Pharmacological Sedation in Paediatric Dentistry

F. Inchingolo[1], A.M. Inchingolo[1] , L. Ferrante[1], E.de Ruvo[1], A. Di Noia[1], A. Palermo[2], A.D.Inchingolo[1], G. Dipalma[1]

[1]*Interdisciplinary Department of Medicine, University of Bari "Aldo Moro", 70124 Bari, Italy*
[2]*College of Medicine and Dentistry, Birmingham B4 6BN, UK*

Email francesco.inchingolo@uniba.it

DOI 10.23804/ejpd.2024.2204

Abstract

Aim This research aims to explore and evaluate various sedation strategies used in paediatric dentistry, focusing on effectively and safely addressing dental anxiety to improve cooperation during dental treatment in paediatric patients.

Materials and methods To identify relevant studies for this systematic review, the Scopus, Web of Science and PubMed databases were used, combining the terms "sedation" with "pediatric dentistry" or "pedodontics" through the Boolean operators "AND" and "OR". Only literature published in English within the last ten years was included. The inclusion criteria were clinical studies, case reports and in vivo studies, while systematic reviews, meta-analyses and studies conducted on animals or in vitro were excluded. After eliminating duplicates, 544 articles were identified, of which 501 were excluded for not meeting the inclusion criteria. A further 27 articles were excluded for various reasons, including lack of retrieval, in vitro nature or being reviews. Finally, 16 articles were selected for inclusion in the review.

Conclusions These findings underscore the importance of pharmacological management in paediatric dental care, offering valuable insights into the selection and application of sedation techniques to mitigate dental anxiety and enhance patient outcomes.

KEYWORDS oral health, general health, well-being, sedation, interdisciplinary, fear, phobia, benzodiazepines, pharmacological sedation.

Introduction

In some cases, anxiety about dental procedures in childhood may require sedation techniques. Over the years, conscious sedation has proven to be particularly useful in the management of small patients which can be difficult due to poor collaboration [Saccomanno et al., 2021; Ashley et al., 2018]. Controlling stress and pain resulting from dental treatments is today's challenge, especially in paediatric dentistry [Viinikangas et al., 2007; Armfield, 2011; Appukuttan, 2016; Primozic et al., 2021; Singh et al., 2023]. Psychological approaches may not be sufficient to reduce levels of anxiety and panic, especially in children, jeopardising the success of dental procedures [Silveira et al., 2020; D'Ettorre et al., 2022; Nelson and Nelson; 2013]. Sedation can be considered a pharmacological method with a relatively safe and effective way to help dental procedures in fragile patients and patients with important clinical problems and uncooperative patients, including children [Memè et al., 2022]. Sedation must follow accurate safety protocols to guarantee an adequate sedation and adequate working times with minimal respiratory depression [Salerno et al., 2023]. Sedation is premedication before general anesthesia to relax patients while preserving cardiopulmonary reflexes [Zommick et al., 1996; Saccomanno et al., 2021]. Recent studies have focused in particular on comparing different sedation approaches to ascertain their effectiveness and safety profiles [Ferrazzano et al, 2006; Lv and Zhang, 2023]. Different agents, inhaled inhalation and intravenous, can be used to achieve different levels of sedation (deep, moderate and mild) [Rossi et al., 2023]. The most frequent anesthetic agents are midazolam, ketamine, meperidine, fentanyl, propofol, sevoflurane and hydroxyzine alone or in combination [Tobias and Leder, 2011]. An alternative is inhalation of nitrous oxide-oxygen (N_2O-O_2) with equilibrium as oxygen sedation (Fig. 1) [Kurdi et al., 2014; Memè et al., 2021]. This technique has analgesic and relaxing properties while preserving the patients' consciousness [Mummolo et al., 2014; Quinzi et al., 2020; Minervini et al., 2023; Uzunçıbuk et al., 2023]. Oral sedation with midazolam or ketamine or both in combination is the oldest and best known technique, but other anesthetic agents can also be used alone or in combination [Wilson et al., 1990; Sheroan et al., 2006; Kupietzky and Houpt, 1993]. Studies comparing oral midazolam alone with the combination of intranasal dexmedetomidine and oral midazolam revealed that the combined approach produces superior sedation outcomes without significant differences in adverse events [Malhotra et al., 2016]. The long-term behavioural benefits of moderate sedation with midazolam or midazolam/ketamine improve treatment outcomes and reduce psychological distress in children [Ferrazzano et al., 2019; Memè et al., 2022]. Advances in monitoring technologies have enabled more accurate assessment of patient responses during sedation, facilitating personalised care and treatment planning [McQueen et al., 2015; Memè et al., 2022; Singam, 2023]. By combining multiple agents with complementary mechanisms of action, doctors can achieve deeper levels of sedation with lower doses, reducing the risk of side effects and complications [American Academy of Pediatrics et al., 2006; Chilkoti et al., 2015]. Additionally, research has explored new drug delivery methods, such as atomised buccal and intranasal administration, to improve sedative efficacy and patient acceptance [Fantacci et al., 2018; Inchingolo et al., 2022; Inchingolo et al., 2023; Amjad et al., 2023]. Safety is a paramount concern in paediatric sedation, with strict adherence to established guidelines and protocols essential to minimise risks [Gómez-Manzano et al., 2022; Nelson and Nelson; 2013]. Pre-operative assessments, such as thorough medical history, physical examination and risk stratification, are crucial to identify patients at increased risk of sedation-related complications [Farronato et al., 2012]. Furthermore, appropriate monitoring during sedation, including continuous monitoring of vital signs and vigilant observation of patient responses, is essential for early diagnosis

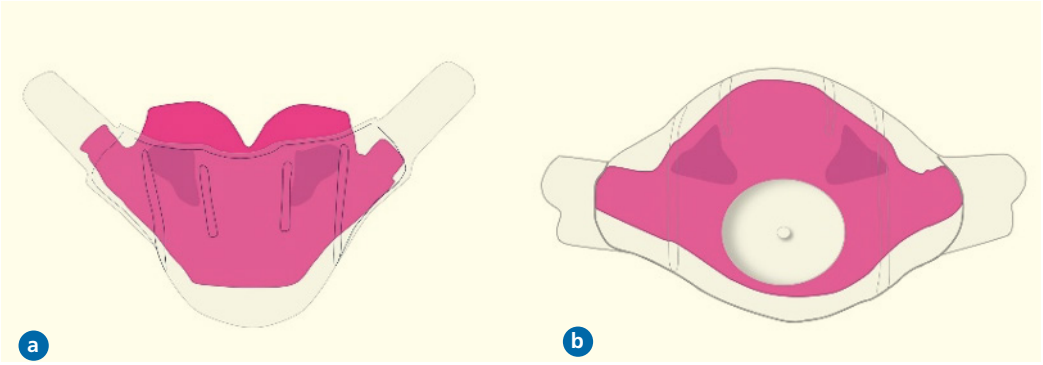

FIG 1
Nasal mask for paediatric sedation with nitrous oxide (N2O)., in top (A) and front (B) projection.

of adverse events and timely intervention [Eddahchouri et al., 2023; Petkar et al., 2023]. Overall, the growing body of research on conscious sedation aims to identify effective clinical protocols and operational guidelines for dental professionals [Marks and Martens, 2003; Inchingolo et al., 2023]. By highlighting the importance of pharmacological management in alleviating dental anxiety, these studies offer valuable guidance to promote positive patient experiences and outcomes in paediatric dentistry [Malviya et al., 1997; Ferrazzano et al., 2019]. The field of paediatric sedation in dentistry therefore continues to evolve, with ongoing research aimed at refining sedation protocols, optimising drug regimens and improving patient outcomes [Mittal et al., 2015; He et al., 2023]. By integrating evidence-based sedation strategies into clinical practice, dental professionals can effectively manage dental anxiety in paediatric patients while ensuring their safety and well-being [Wang et al., 2021; Inchingolo et al., 2022]. Through collaborative efforts among researchers, clinicians and educators, the future of paediatric sedation promises to improve the quality of dental care and promote positive experiences for young patients and their families [Ramos-Gomez, 2014; Mason and Seth, 2019].

Materials and Methods

Protocol and Registration

This systematic review was conducted by the standards of the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) and it was registered under the number ID 527979 on PROSPERO (The International Prospective Register of Systematic Reviews).

Search Processing

The search terms, to select the papers under evaluation, with the Boolean operators "AND" and "OR", utilised on the databases (Scopus, Web of Science, and Pubmed) were: ("sedation") AND ("pediatric dentistry" OR "pedodontics"). The search was restricted to just items released in English during the previous ten years (January 2014 – February 2024) (Table1).

Article screening Strategy	Database: Scopus, Web of Science and Pubmed
	Keywords: A ("sedation"); B ("paediatric dentistry" OR "pedodontics")
	Boolean variable: "AND", "OR"
	Timespan: 2014-2024
	Language: English

TABLE 1 Database search indicators

Eligibility Criteria

The reviewers, who worked in pairs, chose works that satisfied the following criteria for inclusion: 1) clinical studies or case reports, 2) in vivo studies. Exclusion criteria were systematic reviews meta-analyses, animal and in vitro studies.

The review was conducted using the PICO criteria:

- Population: children, male and female, not cooperating with dental treatments
- Intervention: conscious sedation in paediatric dentistry
- Comparison: dental treatment without sedation and different sedation strategies
- Outcome: various sedation methods are increasingly effective and safe, reducing dental anxiety and therefore improving cooperation during dental treatment in paediatric patients.

Data Processing

During the screening process, articles were selected based on their titles and abstracts, excluding any publications that did not align with the study's themes. The full texts of selected publications meeting the inclusion criteria were thoroughly reviewed. Any disagreements among reviewers regarding article selection were resolved through discussion.

Quality Assessment

The quality of the included papers was assessed by two reviewers, R.F. and E.I., using the ROBINS is a tool developed to assess risk of bias in the results of non-randomised studies that compare health effects of two or more interventions. Seven points were evaluated and each was assigned a degree of bias. A third reviewer (F.I.) was consulted in the event of a disagreement until an agreement was reached. The question in the domains evaluated in the ROBINS is the following:

- Bias due to confounding
- Bias arising from measurement of exposure
- Bias in the selection of participants into the study
- Bias due to post-exposure intervention
- Bias due to missing data
- Bias arising from measurement of the outcome
- Bias in the selection of the reported results.

Results

Keyword searches conducted in the Web of Science (188), Scopus (278), and PubMed (324) databases initially identified 790 articles. After removing duplicates (246), 544 unique articles remained. Among these, 502 were excluded for not meeting the inclusion criteria, and an additional 27 were excluded: 1 was in vitro, 2 could not be found, and 24 were reviews. Ultimately, 15 publications were selected for inclusion in this study (Figure 2).

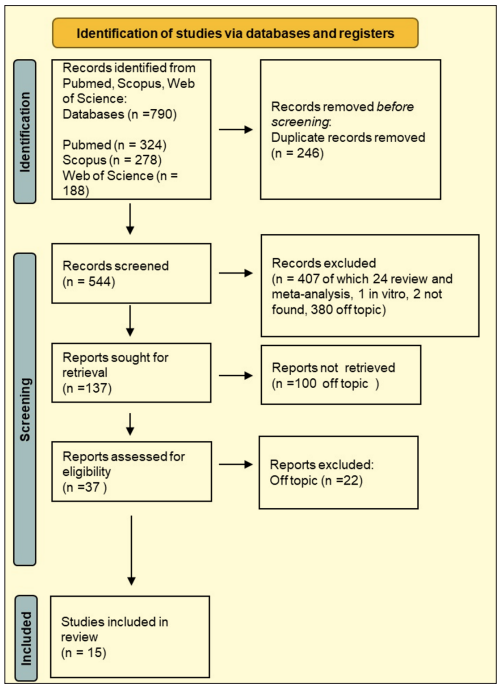

FIG 2 PRISMA flowchart.

Analysing the research design, patient population, intervention, and results led to the selection of study data (Table 3).

Quality Assessment and Risk of Bias of Included Articles

The risk of bias in the included studies is reported in Figure 3. Regarding the bias due to confounding most studies have a low risk. The bias arising from measurement is a parameter with low risk of bias. Many studies have low risk of bias due to bias in selection of participants. Bias due to post exposure cannot be calculated due to high heterogeneity. The bias due to missing data is low in many studies. Bias arising from measurement of the outcome is low. Bias in the selection of the reported results is high in most studies. The final results show that 5 studies have low risk of bias, 2 have a very high risk of bias and five have high risk of bias.

Discussion

Many studies offer an interesting overview of the different sedation strategies used in paediatric dentistry, highlighting the importance of addressing dental anxiety in children effectively and safely [Uchôa et al., 2024]. Nie et al. [2023] study compared the effectiveness of oral midazolam alone versus the combination of intranasal dexmedetomidine and oral midazolam in managing dental anxiety in children. Their study demonstrated that while the combination approach had a longer onset time, it significantly improved the rate of successful sedation compared to oral midazolam alone. Importantly, they found no significant differences in adverse events between the two groups, highlighting the safety of the combination approach [Nie et al., 2023]. Building on this, Antunes et al. [2016] paper discussed the long-term effects of pharmacological management on children's behavior during dental treatment. They found that moderate sedation with midazolam or midazolam/ketamine led to improved behavior in subsequent dental sessions compared to those without sedation. This underscores the importance of effective pharmacological management in reducing the risk of adverse dental experiences that could traumatise children, particularly in the context of early-life caries treatment [Antunes et al., 2016]. Vasakova et al.'s 2020 study focused on the perioral administration of midazolam to induce conscious sedation in children during dental treatments. They emphasised the safety and efficacy of midazolam sedation, noting its ability to significantly reduce blood pressure and heart rate while maintaining acceptable oxygen saturation levels [Cazzolla et al., 2020]. Additionally, they found that older children tended to exhibit better behavior during sedation, highlighting the influence of age on sedation outcomes [Vasakova et al., 2020]. Similarly, Mourad et al. [2003] retrospective study evaluated the success of N_2O sedation for paediatric dental treatment, emphasising its high success rates and its potential as an effective treatment option for pre-operative and anxious children. They identified patient age and practitioner experience as key factors influencing the success of N_2O sedation (Figure 3), further supporting its use in paediatric dental settings [Mourad et al., 2022]. Lastly, Memé et al. [2022] study examined the efficacy and safety of N_2O-O_2 as a treatment approach for paediatric patients

Author and year	Type	Patients	Aim	Material and methods	Results and conclusions
Memè et al. [2022]	Retrospective clinical study	371 children (175 females and 196 males) aged 4–10 years	To assess the effectiveness and safety of N2O-O2 in achieving cooperation in these children.	Children received conservative dental treatment lasting up to 30 minutes. They were initially administered 100% oxygen, followed by a gradual increase in the dose of N_2O to 35%. At the conclusion of the treatment, they were given 100% pure oxygen for 5 minutes.	The research found that using N_2O-O_2 sedation is a safe and effective approach to improve cooperation among young children receiving conservative dental treatment on baby teeth. It significantly enhanced cooperation levels with minimal side effects.
Nie et al. [2023]	RCT (Randomized controlled trial)	83 Children aged 3–12 years	To assess the sedative effectiveness of oral midazolam versus a combination of intranasal dexmedetomidine and oral midazolam in paediatric patients undergoing dental procedures for dental anxiety.	Participants were given either a combination of intranasal dexmedetomidine and oral midazolam, or oral midazolam alone. Sedation was adjusted according to weight, and its effectiveness was assessed using the Ramsay scale score.	The combined administration of oral midazolam and intranasal dexmedetomidine demonstrated greater effectiveness in managing non-cooperative behaviour in children compared to oral midazolam alone.
Antunes et al. [2016]	Prospective clinical study	50 children under four years	To assess children's behavior in subsequent dental sessions after oral rehabilitation with varied pharmacological regimens.	Preschoolers treated for caries were grouped by pharmacological regimen: none, oral midazolam, oral midazolam/ketamine, or general anesthesia.	Pharmacological sedation (midazolam or midazolam/ketamine) improved children's future behavior post-dental treatment, despite initial negative effects. It underscores the importance of pharmacological management for long-term behavioural outcomes in paediatric dentistry.

TAB. 3A Features of the studies included in the analysis.

Author and year	Type	Patients	Aim	Material and methods	Results and conclusions
Vasakova et al. [2020]	Observational clinical study	272 children between 1-12 years of age	To evaluate the effects of midazolam administered to children during dental treatment on their vital conditions and to monitor changes in children's behavior during sedation.	Midazolam sedation during dental procedures. Vital signs monitored pre- and post-midazolam administration. Behavioural changes observed during sedation.	Administering 0.5 mg/kg of midazolam is recommended as a safe dosage for paediatric dental procedures in paediatric dentistry.
Mourad et al.[2022]	Retrospective study	480 patients aged 3 to 17	To evaluate the success rates and potential influencing factors of N_2O sedation for dental treatment in a specialized paediatric dental service.	Study reviewed pediatric dental clinic records (2012-2017) for N_2O sedation, assessing patient age, dentist experience, procedural changes, and sedation/ treatment outcomes.	N_2O sedation achieved over 90% success rate in pediatric dental procedures, improving with patient age and dentist experience.
Hammadyeh et al. [2019]	RCT	40 healthy uncooperative children aged 2–6 years.	To assess dexmedetomidine versus ketamine and atropine IV sedation in uncooperative children during dental procedures.	Group D received intravenous dexmedetomidine, while Group K received intravenous ketamine with atropine. Vital signs, recovery time, adverse effects, and behavior were assessed.	Dexmedetomidine IV sedation was superior to ketamine in uncooperative children, with atropine as an adjunct to ketamine preventing complications
Mehran et al. [2018]	RCT	30 children aged 2-6 years	To compare sedation outcomes, specifically cooperation levels, between two drug combinations (oral midazolam/chloral hydrate and midazolam/promethazine) in paediatric dentistry.	Each child underwent separate dental visits where they received both drug combinations. Vital signs were continuously monitored, and cooperation levels were assessed using the Wilson sedation scale during the procedure.	The midazolam/chloral hydrate combination enhanced cooperation significantly compared to midazolam/ promethazine. While both combinations induced similar sedation levels, chloral hydrate/midazolam resulted in deeper and longer-lasting sedation. However, the promethazine group had fewer postoperative complications.
Tavassoli-Hojjati et al. [2014]	Randomised, cross-over, clinical trial	18 children aged 2.5-6 years	To assess the efficacy, safety, and acceptance of buccal midazolam versus oral midazolam in paediatric dentistry.	Children were randomly assigned to receive buccal or oral midazolam. Vital signs and behaviour were recorded, with blinded administration. Patient and parent satisfaction were assessed post-operatively.	The safe and efficient use of buccal midazolam is indicated for sedating paediatric dental patients.
Mozafar et al., [2018]	Randomise, cross-over, clinical trial	18 children, 3-6 years	The study compared the safety and effectiveness of two drug combinations for conscious sedation during dental treatment of uncooperative children.	N_2O/midazolam at one visit and N_2O/ promethazine at the other. Monitored physiological and behavioural parameters during treatment, assessed patient anxiety and parental satisfaction afterward.	Both drug combinations produced acceptable, efficient, and safe sedation results in a dental treatment setting for uncooperative children.
Malhotra et al. [2016]	RCT	36 children aged 3–9 years	To assess and compare the effects of sedation using intranasal dexmedetomidine and the oral combination drug midazolam–ketamine in children with uncooperative behavior requiring dental treatment.	Group MK: intranasal saline + oral midazolam (0.5 mg/kg) with ketamine (5 mg/kg) in mango juice; Group DX: intranasal dexmedetomidine (1 μg/kg) + oral mango juice; Group C: intranasal saline + oral mango juice. Vital signs monitored; behaviour, sedation, and wakefulness assessed using a modified observer scale.	Both oral midazolam–ketamine combination and intranasal dexmedetomidine can be safely and effectively used for conscious sedation in uncooperative pediatric dental patients.
Sunbul et al. [2014]	RCT	Twenty-five 36- to 72-month-old patient.	To compare behavioural effects of buccal and intranasal midazolam (0.3 mg/kg) in paediatric dental sedation.	The patients were randomly assigned to receive either atomised buccal midazolam in the first visit or intranasal midazolam in the second visit (0.3 mg/kg). method was recorded.	Intranasal midazolam is more acceptable to children, has a faster onset time, and results in less crying compared to buccal administration.
Prud'homme et al. [2019]	Prospective single-center study	76 patients aged 3-15 years	To assess the effects of N_2O-O_2 sedation in pediatric dentistry.	The study comprised all patients who were receiving N_2O-O_2 and were consulting with the Nantes hospital's Dental Service. The effects that the kid experienced, felt, and sought throughout care as well as the evaluation of N_2O-O_2.	62% of patients experienced anxiety reduction and 40% experienced relative analgesia, with 33% showing both effects.
Lenahan et al. [2015]	Retrospective Study	248 paediatric patients	To identify variables influencing sedation efficacy as secondary objectives.	Paediatric dentistry residents assessed each case according to the Frankl behavioural scale. Various factors were analysed for their importance in overall efficacy, including age, gender, ASA status, Frankl score, treatment length, operator experience, dosage, nitrous oxide use, and any related issues.	Over 81% of sedations were rated as very effective or effective, with age, pre-sedation conduct, and drug acceptance being statistically significant factors. Behaviour accounted for less than 5% of sedations stopped, with only one significant issue unrelated to the sedative being identified.
McCormack et al. [2014]	Non randomised cohort study	40 patients (3 to 6 years old).	To assess the frequency of adverse sedation-related events in paediatric dental patients treated with two different multiagent oral sedative regimens.	Patients received either midazolam, meperidine, and hydroxyzine with N_2O (MZ/M/H/N_2O; n=19) or chloral hydrate, meperidine, and hydroxyzine with nitrous oxide (CH/M/H/N_2O; n=21).	Within 8 hours post-discharge, children sedated with MZ/M/H/N_2 O showed increased hyperactivity during dental treatment, as well as slurred speech and difficulty walking. Conversely, those sedated with CH/M/H/N_2O exhibited more sleep, reduced speech and a higher need for postoperative pain medication.

TAB. 3B Features of the studies included in the analysis.

Author and year	Type	Patients	Aim	Material and methods	Results and conclusions
Ilasrinivasan et al. [2018]	Comparative clinical study	30 children aged 3 to 10.	This study compares the efficacy of N_2O-O_2 inhalation with a low-dose oral midazolam-ketamine combination.	A clinical study compared oral ketamine-midazolam and N_2O-O_2 sedation in children with Frankl behavior.	Both the combination of oral midazolam and ketamine and N_2O-O_2 inhalation sedation showed comparable effectiveness in providing anxiety relief during dental treatment for children.

TAB. 3C Features of the studies included in the analysis.

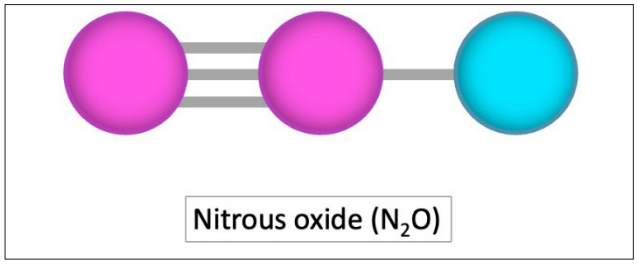

FIG. 3 Molecule configuration of N_2O.

with dental anxiety. Their findings demonstrated a significant increase in children's cooperation during treatment with N_2O-O_2, with a high success rate in completing planned procedures and low rates of transient side effects [Memè et al., 2022]. The study by Prud'homme et al. [2019] evaluates the effects of using the N_2O-O_2 mixture in paediatric sedation in dentistry. The study involved 76 patients aged between 3 and 15 years and the effects during treatment were recorded. Only 62% of patients presented an anxiolytic effect and 40% relative analgesia. Sixteen percent of patients attempted to prolong N_2O-O_2 use, however, no variables were significantly associated with prolongation of N_2O-O_2 use [Hennequin et al., 2012; Prud'homme et al., 2019]. A significant percentage of patients sought prolonged use of N_2O-O_2, indicating a real attraction to nitrous oxide. This is the first study to evaluate a child's appreciation of N_2O. The text provides details on the characteristics of N_2O-O_2, on the indications. N_2O has interesting properties for many specialties. Its use is widespread throughout the world. Although its effectiveness in the context of dental care has been widely demonstrated, the risks associated with its use should not be underestimated [Prud'homme et al., 2019]. The work of Mehran et al. [2018] addresses the challenge of managing dental anxiety in children and the importance of effective sedation techniques to facilitate dental treatment. The paper presents a comparison between the sedative effects of two drug combinations, midazolam/chloralhydrate and midazolam/promethazine, in paediatric dentistry. The study was conducted as a double-blind crossover clinical trial in 30 children aged 2 to 6 years. Each child received both drug combinations at separate dental visits. The results showed that the midazolam/chloralhydrate combination significantly improved cooperation levels compared to midazolam/promethazine. Vital signs such as oxygen saturation and heart rate were monitored during the procedure, with no significant differences between the two groups. The Wilson sedation scale indicated better cooperation after induction of sedation in both groups, but the depth and duration of sedation were more pronounced in the chloralhydrate/midazolam group. The study suggests that the midazolam/chloralhydrate combination is more effective in improving cooperation for dental treatment in young children [Koruk et al., 2010]. However, both combinations showed increased levels of post-sedation cooperation, highlighting the effectiveness of conscious sedation in paediatric dentistry. The importance of addressing dental anxiety in children is highlighted, often managed through premedication to improve behavior during dental procedures. The oral route of sedation is preferred for its effectiveness, although taste can pose a challenge, often mitigated by mixing the medications with sweetened water or juice. While midazolam is effective alone, the study suggests that combining it with chloralhydrate or promethazine reduces the required sedative dose, improving outcomes [Wali et al., 2016]. The use of promethazine is favored due to its lower risk of postoperative nausea and vomiting compared to chloralhydrate. Vital signs, such as oxygen saturation and heart rate, were monitored closely, with no significant differences between the two drug combinations. Although both combinations induced similar levels of sedation, the promethazine group showed fewer postoperative problems [Dallman et al., 2001; Mozafar et al., 2018]. Overall, the study supports the use of low-dose sedation agents for safer and more effective paediatric dental procedures, potentially favoring promethazine over chloralhydrate due to fewer complications [Mehran et al., 2018]. In paediatric dentistry, managing uncooperative children can be challenging, sometimes requiring pharmacological intervention when psychological methods fail. The Hammadyeh et al. study [2019], aims to compare intravenous sedation using dexmedetomidine with ketamine and atropine in uncooperative children during dental treatment. Forty healthy children aged 2–6 years were randomly assigned to either group. Dexmedetomidine showed superior effectiveness in behavior management compared to ketamine, with shorter recovery times. No serious side effects were reported in either group. Dexmedetomidine's safety and efficacy make it a promising option for paediatric sedation in dental settings [Suvvari et al., 2019]. Additionally, the adjunctive use of atropine with ketamine helps prevent complications [Inchingolo et al., 2010; Hammadyeh et al., 2019]. The study of Tavassoli-Hojjati et al. [2014], aims to evaluate the efficacy, safety and acceptability of buccal midazolam in paediatric patients undergoing sedation for dental treatments. The methodology involved 18 uncooperative children, aged 2.5 to 6 years, to receive buccal midazolam (0.3 mg/kg) or oral midazolam (0.5 mg/kg) at their first appointment, with the use of the second appointment alternative. The physiological and behavioural parameters of the patients were recorded during the treatment and, subsequently, the satisfaction of the patients and parents was assessed [Karaca and Durna, 2019; Engle et al., 2021; Russo et al., 2019]. The results showed that both sedation methods produced similar results in terms of efficacy, safety and acceptability. No significant differences in physiological or behavioural parameters were found between the two treatment groups. Most parents rated both sedative agents as "effective" or "very effective," and their children were mostly without anxiety or with less anxiety. Therefore, buccal midazolam can be used safely and efficiently in the sedation of paediatric patients undergoing dental treatments [Tavassoli-Hojjati et al., 2014]. The Malhotra' s study [2016], discusses the importance of behavior management in children for the success of dental treatments. Sedation is presented as a technique that can be used to reduce anxiety, physical discomfort and control behavior during paediatric dental treatments. Midazolam, a sedative drug, is introduced, discussing its properties and various methods of administration, such as the intranasal and buccal routes. A RCT comparing the

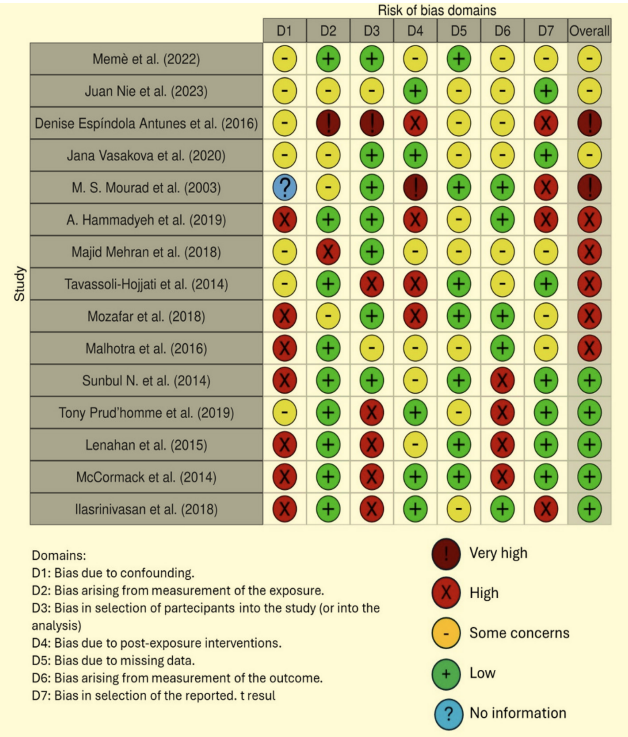

FIG. 3 Bias assessment.

sedative effects of midazolam administered via these two routes (intranasal and buccal) in paediatric dental patients is presented. The results of the study indicate that both routes of administration are effective for paediatric sedation, but the intranasal route was more acceptable for children, had a more rapid onset and resulted in less crying than buccal administration. A detailed analysis of the study results is also provided, which includes the maximum duration of sedative effect, time of onset, acceptability of the drug and patient behavior during treatment [Sunbul et al., 2014]. Both methods of administration of midazolam are safe and effective for paediatric sedation, but the intranasal route seems to offer additional advantages in terms of acceptability by children, rapidity of onset and reduction of crying [Malhotra et al., 2016]. The text of Nada Sunbul et al. [2014] discusses the importance of behavior management in children for the success of dental treatments. Sedation is presented as a technique that can be used to reduce anxiety, physical discomfort and control behavior during paediatric dental treatments [Preethy and Somasundaram, 2021]. Midazolam, a sedative drug, is introduced, discussing its properties and various methods of administration, such as the intranasal and buccal routes. The results of the study indicate that both routes of administration are effective for paediatric sedation, but the intranasal route was more acceptable for children, had a more rapid onset and resulted in less crying than buccal administration. A detailed analysis of the study results is also provided, which includes the maximum duration of sedative effect, time of onset, acceptability of the drug and patient behavior during treatment. Finally, it is concluded that both modes of administration of midazolam are safe and effective for paediatric sedation, but the intranasal route seems to offer additional advantages in terms of acceptability by children, rapidity of onset and reduction of crying [Sunbul et al., 2014; Inchingolo et al., 2022]. The Mozafar's study compares the safety and effectiveness of two drug combinations for conscious sedation during dental treatment of uncooperative children: N_2O and midazolam or N_2O and promethazine. Eighteen healthy, uncooperative children were included in the study. Each child was administered a combination of N_2O/midazolam at one visit and N_2O/promethazine at the other, in a crossover fashion. Physiological and behavioural parameters were monitored during dental treatment, and patients' anxiety and parents' satisfaction were subsequently assessed [Mcdonald et al., 2010]. The results showed that both drug combinations produced acceptable, effective, and safe sedation results. However, children sedated with midazolam were significantly more deeply sedated than the others. Overall, both drug combinations were well accepted by patients and parents [Gazal et al., 2016]. In conclusion, both drug combinations produced acceptable and efficient sedation results in uncooperative children and were safe in terms of heart rate and oxygen saturation [Mozafar et al., 2018]. Few studies have examined the sedation regimen of meperidine and hydroxyzine. The text by Lenahan et al. [2015] has as its primary objective the evaluation of the effectiveness and safety of the combination of meperidine and hydroxyzine as oral sedation for anxious or uncooperative paediatric patients. Among the secondary objectives there was the identification of potential factors that alter the effectiveness of sedation. Two hundred and forty-eight electronic medical records of paediatric patients (131 female, 117 male) who received sedation with meperidine and hydroxyzine were evaluated. The results show that this combination is safe and effective, with over 81% of sedations considered effective or very effective. Factors that influence effectiveness include the patient's age, pre-sedation behaviour, and willingness to take the drug. No serious side effects were found and only 5% of sedations were discontinued due to patient behaviour. From this study it can be seen that the combination of meperidine and hydroxyzine has been evaluated as a good option for paediatric sedation during dental treatments [Lenahan et al. 2015). McCormack's study compares two multi-agent oral sedation techniques in paediatric dental patients: chloral hydrate, meperidine, and hydroxyzine with N_2O (CH/M/H/N_2O) and midazolam, meperidine, and hydroxyzine with nitrous oxide (MZ/M/H/N_2O). It assesses the occurrence of sedation-related adverse events for both sedation protocols within 24 hours post-discharge. The study method involves enrolling 40 healthy patients aged three to six years, undergoing oral sedation due to inability to cooperate with conventional dental treatment. Two dentists specialised in paediatric dentistry perform all sedations following a standard protocol. Patients receive one of the two sedation regimens and are closely monitored during and after treatment. Data are presented through tables comparing the effects of different sedative regimens, focusing on adverse events such as post-sedation drowsiness, speech difficulty, and ambulation. Additionally, risk factors associated with patients' obesity and their impact on sedative effects are examined. The results indicate that patients sedated with MZ/M/H/N_2O show a significant increase in hyperactivity during dental treatment, speech difficulty, or walking difficulty after treatment. On the other hand, patients sedated with CH/M/H/N_2O show a significant increase in drowsiness, speak less than normal, and require more medication. All recorded adverse events were not life-threatening or requiring immediate action. Moreover, no significant correlations were found between patients' age or gender and the incidence of adverse events. However, a positive correlation was found between body mass index (BMI) and central nervous system (CNS) effects, with overweight children showing a higher incidence of CNS effects before discharge. In summary, the study highlights that the two sedation regimens produce different sedation-related adverse events and suggests that the dentist

choose the sedation regimen deemed optimal for the patient, considering the risks and benefits of each option [Damle et al., 2008]. It is also recommended to inform parents about the post-sedation effects expected based on the administered sedation regimen. It is noted that parents of patients sedated with a specific combination of drugs showed greater concern regarding the child's recovery state compared to those sedated with another combination, suggesting that parents may react differently to sedative effects. Finally, it is concluded that there is no recognised standard sedation regimen for such procedures, and each agent or combination can produce variable results and side effects [McCormack et al., 2014; Inchingolo et al., 2023]. Ilasrinivasan et al. [2018] conducted a study comparing nitrous oxide-oxygen inhalation with a low-dose oral combination of midazolam and ketamine for anxiety management in children aged 3 to 10 undergoing dental procedures. Both methods proved effective, but oral sedation had a longer duration [Darlong et al., 2011]. The study involved 30 children divided into two groups, with parameters including mask/drug acceptance, need for physical restraint, sedation scale, facial pain score, sedation duration, time to peak sedation, and adverse reactions. Although statistically insignificant, the midazolam-ketamine oral combination group showed longer sedation duration and time to peak sedation compared to the nitrous oxide group. Both oral midazolam-ketamine and nitrous oxide inhalation were clinically successful in providing anxiety relief during dental treatment [Levine et al., 1993; Lanteri et al., 2020]. However, the study highlights the importance of patient compliance, with nitrous oxide being preferred due to easier administration [Ilasrinivasan et al., 2018]. Dentists can choose the sedative agent based on their preferences, experience, and patient acceptance [Ashley et al., 2018]. The research carried out is a valuable guide for paediatric dentistry professionals, highlighting best practices for the safe and effective sedation of children during dental treatments. Collectively, these studies underscore the importance of pharmacological management in paediatric dental care, providing valuable insights into the effectiveness, safety, and optimal use of various sedation techniques to alleviate dental anxiety and improve patient outcomes [Baakdah et al., 2021].

Conclusions

Numerous studies in paediatric dentistry underscore the importance of addressing dental anxiety in children effectively and safely. Research comparing different sedation strategies reveals valuable insights. For instance, studies comparing oral midazolam alone versus the combination of intranasal dexmedetomidine and oral midazolam demonstrate improved sedation outcomes with the combination approach, with no significant differences in adverse events. Other investigations highlight the long-term behavioural benefits of moderate sedation with midazolam or midazolam/ketamine, emphasising the importance of pharmacological management in improving patient cooperation during dental procedures. Additionally, studies evaluating the safety and efficacy of various sedation methods, such as buccal midazolam, intravenous dexmedetomidine, and N_2O sedation, provide valuable insights into their effectiveness in paediatric dental settings. Overall, these findings serve as a valuable guide for dental professionals, emphasising the importance of pharmacological management in alleviating dental anxiety and improving patient outcomes in paediatric dentistry.

Abbreviations Body Mass Index (BMI), Central Nervous System (CNS), Chloral Hydrate, Meperidine and Hydroxyzine with Nitrous Oxide (CH/M/H/N_2O), Midazolam, Meperidine and Hydroxyzine with Nitrous Oxide (MZ/M/H/N_2O), Nitrous Oxide (N_2O), Nitrous Oxide-Oxygen (N_2O-O_2), Ohio State University Behavioural Rating Scale (OSUBRS), Randomised Controlled Trial (RCT). Author Contributions: Conceptualisation, F.I., G.D., A.D.I, A.M.I., L.F., A.D.N. and E.d.R.; methodology, A.M.I. and G.D.; software, A.P., A.D.I.; validation, F.I., G.D. and A.M.I.; formal analysis, A.P.; investigation, L.F., A.D.N. and E.d.R.; resources, L.F., A.D.N. and E.d.R.; data curation, A.M.I. and A.D.I.; writing—original draft preparation, L.F., A.D.N. and E.d.R.; writing—review and editing, L.F., A.D.N. and E.d.R.; visualisation, A.P.; supervision, F.I., and G.D.; project administration, F.I. All authors have read and agreed to the published version of the manuscript. Funding This research received no external funding. Conflicts of Interest The authors declare no conflicts of interest.

References

- Saccomanno S., Mummolo S., Laganà D., Greco F., Fiasca F., Marzo G., Quinzi V. (2021). The Digital Diagnostic Approach to Stafne's Bone Cavity (SBC): From a Review of the Literature to the Description of a Clinical Case. The Open Dentistry Journal, 15(1).
- Rajwar AS, Goswami M. Prevalence of dental fear and its causes using three measurement scales among children in New Delhi. J Indian Soc Pedod Prev Dent. 2017 Apr-Jun;35(2):128-133.(11)
- Nelson T, Nelson G. The role of sedation in contemporary paediatric dentistry. Dent Clin North Am. 2013 Jan;57(1):145-61. doi: 10.1016/j.cden.2012.09.007. Epub 2012 Oct 23. PMID: 23174615.
- American Academy of Paediatrics et al. (2006) 'Guidelines for monitoring and management of paediatric patients during and after sedation for diagnostic and therapeutic procedures: an update', Paediatrics, 118(6), pp. 2587–2602. Available at: https://doi.org/10.1542/peds.2006-2780.
- Amjad, A., Kordel, P. and Fernandes, G. (2023) 'A Review on Innovation in Healthcare Sector (Telehealth) through Artificial Intelligence', Sustainability, 15(8), p. 6655. Available at: https://doi.org/10.3390/su15086655.
- Antunes, D.E. et al. (2016) 'Moderate sedation helps improve future behavior in paediatric dental patients - a prospective study', Brazilian Oral Research, 30(1), p. e107. Available at: https://doi.org/10.1590/1807-3107BOR-2016.vol30.0107.
- Inchingolo AD, Ceci S, Patano A, Inchingolo AM, Montenegro V, Di Pede C, Malcangi G, Marinelli G, Coloccia G, Garibaldi M, et al. Elastodontic Therapy of Hyperdivergent Class II Patients Using AMCOP® Devices: A Retrospective Study. Applied Sciences. 2022; 12(7):3259. https://doi.org/10.3390/app12073259
- Rossi R, Memè L, Strappa EM, Bambini F. Restoration of Severe Bone and Soft Tissue Atrophy by Means of a Xenogenic Bone Sheet (Flex Cortical Sheet): A Case Report. Applied Sciences. 2023; 13(2):692.
- Appukuttan, D.P. (2016) 'Strategies to manage patients with dental anxiety and dental phobia: literature review', Clinical, Cosmetic and Investigational Dentistry, 8, pp. 35–50. Available at: https://doi.org/10.2147/CCIDE.S63626.
- Armfield, J.M. (2011) 'A comparison of three continuous scales used to determine the prevalence of clinically significant dental fear', Community Dentistry and Oral Epidemiology, 39(6), pp. 554–563. Available at: https://doi.org/10.1111/j.1600-0528.2011.00628.x.
- Artificial Intelligence in Anesthesiology: Current Techniques, Clinical Applications, and Limitations - PubMed (no date). Available at: https://pubmed.ncbi.nlm.nih.gov/31939856/ (Accessed: 23 March 2024).
- Baakdah, R.A. et al. (2021) 'Paediatric dental treatments with pharmacological and non-pharmacological interventions: a cross-sectional study', BMC oral health, 21(1), p. 186. Available at: https://doi.org/10.1186/s12903-021-01555-7.
- Cazzolla, A.P. et al. (2020) 'Taste and Smell Disorders in COVID-19 Patients: Role of Interleukin-6', ACS chemical neuroscience, 11(17), pp. 2774–2781. Available at: https://doi.org/10.1021/acschemneuro.0c00447.
- Chilkoti, G., Wadhwa, R. and Saxena, A.K. (2015) 'Technological advances in perioperative monitoring: Current concepts and clinical perspectives', Journal of Anaesthesiology, Clinical Pharmacology, 31(1), pp. 14–24. Available at: https://doi.org/10.4103/0970-9185.150521.
- Salerno C, Cirio S, Zambon G, D'Avola V, Parcianello RG, Maspero C, Campus G, Cagetti MG. Conscious Sedation for Dental Treatments in Subjects with Intellectual Disability: A Systematic Review and Meta-Analysis. Int J Environ Res Public Health. 2023 Jan 18;20(3):1779.
- Dallman, J.A., Ignelzi, M.A. and Briskie, D.M. (2001) 'Comparing the safety, efficacy and recovery of intranasal midazolam vs. oral chloral hydrate and promethazine', Paediatric Dentistry, 23(5), pp. 424–430.
- Damle, S.G., Gandhi, M. and Laheri, V. (2008) 'Comparison of oral ketamine and oral midazolam as sedative agents in paediatric dentistry', Journal of the Indian Society of Pedodontics and Preventive Dentistry, 26(3), pp. 97–101.
- Darlong, V. et al. (2011) 'Low- versus high-dose combination of midazolam-ketamine for oral premedication in children for ophthalmologic surgeries', Singapore medical journal, 52, pp. 512–6.
- D'Ettorre, G. et al. (2022) 'A comparison between stereophotogrammetry and smartphone structured light technology for three-dimensional face scanning', The Angle Orthodontist, 92(3), pp. 358–363. Available at: https://doi.org/10.2319/040921-290.1.
- Eddahchouri, Y. et al. (2023) 'The Effect of Continuous Versus Periodic Vital Sign Monitoring on Disease Severity of Patients with an Unplanned ICU Transfer', Journal of Medical Systems, 47(1), p. 43. Available at: https://doi.org/10.1007/s10916-023-01934-3.
- Engle, R.L. et al. (2021) 'Evidence-based practice and patient-centered care: Doing both well', Health Care Management Review, 46(3), pp. 174–184. Available at: https://doi.org/10.1097/HMR.0000000000000254.
- Fantacci, C. et al. (2018) 'Intranasal drug administration for procedural sedation in children admitted to paediatric Emergency Room', European Review for Medical and Pharmacological Sciences, 22(1), pp. 217–222. Available at: https://doi.org/10.26355/eurrev_201801_14120.
- Farronato, G. et al. (2012) 'Correlations between malocclusions and dyslalias', European journal of paediatric dentistry : official journal of European Academy of Paediatric Dentistry, 13, pp. 13–8.
- Ferrazzano, G.F., Sangianantoni, S., et al. (2019) 'Assessing changes in oral health-related quality of life and body growth in 3-5 years old children following dental treatment under general anaesthesia due to severe dental caries', European Journal of Paediatric Dentistry, 20(3), pp. 214–218. Available at: https://doi.org/10.23804/ejpd.2019.20.03.09.
- Ferrazzano, G.F., Cantile, T., et al. (2019) 'Oral health status and Unmet Restorative Treatment Needs

(UTN) in disadvantaged migrant and not migrant children in Italy', European Journal of Paediatric Dentistry, 20(1), pp. 10–14. Available at: https://doi.org/10.23804/ejpd.2019.20.01.02.
› Ferrazzano, G.F., Scaravilli, M.S. and Ingenito, A. (2006) 'Dental and periodontal health status in Campanian children and relation between caries experience and socio-economic behavioural factors', European Journal of Paediatric Dentistry, 7(4), pp. 174–178.
› Gazal, G. et al. (2016) 'Pain and anxiety management for paediatric dental procedures using various combinations of sedative drugs: A review', Saudi pharmaceutical journal: SPJ: the official publication of the Saudi Pharmaceutical Society, 24(4), pp. 379–385. Available at: https://doi.org/10.1016/j.jsps.2014.04.004.
› Gómez-Manzano, F.J. et al. (2022) 'Evaluation of Intranasal Midazolam for Paediatric Sedation during the Suturing of Traumatic Lacerations: A Systematic Review', Children, 9(5), p. 644. Available at: https://doi.org/10.3390/children9050644.
› Hammadyeh, A.R., Altinawi, M.K. and Rostom, F. (2019) 'Comparison of two intravenous sedation techniques for use in paediatric dentistry: A randomized controlled trial', Dental and Medical Problems, 56(4), pp. 337–341. Available at: https://doi.org/10.17219/dmp/109929.
› He, H. et al. (2023) 'The Effect of Intranasal Dexmedetomidine on Emergence Delirium Prevention in Paediatric Ambulatory Dental Rehabilitation Under General Anesthesia: A Randomized Clinical Trial', Drug Design, Development and Therapy, 17, pp. 3563–3570. Available at: https://doi.org/10.2147/DDDT.S427291.
› Hennequin, M. et al. (2012) 'A clinical trial of efficacy and safety of inhalation sedation with a 50% nitrous oxide/oxygen premix (KalinoxTM) in general practice', Clinical Oral Investigations, 16(2), pp. 633–642. Available at: https://doi.org/10.1007/s00784-011-0550-y.
› Ilasrinivasan, null et al. (2018) 'A Comparative Evaluation of the Sedative Effects of Nitrous Oxide-oxygen Inhalation and Oral Midazolam-Ketamine Combination in Children', International Journal of Clinical Paediatric Dentistry, 11(5), pp. 399–405. Available at: https://doi.org/10.5005/jp-journals-10005-1547.
› Inchingolo, A.D., Inchingolo, A.M., et al. (2022) 'Effects of Resveratrol, Curcumin and Quercetin Supplementation on Bone Metabolism—A Systematic Review', Nutrients, 14(17), p. 3519. Available at: https://doi.org/10.3390/nu14173519.
› Inchingolo, A.D., Malcangi, G., et al. (2022) 'Oralbiotica/Oralbiotics: The Impact of Oral Microbiota on Dental Health and Demineralization: A Systematic Review of the Literature', Children, 9(7), p. 1014. Available at: https://doi.org/10.3390/children9071014.
› Inchingolo, A.M., Patano, A., et al. (2023) 'Orthognathic Surgery and Relapse: A Systematic Review', Bioengineering, 10(9), p. 1071. Available at: https://doi.org/10.3390/bioengineering10091071.
› Inchingolo, A.M., Malcangi, G., et al. (2023) 'Tooth Complications after Orthodontic Miniscrews Insertion', International Journal of Environmental Research and Public Health, 20(2), p. 1562. Available at: https://doi.org/10.3390/ijerph20021562.
› Inchingolo, F. et al. (2010) 'Severe anisocoria after oral surgery under general anesthesia', International Journal of Medical Sciences, 7(5), pp. 314–318. Available at: https://doi.org/10.7150/ijms.7.314.
› Inchingolo, F. et al. (2023) 'Application of Graphene Oxide in Oral Surgery: A Systematic Review', Materials (Basel, Switzerland), 16(18), p. 6293. Available at: https://doi.org/10.3390/ma16186293.
› Karaca, A. and Durna, Z. (2019) 'Patient satisfaction with the quality of nursing care', Nursing Open, 6(2), pp. 535–545. Available at: https://doi.org/10.1002/nop2.237.
› Koruk, S. et al. (2010) 'Dexmedetomidine-ketamine and midazolam-ketamine combinations for sedation in paediatric patients undergoing extracorporeal shock wave lithotripsy: a randomized prospective study', Journal of Anesthesia, 24(6), pp. 858–863. Available at: https://doi.org/10.1007/s00540-010-1023-1.
› Kurdi, M.S., Theerth, K.A. and Deva, R.S. (2014) 'Ketamine: Current applications in anesthesia, pain, and critical care', Anesthesia, Essays and Researches, 8(3), pp. 283–290. Available at: https://doi.org/10.4103/0259-1162.143110.
› Lanteri, V. et al. (2020) 'Assessment of the Stability of the Palatal Rugae in a 3D-3D Superimposition Technique Following Slow Maxillary Expansion (SME)', Scientific Reports, 10(1), p. 2676. Available at: https://doi.org/10.1038/s41598-020-59637-5.
› Lenahan, M., Wells, M. and Scarbecz, M. (2015) 'A Retrospective Study of 248 Paediatric Oral Sedations Utilizing the Combination of Meperidine and Hydroxyzine for Dental Treatment', The Journal of Clinical Paediatric Dentistry, 39(5), pp. 481–487. Available at: https://doi.org/10.17796/1053-4628-39.5.481.
› Levine, M.F. et al. (1993) 'Oral midazolam premedication in children: the minimum time interval for separation from parents', Canadian Journal of Anaesthesia = Journal Canadien D'anesthesie, 40(8), pp. 726–729. Available at: https://doi.org/10.1007/BF03009769.
› Malhotra, P.U. et al. (2016) 'Comparative evaluation of dexmedetomidine and midazolam-ketamine combination as sedative agents in paediatric dentistry: A double-blinded randomized controlled trial', Contemporary Clinical Dentistry, 7(2), pp. 186–192. Available at: https://doi.org/10.4103/0976-237X.183058.
› Malviya, S., Voepel-Lewis, T. and Tait, A.R. (1997) 'Adverse events and risk factors associated with the sedation of children by nonanesthesiologists', Anesthesia and Analgesia, 85(6), pp. 1207–1213. Available at: https://doi.org/10.1097/00000539-199712000-00005.
› Marks, L.A. and Martens, L.A. (2003) '[Pharmacologic sedation in dentistry: an overview]', Revue Belge De Medecine Dentaire, 58(4), pp. 245–256.
› Mason, K. and Seth, N. (2019) 'Future of paediatric sedation: towards a unified goal of improving practice', British Journal of Anaesthesia, 122. Available at: https://doi.org/10.1016/j.bja.2019.01.025.
› McCormack, L. et al. (2014) 'A comparison of sedation-related events for two multiagent oral sedation regimens in paediatric dental patients', Paediatric Dentistry, 36(4), pp. 302–308.
› Mcdonald, R., Avery, D. and Hartsfield, J. (2010) 'McDonald RE, DR Avery, JK Hartsfield Jr: Acquired and Developmental Disturbances of the Teeth and Associated Oral Structures. In: Dentistry for the Child and Adolescent, ninth edition. JA Dean, DR Avery, and RE McDonald, eds. Mosby, Inc. St. Louis, MO. Pages 85-125, 2010.', in, pp. 85–125.
› McQueen, K. et al. (2015) 'Anesthesia and Perioperative Care', in H.T. Debas et al. (eds) Essential Surgery: Disease Control Priorities, Third Edition (Volume 1). Washington (DC): The International Bank for Reconstruction and Development / The World Bank. Available at: http://www.ncbi.nlm.nih.gov/books/NBK333510/ (Accessed: 23 March 2024).
› Mehran, M. et al. (2018) 'Comparison of sedative effects of oral midazolam/chloral hydrate and midazolam/promethazine in paediatric dentistry', Journal of Dental Research, Dental Clinics, Dental Prospects, 12(3), pp. 221–226. Available at: https://doi.org/10.15171/joddd.2018.034.
› Memè, L. et al. (2021) 'ATR-FTIR Analysis of Orthodontic Invisalign® Aligners Subjected to Various In Vitro Aging Treatments', Materials, 14(4), p. 818. Available at: https://doi.org/10.3390/ma14040818.
› Memè, L., Gallusi, G., et al. (2022) 'Conscious Inhalation Sedation with Nitrous Oxide and Oxygen in Children: A Retrospective Study', Applied Sciences, 12(22), p. 11852. Available at: https://doi.org/10.3390/app122211852.
› Memè, L., Sartini, D., et al. (2022) 'Epithelial Biological Response to Machined Titanium vs. PVD Zirconium-Coated Titanium: An In Vitro Study', Materials, 15(20), p. 7250. Available at: https://doi.org/10.3390/ma15207250.
› Kupietzky A, Houpt MI. Midazolam: a review of its use for conscious sedation of children. Pediatr Dent. 1993 Jul-Aug;15(4):237-41. PMID: 8247896.
› Minervini, G. et al. (2023) 'Prevalence of temporomandibular disorders (TMD) in obesity patients: A systematic review and meta-analysis', Journal of Oral Rehabilitation, 50(12), pp. 1544–1553. Available at: https://doi.org/10.1111/joor.13573.
› Mittal, N. et al. (2015) 'Paediatric Dental Sedation Research: Where Do We Stand Today?', The Journal of Clinical Paediatric Dentistry, 39(3), pp. 284–291. Available at: https://doi.org/10.17796/1053-4628-39.3.284.
› Mourad, M.S. et al. (2022) 'Impact of operators' experience and patients' age on the success of nitrous oxide sedation for dental treatment in children', European Journal of Paediatric Dentistry, 23(3), pp. 183–188. Available at: https://doi.org/10.23804/ejpd.2022.23.03.03.
› Mozafar, S. et al. (2018) 'Comparison of nitrous oxide/midazolam and nitrous oxide/promethazine for paediatric dental sedation: A randomized, cross-over, clinical trial', Dental Research Journal, 15(6), pp. 411–419. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6243808/ (Accessed: 20 March 2024).
› Mummolo, S. et al. (2014) 'Clinical evaluation of salivary indices and levels of Streptococcus mutans and Lactobacillus in patients treated with Occlus-o-Guide', European Journal of Paediatric Dentistry, 15(4), pp. 367–370.
› Nie, J. et al. (2023) 'Oral midazolam vs. intranasal dexmedetomidine plus oral midazolam for sedation of paediatric outpatients: a double-blinded randomized controlled trial', BMC Anesthesiology, 23(1), p. 341. Available at: https://doi.org/10.1186/s12871-023-02289-5.
› Petkar S, Chakole V, Nayak A. Comprehensive Review of Anesthetic Evaluation and Management in Obese Female Patients Undergoing In Vitro Fertilization. Cureus. 2023 Oct 23;15(10):e47521. doi: 10.7759/cureus.47521. PMID: 38021482; PMCID: PMC10664690
› Preethy, N.A. and Somasundaram, S. (2021) 'Sedative and Behavioural Effects of Intranasal Midazolam in Comparison with Other Administrative Routes in Children Undergoing Dental Treatment – A Systematic Review', Contemporary Clinical Dentistry, 12(2), pp. 105–120. Available at: https://doi.org/10.4103/ccd.ccd_470_20.
› Primozic, J. et al. (2021) 'Diagnostic ability of the primary second molar crown-to-root length ratio and the corresponding underlying premolar position in estimating future expander anchoring teeth exfoliation', Orthodontics & Craniofacial Research, 24(4), pp. 561–567. Available at: https://doi.org/10.1111/ocr.12478.
› Prud'homme, T. et al. (2019) 'Assessment of an Equimolar Mixture of Oxygen and Nitrous Oxide: Effects in Paediatric Dentistry', International Journal of Clinical Paediatric Dentistry, 12(5), pp. 429–436. Available at: https://doi.org/10.5005/jp-journals-10005-1658.
› Quinzi, V. et al. (2020) 'Comparison of Mandibular Arch Expansion by the Schwartz Appliance Using Two Activation Protocols: A Preliminary Retrospective Clinical Study', Journal of Functional Morphology and Kinesiology, 5(3), p. 61. Available at: https://doi.org/10.3390/jfmk5030061.
› Ramos-Gomez, F.J. (2014) 'A Model for Community-Based Paediatric Oral Heath: Implementation of an Infant Oral Care Program', International Journal of Dentistry, 2014, p. 156821. Available at: https://doi.org/10.1155/2014/156821.
› Saccomanno, S. et al. (2021) 'Catering Work Profession and Medico-Oral Health: A Study on 603 Subjects', Healthcare (Basel, Switzerland), 9(5), p. 582. Available at: https://doi.org/10.3390/healthcare9050582.
› Ashley PF, Chaudhary M, Lourenço-Matharu L. Sedation of children undergoing dental treatment. Cochrane Database Syst Rev. 2018 Dec 17;12(12):CD003877.
› Sheroan, M.M. et al. (2006) 'A Prospective Study of 2 Sedation Regimens in Children: Chloral Hydrate, Meperidine, and Hydroxyzine Versus Midazolam, Meperidine, and Hydroxyzine', Anesthesia Progress, 53(3), pp. 83–90. Available at: https://doi.org/10.2344/0003-3006(2006)53[83:APSOSR]2.0.CO;2.
› Silveira, E.R. et al. (2020) 'Estimated prevalence of dental fear in adults: a systematic review and meta-analysis'. medRxiv, p. 2020.11.30.20241216. Available at: https://doi.org/10.1101/2020.11.30.20241216.
› Singam A. Revolutionizing Patient Care: A Comprehensive Review of Artificial Intelligence Applications in Anesthesia. Cureus. 2023 Dec 4;15(12):e49887. doi: 10.7759/cureus.49887. PMID: 38174199; PMCID: PMC10762564.
› Singh, J. et al. (2023) 'Assessment of pain in paediatric dental patients during administration of local anesthesia with and without the use of audiovisual distraction', Dental Research Journal, 20, p. 7. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9937933/ (Accessed: 22 March 2024).
› Sunbul, N. et al. (2014) 'Buccal versus intranasal midazolam sedation for paediatric dental patients', Paediatric Dentistry, 36(7), pp. 483–488.
› Suvvari, P. et al. (2019) 'Comparison of Intranasal Dexmedetomidine Versus Intranasal Ketamine as Premedication for Level of Sedation in Children Undergoing Radiation Therapy: A Prospective, Randomised, Double-Blind Study', Turkish Journal of Anaesthesiology and Reanimation, 48. Available at: https://doi.org/10.5152/TJAR.2019.45087.
› Tavassoli-Hojjati, S. et al. (2014) 'Comparison of Oral and Buccal Midazolam for Paediatric Dental Sedation: A Randomized, Cross-Over, Clinical Trial for Efficacy, Acceptance and Safety', Iranian Journal of Paediatrics, 24(2), pp. 198–206. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4268841/ (Accessed: 20 March 2024).
› Tobias, J.D. and Leder, M. (2011) 'Procedural sedation: A review of sedative agents, monitoring, and management of complications', Saudi Journal of Anaesthesia, 5(4), pp. 395–410. Available at: https://doi.org/10.4103/1658-354X.87270.
› Uchôa, S. et al. (2024) 'The care of patients with special needs in paediatric dentistry', in Seven Editora. Available at: https://doi.org/10.56238/sevened2023.007-042.
› Russo S, Jongerius C, Faccio F, Pizzoli SFM, Pinto CA, Veldwijk J, Janssens R, Simons G, Falahee M, de Bekker-Grob E, Huys I, Postmus D, Kihlbom U, Pravettoni G. Understanding Patients' Preferences: A Systematic Review of Psychological Instruments Used in Patients' Preference and Decision Studies. Value Health. 2019 Apr;22(4):491-501. doi: 10.1016/j.jval.2018.12.007. PMID: 30975401.
› Lv LL, Zhang MM. Up-to-date literature review and issues of sedation during digestive endoscopy. Wideochir Inne Tech Maloinwazyjne. 2023 Sep;18(3):418-435. doi: 10.5114/wiitm.2023.127854. Epub 2023 Jun 1. PMID: 37868289; PMCID: PMC10585454.
› Uzunçıbuk, H. et al. (2023) 'Prevalence of temporomandibular disorders in clear aligner patients using orthodontic intermaxillary elastics assessed with diagnostic criteria for temporomandibular disorders (DC/TMD) axis II evaluation: A cross-sectional study', Journal of Oral Rehabilitation [Preprint]. Available at: https://doi.org/10.1111/joor.13614.
› Vasakova, J. et al. (2020) 'Midazolam and its effect on vital signs and behavior in children under conscious sedation in dentistry', Physiological Research, 69(Suppl 2), pp. S305–S314. Available at: https://doi.org/10.33549/physiolres.934511.
› Viinikangas, A. et al. (2007) 'Evaluating a single dental anxiety question in Finnish adults', Acta Odontologica Scandinavica, 65(4), pp. 236–240. Available at: https://doi.org/10.1080/00016350701395932.
› Wali, A. et al. (2016) 'Knowledge, Attitude, and Practices of Dental Surgeons in managing Child Patients', International Journal of Clinical Paediatric Dentistry, 9(4), pp. 372–378. Available at: https://doi.org/10.5005/jp-journals-10005-1393.
› Wang, H.-Y. et al. (2021) 'Association of pharmacological prophylaxis with the risk of paediatric emergence delirium after sevoflurane anesthesia: An updated network meta-analysis', Journal of Clinical Anesthesia, 75, p. 110488. Available at: https://doi.org/10.1016/j.jclinane.2021.110488.
› Wilson, E. et al. (1990) 'Sedation during spinal anaesthesia: comparison of propofol and midazolam', British Journal of Anaesthesia, 64(1), pp. 48–52. Available at: https://doi.org/10.1093/bja/64.1.48.
› Zommick, J. et al. (1996) 'Comparison of general anesthesia and intravenous sedation-analgesia for SWL', Journal of Endourology, 10(6), pp. 489–491. Available at: https://doi.org/10.1089/end.1996.10.489.