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MINIMUM OR CONSCIOUS SEDATION WITH USE OF BENZODIAZEPINES IN PEDIATRIC DENTISTRY

***[1]Karolaine Barbosa de Assis, [1]Carolina Lousada, [1]Daniela Moreira da Silva Esteves, [1]Tayna Gabriele Eschiareti, [1]Ana Maria de Pádua Lemos Benfatti, [1]Patrícia Moreira da Silva Guimarães, [1,2]Idiberto José Zotarelli Filho, [1,2]Ana Paula Bernardes Rosa Maluf Abbud, [1,2]Igor Mariotto Beneti, [1,2]Patrícia Garani Fernandes and [1,2]Leandro Moreira Tempest**

[1]University Center North Paulista (Unorp) Dental School - São José do Rio Preto – SP, Brazil
[2]Post Graduate and Continuing Education (Unipos), Department of scientific production, Street Ipiranga, 3460, São José do Rio Preto SP, Brazil

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ABSTRACT

Minimal or conscious sedation is defined as a state of minimal depression of consciousness obtained with the use of medications in which the patient is able to maintain respiration in a natural and autonomous manner responding to the isolated verbal stimulus or accompanied by tactile stimulation. Among the main drugs used in the minimum sedation are benzodiazepines (BZD), which promote muscle relaxation, lower levels of consciousness, induce drowsiness, reduce anxiety, stress, fear, and phobia. This study aims to analyze the minimal or conscious sedation with the use of BZD in pediatric dentistry through the systematized search of articles in the scientific literature made available in light of the most current knowledge. Minimal or conscious sedation with orally administered BZD is the most recommended and recommended for children due to advantages such as almost universal acceptability, atraumatic route of administration, convenient technique, ease of administration, absence of needles or nasal masks, being economical and low incidence of adverse reactions when obeying the pharmacological protocols of administration, such as vital signs monitoring, detailed anamnesis, emergency kit available in the office. Care these should be taken for greater patient and professional safety. We conclude that minimal or conscious sedation using BZD in pediatric dentistry is efficient, effective being able to promote control of fear, anxiety, and stress, thus ensuring greater tranquility for the patient. Its use is well-founded and guarantees greater safety for pediatric dentists.

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INTRODUCTION

Pediatric dentistry requires quality and comfort treatment through the control of pain, fear, phobia, emotional tension, stress and anxiety in infant dental therapy. These aspects, crucial when well administered, guarantee the professional and the child tranquility, continuity and success in treatment (BORBOSA *et al*., 2015). Several factors such as pain, drill sound, fear of perforation, objective and subjective fear, lack of knowledge about what treatment and fear of the injection can trigger anxiety and stress in children during a dental appointment (FERREIRA *et al*., 2016). Among the infantile patients we can synthetically divide them into two categories: a portion with perfect cognitive ability and adaptive ability, and another portion that does not possess these still emotionally developed qualities that may present fear/phobia, excessive emotional tension, stress and anxiety, both can therefore present conditioning difficulties to therapeutic or preventive care (BORBOSA *et al*, 2015). Regardless of the condition, all of these patients require adequate management and control of pain, fear / phobia, emotional tension, stress, and anxiety that can be achieved through a minimal or conscious sedation protocol that aims to improve treatment

****Corresponding author: Karolaine Barbosa de Assis,***
University Center North Paulista (Unorp) Dental School - São José do Rio Preto – SP, Brazil

experience, possibly influencing future levels of long-term anxiety (COLLADO *et al*., 2013). Excessive emotional tension, stress, and anxiety during pediatric dentistry care are one of the main difficulties for the care of children having cognitive abilities or not, especially for those with fear/phobia objectives (BORBOSA *et al*, 2015). These patients may present with symptoms such as increased blood pressure, heart rate, breathing rate, decreased pain threshold, intrinsic to the anxiety generated by dental procedures in most patients, preventing or greatly hampering appropriate dental treatment, in these cases, use of conscious or minimal pre-operative sedation promotes the control of these parameters in dentistry, allowing normal breathing, minimal depression of consciousness where the patient maintains the control of responses, besides being an adjunct to the induction of anesthesia (FERREIRA *et al*, 2014). One of the main advantages of using minimal or conscious sedation is the need for artificial respiration (YOSHIKAWA *et al*., 2013). There are several means that can be used to control pain, fear and anxiety in dental therapy, among them the pharmacological approach through minimal or conscious sedation with Benzodiazepines (BZD), especially Midazolam and Diazepam (FERREIRA *et al*., 2014).

There are on the market a range of drugs of the class of BZDs such as, Chlordiazepoxide (Librium, Psicossedin); Diazepam (Valium); Clonazepam (Rivotril), Bromazepam (Lexotam), Alprazolam (Frontal), Lorazepam (Lorax), Cloxazolam, among others that safely promote the attenuation of anxiety and stress symptoms with small side effects and at the same time provide satisfactory clinical results (MAIA *et al*., 2018).
These drugs can be administered via numerous routes, such as oral, rectal, inhalation, nasal, intramuscular, subcutaneous and intravenous routes. All these routes have advantages and disadvantages (ALZAHRANI; WYNE, 2012), and the most commonly used routes in dentistry are inhalation, oral and intravenous at the hospital level. The sedation technique most used in pediatric dentistry is oral sedation because it has almost universal acceptability among children. It is an economical, atraumatic, convenient, easily administered route, dispensing needles or nasal masks, with low toxicity, incidence and severity in the adverse reactions (MALAMED, 2012; MAIA *et al*, 2018). On the other hand, it presents as a contraindication a long period of latency (period after drug administration and before its desired effect) and irregular or incomplete absorption by the gastrointestinal tract (MALAMED, 2012). However, the correct and safe use of central nervous system depressant drugs requires knowledge of their pharmacology and pharmacokinetics and training in basic or even advanced cardiopulmonary resuscitation by the pediatric dentistry and its staff. The present study had as objective to analyze the minimal or conscious sedation with the use of Benzodiazepines in pediatric dentistry.

LITERATURE REVIEW

Minimal or Conscious Sedation: Minimal or conscious sedation is intended to promote better patient comfort and relaxation while maintaining safety and access for qualified health professionals. It is currently used if sedation and local anesthesia are used concomitantly during a variety of oral surgical procedures (FERREIRA *et al*, 2014). According to Chen *et al*. (2014) an ideal sedative technique would be one that increases the patient's pain threshold, eliminates undesirable and involuntary movements, minimizes cardiovascular responses caused by anxiety and inadequate analgesia, and allows patient control and cooperation to be safe and predictable, allowing rapid postoperative recovery with minimal side effects.

According to the American Association of Dental Surgeons or American Dental Association-ADA (2016), the stages of central nervous system depression present four levels:

- Anxiolysis or minimal sedation: drug induced state where the patient maintains a minimally depressed level of consciousness but usually responds to tactile stimulation and verbal command although cognitive function and motor coordination may be affected. Ventilatory function and cardiac function remain unchanged. Minimal sedation can be achieved by administering a drug alone (ADA, 2016).
- Minimal or conscious sedation: a controlled state of decreased drug-induced consciousness that allows the maintenance of protective reflexes, such as swallowing and coughing, reducing salivary flow and vomiting reflex, and maintaining the airways independent and continuous, allowing the response to physical stimuli and verbal commands alone or accompanied by light tactile stimulation and, therefore, the patient is easily aroused. They prevent emergency situations such as lipotimia, syncope, and hyperventilation syndrome. No intervention is required to maintain a patent airway and spontaneous ventilation is adequate. Cardiovascular function is generally maintained. Knowledge of the time of onset, peak response and duration of action of each drug is essential to avoid over-sedation (ADA, 2016; MAIA *et al*, 2018).
- Deep sedation: a state of decreased consciousness induced by drugs from which the patient is not easily aroused, and may be accompanied by partial or total loss of protective reflexes and the ability to respond to physical stimuli or verbal commands. But it can respond purposely after repeated or painful stimulation. The ability to independently maintainventilatory function may be impaired. Patients may need assistance in maintaining a patent airway and spontaneous ventilation may be inadequate. Cardiovascular function is generally maintained (ADA, 2016).
- General anesthesia: induced state of drug-induced unconsciousness accompanied by partial or total loss of protective reflexes and inability to maintain independent airways, during which patients are not stimulated, even by painful stimulation. The ability to independently maintainventilatory function is often impaired. Patients generally require assistance in maintaining a patent airway, and positive pressure ventilation may be required because of depression, spontaneous ventilation or drug-induced depression of neuromuscular function. Cardiovascular function may be compromised (ADA, 2016).

Studies have pointed out that sedation levels are notrelated to the route of administration of the drug, but to its dose, route of absorption / excretion and plasma concentration (MAIA *et al*., 2018). The pediatrician who uses moderate sedation should submit the patient to a careful evaluation and prior anamnesis, together with the person responsible for the child / patient

Table 1. Classification of the American Society of Anesthesiology (ASA)

CLASSIFICATION OF THE AMERICAN SOCIETY OF ANESTHESIOLOGY (ASA)		
Classification Definition Moderate sedation procedure	Classification Definition Moderate sedation procedure	Classification Definition Moderate sedation procedure
ASA I	Healthy Patient	Candidate for Moderate Sedation
ASA II	Patient with mild systemic pathology	It presents a higher risk of complications, however it will be a candidate provided that precautions are taken
ASA III	Patient with severe systemic pathology	The procedure should be done in a hospital setting
ASA IV	Patient with severe systemic pathology and is at risk of life	The procedure should be done in a hospital setting
ASA V	Dying patient needing surgery to survive	Not a candidate for conscious sedation
ASA VI	Patient in brain death whose organs will be removed for donation	Not a candidate for conscious sedation

Source: CLOUGH, SHEHABI, MORGAN (2015).

establishing the risks, possible allergies, pre-existing pathologies, analyzing the medical history and possible drug interactions. If the patient has any systemic pathology or uses any medication that may interact with the sedative, it is recommended that the pediatric dentist has the assistance of the doctor who accompanies the patient to jointly perform the risk analysis (KALIBATIENĖ *et al*. 2012 ADA, 2016). In addition to this care, the ADA (2016) recommends that vital signs (heart and respiratory rate, blood pressure, temperature and oxygen saturation) be monitored throughout the procedure and that the pediatric dentist should have emergency equipment and first aid mainly containing oxygen masks, aspiration and medications such as adrenaline, antihistamines such as predizone and bronchodilators minimizing the effects of anaphylaxis. These equipment must be kept in an accessible location and must be constantly renewed (ADA, 2016). The qualified Dentist should have a properly trained clinical staff, continually monitoring patient awareness levels, record all parameters, anesthetic procedures including names and dosages of all drugs given to the patient, administration times including anesthetics monitored physiological parameters (GONÇALVES, 2016). It is essential before the indication of any type of sedation to analyze the medical risk of each patient and to evaluate the risk benefit of this sedation. The medical risks were categorized according to the classification of the American Society of Anesthesiology (ASA), this classification allows an association between the preoperative risks and the results of the procedure (CAVALCANTE *et al*., 2011; GONÇALVES, 2016).

Benzodiazepines

Benzodiazepines (BZD) are lipid-soluble drugs and consequently, their latency period is usually short approximately thirty to fifty minutes after their administration. Its mechanism of action is based on direct action binding to specific receptors of central nervous system structures of the CNS as the Limbic System and acting on the inhibitory systems of neurotransmission of acid-gamma-amino-butyric acid (GABA) which is the main system of neurotransmitter inhibitory CNS (GONÇALVES, 2016). BZD selectively act on postsynaptic gamma aminobutyric acid (GABAA) type A receptors that mediate inhibitory synaptic transmission throughout the central nervous system. Activation of the GABA receptor induces the opening of the chloride (cl-) channels of the neuron membrane, increasing the influx of the anion into the cells, which results in decreased propagation of excitatory impulses (BRUNTON, GOODMAN, GILMAN, 1996). Further, BZD have fewer side effects and have muscle relaxant, hypnotic, sedative, anticonvulsant, high dose neuromuscular block and coronary vasodilatation (BRUNTON, GOODMAN, GILMAN, 1996).Macedo-Rodrigues, Rebouças (2015) recommend that prior to dental care, the infant patient, whose indications wereexposed in thisstudy,should ingest the benzodiazepine prescribed by the dental surgeon one hour before the dental procedure, but in extremely anxious, the prescription may also be made the night before treatment for a quieter night's sleep and lower preoperative stress.Patients with high levels of anxiety present a greater risk of paradoxical effects since the responses by the sympathetic nervous system are increased (GONÇALVES, 2016). Gonçalves (2016) affirms that the administration of local anesthesia is always mandatory in sedated patients and the professional should never compensate for the insufficient administration of local anesthetic with an increase in sedation concentration, as this action may lead to deep sedation (GONÇALVES, 2016). During moderate sedation with benzodiazepines, if the dosing protocol is not followed, deeper sedation may occur, leading to risks to the patient's life (GONÇALVES, 2016). At the end of the care, the child should be accompanied by a responsible person, rest for six hours and not use other drugs depressing the central nervous system, so as not to potentiate the effects of benzodiazepine (MACEDO-RODRIGUES, REBOUÇAS, 2015).

Classification of Benzodiazepines

Benzodiazepines can be classified according to the duration of their anxiolytic or sedative action:

- **Diazepam:** Considered a long-acting agent with elimination half-life between 24 and 72 hours, it is more liposoluble, therefore recommended when a longer postoperative sedation is desired, in contrast to other drugs in the group. Although clinical effects disappear within 2 to 3 hours, somnolence and impairment in psychomotor function may persist due to the production of active metabolites (BRUNTON, GOODMAN, GILMAN, 1996).
- **Lorazepam:** It differs from that said by not producing active metabolites, and the end of its effects is observed after 6 to 8 hours. For this reason, and because itrarely produces paradoxical effects, it is considered by some authors as the ideal agent for the conscious sedation of elderly patients (BRUNTON, GOODMAN, GILMAN, 1996).
- **Alprazolam:** Its highest plasma concentrations are obtained 1 to 2 hours after its administration, with a duration of action of 12 to 15 hours (BRUNTON, GOODMAN, GILMAN, 1996)
- **Midazolam:** Presents anxiolytic, myorelaxant, anticonvulsant and psychosedative properties. It has rapid elimination, and occurs through liver

degradation, independent of the route of administration as well as diazepam is also more liposoluble (BRUNTON, GOODMAN, GILMAN, 1996).

- **Triazolam:** Short-acting benzodiazepine, comparable to lorazepam as a pre-anesthetic medication, but with a faster onset (30 to 60 minutes) and shorter recovery time (around 2 to 4 hours) (BRUNTON, GOODMAN, GILMAN, 1996).

However, the main anxiolytic agents used to induce moderate sedation and used in conscious sedation are benzodiazepines, especially Midazolam and Diazepam (FERREIRA *et al*, 2014).

Midazolam: Pharmacological Aspects and Pharmacokinetics

Currently among the benzodiazepines of choice, midazolam is the drug most suitable for use in pediatric dentistry because it presents desirable pharmacological characteristics such as wide margin of clinical safety, rapid onset of action, anxiolytic properties, sedatives, hypnotics, muscle relaxant and marked amnesic property anterograde, short half-life and duration of sedation adequate small incidence of adverse reactions, being even indicated for children as pre-medication in procedures of short duration (FERREIRA *et al*, 2014; BARBOSA *et al*., 2015).

Mechanism of action: After oral administration midazolam is rapidly absorbed because of its highly lipophilic nature and simultaneously subject to intestinal and hepatic first-pass metabolism, resulting in approximately 40.0 % bioavailability, is metabolized by CYP3A4 a system of enzymes responsible for the primary metabolism of 25.0 % of all drugs used clinically (BRILL *et al*., 2014). The main clinical effects of midazolam are sedation, hypnosis, anxiety reduction, anti-convulsant and muscle relaxation (GONÇALVES, 2016). Midazolam shows water solubility and the production of inactive metabolites.

Posology: Midazolam may be administered by the following routes: oral, rectal, intramuscular, intravenous and intranasal. The most commonly used in pediatric dentistry is the oral route in doses of 7.5 mg to 15 mg, 30 minutes before the procedure (GONÇALVES, 2016). Following oral administration, the plasma concentration of Midazolam increases after about twenty minutes. Its therapeutic period lasts about forty-five minutes and the recovery of the patient is quite fast. The clinical effects of this drug can be reversed using agents with Physostigmine and Flumazenil (GONÇALVES, 2016). In a study involving children, Marques, Gradvohl, Maia, (2010) demonstrated that nine out of ten children presented a high level of anxiety, due to the use of the high-speed turbine and its noise, exodontia, fear associated with the use of and white clothing to previous experiences, somatized to subjective or objective fear. In one study, Marya *et al*. (2012) found that 73% to 79% of patients reported feeling anxious during dental care, and found it difficult to control anxiety, fear, and phobia leading to failure of dental treatment. He also reported that children with past experiences and a history of psychological trauma may find it more difficult to return to the dentist.

Adverse reactions: In general, benzodiazepines can trigger drowsiness, muscle weakness, dizziness, amnesia, increased aggressiveness, and hallucinations. In some cases, the appearance of allergic reactions, mostly cutaneous but also blood, ataxia, and nystagmus with high doses may occur (GONÇALVES, 2016). The serious adverse effects generated by the use of benzodiazepines can be caused by two situations: acute overdosage and continuous administration over a long period of time leading to tolerance and dependence. Acute overdose of benzodiazepines is considered relatively less dangerous than in cases of other anxiolytic drugs (GONÇALVES, 2016). As for Midazolam, serious adverse effects are confusion, aggression, resistance and agitation, fatigue, ataxia, amnesia, cardiac arrest, heart failure, anaphylaxis, thrombosis, laryngospasm, bronchospasm, respiratory depression and respiratory arrest (GONÇALVES, 2016). Although clinical effects disappear within 2 to 3 hours, somnolence and impaired psychomotor function may persist due to the production of active metabolites.

Contraindications and precautions: Side effects of midazolam include post-anesthetic anxiety, diplopia, amnesia, hiccups, anger, and sleep disturbances, uncontrollable shaking of a part of the body, stiffening and spasms of the arms and legs, and aggression (severe side effects are rare, and Midazolam is contraindicated in patients who are hypersensitive to the formula, who have undergone previous prolonged intubation, sleep apnea patients, asthma sufferers, hepatopathies, and congenital heart defects (when combined with other sedative medicinal products) (MAIA *et al*., 2018).

Conclusion

Minimal or conscious sedation using benzodiazepines in pediatric dentistry is effective in being able to promote control of fear, anxiety, and stress, ensuring greater peace of mind for the patient. Minimum or conscious sedation with orally administered benzodiazepines is best for children due to the advantages such as acceptability, atraumatic route, convenient technique, ease of administration, the absence of needles or nasal masks, and low incidence of adverse reactions. The technique requires care such as vital signs monitoring, detailed anamnesis, emergency kit and trained staff for intercurrences. The dosage/weight and administration protocol should be strictly followed as there is a need for constant monitoring of vital signs.

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