

## SYSTEMATIC REVIEW

# Conscious and deep sedation drugs in pediatric dentistry: a systematic review of randomized controlled trials (2019–2024)

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**Abstract**

**Background:** Dental anxiety in children is a common issue that hinders dental treatment, generates negative experiences, and perpetuates fear. This highlights the importance of finding effective solutions. Conscious and/or deep sedation techniques are key tools to improve the pediatric patient's experience and facilitate complex procedures. However, their application requires careful analysis due to the wide variety of available protocols, recommendations and administration routes. **Methods:** A systematic review was conducted following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The electronic search for this review was conducted from October to January (2024–2025). Articles were selected from three databases: PubMed, Scopus, and Web of Science. Specific filters were applied for each database. Eight terms were used for the search strategy and selection criteria was followed. Studies that performed any dental treatment on pediatric patients aged 2 to 12 years who underwent conscious or deep sedation to reduce their anxiety. The risk of bias of the selected articles was assessed. **Results:** The initial electronic search generated 1697 titles from the MEDLINE/PubMed database, 1563 from Web of Science, and 1437 from Scopus, which were later filtered and duplicates eliminated. After analyzing the titles and abstracts of 196 articles, 14 Randomized Controlled Trials (RCTs) that were published during the last 5 years were selected for this review. **Conclusions:** The fastest onset of action is determined by the route of administration. Reported adverse effects were not statistically significant. Nitrous oxide shows the fastest recovery, but drug selection should always be based on the type of dental procedure, its duration, and the child's specific needs. Further research is needed to evaluate parents' level of satisfaction. **The PROSPERO Registration:** The review was registered into PROSPERO (registration number: CRD420250637249).

**Keywords**

Pediatric dentistry; Anti-anxiety agents; In-office sedation

## 1. Introduction

On a daily basis, some of the main factors negatively affecting pediatric dental care are fear, anxiety, and dental phobia (Table 1). The link between fear, anxiety and dentistry has been established over time [1]. Many individuals have experienced dental fear early on childhood or at older age, and these fears are often spread on to their families members [1]. Dental fear affects around 5 to 20% of the pediatric population, nevertheless, it is believed this prevalence could be even higher since many pediatric patients with the most serious dental fear often tend to avoid dental care altogether [2, 3].

Often, parents expect pediatric dentists to handle their children's behavioral issues since "we are specialists in children" [4, 5]. However, in recent years, considering societal changes

and attitudes towards traditional physical restraint, pharmacological behavior management techniques have gained popularity, avoiding uncomfortable situations for both the professional and the child [6].

In order to gain confidence of patients with dental fear, pediatric dental providers often exercise continuous and personalized techniques, even applying them at the moment the patient arrives to the waiting room [1]. The American Academy of Pediatric Dentistry (AAPD) proposes both verbal and non-verbal communication techniques that help manage child behavior [7]. Verbal techniques include "tell-show-do", voice control, and positive reinforcement. On the other hand, non-verbal strategies include distraction, modeling, and recreational activities. These tools are useful in managing children's oppositional behavior [7].

**TABLE 1. Differences between dental fear, anxiety, and phobia.**

Characteristic	Dental fear	Dental anxiety	Dental phobia
Origin	Common fear, fear of pain or discomfort	Excessive worry about the appointment	Irrational and disproportionate fear
Intensity	Moderate	High	Very high, disabling
Duration	Temporary	Long-lasting, anticipatory	Chronic and persistent
Impact	Low	Medium	High, interferes with daily life
Physical symptoms	Mild (palpitations, sweating)	More pronounced (muscle tension, dizziness)	Very intense (panic attacks, fainting)

Different factors such the child's own chronological age, as well as his or her cognitive and psychological development, intellectual disabilities and previous negative experiences at the dentist are linked to the lower level collaboration during a dental procedure and lead to refusal of treatment [3, 8–10]. In addition, some of these patients, especially those with intellectual disabilities, have higher caries prevalence compared to the general population, further complicating the dental treatments and experience [10].

According to the literature, children with low to moderate levels of anxiety can be successfully treated by gaining the children's confidence and trust, not requiring any pharmacological medication. However, extremely fearful or phobic patients often require pharmacological treatments in addition to the application of behavioral techniques. These children often require the use of nitrous oxide, sedation, or even general anesthesia to be treated effectively and safely [3]. However, from these choices general anesthesia comes with higher risks of injury and/or death, in addition to higher cost [10].

This is where sedation plays a safer role and has gained popularity over the years as it can be used when basic behavior guidance techniques fail to be effective, and it can be performed with the administration of different agents and routes. Sedation is an advanced pharmacological behavioral management technique that achieves a minimal level of consciousness depression, where the patient's breathing remains normal and patient stay conscious and retains his/her protective reflexes and is capable of responding to physical and verbal stimulus. During conscious sedation certain gases and/or pharmaceutical agents are used. Sedation is generally performed with either benzodiazepines, which are administered either orally or by IV, or with nitrous oxide (N<sub>2</sub>O) which is inhaled. Benzodiazepines lessen the symptoms of anxiety while prompting muscle relaxation. On the other hand, N<sub>2</sub>O is an anesthetic gas administered at sub-anesthetic dosages that depress the central nervous system triggering an anxiolytic and analgesic effect [10, 11].

In these context, sedation is one of the most frequently used techniques by pediatric dentists to manage anxiety and fear in patients [4, 9]. Moreover, there is currently no fixed pharmacological protocol or guideline for sedation in dental procedures. Benzodiazepines, opioids, and antihistamines are generally employed, apart or in combination, to achieve the desired sedative effect and reduce possible adverse effects from co-administered drugs. The selection of the agent differ depending on the professional's preference, experience, and

complexity of the dental procedure [11]. However, there is a still a need to determine which agents, dosages and protocols are more effective or mostly recommended to follow for the pediatric dental practice.

## 2. Objectives

### 2.1 Main objective

To deepen the understanding of different conscious and/or deep sedation techniques used in pediatric dentistry commonly used to relieve anxiety and manage behavior in pediatric patients undergoing dental procedures, and to analyze which sedative agent is mostly recommended.

### 2.2 Secondary objectives

1. Identify the drug with the fastest onset of action.
2. Determine which agent presents the fewer side effects.
3. Indicate which drug allows for the best recovery.
4. Evaluate what is the most effective method or technique of administration.
5. Evaluate parents' personal experience after their children underwent sedation.

## 3. Methods

### 3.1 Declaration and protocol

This systematic review was conducted following the "Regulations for the Master's Final Project in Pediatric Dentistry and Interceptive and Functional Orthodontics at the Universidad San Pablo CEU" as well as the PRISMA 2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) protocol for systematic reviews, which allows for a more focused methodology for presenting systematic reviews and meta-analyses [12]. It was previously registered on the PROSPERO platform (registration number: CRD420250637249), as we referred in the "Supplementary material 1".

The PICOS question for this review was: What is the safest or most recommended drug for moderate or deep sedation and dental treatment of uncooperative children? (P = children up to 12 years, I = any type of moderate and deep sedation (intravenous, inhalation, oral or combinations thereof), C = any other drug, O = reduction of anxiety reported by measuring biological parameters or by observation scales and S = randomized clinical trials, crossover or not).

### 3.2 Search terms and strategies

The electronic search for this systematic review was conducted from October to January (2024–2025). Initially, to approach the topic, a preliminary search was performed in the EBSCO Discovery metasearch engine, which retrieved an excessively high number of results from different databases. Therefore, it was decided to focus on three of them: PubMed, Scopus, and Web of Science. More specific filters were applied from each of them, allowing us to further narrow the search and identify potentially relevant studies. Eight terms were used for the search strategy, including the Boolean operators “OR” and “AND” to limit the search to the desired result. The search was performed as follows:

((dental care for children) OR (pediatric dentistry) OR (separation anxiety)) AND ((deep sedation) OR (conscious sedation) OR (anti-anxiety agents) OR (anesthetics, dissociative) OR (in-office sedation)).

Inclusion criteria:

- Clinical studies in children under 12 years old.
- Randomized controlled trials.
- Published in the last 5 years.

Exclusion criteria:

- Animal or *in vitro* studies.
- Letters to the editor.
- Case reports.
- Systematic reviews.
- Observational or comparative studies.
- Meta-analyses.
- Studies including general anesthesia.

### 3.3 Intervention

The search was not limited by chronological period, and was supplemented by a manual search of bibliographic references from the documents found to locate studies not identified through the electronic search. Studies that performed any dental treatment on pediatric patients aged 2 to 12 years who underwent conscious or deep sedation to reduce their anxiety during treatment were selected.

The inclusion and exclusion criteria were followed by reading the titles and abstracts. If the criteria were met, then the reviewers read the entire article. Due to the nature of this review only including RCTs, all the articles that did not meet this criteria were excluded for final review. Data was collected by the same two investigators who worked as a continuously as team preparing and editing the manuscript, creating the tables and diagrams. All the relevant data pertaining to the selected articles was summarized into tables.

### 3.4 Study selection process

After searching for articles in the various electronic databases mentioned above, the studies were exported to the bibliography manager Zotero® to facilitate the detection of duplicate articles. After eliminating duplicate articles, the titles and/or abstracts of the studies were read and analyzed, discarding those that were not relevant for this systematic review according to the inclusion and exclusion criteria. The full text was then read to assess eligibility and perform a qualitative synthesis.

Articles that appeared to meet the inclusion criteria, but which were excluded were tabulated.

### 3.5 Data extraction

To summarize the most relevant data from the studies, the following clinical data were extracted: authors, year of publication, study design, number and age of patients, type of drug used and distribution of patient groups, time at which anxiety was measured, onset of side effects, patient recovery, parental satisfaction, and type of anxiety measurement.

### 3.6 Assessing risk of bias in randomized trials

The Cochrane Risk of Bias Tool for Randomized Controlled Trials [13] was used to assess the risk of biased of the selected articles, all of which were randomized controlled trials. This scale evaluates seven domains: random sequence generation, allocation concealment, selective reporting, other biases, masking of participants and personnel, masking of outcomes, and incomplete outcome data. The articles were classified as “high risk of bias”, “low risk of bias”, and “fair risk of bias”. The results were then tabulated.

## 4. Results

### 4.1 Selection of studies and flowchart

The initial electronic search generated 1697 titles from the MEDLINE/PubMed database, 1563 from Web of Science, and 1437 from Scopus. Filtering allowed us to eliminate a large number of articles, and with the help of the bibliographic manager Zotero®, we were able to eliminate duplicates. After analyzing the titles and abstracts of 196 articles, we selected 14 to include in our review. One article that appeared to meet the inclusion criteria but was later excluded is shown in Table 2 [14].

As shown in **Supplementary Table 1** (Ref. [6, 15–27]) refers to the results, **Supplementary Table 2** (Ref. [16, 21–23, 26, 27]) refers to the biological factors and vital signs assessed and **Supplementary Table 3** (Ref. [6, 15–27]) to the measures based on scales/surveys.

The 14 selected articles selected were randomized clinical trials, all published between 2019 and 2024. Fig. 1 displays the search strategy flowchart that was carried out for the identification of articles relevant to the research, identifying those that were excluded for not being related to the objective, for being duplicates, for not having full access to the article or for not meeting the inclusion criteria.

### 4.2 Sample and groups

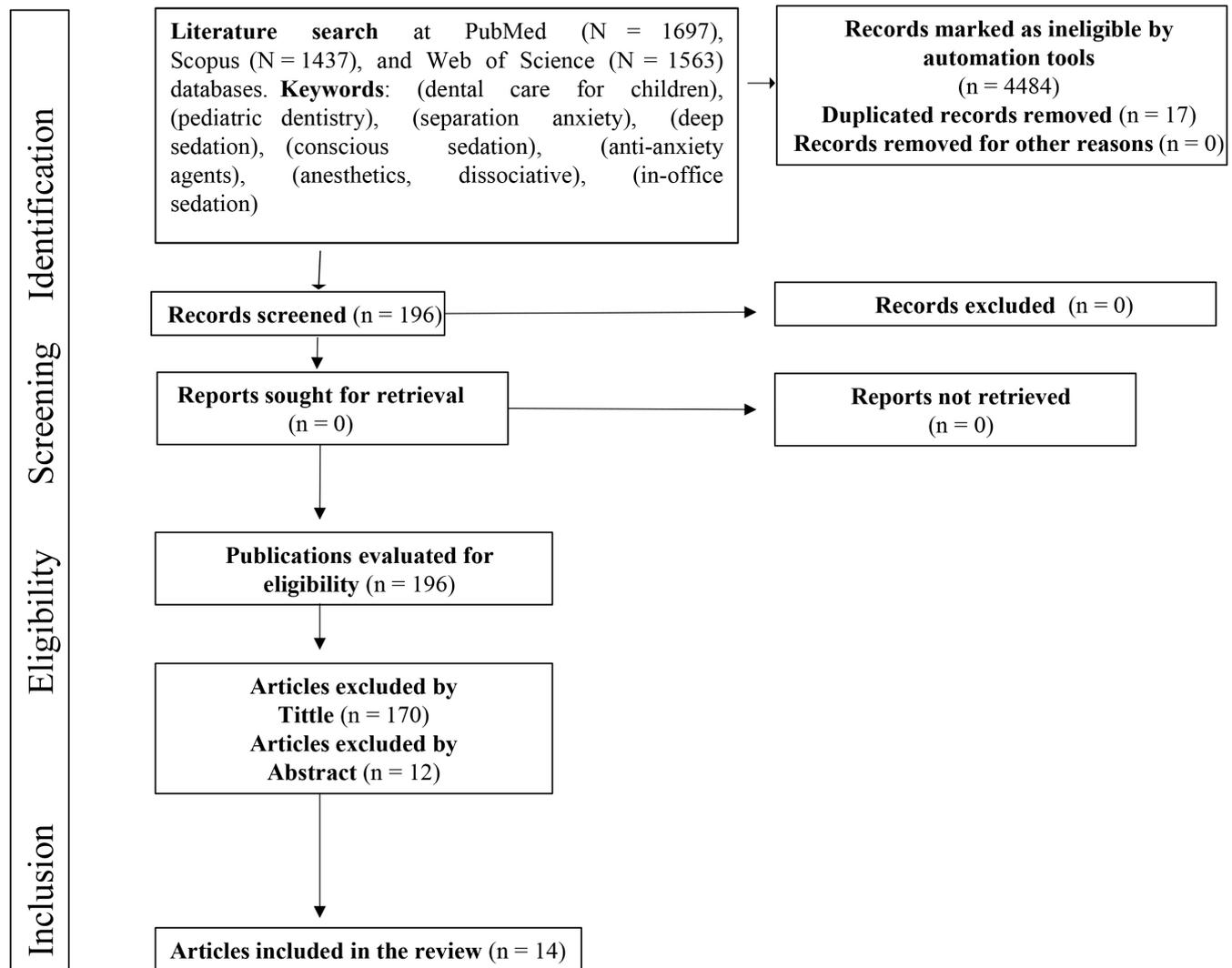
The group distribution for each of the articles included in this review is shown in Table 2. A total of 629 patients were included who underwent different sedation techniques. Children ages ranged from 2 to 12 years.

**TABLE 2. Article that appeared to meet inclusion criteria but was excluded.**

Study that appeared to meet the inclusion criteria, but which was excluded	DOI	Reason for exclusion
The intranasal dexmedetomidine plus ketamine for procedural sedation in children, adaptive randomized controlled non-inferiority multicenter trial (Ketodex): a statistical analysis plan	10.1186/s13063-020-04946-3	Even though the sample covered some of our age limit criteria of children up to 12 years old, some of the participants of this study were older than our age limit, some been up to 17 years old.

DOI: Digital Object Identifier.

### Identification of studies via databases and registers



**FIGURE 1. Search strategy flowchart.**

### 4.3 Type of sedation used and time at which anxiety is measured

In the studies analyzed, different agents and combinations were used for intranasal, oral, intravenous, intramuscular, and nebulized sedation in pediatric patients. Dexmedetomidine (DEX) was used at doses of 3–5  $\mu\text{g}/\text{kg}$  nebulized [15], 2–4  $\mu\text{g}/\text{kg}$  orally [16, 17], 1  $\mu\text{g}/\text{kg}$  intranasally [18] or sublingually [19], and up to 1  $\mu\text{g}/\text{kg}$  intravenously [20–22], in some cases

combined with ketamine (KET) or midazolam (MID).

Ketamine was administered at doses of 7 mg/kg intranasally [23], 5 mg/kg intramuscularly [6], and 2 mg/kg orally or buccally. Midazolam was used at doses of 0.3–0.5 mg/kg by nebulized or intranasal route, and 0.5–0.7 mg/kg orally [24], sometimes combined with dexmedetomidine or fentanyl (FEN) [25]. Nitrous oxide ( $\text{N}_2\text{O}$ ) was included as a control in some protocols [26]. In addition, different intravenous regimens were compared with propofol (20–60  $\mu\text{g}$  kg/min)

alone or in combination with ketamine in 1:3 or 1:4 ratios (ketofol) [27]. These data reflect the variability in the sedation strategies used and the need for comparative studies to determine the optimal protocol in pediatric dentistry that will allow us to perform the necessary dental procedures in a manner that is more comfortable for the patient and easier for the professional.

#### 4.4 Type of anxiety measurement

Anxiety measures were classified into two groups. First, physiological measures included heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), noninvasive blood pressure (NIBP), and the bispectral index (BIS), which assesses the degree of hypnosis by estimating the level of brain electrical activity and pulse oxygen saturation (SpO<sub>2</sub>). The results then tabulated.

Second, measures were made using scales or questionnaires, such as the Modified Observer Assessment of Alertness and Sedation Scale (MOAAS), the Visual Analogue Scale (VAS), the FLACC (Face, Legs, Activity, Cry, Controllability) scale, the OSUBRS (Ohio State University Behavioral Rating Scale), and the Houpt, Ramsay, and Frankl scales. The results also tabulated.

#### 4.5 Risk bias results

According to the Cochrane Risk of Bias Tool for Randomized Controlled Trials, no study with a “high risk of bias” was included in this review Fig. 2 (Ref. [6, 15–27]).

### 5. Discussion

#### 5.1 Most commonly used of sedative agents

Among the evaluated sedatives, Dexmedetomidine (DEX) stands out for its increasing use in pediatric dentistry due to its sedative and analgesic properties and minimal respiratory impact, although it may cause mild bradycardia without clinical consequences [15, 24]. According to Nie *et al.* [24], the sedation produced by DEX is located in the locus

coeruleus and is similar to natural and physiological sleep, unlike other drugs such as Ketamine or Midazolam, which produce anterograde amnesia. Unlike other sedatives such as propofol or benzodiazepines, DEX has a negligible impact on respiration, which is crucial in pediatric patients who are more susceptible to respiratory complications. However, its application must be carefully monitored due to side effects such as mild bradycardia, documented in the study conducted by Elkhatib *et al.* [15]; even though these side effects were clinically insignificant and did not require any intervention.

On the other hand, the combination of DEX with ketamine (KET), with antagonist effects, showed additional benefits. In both recent studies conducted by El-Rouby *et al.* [16, 17], a significant improvement in behavior and rapid recovery compared to DEX alone was emphasized. This may be rationalized by the opposed effect of the anxiolytic effects of DEX and the analgesic effects of KET, which also lessens undesired side effects such as hypersalivation, which is a common problem in pediatric sedation. This is in conformity with the research conducted by Haider *et al.* [21] that documented that DEX diminished this side effect due to its antisialagogue properties.

Although KET is known for its amnesic effect, we found in the study by El-Rouby *et al.* [16] that the number of pediatric patients who presented anterograde amnesia was higher when receiving the combination of DEX KET than when DEX was administered alone, which is consistent with Singh *et al.* [23] in which a higher amount of patients sedated with KET exhibited anterograde amnesia versus patients receiving DEX. It could be theorized that KET could probably induce profound amnesia when administered at full dose [16].

Furthermore, DEX reduces both anxiety and pain due to its marked analgesic effect, thus reducing high-dose local anesthesia and the need for postoperative analgesia, which improves the clinical experience. Despite this, in the study by Elkhatib *et al.* [15], it did not show significant differences compared to midazolam (MID) or DEX/MID in terms of analgesic effect, but its clinical performance surpassed both DEX/MID and MID, thus concluding that DEX was the alternative of choice.

Articles	Risk of Bias Assessment							
	Selection bias: Random sequence generation	Selection bias: Allocation concealment	Reporting bias: Selective reporting	Other bias: Other sources of bias	Performance bias: Blinding	Detection bias: Blinding (outcome assessment)	Attrition bias: Incomplete outcome data	Risk of bias
Elkhatib <i>et al.</i> [15], (2024)	Green	Green	Green	Green	Green	Green	Green	Green
El-Rouby <i>et al.</i> [16], (2024)	Green	Green	Green	Green	Yellow	Green	Green	Yellow
Dubey <i>et al.</i> [23], (2024)	Green	Green	Green	Green	Green	Green	Green	Green
Janiani <i>et al.</i> [26], (2024)	Green	Green	Green	Green	Green	Green	Green	Green
Isik <i>et al.</i> [27], (2024)	Green	Green	Green	Green	Green	Green	Green	Green
Ansari <i>et al.</i> [6], (2024)	Green	Green	Green	Green	Green	Green	Yellow	Yellow
Nie <i>et al.</i> [24], (2024)	Green	Green	Green	Green	Green	Green	Green	Green
Janiani <i>et al.</i> [18], (2024)	Green	Green	Green	Green	Green	Green	Green	Green
Alhaidari <i>et al.</i> [25], (2024)	Green	Green	Green	Green	Green	Green	Green	Green
Rehman <i>et al.</i> [22], (2021)	Green	Green	Green	Green	Green	Green	Green	Green
Shaat <i>et al.</i> [19], (2022)	Green	Green	Green	Green	Green	Green	Green	Green
Haider <i>et al.</i> [21], (2022)	Green	Green	Green	Green	Green	Green	Green	Green
Hammadyeh <i>et al.</i> [20], (2019)	Green	Green	Green	Green	Green	Green	Green	Green
El-Rouby <i>et al.</i> [17], (2024)	Green	Yellow	Green	Green	Yellow	Green	Green	Yellow

FIGURE 2. Risk of bias assessment. Green: low risk bias; Yellow: acceptable risk bias.

Recent studies have shown that combining DEX with Midazolam (MID) or Ketamine (KET) improves sedation quality, however, there are important differences depending on the combinations selected for sedation. For example, the study by Dubey *et al.* [23] shows what happens when a patient is administered the combination of MID and DEX compared to those given KET monotherapy. Intranasal ketamine showed a significantly higher level of acceptability. This could be due to the burning sensation in the nasal mucosa associated with intranasal midazolam. In this regard, DEX-KET yields better pediatric behavior, faster recovery [16, 17], and control of effects like hypersalivation [21], whereas DEX-MID results in lighter sedation [15]. Additionally, the combined use of DEX or MID with opioids or Propofol has proven to optimize sedation, reduce complications, and decrease required dosages [22]. Intranasal KET, although more acceptable than intranasal MID, produces deeper sedation. Finally, the DEX-KET combination is also associated with a higher degree of anterograde amnesia [16] compared to prescribing DEX only [28].

## 5.2 Side effects

According to the articles included in this review none of them reported any significant side effects related to sedation in children. While some studies mentioned mild adverse events such as transient drowsiness or longer-than-expected recovery, none presented serious life threatening complications [6, 16, 18, 21, 24–27]. This suggests that the techniques and drugs used in the analyzed studies have an adequate safety profile in pediatric settings.

According to the literature, combining sedative agents mitigate the risks associated with high individual doses, as demonstrated by the 1:4 ketofol approach, which is the combination of propofol with ketofol. According to the study by Gizem *et al.* [27] this combination maintains hemodynamic and respiratory stability while optimizing sedation and achieving the desired relaxing effects.

In the study conducted by Ansari *et al.* [6], the combination of diazepam, such as midazolam with ketamine, has demonstrated to be useful in reducing undesired side effects such as vomiting or flushing commonly associated with ketamine. In this study an increase in heart rate was observed in both study groups after administering local anesthesia [6]. This increase in heart rate may be due to the effects of ketamine or the epinephrine content of lidocaine. However, the combination of atropine in conjunction with a sedative drug, may also contribute in the increase in heart rate. In addition, pain during the administration of injections or to the dental treatment is also considered a contributing factor for the increased heart rate [6]. However, further research is recommended to strengthen evidence regarding long-term safety and efficacy in different patient populations.

## 5.3 Administration techniques

Various routes of sedative administration in pediatric dentistry have been evaluated, including intranasal (IN) and intramuscular (IM) [6]. However, IN administration is less invasive and suitable for shorter procedures, although it may cause nasal irritation [6]. The IN route, although less invasive,

virtually pain free, and is better tolerated by children, offers an acceptable level of sedation only for short procedures lasting a maximum of 15 minutes, approximately. One of its benefits is that this route avoids the gastrointestinal tract and hepatic metabolism, which is a drawback with the oral route. However, there are reports of a burning sensation, irritation, and mucosal inflammation after intranasal administration, which can be lessened by applying topical anesthetic spray before administering the sedative drug [6].

In contrast, the IM route, which is more effective and preferred by parents, is ideal for longer treatments [6]. Ketamine showed greater bioavailability via the IM route (approximately 93% vs. 50% for IN) [6]. Intranasal midazolam has better acceptance than nitrous oxide [18], and its sublingual route has superior acceptance compared to the IN administration [21], albeit with a slower onset of action. Finally, although Propofol provides rapid induction, it may be associated with respiratory events, underscoring the need for thorough preoperative screening [21].

The best results is the KET-DEX combination, compared to MID which is considered the “gold standard”. It concludes recommending comparing intranasal sedation with other routes [19]. Therefore, we have decided to include all types of routes in our review without excluding any, so that standardized protocols can be established in the future to optimize its use in pediatric dentistry.

## 5.4 Parental experience

According to an article published by Arenas *et al.* [5], parents are increasingly choosing pharmacological techniques such as general anesthesia over behavioral modification, citing that it is due to increasingly permissive parenting norms. Given this trend, it would be useful for dental school educators to introduce these concepts into university curricula—both undergraduate and postgraduate—to adequately prepare the students [5].

In this review, only three of the selected articles evaluated parental satisfaction with the sedation provided to their children and all measured in different ways [6, 21, 24]. In the RCT conducted by Haider *et al.* [21] no statistical difference ( $p = 1$ ) was reported for parental satisfaction in the two study groups as the parents reported being “satisfied” and “very satisfied” after completing a 5-point Likert-scale questionnaire ((5) very satisfied, (4) satisfied, (3) neutral, (2) dissatisfied, (1) very dissatisfied) [21]. In the study of Nie *et al.* [24] the parents reported that all adverse events had disappeared without any new adverse events after a time-frame of one day. In midazolam (M) group, the parents of twenty-three participants were “very satisfied” with the sedation treatment, the parents of twenty participants were “generally satisfied”. No parents reported been “dissatisfied”. However, in the dexmedetomidine-midazolam (DM) group, the parents of thirty-four participants responded been “very satisfied”, four parents reported been “generally satisfied”, while two parents responded been “dissatisfied”. According to this study, overall parental satisfaction was higher in the DM group ( $p = 0.001$ ). This study also took the factor time into account as the satisfaction questionnaire was emailed to

the parents 24 hours after treatment, asking whether their child suffered any unexpected or harmful reactions associated with the medical treatment, and asking if they were satisfied with the sedation treatment. Parent's satisfaction was categorized as either very satisfied, generally satisfied or dissatisfied [24]. In the study conducted by Ansari *et al.* [6], parents were also called 24 hours after the intervention. In this study the parents favored the IM route reporting that "it was much more effective" ( $p < 0.05$ ) [6].

## 5.5 Monitoring and safety preparedness

According to the latest American Association of Pediatric Dentistry, there are guidelines to follow during the entire process of sedation in order to prevent or recover from complications. They highlight the importance of knowing safety it is common for children to die from sedation complications. According to the guideline those cases who are in American Society of Anesthesiologists (ASA) classes I and II are normally considered safe for minimal, moderate, or deep sedation [29].

However, some patients require further monitoring and skills such as airway maintenance and patency, which is the main source of complication during sedation. For example, they state that children with compromised airways, such as those with apnea, laryngospasm, and/or airway blockade does require patency of the airway and the healthcare provider needs to know how to provide continuous positive airway pressure (CPAP) and knowledge using bag-valve-mask (BVM) ventilation, among others in order to maintain airway patency [29].

Healthcare providers thus require an emergency kit easily accessible during the sedation including oral and nasal airways masks, BVMs, laryngeal mask and blades, tracheal tubes, face masks, blood pressure (BP) cuffs, intravenous catheters, among others to revive and provide vital life support [29].

## 5.6 Limitations

The main limitation of this work is the lack of uniformity among clinical trials in the literature, particularly regarding the scales used to measure sedation levels, which vary significantly. Most studies lacked a placebo-controlled group or comparisons with a known-effective sedative. Future research should consider using oral midazolam or nitrous oxide sedation as standard references to evaluate the efficacy of other methods [4].

It's also important to consider the age of the children included in the studies as limitation. Children should ideally be segmented into three broad age groups, as recommended by the British National Formulary (BNF) for pediatric prescriptions: 1–6 years, 6–12 years, and over 12 years, since reasons for sedation may vary notably across these groups [4].

In most reviewed studies, children were healthy or had mild systemic conditions, consistent with ASA physical status classifications I and II [30]. However, some techniques may be more suitable for children with more complex medical conditions, as in the study conducted by Garret-Bernardin *et al.* [31], which included patients with physical and psychological impairments and thus provides a broader view of the types of patients managed under nitrous oxide sedation.

Another aspect to point out is that there was limited information on regard to the dental restoration procedures performed in the studies, although some mentioned the use of local anesthesia, bite blocks, and rubber dams. Undoubtedly, we believe this detail is important to be added in these kind of studies as the type of procedure performed can influence both behavior and anxiety levels [4].

Initially, we intended to exclude articles allocated to deep sedation, but this was not feasible due to ambiguity in many studies regarding the type of sedation used. In several cases, it was not specified whether the sedation was conscious or deep, and patient drowsiness was vaguely described [4]. In some studies, children reportedly fell asleep, and oral devices were used, suggesting the sedation may have been deeper than indicated. This highlights the need to establish a standardized definition of conscious sedation, or at the very least, use universally accepted terminology. Without clear classification, it is difficult for researchers to properly interpret and apply published data [4].

## 6. Conclusions

The choice of sedative protocol and route of administration should be individualized, taking into account the procedure's complexity, the patient's characteristics, and its potential side effects. DEX is emerging as a versatile drug, especially in combination therapies, to optimize pediatric dental sedation, while ketamine and midazolam remain key components in specific protocols.

The fastest onset of action is determined by the administration route. As of today, Propofol, administered intravenously, induces sedation most rapidly.

In all studies included in this review, the reported adverse effects were not statistically significant. However, nitrous oxide was the sedative drug with the lowest risk of complications, which were nearly negligible.

For rapid recovery without residual effects, nitrous oxide is the drug of choice. However, for calm, agitation-free recovery, dexmedetomidine is preferred, although it may cause mild bradycardia without clinical consequences. For minor procedures requiring a balance between quickness and efficacy, midazolam is ideal. Nonetheless, the choice always depends on the type of procedure, its duration, and the child's specific needs.

There is no single "best" technique for all the cases. However, combinations and personalization of the strategy appear to yield better outcomes: intranasal or inhalation routes for short procedures, oral for moderate ones, and intravenous for deep sedation in longer procedures.

Although few studies evaluated parental satisfaction, it is evident in the few studies that reported it that parents tend to favor approaches that balance efficacy, safety, and comfort for their children. The lack of information on this regard entails that further research is needed to evaluate parental comfort and satisfaction when their children undergo these types of interventions.

## AVAILABILITY OF DATA AND MATERIALS

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## AUTHOR CONTRIBUTIONS

MNM and EMMP—organized the conceptualization. JCV and MRV—wrote the original draft. CSGD—analyzed the manuscript and wrote the original draft. MNM, MBDC and CSGD—did the methodology and revised the original draft. All the authors contributed and agreed on the final manuscript.

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

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## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found, in the online version, at <https://oss.jocpd.com/files/article/2028734991175696384/attachment/Supplementary%20material.zip>.

## REFERENCES

- [1] Santiago EP, Brito T de S, Almeida SA. Dentistphobia and the conduct of the dentist: an integrative review of the literature. *Facit Business and Technology Journal*. 2021; 1: 103–117.
- [2] Baier K, Milgrom P, Russell S, Mancl L, Yoshida T. Children's fear and behavior in private pediatric dentistry practices. *Pediatric Dentistry*. 2004; 26: 316–321.
- [3] Gao F, Wu Y. Procedural sedation in pediatric dentistry: a narrative review. *Frontiers in Medicine*. 2023; 10: 1186823.
- [4] Ashley PF, Chaudhary M, Lourenço-Matharu L. Sedation of children undergoing dental treatment. *Cochrane Database of Systematic Reviews*. 2018; 12: CD003877.
- [5] Arenas M, Barbería E, Marotom M, Gómez B. Paternal demand of paediatric dental treatment using general anaesthesia: a surprising reality. *RCOE*. 2006; 11: 351–356. (In Spanish)
- [6] Ansari G, Toomarian L, Masoum T, Shayeghi S, Eftekhar L. Evaluation of the sedative effect of intranasal versus intramuscular ketamine in 2–6-year-old uncooperative dental patients. *Dental and Medical Problems*. 2024; 61: 35–41.
- [7] Clinical Affairs Committee–Behavior Management Subcommittee, American Academy of Pediatric Dentistry. Guideline on behavior guidance for the pediatric dental patient. *Pediatric Dentistry*. 2015; 37: 57–70.
- [8] Zhang Q, Deng X, Wang Y, Huang R, Yang R, Zou J. Postoperative complications in Chinese children following dental general anesthesia: a cross-sectional study. *Medicine*. 2020; 99: e23065.
- [9] Álvarez AM, Álvarez M. Oral sedation: clinical foundations for its application in dentistry. *CES Odontología*. 2006; 19: 61–73. (In Spanish)
- [10] Salerno C, Cirio S, Zambon G, D'Avola V, Parciannello RG, Maspero C, *et al.* Conscious sedation for dental treatments in subjects with intellectual disability: a systematic review and meta-analysis. *International Journal of Environmental Research and Public Health*. 2023; 20: 1779.
- [11] Lee R, Wang K, Forsyth A, Garcia M, Scott J, Nelson T. The effect of temperament on outcomes of opioid and non-opioid pediatric dental sedation. *Journal of Dentistry for Children*. 2024; 91: 18–24.
- [12] Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, *et al.* The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *The BMJ*. 2021; 372: n71.
- [13] Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, *et al.*; Cochrane Bias Methods Group; Cochrane Statistical Methods Group. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *The BMJ*. 2011; 343: d5928.
- [14] Heath A, Rios JD, Pullenayegum E, Pechlivanoglou P, Offringa M, Yaskina M, *et al.*; PERC-KIDSCAN Ketodex Study Group. The intranasal dexmedetomidine plus ketamine for procedural sedation in children, adaptive randomized controlled non-inferiority multicenter trial (Ketodex): a statistical analysis plan. *Trials*. 2021; 22: 15.
- [15] ElKhatib AA, Ghoneim TAM, Dowidar KML, Wahba NA. Effect of Dexmedetomidine with or without Midazolam during procedural dental sedation in children: a randomized controlled clinical trial. *BMC Oral Health*. 2024; 24: 1298.
- [16] El-Rouby SH, O Crystal Y, M Elshafie A, A Wahba N, El-Tekeya MM. The effect of dexmedetomidine-ketamine combination versus dexmedetomidine on behavior of uncooperative pediatric dental patients: a randomized controlled clinical trial. *Journal of Applied Oral Science*. 2024; 32: e20240057.
- [17] El-Rouby SH, Crystal YO, Elshafie AM, Wahba NA, El-Tekeya MM. Effectiveness of buccal administration of dexmedetomidine and ketamine combination in paediatric dental sedation: a randomized controlled clinical trial. *International Journal of Paediatric Dentistry*. 2025; 35: 359–368.
- [18] Janiani P, Gurunathan D, Nuvvula S. Influence of temperament on the acceptance of two conscious sedation techniques in toddlers undergoing dental treatment: a randomised cross over trial. *Pain Research and Management*. 2023; 2023: 6655628.
- [19] Shaat MA, Bakry NS, Elshafie AM, Talaat DM. Intranasal versus sublingual route of dexmedetomidine sedation in paediatric dentistry: a randomized controlled clinical trial. *International Journal of Paediatric Dentistry*. 2022; 32: 232–239.
- [20] Hammadyeh AR, Altinawi MK, Rostom F. Comparison of two intravenous sedation techniques for use in pediatric dentistry: a randomized controlled trial. *Dental and Medical Problems*. 2019; 56: 337–341.
- [21] Haider K, Mittal N, Srivastava B, Gupta N. A double-blind randomized controlled trial to compare the safety and efficacy of dexmedetomidine alone and in combination with ketamine in uncooperative and anxious paediatric dental patients requiring pulpextomy. *European Archives of Paediatric Dentistry*. 2022; 23: 465–473.
- [22] Rehman F, Goyal A, Gauba K, Jain K, Kapur A. Safety and efficacy of IV dexmedetomidine as an adjunct to propofol to sedate anxious and uncooperative pediatric dental patients: a randomized controlled trial. *Journal of Clinical Pediatric Dentistry*. 2021; 45: 428–432.
- [23] Dubey B, Singh N, Kumar S. Comparison of intranasal ketamine with intranasal midazolam and dexmedetomidine combination in pediatric dental patients for procedural sedation: a crossover study. *Journal of Indian Society of Pedodontics and Preventive Dentistry*. 2024; 42: 217–225.

- <sup>[24]</sup> Nie J, Chen C, Xie J, Ding G. Oral midazolam vs. intranasal dexmedetomidine plus oral midazolam for sedation of pediatric outpatients: a double-blinded randomized controlled trial. *BMC Anesthesiology*. 2023; 23: 341.
- <sup>[25]</sup> Alhaidari RI, AlSarheed M, Sheta SA, Aldhubaiban M. Intranasal fentanyl combined with oral midazolam for pediatric dental sedation: a controlled randomized blinded crossover clinical trial. *Pediatric Dentistry*. 2022; 44: 255–260.
- <sup>[26]</sup> Janiani P, Gurunathan D, Manohar R. Comparative evaluation of intranasal dexmedetomidine, intranasal midazolam, and nitrous oxide for conscious sedation of anxious children undergoing dental treatment: a randomized cross-over trial. *Journal of Indian Society of Pedodontics and Preventive Dentistry*. 2024; 42: 141–148.
- <sup>[27]</sup> Isık G, Alpay N, Daglioglu G, Ciftci V. Effects of propofol, ketamine-propofol mixture in pediatric dental patients undergoing intravenous sedation: a clinical study. *Scientific Reports*. 2024; 14: 11806.
- <sup>[28]</sup> Singh C, Pandey RK, Saksena AK, Chandra G. A comparative evaluation of analgo-sedative effects of oral dexmedetomidine and ketamine: a triple-blind, randomized study. *Pediatric Anesthesia*. 2014; 24: 1252–1259.
- <sup>[29]</sup> Coté CJ, Wilson S; American Academy of Pediatrics; American Academy of Pediatric Dentistry. Guidelines for monitoring and management of pediatric patients before, during, and after sedation for diagnostic and therapeutic procedures. *Pediatrics*. 2019; 143: e20191000.
- <sup>[30]</sup> Bastarrechea Milián M de las M, Rodríguez Soto A, Morales Navarro D. Medical risk in dental patients according to the ASA classification. *Revista Habanera de Ciencias Médicas*. 2020; 19: e3032.
- <sup>[31]</sup> Garret-Bernardin A, Festa P, Matarazzo G, Vinereanu A, Aristei F, Gentile T, *et al.* Behavioral modifications in children after repeated sedation with nitrous oxide for dental treatment: a retrospective study. *International Journal of Environmental Research and Public Health*. 2023; 20: 4037.

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