Considerations for the Use of Enteral Sedation in Pediatric Dentistry

Jeffrey S. Yasny*/ Ali Asgari **

Treating an uncooperative, uncontrollable child can be unpleasant for all parties involved. Despite the dentist's best efforts to employ traditional techniques, the behavioral management of challenging pediatric dental patients often requires more than "tell, show, do." Consequently, pre-operative pharmacological intervention may be necessary. Enteral sedation may be the optimal adjunct for the dental treatment of such a challenging patient population. However, it must be utilized with caution and is not an appropriate treatment modality for all. This paper will present various considerations for the safe, appropriate and effective use of enteral sedation in contemporary pediatric dentistry. With the strong demand for this service, properly trained practitioners can broaden their practice and provide a win-win scenario for themselves and their patients.

Keywords*: enteral sedation, oral sedation, anesthesia, pediatric dentistry*
J Clin Pediatr Dent 32(2): 85–94, 2007

INTRODUCTION

In the pediatric dental practice, patients present the practitioner with a wide variety of challenges that may preclude treatment, despite the dentist's best efforts to employ traditional behavioral management techniques. Interacting with an uncontrollable child who is screaming, crying, and/or throwing a tantrum is unpleasant for all parties involved. It is also unsafe, and often unsuccessful. At the end of this type of appointment, the parents may be exasperated, the dentist and his/her staff may feel fatigued and disappointed, and the child may remain untreated and perhaps psychologically scarred with a poor association with the dental office. Not exactly a win-win-win situation. Since optimizing the patient's dental experience is the common goal, the behavioral management of challenging pediatric dental patients may require more than "tell, show, do". Thus, in certain circumstances, the need for pre-operative pharmacological intervention may be warranted. However, careful considerations must also be addressed prior to proceeding with such a treatment plan. This paper will present various considerations for the safe, appropriate and effective use of enteral sedation in contemporary pediatric dentistry.

* Jeffrey S. Yasny, DDS, FADSA Assistant Professor, Departments of Dentistry and Anesthesiology, The Mount Sinai School of Medicine

** Ali Asgari, Practicing Pediatric Dentistry in New York City

Send all correspondence to: Jeffrey S. Yasny, Assistant Professor, Mount Sinai School of Medicine, Department of Anesthesiology, One Gustave L. Levy Place, Box 1010, New York, New York 10029-6574

Telephone: (212) 241-7467
Fax: (212) 876-3906

E-mail: jeffrey.yasny@mssm.edu

The need for sedation in pediatric dentistry

The practice of pediatric dentistry has certainly changed over the past several decades. While dental materials and clinical techniques have made impressive progress, the pediatric dental population itself seems to have experienced a qualitative transformation. Supporting this statement was the survey of pediatric dentists that found children are less cooperative than in previous years. This conclusion was attributed to changes in parenting styles, primarily the failure of parents to set limits on children's behavior.[1] While the high caries rate in children may be associated with patients of a lower socioeconomic status,[2] it seems that over the past few decades the overall behavior of children in general has not improved significantly, and may have become even more challenging for the pediatric dentist.[3]

The source of the behaviorally challenging patient may be one of extreme fear or apprehension, a young or emotionally challenged child who cannot cooperate, or a patient with cognitive impairment who is unable to cooperate. So how does one proceed with such challenges? Initially, the most conservative behavioral approach should be attempted. However, some patients may have experienced multiple dental visits that employed conventional behavioral techniques unsuccessfully, without achieving any treatment. While not every child is a candidate for sedation, it should be noted that not every child will respond to "tell, show, do" either.

Without pharmacological intervention, the patient may be at risk for psychological and/or physical trauma. For the dentist, attempting to treat an otherwise uncooperative child can result in a difficult, stressful, and dangerous task.[4] Moreover,

if the practitioner plans to use invasive rotary instrumentation for a patient who may become wildly combative, it may inevitably place the child in harm's way.[5] Passive restraint may also prove to be insufficient for some of these patients. Sedating the patient may be the only effective means of treating them.[6] Therefore, it may be necessary to consider an adjunctive form of treatment (i.e. enteral sedation), upon weighing the associated risks and benefits.

Advantages and disadvantages of enteral sedation

Common routes of administration for sedation in dentistry have been defined as enteral (i.e. oral, sublingual, rectal) in which the agent is absorbed through the gastrointestinal (GI) tract or oral mucosa; or parenteral routes (i.e. intranasally, intramuscularly, intravenously, submucosally, subcutaneously), whereby the drug bypasses the GI tract.[7]

There are several significant advantages of utilizing enteral sedation as an adjunct to dental treatment for a fearful or uncooperative patient. The lack of needles can diminish a patient's fear; it is generally accepted by patients; easy to administer; and the cost of medications is minimal to the practitioner. Also, there is a decreased incidence and severity of adverse and allergic reactions to medications when administered orally. Enteral sedation may also serve as an effective "middle ground" therapy between the traditional non-pharmacological approach and general anesthesia. However, sedation is not without risk. If not administered carefully, by properly trained professionals, it has the potential for serious or dire consequences including an unexpectedly deep sedation, respiratory depression, cardiac arrest and death.[8,9]

Consequently, the disadvantages of this treatment modality must also be examined. The success of enteral sedation is initially dependent on the patient's ability or willingness to take the medication (i.e. compliance), which may not be possible in severely phobic or behaviorally challenging individuals. Compared with intravenous administration, the onset of action is slow (i.e. the latent period is relatively long), usually 30-60 minutes. Moreover, there is a lack of control over the drug's action. Once administered to the patient, the practitioner does not have the ability to titrate to effect (i.e. lighten or deepen the level of sedation). The results are less predictable due to a first pass effect and a variable absorption from the gastrointestinal tract. Furthermore, the prolonged duration of action can also affect optimal recovery times.[10]

Patient assessment as a candidate for sedation

Minimizing the potential morbidity involved with sedation requires several considerations prior to the sedation appointment. Of paramount importance is appropriate patient selection. Not everyone is an acceptable candidate for this treatment. Prior to the sedation a complete history and physical should be performed; ideally by the patient's pediatrician. A review of the patient's past medical and surgical histories, current medications and any known drug allergies should also be documented. The physical status of patients treated in the dental office for enteral sedation should belong to either one of the following two classifications: A healthy patient without systemic disease (A.S.A. I), or a patient with mild systemic disease (A.S.A. II).[11] In addition, the patient should be evaluated for their ability and willingness to cooperate. For example, a mentally or physically handicapped child who is incapable of undergoing the dental procedure without the use of sedation must be evaluated thoroughly.[12] The psychological and physical age of the child and whether or not they coincide, must also be determined in order to estimate the potential for successful acceptance of the treatment.[13]

Importance of airway assessment and management

The patient's airway must be meticulously assessed. For the practitioner involved with the sedation, airway management is vital. Patients should be able to maintain their own patent airway and their normal physiological reflexes should be intact if enteral sedation is the desired method of sedation. An examination of the patient may reveal enlarged tonsils which can compromise the airway during a sedation.[14] Additional anatomic considerations such as macroglossia, micrognathia, limitations of mouth opening or neck mobility which could potentially compromise the airway must be addressed prior to the sedation. For example, patients with micrognathia may have an associated syndrome such as Pierre-Robin's, Treacher-Collins, Goldenhar's, Cornelia de Lange, or mucopolysaccharidosis that likely negates this type of treatment.[15] Furthermore, patients with obstructive sleep apnea (O.S.A.) are generally not good candidates for this therapy. It was found that the perioperative risk to patients increases in proportion to the severity of sleep apnea.[16]

If an upper respiratory tract infection (URI) is suspected preoperatively, the practitioner is faced with an interesting dilemma. One must thoroughly assess the risk/benefit ratio prior to proceeding with the sedation. In the past, there was a blanket cancellation of surgery for the child with a URI; however, more recent literature supports the cancellation on a more selective, case-by-case basis.[17] A national survey of anesthesiologists found that younger practitioners with less than 10 years of experience are less likely to cancel a procedure due to a patient's URI than their more experienced colleagues.[18] Emotional and economic burdens may also be placed on the parents due to a cancellation.[19] In addition, it is common for children to experience six to eight URIs per year, and young children attending day care or nursery school may demonstrate an even higher frequency annually.[20] As a result, it may be difficult to precisely find a convenient, symptom-free time for an elective procedure such as dental treatment.

The patient should be evaluated for signs and symptoms of an URI including the following: fever, dyspnea, productive cough, sputum production, nasal congestion, wheezing and lethargy.[21] Nasal congestion, sputum production, and a history of reactive airway disease have been identified as predictors of adverse respiratory events.[22,23] Moreover, it has

been found that airway hyperreactivity persists for several weeks following an URI.[24,25] Therefore, when deciding whether to proceed or not, one may consider the following suggestions: any child with severe symptoms such as a productive cough, fever of >38ºC, mucopurulent secretions, nasal congestion and lethargy should have their procedure postponed for at least 4 weeks. Children who present with an uncomplicated URI (i.e. clear secretions, afebrile), and are otherwise healthy, should be able to undergo the procedure.[26]

Preoperative guidelines for sedation

Preoperative instructions should be made clear to the parent(s) or legal guardian. Patients are not to have any food or drink for several hours prior to the sedation.[27] Refraining from the ingestion of food and liquid for hours prior to the sedation has been shown to minimize the risk of nausea, vomiting and aspiration of gastric contents.[28] Currently, the following intake restrictions are recommended: Clear liquids (i.e. apple juice, tea, water) for at least 2-3 hours. Breast milk should not be ingested for at least 4 hours prior to the procedure. Liquids such as milk and any juice containing pulp are considered to be "not clear" and are classified as solids.[29] Milk and solids should be restricted from intake for at least 6 hours for a child less than 3 years of age, and at least 8 hours for children greater than 3 years of age.[30]

Medications taken routinely in the morning by the patient should not be ignored and taken with small sips of water. Insulin or oral hypoglycemics should be avoided on the morning of a procedure involving sedation, in accordance with the fasting regimen and altered glucose levels. The patient should wear loose, comfortable clothing, remove any jewelry or optical aids, and visit the restroom prior to the procedure. Prior to proceeding with the procedure, expectations of the sedation should be clarified to the patient's parent(s) or legal guardian. It should be clearly established that this adjunct to traditional therapy may not be successful. If the dental treatment cannot be safely performed utilizing enteral sedation, it may be postponed until another day using another dose or sedation agent. Alternatively, another therapeutic mode may be required (i.e. general anesthesia). Thus, the potential for an additional appointment should be discussed ahead of the sedation in order to eliminate any heightened or false expectations. Finally, the practitioner should document the major components of the pre-operative discussion.

An unsuccessful enteral sedation may be due to any of the following reasons: a patient may not be entirely compliant, ingesting only a portion of the intended dose and limiting its effectiveness; severe patient anxiety can overwhelm the drug's action; since drug absorption through the GI tract is erratic, the desired effect of the medication(s) may be compromised; the timing of the drug to achieve peak blood levels may not coincide with the timing of the procedure; the response to medications by the patient population is a bell shaped curve whereby dosages and the desired effects do not apply universally to all patients, evident in some patients who may be classified as hypo or hyper responders. Finally, the drug type used (i.e. opiod versus benzodiazepine) may not have been ideal for that individual.

Different sedative agents

Several sedative-hypnotic agents have been utilized effectively for sedating children in the dental setting. This paper will discuss certain drugs of various classifications including benzodiazepines, antihistamines, opiods, and non-barbituates. All of these agents can be used alone, or in concert with other sedative agents to potentiate the effects of the mixture and achieve a deeper level of sedation. It is essential that any dental practitioner who opts to utilize these medications, thoroughly understands the clinical pharmacology of these drugs, and possesses the ability to initiate appropriate resuscitation during an untoward event.

Benzodiazepines- Pharmacology and physiology

Currently, benzodiazepines are the class of drugs most frequently used as an oral sedative in the dental practice. Gamma-aminobutyric acid (GABA) is the major inhibitory neurotransmitter in the central nervous system, and binds to its receptor within the protein complex of a neuronal cell membrane. Benzodiazepines attach selectively to their receptor sites located on the alpha sub-units of GABA receptors within this GABA-Chloride ionophore complex, and facilitate the inhibitory actions of GABA.[31] Benzodiazepines do not open chloride channels themselves. Rather, they enhance the chloride channel's response to GABA. The binding of GABA by agonist benzodiazepines causes a conformational change in the receptor site that opens chloride channels. Consequently, the increased influx of chloride ions hyperpolarizes cell membranes, making them more resistant to excitation and less likely to transmit an action potential.[32] GABA receptors are anatomically distributed almost entirely within the central nervous system (C.N.S.), resulting in effects on the C.N.S. primarily. Primary therapeutic effects of benzodiazepines include sedation, anxiolysis, and anterograde amnesia – all beneficial for the treatment of the fearful pediatric dental patient. These drugs possess muscle relaxant and anti-convulsant properties as well. Overall, benzodiazepines demonstrate a wide margin of safety and a wide therapeutic index which represents the dosage difference between an effective dose and a lethal dose. Its onset and duration of action are relatively short when compared with other orally administered sedatives. Minimal adverse reactions are associated with these drugs, and a reversible agent is available.

Although generally safe, some undesirable effects can occur with benzodiazepines. Particularly significant clinically is that benzodiazepines administered alone can cause respiratory depression, an effect that is amplified when given in combination with opioids.[33] Moreover, this synergistic effect causing significant respiratory depression can also occur when benzodiazepines are administered in the presence of other CNS depressants such as a patient's own medications. Untoward physiological effects may include nausea, vomiting and/or unsteady movements (ataxia). This

latter condition can manifest as a loss of head control, leading to a compromise of the patient's airway. Other undesirable responses may include a paradoxical or angry response, whereby the patient appears irritable, agitated and/or combative.[34,35] Benzodiazepines should be avoided in patients with acute narrow angle glaucoma, and are contraindicated for patients with a known allergy or hypersensitivity to them or any of their components.

Midazolam (Versed®)- Pharmacology and advantages/disadvantages

Midazolam (Versed®) is a widely used, short-acting, benzodiazepine with minimal side effects. It can be administered orally, intranasally, intramuscularly, or intravenously. Like most drugs, its onset of action varies greatly depending upon its route of administration. Intravenous administration will result in the most rapid onset of action due to its immediate deposit into a patient's circulation. However, when administered orally, the drug is exposed to metabolic clearance mechanisms in the intestine and liver, and will take longer to produce its pharmacological effects pending its eventual deposit into the circulatory system and action at receptors. For pediatric dental patients, it is commonly administered orally, in doses of 0.25 – 0.75 mg/kg, with an upper limit of up to 1.0 mg/kg.[36] An effective dose is usually 0.5 mg/kg and should not exceed the maximally recommended dose of 20 mg. In obese children, the dose should be calculated based on ideal body weight.[37] When supplied as an oral formulation, the bitter taste often requires an accompanying flavoring agent, (i.e. apple juice) for patient acceptance. In order to enhance analgesia, the sedative can be mixed with an acetaminophen elixir, at a dosage of 15 mg/kg.[38] The oral form of midazolam has a cherry flavored vehicle that can be mixed with children's flavored aspirin or acetaminophen to increase the palatability.[39] Qualities that increase its appeal over similar drugs in this class, are its relatively high lipid solubility which produces a short onset of 10-30 minutes, and that its short half-life does not tend to produce excessive sedation or recovery times. Acting on GABA receptors, it depresses the C.N.S., and has a minimal effect on the cardiovascular system. Paradoxical responses have been reported.[40]

Certain medications can potentiate or diminish the effects of midazolam. The major cytochrome responsible for the biotransformation of many sedatives is Cytochrome P450 3A (CYP3A).[41] Concomitantly present medications such as Erythromycin and Clarithrimycin can increase the levels of sedation up to 240% by inhibiting CYP3A. Interactions with azole antifungals such as ketoconazole, itraconazole, fluconazole, HIV protease inhibitors such as ritonavir, indinavir, saquinavir, nelfinavir, can also increase sedation effects by limiting the CYP3A biotransfomation as well.[42,43] Another factor that can increase the level of sedation is the consumption of grapefruit juice. Inhibition of the CYP3A from grapefruit juice consumption results in a delayed absorption and reduced first pass effect of midazolam. This has been found to increase blood plasma levels of midazolam by 56% and increase its bioavailability by 35%, leading to excessive levels of sedation for the pediatric patient.[44] Conversely, carbamazepine, an anti-seizure medication, induces the CYP3A pathway, decreasing the plasma concentration of midazolam and reducing its effectiveness.[45]

Diazepam (Valium®)- Pharmacology and advantages/disadvantages

Diazepam (Valium®) is the prototypical benzodiazepine, having been widely used by adult patients for decades. Reversibly binding to GABA receptors, its effects on a patient's central nervous system are similar to that of midazolam. It is 2-4 times less potent than midazolam, and is typically administered orally for sedation purposes in doses of 0.2 – 0.3 mg/kg, with a maximal dose of 10 mg.[46] Its onset of action (30-60 minutes) is longer than midazolam, and has a prolonged duration and recovery. The half-life of diazepam is 20-96 hours, compared with the 2-4 hour half-life of midazolam. Unlike midazolam which produces no active metabolites, diazepam produces two principal active metabolites during its metabolism in the liver; desmethyldiazepam and oxazepam, which may accumulate and potentially prolong the duration of action.[47] This can result in an undesirable sedation that includes a second sleep effect, whereby the patient appears to awaken, only to be resedated later by these lingering chemicals.

Benzodiazepine Antagonist: Flumazenil (Romazicon®)- Pharmacology

One of the benefits of using benzodiazepines is the ability to reverse possible undesirable effects such as oversedation. Flumazenil (Romazicon®) is a benzodiazepine antagonist, acting competitively at the benzodiazepine site of the GABA receptor, but without altering its morphology. This reversal agent is typically administered intravenously and its onset of action is usually within 1 minute. The first dose administered is 0.01 mg/kg with a maximum dose of 0.2 mg. Doses should be administered slowly over 15-30 seconds, and may be repeated every minute at 0.01 mg/kg for up to 5 doses or a maximum cumulative dose of 1.0 mg.[48] The duration of action of flumazenil is about 30 minutes, less than the half-life of the benzodiazepine being reversed. Therefore, the patient should be carefully monitored after its administration for any signs of resedation and hypoventilation. If such undesirable signs occur, another dose may be required or an infusion may need to be initiated.[49]

Antihistamines- Pharmacology and physiology (Hydroxyzine)

In addition to providing beneficial therapy for allergic reactions, emesis, and pruritis, antihistamines are another class of drugs that have also been effective in the treatment of the fearful pediatric dental patient. Hydroxyzine is available in two forms, Hydroxyzine hydrochloride (Atarax®) which contains alcohol, and Hydroxyzine pamoate (Vistaril®). It has been used effectively in combination with several other agents to reduce the incidence of nausea and vomiting

during sedation.[50] The dosage form is supplied in varying concentrations as an oral syrup. The antihistaminic effect is due to cetirizine, one of its metabolites and a potent H_1-antagonist[51] Hydroxyzine competes with histamine for H_1 receptor sites on effector cells in the GI tract, blood vessels and respiratory tract. Hydroxyzine is administered orally at a dose of 0.5-1.0 mg/kg. It is rapidly absorbed from the gastrointestinal tract and its clinical effects are usually noted within 15 to 30 minutes after oral administration.[52] Hydroxyzine's half-life can be as low as 5 hours for small children, which is beneficial because of the diminished opportunity for a prolonged sedation. Side effects of this medication may include dizziness, ataxia, hypotension and xerostomia. There are no specific reversal agents for this medication.

Promethazine (Phenergan®)

Promethazine (Phenergan®) is another anitihistamine that can be administered orally. Similar to hydroxyzine, its onset of action is usually within 20 minutes. A typical oral dose is 0.5 mg/kg, with a maximal dose of 25 mg.[53] Undesirable neurologic effects such as extra-pyramidal reactions, dystonia, confusion and excitation may occur. Other side effects such as thickening of bronchial secretions, and pharyngitis have been reported with the use of this medication. A survey published in 1987 found it to be the third most commonly used premedication on its own, and the most commonly used combination drug (with meperidine).[54] However, recently its use for sedation in dentistry has diminished markedly.

Opiods- Pharmacology and physiology

Opiods, also known as narcotics, or opiates, are named for the class of drugs that were derivatives of opium. Currently, opiod is the preferred term since these medications specifically bind opiod receptors (mu, kappa, delta) primarily in the brain and spinal cord, producing generalized CNS depression. These drugs act on many systems producing a myriad of effects that can include sedation, mood alteration, respiratory depression, bradycardia, nausea, vomiting, constipation and pain relief. Analgesia is achieved by inhibiting afferent transmission of pain sensation in the brain and spinal cord, resulting in a patient's increased pain threshold and tolerance. Clinically, a patient's respiratory pattern in the presence of opiods may manifest as a reduced rate of breathing, accompanied by a greater tidal volume. With the presence of other CNS depressants, opiods may act synergistically to produce a more profound sedation and significantly depress respiration.[55] One of the hallmarks of opiod overdose is miosis, or pinpoint pupils, caused by the drug's action at the nucleus of the oculomotor nerve (C.N. III). In the early 1980s, this was the most common class of drugs used for sedation in dentistry.[56]

Meperedine (Demerol®)- Pharmacology and physiology

Meperidine (Demerol®) is a pure mu agonist opioid that can be administered orally at a dose of 1-2 mg/kg, with a maximum dose of 100 mg. Its onset of action is usually within 10-15 minutes. The duration of action is 2-3 hours.[57] Most metabolites produced by opiods are inactive. However, like morphine, meperidine produces an active metabolite, normeperidine, which has been associated with toxicity that may precipitate CNS excitation, twitches, tremors or seizures. McKee *et al* found a dose-dependent increase in adverse outcomes with this medication.[58] Contraindications include hypersensitivity to meperidine or any component, and the use of MAO inhibitors by a patient within the past 14 days. Similar to morphine, meperidine can cause histamine release, and should also be avoided in patients with a history of asthma.[59]

Fentanyl (Sublimaze®)- Pharmacology and physiology

Fentanyl (Sublimaze®), like meperidine, is a synthetic compound classified according to chemical structure as a phenylpiperidine, and is in a different chemical class than morphine or codeine, a consideration if a true allergy to one of these medications exists. Fentanyl is 100 times more potent, and 7,000 times more lipid soluble than morphine.[60] Consequently, it can more readily penetrate membranes such as the blood brain barrier, and become rapidly absorbed into the C.N.S. where it binds with stereospecific opiod mu receptors at many sites to produce its effects.[61] Its indications include sedation and analgesia. It does not release histamine but it has the potential to produce side effects such as respiratory depression, bradycardia, hypotension, vomiting, and constipation. Complications may include chest wall rigidity, seizures, and facial pruritis. Of particular significance is that it is often used in combination with benzodiapenines, synergistically increasing sedative properties and concomitantly depressing respirations. This medication is routinely administered intravenously. Intranasally, fentanyl is supplied as an injection solution of 0.05 mg/ml and may be administered in a dose of 1-2 mcg/kg. When administered orally, its onset of action is slightly quicker than meperidine, and produces a shorter duration of action. Although it has been previously available for oral sedation as a lollipop, this form of administration is not currently a common practice in dentistry. It should not be used in patients with a hypersensitivity or intolerance to fentanyl or any component.

Opiod antagonists: Naloxone (Narcan®)- Pharmacology and physiology

Naloxone (Narcan®) is an opioid receptor antagonist, competitively displacing opiods at receptor sites. It is indicated to reverse C.N.S. and respiratory depression secondary to opiod overdose. For the pediatric population, doses of 0.01 mg/kg are administered intravenously and repeated every 2 minutes until normal patient function returns. The maximal recommended dose is 0.2 mg. It is supplied in concentrations of 0.4 mg/ml, so a 1ml vial should be diluted with an additional 9 ml of normal saline to obtain a safer concentration of 0.04 mg/ml. Naloxone antagonizes mu, kappa, delta and sigma receptors, reversing the undesirable sedative and respiratory opiod effects, but also antagonizing the analgesic effects. It will not reverse nausea and vomiting. Since the duration of action of naloxone is only 10 minutes, it is

possible that the patient may experience intense pain, leading to a catecholamine release after receiving an initial dose.[62] Side effects may include nausea, vomiting, tachycardia, hypertension and pulmonary edema.[63] After its administration, the patient should be carefully monitored.

Chloral Hydrate (Somnote®)- Pharmacology and physiology

Chloral Hydrate (Somnote®) is classified as a non-barbituate, a hypnotic that has been widely used as a sedative in pediatric dentistry for decades. It may be administered orally at a dose of 25-50 mg/kg,[64] with a maximal total dose of 1,000 mg. Its onset of action is 30-60 minutes and duration of up to 5 hours. Its mechanism of action is unknown, yet its depressant effects on the C.N.S. are primarily due to its active metabolite, trichloroethanol (TCE), a carcinogen in mice. A major disadvantage of this medication is that of all the orally administered sedative medications, it may have the worst taste. Moreover, its liquid concentration is a mucosal irritant that can cause nausea, vomiting or even laryngospasm.[65] Compared with other agents, other notable side effects include its delayed onset, prolonged recovery, possible cardioirregularity at higher doses, and no analgesic properties.[66] Chloral hydrate depresses genioglossus activity causing hypotonicity of the tongue which can lead to it falling backward against oropharyngeal structures, depressing respiration and compromising the patient's airway.[67] Moreover, it has no reversal agent.[68] Although this medication was the standard of oral sedation in pediatric dentistry for many years, it has more recently fallen out of favor with pediatric dentists and training programs.[69]

Review of the literature- Studies on sedation

Decades of research have confirmed the safe and effective means of sedating an otherwise uncooperative child prior to performing dental procedures. Numerous studies both prospective and retrospective have demonstrated the safety and efficacy of enteral sedation in dentistry. Several studies have also shown the effectiveness of the various sedation agents either alone or in concert with other medications. There have also been many studies comparing and contrasting various sedation agents in terms of onset of action, recovery period, as well as duration and level of sedation. Although not every study will be noted, some of the more conclusive ones will be mentioned.

In a study of 1,112 outpatient children given either nitrous oxide or midazolam over a 10 year period, there was a very low complication rate associated with the procedure and induction of the sedative agent.[70] Erlandsson *et al* found the oral administration of midazolam to be a safe form of premedication in 160 children with a mean age of 6.7 +/- 2.6 years referred for dental treatment due to behavioral problems. The advantages of its short waiting-time and half-life, and level of sedation obtained were specifically sited.[71]

Comparisons of medications have also been made. Haas *et al* found that children who were administered 0.60 mg/kg of midazolam prior to the administration of a local anesthetic, demonstrated an increased level of sedation compared with patients who had received 50 mg/kg of chloral hydrate.[72] Another study measured the efficacy of midazolam versus diazepam when both were used in concurrence with nitrous oxide. Although both groups demonstrated a clinically acceptable level of sedation, the group receiving the midazolam had higher levels of sedation at increased levels of stimulation, whereas the group that had received the diazepam was more easily aroused with less of a stimulus.[73]

Chloral hydrate has been used in concert with other agents utilized in pediatric dentistry with varying degrees of success. It was found that children receiving a sedative cocktail of chloral hydrate and hydroxyzine, compared with children who were administered a similar mixture with an added dose of meperidine, demonstrated no significant differences in their measured levels of compliance and sedation.[74] In a similar study, it was demonstrated that the addition of the meperidine increased the compliance and sedation levels of the patients, without the added risk of increasing the respiratory distress.[75] In another study, a group of children that received 50 mg/kg of chloral hydrate and 1 mg/kg of promethazine was compared with a group that received 50 mg/kg of chloral hydrate and 1 mg/kg of meperidine. No significant differences in the vital signs of the two groups were noted, with all subjects being responsive throughout the procedure.[76] Chloral hydrate has also been used in conjunction with promethazine. In one study, two groups received different drug regimens. The first group received 50 mg/kg of chloral hydrate and 1 mg/kg of promethazine. The second group received 1 mg/kg of meperidine and 1 mg/kg of promethazine. The first group demonstrated better results, experiencing less crying and more sleep throughout the procedure.[77]

The mixture of various sedative agents in order to obtain a higher degree of sedation, achieve a longer and more effective treatment time, while producing less patient agitation has been examined. In order to determine the efficacy of diazepam as a sedation agent, Houpt *et al* compared one group of children who received 0.5 mg/kg of this drug alone, with another group that received the same dosage of diazepam in combination with nitrous oxide at a concentration of 50:50. It was demonstrated that the nitrous oxide augmented the efficacy of the sedations by 50%.[78]

Polypharmacy or more of one drug (or drugs), does not necessarily ensure better results. In one study, 120 apprehensive children aged 24-48 months were orally administered varying dosages of midazolam, mixed with varying dosages of meperidine. The levels of cooperation and need for restraint were measured for each combination. Combined higher doses of both agents demonstrated somnolence and oversedation. The higher dose of midazolam mixed with the lower dose of meperidine was the most effective combination, allowing the successful completion of all visits with no need for restraint, no loss of consciousness throughout appointments, and no adverse reactions. There appeared to be a synergistic effect of the two medications, increasing the working time and facilitating the sedation.[79]

Routes of Administration

Other research has compared different routes of administrations of sedatives. One study found no significant difference in efficacy or safety when the combination of meperidine and hydroxyzine was administered orally or submucosally.[80] Moreover, a comparison of midazolam given orally (0.7 mg/kg) with 0.3 mg/kg administered intranasally (IN), showed overall behavior of the pediatric dental patients to be similar, with no significant differences in vital signs. With IN administration, mean onset time was approximately 3 times faster, but working time was 10 minutes shorter and toward the end of the session more patient movement and less sleep was demonstrated.[81] Also, sedatives are not necessarily an indication of cooperative behavior at appointments subsequent to the sedation. The sedation likely alters the uncooperative behavior only temporarily. Comparing children aged 39-71 months who had previously received sedation with ones that had not, McComb *et al* found no relationship between oral conscious sedation and the future behavior of children in the dental setting.[82]

Patient monitoring and safety training for sedation procedures:

Although numerous sedation medications have been mentioned and their pharmacology and physiology discussed, the ultimate safety and wellbeing of the patients receiving sedation is paramount and ultimately the responsibility of the person administering the sedation. In an effort to optimize the safe practice of enteral sedation in the dental practice, national guidelines have been established and will most likely be modified in the future. In addition to possessing proper knowledge of the pertinent pharmacology, the operating dentist should possess current completion of a Basic Life Support (B.L.S.) course and when treating children, Pediatric Advanced Life Support (P.A.L.S.) is vital. He/she should be capable of performing bag-valve-mask ventilation, and maintaining advanced airway skills, should the necessity to initiate rescue therapies become indicated.

Monitoring the patient clinically and with adjunctive medical equipment is extremely critical. An adequate oxygen supply must be determined and baseline vital signs of the patient obtained contemporaneously with direct clinical observation of the patient. The patient should be monitored prior to the sedation, during the procedure, as well as postoperatively for effective recovery from the sedation. The triad of proper monitoring includes oxygenation, ventilation, and circulation. This involves the use of equipment such as a pulse oximeter for oxygen saturation, capnography and pretracheal stethoscopes to obtain respiratory information, continual evaluation of heart rate and blood pressure with an appropriately sized non-invasive cuff and finally direct observation of chest excursions.

Documentation is also imperative during sedation both legally and ethically. It is critical to have this information prior to discharge of the patient. An appropriate time-oriented anesthetic record must be maintained that includes the individuals present during the administration of the sedative agents and during the sedation at least one additional person should be present in addition to the dentist who is trained in basic life support. During the recovery phase, patients must have continuous supervision until oxygenation, ventilation and circulation are stable and the patient is appropriately responsive for discharge from the facility. It is the dentist who must determine and document that the patient is stable and meets appropriate discharge criteria. Furthermore, the dentist must provide explanation and documentation of postoperative instructions to the responsible adult escorting the patient home.[83,84]

Despite being discharged safely from the sedation site, a patient may still become susceptible to tragic outcomes. Unfortunately, with the use of sedation in dentistry, dire consequences such as death and permanent neurologic injury from respiratory compromise have been reported.[85] Following an appointment involving sedation, the patient must be carefully monitored during his/her transportation home. For example, if a young patient is placed into the infant seat of a parent's car, and is unsupervised, then during the ride home the patient's head can flex forward and downward, compromising the airway and leading to its obstruction. Respiratory arrest can ensue (the primary cause of cardiac arrest in children), leading to morbidity and possibly mortality.[86] Therefore, postoperatively, it is imperative that a responsible adult continuously monitor the patient for any poor head positioning and/or respiratory depression.

CONCLUSION

In conclusion, the current care of pediatric dental patients appears to be evolving into three main categories: behavioral management with "tell, show, do"; sedation with orally administered midazolam and/or nitrous oxide and oxygen via inhalation; and general anesthesia.[87] Yet this can also present complications when children with management problems in some areas of the United States have recently experienced an increase in the waiting time for sedation services or general anesthesia[88] Coincidentally there has been an increased demand for continuing education courses that focus on enteral sedation recently.[89] Courses that involve patient simulators provide a dynamic hands-on education mimicking potential real-life situations. This is similar to many areas of health care which have utilized similar benefits of combining the cognitive skills taught through didactic lectures with the psychomotor skills obtained in the use of a mannequin-based simulator.[90]

Enteral sedation in pediatric dentistry is a valuable adjunct to dental treatment but it must be exercised with caution. Preoperatively, patients must be thoroughly examined and medically optimized when necessary. Since the degree of sedation and respiratory depression provided by oral sedative medications is difficult to predict, this treatment modality is not recommended for all patients. However, with appropriate patient selection, judicious use of medications, careful monitoring through adequate equipment, and effective communication, this form of treatment can be safely and effectively administered. With the strong demand for oral

sedation services evident, properly trained practitioners who opt to utilize this vital form of treatment can reach out to a wider patient population, and provide a win-win scenario for themselves and their patients.

REFERENCES

1. Casamassimo PS, Wilson S, Gross L. Effects of changing U.S. parenting styles on dental practice; perceptions of diplomats of the American Board of Pediatric Dentistry presented to the College of Diplomates of the American Board of Pediatric Dentistry 16th Annual Session, Atlanta, GA. Pediatr Dent, 24(1): 18–22, 2002.
2. Peres MA, Peres KG, de Barros AJ, Victoria CG. The relation between family socioeconomic trajectories from childhood to adolescence and dental caries and associated oral behaviours. J Epidemiol Community Health, 61(2): 141–5, 2007.
3. Arnup K, Broberg KG, Berggren U, Bodin L. Lack of cooperation in pediatric dentistry—the role of the child personality characteristics. Pediatr Dent, 24: 119–128. 2002
4. Baier K, Milgrom P, Russell S, Mancl L, Yoshida T. Children's fear and behavior in private pediatric dentistry practices. Pediatr Dent, 26: 316–321, 2004.
5. AAPD Guidelines on Behavior Guidance for the Pediatric Dental Patient. Pediatr Dent, 27(7): 92–100, 2006.
6. Nathan JE. Effective and safe pediatric oral conscious sedation: philosophy and practical considerations. Alpha Omegan, 99(2): 78–82, 2006.
7. Guidelines for teaching the comprehensive control of anxiety and pain in dentistry, as adopted by the American Dental House of Delegates, October 2005.
8. Cote CJ, Karl HW, Notterman DA, Weinberg JA, McCloskey C. Adverse sedation events in pediatrics: Analysis of medications used for sedation. Pediatrics, 106: 633–44, 2000.
9. Cote CJ, Karl HW, Notterman DA, Weinberg JA, McCloskey C. Adverse sedation events in pediatrics: A critical incident analysis of contributing factors. Pediatrics, 105: 805–14, 2000.
10. Malamed SF. Sedation - A Guide to Patient Management. 3rd ed. St. Louis:Mosby, 8–11, 1995.
11. American Society of Anesthesiologists: New classification of physical status, Anesthesiology, 24: 111, 1963.
12. Radis FG, Wilson S, Griffen AL, Coury DL. Temperament as a predictor of behavior during initial dental examination in children. Pediatr Dent,16: 121–27. 1994.
13. Rothbart MK, Ahadi, SA, Hershey, KL, Fisher P. Investigation of temperament at three to seven years: The children's Behavior Questionnaire. Child Development, 72: 1394–08, 2001.
14. Fishbaugh DF, Wilson S, Preisch JW, Weaver JM. 2nd Relationship of tonsil size on an airway blockage maneuver in children during sedation. Pediatr Dent, 19: 277–81, 1997.
15. Jones, KL. Smith's Recognizable Patterns of Human Malformation 6th ed, Philadelphia:WB Saunders, 82–3, 262–3, 280–1, 738–9, 888–9, 1997.
16. Practice guidelines for the perioperative management of patients with obstructive sleep apnea: a report by the American Society of Anesthesiologists task force on perioperative management of patients with obstructive sleep apnea. Anesthesiology, 104(5): 1081–93, 2006.
17. Cote CJ. The upper respiratory tract infection (URI) dilemma: fear of complication or litigation? Anesthesiology, 95: 283–5, 2001.
18. Tait AR, Reynolds PI, Gutstein HB. Factors that influence an anesthesiologist's decision to cancel elective surgery for the child with an upper respiratory tract infection. J Clin Anesth, 7: 491–9, 1995.
19. Tait AR, Voepel-Lewis T, Munro HM, Gutstein HB, Reynolds PI. Cancellation of pediatric outpatient surgery: economic and emotional implications for patients and their families. J Clin Anesth, 9: 213–9, 1997.
20. Gwaltney J Jr. The common cold. In: Mandell G, Bennett J, Dolin R, eds. Principles and practice of infectious diseases. New York:Churchill Livingstone, 561–6, 1995.
21. Tait AR, Malviya S. Anesthesia for the Child with an Upper Respiratory Tract Infection: Still a Dilemma? Anesth Analg, 100: 59–5, 2005.
22. Parnis SJ, Barker DS, Van der walt JH. Clinical predictors of anaesthetic complications in children with respiratory tract infections. Pediatric Anesthesia, 11: 29–40, 2001.
23. Tait AR, Malviya S, Voepel-Lewis T, Munro HM, Seiwert M, Pandit UA. Risk factors for perioperative adverse respiratory events in children with upper respiratory tract infections. Anesthesiology, 95: 299–306, 2001.
24. Empey DW, Laitinen LA, Jacobs L, Gold WM, Nadel JA. Mechanisms of bronchial hyperactivity in normal subjects after upper respiratory infection. Am Rev Respir Dis, 113: 131–9, 1976.
25. Aquilina AT, Hall WJ, Douglas RG Jr, Utell MJ. Airway reactivity in subjects with viral upper respiratory tract infections; the effects of exercise and cold air. Am Rev Respir Dis, 122: 3–10, 1980.
26. Rolf N, Cote CJ. Frequency and severity of desaturation events during general anesthesia in children with and without upper respiratory infections. J Clin Anesth, 4: 200–3, 1992.
27. Bahn EL, Holt KR. Procedural sedation and analgesia: a review and new concepts. Emerg Med Clin North Am., 23(2): 503–17, 2005.
28. Murphy GS, Ault ML, Wong HY, Szokol JW. The effect of a new NPO policy on operating room utilization. J Clin Anesth, 12(1): 48–1, 2000.
29. Agrawal D, Manzi SF, Gupta R, Krauss B. Preprocedural fasting state and adverse events in children undergoing procedural sedation and analgesia in a pediatric emergency department. Ann Emerg Med, 42(5): 636–46, 2003.
30. Soreide E, Eriksson LI, Hirlekar G, et al. Pre-operative fasting guidelines: an update. Acta Anaesthesiol Scand, 49(8): 1041–7, 2005.
31. Abrams, AC. Clinical Drug Therapy Rationale for Nursing Practice. 8th Edition Philadelphia: Lippincott, 2001: 111–128.
32. Katzung BG. Sedative-Hypnotic Drugs. In: Basic and Clinical Pharmacology, 8th ed. USA: The McGraw Hill Companies, Inc., 364–81, 2001.
33. Kost, M. Moderate Sedation/Analgesia Core Competencies For Practice. Missouri:Saunders, 83–6, 2004.
34. Van der Bijl P, Roelofse JA, Joubert JJ, van Zyl JF. Comparison of various physiologic and psychomotor parameters in patients sedated with intravenous lorazepam, diazepam, or midazolam during oral surgery. J Oral Maxillofac Surg, 49(7): 672–9, 1991.
35. Fraone G, Wilson S, Casamassimo PS, Weaver J, Pulido AM. The effect of orally administered midazolam on children of three age groups during restorative dental care. Pediatr Dent, 21(4): 235–41, 1999.
36. Bayrak F, Gunday I, Memis D, Turan A. A comparison of oral midazolam, oral tramadol, and intranasal sufentanil premedication in pediatric patients. J Opioid Manag, Mar-Apr; 3(2): 74–8, 2007.
37. Yemen, TA. Pediatric Anesthesia Handbook. New York: McGraw-Hill Medical Publishing, 47–53, 2002.
38. Reeves ST, Wiedenfeld KR, Wrobleski J, Hardin CL, Pinosky ML. A randomized double-blind trial of chloral hydrate/hydroxyzine versus midazolam/acetaminophen in the sedation of pediatric dental outpatients. ASDC J Dent Child, 63(2): 95–100, 1996.
39. Rosenberg M. Oral Midazolam Syrup as a Safe Sedative for Pediatric Dentistry. J Mass Dent Soc, 49(2): 32–5, 2000.
40. Marshall WR, Weaver BD, McCutcheon P. A study of the effectiveness of oral midazolam as a dental pre-operative sedative and hypnotic. Spec Care Dentist, 19(6): 259–66, 1999.
41. de Wildt SN, de Hoog M, Vinks AA, van der Giesen E, van den Anker JN. Population pharmacokinetics and metabolism of midazolam in pediatric intensive care patients. Crit Care Med, 31(7): 1952–8, 2003.
42. Sagir, A, Schmitt M, Dilger K, Haussinger D. Inhibition of cytochrome P450 3A: relevant drug interactions in gastroenterology. Digestion, 68(1): 41–8, 2003.
43. Dresser GK, Spence JD, Bailey DG. Pharmacokinetic-pharmacodynamic consequences and clinical relevance of cytochrome P450 3A4 inhibition. Clin Pharmacokinet, 38(1): 41–57, 2000.
44. Goho C. Oral midazolam-grapefruit juice drug interaction. Pediatr Dent, 23(4): 365–6, 2001.

45. Yuan R, Flockhart DA, Balian JD. Pharmacokinetic and pharmacodynamic consequences of metabolism-based drug interactions with alprazolam, midazolam, and triazolam. J Clin Pharmacol, 39: 1109–25, 1999.
46. Martinez JL, Sutters KA, Waite S, Davis J, Medina E, et al A comparison of oral diazepam versus midazolam, administered with intravenous meperidine, as premedication to sedation for pediatric endoscopy. J Pediatr Gastroenterol Nutr, Jul; 35(1): 51–8, 2002.
47. Wiener-Kronish, Jeanine P, Gropper, MA. Conscious Sedation. Philadelphia: Hanley & Belfus, 2001: 8–10.
48. Shannon M, Albers G, Burkhart K, Liebelt E, Kelley M, et al. Safety and efficacy of flumazenil in the reversal of benzodiazepine-induced conscious sedation. The Flumazenil Pediatric Study Group. J Pediatr, Oct; 131(4): 582–6, 1997.
49. Euliano TY, Gravenstein JS. Essential Anesthesia From Science To Practice. New York: Cambridge University Press, 169, 2004.
50. Kost, M. Moderate Sedation/Analgesia Core Competencies For Practice. Missouri: Saunders, 249–51, 2004.
51. Christophe B, Maleux MR, Gillard M, Chatelain P, Peck MJ, Massingham M. The histamine H(1)-receptor antagonist cetirizine does not interact with bradykinin B(1) or B(2)-receptors in vitro. Inflamm Res, 53(1): 81–2, 2004.
52. Martinez D, Wilson S. Children sedated for dental care: a pilot study of the 24-hour postsedation period. Pediatr Dent, 28(3): 260–4, 2006.
53. Alfonzo-Echeverri EC, Berg JH, Wild TW, Glass NL Oral ketamine for pediatric outpatient dental surgery sedation. Pediatr Dent, May-Jun; 15(3): 182–5, 1993.
54. Wright GZ, Chiasson RC. The use of sedation drugs by Canadian pediatric dentists. Pediatr Dent, 9: 308, 1978.
55. Dionne RA, Yagiela JA, Moore PA, Gonty A, Zuniga J, Beirne OR. Comparing efficacy and safety of four intravenous sedation regimens in dental outpatients. JADA, 132: 740–51, 2001.
56. Aubuchon RW. Sedation liabilities in pedodontics. Pediatr Dent, 4: 171–80, 1982.
57. Gregory, GA. Pediatric Anesthesia. Pennsylvania: Churchill Livingstone, 36–7, 2002.
58. McKee KC, Nazif MM, Jackson DL, Barnhart DC, Close J, Moore PA. Dose-response characteristics of meperidine sedation in preschool children. Pediatr Dent,12: 222–7, 1990.
59. Wiener-Kronish, Jeanine P, Gropper MA. Conscious Sedation. Philadelphia: Hanley & Belfus, 10–2,102, 2001.
60. Chudnofsky CR, Wright SW, Dronen SC, Borron SW, Wright MB. The safety of fentanyl use in the emergency department. Ann Emerg Med, Jun; 18(6): 635–9. 1989.
61. Litman, RS. Pediatric Anesthesia The Requisites in Anesthesiology. Pennsylvania: Elsevier Mosby, 151,201,202, 2004.
62. Buck ML. Naloxone For The Reversal Of Opoid Adverse Effects. Pediatric Pharmacotherapy, 8(8): 1–5, 2002.
63. Bell C, Kain ZN. The Pediatric Anesthesia Handbook. 2nd Edition. St. Louis. Mosby, 378, 1997.
64. Chowdhury J, Vargas KG. Comparison of chloral hydrate, meperidine, and hydroxyzine to midazolam regimens for oral sedation of pediatric dental patients. Pediatr Dent, May-Jun; 27(3): 191–7, 2005.
65. Twersky RS. The Ambulatory Anesthesia Handbook. St. Louis: Mosby, 348–9, 1995.
66. Krauss B, Brustowicz RM. Pediatric Procedural Sedation and Analgesia. Philadelphia: Lippincott Williams & Wilkins, 39–45, 1995.
67. Hershensen M, Brouillette RT, Olsen E, Hunt CE. The effect of chloral hydrate on genioglossus and diaphragmatic activity. Pediatr Res, 18: 516–19, 1984.
68. Hardman JG, Lee EL. Goodman & Gilman's: The Pharmacological Basis of Therapeutics. 10th ed. New York: McGraw-Hill, 419–21, 2001.
69. Wilson S, Farrell K, Griffen A, Coury D. Conscious Sedation Experiences in Graduate Pediatric Dentistry Programs. Pediatr Dent, 23: 307–14, 2001.
70. Hulland SA, Freilich MM, Sandor GK. Nitrous oxide or oral midazolam for pediatric outpatient sedation. Oral Surg Oral Med Oral Pathol Oral Radiol Endod, 93(6): 643–6, 2002.
71. Erlandsson AL, Backman B, Stenstrom A, Stecksen-Blicks C. Conscious sedation by oral administration of midazolam in pediatric dental treatment. Swed Dent J, 25(3): 97–104, 2001.
72. Haas DA, Nenniger SA, Yacobi R. A Pilot study of the efficacy of oral midazolam for sedation in pediatric dental patients. Anesth Prog, 43(1): 1–8, 1996.
73. Pisalchaiyong T, Trairatvorakul C, Jirakijja J, Yuktarnonda W. Comparison of the effectiveness of oral diazepam and midazolam for the sedation of autistic patients during dental treatment. Pediatr Dent, 27(3): 198–206, 2005.
74. Poorman T, Farrington FH, Mourino AP. Comparison of chloral hydrate/hydroxyzine combination with and without meperidine in the sedation of pediatric dental patients. Pediatr Dent, 12(5): 288–91, 1990.
75. Hasty MF, Vaan WF, Dilley DC, Anderson JA. Conscious sedation of pediatric dental patients: an investigation of chloral hydrate, hydroxyzine pamoate, and meperidine vs. chloral hydrate and hydroxyzine pamoate. Pediatr Dent, 13(1): 10–9, 1991.
76. Sams DR, Russell CM. Physiologic response and adverse reactions in pediatric dental patients sedated with promethazine and chloral hydrate or meperdine. Pediatr Dent, 15(6): 422–24, 1993.
77. Sams DR, Cook EW, Jackson JG, Roebuck BL. Behavioral assessments of two drug combinations for oral sedation. Pediatr Dent, 15: 186–9, 1993.
78. Houpt MI, Kupietzky A, Tofsky NS, Koenigsberg SR. Effects of nitrous oxide on diazepam sedation of young children. Pediatr Dent, 18(3): 236–41, 1996.
79. Nathan JE, Vargas KG. Oral midazolam with and without meperidine for management of the difficult young pediatric dental patient: a retrospective study. Pediatr Dent, 24(2): 129–38. 2002.
80. Cathers JW, Wilson CF, Webb MD, Alvarez ME, Schiffman T, Taylor S. A comparison of two meperidine/hydroxyzine sedation regimens for the uncooperative pediatric dental patients. Pediatr Dent, 27(5): 395–400, 2005.
81. Lee-kim SJ, Fadavi S, Indru P, Koerber A. Nasal versus oral midazolam sedation for pediatric dental patients. J Dent Child, 71: 126–30, 2004.
82. McComb M, Koenigsberg Sr, Broder HL, Houpt M. The Effects of oral conscious sedation on future behavior and anxiety in pediatric dental patients. Pediatr Dent, 24(3): 207–11, 2002.
83. Guidelines for the use of conscious sedation, deep sedation and general anesthesia for dentists. Adopted by the American Dental Association House of Delegates, October, 2005.
84. Cote CJ, Wilson S. Guidelines for monitoring and management of pediatric patients during and after sedation for diagnostic and therapeutic procedures: an update. Pediatrics, 118(6): 2587–602, 2006.
85. Cote CJ, Karl HW, Notterman DA, Weinberg JA, McCloskey C. Adverse sedation events in pediatrics: analysis of medications used for sedation. Pediatrics, 106(4): 633–44, 2000.
86. Cote CJ, Notterman DA, Karl HW, Weinberg JA, McCloskey C. Adverse sedation events in pediatrics: a critical incident analysis of contributing factors. Pediatrics, 105: 805–14, 2000.
87. Dionne R, Yagiela JA, Cote CJ, et al. Balancing efficacy and safety in the use of oral sedation in dental outpatients. JADA, 137: 502–13, 2006.
88. Lewis CW, Nowak AJ. Stretching the safety net too far waiting times for dental treatment. Pediatr Dent, 24(1) 6–10. 2002.
89. Weaver JM. Managing real anesthesia emergencies on human simulators. Anesth Prog, 53: 117–18, 2006.
90. Loyd GE, Lake CL, Greenberg RB. Practical Health Care Simulations. Philadelphia: Hanley & Belfus Medical Publishers, 230–3, 2004.