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Sedation in pediatric dentistry: A scoping review

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Abstract
Introduction: Pediatric dentists face the daily challenge of treating patients with anxiety, phobias and fears, and it is important to know the drugs for each patient.
Objective: To analyze the literature on drugs used for sedation, particularly dexmedetomidine, ketamine, midazolam and nitrous oxide.
Methodology: Articles were searched in databases such as PubMed, Google Scholar, using keywords: sedation, drugs, pediatric dentist, pediatric patient.
Results: Dexmedetomidine provides sedation, analgesia and sympathicolysis, is safe and acceptable in infants and children without respiratory depression, and adverse events such as hypoxemia and bradycardia may occur. Ketamine is a drug that presents multiple routes of administration and has analgesic, hypnotic, amnesic, anti-inflammatory and sympathomimetic properties, having undesirable side effects such as delirium, psychosis, perception disorders, arterial and intraocular hypertension. Midazolam is a fast-acting and short-acting drug, which can be administered by different routes. It presents adverse reactions such as disinhibition, hallucinations and marked respiratory depression. Oral absorption and action time are prolonged. Nitrous oxide has analgesic and anesthetic effect, as well as its rapid elimination from the body, does not affect respiration, so it is possible to administer it in patients with respiratory ailments, its use is limited to short or non-invasive procedures and can cause side effects such as nausea, vomiting, headache and fatigue.
Conclusion: All the drugs reviewed have unacceptable systemic side effects, and if it is necessary to choose one, it would be nitrous oxide as the best drug to use for sedation in pediatric dentistry.

Keywords: Sedation, drugs, midazolam, nitrous oxide, ketamine, dexmedetomidine

1. Introduction
Every day the pediatric dentist is faced with patients who require extensive treatment and who suffer from anxiety due to previous experiences and/or phobias that influence the behavior of the patients at the time of the dental consultation, for this reason, using medication to perform sedation is an alternative method to attend patients in a comprehensive manner [1]. According to the American Academy of Pediatric Dentistry, the purpose of performing sedation in the area is to: promote, facilitate and enhance good patient care, reduce disruptive behaviors, promote a positive response to dental intervention, as well as patient well-being and safety [2]. The American Society of Anesthesiologists adopted a standard since 1962 to classify the physical status of patients, estimating the risk that they present before a surgical procedure is performed and that should be taken into account when deciding whether or not a patient is fit to be submitted under sedation. This classification is called ASA. The AAPD advises that patients who are candidates for sedation in the dental office should be within ASA I and II, which are patients without any systemic disease or patients with mild or moderate systemic disease [3]. A current analysis of the literature allows us to detect the need for a systematic review of the different drugs used for sedation in pediatric dentistry, therefore, the objective is to review the current literature on the most commonly used drugs for intravenous sedation in pediatric patients. We will compare the use of dexmedetomidine, ketamine, midazolam and nitrous oxide studying the advantages and disadvantages of their use in pediatric patients.

2. Materials and Methods

Information was collected from articles published in PubMed, SCOPUS and Google Scholar servers, with emphasis on the last 5 years. The quality of the articles was evaluated based on the standard guidelines, i.e., identification, review, choice and inclusion. The quality of the review was assessed using the measurement instrument for evaluating systemic reviews. Boolean logical operators AND, OR and NOT were used in the search. It was performed with the words "pediatric dentistry", together with the following terms: Drugs, sedation, dexmedetomidine, ketamine, midazolam and nitrous oxide. The keywords were used individually, as well as each of them related to each other.

3. Results & Discussion

3.1 Dexmedetomidine

3.1.1 Advantages

Dexmedetomidine is a drug with multiple therapeutic properties, such as sedation, analgesia, anxiolysis, sympatholysis and opioid sparing. In addition, unlike other drugs, it has been shown to produce less delirium in patients [4]. It also decreases the need to administer inhaled and/or intravenous opioids and anesthetics, and its sympatholytic effect provides stable hemodynamics during the operative procedure [5]. Another benefit of dexmedetomidine is that it does not produce strong respiratory depression, making it safe and acceptable. It has even been proven safe in infants and children, preventing hypoxia and preserving reactivity and increased CO2. In addition, its unique ability to provide sedation and analgesia without respiratory depression makes it a new agent with a wide margin of safety and excellent sedative capabilities and moderate analgesic properties [6]. In patients with bipolar disorder and mild to moderate agitation, dexmedetomidine was shown to be more effective than placebo in reducing the agitation score at 2 hours, although it was also associated with a higher incidence of serious adverse events, especially hypoxemia and bradycardia [7].

3.1.2 Disadvantages

Dexmedetomidine is a drug that does not produce respiratory depression, but its hemodynamic effect is complex and, therefore, it is necessary to have a careful selection of patients, choose the appropriate dose and carry out continuous monitoring [8]. Despite its use in clinical practice, there is still no general consensus on the indications, dosage and timing of administration of this drug [9]. In addition, quality studies and in-depth pharmacokinetic analyses are needed to establish the pharmacological profile in different pediatric ages and procedures [10]. It is important to note that the use of dexmedetomidine may also increase the incidence of serious adverse events, such as hypoxemia and bradycardia. Therefore, a careful risk-benefit assessment needs to be performed before using this drug in any patient [11].

Dexmedetomidine has a weak sedation effect and we have to be very careful with the patients to whom we administer it since it has important side effects such as bradycardia, hypotension, hypertension, etc. The patient must be systemically healthy and the drug dose must be administered very carefully.

3.2 Ketamine

3.2.1 Advantages: This drug is considered as an ideal anesthetic since it presents several routes of administration thanks to the fact that it is soluble in aqueous and lipid solutions [12], it can be administered orally, nasally, rectally, intravenously, intramuscularly, subcutaneously, trans dermally, sublingually and intraosseously [13]. It manages acute and chronic pain, has hypnotic, amnesic, analgesic, anti-inflammatory and sympathomimetic properties, maintaining laryngeal, respiratory and cardiovascular reflexes [14]. Likewise, it has been shown to have an effect on stress and depression from the time Ketamine is administered, and has a rapid onset and termination effect due to its analgesic properties making it an ideal choice for pediatric outpatients [15].

3.2.2 Disadvantages

Its undesirable side effects are related to psychomimetic actions such as delirium, psychosis, perception and hallucination disorders [16], it also presents sympathomimetic actions such as arterial and intraocular hypertension [17], mucus hypersecretion in the respiratory tract area. It has also been shown to increase salivation, heart rate, systemic blood pressure and intracranial pressure, requiring careful control at the time of administration [18]. At low doses it has been shown to present adverse effects called k-hole where immobilizing and hallucinogenic effects occur, all depending on the dose administered [19].

The drug Ketamine is considered an ideal anesthetic due to its ability to be administered through various routes, including oral, nasal, rectal, intravenous, intramuscular, subcutaneous, transdermal, sublingual, and intraosseous. In addition, it can treat both acute and chronic pain and has hypnotic, amnesic, analgesic, anti-inflammatory and sympathomimetic properties. However, Ketamine can also have undesirable side effects, such as delirium, psychosis, perceptual disturbances and hallucinations, and increase blood pressure and heart rate. In low doses, it may produce an adverse effect called "k-hole". Careful monitoring is recommended when administering this drug.

3.3 Midazolam

3.3.1 Advantages

Benzodiazepines (midazolam) have a rapid and short-acting action, exerts anxiolytic, anticonvulsant, muscle relaxant and amnesic effects [20]. It has several routes of administration, such as oral, trans mucosal, intravenous, intramuscular and rectal [21]. Midazolam has been the most commonly used sedative for anxiolysis in pediatric patients with intervention anxiety [22]. It is generally administered orally, making it a simple administration for patients who have needle phobias and are difficult to administer medications parenterally [23].

3.3.2 Disadvantages

It is possible that midazolam may present adverse reactions such as disinhibition, hallucinations, agitation, inconsolable crying, restlessness and disorientation, especially in young children, accounting for 1.4% of cases [24]. It is contraindicated in patients with pulmonary disease and who are sensitive to benzodiazepines [25]. This drug also presents complications in occasional marked respiratory depression, requiring oxygen and the full equipment required for respiratory depression by positive pressure ventilation in the operating room [26]. When administered orally, one of the disadvantages is that its absorption and time of action is prolonged, since it takes about 30 minutes to exert sedative effects [27].

Benzodiazepines are fast-acting drugs with a short duration of action. They can be administered by various routes, including oral, trans mucosal, intravenous, intramuscular, and rectal.

Midazolam is a sedative used to treat anxiety in pediatric patients. Although it is easy to administer orally, it can produce side effects such as disinhibition, hallucinations, excitement and restlessness, especially in young children. It may also cause marked respiratory depression at times and is contraindicated in patients with pulmonary disease and sensitivity to benzodiazepines. Oral absorption of the drug is slow and takes about 30 minutes to produce sedative effects.

3.4 Nitrous oxide

3.4.1 Advantages

Some of the advantages of nitrous oxide are its analgesic and anesthetic effect, it has been used in dental and minor surgical procedures [28], it provides rapid pain relief without the need for injections, having a fast action because its effect is through inhalation with a nasal mask minimizing the risk of needle infection [29]. Another advantage is its excretion, since it is eliminated from the body quickly, increasing its safety. It has also been used to reduce anxiety in patients with dental phobia or anxiety before medical procedures [30].

It does not present respiratory affectation, making its administration possible in patients with respiratory conditions [31].

3.4.2 Disadvantages

Nitrous oxide is not suitable for procedures that are long or invasive because its effect is of short duration. In some cases, the use of nitrous oxide can cause nausea and vomiting, especially if used in high doses, and can cause side effects such as headache, dizziness, sweating, chills and fatigue. Excessive use or abuse of administration can cause brain damage and other serious side effects [32]. For its administration, it is necessary to ask the patient's medical history to know if he/she has cardiovascular diseases, since the gas can increase the heart rate and respiratory frequency, increasing the oxygen demand of the heart. If the patient is allergic to the gas administered, there may be skin rashes accompanied by urticaria, as well as difficulty breathing, coughing or wheezing, a possible sign of bronchospasm or inflammation of the airways [33].

The patient may present with swelling of the face, tongue or throat [34]. Gas allergy may cause a decrease in blood oxygen level, which may cause heart palpitations along with other symptoms. When these manifestations occur, it is necessary to discontinue administration and be intervened by emergency physicians for early treatment to avoid serious complications [35]. Nitrous oxide is a gas used in dental and minor surgical procedures for its analgesic and anesthetic effects. It is administered through a nasal mask, which minimizes the risk of needle infection. In addition, it is safe and does not affect breathing, which makes it suitable for patients with respiratory diseases and dental phobia. However, its effect is short-lived, it is not suitable for long or invasive procedures and may cause side effects such as nausea, vomiting, headache and dizziness. Precautions should also be taken in patients with cardiovascular disease and allergies to this gas. If signs of allergy occur, administration should be discontinued and immediate medical attention sought.

4. Conclusion

Four different drugs used for sedation in pediatric dentistry were reviewed, i.e. the advantages and disadvantages of Dexmedetomidine, Ketamine, Midazolam and Nitrous Oxide. The drug that showed the best results and the least adverse effects was nitrous oxide, since its route of administration is by gas, without the need for needles, and it is possible to use it in patients with respiratory problems, as long as there is an adequate dose and a good clinical history.

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