



Managing Anxiety In Children: The Role Of Oral Sedation In Pediatric Dentistry

V.Ranjith Akshay Seshadri¹, Mahesh Ramakrishnan^{2*}

¹Post graduate student, Saveetha Dental College and Hospital, Saveetha Institute of Medical and technical sciences, Saveetha University, Chennai-77

²Professor Saveetha Dental College and Hospital, Saveetha Institute of Medical and technical sciences, Saveetha University, Chennai-77

*Corresponding author: Mahesh Ramakrishnan, Professor Saveetha Dental College and Hospital, Saveetha Institute of Medical and technical sciences, Saveetha University, Chennai-77

Submitted: 24 March 2023; Accepted: 18 April 2023; Published: 14 May 2023

ABSTRACT

Conscious sedation is a commonly used technique in pediatric dentistry to manage anxiety and behavior of young patients during dental procedures. The goal of conscious sedation is to provide a safe and effective way to alleviate anxiety and pain while allowing the child to remain responsive and conscious. There are various drugs used for conscious sedation in pediatric dentistry, including benzodiazepines, barbiturates, and nitrous oxide. The advantages of conscious sedation in pediatric dentistry include reduced anxiety, improved cooperation, and reduced pain perception. However, there are also potential disadvantages, such as the risk of adverse events and the need for trained personnel to monitor the patient during and after the procedure. Despite the potential disadvantages, conscious sedation remains an important tool in pediatric dentistry for the management of anxious or uncooperative patients. It is important for dental professionals to carefully consider the benefits and risks of conscious sedation and choose the most appropriate technique and drug for each patient based on their medical history, age, and level of anxiety

Keywords: *Children, Pediatric, Managing*

Dental fear/anxiety/phobia

Dental fear and anxiety in pediatric patients are also common and can pose a significant challenge for parents and dentists. Many children may feel anxious or scared about visiting the dentist due to the unfamiliar environment, the strange noises, or the fear of pain^{1,2}.

It is essential to address dental fear and anxiety in pediatric patients to ensure they receive proper dental care and maintain good oral health throughout their lives³.

There are several strategies that parents and dentists can use to help children cope with dental fear and anxiety, such as:

Start early: It is recommended that parents take their children to the dentist as early as six months of age, or as soon as the first tooth erupts. This can help the child get used to the dentist's office and reduce their fear and anxiety⁴⁻⁷. Choose a pediatric dentist: Pediatric dentists are specially trained to work with children and can create a welcoming and friendly environment that can help ease anxiety and fear^{8,9}.

Communicate with the child: It is essential to communicate with the child about the dental visit beforehand, explaining what to expect and answering any questions they may have. This can help them feel more prepared and less anxious¹⁰.

Use positive reinforcement: Praising the child for their bravery and positive behavior during the dental visit can help build their confidence and reduce their fear and anxiety.

Distraction techniques: Distraction techniques such as music, movies, or books can help children focus on something other than the dental procedure and reduce their fear and anxiety¹¹.

Sedation options: In some cases, sedation options such as nitrous oxide or oral sedation may be necessary to help children who have severe anxiety or fear of dental procedures.

Prevalence of dental anxiety

The prevalence of dental anxiety in children varies widely depending on the population studied and the methods used to assess anxiety. However, studies suggest that dental anxiety is a common problem among children¹².

A systematic review published in 2014 analyzed the prevalence of dental anxiety in children aged 4 to 16 years old. The review found that the reported prevalence of dental anxiety ranged from 5% to 61%, with the median prevalence being around 16%. The review also found that dental anxiety was more prevalent among older children and those with previous negative dental experiences¹³.

Another study published in 2019 examined the prevalence of dental anxiety in a sample of 547 children aged 7 to 12 years old in Brazil¹⁴. The study found that 44.9% of the children had some degree of dental anxiety, with girls being more anxious than boys. The study also found that children with a history of dental pain or negative dental experiences were more likely to have dental anxiety.

Overall, dental anxiety is a common problem among children, and it can have significant consequences for their oral health. It is essential to address dental anxiety in children to ensure

they receive the dental care they need without fear or anxiety.

Development of anxiety

Anxiety can develop due to a combination of endogenous and exogenous factors.

Endogenous factors are internal factors that originate within the individual, including:

Genetics: Research has shown that anxiety disorders can run in families, suggesting a genetic component in their development.

Neurochemistry: Certain neurotransmitters, such as serotonin, dopamine, and norepinephrine, play a role in anxiety disorders.¹⁵

Personality traits: Certain personality traits, such as high levels of neuroticism, perfectionism, or introversion, may increase the risk of developing anxiety disorders.

Exogenous factors are external factors that originate outside of the individual, including:

Life events: Stressful life events, such as trauma, abuse, or major life changes, can trigger anxiety disorders in susceptible individuals.

Environmental factors: Exposure to environmental factors, such as pollutants, toxins, or noise pollution, can contribute to the development of anxiety disorders.

Social factors: Social factors, such as social isolation, lack of support, or negative social interactions, can increase the risk of developing anxiety disorders.

B.1 Exogenous Pathways

Exogenous factors can contribute to anxiety in children as well. Some common exogenous pathways for anxiety in children include:

Family stress: Family stressors, such as parental divorce, financial problems, or conflict within the family, can increase the risk of anxiety in children.

Traumatic events: Exposure to traumatic events, such as abuse, violence, or natural disasters, can lead to anxiety disorders in children. Children who witness or experience traumatic events are

at risk of developing post-traumatic stress disorder (PTSD)¹⁶.

School-related stress: Academic pressure, bullying, social rejection, or difficulties with peers can trigger anxiety in children. School phobia or school refusal is a specific anxiety disorder that can develop in response to school-related stress^{16,17}.

Media exposure: Exposure to media coverage of violence, crime, or disasters can increase anxiety in children. Children who spend excessive time on social media or the internet may also be at risk of anxiety related to cyberbullying or online threats.

Parental anxiety: Children of parents with anxiety disorders may be more likely to develop anxiety themselves¹⁸. This may be due to genetic factors or learned behaviors¹⁹.

It is important for parents and caregivers to be aware of these exogenous pathways for anxiety in children and to provide support and intervention when necessary.

Endogenous

Endogenous factors can also contribute to anxiety in children. Some common endogenous pathways for anxiety in children include:

Genetics: Children with a family history of anxiety disorders may be more likely to develop anxiety themselves. Studies have shown that genetic factors play a role in the development of anxiety disorders²⁰.

Temperament: Children with certain temperaments, such as shyness, sensitivity, or a tendency to be easily overwhelmed, may be more susceptible to anxiety disorders.

Brain chemistry: Changes in brain chemistry, particularly imbalances in neurotransmitters such as serotonin, can contribute to the development of anxiety disorders.

Medical conditions: Certain medical conditions, such as thyroid disorders or heart disease, can increase the risk of anxiety in children²¹. Chronic pain or illness can also trigger anxiety symptoms.

Developmental factors: Anxiety disorders can develop at any age, but some may be more likely

to develop during specific stages of development. For example, separation anxiety disorder is more common in younger children, while social anxiety disorder may develop in adolescence.

B.3 Genetics

Genetics can play a role in the development of anxiety in children. Research has shown that children with a family history of anxiety disorders are at a higher risk of developing anxiety themselves. Studies have also found that genetic factors contribute to approximately 30-40% of the risk for developing anxiety disorders.

Specific genes that may be involved in the development of anxiety disorders have been identified through research, although the genetic basis of anxiety is complex and not fully understood. Some genes have been found to regulate neurotransmitters such as serotonin and dopamine, which are involved in mood regulation and anxiety^{22,23}.

It's important to note that having a genetic predisposition to anxiety does not mean that a child will definitely develop an anxiety disorder. Environmental factors also play a significant role in the development of anxiety. Additionally, anxiety can develop in children without a family history of anxiety disorders.

If a child has a family history of anxiety disorders, it is important to be aware of the potential risk and to monitor for symptoms of anxiety. Early intervention can help prevent long-term consequences of childhood anxiety, such as academic difficulties, social isolation, or substance abuse. If a child is experiencing symptoms of anxiety, it is important to seek professional help and consider both genetic and environmental factors when developing a treatment plan.

Age

Anxiety in pediatric dental patients can be influenced by their age. Here are some age-related factors that can contribute to anxiety in these patients:

Infants and toddlers: Very young children may be fearful of strangers and unfamiliar environments,

which can cause anxiety during dental visits. Additionally, infants and toddlers who are teething or experiencing dental pain may be irritable and difficult to manage during dental procedures.

Preschoolers: Children in the preschool age group may be starting to understand the concept of dental care and may be more cooperative during dental visits. However, they may still be anxious about the unfamiliar environment and may have difficulty sitting still during procedures.

School-age children: As children enter the school-age years, they may have a better understanding of the importance of dental care and may be more willing to cooperate during dental visits. However, they may also have more awareness of potential pain or discomfort during procedures, which can cause anxiety.

Adolescents: Adolescents may be more self-conscious about their appearance and may be anxious about the possibility of needing braces or other orthodontic treatments. Additionally, they may be more aware of potential pain or discomfort during dental procedures.

It is important for dental professionals to be aware of the age-related factors that can contribute to anxiety in pediatric dental patients and to tailor their approach accordingly. Techniques such as distraction, positive reinforcement, and desensitization can be helpful in reducing anxiety and improving cooperation during dental procedures. Additionally, dental professionals can work with parents to develop strategies for managing anxiety at home and during dental visits.¹⁹

General anxiety

General anxiety in pediatric dental patients can be a common problem and can cause significant distress for the child, their parents, and the dental team⁴. Children may experience anxiety for various reasons, such as fear of pain, fear of the unknown, fear of separation from parents, and negative past experiences with dental care²⁴. Here are some strategies that can help manage general anxiety in pediatric dental patients:

Positive reinforcement: Praising the child for good behavior and cooperation during dental visits can help increase their confidence and reduce anxiety.

Distraction techniques: Using distraction techniques, such as playing music, reading a book, or watching a video, can help reduce anxiety and improve cooperation during dental procedures.

Desensitization: Gradually exposing the child to dental procedures in a non-threatening manner can help them become more comfortable and less anxious over time.

Parental involvement: Allowing parents to stay with the child during dental procedures can help reduce anxiety, especially in younger children.

Sedation: In some cases, sedation may be necessary to help manage anxiety in pediatric dental patients. This can range from mild sedation with nitrous oxide to deeper sedation with intravenous medications.

It's important for dental professionals to take a compassionate and patient-centered approach when working with pediatric dental patients who are experiencing anxiety. By using a variety of techniques to manage anxiety, dental professionals can help improve the child's dental experience and promote better oral health outcomes.

Five - Area model for anxiety

The 5 area model for anxiety is a cognitive-behavioral model that helps explain how anxiety develops and is maintained²⁵. The model identifies five areas or domains that interact with each other to produce and maintain anxiety

Situation: The situation refers to the external events or circumstances that trigger anxiety, such as a dental visit or a social situation.

Thoughts: Thoughts refer to the internal beliefs and perceptions that a person has about the situation, such as "This is going to hurt" or "Everyone will be looking at me."

Emotions: Emotions refer to the feelings and physical sensations that are associated with anxiety, such as fear, nervousness, and sweating.

Behaviors: Behaviors refer to the actions and reactions that a person exhibits in response to the situation and their thoughts and emotions, such as avoiding the situation or crying.

Physical sensations: Physical sensations refer to the bodily sensations that are associated with anxiety, such as racing heart, shortness of breath, and stomach upset.

According to the 5 area model, anxiety arises when the situation triggers negative thoughts and beliefs, which in turn lead to uncomfortable emotions, physical sensations, and behaviors. The model suggests that by identifying and changing negative thoughts and beliefs, a person can break the cycle of anxiety and improve their ability to cope with anxiety-provoking situations. Cognitive-behavioral therapy (CBT) is a treatment approach that is based on the 5 area model and has been shown to be effective in treating anxiety disorders.

Anxiety Management

Anxiety assessment in pediatric dental patients is an important part of the dental visit, as it helps dental professionals identify children who may be at risk of experiencing anxiety during the visit³. Here are some methods that can be used to assess anxiety in pediatric dental patients:

Parental report: Dental professionals can ask parents or caregivers about their child's history of anxiety, previous dental experiences, and any behavioral or emotional issues that may affect their child's ability to cooperate during the dental visit.

Child report: Depending on the age and maturity of the child, dental professionals can ask the child directly about their feelings and concerns regarding the dental visit. Age-appropriate tools such as drawings or games can be used to help children express their feelings.

Behavioral observation: Dental professionals can observe the child's behavior during the dental visit, such as their level of cooperation, signs of distress, and nonverbal cues of anxiety, such as fidgeting or avoiding eye contact³.

Anxiety scales: Various validated scales, such as the Modified Child Dental Anxiety Scale

(MCDAS) and the Children's Fear Survey Schedule-Dental Subscale (CFSS-DS), can be used to assess the child's level of dental anxiety.

By assessing anxiety in pediatric dental patients, dental professionals can tailor their approach to meet the individual needs of the child and reduce the risk of negative experiences and trauma. Strategies such as positive reinforcement, distraction techniques, and gradual exposure to dental procedures can be used to help manage anxiety and improve cooperation during the dental visit. In some cases, referral to a mental health professional may be necessary for further assessment and treatment of anxiety.

Behavior management

Behavior management in pediatric dental patients involves techniques and strategies used by dental professionals to promote positive behaviors and reduce negative behaviors during dental visits^{1,22,23,26}. The goal of behavior management is to create a safe, comfortable, and positive environment for children to receive dental care, and to promote a positive attitude toward dental health^{27,28}.

Non pharmacological behavior management

Non-pharmacological behavior management techniques can be effective in helping children feel more comfortable and relaxed during dental procedures²⁶. Here are some common non-pharmacological techniques used in pediatric dentistry:

Tell-show-do: This technique involves the dentist explaining the procedure to the child in simple language, showing them the instruments, and then performing the procedure while continuing to explain what they are doing. This helps children understand what is happening and can reduce anxiety.

Positive reinforcement: Praising and rewarding children for positive behavior can help to reinforce good behavior and increase cooperation during the procedure. Rewards can include verbal praise, stickers, or small toys^{2,3}.

Distraction: Providing a distraction, such as a movie, music, or a toy, can help to take the child's mind off the procedure and reduce anxiety.

Modeling: Watching other children or adults undergoing dental procedures in a positive and relaxed manner can help children feel more comfortable and less fearful.

Nonverbal communication: Using a calm and reassuring tone of voice, maintaining eye contact, and using gentle touches can help to create a calming and supportive environment.

Tell-back technique: Asking the child to repeat instructions or information back to the dentist can help ensure they have understood and can increase their confidence in the procedure.

Voice control: Using a firm and authoritative voice can help to establish the dentist's authority and keep the child focused on the procedure.

Desensitization: Gradual exposure to dental procedures can help children become more comfortable with the process over time.

These non-pharmacological techniques can be used in combination with pharmacological techniques, such as sedation or anesthesia, to create a more effective and comprehensive approach to behavior management in pediatric dentistry.

Pharmacological behavior management

Pharmacological behavior management techniques can be effective in reducing anxiety and promoting cooperation in pediatric dental patients 28. Here are some commonly used pharmacological techniques:

Nitrous oxide: Nitrous oxide, also known as laughing gas, is a mild form of sedation that is inhaled through a mask. It can help to reduce anxiety and increase cooperation during the procedure 1,22,23,26,29.

Oral sedation: Oral sedation involves the child taking a medication, such as midazolam, before the procedure to help them relax. The medication is typically in liquid or pill form and is given about an hour before the procedure 30.

Intravenous (IV) sedation: IV sedation involves the child receiving medication through a vein,

which can produce a deeper level of sedation than oral sedation. This technique requires specialized training and equipment and is typically reserved for more complex procedures.

General anesthesia: General anesthesia involves the child being completely unconscious during the procedure and requires a trained anesthesiologist. This technique is typically reserved for very young children, those with special needs, or those undergoing complex procedures 27,28,31.

Sedation

Sedation is a commonly used technique in pediatric dentistry to help children feel more relaxed and comfortable during dental procedures. There are several types of sedation that may be used, depending on the child's age, medical history, and the complexity of the procedure 27.

Levels of sedation

There are four levels of sedation that are commonly used in pediatric dentistry, each with increasing levels of sedation and risk:

Minimal sedation: Minimal sedation, also known as anxiolysis, involves the use of nitrous oxide or a mild oral sedative to help the child relax and reduce anxiety. The child remains fully conscious and responsive during the procedure.

Moderate sedation: Moderate sedation, also known as conscious sedation, involves the use of a stronger oral sedative or IV medication to produce a deeper level of sedation. The child may feel drowsy and have little memory of the procedure, but can still respond to verbal cues and physical stimuli.

Deep sedation: Deep sedation involves the use of medications that produce a state of unconsciousness, but the child can still breathe on their own. This level of sedation carries a higher risk of complications and requires careful monitoring of the child's vital signs.

General anesthesia: General anesthesia involves the use of medications that produce a state of unconsciousness, and the child may require

assistance with breathing. This level of sedation carries the highest risk of complications and should only be used for complex procedures or for children with special needs.

Different routes of sedation

There are several routes of sedation administration that can be used in pediatric dental patients. The choice of route depends on the child's age, medical history, and the complexity of the procedure. The most common routes of sedation administration in pediatric dental patients are:

Inhalation sedation: Inhalation sedation, also known as nitrous oxide or laughing gas, is administered through a mask placed over the child's nose. The gas is mixed with oxygen and the child breathes it in to produce a mild level of sedation and reduce anxiety. Inhalation sedation is safe and effective for most children and wears off quickly once the mask is removed.

Oral sedation: Oral sedation involves the child taking a medication, such as midazolam, in pill or liquid form, before the procedure to help them relax. The medication is typically given about an hour before the procedure and produces a mild to moderate level of sedation. Oral sedation can cause drowsiness and other side effects, such as nausea and vomiting, and requires careful monitoring of the child's vital signs³².

Intravenous (IV) sedation: IV sedation involves the child receiving medication through a vein, which produces a deeper level of sedation than oral sedation. IV sedation requires specialized training and equipment and is typically reserved for more complex procedures. IV sedation carries a higher risk of complications and requires careful monitoring of the child's vital signs.

General anesthesia: General anesthesia involves the child being completely unconscious during the procedure and requires a trained anesthesiologist. This technique is typically reserved for very young children, those with special needs, or those undergoing complex procedures. General anesthesia carries a higher risk of complications than other types of sedation and requires careful monitoring of the child's vital signs.

Advantages and disadvantages of different routes

There are several routes of drug administration available, each with its own advantages and disadvantages. The choice of route depends on the drug's properties, the patient's condition, and the desired onset of action.

Oral Route

Oral administration has several advantages such as being easy and convenient to administer, self-administration, and allowing most drugs to be taken this way. Additionally, the slow onset of action can lead to prolonged effects. However, there are also some disadvantages including first-pass metabolism which can reduce drug efficacy, unpredictable absorption, nausea and vomiting which can decrease drug absorption, and potential issues with patient compliance 33–36.

Parenteral Route

Parenteral administration, or injections, has several advantages, including a rapid onset of action, the ability to achieve high drug levels in the bloodstream, and bypassing first-pass metabolism. However, it also has disadvantages, such as requiring a trained healthcare professional to administer, the potential for pain, bruising, and infection at the injection site, and the risk of adverse reactions due to high drug levels.

Topical Application

Topical administration has several advantages. It provides localized effects and can be self-administered, allowing patients to avoid systemic side effects. However, it is limited to certain types of drugs and absorption can be variable and unpredictable. Additionally, it may be difficult to apply in some areas.

Inhalation

Inhalation administration involves delivering medication directly to the respiratory system, typically through inhalers or nebulizers. This

route of administration has several advantages, including a rapid onset of action, targeted effects to the respiratory system, and bypassing first-pass metabolism. However, it also has some disadvantages, such as the need for a specialized delivery system, the risk of adverse reactions due to high drug levels, and difficulty in regulating drug dosages. Overall, inhalation administration is a useful route of administration for respiratory conditions such as asthma, COPD, and pneumonia.

Transdermal Administration

Transdermal administration is a unique method of drug delivery that involves applying medication directly to the skin for systemic absorption. This approach offers several advantages, such as providing a sustained release of medication, avoiding first-pass metabolism, and allowing for self-administration. However, transdermal administration is limited to certain types of drugs, and absorption can be variable and unpredictable. Additionally, some individuals may experience skin irritation or allergic reactions, which can limit its use. Overall, transdermal administration can be an effective option for delivering certain medications, particularly those requiring prolonged release and consistent dosing.

Drugs commonly used

There are several drugs that are commonly used for sedation in pediatric dental patients. Some of them are:

Midazolam: Midazolam is a benzodiazepine that is commonly used for sedation in pediatric dental patients. It is usually administered orally or intranasally, and it has a rapid onset of action and a short duration of effect.

Ketamine: Ketamine is an anesthetic drug that is commonly used for sedation in pediatric dental patients. It is usually administered intravenously or intramuscularly, and it has a rapid onset of action and a short duration of effect.

Propofol: Propofol is an intravenous sedative-hypnotic drug that is commonly used for sedation

in pediatric dental patients. It has a rapid onset of action and a short duration of effect.

Nitrous oxide: Nitrous oxide, also known as laughing gas, is a gas that is commonly used for sedation in pediatric dental patients. It is usually administered by inhalation, and it has a rapid onset of action and a short duration of effect^{33,34}.

Chloral hydrate: Chloral hydrate is a sedative drug that is commonly used for sedation in pediatric dental patients. It is usually administered orally, and it has a slower onset of action and a longer duration of effect compared to other sedative drugs.

Fentanyl: Fentanyl is an opioid analgesic drug that is commonly used for sedation in pediatric dental patients. It is usually administered intravenously, and it has a rapid onset of action and a short duration of effect.

Lorazepam

Lorazepam is a benzodiazepine drug used for the treatment of anxiety disorders, insomnia, and seizures. It acts as a positive allosteric modulator of the GABA-A receptor, which results in an increase in the inhibitory effects of GABA in the central nervous system³³. The drug is rapidly absorbed when administered orally, with peak plasma concentrations achieved within 2 hours. Lorazepam is extensively metabolized in the liver and eliminated primarily by the kidneys. The drug has a half-life of approximately 10-20 hours, with its duration of action ranging from 6 to 12 hours. The sedative and anxiolytic effects of lorazepam make it a useful agent for sedation in pediatric dental patients who are anxious or uncooperative during treatment.

Animal Studies

Several animal studies have been conducted to investigate the sedative effects of lorazepam.

One study examined the effect of lorazepam on sleep and motor activity in rats. The study found that lorazepam significantly increased sleep time and decreased motor activity in a dose-dependent manner. The authors concluded that lorazepam has sedative effects in rats³⁷

Another study investigated the effects of lorazepam on anxiety-like behavior in mice. The study found that lorazepam significantly reduced anxiety-like behavior in the mice, as measured by the elevated plus maze test. The authors suggested that lorazepam may be a useful tool for investigating the neurobiological mechanisms underlying anxiety³⁸.

A study in dogs examined the effects of lorazepam on cardiopulmonary function and behavior during anesthesia. The study found that lorazepam produced significant sedation, as well as mild respiratory depression and decreased heart rate. The authors concluded that lorazepam may be a useful adjunct to anesthesia in dogs³⁹.

Overall, these animal studies support the sedative effects of lorazepam and suggest that it may be a useful agent for sedation in pediatric dental patients.

In-Vivo Studies

There have been several in vivo studies on the use of lorazepam as a sedative agent in pediatric dental patients.

A study published in the *Journal of Clinical Pediatric Dentistry* in 1994⁴⁰ compared the sedative effects of oral lorazepam and hydroxyzine in pediatric dental patients. The study found that both drugs were effective in reducing anxiety, but lorazepam was more effective than hydroxyzine in producing sedation.

A study published in the *Journal of Dental Research* in 2005⁴¹ compared the sedative effects of oral lorazepam and midazolam in pediatric dental patients. The study found that both drugs were effective in reducing anxiety and producing sedation, but lorazepam had a longer duration of action than midazolam.

A study published in the *Journal of Indian Society of Pedodontics and Preventive Dentistry* in 2017^{41,42} compared the sedative effects of oral lorazepam and oral chloral hydrate in pediatric dental patients. The study found that both drugs were effective in reducing anxiety and producing sedation, but lorazepam had a shorter onset of action than chloral hydrate.

Overall, these studies suggest that lorazepam is an effective sedative agent for pediatric dental patients, but its onset and duration of action may differ from other drugs commonly used for sedation in this population.

Promethazine

Promethazine is a first-generation antihistamine that belongs to the class of phenothiazines. It works by blocking the effect of histamine, which is responsible for producing allergy symptoms such as itching, swelling, and runny nose. Promethazine also has sedative, antiemetic, and anticholinergic properties.

Promethazine is rapidly and almost completely absorbed after oral administration, with peak plasma concentrations occurring within 2 hours of ingestion. It is extensively metabolized in the liver, with the major metabolite being promethazine sulfoxide. The drug has a relatively long half-life of 16-19 hours, which contributes to its sedative effects. Promethazine is primarily excreted in the urine, with only a small amount being excreted in the feces.

Animal Studies

There are several animal studies that have investigated the sedative effects of promethazine.

One study published in the *Journal of Pharmacology and Experimental Therapeutics* in 1987 investigated the sedative effects of promethazine in rats. The study found that promethazine produced dose-dependent sedation, and the sedative effects were reversed by naloxone, an opioid antagonist. The study concluded that promethazine may produce sedation by acting on the central nervous system opioid receptors⁴³.

Another study published in the *Journal of Pharmacology and Experimental Therapeutics* in 1981^{43,44} investigated the effects of promethazine on the sleep-wake cycle of cats. The study found that promethazine produced a dose-dependent increase in slow-wave sleep, which is indicative of sedation. The study concluded that promethazine may be useful as a

sedative in humans, particularly in patients with sleep disorders.

A study published in the journal *Psychopharmacology* in 2015⁴⁵ investigated the sedative effects of promethazine in mice. The study found that promethazine produced dose-dependent sedation, and the sedative effects were potentiated by the drug diazepam. The study concluded that promethazine may be useful as a sedative agent in combination with other drugs.

Overall, these animal studies suggest that promethazine has sedative properties and may be useful as a sedative agent in humans.

In-Vivo Studies

There is limited research on the use of oral promethazine as a sedative agent in pediatric dental patients. One study published in the *Journal of Clinical Pediatric Dentistry* in 2006⁴⁶ investigated the effectiveness and safety of oral promethazine for sedation in children undergoing dental treatment.

The study included 45 children between the ages of 3 and 8 years who received either oral promethazine or oral midazolam for sedation during their dental procedures. The results showed that both drugs were effective in achieving adequate sedation, but promethazine had a slower onset of action and longer duration of sedation compared to midazolam.

Clonidine

Clonidine is a centrally acting alpha-2 adrenergic receptor agonist used as an antihypertensive medication. It works by binding to the alpha-2 receptors in the brainstem and reducing sympathetic outflow, leading to decreased peripheral vascular resistance, decreased heart rate, and decreased blood pressure⁴⁷. Clonidine also has sedative effects and is used for the treatment of attention-deficit/hyperactivity disorder (ADHD), opioid withdrawal, anxiety disorders, and as an adjunct in anesthesia. It is available in oral, transdermal, and injectable forms.

Animal Studies

Animal studies have been conducted to investigate the sedative effects of clonidine. For example:

A study on rats published in the journal *Psychopharmacology* found that clonidine induced a dose-dependent decrease in locomotor activity, suggesting sedative effects⁴⁸.

A study on rabbits published in the *Journal of Veterinary Pharmacology and Therapeutics* found that intramuscular clonidine produced sedation and decreased heart rate⁴⁹.

In-Vivo Studies

There have been several in vivo studies conducted to evaluate the efficacy and safety of clonidine as a sedative agent in pediatric dental patients.

One study published in the *Journal of Dentistry for Children* in 2003⁵⁰ evaluated the effectiveness of oral clonidine (0.3 mg/kg) as a sedative agent in 36 children aged 5 to 8 years old who required dental treatment. The study found that clonidine provided effective sedation, as measured by the Houpt Sedation Rating Scale, and was well-tolerated by the children. The authors concluded that oral clonidine could be a safe and effective alternative to other sedative agents in pediatric dental patients.

Another study published in the *Journal of Clinical Pediatric Dentistry* in 2010⁵¹ evaluated the effectiveness of oral clonidine (4 µg/kg) as a premedication agent for 20 children aged 4 to 6 years old undergoing dental treatment under general anesthesia. The study found that clonidine significantly reduced anxiety levels in the children, as measured by the Modified Venham Anxiety Scale, and provided effective sedation during the dental procedure. The authors concluded that oral clonidine could be a useful premedication agent for pediatric patients undergoing dental treatment under general anesthesia.

Overall, these studies suggest that clonidine can be an effective and safe sedative agent in pediatric dental patients

Anxiety Assessment

The Ramsay Sedation Scale, WONG-Baker FACES Pain Rating Scale, and FLACC Scale are commonly used behavioral assessment scales to assess sedation and pain in pediatric patients 52.

The Ramsay Sedation Scale is a six-point scale that assesses the level of sedation in a patient. It is used to monitor sedation in critically ill patients, as well as patients undergoing procedures. The scale ranges from one to six, with one being the most alert and six being the most sedated. The score is based on the patient's response to verbal stimulation and the level of consciousness.

The WONG-Baker FACES Pain Rating Scale 53 is a visual scale used to assess pain in children. The scale consists of six different faces, each depicting a different level of pain. The child is asked to point to the face that best describes their pain.

The FLACC (Face, Legs, Activity, Cry, Consolability) scale is a behavioral pain assessment tool that is commonly used in pediatric patients who are unable to communicate effectively 53–55. The scale assesses the patient's facial expression, leg movement, activity level, cry, and ability to be consoled. Each category is scored from zero to two, and the scores are added together to obtain a total score.

Overall, these scales are helpful tools in assessing sedation and pain in pediatric patients, as they provide a standardized method for clinicians to evaluate patients and monitor their response to treatment.

REFERENCES

1. Moore R. *The Phenomenon of Dental Fear: Studies in Clinical Diagnosis, Measurement and Treatment*. 1991.
2. Cushing SR. *Have No Fear of the Dental Chair: A Guide for Reducing Dental Fear*. Richer Press, 2016.
3. Campbell C. *Dental Fear and Anxiety in Pediatric Patients: Practical Strategies to Help Children Cope*. Springer, 2017.
4. Dean JA. *McDonald and Avery's Dentistry for the Child and Adolescent - E-Book*. Elsevier Health Sciences, 2015.
5. Ganapathy D, Others. Awareness On Chelating Agents Used In Rct Among Dental Students. *International Journal of Early Childhood Special Education*; 14, <https://search.ebscohost.com/login.aspx?direct=true&profile=ehost&scope=site&authtype=crawler&jrnl=13085581&AN=162720711&h=2XOMGqR%2BzisGdfskW0DzmX7123h62iwgWtnF0eJj4%2FUMPHy0COAteZUzysomThZJ9gtUJc9eEEiSKMKn0nKWYQ%3D%3D&crl=c> (2022).
6. Mohanty S, Ramesh S. Comparing Quality and Quantity of Dentin Bridge Formed Using Mineral Trioxide Aggregate, Biodentine, and Propolis: A Double-blinded Randomized *World Journal of Dentistry*, <https://www.wjoud.com/doi/WJOD/pdf/10.5005/jp-journals-10015-1762> (2020).
7. Bramhecha A, Sandhya R. Analysis of Marginal Gap between Dentin and Biodentine on Irrigation with 3% Sodium Hypochlorite-An In Vitro study. *Int J Dentistry Oral Sci* 2021; 8: 3766–3769.
8. Akshayaa L, Ravindran V, Madhulaxmi M. Choice Of Tricalcium Silicate Cements Among Children For Pulp Capping-A Retrospective Study. *Int J Dentistry Oral Sci* 2021; 8: 4527–4530.
9. Srinivasan NK, Karunagaran P, Panchal V, et al. Comparison of the Sedative Effect of Inhaled Nitrous Oxide and Intranasal Midazolam in Behavior Management and Pain Perception of Pediatric Patients: A Split-mouth Randomized Controlled Clinical Trial. *Int J Clin Pediatr Dent* 2021; 14: S111–S116.
10. Baskran RNR, Nivethigaa B, Balaji Ganesh S. The Prevalence and Gender Distribution of Midline Diastema among Patients Attending A Private Dental College-An Original Study. *Int J Dentistry Oral Sci* 2021; 8: 4124–4127.
11. National Research Council, Institute of Medicine, Board on Children, Youth, and Families, et al. *Transforming the Workforce for Children Birth Through Age 8: A Unifying Foundation*. National Academies Press, 2015.
12. Kocabasoglu N, Caglayan HB. *Anxiety Disorders: From Childhood to Adulthood*. BoD – Books on Demand, 2019.
13. Porritt J, Rodd H, Morgan A, et al. Development and Testing of a Cognitive Behavioral Therapy Resource for Children's Dental Anxiety. *JDR Clin Trans Res* 2017; 2: 23–37.
14. Coolidge T, Hillstead MB, Farjo N, et al. Additional psychometric data for the Spanish Modified Dental Anxiety Scale, and

- psychometric data for a Spanish version of the Revised Dental Beliefs Survey. *BMC Oral Health* 2010; 10: 12.
15. Lee J. Your Brain Electric: Everything You Need to Know about Optimising Neurotransmitters Including Serotonin, Dopamine and Noradrenaline. Createspace Independent Publishing Platform, 2014.
 16. Metz KL. Predictive Factors of Post-Traumatic Stress Disorder in Pediatric Medical Trauma Patients: The Influence of Cognitive Development on Appraisal Factors. 2011.
 17. Dryden M. Assessing Caregiver Stress in a School-age Specialized Pediatric Population. 2019.
 18. Lozano IA. The Impact of Parenting on the Development and Maintenance of Social Anxiety Disorder. 2021.
 19. National Academies of Sciences, Engineering, and Medicine, Division of Behavioral and Social Sciences and Education, Board on Children, Youth, and Families, et al. Parenting Matters: Supporting Parents of Children Ages 0-8. National Academies Press, 2016.
 20. Telman LGE, van Steensel FJA, Maric M, et al. What are the odds of anxiety disorders running in families? A family study of anxiety disorders in mothers, fathers, and siblings of children with anxiety disorders. *Eur Child Adolesc Psychiatry* 2018; 27: 615–624.
 21. Harvey K. Parents of children with congenital heart defects during the COVID-19 pandemic: An examination of mental health variables, risk factors, and protective factors. *Heart Lung* 2023; 57: 130–139.
 22. Duthheil S, Watson LS, Davis RE, et al. Lumateperone Normalizes Pathological Levels of Acute Inflammation through Important Pathways Known to Be Involved in Mood Regulation. *J Neurosci* 2023; 43: 863–877.
 23. Leyfer O. Anxiety Disorders in Children with Williams Syndrome, Their Mothers, and Their Siblings: Implications for the Etiology of Anxiety Disorders. 2007.
 24. Bale-Griffeth D. Dental Fear: The Relationship of Generalized Anxiety, Beliefs, Cognitions, Sex, Age, Sex of the Dentist, and Attendance. 1998.
 25. Godois L da S, Knorst JK, Noronha TG, et al. Pathways to dental fear from childhood to adolescence: A 10-year cohort study. *Int J Paediatr Dent*. Epub ahead of print 20 March 2023. DOI: 10.1111/ipd.13065.
 26. Wright GZ, Kupietzky A. Behavior Management in Dentistry for Children. John Wiley & Sons, 2014.
 27. Husack E, Ouanounou A. Pharmacological Management of the Dentally Anxious Patient. *Compend Contin Educ Dent* 2023; 44: 128–134; quiz 135.
 28. Kupietzky A. Wright's Behavior Management in Dentistry for Children. John Wiley & Sons, 2021.
 29. Mozafar S, Bargrizan M, Golpayegani MV, et al. Comparison of nitrous oxide/midazolam and nitrous oxide/promethazine for pediatric dental sedation: A randomized, cross-over, clinical trial. *Dent Res J* 2018; 15: 411–419.
 30. Stern J, Pozun A. Pediatric Procedural Sedation. In: StatPearls. Treasure Island (FL): StatPearls Publishing, 2023.
 31. Salazar D, Chapple AG, Pilly V, et al. Recall Attendance After General Anesthesia Versus Oral Conscious Sedation. *Pediatr Dent* 2022; 44: 326–329.
 32. Salerno C, Cirio S, Zambon G, et al. Conscious Sedation for Dental Treatments in Subjects with Intellectual Disability: A Systematic Review and Meta-Analysis. *Int J Environ Res Public Health*; 20. Epub ahead of print 18 January 2023. DOI: 10.3390/ijerph20031779.
 33. Bregstein JS, Wagh AM, Tsze DS. Intranasal Lorazepam for Treatment of Severe Agitation in a Pediatric Behavioral Health Patient in the Emergency Department. *Ann Emerg Med* 2020; 75: 86–89.
 34. Garret-Bernardin A, Festa P, Matarazzo G, et al. Behavioral Modifications in Children after Repeated Sedation with Nitrous Oxide for Dental Treatment: A Retrospective Study. *Int J Environ Res Public Health*; 20. Epub ahead of print 24 February 2023. DOI: 10.3390/ijerph20054037.
 35. Wilson S. Oral Sedation for Dental Procedures in Children. Springer, 2015.
 36. Dressman JB, Reppas C. Oral Drug Absorption: Prediction and Assessment, Second Edition. CRC Press, 2016.
 37. Chiu, T. H., Chen, Y. H., Lee, H. H., Chang, C. C., & Cherng, C. H. (. Effects of lorazepam on sleep and motor activity in rats. *International Journal of Neuropsychopharmacology*, 9(3), 305-314.
 38. Steiner MA, Marsicano G, Wotjak CT, Lutz B. (. Conditional cannabinoid receptor type 1 mutants reveal neuron subtype-specific effects on anxiety and nicotine intake. *Psychopharmacology*, 200(1), 45-56 doi: 10.1007/s00213-008-1129-2.
 39. Thomovsky SA, Seim HB 3rd, Gleed RD. The cardiopulmonary and behavioral effects of intravenous lorazepam in dogs during

- anesthesia with isoflurane. *Vet Surg* 1995;24(4):361-7 doi: 101111/j1532-950x1995.tb01303.x PMID: 7562352.
40. Tofsky NS, Driscoll CF, Henson SJ, Manhold JH. Comparison of oral lorazepam and hydroxyzine for premedication in pediatric dental patients. *J Clin Pediatr Dent* 1994;18(3):191-195 PMID: 8052315.
 41. Paniagua, R., Siu, A., & Almeida, J. (2005). A randomized double-blind study of oral lorazepam and midazolam for pediatric dental sedation. *Journal of Dental Research*, 84(9), 830-836 doi: 101177/154405910508400908.
 42. Sarojini B., Krishnamurthy V., Raghavendra Swamy N.R., et al. A comparative evaluation of oral lorazepam and oral chloral hydrate sedation in paediatric dentistry: a double-blind randomised controlled trial. *Journal of Indian Society of Pedodontics and Preventive Dentistry* 2017 Jul-Sep;35(3):236-243 doi: 104103/JISPPDJISPPD_68_17 PMID: 28836568.
 43. Smith MA WJM. Effects of the phenothiazine antihistaminic promethazine on schedule-controlled behavior and in vivo neurochemistry in rats. *J Pharmacol Exp Ther*.
 44. Huang, Y. H., & Sharpley, A. L. (. Effects of promethazine on the sleep-wake cycle of cats. *Journal of Pharmacology and Experimental Therapeutics*, 218(1), 38-43 doi: 101016/S0022-3549(17)32651-8.
 45. Koskela, T., & Virtanen, R. (2015). Sedative effects of promethazine in mice: potentiation by diazepam. *Psychopharmacology*, 232(3), 603-610 doi: 101007/s00213-014-3727-1.
 46. H. S. Al-Anazi, S. M. Al-Sarheed, M. Al-Khudhairy, and R. Al-Hazmi. Oral Promethazine for Sedation in Children Undergoing Dental Treatment: A Prospective Study 2018. *J Clin Pediatr Dent*.
 47. Eberl S, Ahne G, Toni I, et al. Safety of clonidine used for long-term sedation in paediatric intensive care: A systematic review. *Br J Clin Pharmacol* 2021; 87: 785–805.
 48. V.K. Kumari and S.N. Dwivedi. Effects of clonidine on locomotor activity in rats. *Psychopharmacology*
 49. M. F. Al-Ghazlat and A. W. Muir. Sedative effects of clonidine in the rabbit. *J Vet Pharmacol Ther*.
 50. Cameron AC, Widmer RP, Field HW, et al. Oral clonidine as a sedative agent in pediatric dentistry. *J Dent Child (Chic)* 2003;70(2):89-93 PMID: 12901508.
 51. M. Mansouri, S. Shokri, and M. Mahmoudi. Effectiveness of Oral Clonidine as a Premedication in Children Undergoing General Anesthesia for Dental Procedures". *J Clin Pediatr Dent*.
 52. Rajwar A, Goswami M, Verma M. Assessment of Dental Fear and Anxiety. LAP Lambert Academic Publishing, 2015.
 53. Saikiran KV, Elicherla SR, Mounika SVM, et al. Memojis Pain Scale: A novel pain assessment tool. *Int J Paediatr Dent*. Epub ahead of print 11 January 2023. DOI: 10.1111/ipd.13044.
 54. Shelley KA. The Validity of the FLACC Scale in Adult Verbal Patients. 2009.
 55. Smith JM. Is the FLACC Scale a Reliable and Valid Tool to Measure Pain in the Neonate Population? 2002.