with increased complications. A thorough health history and physical examination can reveal many of them.

First, the provider should find out why the child is having the procedure or test. The provider should then find out whether the child has medical issues that could put them at increased risk for complications. Recent upper respiratory illness symptoms, especially coughing, wheezing, or nasal congestion, can increase the risk of airway irritability and respiratory complications, including hypoventilation, desaturation, and laryngospasm. Similarly, a history of recent vomiting or symptomatic gastroesophageal reflux can be cause for concern, as emesis during sedation, when airway-protective reflexes may be blunted, could lead to aspiration and initiate laryngospasm. Significant obesity, an increasing problem in the pediatric population, may be associated with an increased risk of airway obstruction, especially with deeper levels of sedation. Overt obstructive sleep apnea symptoms are clearly associated with airway obstruction during sedation; however, many families are unable to say how frequently or how badly their children snore. Even occasional audible snoring makes the need for airway repositioning and nasopharyngeal airway placement more likely.

Physicians should also be aware of underlying medical conditions that increase the potential for airway compromise during sedation. A number of genetic syndromes

are associated with anatomic and/or developmental airway differences as well as altered respiratory mechanics; several excellent articles describe these [14,15]. Infants born prematurely have immature respiratory drive physiology, increasing the likelihood of sedation-related apnea in the first months of life. Currently, many sedation programs choose to monitor infants less than 60 weeks postconceptual age for a longer time period than they do older children prior to discharge. For example, at Children's Hospitals and Clinics of Minnesota, we monitor these infants for a 12-h period, discharging them to home only if they have not had any episodes of apnea during that time. Changes in respiratory physiology during procedural sedation can aggravate underlying asthma or bronchopulmonary dysplasia, potentially leading to bronchospasm and/or desaturation.

Physical examination should focus on findings that could affect the course of the child's sedation. The physician should look for craniofacial abnormalities that could be problematic if the patient should need bag-mask ventilation or endotracheal intubation. These include, but are not limited to, facial anomalies such as retrognathia that can prevent good mask seal and interfere with airway visualization, tonsillar hypertrophy that can prevent adequate air entry, and limited neck mobility that can prevent adequate airway positioning. Physicians should also remember to look for braces and other orthodontia. Many neuromuscular disorders are associated with decreased ability to handle oral secretions; these secretions can pool in the hypopharynx and lead to coughing, laryngospasm, or aspiration when airway reflexes are blunted. Children who have obvious wheezing or other respiratory difficulties should have their test or procedure rescheduled. If the procedure or test is deemed to be an emergency, an anesthesia consultation should be sought. Significant abdominal distension can increase the risk of vomiting and aspiration.

Although the need for strict nothing by mouth (NPO) guidelines for urgent and emergent sedations continues to be a topic of debate, most physicians should plan to adhere to the recommended ASA guidelines [1]. These suggest the following NPO times:

- Clear liquids: 2 h
- Breast milk: 4 h
- Infant formula, other nonhuman milk, solids: 6 h
- Full meal: 8 h

For children requiring sedation who do not meet the ASA NPO guidelines, recommended options include delaying the procedure or seeking an anesthesia consultation [16]. The literature suggests that the aspiration risk for procedural sedation and analgesia is lower than that of general anesthesia because the principal risk factors (airway manipulation, absence of protective airway reflexes, and poor ASA physical status) are not present routinely in this setting [17,18]. As a reflection of this evidence, some emergency physicians disregard preprocedural fasting guidelines. However, even though published studies suggest that strict adherence to the fasting guidelines is not necessary, their sample size and/or designs are insufficient to safely practice the liberalized preprocedural fasting guidelines and to justify changes in emergency department procedural sedation and analgesia policies.

5.5 Preparation and Setup for Sedation and Analgesia

The single best way to monitor a sedated child is continuous direct observation by one or more trained providers not directly involved with the procedure itself. Beyond this basic tenet, the frequency and intensity of monitoring depend on the depth of the sedation being performed. At a minimum, all sedated patients should be monitored with continuous pulse oximetry. The ASA also recommends that respiratory function be continuously monitored by observation, auscultation, and/or capnography. Electrocardiography (ECG) should be used and blood pressure (BP) should be measured intermittently during deep sedation.

Equipment needs are based on patient management and rescue. A number of mnemonics can help the sedation provider remember the essentials; one of the most popular is the SOAPME mnemonic:

- suction: appropriately sized large-bore suction catheters, smaller catheters for nasal or endotracheal suctioning, functional vacuum apparatus;
- oxygen: adequate supply, functioning flow meters;
- airway equipment: appropriately sized masks, self-inflating or anesthesia bag-valve-mask (BVM) systems, nasopharyngeal and oropharyngeal airways, laryngeal mask airways, laryngoscope blades and handles, endotracheal tubes;
- pharmacy: sedative analgesic medications, reversal agents, emergency resuscitation, and airway medications;
- monitors: pulse oximetry, cardiorespiratory monitor with ECG and BP capability, stethoscope, end-tidal carbon dioxide monitor; and
- extras: intravenous access catheters, isotonic resuscitation fluid, emergency drug sheet, calculator.

The type of procedure being performed may also dictate other equipment needs. Documentation of sedation encounters should include informed consent, postsedation instructions, and contact information for the parent or guardian. A focused history and physical examination should be performed and documented at the time of sedation. The plan for procedural sedation as well as an assessment of the child's sedation risks and ASA classification should be included in the documentation. A time-based recording of vital signs, sedation scores, and administered medications is required. Also, any adverse events and associated interventions should be noted.

5.6 Personnel and Training

The provider responsible for sedation in pediatric patients must be familiar with monitoring, as per the AAP guidelines, and competent in managing the complications. The sedation may exceed the intended level and the provider should be sufficiently skilled to rescue the child from a deeper level of sedation. The provider must be trained in and capable of providing BVM ventilation and advanced airway skills if required, to keep the child oxygenated. At least one individual must

be present who is trained in advanced pediatric life support. Human simulators offer an extremely promising technology in the promotion of the safe administration of pediatric procedural sedation. This technology will train the sedation providers to recognize the critical airway emergencies and initiate resuscitation. The study [19] carried out to measure the system safety and errors supports the feasibility of using available human simulation.

5.7 Vascular Access and Monitoring

Children receiving deep sedation should have an intravenous access placed at the start of the procedure. An intraosseous needle should be available in the event of failure to place an intravenous line, or if the intravenous line becomes nonfunctional in an emergency situation. If the child is receiving sedative agents other than via the intravenous route, for example, intranasal, oral, or rectal, the need for intravenous access is debatable. Most authors recommend the placement of intravenous access for the administration of emergency medications, including reversal agents, during procedural sedation.

Prior to administration of sedative medication, a baseline determination of vital signs should be documented. The selection of medication with appropriate concentration and labeling is essential to prevent medication errors [7]. Medications with minimal effect on respiration are associated with fewer respiratory adverse events [20], and titration of the medication dose guided by the bispectral index (BIS) may be useful in preventing oversedation [21]. Continuous monitoring of oxygen saturation, heart rate, and respiratory rate using capnography and intermittent measurement of BP should be documented. The new-generation pulse oximeters are less susceptible to motion artifacts. Oximeters that change the tone with changes in hemoglobin saturation provide immediate aural warning to everyone within hearing distance. The oximeter probe must be properly positioned; clip-on devices can be easily displaced and could result in a false reading. Capnography is valuable in monitoring respiration, especially in children sedated in less accessible locations, such as during a magnetic resonance imaging (MRI) or computerized tomography (CT) scan, or in darkened rooms. Nasal cannulae that allow the simultaneous delivery of oxygen and measurement of expired CO_2 are very useful in making the diagnosis of airway obstruction or apnea during sedation. In a recent randomized controlled trial, investigators examined the use of a capnography monitor during emergency department sedation using propofol and opioids in adults [22]. They concluded that the addition of capnography to standard monitoring reduces hypoxic events and also provides early warning of the development of hypoxemia. Capnography has been demonstrated to improve patient safety during procedural sedation by reducing the apnea/hypoxia events [23]. Any restraining devices should be checked to prevent airway obstruction or restriction of chest movement.

5.8 Sedatives and Analgesics: a Difficult Choice

A number of medications are used for pediatric procedural sedation. There is rarely a right or wrong choice with regard to medication selection; however, the physician's familiarity and experience with various agents are important considerations. Many of the more commonly used sedation agents have no analgesic component, so adding a medication for pain control or choosing a different regimen may be more appropriate for painful procedures.

Benzodiazepines have been a mainstay of procedural sedation for many years. A drug in this class can be used as a single agent for brief, nonpainful procedures and as an adjunct in combination with opioids or ketamine for more painful ones. The pharmacokinetics of midazolam make it most suited for procedural sedation. Onset of action occurs in less than 60 s when administered intravenously (IV), and its duration is usually a few minutes. Midazolam may be administered via many different routes: IV, orally, rectally, or intranasally. Although the combination of midazolam and an opioid analgesic can provide excellent sedation and analgesia for painful procedures, the combination is also associated with a higher incidence of respiratory depression.

Nitrous oxide, a longtime favorite sedative/analgesic agent for dental procedures, is becoming increasingly popular as a minimally sedating agent for a variety of pediatric procedures, including IV catheter placements, VCUGs, lumbar punctures, and other brief, painful procedures. Nitrous oxide is delivered as either a fixed 50/50 mixture with oxygen or in titratable concentrations of 30–70%. Onset of action generally takes place within 2–3 min, and its effect rapidly ends when the gas is discontinued. Nitrous oxide may also be combined with an opioid analgesic for more painful procedures such as joint taps, but this combination can induce moderate or even deep levels of sedation. The incidence of nausea and vomiting following nitrous oxide administration is approximately 5% [9]. Challenges with inhalation equipment and appropriate waste anesthetic gas scavenging have limited the use of nitrous oxide in some locations.

Chloral hydrate has been used as a sedative hypnotic agent for more than 100 years. It is particularly useful for inducing a sleep state in children younger than 2 years of age for a nonpainful procedure such as a CT/MRI scan or an auditory brain stem response (ABR) test for hearing. Chloral hydrate is administered orally, with an onset of action usually within 20–30 min, although onset of action can be somewhat variable. Duration of action can be even more unpredictable. Most children sleep for 60–120 min, but the long elimination half-life of chloral hydrate occasionally can result in prolonged sedation states that can last more than 12 h. Because of the unpredictable duration of action, there have been reports of serious adverse events and even death following discharge for children who received chloral hydrate for sedation [10]. Rates for successful sedations are between 85% and 95%. In rare instances, younger children never achieve the depth of sedation required to complete the associated procedure. The rate of failed sedation increases markedly for children over the age of 3 years. Although chloral hydrate administration is generally associated with a moderate level of sedation and rarely with res-

piratory depression, the incidence of respiratory complications is higher in infants, especially those younger than 2 months of age [24].

Barbiturates, most commonly pentobarbital, have also been mainstays of sedation for nonpainful pediatric procedures in the past. Although the use of pentobarbital has been largely supplanted by newer agents such as propofol and dexmedetomidine, it is still used for moderate sedation for procedures such as MRI scans. The advantages of pentobarbital include its 1–2 min IV onset time, the ability to provide repeat dosing in as little as 5–10 min, and limited respiratory and hemodynamic effects in otherwise healthy children. However, children with underlying respiratory or cardiovascular issues may be more susceptible to associated cardiopulmonary instability. Although children can become quite deeply sedated, and even anesthetized, with pentobarbital, it does not provide any analgesic effects. The disadvantages of using pentobarbital for procedural sedation include its potential for prolonged deep sedation and unpredictable recovery time, which can range from 60 min to more than 12 h, as well as its association with recovery dysphoria and agitation (unaffectionately labeled "pentobarb rage") [25].

Dexmedetomidine is a relatively new, highly selective central alpha-2 adrenergic receptor agonist with both sedative and analgesic properties. Already in use as an intensive care unit sedative analgesic, dexmedetomidine has migrated to the procedural sedation arena, where it is a preferred agent for many providers because of its limited effects on respiration. Dexmedetomidine is generally associated with a moderate level of sedation that, according to electroencephalogram (EEG), mimics normal sleep. Therefore, many pediatric neurologists prefer dexmedetomidine for children who require sedation for successful completion of EEGs. Dexmedetomidine has also proven to be useful for the sedation of children with autism or other developmental concerns, as the recovery period seems to be associated with a much less troublesome emergence [26]. Most often, dexmedetomidine is administered as an IV agent, with a slow initial bolus over 5–10 min followed by a continuous infusion; it also can be given orally or buccally with good success. Dexmedetomidine can be associated with clinically significant cardiovascular effects, especially bradycardia, because of its effects on cardiac conduction times.

Many children's hospitals have built their sedation programs around the sedative/anesthetic agent propofol. By far the most commonly used agent for pediatric procedural sedation, it is used both as a single agent for nonpainful procedures such as CT, MRI, and ABR testing, and in combination with analgesics such as ketamine and fentanyl for a variety of painful procedures. Propofol is administered intravenously and its many advantages include onset in 30–60 s, offset generally in 5–15 minutes, and ease of titration to effect. For longer procedures, bolus propofol is used for induction, and deep sedation is maintained by a continuous IV infusion. Propofol use is associated with a high incidence of respiratory depression and induction can easily lead to rapid loss of airway reflexes and apnea [27]. Physicians who administer propofol must be able to rescue patients from a general anesthetic state and have expertise in both BVM ventilation and endotracheal intubation. Because of the risk of rapid respiratory decompensation, some

hospitals restrict the use of propofol to anesthesia providers. In addition, propofol can lead to bradycardia and hypotension, although these effects are typically mild and do not become clinically significant in otherwise healthy children.

For decades, opioids have been the most commonly administered analgesic medications. Although they have no inherent amnestic qualities and limited sedative effects when used independently, they may be used in combination with sedative/hypnotic agents to facilitate deep sedation for painful procedures. Fentanyl is the most commonly used procedural opioid because of its pharmacokinetic profile and low cost. The onset of an IV dose of fentanyl occurs within 2–3 min, with peak effect at 5 min. This more rapid onset allows for more titratable dosing for procedural analgesia than morphine, which has an onset of action of 5–10 min. As with all opioids, fentanyl leads to dose-dependent respiratory depression, especially when used in combination with another sedative agent.

Ketamine is a favorite medication to facilitate sedation for painful procedures in the emergency department. Ketamine is a derivative of phencyclidine and it is uniquely associated with sedative, dissociative, amnestic, and analgesic properties. At lower doses, ketamine leads primarily to anxiolytic and analgesic effects. With higher doses, ketamine produces antegrade amnesia and a dissociative state of sedation/anesthesia. On awakening, children often report having experienced very vivid dreams or hallucinations. Ketamine may be administered via IV, intramural, oral, rectal, or nasal routes. Deep levels of sedation are generally achieved. Typically, patients maintain spontaneous respiratory drive and adequate airway-protective reflexes, although ketamine is a sialagogue, and the additional saliva it produces can increase the risk for laryngospasm. Ketamine also leads to increased heart rate, BP, and cardiac output in previously hemodynamically stable children. Unique side effects associated with ketamine include a potential increase in intracranial and intraocular pressure as well as negative neuropsychiatric effects with emergence delirium and significant agitation. The incidence of vomiting with ketamine sedation ranges from 12% to 25% but does seem to be decreased with the coadministration of midazolam and/or ondansetron.

5.9 Postsedation Recovery and Discharge

Ongoing monitoring and observation are critical during recovery from procedural sedation and should continue until the child's vital signs and level of interaction have returned to their presedation baselines. Significant adverse events can occur during emergence, especially if medications with longer half-lives were used. The recovery area should be equipped with the same monitoring and resuscitation equipment as the sedation and procedural area itself, and the same rescue resources should be available. Children should be discharged only when they have met specific preestablished recovery criteria and after the family has received detailed instructions for postsedation care, including instructions on how to seek follow-up medical care if needed.

5.10 Conclusions

Pediatric sedation requires careful consideration of the balance between the patient's risk factors, the procedure being performed, and the provider's experience and expertise. With appropriate preparation, physicians can offer safe and effective procedural sedation to meet the needs of their pediatric patients.

Sedation and analgesia in children for procedures outside the operating room are rapidly expanding, and are being driven to be more cost-effective and efficient. Highly motivated and organized sedation/anesthesia services are likely to reduce serious adverse outcomes, but minor adverse events are actually common. The majority of the adverse events associated with pediatric sedation and analgesia are respiratory/airway-related, which can be managed with simple maneuvers. There should be a real collaboration between the anesthesiology department and other concerned departments to enhance the safe and effective management of pediatric sedation and analgesia outside the operating room.

5.11 Future Developments

With the increasing frequency of diagnostic and therapeutic procedures in children, the demand for sedation and analgesia for children outside the operating room setting is exceeding the capacity of anesthesia services. The number of children requiring sedation outside the operating room may approach the number of children requiring anesthesia in the operating room in 5 years time, and as a result, more nonanesthesiologists could be asked to provide procedural sedation outside the operating room. Hospitals are likely to set up multidisciplinary pediatric sedation teams that will not only administer procedural sedation, but will also be responsible for training and credentialing for all nonanesthesiologists in procedural sedation. The anesthesiology department should collaborate with other providers and establish structured training involving human simulation, with emphasis on critical events. There is a need for pharmacological agents with minimal respiratory and cardiovascular depression; newer drugs such as the alpha-2 adrenergic receptor agonist dexmedetomidine offer significant advantages and huge potential for widespread use. The use of brain function monitors, such as the BIS, and respiratory monitors, such as end-tidal CO_2 monitoring, will be routinely used to provide safe and effective sedation. Results from the pediatric sedation research consortium and other studies could help us identify strategies to prevent and manage adverse events during procedural sedation in children.

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