

Republic of Iraq Ministry of Higher Education and Scientific Research University of Baghdad College of Dentistry



Life Threatening Reaction After Using Pedodontic Sedation

A project submitted to

The College of Dentistry, University of Baghdad, Department of Pediatric and Preventive Dentistry in partial fulfillment of the requirement for the Degree of Bachelor of Dental Surgery (B.D.S)

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Certification of the Supervisor

I certify that this project entitled "Life Threatening Reaction After Using Pedodontic Sedation" was prepared by the fifth-year student Maryam Ahmed Abdulrazzaq under my supervision at the College of Dentistry/University of Baghdad in partial fulfilment of the graduation requirements for the Bachelor Degree in Dentistry.

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Dedication

This project is dedicated to the Prophet Muhammad and His Chastity Family. Those who taught me the meaning of patience and the importance of knowledge, learning and giving, who instilled in me the love of God and the love of doing good, and the best kind of goodness is giving knowledge and relieving people's pain.

To my parents who have always given me all the support, for fulfilling all my needs since I was born and for teaching me that even the largest task can be accomplished if it is done one step at a time.

To my mother, thank you for never failing to be my role model for all these years and future to come. Your hard work has inspired me to always pursue the best version of myself and never stop learning and chasing my dreams.

To my father, sisters Meinah and May and brother Ihsan, thank you for always being there for me. I am truly blessed to have such an amazing family.

To my friends, thank you for always encouraging me, special thanks to my best friend Maryam Ayoub for all the hours of reading we did and always pushing me to accomplish the best I could. I am also grateful to my friend "Kawther Ali" who supported me throughout this venture.

To all children in the world who deserve peace and the best possible care...

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List of Abbreviations

CNS	Central nervous system.
FDA	Food and Drug Administration.
GIT	Gastrointestinal tract.
N ₂ O	Nitrous oxide.
PR	Paradoxical reaction.

The Aim of the Study

The main objective of this review is how to deal with the over dose sedation and reaction between drugs combination, how to recognize early signs and symptoms of an adverse reaction of sedation and how to avoid a lethal dosage of sedation before, after and during a dental procedure by knowing exact dosing and emergency skills. This topic also explains the main sedatives that are used in pediatric dentistry and the route of administration.

Introduction

Young children are not miniature adults, and the safe sedation that is given to them largely for behavior control necessitates medical monitoring and understanding of the distinctions between children's and adults' anatomy, as well as the medical condition of the child and the side effects of the drugs and their doses, as well as the interaction between them. Also, the dentist must have a clear understanding of the pharmacodynamic and pharmokinetic effects of the prescribed sedation (**Girdler** *et al.*, **2017**).

Many sedation-related problems may be predicted; thus, crises can be avoided with careful preparation and skill. The need of a comprehensive and meticulous of patient evaluation can't be overstated. Each patient's ability to endure sedation-assisted therapy, as well as the danger that sedation poses to the patient, must be examined individually (**Coté** *et al.*, **2019**).

1.1 Definition of Sedation

Conscious Sedation is a medically controlled state of depressed consciousness that allows protective reflexes to be maintained, retains the patient's ability to maintain a patent airway independently and continuously, and permits appropriate response by the patient to physical stimulation or verbal command, e.g., "open your mouth". In other words, it is a technique in which the use of a drug or drugs produces a state of depression of the central nervous system enabling treatment to be carried out, but during which verbal contact with the patient is maintained throughout the period of sedation (Welbury *et al.*, 2005; Hallonsten *et al.*, 2020).

Also it is a type of medication that given to the child before dental procedure to make him more relaxed, calmer and less distress about the dental procedure, it can be inhaled as a gas or given as injection or can be given to the child orally as a pill or as a syrup, sedation should be safe and the child should return to the normal status before the end of the procedure and make the child forget any distress (**Hallonsten** *et al.*, **2020**).

1.2 History of Sedation

For a long time, dentists have represented a terrifying idea for many people, and it took years to find a way to make the patient more relaxed and calm, first with the discovery of nitrous oxide by Joseph Priestly 1772, and experimented and published by Humphry Daly 1799, then nitrous oxide brought to dentistry by Horace Wells first in 1844 during tooth extraction, then in the 1900s, sedation was discovered and given by dentists, and it was perfected in the 1930s. They also discovered that IV sedation is safer than general anesthesia 1943 (**Yagiela, 1999**).

1.3 Objective of Sedation

Objectives for sedation in pediatric dental care consider both the needs of the child and the dentist (Hallonsten *et al.*, 2020):

- The child
 - Reduce fear and perception of pain during the treatment.
 - Facilitate coping with the treatment.
 - Prevent development of dental fear and anxiety.
- The dentist
 - Facilitate accomplishment of dental procedures.
 - Reduce stress and unpleasant emotions and prevent unwanted behavior or physical movement to provide safe procedure.
 - Prevent "burn-out" syndrome.

And the important point to be considered is that under medical care, the patient should be able to return to his normal state.

1.4 The Continuum of Anesthesia and Sedation

The continuum of sedation contains four important degrees (Green *et al.*, 2020; Mason *et al.*, 2021):

1. Minimal Sedation (Anxiolysis) is a drug-induced state during which patients respond normally to verbal commands. Although cognitive function and physical coordination may be impaired, airway reflexes, and ventilatory and cardiovascular functions are unaffected.

2. Moderate Sedation "Conscious Sedation" is a drug-induced depression of consciousness during which patients respond purposefully to verbal commands,

either alone or accompanied by light tactile stimulation. No interventions are required to maintain a patent airway, and spontaneous ventilation is adequate. Cardiovascular function is usually maintained.

3. Deep Sedation is a drug-induced depression of consciousness during which patients cannot be easily aroused but respond purposefully following repeated or painful stimulation. The ability to independently maintain ventilatory function may be impaired. Patients may require assistance in maintaining a patent airway, and spontaneous ventilation may be inadequate. Cardiovascular function is usually maintained.

4. General Anesthesia is a drug-induced loss of consciousness during which patients are not arousable, even by painful stimulation. The ability to independently maintain ventilatory 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, table (1).

	Minimal Sedation Anxiolysis	Moderate Sedation/ Analgesia "Conscious Sedation"	Deep Sedation/ Analgesia	General Anesthesia
Responsiveness	Normal response to verbal stimulation	Purposeful response to verbal or tactile stimulation	Purposeful response following repeated or painful stimulation	Unarousable even with painful stimulus
Airway	Unaffected	No intervention required	Intervention may be required	Intervention often required
Spontaneous Ventilation	Unaffected	Adequate	May be inadequate	Frequently inadequate
Cardiovascular Function	Unaffected	Usually maintained	Usually maintained	May be impaired

Table (1): The Continuum of anesthesia and sedation (Mason et al., 2021)

Because sedation is a continuum, it is not always possible to predict how an individual patient will respond and the studies have shown that it is common for children to pass from the intended level of sedation to a deeper, unintended level of sedation, making the concept of rescue essential to safe sedation. Practitioners of sedation must have the skills to rescue the patient from a deeper level than that intended for the procedure. For example, if the intended level of sedation is "minimal," practitioners must be able to rescue from "moderate sedation"; if the intended level of sedation is "moderate," practitioners must have the skills to rescue from "deep," practitioners must have the skills to rescue from a state of "general anesthesia." The term "rescue" is often used to describe this management, and refers to steps taken to return the patient to the initially desired level of sedation (**Motas et al, 2004; Gamble et al., 2012**).

<u>1.5 Indications For Sedation</u>

Indications for sedation should be based on a combined assessment of patient and dental indications (Koch and Poulsen, 2009):

- 1. Patient indications:
- Patients with inadequate coping ability.
- Patients with high dental fear/dental anxiety/ odontophobia.
- Need for reduction of patient's pain perception (prevent fear-induced pain).
- 2. Dental indications:
- Oral examinations and treatments of moderate extent and complexity (extensive treatment needs should be accomplished under general anesthesia).
- Emergency treatment (e.g., extractions and emergency treatment of traumas).

1.6 Most Common Drugs Used in Sedation

1.6.1 Hydroxyzine

Hydroxyzine is an antihistamine with weak sedative, anticholinergic, and antiemetic properties with no depressant effects on cardiac or respiratory function in normal doses. Recovery is slow by modern standards, reflected by the mean half-life of 3 hours. There are two forms of hydroxyzine (**Thakkar, 2011; Dean, 2021**).

1.6.1.1 Routes of administration of Hydroxyzine

There are two routes of hydroxyzine administration (Dean, 2021):

- 1. The oral route is preferred for administration and the dosage ranges from 0.5 to 1.0 mg/kg.
- 2. A deep intramuscular injection into a big muscle mass is available with 1 mg/kg dosage.

Hydroxyzine should not be administered subcutaneously or intravenously because of the risk of tissue necrosis and hemolysis.

1.6.2 Benzodiazepine Agonists and Antagonists

The drugs of first choice for sedation of anxious children are the benzodiazepines, due to its anxiolytic, sedative/hypnotic, and muscle relaxing effect (wide therapeutic index), shallow dose-response curve, and its specific effects on the central nervous system (Mason, 2011).

Side-effects are few, although anterograde amnesia can be expected and is frequently cited as an advantage (**Berthold**, **2007**).

Benzodiazepines such as midazolam, diazepam and others have similar pharmacological properties, but different duration time, and the choice between them may therefore be based on the length of time that sedation is needed (Koch *et al.*, 2017).

1.6.2.1 Midazolam (Agonist of Benzodiazepine)

It is a water-soluble type of benzodiazepine. This property accounts for its stability in aqueous solutions, making it nonirritating to tissues following intravenous or intramuscular administration. Midazolam has the shortest working time of benzodiazepines because of fast elimination half time about 1-4 hours and is therefore most suitable for perioperative sedation under treatments of short duration (Koch *et al.*, 2017).

1.6.2.1.1 Routes of administration of Midazolam

Routes of midazolam administration are as the following (Koch *et al.*, 2017; Dean, 2021):

- 1. Intravenous sedation is the most effective in terms of fast response, effect and possibility to adjust the dosage to an optimal level of effect, but this is usually not practicable in a dental setting, since it demands assistance of a specialist in anesthesiology.
- 2. Oral administration is generally preferred from a practical point of view with dosage ranges from 0.25 to 1.0 mg/kg, but some children are unable or unwilling to take an oral medication., however, a trick may be used in children who are unwilling to drink from a cup by placing the solution in the retromolar area from a needleless syringe, Figure (1).
- 3. The rectal and nasal route could be alternative to the oral route in the aforementioned case.

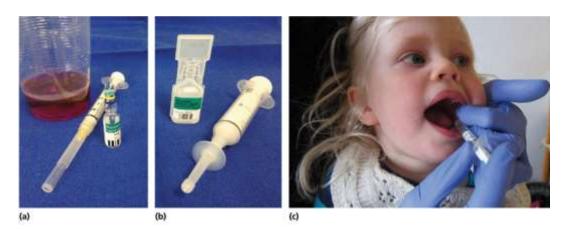


Figure (1): (a) Oral administration with midazolam mixed in a juice. (b) Applicator for rectal administration of midazolam. (c) Oral sedation with needleless syringe in a 2-year-old child (Koch *et al.*, 2017).

Benzodiazepines have negligible effects on cardiovascular or respiratory function when used as single agents (**Dean, 2021**).

1.6.2.2 Flumazenil (Antagonism of Benzodiazepine)

Flumazenil is a direct, specific reversal agent used in clinical practice for reversing unexpected over-sedation from orally, intravenously, or rectally administered benzodiazepine. Pharmacologically, it acts as a competitive antagonist at the benzodiazepine receptor sites in the CNS. In selected situations, the drug is able to rescue patients from the effects of benzodiazepine overdose in some instances (Welbury *et al.*, 2018; Dean, 2021).

The FDA has authorized flumazenil for intravenous use. Alternative methods of administration include intraoral submucosal injection in the sublingual region. which has a delayed start of action (**Faccini** *et al.*, **2016**).

1.6.3 Opioid Agonists and Antagonists

Opioids are drugs that bind to receptors in the endogenous opioid system. Because of their capacity to inhibit the cough reflex and produce analgesia, opioids are most helpful during moderate sedation (**Blanco and Volkow**, 2019; **Dean**, 2021). Opioids differ from the benzodiazepines in several critical ways that are relevant to the clinician seeking to provide sedation. They produce analgesia in different ways and at sedative doses, opioids produce analgesia while not affecting awareness and memory, whereas benzodiazepines produce profound, dose-dependent amnesia (**Dean, 2021**).

1.6.3.1 Meperidine (Agonist of Opioid)

Meperidine is a synthetic opiate agonist and water soluble drug, but many other medicines in solution are incompatible with it (**Preuss** *et al.*, **2019**).

Meperidine enteral or parenteral delivery is possible, however, oral administration is only approximately half as effective as intramuscular injection (Marsden *et al.*, 2019).

1.6.3.2 Naloxone (Antagonism of opioid)

Naloxone is a semisynthetic opioid receptor antagonist with no intrinsic agonist action that is used to counteract the symptoms of opioid medication overdose. Reversal starts within 2 to 5 minutes after a subcutaneous or intramuscular injection, compared to 30 seconds to 2 minutes after an intravenous injection. The reversal lasts around 45 minutes, depending on which route you take (**Dean, 2021**).

1.6.4 Hypnotics (Chloral Hydrate)

Chloral hydrate is a kind of aldehyde that the liver breaks down. It's a skin and mucous membrane irritant associated to a significant risk of nausea and vomiting, particularly when consumed on an empty stomach, therefore it's best to dilute it in a flavored vehicle (**Zeilinska** *et al.*, **2019**).

This medication may be a poor option for many juvenile children due to the wide range of adverse effects such as respiratory depression, general anesthesia when taken in big doses, also large dosages make the myocardium more susceptible to the actions that cause arrhythmias, therefore they should be avoided in individuals with heart problems. In some cases, with consumption of 4 g has been linked to death (**Mataftsi** *et al.*, **2017**).

Recently, there has been concern that there is a risk of carcinogenesis. Although it is still in widespread use around the world it is gradually becoming obsolete, for example in the United States, chloral hydrate is no longer commercially accessible (Welbury *et al.*, 2018; Dean, 2021).

Dosage ranges from 25 to 50 mg/kg and the total dosage of no more than 1g. be given to young children (**Mataftsi** *et al.*, **2017**).

1.6.5 Nitrous Oxide

For minimal sedation, nitrous oxide–oxygen is the method most commonly used and its high success rate and safety are well documented, Figure (2). Nitrous oxide is a colorless, slightly sweet-smelling, inert gas that is heavier than air. It is compressed in cylinders as a liquid that vaporizes on release. The gas is nonflammable but will support combustion (**Clark and Brunick, 2015**).



Figure (2): Nitrous oxide-oxygen sedation (Koch et al., 2017).

Although nitrous oxide is deemed safe use in medicine and dentistry, it may not be appropriate for all individuals. It's critical to evaluate a patient's medical history and consider the tiny number of circumstances in which nitrous oxide sedation may be contraindicated or at least offer a relative contraindication (Attri *et al.*, 2017).

1.6.5.1 Inhalation Techniques Units of sedation

Inhalation techniques divided in two types flow according to the oxygen and nitrous oxide flow (**Krishna** *et al.*, **2016**):

- 1. Gases are given intermittently (demand flow) according to the patient's respiratory demand and needs.
- 2. Continuous flow: continuous gas flow (safer and more precise).

1.6.5.2 Mechanism of sedation (Stages of Sedation) using Nitrous oxide

The patient during induction of nitrous oxide will pass in four stages in each stage the patient will felt different sensations (**Emmanouil**, **2020**):

1. The sensation of tingling (Paresthesia - tingling of hands, feet).

2. Followed by a pleasant sensation (Vasomotor - warm sensations).

3. A sense of well-being may develop, and hearing may turn into electronic pounding, (Drift - exhilaration, centrally fixed pupils, floating feeling).

4. Nausea, sleepiness, and the possibility of a dream (Dream - eyes closed but will open in response to questions, difficulty in speaking, jaw sags open).

1.7 Adverse Sedation Events in Pedodontics

Procedural sedation of pediatric patients has serious associated risks. These adverse responses during and after sedation for a diagnostic or therapeutic procedure may be minimized, but not completely eliminated, by a careful preprocedure review of the patient's underlying medical conditions and consideration of how the sedation process might affect or be affected by these conditions (Chiaretti *et al.*, 2014; Coté *et al.*, 2019).

The groundbreaking studies show a low but persistent rate of potential sedation-induced life-threatening events, such as apnea, airway obstruction, laryngospasm, pulmonary aspiration, desaturation, and others, even when the sedation is provided under the direction of a motivated team of specialists (**Cravero** *et al.*, **2009**).

Nausea and vomiting even they are not life-threating events but they are not uncommon adverse events of some sedative drugs such as opioids and nitrous oxide. Vomiting can be caused by an excessive amount of sedative administration for a long time, influenza or a previous GIT infection (**Coté** *et al.*, **2019**)

Vomiting can be avoided by the following (**Cameron and Widmer, 2008; Coté** *et al.*, **2019**):

- 1. Usage of a minimum effective concentration in the case of opioids or nitrous oxide usage.
- 2. Keep the operation as short as possible in the case of nitrous oxide usage.
- 3. Inhalation from an empty stomach in the case of nitrous oxide usage.
- 4. The use of rubber dam for restorative procedures under inhalation sedation is highly recommended as it improves patient comfort and reduces nausea as it limits mouth breathing since nausea in children is often brought about by fluctuating concentrations of nitrous oxide due to alternate breathing through the mouth and nose, Figure (3).



Figure (3): The use of nitrous oxide with rubber dam (Cameron and Widmer, 2008)

1.7.1 Hydroxyzine's Adverse Effects

The following are some of the most prevalent adverse effects of hydroxyzine especially in large doses; sleepiness, headache, dry mouth, a rash on the skin, prolonged drowsiness and ataxia. In children, paradoxical reactions may occur at sedative doses (**Dean, 2021**).

1.7.2 Benzodiazepine's Adverse Effects

Side-effects are few, although anterograde amnesia can be expected and is frequently cited as an advantage (**Berthold**, **2007**).

Benzodiazepines have negligible effects on cardiovascular or respiratory function when used as single agents. Therefore, the combination of hydroxyzine (3.7 mg/kg) with midazolam (0.3 mg/kg) administered 30 minutes before treatment resulted in safe and effective sedation for the dental treatment of young children. Also sedation can be done by a combination of midazolam with opioids which accounts for approximately 75% of routine procedural sedations. This combination's use might be more advantageous when compared to midazolam alone, resulting in

less crying and movement during the first 30 and 20 minutes, respectively (**Dean**, **2021; Sivakumar** *et al.*, **2021**).

1.7.2.1 Paradoxical Reactions

Paradoxical reactions are one of the benzodiazepine's adverse effects. The central features of paradoxical reactions are emotional lability, agitation, excessive movement, and confusion. This may be associated with increased autonomic activity including tachycardia, hypertension, and tachypnea and relatively uncommon and occur in less than 1% of patients. The exact mechanism of paradoxical reactions remains unclear. Most cases are idiosyncratic; however, some evidence suggests that these reactions may occur secondary to a genetic link. Even they are relatively uncommon, have low prevalence and are not life-threatening, they have to be treated promptly (**Farkas, 2015; Sivakumar et al., 2021**).

1.7.2.2 The Management of Paradoxical Reactions

The management of the paradoxical reactions should be done in the following sequence (Farkas, 2015):

Step 1: Stop the offending agent.

The most important aspect is recognizing the PR and discontinuing the causative medication. Failure to diagnose that the patient is experiencing a PR may lead to progressive up-titration of sedative dose, leading to a vicious cycle, Figure (4).

Step 2: Counteract residual drug: Flumazenil.

Flumazenil appears to be an excellent treatment if not contraindicated (e.g. by chronic benzodiazepine use). About a dozen case reports describe flumazenil as being uniformly effective in rapidly terminating a PR due to a benzodiazepine.

Step 3: Add another sedating medication.

If the patient still requires sedation following the above steps, an alternative sedative such as opioids may be added.

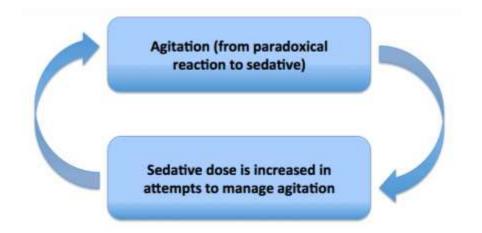


Figure (4): The vicious cycle between agitation and sedative dose in paradoxical reaction (Farkas, 2015).

1.7.2.3 The Use of Flumazenil as Antagonism of Benzodiazepine

Flumazenil's function in sedative situations is misunderstood, which is a more pernicious problem. The majority of sedation-related morbidity and death is due to respiratory problems and the administration of flumazenil as a first step for the management of hypoventilation or apnea during benzodiazepine sedation is a common practice in children, and one might be led to believe that it is an appropriate first step for the management of hypoventilation or apnea during benzodiazepine sedation. When respiratory distress occurs, the first approach should always be proper and effective airway control. Delaying airway management to give flumazenil can lead to hypoxia, severe morbidity, or death (**Nordstrom and Wilson, 2018; Dean, 2021**).

1.7.3 Opioids' Adverse Effects

Overdose or rapid administration of meperidine can lead to a number of serious adverse effects, including respiratory depression, apnea, rigidity and bradycardia. If these remain untreated, respiratory arrest, circulatory arrest or cardiac arrest may occur (Blanco and Volkow, 2019; Marsden *et al.*, 2019).

1.7.3.1 Naloxone as Antagonism of Opioids

Naloxone overdose can lead to nausea, vomiting, sweating, hypotension, hypertension, ventricular tachycardia and fibrillation, and pulmonary edema are all possible side effects of excessive or fast reversal. As a result, naloxone should be dosed carefully. The use of naloxone, like benzodiazepine reversal, should never take precedence over basic airway care and resuscitative efforts (**Olfson** *et al.*, **2018**).

1.7.3.2 The Management of Apnea

Apnea is defined by the American Academy of Sleep Medicine (AASM) as the cessation of airflow for at least 10 seconds. Apnea may last for 30 seconds or even longer (**Mansukhani** *et al.*, **2014**).

Apnea can be occurred as a result to over sedation with meperidine and it should be managed immediately to avoid more severe events (**Coté** *et al.*, **2019**), Figure (5).

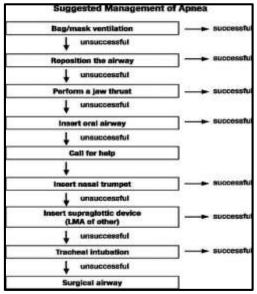
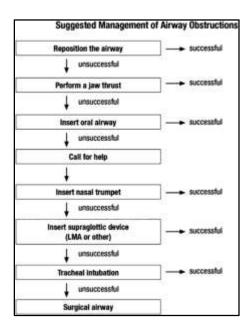


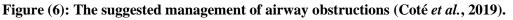
Figure (5): The suggested management of apnea (Coté et al., 2019).

1.7.4 Nitrous Oxide's Adverse Effects

Most of issues during N₂O induction occur due to increase the concentration of nitrous oxide above the allowing level and other problems are due to wrong application and the common N₂O adverse effects are (**Coté** *et al.*, **2019; Kayla**, **2021**):

- 1. During the operation, the patient may fall asleep, and periodic arousal or conversation is necessary.
- Obstruction of the airway: In this situation, hyper stretching to the jaw, mobilization of the tongue forward and frequent head movements is required, Figure (6).





3. Diffusion hypoxia: Because N₂O has a lower blood solubility, it quickly diffuses into the alveoli and dilutes the alveolar air, producing a drop in the partial pressure of oxygen in the alveoli; to avoid this, oxygen inhalation for 10 minutes is helpful.

- An increase in the concentration of N₂O: This should be avoided at all costs, since it will produce pressure in the air-filled bodily cavities, particularly in the middle ear.
- 5. Visual and auditory hallucinations: This can happen if the dentist provides a high concentration of N₂O (>60%), thus lower the N₂O dose could help to reduce the hallucinations.

1.7.4.1 Nitrous oxide Exposure for a Long Time

Long-term (chronic) exposure to sufficient amounts of nitrous oxide can result in lasting detrimental changes, thus dental professionals who work in circumstances where nitrous oxide is administered to patients should be cautious. (Wadha, 2018).

Chronic exposure can lead to problems with the respiratory system, hematology, immunology, liver, kidneys, and the nervous system, including loss of focus, numbress and paresthesia, ataxia, bladder control loss, and bowel sphincter control loss (Zaffina *et al.*, 2019).

In the operatory, controlling N₂O concentration and minimize the risks as much as possible by the following (**Mcglothin** *et al.*, **2019**):

- 1. use a good scavenging system and provide enough room air movement,
- 2. The patient restricts his speech and breathes via his lips.
- 3. The correct selection of nasal hood size.

1.8 Risk Factors of Adverse Sedation Events in Pedodontics

Four factors considered as risk factors that increase the likelihood of adverse sedation events and the dentist must recognize them to avoid the negative consequences (Kamat *et al.*, 2020):

- 1. First factor is the use of various medication methods without first recognizing possible interactions. Sedation is used as part of a combination medication.
- 2. Second factor is the excessive dose of sedative.

- 3. Third factor is the inability to detect early indications of respiratory depression.
- 4. Fourth factor is the unsuccessful emergency care that focuses on reactions.

1.9 Drug Dosage Individualization

The determination dose depends on the following (Dušková et al., 2017):

- Body mass index or body surface area.
- Age extremes.
- Medical history.
- Concurrent medications.
- Chemical dependency.
- Anxiety level.

For children, a therapeutic dosage can be as little as a few tenths of a milliliter, and a toxic overdose also, especially with narcotic analgesics, can be fatal. In recent years, suggested doses for several of these medicines have been lowered downward, If the administration of the drug at carefully selected dosage is insufficient, a change in treatment strategy should be explored rather than raising the dose above the suggested levels, (**Padmanabhan** *et al.*, **2019**).

The dosage of each treatment must be carefully selected while taking a combination of medicines. Drug combinations appear to cause a cascade of negative consequences. Therefore, to establish an acceptable margin of safety, each agent's dose must be reduced to levels below what is typically regarded the maximum advised for the medication when taken alone. The necessity for dose decrease is indicated by conditions such as liver disease and asthma (**Padmanabhan** *et al.*, **2019**).

1.10 Emergency Preparation for Pediatric Over Sedation

It is critical to have a setting where both respiratory and cardiovascular indicators can be continually monitored. Suitable emergency medicines, such as oxygen, naloxone, and epinephrine, should be accessible, as well as staff skilled in emergency care administration. Because a variety of sedative medication methods can quickly produce unconsciousness, respiratory arrest, and convulsions, practitioners should be prepared to detect and handle these events (Scherrer *et al.*, **2018**).

1.10.1 Essential Emergency Drugs

Essential emergency drugs that should be available (Kenneth, 2021):

- 1. Oxygen.
- 2. Adrenaline injection (1:1000, 1 mg/ml).
- 3. Oral glucose solution/tablets/gel/powder.
- 4. Glucagon injection 1 mg.
- 5. Glyceryl tri-nitrate (GTN) spray (400 micrograms/dose).
- 6. Salbutamol aerosol inhaler (100 micrograms/actuation).
- 7. Aspirin (300 mg).
- 8. Buccal Midazolam 10 mg/ml.
- 9. Flumazenil (500 ug/5 ml).

<u>1.10.2 Emergency Equipment</u>

Emergency equipment that should be available for sedation (**Dugaal** *et al.*, **2013**):

- 1. Positive pressure ventilation with self-inflating bag.
- 2. Emergency supply of oxygen in addition to working supply.

- 3. Appropriate face masks for children and adolescents.
- 4. Various sizes of oral airway.
- 5. Good high-volume suction with a long extension capacity.

1.11 Recommendations

- The dental staff should be trained properly on how to manage the adverse effects' cases quickly and proficiently.
- The selection of the lowest dose of sedative with the highest therapeutic index for the procedure is helpful and may be the best way to avoid the adverse effects of high sedative dosage.
- Every dental clinic that uses sedation in its treatment plan for children should have a mini-pharmacy containing essential emergency drugs for the purpose of rapid intervention in the event of adverse effect occurrence.

2.1 Conclusion

- Good identification of sedatives and appropriate treatment must be done by the dentist and dental stuff to avoid any critical situations and any severe negative consequences.
- Adverse events of pediatric sedation can be fatal if they are not treated or managed properly.
- The sedation prescription should be done using standardized dosing regimens, and double-checking all doses before their administration.

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