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Sedation for pediatric dental patients

Michael D. Webb, DDS[a,b,c],
Paul A. Moore, DMD, PhD, MPH[d,*]

[a]*Department of Pediatric Dentistry, Baylor College of Dentistry, USA*
[b]*Clinical Department of Dentistry, Children's Medical Center of Dallas, USA*
[c]*Texas Scottish Rite Hospital for Children, USA*
[d]*Department of Dental Public Health, University of Pittsburgh School of Dental Medicine, 552 Salk Hall, 3501 Terrace Street, Pittsburgh, PA 15261, USA*

There are few areas of dental therapeutics as controversial as the pharmacologic management of fearful and uncooperative pediatric dental patients. A pediatric dentist is faced with one of the most difficult tasks in our profession: maximizing comfort and cooperation while minimizing risks and costs of dental care for the unmanageable child. Pharmacosedation provides the means for children to avoid psychologically traumatic experiences that might inhibit regular oral health care when they become adults. By controlling disruptive behaviors, the pediatric dentist is able to provide quality dental care in an environment that is pleasant for the child, the parent, and the practitioner.

It is generally agreed that most fearful and uncooperative children can and should be managed with behavioral (nonpharmacologic) management procedures [1]. These include behavior modification techniques such as tell-show-do, positive reinforcement, controlled expectations, modeling, and suggestion. Unfortunately, there is a small percentage of the pediatric population that cannot be successfully managed solely through behavioral management techniques. When behavioral management strategies fail, some form of pharmacologic sedation or anesthesia may be a valuable and necessary alternative.

The sedative agents and techniques used by dentists who treat children vary with the practitioner's experience and training. Dentists with limited knowledge and experience in providing sedation to children should adhere to single drug regimens that have a wide margin of safety. Conversely,

* Corresponding author.
E-mail address: pam7@pitt.edu (P.A. Moore).

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pediatric dentists and practitioners who have advanced training in anesthesiology and management of sedation complications in the pediatric population may elect to use multiple drug regimens that are likely to produce deeper levels of sedation.

Levels of sedation and anesthesia have been classified by the American Dental Association into three categories: conscious sedation, deep sedation, and general anesthesia [2]. None of these anesthetic strategies is ideal for treating all pediatric patients (see box below). Sedation regimens that provide conscious sedation for young, uncooperative patients are not effective for every child. Deep sedation techniques are also less than 100% successful and require added anesthesia training or certification for their safe and proper use. General anesthesia is an effective and reliable means of treating unmanageable pediatric patients but is expensive, inconvenient, and not without added risk [3].

Drugs commonly used to produce conscious sedation are nitrous oxide, opioids, benzodiazepines, chloral hydrate, barbiturates, and antihistamines (Table 1). Oral administration is the most common route of administering sedative agents to children. It is recommended that preoperative medications not be administered outside the treatment facility: chloral hydrate, opioids,

Definitions of sedation/anesthesia[a]

Conscious sedation

A minimally depressed level of consciousness that retains the patient's ability to independently and continuously maintain an airway and respond appropriately to physical stimulation and verbal command.

Deep sedation

An induced state of depressed consciousness accompanied by partial loss of protected reflexes, including the inability to continually maintain an airway independently and/or to respond purposefully to verbal command.

General anesthesia

An induced state of unconsciousness accompanied by partial or complete loss of protected reflexes, including the inability to independently maintain an airway and respond purposefully to physical stimulation or verbal command.

[a] American Dental Association. The use of conscious sedation, deep sedation, and general anesthesia in dentistry. Chicago: American Dental Association; 1996.

Table 1
Sedation regimens for pediatric dental patients

Agent	Formulation	Dosage	Route	Onset time	Comments
Chloral hydrate					
Chloral hydrate syrup	500 mg per 5 ml	50–60 mg/kg	PO	30–45 min	Chloral hydrate is irritating to mucosa Nausea and vomiting may occur Multiple drug interactions
Opioids					
Meperidine (Demerol®)	50 mg per 5 ml	2.0 mg/kg	PO	45–60 min	Poor bioavailability orally Respiratory depression may occur Increases local anesthetic toxicity
Fentanyl Oralet®	200 mcg	5–15 mcg/kg	Transmucosal	20–30 min	Child's minimum weight must be 15 kg
	300 mcg	5–15 mcg/kg	Transmucosal	20–30 min	Severe hypoventilation possible
	400 mcg	5–15 mcg/kg	Transmucosal	20–30 min	Limited to hospital setting only
Benzodiazepines					
Midazolam (Versed®)	5.0 mg per ml	0.5–0.75 mg/kg	PO	15–20 min	Usual maximum dose is 15 mg
	1.0 mg per ml	0.2–0.3 mg/kg	Intranasal	10–15 min	Short half-life (106 min)
Diazepam (Valium®)	2-, 5-, 10-mg tablets	0.15–0.25 mg/kg	PO	30–60 min	Effective for 6–12-year-old anxious children
	5 mg/5ml		PO		Usual maximum dose is 15 mg
Inhalational sedation					
Nitrous oxide/oxygen	Pure gases	25–60%	Inhalational	2–4 minutes	Effective for mild to moderate anxiety Waste gases must be controlled Rapid elimination and recovery

and other sedatives should be administered in the controlled environment of the dental facility. Many pediatric dentists have decreased their use of parenteral sedation in response to concerns of safety, state certification requirements, and malpractice costs. The goal of sedating the pediatric dental patient is to safely control the child's behavior so that quality dental care can be provided while helping the child cope with the stress of dental treatment. These goals may not always be met with conscious sedation techniques. Deeper forms of sedation or general anesthesia may be needed to provide necessary dental care to uncooperative children.

Sedation is not a substitute for effective local anesthesia. Dosage guidelines for local anesthesia based on weight should be strictly followed. Multiple drug techniques that include opioids seem to pose even greater problems when local anesthesia dosages are exceeded because of the significant incidence of serious side effects and the difficulty of managing the life-threatening respiratory emergencies that may develop [4,5]. A more detailed discussion of adverse reactions to local anesthetics is presented elsewhere in this issue of the *Dental Clinics of North America*.

Nitrous oxide inhalation sedation

Nitrous oxide is used in pediatric dentistry to induce relaxation and to modify the noxious stimuli of dental treatment. It may be used as the sole sedative agent or as an adjunct to other agents. Its unique pharmacokinetics and proven safety record support its continued use in pediatric dentistry [6].

The absorption of N_2O through the pulmonary alveoli is rapid, with blood levels and clinical effects being seen within minutes of its administration [7]. The distribution of N_2O is limited when compared with other anesthetic gases and therefore large tissue reservoirs of the gas that would delay recovery are not established. Metabolism of N_2O is essentially nonexistent and excretion rapidly occurs primarily through the lungs at a rate similar to its absorption. The clinical consequences of N_2O's unique pharmacokinetics include rapid induction and recovery, ability to titrate and adjust to desired sedative endpoint, and reversibility.

The induction process for a child who is familiar with nitrous oxide/oxygen inhalation sedation can be nearly complete in 3–5 minutes. Children who have not experienced the effects of nitrous oxide need more explanation of the experience and require a slower, more controlled induction. Subjective symptoms such as tingling of the extremities or a feeling of warmth usually occur within the first few minutes.

Within 5–10 minutes after discontinuing nitrous oxide, the patient has eliminated most of the gas from the body. Because of a higher cardiac output, recovery may be more rapid in children than adults. After a 10–15 minute observation period, full recovery is apparent and the child may usually leave the office and return home.

Because of rapid elimination during the initial 3–5 minutes, large volumes of nitrous oxide are exhaled. As nitrous oxide leaves the plasma and enters the alveoli, it dilutes the ambient air (21% oxygen) that is being inhaled. The result is a theoretic drop in the oxygen concentration to hypoxic levels, frequently referred to as "diffusion hypoxia." In clinical practice, diffusion hypoxia is not a significant problem when administering N_2O sedation. A child who has received nitrous oxide:oxygen sedation has been breathing high concentrations of oxygen (at least 40–50%) and the excess oxygen prevents the dilution of oxygen in air [8]. Diffusion hypoxia is likely to be a problem only after general anesthesia in which the nitrous oxide:oxygen ratio is often higher (75%:25%) and other respiratory depressant drugs have been administered [6]. Nevertheless, a common practice in dentistry is to administer 100% oxygen at the conclusion of nitrous oxide sedation. This procedure has been recommended primarily because it is believed to prevent nausea [9].

The rapid elimination of nitrous oxide permits the pediatric dentist to reverse the effect of the sedation. This reversibility is one of the major reasons for nitrous oxide's record of safety. If a child becomes unexpectedly oversedated, the nitrous oxide concentration can be decreased and the child immediately returns to a more comfortable level of sedation.

One of the absolute advantages of nitrous oxide's rapid absorption and elimination is that the sedative effects can be adjusted to the amount of stimulation that occurs during the procedure. By adjusting the concentration, the sedation can be titrated to the child's moment-to-moment needs.

Pediatric dentists commonly use nitrous oxide/oxygen inhalational sedation. A survey of members of The American Academy of Pediatric Dentistry indicated that 85% of the respondents used nitrous oxide/oxygen analgesia with most using it more frequently than five times per week [10]. In a study that looked at the effect of nitrous oxide-oxygen on physiologic and behavioral parameters in children, there were significant reductions in adverse behavior with no effect on oxygen saturation when a nitrous oxide-oxygen mixture was compared with 100% oxygen [11]. Nitrous oxide has been combined with other agents to provide additive sedative effects. It has been found to augment the effects of diazepam and to result in "deep" rather than "conscious" sedation when combined with chloral hydrate [12–14]. Nitrous oxide-oxygen analgesia seems to be a safe and useful tool in the sedation of pediatric dental patients.

Opioid sedation

Opioid analgesics decrease a patient's psychologic reaction to painful stimuli, produce sedation, and reduce disruptive motor activity. Side effects of opioids include nausea and vomiting that is induced by direct stimulation of the chemoreceptor trigger zone [15]. Respiratory depression, a consequence of decreased sensitivity to CO_2, may also be seen [16]. An estimate

of the comparative frequency of these two side effects reveals that mild respiratory depression is more commonly observed than nausea and vomiting [17].

When used for pediatric sedation, the dosage ranges for opioids are invariably higher than required for analgesia. For example, the recommended dosage guidelines in pediatric dentistry are up to 2.0 mg/kg for meperidine (Demerol®). When used concomitantly with other central nervous system (CNS) depressant drugs, these guidelines should be adjusted downward [4,18].

Sedation using opioids has maintained a degree of popularity among pediatric dentists. The most common opioid used for oral sedation in pediatric dentistry is meperidine. It is rapidly absorbed from the gastrointestinal tract and has an onset of 30–60 minutes. First-pass metabolism breaks down nearly 75% of the administered dose. The maximum clinical effect is seen after approximately 1 hour with a duration of action of less than 2 hours. Supplemental drugs frequently used for their added sedative effects and antiemetic effects are promethazine and hydroxyzine [4].

A less commonly used oral opioid sedation technique is oral transmucosal fentanyl citrate (OTFC). This formulation is available as a lozenge on a plastic stick (Fentanyl Oralet®). The child sucks on the lozenge and slowly releases the sedative drug, fentanyl, into saliva, that is then absorbed across the mucous membranes of the oral cavity. The advantages of the OTFC are patient acceptance, rapid onset, and a high bioavailability compared with oral administration that must undergo significant first-pass metabolism [19,20]. Three different formulations are available (200, 300, and 400 micrograms), depending on the child's weight. Dosing recommendations are for 5–15 mcg/kg; doses higher than 15 mcg/kg are contraindicated because they are associated with an excessive frequency of hypoventilation [21]. The use of a pulse oximeter is necessary during administration. Once the desired level of preoperative sedation is achieved, the lozenge should be removed. The formulation is marketed only to hospitals and monitored anesthesia care settings. Respiratory depression, hypotension, itching of the eyes and nose, nausea, and vomiting have been reported [20,22].

Benzodiazepine sedation

Although benzodiazepines have been used extensively in the management of adults who are anxious and fearful of dental procedures, their clinical use in pediatric dentistry has only recently been initiated. The benzodiazepines lack significant respiratory depressant effects at therapeutic doses. There is a specific benzodiazepine antagonist available (flumazenil) that can reverse the central nervous system (CNS) depressant effects seen with overdose [23,24].

Diazepam has been used to provide sedation of pediatric dental patients. Although the drug's elimination may be delayed in the neonate, the pharmacokinetics of diazepam seems to be similar for young children and adults. It

has an apparent long duration of action caused by an active metabolite, desmethyldiazepam, that is slowly eliminated and retains some sedative activity.

In pediatric dentistry, diazepam seems to be an effective sedative, particularly if the lack of cooperation is from fear and apprehension [25]. Its large therapeutic index and linear dose-response relationship are valuable assets for a pediatric sedative that is administered orally [26,27]. The recommended dose for oral diazepam is 0.15–0.25 mg/kg given 1 hour before the appointment.

Newer benzodiazepine derivatives such as midazolam and triazolam are now being studied to determine appropriate dosages and to address safety concerns in younger children [28–30]. Midazolam offers the advantage of having a shorter onset and duration of action. It is commonly used as a preanesthetic sedative and is becoming popular in pediatric dentistry. There is a flavored oral preparation available that has eliminated the need to mix the intravenous formulation in a vehicle to make it palatable. The dosage regimen of midazolam for pediatric dentistry is 0.5–0.75 mg/kg, administered approximately 30 minutes before the procedure. Duration of action is approximately 30 minutes. A shorter onset period may be an advantage in some clinical situations. Triazolam has not gained widespread acceptance in pediatric dentistry in part because few studies have demonstrated its safety or efficacy in children undergoing dental procedures. The lack of a commercially available liquid formulation of triazolam also limits it usefulness as a pediatric premedicant.

In addition to oral administration of various benzodiazepines, intranasal administration of midazolam, a water soluble, short-acting benzodiazepine, has been evaluated clinically because of its rapid onset (10–15 minutes) and rapid elimination [31]. Although the drug is reliably absorbed, the formulation is somewhat irritating and may cause stinging and discomfort when initially administered. Dosages of 0.2–0.3 mg/kg have been reported to provide adequate sedation with rapid onsets and minimal delay in recovery [22].

Chloral hydrate sedation

Liebig first introduced chloral hydrate into practice in 1832 and it is the oldest and best-studied sedative-hypnotic used in pediatric dentistry. The sedative-hypnotic activity of chloral derivatives is probably caused by the active metabolite trichloroethanol. Following absorption, chloral hydrate is rapidly metabolized to trichloroethanol (TCE) and to a lesser extent to trichloroacetic acid (TCA). Plasma half-life of TCE is estimated to be 8 hours. Peak plasma concentrations of TCE are reached in 20–60 minutes. Plasma concentrations of chloral hydrate are nearly undetectable after oral dosing. Rectal absorption of chloral hydrate formulations containing polyethylene glycol vehicles is nearly as rapid as oral absorption, although somewhat less complete [32,33].

Although definitive studies in children are sparse, it is generally assumed that therapeutic doses of chloral hydrate have minimal effects on respiratory and cardiovascular function [34]. Changes in respiratory function (pCO_2, respiratory rate, tidal volume) are comparable to natural sleep. Asthmatic patients may be somewhat more sensitive to chloral hydrate's minimal respiratory depressive properties [35]. The CO_2 chemoreceptor response seems to be unchanged in infants administered 50 mg/kg chloral hydrate [36].

The primary pharmacologic effect of chloral hydrate is CNS depression. Signs and symptoms following ingestion of increasing doses of chloral hydrate progress from relaxation, lethargy, drowsiness, and hypnosis to loss of consciousness and coma. Given alone, chloral hydrate provides measurable sedation at doses more than 40 mg/kg with therapeutic doses ranging from 50–60 mg/kg. When administered in combination with other CNS depressants, a lower dose of chloral hydrate also may be effectively prescribed [37].

Adverse effects of chloral hydrate administration are rare. When used as a hypnotic, untoward reactions occur in approximately 2% of cases. Overt CNS depression, characterized by disorientation, and prolonged drowsiness account for half of these reactions. The reports of reactions in dental premedication are generally similar although dose-related reactions such as prolonged CNS depression and vomiting occur more frequently in younger ambulating populations. With extremely high doses of chloral hydrate (ie, 75 mg/kg) a significant incidence of vomiting has been reported [38]. The maximum recommended dose in children, irrespective of body weight, is 1000–1500 mg [39].

Chloral hydrate may induce cardiac arrythmias, and in overdose situations cardiac arrest has been reported [34]. Cutaneous reactions to chloral hydrate, although described frequently in textbooks, seldom occur. Skin eruptions are usually erythematous, eczematous, and scarlatiniform [40]. Fixed eruptions, skin lesions occurring at the same site on repeated administration, have also been reported [41].

Chloral hydrate has been implicated in a variety of drug interactions. As one might expect, chloral hydrate produces additive CNS depression when administered with other sedatives. This additive drug interaction permits one to decrease the dose of both depressants, thereby limiting the side effects of the drugs. The reduced dosages when chloral hydrate is combined with the antiemetic promethazine have been shown to appreciably decrease the incidence of nausea and vomiting [38,42]. Nitrous oxide/oxygen in combination with 60 mg/kg chloral hydrate may increase the level of CNS depression to such an extent that the child's protective reflexes may be compromised [14].

Three inadvertent overdose reactions have been described by Hayden [43]. These mishaps were caused by either incorrect calculation of dose or lack of communication among the dentist, staff, parent, and patient. A low dose (250 mg) has reportedly induced laryngospasm and cardiac arrest when chloral hydrate elixir, a known irritant to mucous membranes, was rapidly introduced into the oropharynx with a syringe.

Because vomiting is frequent with doses greater than 60 mg/kg, consumption of a large overdose is often prevented. In children, hypotension and cardiac arrhythmias commonly occur with overdose. These symptoms are distinctly different from local anesthetic or narcotic overdose in which convulsions and respiratory depression are usually reported. The high incidence of nausea and vomiting, concerns for its possible mutagenicity, and the risk for cardiovascular collapse have decreased the use of chloral hydrate in recent years.

Barbiturate sedation

The barbiturate sedative-hypnotics were the primary therapeutic agents for treating anxiety and induction of sleep before the introduction of benzodiazepines. As premedicants in pediatric dentistry, the most frequently prescribed agents are secobarbital and pentobarbital [44]. The barbiturates produce dose-dependent effects ranging from relaxation and sedation to hypnosis and general anesthesia. They have minimal effects on respiratory function at therapeutic doses although respiratory drive may be inhibited at higher doses.

The use of barbiturates in pediatric dentistry has been limited for two reasons: their reputed ability to induce paradoxic excitement and their limited therapeutic dosage range. Inadequate doses are ineffectual and may actually cause some uncooperative children to become more unmanageable. Even at higher doses in the therapeutic range, a few children, particularly when stimulated, demonstrate paradoxic excitation [45]. This reversal of sedative effects, seen with less than 5% of pediatric patients, may be caused by barbiturates' anti-analgesic properties or may be attributable to respiratory depression and subsequent agitation.

Precautions

Overall, the safety and efficacy of pediatric pharmacosedation is a function of a practitioner's ability and preparedness, drug and dosage selection, and awareness of a child's unique physical and psychologic makeup (see list below).

- Unique characteristics of pediatric sedation
- Child's weight and volume of distribution
- Unique physical anatomy
- Responsiveness to oral sedatives
- Limitations for route of drug administration
- Psychologic makeup and coping skills

When compared with adults, pediatric patients have unique characteristics that seem to increase the risks associated with sedation [3]. The most obvious anatomic difference between the adult and pediatric patient is body size. An increased awareness of dosage adjustment in pediatric patients has

developed in the last few years within dentistry. Available data as reported by Aubuchon's survey [46], and by Moore and Goodson's case report analysis [5] reinforce the belief that serious adverse reactions in pediatric sedation are commonly caused by inadequate weight-based dosage reduction.

The pediatric airway anatomy is an important factor in airway complications when sedating children. Infants and young children have narrow nares, a large tongue, a high glottis, and slanting vocal cords. In an infant, the narrowest point of the upper airway may be at the level of the cricoid ring rather than the vocal cords. Airway obstruction is therefore more likely to occur below the vocal cords in pediatric patients [47]. Additionally, because of the smaller caliber of the airway passages, acute bronchial inflammation can present a significantly more severe obstruction in younger patients. Because children have significantly higher metabolic rates, hypoxia develops rapidly when airway obstructions occur.

Children's responsiveness to sedatives may differ from that of adults because of differences in pharmacokinetics or pharmacodynamics. Fortunately, differences in drug absorption, distribution, and excretion occur primarily in the perinatal period and are usually not relevant to office practice, where treatment is usually limited to children over 2 years of age.

It has been reported that young children may be unexpectedly sensitive to the CNS depressants used for sedation in pediatric dentistry. Transient airway obstruction was seen in 4 of 15 preschool children who were administered 60 mg/kg of chloral hydrate in combination with nitrous oxide. These four children were found to be among the youngest in this treatment group [14]. This finding supports empiric findings by Grimes, who recommends reducing weight-based dosages for patients under 2 years of age [48]. Wilson reported a similar response and believed that children with large tonsils and adenoids were most at risk [49].

Children, particularly uncooperative preschool children, come to a dental office under circumstances different from those of adults. Although children are anxious and fearful, unlike adults, they have not arrived at a dental office of their own desire. A 2- or 3-year-old does not consider acquiring good dental health a significant motivator to tolerate treatment and, in fact, sees no obvious benefits in cooperating with therapy. Additionally, children lack experience with uncomfortable situations and have inadequate coping skills with which to tolerate treatment. These differences in a child's psychologic development limit the success of any sedation therapy in many instances.

As a consequence of these differences, dose-response curves for sedatives used in pediatric dentistry are flat, placebo effects seem nearly comparable to effective doses, and high failure rates are frequently reported [14,50]. Strategies for correcting these pharmacologic inadequacies, such as remedicating unsuccessfully sedated patients and using a variety of drug combinations, may increase the likelihood of adverse responses. Using large doses of synergistic agents decreases the therapeutic index of sedation procedures and significantly affects the overall safety.

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