Artículo de Revisión

Volumen 16, N° 33. Julio-diciembre 2026
Madhura Joshi y Col.
Pg. 367-440

DOI:

Acta BIOCLÍNICA
ISSN Electrónico: 3105-403X

# PAIN AND ANXIETY MANAGEMENT USING SEDATION IN MODERN PEDIATRIC DENTISTRY. A REVIEW

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## ABSTRACT

Sedation is a valuable tool in dentistry, yet it is like a loaded gun; when used correctly, it can serve and protect and if used inappropriately, it can shoot to kill. The most common reason for referral to new patient pediatric dentistry consultant clinics is the management of dental anxiety. Not only are there risks associated with dental extractions under general anaesthesia but this can also contribute to dental anxiety in later life. As a Pediatric Dentist it is our duty to allay anxiety of the patient. Successful outcomes depend on a systematic approach as well as having the knowledge and skills to manage adverse events.

**KEYWORDS:** sedation; anesthesia; pediatric dentistry; nitrous oxide; behaviour management.



Received: March 22, 2026
Accepted: April 30, 2026

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# MANEJO DEL DOLOR Y LA ANSIEDAD MEDIANTE SEDACIÓN EN LA ODONTOLOGÍA PEDIÁTRICA MODERNA. UNA REVISIÓN

## RESUMEN

La sedación es una herramienta valiosa en odontología, pero es como un arma cargada: si se usa correctamente, puede proteger y, si se usa de forma inapropiada, puede ser mortal. El motivo más común de derivación a las consultas de odontología pediátrica para pacientes nuevos es el manejo de la ansiedad dental. No solo existen riesgos asociados con las extracciones dentales bajo anestesia general, sino que esto también puede contribuir a la ansiedad dental en la edad adulta. Como odontólogos pediátricos, es nuestro deber aliviar la ansiedad del paciente. Los resultados exitosos dependen de un enfoque sistemático, así como de contar con el conocimiento y las habilidades para manejar eventos adversos.

**PALABRAS CLAVE:** sedación; anestesia; odontología pediátrica; óxido nitroso; manejo del comportamiento.

## INTRODUCTION

Clinically children with dental fear problem differ from that presenting dental behavior management problem (BMP). Dental fearful children can be shy and silent in their initial contact with the dentist and passive during dental treatment. Children with BMP, on the other hand, are more outgoing in their general behavior and often rebellious during dental treatment. Thus clinical evidence suggests that there is a temperamental difference between



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children with dental fear and children with BM (Malamed, 2004).

Success in dentistry, to a large degree, requires the recognition and effective treatment of fear and anxiety in patients. A broad range of anxiety control methods are available in dentistry today. With the exception of hypnosis and acupuncture, all methods employ the use of drugs that produce effects from mild forms of sedation to general anesthesia. According to a 1999 report from the Institute of Medicine, anesthesia care today is nearly times safer than it was 20 years ago. But not all the surgical procedures require anesthetic. Sometimes no anesthetic is required, and sedation is used, which doesn't result in loss of consciousness or significant analgesia, but frequently produces a degree of amnesia, and relaxes the patient.

The number of noninvasive and minimally invasive procedures performed outside of the operating room has grown exponentially over the last several decades. Sedation, analgesia, or both may be needed for many of these interventional or diagnostic procedures. Medications that elicit pharmacologic effects, such as anxiolytics, amnesia, or analgesia, provide patient comfort during various procedures.

This review mainly focuses on providing an in-depth insight to the various aspects of sedation which is the most advanced and the most effective pain & anxiety management technique used in modern pediatric dentistry.



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**SEDATION**

Sedation is a depressed state involving a lack of total consciousness but short of anaesthetic sleep. A state that allows patients to tolerate unpleasant procedures while maintaining adequate cardiorespiratory function and the ability to respond purposefully to verbal command and/or tactile stimulation.

The use of sedation is advocated in children lacking cooperation for short procedures. It can also be done in cases where pre-medication is required. This serves the purpose of making treatment more acceptable and less anxiety prone.

**SEDATION LEVELS**

This is accomplished along a continuum of (American Society of Anesthesiologists, Position on Monitored Anesthesia Care, Last Amended on October 17, 2018)(Non-Anesthesiologists & An Updated Report by the American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologists, 2002)

Minimal sedation **(anxiolysis):**

A drug-induced state during which patients respond normally to verbal commands, although cognitive function and coordination might be impaired, respiratory and cardiovascular functions are unaffected.

**Moderate sedation (formerly conscious sedation):**

A drug-induced depression of consciousness during which patients respond purposefully



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to verbal commands, either alone or accompanied by light tactile stimulation.

*Conscious sedation*

Conscious sedation is a controlled drug-induced state, with minimally depressed consciousness during which patients are able to maintain ventilator function and respond to verbal or physical stimulations. It allows protective reflexes to be maintained; retains the patient's ability to maintain a patent airway independently and continuously; Permits appropriate response by the patient to physical stimulation or verbal command, e.g. 'open your eyes!' American academy of pediatrics (1985, 1993)

**Dissociative sedation**

A trance-like cataleptic state induced by the dissociative drug ketamine characterised by profound analgesia and amnesia, with retention of protective airway reflexes, spontaneous respirations, and cardiopulmonary stability (Krauss & Green, 2000)

**Deep sedation**

A drug-induced depression of consciousness during which patients cannot be easily aroused but respond purposefully after repeated verbal or painful stimulation (e.g., purposefully pushing away the noxious stimuli).

**RELATIVE ANALGESIA**

It is a technique in which the dose of nitrous oxide is titrated to the need of the



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individual patient, and the inspired concentration is always kept to the minimum necessary.(Langa, 1968)

**General Anesthesia**

A drug induced loss of consciousness, during which patients are not arousable even by painful stimulation. The ability to independently maintain ventilator function is often impaired. Patients often require assistance in maintaining a patent airway, and positive pressure ventilation may be required because of depressed spontaneous ventilation or drug-induced depression of neuromuscular function. Cardiovascular function may be impaired.

Dental procedures under general anesthesia are a therapeutic option for many children since it can provide for a broad and high quality dental care, when conventional dental treatment is not a viable option (Silva et al., 2015)

*THE STAGES OF GENERAL ANESTHESIA*

In the mid-1840s Francis Plomley described three stages of general anesthesia .("A Synopsis of Surgical Anatomy. Ed. 7. Alexander Lee McGregor, M.Ch. (Edin.), F.R.C.S. (Eng.). Bristol, England, John Wright and Sons Ltd.; Baltimore, The Williams and Wilkins Company, 1950," 1951) In 1847 John Snow added a fourth, overdose [Snow, 1847]. It was not until World War I, that Guedel in 1937 ,more clearly described the signs and symptoms of the various stages of anesthesia [Guedel's classification which was accepted throughout the world and is considered to be one of the important



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contributions to the Science of anesthesiology. ("Book Review," 1937)

Four stages of anesthesia are described:

I. Stage of analgesia
II. Stage of delirium
III. Stage, of surgical anesthesia
IV. Stage of respiratory paralysis

## HISTORY

### Early local anesthetics

The first effective local anesthetic was cocaine. Isolated in 1859 was used by Karl Koller, at the suggestion of Sigmund Freud, in ophthalmic surgery in 1884. Before that doctors had used a salt and ice mix for the numbing effects of cold, which could only have limited application. Similar numbing was also induced by a spray of ether or ethyl chloride. A number of cocaine derivatives and safer replacements were soon produced, including procaine (1905), Eucaine (1900), Stovaine (1904), and Lidocaine (1943). Opioids were first used by Racoviceanu- Pitesti, who reported his work in 1901(Barash et al., 2013)[17].

## ORIGIN OF ANESTHESIA

The word anesthesia was first introduced by Oliver Wendell Holmes in 1846, four weeks following the first demonstration of ether anesthesia at the Massachusetts General Hospital. Dr. Holmes taught anatomy and physiology at Harvard Medical School. He went on to become dean of Harvard Medical School. Ether was demonstrated as a means of rendering a patient unconscious and free from surgical pain. He derived this



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English word from the Greek word anaisthesis, which means insensibility or loss of sensation with or without the loss of consciousness. This is described in a letter to William T. G. Morton, the dentist who performed this demonstration:

In modern times, general anaesthesia can be clinically defined by four criteria:

- Amnesia (loss of recall for the event)
- Analgesia (insensibility to pain)
- Hypnosis (unconsciousness)
- Muscle relaxation.

**A note on the Indian Pioneer - Sushruta**

Of all the Hindu healers, Sushruta was deservedly the most famous, perhaps because he achieved a remarkable level of scientific understanding and success for someone practicing medicine in the fifth and sixth century. His extraordinary surgical exploits and self-made instruments were recorded in a series of Sanskrit medical texts known as the Sushruta Samhita. Among some of his more impressive firsts were rhinoplasty, prostatectomy and abscess lancing. For example, in the Sushruta Samhita, written perhaps as early as 400 BC, it was advised that alcohol be used before surgery to produce insensibility to pain. Some of the earliest pharmacological methods of pain relief included the plant derivatives: cannabis, mandrake, opium and alcohol. These analgesics were used for surgical analgesia as long as 2500yr ago (Hamilton & BAskett, 2000).



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**Local anesthesia consideration during sedation:**

All local anesthetic agents can become cardiac and CNS depressants when administered in excessive doses. There is a potential interaction between local anesthetic and sedative used in pediatric dentistry which can result in enhanced sedative effect. Therefore, particular attention should be paid to doses used in pediatrics to avoid excessive doses for the patients who are going to be sedated, a maximum recommended dose in mg/kg or mg/lb. should be calculated, and the dose administered should be recorded for each patient prior to administration for all sedative and local anesthetics.

**FACTORS INFLUENCING PATIENT RESPONSE**

A number of factors will interact to determine whether the pediatric patient will face the scheduled visit to the dentist or physician with eager anticipation or with fearful Dread. These include the influence of the parent, of the child's peers, of the doctor, and of the office staff. Another factor is the child's prior experience with health professionals. Parents attitudes and feelings will be transferred to the child via nonverbal communication. Children may overhear their parents discussing their experiences or may see their parent suffering either before or after a Dental appointment.



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Kimmelman has stated that firmness with kindness and a soft, clear voice is an asset in dealing with children. The dress of the doctor is important: White uniforms may provoke negative feelings in younger patients, and colorful uniforms or the absence of uniforms may evoke a more positive response. With universal precautions (gloves, glasses, and masks being mandatory), explanations and role playing with the child to make them comfortable with our safety garb is suggested.

The time of day at which the appointment is scheduled may have bearing on a child's behavior, especially the younger child. Interference with a child's sleep or eating habits should be avoided, if possible. The length of the appointment should not exceed the child's attention span (Kimmelman, 1964).

The office environment is another factor that influences the patient's behavior. An office in which many children are treated should offer an environment that is appealing to children. Although most pediatric medical and dental offices are designed with this in mind, even in the office of the busy generalist a separate area of the reception area might be set aside for younger patients.

**BEHAVIORAL EVALUATION OF THE PEDIATRIC PATIENT**

There are innumerable factors that interact to influence a child's behavior in the dental office; the doctor must still be able to



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evaluate this patient's ability to cope with the planned treatment. Two of the more commonly used systems are the Frankl Behavioral Rating Scale (Frankl, 1962) and the System devised by Wright (Wright & Kupietzky, 2014).

In the Frankl system the doctor places the child's behavior into one of four categories:

1. Definitely positive behavior
2. Positive behavior
3. Negative behavior
4. Definitely negative behavior

Johnson has stated that the Frankl scale appears to be closely related to the attitude of the parent toward dentistry (Winer, 1982) .

Wright's classification presents three major groups:

1. Cooperative
2. Lacking cooperative ability and
3. Potentially uncooperative behavior, with multiple subgroups.

Wright has stated that most doctors, either consciously or subconsciously, categorize the behavior of children into one of these groups.

Successful treatment of the patient who lacks the ability to cooperate usually requires the use of one of the techniques of sedation. If these techniques fail to prove adequate, general anesthesia may be required. The potentially uncooperative patient may or may not require the use of sedation for successful treatment.



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**Clinical Signs of Sedation** (Houpt et al., 2004)

**OBJECTIVE SIGNS**

These signs assessed the clinical features and condition of the patient's face, hands, legs, and feet to determine the effects of nitrous oxide. The signs include open or closed eyes, tears, trance like state, speaking, clenched hand, abducted feet and laughing

**SUBJECTIVE SYMPTOMS**

Subjective symptoms addressed the child's perception of the nitrous oxide effects. Questions regarding the child's perception of the nitrous oxide effects on the head, abdomen, fingers, toes, and overall condition were asked prior to and 5 minutes after nitrous oxide administration.

**PSYCHOMOTOR EFFECTS**

These were evaluated by asking the patient to draw four figures from the Bender Visual Motor Gestalt Test before and 5 minutes after the nitrous oxide administration This determines the Visio-motor capacity of the child.(Bender, 1946)

**NON-DRUG TECHNIQUES OF SEDATION**

Psychosedation describes a drug capable of producing relaxation of the patients mind.

The two major categories of psychosedative techniques are:

1. Iatrosedative techniques and
2. Pharmacosedation techniques.



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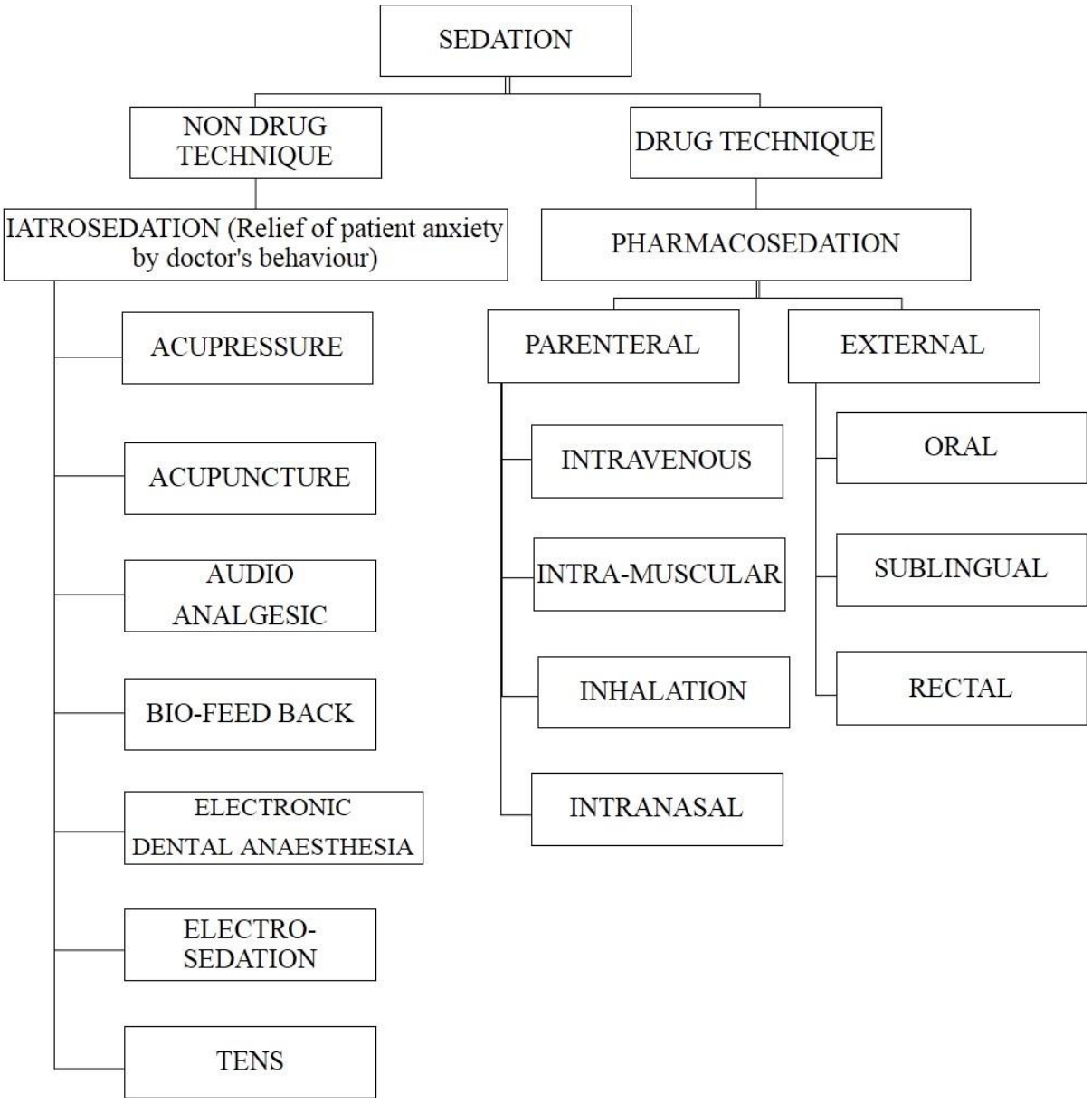



**Figure 1**



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**Latrosedation**: Iatrosedation refers to the relief of anxiety through the doctor's behavior and not by drugs (Mann & Hunt, 2013). This term was described by Dr. Nathan Friedman. General definition of iatrosedation involves the technique achieving sedation without any drugs. Types of iatrosedative techniques include Acupressure, Acupuncture, Audio analgesia, Biofeedback, Electro anesthesia (EA), Electro sedation, Electronic dental anesthesia (EDA), Hypnosis, TENS Cranial electro stimulations

Egbert et al 1962 demonstrated the value of the preoperative visit by the anesthesiologist to patients about to undergo surgery the next day and concluded that both preoperative drug and preoperative visit makes the patient drowsy and calm (L. D. Egbert et al., 1963).

A second study by Egbert conducted a study where two groups I and II who were not told about post-operative discomfort & pain but were told that analgesics would be available if they were required and were told about the post-operative discomfort and pain respectively. They observed that Group I required twice the dose of analgesic than Group II. Group II patients were discharged earlier than Group I (Lawrence D. Egbert et al., 1964)

**FACTORS GOVERNING DRUG ADMINISTRATION**

Various factors govern the determination of drug dosages for children. These are



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generalized, with exceptions to be anticipated:

1. Age of the child:
2. Weight of the child:
3. Mental attitude of the child:
4. Level of sedation desired:
5. Physical activity of the child:
6. Contents of the stomach:
7. Time of day:
8. Ability to titrate:

**Formulas**

Young's rule and Clark's rule have been suggested as aids in determining pediatric dosages as a fraction of the adult dose. The success of such rules is haphazard at best and cannot be recommended (Shashikiran et al., 2006).

**Young's rule:**

$$\text{Fraction of adult dose for children} = \left( \frac{\text{Age of patient}}{\text{Age} + 12} \right)$$

**Clark's rule:**

$$\text{Fraction of adult dose for children} = \left( \frac{\text{Weight in pounds}}{150} \right) \text{ OR } \left( \frac{\text{Weight in kilograms}}{70} \right)$$



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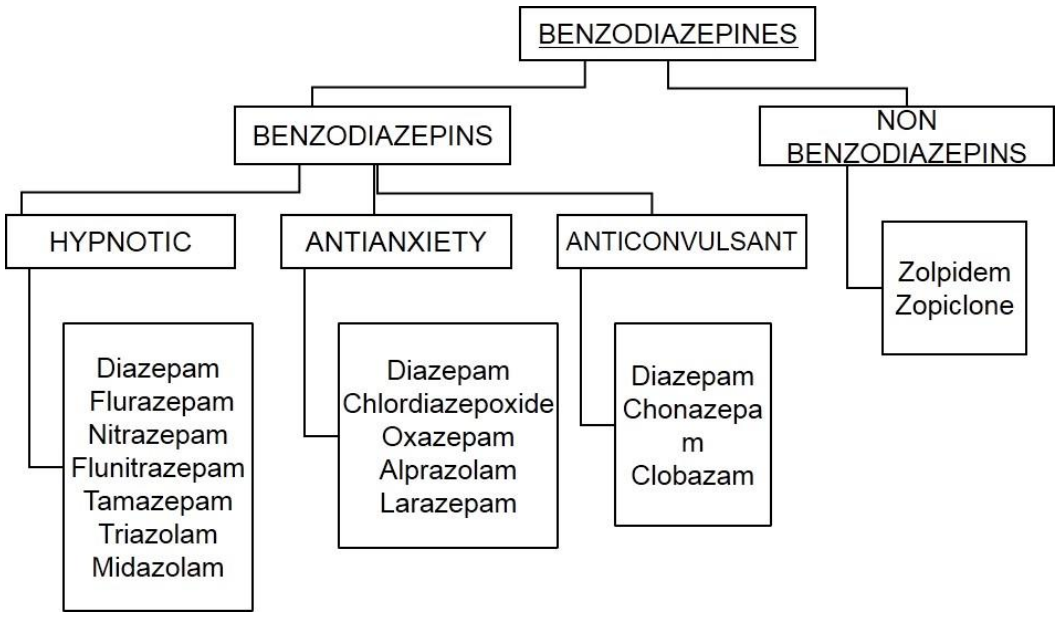
**BENZODIAZEPINES and NON-BENZODIAZEPINES (Figure 2)**

*BENZODIAZEPINES*

Benzodiazepines are most widely used anxiolytic drugs. They have largely replaced Barbiturates and Meprobamate in the treatment of anxiety, since the benzodiazepines are most effective and safer.

**Mode of action**

Benzodiazepines bind to a specific benzodiazepine receptor on GABA receptor complex, thereby increasing GABA affinity for its receptor. The final result is a sedative-hypnotic effect. Act on the limbic system, resulting in sedative, anxiolytic, anticonvulsant, and amnestic effects, however no analgesic effects seen.






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**2. BARBITURATES (Figure 3)**

The barbiturates represented the first truly effective drugs for the management of anxiety and were widely prescribed. Barbiturates are generalized CNS depressants, depressing the cerebral cortex, the limbic system at therapeutic blood level. These actions produce a reduction in the anxiety leave, decreased mental acuity, and drowsiness. At higher dosages, depression of medulla occurs, leading to respiratory depression and possible cardiovascular depression. Barbiturates are capable producing any level of CNS depression. Ranging from light conscious sedation through hypnosis, general anaesthesia, coma, and death.

| DRUG NAME | HALF LIFE (in hours) | ACTIVE METABOLITE | PEAK PLASMA LEVEL |
|---|---|---|---|
| Triazolam | 1.5-5.5 | No | 1.3 |
| Midazolam | 1.2-12.3 | No | 0.5 |
| Lorazepam | 12 | No | 2 |
| Diazepam | 20-70 | Yes | 2 |
| Chlrodiazepoxide | 24-48 | Yes | 4 |
| Alprazolam | 12-15 | No | 1-2 |



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## OPOIDS (Figure 4)

Opioid analgesics among the most commonly used medications in the emergency department and are most often used for pain control. They have analgesic properties, cause some sedation and have no amnestic properties. Commonly used agents include morphine, meperidine and fentanyl. Their advantages include a variety of administration routes (e.g. oral, intravenous, rectal, intramuscular, subcutaneous, transmucosal, intranasal routes).

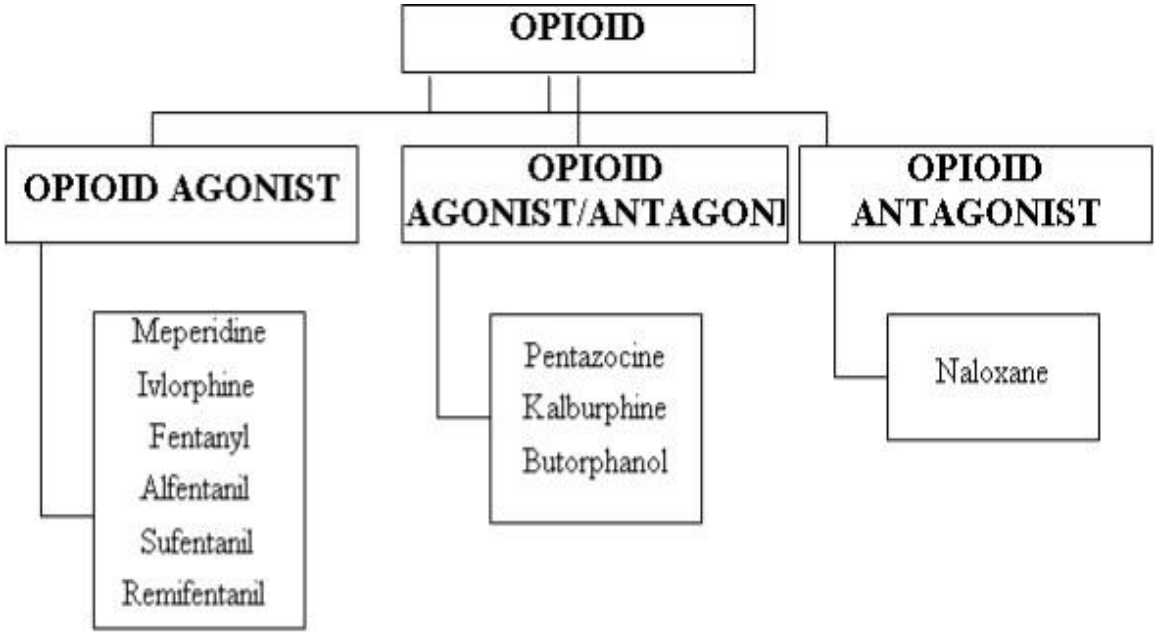



Figure 4



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**ANTICHOLINERGICS**

A. Natural Alkaloids: Atropine, Hyoscine
B. Semisynthetic Derivatives: Homatropine, Hyoscine, Butyl Bromide, Ipratropium Bromide
C. Synthetic Compounds: Cyclopentolate, Tropicamide, Isopropamide,

**ANTIHISTAMINES ($H_1$ Antagonists) (Figure 5)**

The most popular antihistamine is hydroxyzine, although promethazine and diphenhydramine are sometimes used in sedative combinations. These antihistamines have other properties including antiemetic effects. Antihistamines can also be used as a singular sedative agent; however, the amount of sedation achieved in therapeutic doses is minimal especially under challenging conditions associated with dental procedures. The use of communicative behavior guidance techniques, antihistamines, and nitrous oxide can produce amazingly good results for children who have mild anxiety.

*Hydroxyzine*

A Di-Phenyl-Ethane has been one of the most popular psychosedative agents in pediatric dental practice. It is given orally in a dose of 3.7 mg/kg body weight, 45 minutes to one hour before the appointment or in divided doses or 25mg/5cc. Hydroxyzine used in combination with other sedatives may reduce the incidence of nausea or vomiting. Hydroxyzine has some other benefits that suggest its use as an adjunct with other sedatives including broncho-dilatation,



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antiarrhythmic properties, very mild analgesia, and drowsiness. Its mechanism of action is not fully appreciated, but the primary target appears to be subcortical portions of the CNS. Hydroxyzine is rapidly absorbed from the gut with noted effects within 15–30 min. It is metabolized in the liver and excreted through the kidney and has a wide margin of safety.

Promethazine:

A phenothiazine derivative administered in dose of 1.2 mg/kg body weight, one hour prior to the appointment. Promethazine is not particularly effective as a sole agent for sedation, though it does help in calming lesser degree of anxiety. It is, therefore, most commonly employed in combination with other sedative drugs such as Chloral Hydrate, Hydroxyzine, and Meperidine etc. Side effects include paradoxical hyper-excitability, hallucinations and mild hypertension.

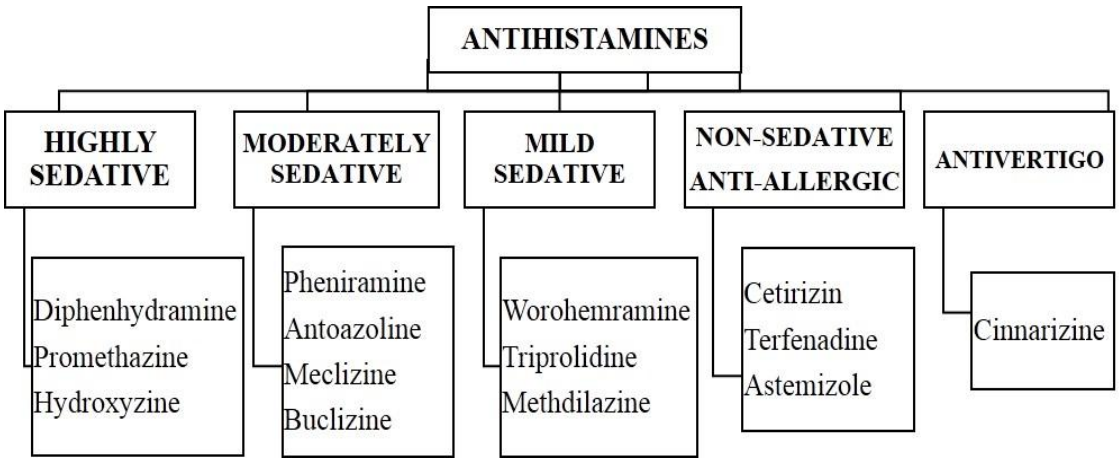



**Figure 5**



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**Others**

A. Inhalation:

   Gas: nitrous oxide

   Liquid: ether, halothane, enflurane, isoflurane, sevoflurane

B. Inducing agent: propofol, thiopentone sodium.
C. Dissociative anaesthesia: ketamine
D. Neuroleptic analgesia: fentanyl + droperidol.
E. Chloral derivative: chloral hydrate
F. D-iso-propylphenol: propofol

**ANTIDOTE DRUGS/ REVERSAL AGENTS:**

Specific reversal agents to antagonize the drug Effect in case of over dosage and inadvertent adverse Drug effects exist for benzodiazepines and opioids. Sedation providers must understand their use in order To responsibly utilize either of these classes of agents.

**Drugs classification:**

A. Opioid antagonist: Naloxane, nalbuphine.
B. Benzodiazepine antagonist: flumazenil
C. Agents for reversal of emergence dilirium: Physostigmine
D. Vasodilator for extra vascular or intra-arterial drug administration: procaine

**Naloxone:**

Naloxone (narcan) is an opioid antagonist and can be given intravenously, intramuscularly, Or subcutaneously but the preferred route of Administration is intravenous. The drug should be given in a



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slowly titrated manner when possible. The dose for children is 0.1 mg/kg for children under 20 Kg. The drug is incredibly effective in reversing the depressive effects of the Opioids. Children will often be quite disturbed when they are awakened from sedation by administering naloxone. The most Common side effect is nausea.

**Flumazenil**

Flumazenil can be used to reverse the effects of benzodiazepines and should be immediately available when using benzodiazepines for sedation. A dose of 0.01mg/kg may be repeated 4 times as needed. Careful observation for this re-sedation should be maintained for at least an hour following the administration of flumazenil.

*NITROUS OXIDE*

Dr. Horace wells introduced nitrous oxide as a general anaesthetic in 1844. The only agent, used with inhalation technique that meets the requirements of sedation is nitrous oxide. It is delivered by means of a flow meter utilizing nasal masks or hoods.

**EVOLUTION OF NITROUS OXIDE**

- 1973 - Wright and MacAulay 44% using nitrous oxide
- 1996 - Wright 66.3% using nitrous oxide
- 2002 - Houpt 61% using nitrous oxide
- 2007 - Lynch 74% using nitrous oxide
- 2011 - Wilson and Alcaino's recent international survey, based on 311 replies, revealed that at least 56% of



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Accepted: April 30, 2026

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the respondents used nitrous oxide in their practices.

**NITROGEN IN $N_2O$**

It is the most frequently used sedation agent by pediatric dentist. It is sweet smelling, colorless, non-inflammable, inert gas and is compressed in cylinders at 750 psi as liquid that vapourises on release. It has a blood gas co-efficient of 0.47 and has rapid onset and recovery due to low blood solubility. It has low tissue solubility and minimum alveolar concentration value in excess of one atmosphere, rendering full anesthesia without hypoxemia impossible at normal atmospheric pressure. Poor tissue solubility ensures its effect is characterised by rapid onset and fast recovery. It is weak analgesic; effect can be influenced by psychological preparation of the child.

*It is a cost effective alternative to general anaesthesia with minimal effect on cardiovascular and respiratory function and the laryngeal reflex, Poor tissue solubility ensures rapid onset and it is commonly used in the management of uncooperative children and Minimum side effects. Inspite of the advanmtages, it is asociatd with nausea, impotence, liver toxicity and recreational abuse and vitamin $B_{12}$ activity resulting in impaired synthesis of RNA. The Toxic effects of N2O is that is a potential Carcinogenic agent,Bone marrow depression may occur after prolonged use (Becker & Rosenberg, 2008).*

**OXYGEN IN $N_2O$**

First prepared in 1727 by Stephen Hales and discovered as an element in 1771 by Joseph Priestley and almost simultaneously by Karl



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Scheele (1771). $O_2$ is the second component of the inhalation sedation (Girdler et al., 2004).

*Special indications nitrous oxide-oxygen inhalation sedation(Table 2)*

*It is indicated in children with mild-to-moderate anxiety to enable them to accept dental treatment better and to facilitate coping across sequential visits (Bowen, n.d.)*

**EQUIPMENTS for Inhalation Sedation While Using $N_2O$**

It is administered by closely fitting nasal hood with two ports. One for administration of agent and Other for expired gases to be scavenged out without contaminating the operating room. The drug may be delivered alone at concentrations of 30-50% for moderately painful procedures or in combination with a Mild sedative at lower concentrations for similar effect. Onset of sedation and analgesia occurs in minutes and is terminated rapidly when the gas is discontinued. Nitrous oxide is 34 times more soluble in Blood than nitrogen. As a result oxygen concentration in the alveoli falls and patient becomes hypoxic. To overcome this problem - nitrous oxide concentration during maintenance phase should be kept as low as possible (should not exceed 30%).

On administration of nitrous oxide, patients feel lightheaded and though the pain is felt, response to it is altered. With the onset of sedative effect tingling sensation is felt in hands, feet and oral cavity, etc. due To



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paraesthesia of sensory nerves induced by Nitrous Oxide. Facial flushing and perspiration is usually observed. Administration of Nitrous Oxide is sometimes accompanied by hallucinations and for this reason its use is contraindicated in psychiatric patients.

During the end of the procedure it is necessary to administer 100% oxygen to prevent hypoxia due to quick washing of alveolar gases because of higher perfusion pressure of nitrous oxide. This phenomenon is called as diffusion hypoxia. It is recommended that the patient should be maintained on 100% oxygen for 5-10 minutes after the procedure. There should also be an oxygen flush lever that will deliver 100% oxygen at 30L/min. The designs for converting this system into one using a full mask and intermittent positive pressure ventilation for emergency resuscitation are available (Nozik-Grayck et al., 2014)

The gas cylinders are required to be colour coded green (oxygen) and blue (nitrous oxide). The nitrous oxide cylinders should be of medical quality to assure freedom from inadvertent contamination by toxic byproducts such as nitrous dioxide and nitric oxide. The nitrous oxide is packaged by compressing the gas into its liquid form and stored at 650 to 800 psi (King et al., 2020)



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**Procedure of Administration** (Sweeney, 1974)(Figure 6)

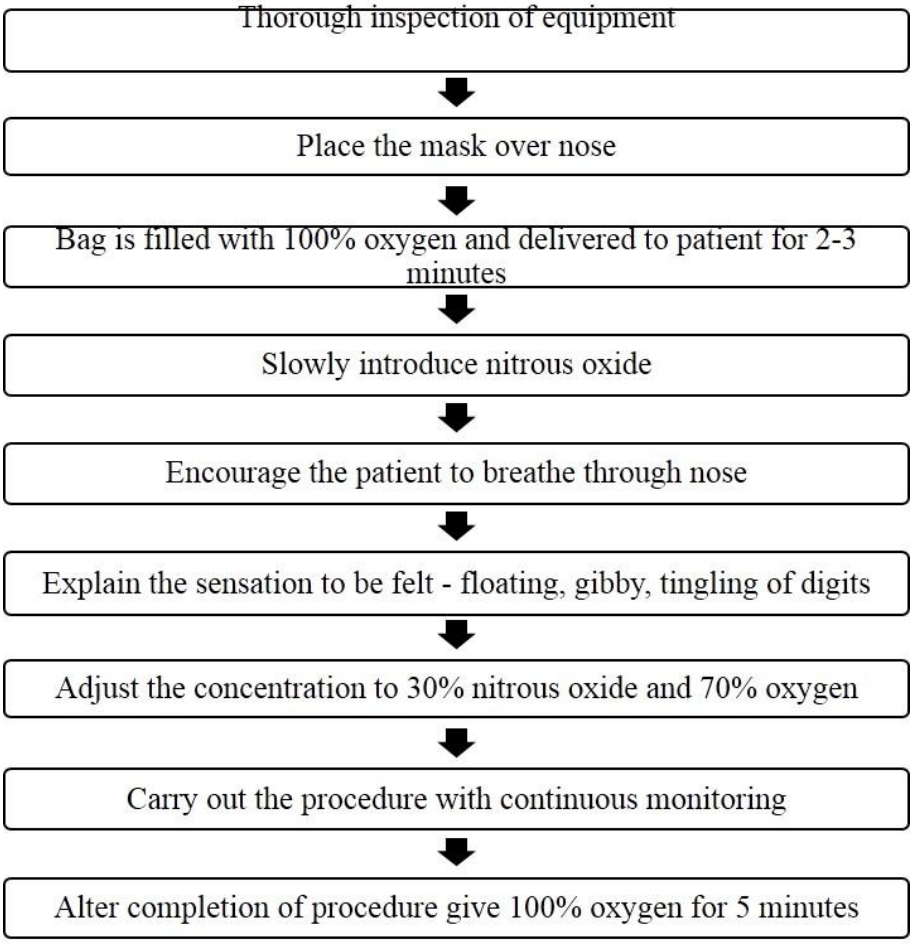



Figure 6



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**EFFECTS OF NITROUS OXIDE ON VARIOUS SYSTEMS**

Nitrous oxide exerts CNS depressant action, amnesia is possible only at higher concentrations. Hallucinations can also occur. It also reduces $CO_2$ stimulated respiratory drive therefore respiratory depression may result, if used in combination with narcotics. Decreases cardiac output is decreased while there is increase in Peripheral vascular resistance. Significant in patients suffering from cardiac problems. Vomiting may be induced depending on the length of exposure and concentration of the drug.

Signs and symptoms of $N_2O$ **(Shashikiran et al., 2006)**

| SYMPTOMS | SIGNS |
|---|---|
| 1. Light headedness (dizziness)<br>2. Tingling of hands and feet<br>3. Wave of warmth<br>4. Feeling of vibration throughout body.<br>5. Numbness of hands and feet. Soft tissues of oral cavity.<br>6. Feeling of euphoria, laughing, crying.<br>7. Feeling of lightness or heaviness of | 1. Blood pressure, heart rate elevated slightly early in procedure, then returns to baseline values.<br>2. Respirations are normal, smooth peripheral vasodilation.<br>3. Decreased muscle tone as anxiety decreases (arms and legs relax).<br>4. Flushing of extremities, face |



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| | |
|---|---|
| extremities analgesia.<br>8. Hearing, especially of distant sounds, becomes more acute.<br>9. Visual images become confused (patterns on ceiling begin to move).<br>10. Sleepiness, dreaming, nausea<br>11. Sweating increases | 5. Increased movement<br>6. Increased heart rate, blood pressure<br>7. Increased rate of respiration.<br>8. Increased sweating possibly lacrimation. |

**STAGES OF NITROUS OXIDE ANALGESIA**

Depending on the concentration and length of administration of gas, four levels of sedation can be experienced or described (after an initial feeling of light-headedness). A tingling sensation, especially in the arms and legs, or a feeling of vibration (paraesthesia) Quickly followed by warm sensations, and a feeling of well-being, euphoria and/or floating. During heavier sedation, hearing may dissolve into a constant, electronic-like throbbing. They feel like they are flying in air. At a deeper level of sedation again, sleepiness, ("dream") can occur. If nausea set in, it indicates definite over-sedation.



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**Concentration of nitrous oxide and oxygen during various stages of sedation:**

| | |
|---|---|
| **INDUCTION** | Slow □ 0.5-1 lit/min<br>Rapid 2-4 lit/min.<br>40% nitrous oxide<br>60% oxygen |
| **MAINTENANCE** | 20-30% nitrous oxide |
| **REVERSAL** | 100% oxygen |

**EFFECTS OF NITROUS OXIDE ON VARIOUS SYSTEMS**

CNS depressant action, amnesia is possible only at higher concentrations. Hallucinations can also occur. Reduces $CO_2$ stimulated respiratory drive therefore respiratory depression may result, if used in combination with narcotics. Decreases cardiac output and increases Peripheral vascular resistance. Significant in patients suffering from cardiac problems. Vomiting may be induced depending on the length of exposure and concentration of the drug.

**Nitrous oxide hazards**

Since 1970s, studies have indicated that chronic exposure to inhalation anaesthetics could be a health hazard. The hazards of nitrous oxide have been reported by Cohen (1970) (Cohen et al., 1971). Several studies on occupational safety and health report



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that with nitrous oxide 25-400 ppm is the safety level. However, levels of nitrous oxide in dental environment have been reported to vary from 500 to 1000 ppm. Therefore, precautionary measures must be undertaken to limit exposure of staff to the vapours[82] If enclosed spaces - contra indicated such as pneumothorax, upper respiratory tract infection, respiratory depression. Pregnancy as spontaneous abortions may occur, diffusion hypoxia, DNA synthesis affected vitamin $B_{12}$ oxidation may be suppressed even with brief exposures of at least 6 hrs, altered hematopoesis and pernicious anaemia. Bone Marrow Toxicity; agranulocytosis, thrombocytopenia. 6% reduction in chances of conception in DSA > 5hrs./day (Rowland et al., 1992) Spontaneous abortion risk increases, 1.5 times risk (Boivin, 1997)

COSHH (Control Of Substances Hazardous to Health)

It was aimed to minimize the exposure to hazardous substance regulations in 1994. It is estimated in TWA, Time Weighted Average. The average exposure to contaminant or condition to which workers may be exposed without adverse effects over the period such as in an 8hr/day or 40hr/week.

- **USA**
  - **ADA;** 50ppm 8hr TWA
  - **NIOSH;** 25ppm 8hr TWA
- **Europe**
  - 25ppm 8hr TWA
  - Greece banned



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**Conscious sedation in children:**

Conscious sedation can be defined as a technique that can be performed using one or more drugs that produce a state of depression in the central nervous system, allowing the desired treatment to be made. Verbal contact with the patient must be always maintained throughout the period of sedation, which means that it is a medically controlled state of depression of conscience that allows the patient to preserve his protective reflexes, a free respiratory airway and also present an appropriate response to physical stimulus and verbal commands such as, e.g., "open your mouth". (Silva et al., 2015)

I) Inhalational agents

Inhalational agent commonly used is Nitrous Oxide with oxygen supplementation in different Concentrations. This is also known as relative Analgesia. Other drug of choice are: Desflurane and Sevoflurane

II) Systemic agents

Systemic agents are usually administered by various routes including oral, sub mucous, rectal, Intranasal, intramuscular and intravenous. Drugs in this method can be classified as:

A. CONVENTIONAL

I. Lytlc Cocktalls
II. Barbiturates E.g. Phenobarbitone
III. Chloral Hydrate
IV. Anti – Histiminies E.g. Promethazine, hydroxyzine



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B. CONTEMPORARY

I. Newer Benzodiazepines E.g. Midazolam, Triazolam

II. Newer Antihistamines E.g. Loratidine

Conscious Sedation with Nitrous Oxide presents fast action on induction as well as during recovery (these effects occur within a few minutes). It presents low solubility in the tissues, as well as a minimal alveolar concentration (MAC) which is so high that its anesthetic effect is poor under normal atmospheric pressure (Gupta et al., 2015). In 2008, a Cochrane review reports high probability of beneficial effects on behavior and anxiety when N2O is used. Furthermore, this technique has been described as standard technique in pediatric dentistry and can be successful in up to 90% of the cases, provided that patients are carefully selected. (Ashley et al., 2018)

Machines intentionally designed for the administration of inhalation sedation in dentistry should be used and be capable of administrating N2O to a maximum limit of 70% with not less than 30% of oxygen in volume, even though in the majority of cases, adequate analgesia is achieved with concentrations of N2O that do not exceed 50% in volume.

**DISSOCIATIVE sedation in children:**

Ketamine

It is in use since 1970, is often referred to as a dissociative agent causing a functional and electro-physiologic dissociation between



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the thalamo-neocortical and limbic areas of the brain leading to a trancelike cataleptic state characterized by profound analgesia and amnesia, with retention of protective airway reflexes, spontaneous respiration, and cardiopulmonary stability (Pandey et al., 2011)

Ketamine was the medication used most frequently for Procedural Sedation Analgesia. Ketamine is unique in that it does not follow the dose-dependent sedation spectrum of minimal, moderate, deep and general anaesthesia. Ketamine/Propofol and Propofol alone had higher rates of apnoea than ketamine alone. Ketamine did have a relatively high incidence of vomiting at 8%, compared with all of the other medications, followed by nitrous oxide at 6.8%.(Bellolio et al., 2016)

Ketamine/Propofol or “Ketofol”

In recent years, the combination of propofol and ketamine (nicknamed “ketofol”) has been increasingly used and reported in the literature. The advantage of such a combination over ketamine alone is a shorter recovery time, decreased incidence of nausea and vomiting, and lower incidence of emergence reactions. In addition, combining propofol and ketamine appears to result in smaller doses of each medication needed than either alone; with propofol in particular, smaller drug doses may mean fewer adverse respiratory events. Multiple regimens have been described in the literature, with no one



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method being described as favourable over others (Coté et al., 2016) .

In 2010, Andolfatto and Willman published a series of 219 pediatric patients who received a 1:1 mixture of 10 mg/mL ketamine and 10 mg/mL propofol in a single syringe. Their study found that the median dose needed for adequate PSA was 0.8 mg/kg of each medication. The overall incidence of adverse effects was low and the median recovery time of 14 minutes was shorter than that observed with ketamine alone. Adequate sedation was achieved in all patients and both families and staff were very satisfied with performance of the drug mixture (Andolfatto & Willman, 2010).

Dexmedetomidine

It is a potent, highly selective alpha-2 agonist that has sedative and analgesic effects. It acts on adrenoceptors in many tissues, including the nervous, cardiovascular and respiratory systems. When administered within the recommended doses, it causes analgesia with no accompanying respiratory depression. The ideal sedative for the outpatient dental clinic would be effective, easy to titrate, fast in onset and offset, predictable in response, able to preserve the airway tone, inexpensive, minimal cardiovascular or respiratory effects, and minimal risk of the central nervous system (CNS) depression. Despite these excellent attributes, data regarding the use of dexmedetomidine in pediatric dentistry is



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still limited. Gyanesh et al., who reported that children in the dexmedetomidine group had an earlier awakening and discharge than those in the ketamine group, but this difference was statistically non-significant (Hammadyeh et al., 2019). Potential complication include nausea and vomiting due to presence of food in the stomach, over-sedation, vertigo, bowel discomfort, claustrophobic effect

**OTHER PROCEDURES THAT USE NITROUS OXIDE**

RELATIVE ANALGESIA

The specific technique of Relative Analgesia is described fully by Langa (1968) (Langa, 1963). It is a technique in which the dose of nitrous oxide is titrated to the need of the individual patient, and the inspired concentration is always kept to the minimum necessary. This emphasizes the fundamental point that Relative Analgesia is not a simple pharmacological technique (Allen, 1984).

It Alleviates fear by producing anxiolysis, reduces pain by inducing analgesics and improves patient co-operation so that the dental treatment can be performed. **It includes a triad of elements;**

1. The administration of low to moderate titrated concentration of nitrous oxide in oxygen to patient who remain conscious
2. The use of superficially designed machine with number of safety features, including the ability to deliver minimum of 30% oxygen and a fall-safe



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device that cuts off delivery of nitrous oxide if the oxygen supply falls.

3. The use of semi-hypnotic suggestion to reassure and encourage the patient through-out the period of sedation and treatment.

There machines developed and manufactured in India such as Noiseless NOIS (Nitrous Oxide Inhalation Sedation) Nitrox, ConsEd and SmartSed.

ENTONOX

The drug; $N_2O$ must be delivered with oxygen to avoid a hypoxic gas mixture. This may be accomplished through the use of flow meters from separate sources or through the delivery of a fixed mixture of 50% $N_2O$ and 50% oxygen. This mixture 50:50 is ENTONOX and is supplied in cylinders colour blue with a quartered white and blue collar. Used by midwives for pain control during labour and has been used in combination with oxygen for dental sedation. This technique is not flexible as relative analgesic and thus specially adapted medicine is necessary (Parsa et al., 2017).

**Routes of administration in pediatrics**

The routes for administration of sedation in Pediatrics are mainly through the:

1. Inhalation
2. Intramuscular
3. Intravenous
4. Oral
5. Submucosal

Two routes of drug administration predominate, with more than 60% of the



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respondents indicating that they employ the oral route

Approximately 43% employing inhalation sedation, although a wide variety of drugs are available for the management of anxiety, Pediatric dentists and general practitioners who manage large numbers of children rely on a rather limited number of well-established drugs. Nitrous oxide is the drug of choice in the recent day's scenario.

**INTRANASAL**

Use of this route is in very uncooperative young patients who are unwilling to accept oral medication and has the advantage of avoiding other painful invasive routes to increase patient comfort. Rapid absorption of drug takes place from the highly vascular nasal mucosa. It avoids first pass effect of liver. Concentrated solutions are used for intranasal administration. The major drawback of this route is burning sensation produced during drug administration which sometimes elicits the crying response in children, thus making the whole process counterproductive.

It is particularly well suited to pediatric procedures and provides better sedation with fewer respiratory complications than midazolam/ fentanyl making a quite ideal agent for pediatric dental sedation (Pandey & Bahetwar, 2011) Midazolam, ketamine, fentanyl like drugs may be given by this route. Mild to moderate levels of sedation can be achieved with 0.5 mg/kg of midazolam when administered orally; however, the recommended dose for the IN route to obtain a similar effect is 0.2–0.3



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mg/kg. IN administration of many sedative agents can be achieved. Certain agents such as chloral hydrate would be contraindicated because of its thicker consistency and extreme mucosal irritation.

Midazolam

It is hydrophilic, short-acting benzodiazepine, which produces sedation, anxiolysis, and amnesia, time of onset is dose dependent Intranasal midazolam was administered in a dose ranging from 0.1-0.5 mg/kg. An optimal dose of 0.2mg/kg produced rapid, non-invasive and safe preoperative sedation. Higher doses did not have clinical benefits and were associated to coughing, sneezing, and expulsion of the solution (AlSarheed, 2016).

Dexmedetomidine

It is an α2 agonist with analgesic and sedative properties. Moreover, it is least likely to produce respiratory depression in comparison with other commonly used sedatives. It is widely used in pediatric patients. Besides other routes, dexmedetomidine is conveniently and effectively given by oral as well as intranasal route and is well tolerated by both. Rccommended dosage is 1 µg/kg and 2 µg/kg (Patel et al., 2018)

**Efficacy of drugs**

Several large studies document that it has a wide margin of safety. However, it has been used by few researchers for pediatric dental sedation. INK with either mode of administration provides good sedation and



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represents a safe and effective pharmacological technique for procedural sedation of young, uncooperative pediatric dental patients (Attri et al., 2017)

AM Al-Zahrani et al. found that oral midazolam alone resulted in a superior sedation to IN administration of midazolam alone, IN midazolam plus oral transmucosal fentanyl citrate (the fentanyl patch) and IN administration of both midazolam and sufentanil. (Al-Zahrani et al., 2009)

Bahetwar et al. showed that IN ketamine alone (6 mg/ kg) or IN midazolam (0.2 mg/kg) plus IN ketamine (4 mg/kg) resulted in much more successful sedations than IN midazolam (0.3 mg/kg) alone (Bahetwar & Pandey, 2011).

**INTRA MUSCULAR**

The intramuscular (IM) route of drug administration is a parental technique where the drug enters the cardiovascular system and bypasses first phase metabolism. Technically, the IM of administration might be considered the easiest of all routes. It requires no special equipment except a syringe and needle. In the child the IM route is more frequently indicated; as both IV and inhalation conscious sedation requires a degree of patient cooperation for success to be achieved.

The IM route of drug administration involves injection of the sedative agent into a skeletal muscle mass. Its use in pediatric health care has been primarily a precursor route for sedative administration prior to



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intravenous catheter placement or induction of general anesthesia.

Proper site selection varies from patient to patient and is an important factor in the safety of this technique. The sites most commonly chosen for the administration of IM drugs are the following (Jensen et al., 1980): Gluteal area, Ventro-gluteal area, Vastus lateralis and Mid-Deltoid area. For most patients the upper outer quadrant of gluteal region is safest but in small children anterior thigh (Vastus Lateralis muscle) is the preferred site.

It is painful, invasive and one of the most unpleasant routes of drug administration. It can, however, be used as a rescue in those patients who refuse to accept oral medication and in whom gaining venous access is rather impossible because of poor cooperation. In such cases, patient needs to be restrained momentarily and onset of sedative effect is achieved within minutes. Absorption from an injection deep into a large muscle is much faster and more dependable than absorption from the oral route.



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**COMMONLY USED INTRAMUSCULAR DRUGS AND ITS COMBINATIONS**

| | |
|---|---|
| 1. Diazepam & Morphine | Longer duration – 7hrs |
| 2. Diazepam & Meperidine | Duration – 3-4 hrs. |
| 3. Diazepam & Fentanyl / Alphaprodin | Duration – 2-4 hrs. |
| 4. Promethazine/ Hydroxyzine & Meperidine | Duration – 2-4 hrs. |

Other drugs can be administred IM are Lytic cocktail/ DPT: Meperidine (Demerol), promethazine (Phenergan), & chlorpromazine (Thorazine) Dose:-1: 1/4:1/4. 1mg/kg. Hydroxyzine plus opioid, Barbiturate plus opioid, Pentobarbital, Meperidine, and Scopolamine, Meperidine, Promethazine, and Chlorpromazine:



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| GENERIC NAME | PROPRIETARY | HALF LIFE |
|---|---|---|
| 1. Ultra-short acting | | |
| a. Hexobarbital | Sombulex | 5 hours |
| b. Methohexital sodium# | Brevital, Brietal | 3.5-6 hours |
| c. Thiamylal sodium# | Surital | - |
| d. Thiopental sodium# | Pentothal | 3-8 hours |
| 2. Short acting | | |
| a. Pentobarbital sodium | Nembutal | 21-42 hours |
| b. Secobarbital sodium | Seconal | 20 - 28 hours |
| 3. Intermediate acting | | |
| a. Amobarbital | Amytal | 14-42 hours |
| b. Butabarbital | Butisol | - |
| 4. Long acting | - | 24 - 96 hours |
| a. Phenobarbital | | |

**Complications:**

Some of the complications with IM route include injury to the nerve rsulting in paralysis, paraesthesia and hyperesthesia, intravenous or intra-arterial air embolism, periostitis, hematoma, abscess, cyst and scar formation.

**INTRAVENOUS**

It is one of the most common routes employed for achieving Sedation and Analgesia. Rapid wearing off of drug effect are the obvious advantages. Because of the rapidity of drug effect with this route, titrated effect can be produced. It requires skilled personnel for venipuncture. Dentist need not be an anaesthesiologist to administer an intravenous injection. Intravenous sedation merely is a more direct method of depositing a chemical into the blood stream



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The IV route is the optimal and ideal route for administration of sedation. In fact, the American Society of Anesthesiologists (ASA) discourages oral sedation protocols, especially for children, and states in the 2002 publication "Practice guidelines for sedation and analgesia by non - anesthesiologists" that "intravenous administration of sedative and analgesic medications increases the likelihood of satisfactory sedation for both moderate and deep sedation. They also agree that it decreases the likelihood of adverse outcomes." (Non-Anesthesiologists & An Updated Report by the American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologists, 2002)

The primary advantage of IV sedation is the ability to achieve their maximal effect. And a baseline level of sedation followed by maintaining a "therapeutic window," wherein small doses of sedative and/or analgesic agents can be administered as needed to maintain the desired level of sedation (Jin et al., 2015). It is possible to predictably increase or decrease the depth of sedation during treatment depending on the patient's response and the procedure being performed. Administration of emergency drugs is almost always best accomplished through the IV route. Thus avoiding under- or overdosing with a standardized single bolus dose, as is necessary with oral, IM, or SM injections.



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**Disadvantages**

Venipuncture is necessary and complication may occur, More intense monitoring required, Recovery may not be complete, Most IV agent cannot be reversed. Intravenous sedation is not recommended in pre- Cooperative children. Dentists should consider whether the provision of an elective general anaesthetic might be preferable in such circumstances. An additional disadvantage of IV sedation for pediatrics is the need to induce at least a moderate level of sedation and often deep sedation.

**COMMONLY USED TECHNIQUES FOR IV SEDATION**

**The butterfly NEEDLE:**

The butterfly is a very convenient one-piece needle and extension tube Sedation technique. The dentist may begin to sedate the patient once the vein has been entered, the tourniquet has been released, and the needle and tube have been securely taped.

**The Loma Linda (Jorgensen) Technique**

Venipuncture is performed with a 2 cc syringe containing 50mg/cc of Nembutal. The drug is injected slowly until the patient experiences dizziness or blurring of vision. The syringes may be changed one or two or more times and the patient may require 300 mg of the drug. 10% more than the latter base dose should be added, the



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Accepted: April 30, 2026

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syringe is then detached from the needle. It is replaced by a fresh syringe 25 mg of Meperidine and 0.32mg of Scopolamine which have been diluted with up to 5 ml of distilled water. Demerol is administered if patient received 100 mg of Nembutal. 25 mg Demerol should be administered, or proportionally less depending on the dose of Nembutal. The local injection is administrated. The needle is removed. Dental treatment is instituted. The Loma Linda Technique is an innocuous method, which could be likened to instant premedication on minor operative, short-term procedures. (Jorgensen & Leffingwell, 1967)

**The Monheim Technique**

This technique involves an excellent mechanical arrangement: a single venipuncture, kept patent by dripping dextrose in water. Medications are given at sites: Nembutal 50-100 mg. Demerol 25 mg is mixed with Phenergan 25 mg. Sign and symptom includes, drowsiness; local sedation is maintained by inhalation 50/50 nitrous oxygen. The Monheim Technique basically is an inhalation technique with premedication. It is excellent for short procedures, but has all the deficiencies of Nitrous analgesia in longer treatments (Giovannitti et al., 2019).

**The Shane Technique**

A 5cc syringe is filled with Alphaprodine, Hydroxyzine, and Atropine diluted with normal saline to 5ml and mixed in a larger syringe filled with 1% Methohexital, to induce amnesia. Sign and symptoms are eccentric eyes. The Shane Technique is an



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excellent intravenous technique which would be improved if the medications were delivered in separate syringes and if the warnings on IV Vistaril were non-existent. (Shane, 1966)

**POTENTIAL COMPLICATIONS**

Extravasations of drug into the tissues, hematoma formation, and inadvertent intra-arterial injections are possible complications of a misplaced IV catheter. Thrombophlebitis is a rare complication that may be attributable to the IV cannula or drugs. An immediate anaphylactic allergic reaction will become life threatening more rapidly if it is due to an IV bolus of a drug than if it is due to an oral or intramuscular dose. Significantly, a papoose which is too tight may restrict respiratory efforts resulting in hypoxia in a sedated child.

**PRECAUTIONS**

It should be administered only an experienced dental sedationist with a trained dental nurse in an appropriate facility. A pulse oximeter, at least, should be used to augment alert clinical observation. I.V for children less than 14 years should he carried out in a hospital facility.

**ORAL SEDATION**

Oral sedation is a valuable technique in pediatric dentistry. It is a popular mode of administration. It is simple, safe, convenient and most economical mode. One of its major advantages is the fact that it



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minimizes the need of syringes, needles and trained personnel: there is no need for the use of a needle (IM, SM, SC, and IV) or of a nasal hood (inhalation) to produce a clinical effect. When chairside behavior management techniques are not effective, oral sedation is an effective option available to promote successful dental treatment. Oral sedation is most accepted by pediatric patients, in comparison to intranasal, intravenous and intramuscular sedation (Parikh, 2017)

According to the American Academy of Pediatric Dentistry (AAPD), moderate oral sedation is the “drug-induced depression of consciousness” during which patients respond purposefully to verbal commands. There is no intervention necessary to maintain an open airway, and spontaneous ventilation is adequate while cardiovascular function is maintained.

Patients medically qualified for moderate sedation must be relatively healthy with minimal obstruction of the airway to minimize adverse events. This is classified by the American Society of Anesthesiologists (ASA) as class I-II with a Brodsky tonsillar classification of 0-2 (Parikh, 2017)

It is the most universally accepted and easiest route of drug administration. This route is mostly recommended for premedication and combination therapy. There is considerable duration between administration of drug and attainment of



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therapeutic effect. Greater patient acceptance and compliance, Reduced severity and incidence of adverse reactions Potential disadvantages include absorption of the drug by this route can be potentially erratic and incomplete. There is inability to titrate the drug level, inability to alter the sedation on demand, Objectionable taste and difficulty in reversal of unwanted effect and slow recovery time.

Oral sedation involves a wide spectrum of medications;

1. Benzodiazepines such as Midazolam and Diazepam
2. Antihistamines such as Hydroxyzine
3. Opioids such as Meperidine
4. Chloral Hydrate has been used individually or in combination for oral sedation in pediatric dentistry for years.
5. Nitrous oxide, an inhalation agent, is usually always used during oral moderate sedation for pediatric dentistry patients.

Various formulations for oral administration are tablets, capsules, syrups, linctuses, gels etc.

The triple regimen of oral moderate sedation proves to be beneficial as the pharmacokinetics and pharmacodynamics help to minimize any potential side effect an individual medication may have.

**Midazolam**

Midazolam is a short acting, water soluble benzodiazepine. The drug has become



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particular popular because of its short duration, predictable onset, and lack of active metabolites. It provides skeletal muscle relaxation, amnesia, and anxiolysis. The recommended oral dose is 0.5-0.75 mg/kg onset of sedation in approximately 15 minutes, with rapid offset approximately 30 minutes after the peak effect is noted. It can be given via oral or intranasal administration and has fewer metabolites than Diazepam (Dundee et al., 1984). Due to a bitter taste and has to be administered with sweet tasting masking agents like fruit juices, honey, flavored syrups, etc. But, recently premixed oral syrup has become available for use. Midazolam has been shown to be an effective tool for quick procedures due to its fast onset time, but may induce restlessness, agitation, anxiety and sometimes aggressive behavior.

**Hydroxyzine**

Hydroxyzine is a medication with both antihistaminic and antiemetic effects. It causes Central Nervous System (CNS) depression, anxiolysis, analgesia, sedation and bronchodilation. It's onset time is 15 to 30 minutes with 1.0 mg/kg orally, and it may potentiate the effects of Meperidine as well as other CNS depressants (Schaefer & Zito, 2020). Meperidine: It Is a narcotic analgesic which causes CNS, cardiovascular, and respiratory depression, produces sedation, analgesia, euphoria, and lowers the seizure threshold. Onset time is 30 minutes, peak effect is at 1 to 2 hours, dosage ranges from 1 to 2 mg/kg orally and maximum dosage is 50 mg. Meperidine acts



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at the mu receptor, which functions as an inhibitory modulator of synaptic transmission in the CNS. One undesirable effect is that Meperidine can lead to non-immunologic histamine release. Therefore, combining it with Hydroxyzine will aid to counteract this histaminic effect (Swerdlow, 1967).

**Diazepam**

They act on the limbic system, thalamus, and hypothalamus through mediation of the inhibitory neurotransmitter GABA. It has an onset time of 45 to 60 minutes and has a peak effect of 60 minutes. It has a dosage of 0.25 to 0.3 mg/kg orally, with a max dose of 10mg. However, Diazepam has a long half-life because it has multiple active metabolites (Griffin et al., 2013).

**Fentanyl**

Fentanyl is a powerful synthetic opioid which is 100 Times more potent than morphine. The recommended Dosage is 15-20ug/kg orally. Sedation reliably occurs within 15-30 minutes. It can be administered via oral transmucosal route. Respiratory depression with oxygen desaturation to less than 90% has been reported in 5% of children but usually resolves with verbal prompting (Farrar et al., 1998)

Associated Nausea and vomiting that occurs in about 15-20% of Cases, and the need for more intensive monitoring and Observation than other oral sedatives have limited Its popularity to date. The use of pulse oximeter is mandatory in these patients even when they appear Awake and alert .



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**PRECAUTIONS IN ORAL SEDATION**

Only one dose of the drug is prescribed to avoid any adverse effects. In addition, very explicit verbal as well as written instructions should be given to the person who will administer the drug to the patient. Children who are given an oral sedative should be placed in quiet room together with their escort and a competent member of staff and should be monitored clinically and electronically.

Ultimately, the goal is to promote cooperative behavior in order to safely complete dental treatment. Due to sleepiness, drug-specific motor imbalance, and sleep during transit and recovery times greater than four hours, “vigilant adult supervision” is recommended post-discharge.

**SUBMUCOSAL ROUTE**

The SM route of administration is another route that has been more popular in previous decades than today. Like the intranasal route, the dose of an agent administered submucosally is less than that of the oral route. Also, the agent must be non-irritating to tissues.

**Technique**

The SM route was originally used for the administration of opioid agonists such as Alphaprodine. The technique has fallen into disfavour because of a significant number of serious adverse reactions that were noted



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in conjunction with the SM administration of Alphaprodine.

The traditional location for the submucosal route of administration is in the buccal vestibule just between the 1st and 2nd primary molar of children. This injection is similar to that of local infiltration of local anesthetic to anesthetize the 1st primary molar. There is a fairly large venous complex in the pterygoid fossa of children, and thus, needle entry into the buccal mucosa pointed distal to the 2nd primary molar or maxillary tuberosity is highly likely to produce IV administration of a fairly large bolus of sedative and thus contraindicated.

For dental procedures, some drugs may be injected SM within the oral cavity, usually into the buccal mucosa between the 1st and 2nd primary molar. This may be less objectionable to some patients and parents than other injection sites, and it may be more comfortable and convenient for the dentist to perform.

**Drugs**

Meperidine can also cause localized release of histamine causing a red inflammatory wheal over the malar bone and area of injection. Significant pruritus is also notable requiring light rubbing of the area to counter the itching effect.

Several studies have shown successful sedation can be achieved via the submucosal route.

Pandey et al. in a blinded randomized crossover trial of 23 children compared oral



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midazolam (0.5 mg/kg) alone to the same oral dosage of midazolam with addition of a submucosal injection of fentanyl (3 micrograms/kg). The combination of midazolam and fentanyl was statistically significantly superior to oral midazolam alone for completion of dental treatment although four children in the combination group did suffer transient desaturations which were readily corrected by changes in head position (Pandey et al., 2010).

Myers et al. have demonstrated that submucosal administration of midazolam can augment a failing sedation. In study, in which children had received chloral hydrate (50 mg/kg) prior to dental treatment, submucosal injection of midazolam at 0.2 mg/kg deepened the sedation and improved behavior such that planned treatment could be completed (Myers et al., 2004).

**SEDATION IN MEDICALLY COMPROMISED CONDITIONS**

**Medically compromised patients:**

The most important are relating to the cardiovascular and respiratory systems, some musculoskeletal disorders are also significant. The administration of supplemental Oxygen may be indicated in the management of many of these patients.

**Asthma:**

Well-controlled asthma is not a contraindication to the use of sedation. Poorly controlled, even with medication (brittle asthma), great care must be exercised. Sedation may be helpful, but a



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detailed assessment of the patient on each day of treatment is essential as asthma is notoriously labile.

**Chronic obstructive pulmonary disease (COPD):**

Supplemental oxygen should be started before the induction of sedation in these cases. Patients with very severe bronchitis who may have a hypoxic respiratory drive should not be sedated with benzodiazepines or other respiratory depressant agents.

**Epilepsy**

Patients with well-controlled epilepsy usually present few problems, whereas the uncontrolled or poorly controlled patient must be referred for specialist care. Anti-epileptic drugs all depress the central nervous system often resulting in unpredictable over- or under-sedation and a shortened period of effective anxiolysis. Nonetheless, intravenous midazolam usually provides excellent sedation and also reduces the risk of stress-induced seizures.

**Movement disorders**

In patients with uncontrolled movements or spasticity, intravenous Benzodiazepine sedation will often reduce or suppress excess activity, making treatment easier for both the dentist and the patient.

**Neurological conditions**

The presence of a neurological impairment can be a major barrier to the receipt of oral care. The ability to receive dental treatment relies on patients being able to sit in the dental chair, open their mouth and allow procedures to be carried out. This is not always possible for those who are restricted



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physically or who present with involuntary muscle co-ordination. Providing muscle relaxation by way of conscious sedation is of great benefit to patients and clinicians. It is important to be aware that many patients may have an impaired swallowing ability as a result of their condition and when providing treatment under conscious sedation the patient should be kept in the semi-prone position.

**Learning disability**

Many individuals with Autism, Down syndrome, Attention deficit and hyperactivity disorder (ADHD), Cerebral palsy, Other congenital or genetic disorders. may have associated disability including physical, sensory or medical impairments. The main problem delivering care to those with a learning disability lies in the patient's level of co-operation and understanding.

**Sensory impairment**

Hearing impairment can range from mild to profound hearing loss or deafness and people will communicate in a variety of ways by use of sign language, lip reading, hearing aids and body language. A patient who is sedated will be less alert and communicative and this situation will be compounded for those with a hearing impairment.

**Mental health problems**

People with mental health problems can experience anxiety about dental care which may be compounded by their condition. The use of conscious sedation to help alleviate stress and anxiety during care can therefore be extremely valuable. The



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provision of sedation for those with mental health problems may be influenced by the level and stability of the patient's condition, the type of medication the patient may be taking, and the patient's level of mental capacity.

Premedication can be easily administered, should this be felt necessary, to help the patient cope with the sedation technique and subsequent treatment. In the event of an untoward incident, emergency care is readily available. The deciding factor for location of treatment will rest with the patient's ASA classification, which depends on the severity of their disability and any concomitant systemic conditions.

**Pregnancy**

There is no sedation drug which is guaranteed to be safe during pregnancy. As far as possible the use of sedation should be avoided in the first trimester. If dental treatment cannot be deferred, nitrous oxide is probably preferable to midazolam. In later Pregnancy, the use of nitrous oxide is generally considered to be safe.

Mothers who are breast feeding should be warned that some sedative drugs - for example, Midazolam - are secreted in breast milk and can produce a degree of sedation in their infant. This may not always be perceived as an unwelcome side effect.

**Advanced Cardio-Respiratory disease**:

Patients who are breathless at rest or after minimal exertion should not be considered



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for treatment under conscious sedation anywhere other than a specialist centre.

**Active liver disease:**

If there is known liver failure, or impairment of liver function, or active liver disease, drug effects may be magnified due to changes in plasma protein concentrations.

**Severe psychological illness:**

Individuals with unpredictable behaviour react abnormally to sedative drugs due to concurrent psychoactive medication and also present management problems. Recovery and post-sedation behaviour are unpredictable.

**Drug and alcohol abuse:**

These conditions are often associated with psychiatric disease. Even where this is not the case, the impact of drugs and alcohol may result in a variety of difficulties. Liver failure and chronic viral infections are common.

**Obesity**

Individuals with a body mass index (BMI) greater than 25 may not be suitable for treatment under conscious sedation in the dental surgery. Obese patients often have difficult veins. In the event of a collapse, there may be airway management and patient handling problems. Some dental chairs may become unstable or fail to operate correctly if their maximum load is exceeded.

**Concurrent medication**

Medicines can alert the sedationist to undisclosed disease and raise the possibility of potential drug interactions. Drugs with potential interactions include



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antidepressants, other benzodiazepines, antihistamines, Opioid analgesics, alcohol, $H_2$ receptor antagonists, protease inhibitors and erythromycin or these drugs represents an absolute contraindication to the use of sedation.

**Neonates and Former Preterm Infants**

Neonates and former preterm infants require specific management, because immaturity of hepatic and renal function may alter the ability to metabolize and excrete sedating medications, resulting in prolonged sedation and the need for extended post sedation monitoring. Former preterm infants have an increased risk of post anesthesia apnea, but it is unclear whether a similar risk is associated with sedation, because this possibility has not been systematically investigated. At this point, the research in this area is preliminary and inconclusive at best, but it would seem prudent to avoid unnecessary exposure to sedation if the procedure is unlikely to change medical/dental management (e.g., sedated MRI purely for screening purposes in preterm infants) (Coté et al., 2016)

**SEDATION FOR IMAGING STUDIES**

Imaging can often be performed without sedation in older cooperative children and young infants (up to six months of age) that are bundled and recently fed. Furthermore, as newer technologies decrease the image capture time for computed tomography (CT), some younger infants and many uncooperative patients can be imaged



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without sedation. However, a significant number of older infants, toddlers, and older children with intellectual disability cannot cooperate even for brief imaging tests (e.g, helical CT) and warrant sedation to ensure accurate imaging without excessive radiation exposure. Ideally, the chosen agent or agents should have a quick onset of action that permits successful and safe completion of the imaging study, maintains airway reflexes, and has limited impact on breathing and hemodynamic stability. The regimen should also permit rapid recovery with few side effects, such as nausea or agitation. Because imaging studies are not painful, analgesia is not necessary (Arlachov & Ganatra, 2012).

**Computed tomography**

Successful imaging with helical CT is less sensitive to patient movement than MRI and, given the rapid speed of imaging, can frequently be done without sedation or requires only brief sedation (approximately 5 to 10 minutes). Modern computed tomography can take just 5 min. If a child will not lie still, either oral chloral hydrate, triclofos, or midazolam is usually effective. Anaesthesia will be necessary occasionally (Sury, 2004).\

**Magnetic resonance imaging**

MRI often necessitates sedation for up to one hour. Furthermore, machine noise and lack of patient access pose additional challenges to achieving safe and effective sedation. Healthy infants and children



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undergoing MRI should receive sedation using propofol or dexmedetomidine. Because it has a shorter time to recovery and discharge, experienced providers often administer propofol given as a bolus of 2 to 4 mg/kg followed by an infusion at 150 to 200 mcg/kg/minute. Infants <3 months should sleep naturally after a feed and children aged >8 yr may be cooperative enough but otherwise, the vast majority of other children need drug-induced sleep. Propofol may also be preferred in children with increases in pulmonary artery pressure, decreases in cardiac output, children with AV node conduction delay, or those receiving digoxin, beta blockers or other medications that slow AV node conduction. Melatonin may be useful. Either propofol or dexmedetomidine can be used safely for MRI sedation (Sahyoun & Krauss, 2015)

**Transthoracic echocardiography**

Irritable infants and small children can be calmed by oral chloral hydrate, triclofos or midazolam. Anaesthesia is required for trans-oesophageal echocardiography.

**Radiotherapy**

Radiotherapy requires immobility for 10–20 min repeated each day for two or more weeks. Deep sedation or anaesthesia is necessary for uncooperative children. The EEG is changed by sedation so natural sleep is preferred. Sleep deprivation or melatonin are useful measures for successful recordings. For brain stem-evoked responses, many deaf children are restless and need deeper sedation or light anaesthesia.



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Accepted: April 30, 2026

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**Painful procedures**

Many children undergo repeated lumbar punctures, intrathecal injections and bone marrow aspirations. In cooperative children, behavioural techniques are worthwhile and conscious sedation using nitrous oxide alone or midazolam with fentanyl can be successful with local anaesthesia. Nevertheless, large numbers need anaesthesia. Deep sedation with combinations of midazolam, opioids and ketamine is possible but unreliable; it is not recommended.

**Interventional radiology**

Percutaneous biopsy of solid organs and tumours, drainage of abscesses and cysts, dilatation of stenoses and strictures, insertion of gastrostomy and nephrostomy tubes, and central venous catheters are now within the service capability of radiology departments. As almost all of these are painful, unpredictable and last a variable length of time, anaesthesia is preferable. Ketamine has been used with limited success but is a poor substitute for other anaesthesia techniques.

**Cardiac angiography**

Femoral cannulation is almost painless under local anaesthesia but can be technically challenging. Immobility is needed for both imaging and measurement of intravascular pressures that require steady state cardio-respiratory function. Balloon dilatations, insertion of coils and stents, cyanosis and cardiac failure are obvious potential hazards to consider.



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Virtually all cardiac angiography should be conducted under general anaesthesia because it provides optimum and reproducible steady state conditions with maximum safety.

**The Consequences of the 2019 AAPD Sedation Guidelines**

An independent observer staff person must remain with the patient. These specific personnel must be skilled to assist with any potential medical emergency. Both this independent observer and operating dentist are required to be certified in Pediatric Advanced Life Support (PALS). From the time of initial anesthesia delivery, continuing through the entire phase of anesthesia and clinical treatment, and throughout the patient's time in recovery, the independent anesthesia practitioner would remain committed to continual patient observation. The observer would be solely committed to remaining with the assigned anesthesia patient. (Hin et al., 2019)

**EMERGENCIES DURING SEDATION**

The standard of care for emergencies arising as part of sedation treatment is the same as during other situations in that the health care professional must act as a correspondingly qualified health professional would in the same or similar circumstances. However, by their very nature, emergencies lend themselves to a different analysis of the health professional's conduct.



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An emergency scenario does not lend itself to typical dentist-patient circumstances. For instance, in an emergency, there is generally not time for leisurely reflection about the problem, consultation with colleagues, the patient, the patient's family, or even proffering of informed consent, let alone bare consent.

**Consent during Emergencies**

Emergency situations present a different paradigm for consent evaluation. During an emergency, there simply may be no reasonable opportunity to obtain consent.

ADA itself lists the following as dental emergencies: "bitten lip or tongue; broken tooth; cracked tooth; jaw-possibly broken; knocked out tooth; objects caught between teeth; toothache."

Not unlike other scenarios in the health professions or in general, one man's emergency will be part and parcel or routine for another. Dentists who are trained for and use only local anesthesia might very well define a patient's loss of consciousness and momentary apnea as an emergency.

On the other hand, dentists trained in sedation will likely see loss of consciousness and apnea on a routine basis and should be able to treat these clinical findings seamlessly. Further, dentists who routinely administer general anesthesia actually have as a goal patient unconsciousness and expect to see patient apnea from time to



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time, so these findings are not emergencies to, for instance, dentist anesthesiologists or oral and maxillofacial surgeons who use general anesthesia. Importantly, however, dentists should be able to provide successful emergency treatment at a level above what they commonly are comfortable with.

**THE UNIQUE STATUS OF SEDATION IN DENTISTRY**

Sedation, particularly intravenous, is generally regulated in states by statute or via dental practice acts. The reasons for these regulations are multiple, but essentially they are in place first because dentists are not routinely trained to be proficient in advanced forms of sedation. Sedation proficiency generally requires postgraduate training consisting of relatively short oral sedation courses to accredited residency training in general anesthesia lasting 2 or more years. Intravenous sedation courses fall somewhere in the middle temporally.

A second reason that sedation is specifically regulated is that the vast majority of dentists use local anesthesia alone for invasive procedures. It is somewhat ironic that although dentists introduced safe, predictable, and reproducible anesthesia to the world, the profession has largely lost that heritage in its gravitation toward local anesthesia. Advanced pain control techniques are not readily available to our patients today despite the overwhelming patient perceived need and demand.



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Accepted: April 30, 2026

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Dentist anesthesiologists and dentists who limit their practices to sedation-only procedures are literally as busy as they desire. Anesthesiology is a specialty in medicine, veterinary medicine, and for dentists in Japan and Canada.

**LIMITING LIABILITY FOR EMERGENCIES**

Just as injudicious practice protocols will lead to an increased incidence of complications and emergencies, careful practice within the standard of care of the profession will minimize adverse sequelae, including emergencies, in an office practice. However, even the most careful practitioner through no fault of his or her own will, given a long enough career, experience emergency situations.

**DEALING WITH SEDATION-RELATED INCIDENTS:** The incidence of complications from patients undergoing simple sedation for dental treatment is extremely low. However, there have been reports of critical episodes, some of which have led to serious morbidity. In such cases there will be a sequence of procedures to be followed and questions to be asked. If the dentist can give reasons, for the first question and answer the remaining questions positively, there will be little cause for concern. If not, the failings need to be identified so that the courts can determine a verdict in relation to the adverse event. It is recommended that oximeter becomes standard practice for all patients receiving intravenous sedation[98], for IV sedation with benzodiazepines pulse oximeter is mandatory. Dental education



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Accepted: April 30, 2026

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ISSN Electrónico: 3105-403X

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should incorporate appropriate training methods in the dental curriculum and thus contribute to continuing toward acceptable ethical behavior in the practice of the dental profession. This would help in providing quality oral healthcare to patients and society at large.

## CONCLUSION

Sedation in pediatric population should be provided by only those persons, who have been trained in its administration, monitoring, and its emergencies management provided by the concerned body. Successful outcomes depend on a systematic approach as well as having the knowledge and skills to manage adverse events.

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Accepted: April 30, 2026

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