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REVIEW ARTICLE

Nitrous Oxide Sedation in Pediatric Dental Practice: Current Status and Nanomedicine-Based Prospects, A Narrative Review

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ABSTRACT

Pediatric dental anxiety significantly compromises treatment cooperation and oral health outcomes, necessitating effective behavior management strategies in clinical practice. Nitrous oxide–oxygen inhalation sedation remains one of the most widely used pharmacological approaches in pediatric dentistry due to its rapid onset, titratability, anxiolytic and analgesic properties, and favorable safety profile. This review synthesizes current evidence regarding the scientific basis, clinical indications, contraindications, effectiveness, and safety considerations of nitrous oxide sedation in children. Available data support its role in improving patient cooperation, facilitating minimally to moderately invasive procedures, and reducing the need for general anesthesia in appropriately selected cases. Although adverse effects are generally mild and transient, appropriate patient selection, adherence to monitoring protocols, and compliance with established guidelines are essential to ensure safe practice. The review also discusses occupational and environmental considerations, current clinical limitations, and variability in patient response. Emerging adjunctive technologies, including virtual reality–based distraction, artificial intelligence–assisted monitoring, and advanced delivery systems, are highlighted as complementary strategies to enhance patient experience and procedural efficiency. Furthermore, the potential application of nanomedicine-based drug delivery systems is explored as a future direction for improving sedation precision and minimizing systemic exposure, although regulatory and long-term safety challenges remain. Integrating established sedation protocols with technological and nanomedical innovations may contribute to more individualized, effective, and safer management of pediatric dental anxiety.

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INTRODUCTION

Pediatric dental anxiety remains a major barrier to the delivery of effective oral healthcare, often resulting in avoidance of treatment, delayed intervention, and compromised oral health outcomes [1]. Dental fear and anxiety (DFA) in children significantly interfere with cooperation during clinical procedures, making behavior management a central component of pediatric dental practice [2]. Although non-pharmacological techniques such as tell–show–do, distraction, and cognitive-behavioral approaches are valuable, they are not always sufficient for highly anxious or semi-cooperative children, thereby necessitating pharmacological interventions [2]. Among these, nitrous oxide inhalation sedation is recognized as one of the most widely used and reliable techniques in pediatric dentistry. Owing to its anxiolytic, sedative, analgesic, and mild amnesic properties, nitrous oxide facilitates the safe and efficient completion of dental procedures while maintaining patient consciousness and protective reflexes [3, 4]. Its rapid onset, titratability, quick recovery, and favorable safety profile have made it a cornerstone of contemporary pediatric behavior management[5, 6]. Furthermore, its use has been shown to significantly reduce the need for dental general anesthesia, particularly in anxious or semi-cooperative children with extensive treatment needs [7].

Despite its long-standing clinical use and

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established safety record, continuous evaluation of nitrous oxide sedation remains essential, particularly in light of emerging biomedical technologies and evolving clinical standards[4]. This narrative review aims to provide a comprehensive synthesis of the current status of nitrous oxide sedation in pediatric dental practice, including its indications, advantages, limitations, and safety considerations[2]. In addition, it explores future directions, particularly the integration of nanomedicine-based strategies to enhance the precision, efficacy, and safety of sedation techniques[8]. Advances in nanotechnology may enable the development of targeted drug delivery systems and improved pharmacokinetic control, potentially optimizing sedation outcomes while minimizing adverse effects[8, 9]. Moreover, complementary modalities such as virtual reality and other innovative behavioral interventions are gaining attention as adjunctive approaches to reduce pediatric dental anxiety and improve patient cooperation[10]. By critically examining existing evidence and identifying gaps in the literature, this review seeks to inform clinical practice and guide the development of next-generation strategies for managing pediatric dental anxiety.

PEDIATRIC DENTAL ANXIETY AND BEHAVIOR MANAGEMENT

Pediatric dental anxiety represents a substantial clinical challenge, influencing treatment acceptance, procedural efficiency, and long-term oral health trajectories. Epidemiological studies consistently demonstrate a high prevalence of dental anxiety among children, with significant associations between anxiety levels and reduced willingness to undergo dental procedures as well as poorer oral health outcomes [11, 12]. Anxious children are more likely to postpone or avoid dental visits, perpetuating a cycle of untreated disease and escalating fear[11]. Early identification and appropriate management are therefore essential to prevent behavioral deterioration and ensure optimal care delivery[13, 14].

The etiology of pediatric dental anxiety is multifactorial, involving psychological, environmental, and neurobiological determinants. Personality traits such as shyness, behavioral inhibition, and heightened fear sensitivity contribute to vulnerability, while neurobiological pathways involving the amygdala and prefrontal cortex play central roles in fear processing and emotional regulation[11]. Genetic predispositions may further explain interindividual variability in anxiety responses, underscoring the importance of individualized management strategies[11]. Additionally, traumatic or negative dental experiences during early childhood can reinforce maladaptive fear responses, highlighting the importance of positive early encounters and preventive behavioral guidance.

Non-pharmacological behavior management techniques remain the foundation of pediatric dental care and are generally considered first-line interventions. Cognitive-behavioral therapy, guided imagery, distraction techniques, and virtual reality-based interventions have demonstrated effectiveness in reducing anxiety and improving cooperation [12, 15]. Traditional approaches such as Tell–Show–Do (TSD), modeling, and audiovisual distraction are widely implemented in routine practice; however, their success may vary according to the child's developmental stage, temperament, and procedural complexity[15, 16]. While these techniques offer the advantage of avoiding pharmacological risks, they may not achieve adequate behavioral control in children with moderate to severe anxiety[12].

When behavioral approaches alone are insufficient, pharmacological interventions become indicated. Nitrous oxide inhalation sedation is among the most commonly employed and well-established pharmacological modalities in pediatric dentistry, particularly for children with moderate anxiety or limited cooperative capacity[2, 17]. It is characterized by rapid onset, ease of titration, quick recovery, and a low incidence of adverse effects, contributing to its strong safety profile[3, 18]. Importantly, its use enhances treatment acceptance and may significantly reduce the need for more invasive modalities such as general anesthesia, thereby offering a balanced and patient-centered approach to managing pediatric dental anxiety while maintaining high standards of safety and comfort [2, 3].

NITROUS OXIDE SEDATION: SCIENTIFIC AND CLINICAL FOUNDATIONS

Nitrous oxide sedation has occupied a central role in dental practice for more than 150 years, following its early recognition as an anesthetic and analgesic agent in the nineteenth century[19, 20]. Over time, its application has evolved from experimental anesthesia to a refined technique

for conscious sedation, particularly in pediatric dentistry where anxiety control is paramount. Its favorable safety profile and clinical effectiveness have established nitrous oxide as a preferred modality for managing dental fear and facilitating cooperation in children[3, 21]. Technological advances, including the development of modern inhalation sedation units, have significantly enhanced precision and safety. Contemporary systems allow accurate titration of gas concentrations, continuous flow delivery, and integration of multiple safety mechanisms, thereby improving clinical control and minimizing risk[3].

From a pharmacological perspective, nitrous oxide is a small inorganic molecule with sedative, anxiolytic, and analgesic properties[19]. It is rapidly absorbed through the pulmonary alveoli and quickly diffuses into the bloodstream, reaching the central nervous system within minutes and producing a fast onset of action. Its low blood–gas solubility facilitates rapid elimination once administration is discontinued, allowing swift recovery and making it particularly suitable for outpatient pediatric dental procedures[4]. Mechanistically, the analgesic effects of nitrous oxide are believed to involve activation of endogenous opioid pathways, whereas its anxiolytic properties are associated with modulation of γ-aminobutyric acid type A (GABAA) receptors, producing effects comparable to benzodiazepines[19]. Additionally, interactions with N-methyl-D-aspartate (NMDA) receptors contribute to its anesthetic and analgesic profile, supporting its efficacy in reducing both pain perception and anxiety during dental interventions[19].

Clinically, nitrous oxide is administered via a continuous-flow delivery system equipped with a nasal hood, which permits effective sedation while maintaining full access to the oral cavity for operative procedures[3]. Modern delivery units incorporate essential safety features, including oxygen fail-safe mechanisms, flow meters, and scavenging systems designed to reduce occupational exposure and environmental contamination[3]. Appropriate administration requires gradual titration to achieve the desired sedative effect while minimizing adverse reactions, with careful patient assessment, monitoring, and documentation forming integral components of sedation protocols[2, 20]. Comprehensive practitioner training is critical to ensure competence in case selection, dosage adjustment, and management of potential complications, thereby optimizing clinical outcomes and maintaining high standards of patient safety[3, 22].

CLINICAL APPLICATIONS IN PEDIATRIC DENTAL PRACTICE

Nitrous oxide-oxygen inhalation sedation is widely utilized in pediatric dentistry because of its established safety profile, rapid onset, and effectiveness in reducing anxiety and discomfort in young patients. It is primarily indicated for children who exhibit dental fear, limited cooperation, exaggerated gag reflex, or mild behavioral management challenges that interfere with routine dental care[2, 3]. Owing to its anxiolytic, sedative, and mild analgesic properties, nitrous oxide is particularly beneficial during minimally invasive and short-duration procedures, facilitating improved communication and cooperation[8]. Careful case selection and comprehensive preoperative assessment are essential, especially in children aged 3–6 years, to ensure optimal safety and clinical success[23].

Despite its favorable safety margin, nitrous oxide sedation is contraindicated in specific clinical situations. Children with significant respiratory compromise, such as severe asthma or chronic obstructive pulmonary disease, may be at increased risk because effective nasal breathing is required for gas delivery. Additional contraindications include acute upper respiratory tract infections, inability to tolerate the nasal hood, certain psychological or behavioral disorders that prevent communication, and a history of substance misuse[2, 3]. When appropriately administered, nitrous oxide demonstrates high clinical effectiveness, with reported success rates of approximately 86% in achieving satisfactory cooperation during pediatric dental procedures[24]. Its rapid onset and recovery profiles enhance clinical efficiency, and adverse effects—such as nausea, dizziness, or headache—are generally mild and occur in a small percentage of cases[3].

Compared with other sedation modalities, nitrous oxide offers distinct advantages, including titratability, minimal respiratory depression, and a broad margin of safety[8]. The ability to adjust sedation levels incrementally allows clinicians to maintain protective reflexes while optimizing patient comfort[3]. Furthermore, its rapid pulmonary elimination minimizes residual sedative effects, making it particularly suitable for

outpatient and short procedures. Importantly, the effective anxiolysis and behavioral control achieved with nitrous oxide can substantially reduce the need for general anesthesia in selected pediatric patients, including those who are fearful, precooperative, or have special healthcare needs[24, 25]. This reduction not only lowers healthcare costs but also decreases exposure to the greater risks and recovery time associated with general anesthesia[24].

SAFETY PROFILE AND RISK MANAGEMENT

The safety profile of nitrous oxide–oxygen inhalation sedation in pediatric dentistry is well established, although careful risk assessment remains essential. The most common immediate adverse effects are nausea and vomiting, which are typically mild, transient, and self-limiting[26-28]. More serious complications, such as aspiration of gastric contents, are rare and are usually associated with failure to follow appropriate preoperative instructions, including fasting recommendations when indicated[28]. Nitrous oxide should be avoided in children with specific contraindications, including significant obstructive pulmonary disease, recent middle ear or tympanic membrane surgery, and conditions that impair nasal breathing, as these factors may increase the risk of adverse outcomes[27].

Occupational exposure and environmental considerations also represent important components of risk management. Chronic exposure to trace levels of nitrous oxide has been associated with potential health risks among dental personnel, including reproductive and neurological concerns, underscoring the necessity of effective scavenging systems and adequate operatory ventilation[26, 27]. In addition, nitrous oxide is recognized as a greenhouse gas with a measurable environmental impact, and its routine use in clinical settings contributes, albeit modestly, to atmospheric emissions[29]. Implementation of properly maintained delivery systems, active scavenging units, and adherence to recommended exposure limits are therefore essential to minimize occupational and environmental risks.

Safe administration further depends on strict adherence to monitoring standards, appropriate equipment, and clinician training. Contemporary sedation units incorporate multiple safety features such as fail-safe oxygen delivery systems and flow controls to reduce the likelihood of hypoxic mixtures, while providers must be adequately trained to recognize and manage potential complications[3]. Evidence-based guidelines from professional organizations, including the American Academy of Pediatric Dentistry and other international bodies, outline protocols for patient selection, monitoring, documentation, and emergency preparedness to ensure safe practice[2, 30]. From a long-term perspective, ongoing surveillance of occupational exposure levels and the establishment of clear regulatory standards for non–operating room settings are necessary to safeguard both patient and staff health [26, 31].

LIMITATIONS AND CURRENT CHALLENGES

The use of nitrous oxide sedation in pediatric dental practice presents several limitations and challenges that need to be addressed to optimize its effectiveness and safety. These challenges include variability in patient response, behavioral unpredictability, equipment and training requirements, access and cost considerations, and evidence gaps in special populations. Each of these factors plays a critical role in the successful implementation of nitrous oxide sedation in pediatric dentistry.

The effectiveness of nitrous oxide sedation can vary significantly among pediatric patients due to differences in age, health status, and individual temperament[32]. Children with certain metabolic disorders, such as cobalamin and folate deficiencies, may experience adverse effects, highlighting the need for careful patient selection[33].

Specialized equipment is required to administer nitrous oxide safely, including systems to blend the gas with oxygen and mechanisms to scavenge excess nitrous oxide to prevent occupational exposure. Adequate training for dental practitioners is essential to manage potential complications and ensure the safe administration of nitrous oxide[3].

While nitrous oxide is considered cost-effective, the initial investment in equipment and training can be a barrier for some dental practices[33]. Access to nitrous oxide sedation may be limited in certain regions due to regulatory and financial constraints, affecting its availability for pediatric patients[32].

There is a lack of comprehensive data on the use of nitrous oxide in special populations, such as children with disabilities or those with specific health conditions, which can affect sedation outcomes[24]. More research is needed to establish evidence-based guidelines for these groups to

ensure safe and effective sedation practices[2].

While nitrous oxide sedation offers significant benefits in pediatric dental practice, including rapid onset and recovery, its application is not without challenges. Addressing these limitations requires a multifaceted approach, including improved training, better equipment, and more research into its effects on diverse patient populations. This will help ensure that nitrous oxide sedation remains a viable and effective option for managing dental anxiety and facilitating treatment in children.

EMERGING ADJUNCTIVE TECHNOLOGIES IN PEDIATRIC SEDATION

Emerging adjunctive technologies in pediatric sedation are transforming the landscape of pediatric dental care by offering innovative solutions to manage pain and anxiety. These technologies, including virtual reality (VR), AI-assisted monitoring systems, and improvements in sedation delivery devices, are being integrated into clinical practice to enhance patient experience and outcomes. This section will explore these technologies, focusing on their application in pediatric sedation, particularly in the context of nitrous oxide sedation in dental practice.

VR has been shown to significantly reduce pain and anxiety in pediatric patients during various medical procedures. Studies have demonstrated that VR can serve as an effective distraction tool, reducing the need for pharmacological sedation and minimizing associated risks such as laryngospasm and hypoxia[34, 35]. In pediatric dentistry, VR has been used to manage anxiety and pain during procedures, providing an immersive experience that diverts attention from the clinical environment. This has been particularly effective in reducing distress during local anesthesia and other invasive dental procedures[36, 37]. Research comparing VR to traditional sedation methods, such as nitrous oxide, indicates that VR can be a viable alternative, offering similar or superior outcomes in terms of pain reduction and patient satisfaction[38, 39].

AI-assisted systems are being developed to improve the monitoring of pediatric patients during sedation. These systems can provide real-time data analysis, alerting clinicians to potential adverse events and allowing for timely interventions.By integrating AI technology with existing sedation protocols, healthcare providers can enhance the safety and efficacy of sedation practices, reduce the likelihood of complications and improve overall patient care.Advances in sedation delivery devices, such as the PediSedate®, combine nitrous oxide delivery with interactive video components to enhance the sedation experience. This approach not only reduces distress but also improves cooperation and acceptance among pediatric patients[39]. New devices, such as jet injectors, offer needle-free anesthesia options, minimizing pain and anxiety associated with traditional needle-based methods. These innovations are particularly beneficial in pediatric dental care, where patient comfort is paramount[36].

While these emerging technologies offer promising advancements in pediatric sedation, it is important to consider the broader context of their implementation. The integration of VR, AI, and improved delivery devices into clinical practice requires careful consideration of cost, accessibility, and training for healthcare providers. Additionally, further research is needed to fully understand the long-term effects and potential limitations of these technologies in pediatric care. As these technologies continue to evolve, they hold the potential to significantly enhance the quality of care and patient experience in pediatric dental practice.

NANOMEDICINE-BASED PROSPECTS

Nanomedicine offers promising prospects for enhancing nitrous oxide sedation in pediatric dental practice by leveraging advanced drug delivery systems and targeted therapies. This approach aims to improve the efficacy, safety, and patient experience associated with sedation in dentistry. The integration of nanotechnology into dental practices could revolutionize sedation techniques, offering more controlled and effective outcomes. The following sections explore various aspects of nanomedicine in dentistry, focusing on its potential applications in pediatric sedation.

Nanomedicine involves the application of nanotechnology to develop novel therapeutic and diagnostic tools in dentistry.It enhances treatment precision and patient outcomes by utilizing nanoparticles and nanostructures for targeted drug delivery and regenerative medicine[40, 41]. In dentistry, nanotechnology has been applied to improve the mechanical, antimicrobial, and biocompatible properties of dental materials, leading to better restorative and preventive treatments[40].

Nano-based drug delivery systems optimize targeted therapies with minimal systemic side effects, which is crucial in pediatric dentistry[40]. These systems include nanoparticles, nanorods, and nanotubes, which have been integrated into various dental applications to improve treatment efficacy[40, 41]. Polymer-based drug delivery systems, especially those using natural polysaccharides, demonstrate potential in addressing prevalent dental issues in children by performing targeted therapy and reducing drug dosages[42].

Nanotechnology enables the development of drug delivery systems that provide controlled and sustained release of sedatives, enhancing the management of anxiety and pain in pediatric patients[41]. These systems can be designed to release sedatives in response to specific stimuli, ensuring precise control over sedation levels[42]. The use of nanocomposite hydrogels and nanoparticles for sedative delivery is being explored to improve the safety and efficacy of sedation in dental procedures[43].

Nanomedicine-based sedation techniques offer several advantages over conventional methods, including improved drug targeting, reduced side effects, and enhanced patient comfort[41, 44]. These techniques can potentially lower the required dosage of sedatives, minimizing the risk of adverse effects and improving the overall safety profile of sedation[42]. The ability to deliver sedatives directly to the target site can enhance the effectiveness of sedation, leading to better patient outcomes[43].

Despite the potential benefits, there are concerns regarding the cytotoxicity and long-term biocompatibility of nanomaterials used in dental applications[40, 42]. Regulatory challenges and high costs are significant barriers to the widespread clinical adoption of nanotechnology in dentistry[40]. Ongoing research is needed to address these challenges, improve cost-effectiveness, and establish standardized regulatory guidelines to ensure the safe integration of nanomedicine into dental practice[40, 43].

While nanomedicine holds great promise for enhancing sedation techniques in pediatric dentistry, it is essential to consider the potential risks and challenges associated with its implementation. The development of safe, effective, and cost-efficient nanotechnology-based solutions requires rigorous scientific validation and regulatory oversight. As research progresses, the integration of nanomedicine into dental practices could lead to significant advancements in patient care and treatment outcomes.

FUTURE PERSPECTIVES

The integration of nanotechnology into clinical sedation protocols represents a promising frontier in medical innovation, offering potential improvements in drug delivery, precision, and patient outcomes. However, realizing this potential requires addressing several key areas, including interdisciplinary research, regulatory and ethical considerations, and the direction of clinical trials. These aspects are crucial for the successful translation of nanotechnology from research to clinical practice.

Nanotechnology can enhance drug delivery by improving solubility, bioavailability, and targeted delivery, which are critical for effective sedation protocols[45, 46]. The use of nanoparticles, such as liposomes and dendrimers, allows for controlled drug release and minimized systemic toxicity, which is particularly beneficial in sedation where precision is paramount[45]. Nanorobots and nanosensors could enable real-time monitoring and adjustment of sedation levels, enhancing patient safety and treatment efficacy[47].

Successful integration of nanotechnology into clinical sedation requires collaboration between chemists, engineers, and medical professionals to translate lab research into clinical applications[45]. Interdisciplinary research is essential to address the complex challenges of biocompatibility, potential toxicity, and the development of smart nanocarriers that respond to biological stimuli[45, 46]. Combining expertise from various fields can facilitate the design of more effective nanoparticles and expand applications beyond current limitations[45].

The lack of clear regulatory guidelines for nanomedicine poses a significant barrier to clinical adoption. There is a need for standardized safety protocols and regulatory frameworks to ensure responsible implementation[48]. Ethical considerations, such as patient autonomy, neuroprivacy, and long-term safety, must be addressed to gain public acceptance and trust in nanotechnology-based sedation protocols[49]. The development of international definitions and consistent regulatory policies is crucial to avoid discrepancies that could hinder research and development[48].

Clinical trials for nanotechnology in sedation should focus on demonstrating safety, efficacy, and the potential for personalized medicine[46]. There is a growing need for trials that explore the use of AI in designing nanoparticles and managing nanorobots, which could revolutionize personalized sedation protocols[49]. Enhanced transparency and interdisciplinary cooperation are essential to overcome translational obstacles and bridge the gap between innovation and patient accessibility.

While the integration of nanotechnology into clinical sedation protocols holds immense promise, it is essential to consider the broader implications and challenges. The potential for nanotechnology to revolutionize healthcare is significant, but it requires careful navigation of regulatory, ethical, and interdisciplinary landscapes. Addressing these challenges will be crucial for the successful implementation of nanotechnology in clinical settings, ultimately improving patient outcomes and advancing medical practice.

CLINICAL IMPLICATIONS FOR PEDIATRIC DENTISTS

The clinical implications for pediatric dentists involve a multifaceted approach to managing pain and anxiety in children, which is crucial for improving their dental experiences and outcomes. Pediatric dentists must integrate both pharmacological and non-pharmacological strategies to effectively address these challenges. This involves practical recommendations, case selection strategies, combining different approaches, and considering training needs for dental professionals. The following sections delve into these aspects, providing insights from recent research.

Non-pharmacological interventions such as virtual reality, guided imagery, and cognitive strategies have shown significant effectiveness in reducing anxiety and pain in pediatric dental settings. These methods can decrease anxiety levels by up to 40% and pain scores by 35[12]. Pharmacological approaches, including the use of pre-emptive oral analgesics and procedural sedation, are recommended for managing intra-operative and post-operative pain. These methods have been strongly recommended based on moderate evidence, with benefits outweighing potential harms[50, 51].

Dentists should assess the severity of dental anxiety and fear in children to tailor interventions appropriately. Early identification of these conditions is crucial for implementing effective management strategies[52]. The choice between pharmacological and non-pharmacological methods should be based on the complexity of the case and the child's specific needs. For instance, non-pharmacological techniques like the "tell-show-do" method and desensitization are effective for less severe cases, while pharmacological interventions may be necessary for more complex situations.

An integrated approach that combines both pharmacological and non-pharmacological methods can enhance the management of pain and anxiety. For example, using behavior management technology alongside sedation can reduce the required medication dosage and minimize adverse events[51]. Behavioral interventions, mechanoreceptor stimulation, and thermal receptor stimulation have been shown to effectively reduce intra-operative pain, while pharmacological methods can address post-operative discomfort[50].

There is a need for comprehensive training programs that equip pediatric dentists with the skills to manage dental anxiety and behavior management problems. A proposed curriculum includes assessment, non-pharmacological and pharmacological approaches, and decision-making skills. Training should also address the variability in exposure to different sedation techniques and pharmacological agents, ensuring that dentists are well-prepared to handle a range of clinical scenarios[53].

While the integration of pharmacological and non-pharmacological approaches is essential, it is important to consider the potential limitations and challenges. For instance, the use of sedation in pediatric dentistry is becoming less common, which may lead to an over-reliance on non-pharmacological methods or physical restraint in some cases[53]. Additionally, cultural differences and family dynamics can influence the effectiveness of anxiety management strategies, highlighting the need for individualized treatment plans[52]. Overall, a balanced approach that considers the unique needs of each child and the available resources is crucial for optimizing dental care in pediatric patients. To synthesize the key clinical, safety, technological, and future-oriented aspects discussed throughout this review, Table 1 provides

Table 1. Overview of Nitrous Oxide Sedation in Pediatric Dentistry: Clinical Applications, Safety, Challenges, and Future Directions

Domain	Key Aspects	Clinical Implications
Indications	Moderate dental anxiety, limited cooperation, exaggerated gag reflex, minor to moderately invasive procedures	Facilitates safe and efficient treatment while maintaining consciousness and protective reflexes
Advantages	Rapid onset and recovery, titratability, minimal respiratory depression, high safety margin	Suitable for outpatient pediatric care; reduces need for general anesthesia
Contraindications	Severe respiratory disease, nasal obstruction, recent middle ear surgery, inability to communicate	Requires careful patient selection and preoperative assessment
Adverse Effects	Mild nausea, vomiting, dizziness (rare serious complications such as aspiration)	Generally self-limiting; minimized with proper fasting and monitoring protocols
Occupational & Environmental Considerations	Risk of chronic staff exposure; greenhouse gas emissions	Requires scavenging systems, ventilation, and adherence to exposure limits
Current Challenges	Variable patient response, equipment costs, training requirements, limited data in special populations	Emphasizes need for standardized training and further research
Emerging Adjunctive Technologies	Virtual reality, AI-assisted monitoring, advanced delivery systems	May enhance patient cooperation and reduce sedative dosage
Nanomedicine Prospects	Targeted drug delivery, controlled release systems, reduced systemic toxicity	Potential to improve sedation precision, safety, and personalization; requires regulatory validation

a structured overview of nitrous oxide sedation in pediatric dentistry. This summary highlights current indications, advantages, limitations, safety considerations, and emerging innovations, including nanomedicine-based approaches, thereby offering clinicians a concise reference framework for evidence-based decision-making.

CONCLUSION

Nanomedicine-enhanced pediatric sedation represents an emerging and promising advance in child healthcare, with the potential to refine drug delivery, improve efficacy, and enhance safety. By improving solubility, stability, and targeted delivery of sedative agents, nanotechnology may help address the distinct physiological and developmental characteristics of children, while also reducing systemic exposure and adverse effects. At the same time, this field remains at an early stage, and important questions regarding long-term safety, biocompatibility, and regulatory pathways still limit widespread clinical adoption.Current evidence from pediatric and related therapeutic areas indicates that nanotechnology-based systems can optimize pharmacokinetics and enable more predictable sedation, suggesting meaningful advantages over conventional formulations. Nonetheless, the clinical data specific to pediatric sedation are still relatively limited, underscoring the need for robust trials and longitudinal safety studies. In this context, traditional sedatives such as oral ketamine and remimazolam, which already possess established efficacy and safety profiles, will continue to form the backbone of pediatric sedation practice in the near term.Looking ahead, advances in nanotechnology are likely to generate novel sedative formulations and delivery platforms that could further individualize and improve pediatric sedation. Realizing this potential will depend on rigorous research, careful evaluation of toxicity and long-term outcomes, and navigation of complex regulatory frameworks. Ultimately, nanomedicine should be viewed as a complementary extension of existing pediatric sedation strategies, integrated thoughtfully to balance innovation with patient safety. A nuanced understanding of both conventional and nanomedicine-based approaches will be essential for clinicians aiming to optimize sedation care for children in the coming years.

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CONFLICT OF INTEREST STATEMENT

The authors declare that there are no conflicts of interest related to the research, authorship, or publication of this manuscript. All authors have disclosed any financial or personal relationships that could potentially influence or bias the work presented.

REFERENCES

1. Birajee G, et al. Assessment of Dental Fear and Anxiety in Children Undergoing Nitrous Oxide-Oxygen Inhalation Sedation visiting BPKIHS. J Nepal Assoc Pediatr Dent. 2023;4(1):12-17. https://doi.org/10.3126/jnapd.v4i1.68689
2. Ibrahim DFA, Hussein AS, Hamzah SH. Nitrous oxide inhalation sedation in pediatric dentistry: an overview of the available guidelines. Jordan Med J. 2022;56(2):159-169. https://doi.org/10.35516/jmj.v56i2.239
3. Lim JW, et al. Nitrous Oxide-Oxygen Inhalation Sedation in Paediatric Dental Patients: A Review. Malays J Paediatr Child Health. 2022;28(1):91-100. https://doi.org/10.51407/mjpch.v28i1.163
4. Khinda V, Rao D, Sodhi SPS. Nitrous oxide inhalation sedation rapid analgesia in dentistry: An overview of technique, objectives, indications, advantages, monitoring, and safety profile. Int J Clin Pediatr Dent. 2023;16(1):131-136. https://doi.org/10.5005/jp-journals-10005-1807
5. Silva TAP, Silva IAPS, de Andrade RS. Sedação inalatória com óxido nitroso na prática clínica odontológica: revisão integrativa. Braz J Implantol Health Sci. 2023;5(5):2740-2764. https://doi.org/10.36557/2674-8169.2023v5n5p2740-2764
6. Ghabchi B, et al. Evaluation of dental treatments under nitrous oxide-oxygen inhalation sedation in pediatric patients with dental anxiety: a 10-Year retrospective study. BMC Oral Health. 2025;25(1):1171. https://doi.org/10.1186/s12903-025-06588-w
7. Mourad MS, et al. Potential for nitrous oxide sedation in pedodontics practice to reduce the need for dental general anesthesia. Quintessence Int. 2022;53(7):620-627.
8. Saturnino TS, Santos LRS, de Souza Matos D. Benefícios da sedação mínima no atendimento odontológico pediátrico: uma revisão narrativa da literatura. Braz J Health Rev. 2024;7(5):e73133. https://doi.org/10.34119/bjhrv7n5-275
9. Seifi N, et al. Anti-cancerous effect and biological evaluation of green synthesized Selenium nanoparticles on MCF-7 breast cancer and HUVEC cell lines. Nanomed Res J. 2023;8(4):373-382.
10. Potgieter N, Streit G. Predictable sedation: Safe administration of oral Midazolam and nitrous oxide gas for paediatric patients in the general dental practice. S Afr Dent J. 2021;76(8):471-476. https://doi.org/10.17159/2519-0105/2021/v76no8a4
11. Muhabes MH, Al-Obaidi NS. Understanding and addressing pediatric dental Anxiety: A contemporary overview. Al-Azhar J Dent Sci. 2024;27(4):585-593. https://doi.org/10.21608/ajdsm.2024.320184.1575
12. Aldawsari OAS, et al. Non-Pharmacological Approaches to Manage Pain and Anxiety in Pediatric Care. Adv Clin Exp Med. 2023;10(1):1-12.
13. Achmad H. Management of Pediatric Patients with Anxiety on Dental Care: A Systematic Review. Ann Rom Soc Cell Biol. 2021;25(2):1868-1883.
14. Soltani S, et al. The green-synthesized metal and metal oxide nanoparticles in dental implant applications. Nanomed Res J. 2023;8(3):218-230.
15. Kaur K, et al. Analyzing Nonpharmacological Behavior Management in Children With Dental Anxiety: A Systematic Review and Meta-Analysis. Health Sci Rep. 2025;8(8):e71176. https://doi.org/10.1002/hsr2.71176
16. Almarzouq SS, et al. Effectiveness of nonpharmacological behavioural interventions in managing dental fear and anxiety among children: a systematic review and meta-analysis. Healthcare (Basel). 2024;12(12):1200. https://doi.org/10.3390/healthcare12050537
17. Cavalcante LB, et al. Sedação consciente: um recurso coadjuvante no atendimento odontológico de crianças não cooperativas. Arq Odontol. 2011;47(1):1-7.
18. Jeglitsch A, Mathers F, Bürkle V. Lachgassedierung in der Kinderzahnheilkunde. Stomatologie. 2014;111(4):182-187. https://doi.org/10.1007/s00715-014-0332-7
19. Emmanouil D. The pharmacology, physiology and clinical application in dentistry of nitrous oxide. In: Pediatric Sedation Outside of the Operating Room: A Multispecialty International Collaboration. Springer; 2021. p. 199-209. https://doi.org/10.1007/978-3-030-58406-1_12
20. Clark MS, Brunick AL. Handbook of Nitrous Oxide and Oxygen Sedation. 3rd ed. St. Louis: Mosby Elsevier; 2008.
21. Tian Z, Daoyong H. Technology of nitrous oxide/oxygen inhalation sedation and its clinical application in pediatric dentistry. West China J Stomatol. 2014;32(1):1-5.
22. Holroyd I. Inhalation sedation with nitrous oxide in paediatric dentistry: a review. Dent Nurs. 2007;3(2):68-70. https://doi.org/10.12968/denn.2007.3.2.29670
23. Gupta K, Ritwik P. Clinical application of nitrous oxide in pediatric dentistry. In: Nitrous Oxide in Pediatric Dentistry: A Clinical Handbook. Springer; 2020. p. 151-206. https://doi.org/10.1007/978-3-030-29618-6_5
24. Galeotti A, et al. Inhalation conscious sedation with nitrous oxide and oxygen as alternative to general anesthesia in precooperative, fearful, and disabled pediatric dental patients: a large survey on 688 working sessions. Biomed Res Int. 2016;2016:7289310. https://doi.org/10.1155/2016/7289310
25. Dziedzic A. The role of general anaesthesia in special care & paediatric dentistry; inclusion criteria and clinical indications. SAAD Dig. 2017;33(1):48-54.
26. Zaffina S, et al. Nitrous oxide occupational exposure in conscious sedation procedures in dental ambulatories: a pilot retrospective observational study in an Italian pediatric hospital. BMC Anesthesiol. 2019;19(1):42. https://doi.org/10.1186/s12871-019-0714-x
27. Zier JL, Farrell M. Nitrous Oxide. In: The Pediatric Procedural Sedation Handbook. Oxford University Press; 2018. p. 314. https://doi.org/10.1093/med/9780190659110.003.0049
28. Muñoz L V, et al. Adverse Events and External Factors Affecting Nitrous Oxide Dental Sedation in an Academic Center. Pediatr Anesth. 2025;35(4):321-322. https://doi.org/10.1111/pan.15064
29. Gordon DW, Chatterjee D, McGain F. It's time to stop using nitrous oxide for pediatric mask induction. Pediatr Anesth. 2024;34(2):104-107. https://doi.org/10.1111/pan.14778
30. Barbosa ACBM, et al. Inhalation conscious sedation with

nitrous oxide/oxygen in pediatric dentistry. Rev Bras Anestesiol. 2014;64(2):102-104.
31. Moscato U, et al. Low-level nitrous oxide: risk assessment and risk management. G Ital Med Lav Ergon. 2016;38(3):242-244. https://doi.org/10.4081/gimle.711
32. Wilson S. Sedation of pediatric patients for dental procedures. In: Mason's Pediatric Sedation Outside of the Operating Room: A Multispecialty International Collaboration. Springer; 2025. p. 465-485. https://doi.org/10.1007/978-3-031-68468-5_22
33. Gupta N, Gupta A, MR VN. Current status of nitrous oxide use in pediatric patients. World J Clin Pediatr. 2022;11(2):93-104. https://doi.org/10.5409/wjcp.v11.i2.93
34. Sanna G, et al. Virtual sedation as a substitute to pharmacological sedation during PICC placement in pediatric patients: A feasibility study. J Vasc Access. 2024;25(1):313-317. https://doi.org/10.1177/11297298221085424
35. Priyadarshini S, et al. Is virtual reality effective in decreasing Pain during clinical procedures among children: a systematic review and Meta-analysis. J Indian Assoc Pediatr Surg. 2024;29(5):465-478. https://doi.org/10.4103/jiaps.jiaps_62_24
36. Kaswindiarti S, et al. Pengaruh Distraksi Virtual Reality Terhadap Perubahan Denyut Nadi Selama Prosedur Anestesi Lokal Jet Injektor Pada Perawatan Gigi Anak. B-Dent J Kedokt Gigi Univ Baiturrahmah. 2021;8(3):249-255. https://doi.org/10.33854/jbd.v8i3.600
37. Barros Padilha DX, et al. Virtual reality and behaviour management in paediatric dentistry: a systematic review. BMC Oral Health. 2023;23(1):995. https://doi.org/10.1186/s12903-023-03595-7
38. Scherer C, et al. A randomized controlled trial comparing immersive virtual reality games versus nitrous oxide for pain reduction in common outpatient procedures in pediatric surgery. Trials. 2025;26(1):21. https://doi.org/10.1186/s13063-025-08718-9
39. Brown SC, et al. Reducing distress for children during invasive procedures: randomized clinical trial of effectiveness of the PediSedate. Pediatr Anesth. 2009;19(8):725-731. https://doi.org/10.1111/j.1460-9592.2009.03076.x
40. Cheraghiyan M. Nanotechnology in dentistry: Potential applications and future perspectives. J Oral Dent Health Nexus. 2025;2(1):1-13. https://doi.org/10.61838/kman.jodhn.2.1.1
41. Renugalakshmi A, Sekar Vinothkumar T, Kandaswamy D. Nanodrug delivery systems in dentistry: a review on current status and future perspectives. Curr Drug Deliv. 2011;8(5):586-594. https://doi.org/10.2174/156720111796642336
42. Alavi SE, et al. Bioresponsive nanotechnology in pediatric dental drug delivery. J Drug Deliv Sci Technol. 2024;93:105436. https://doi.org/10.1016/j.jddst.2024.105436
43. Narang RS, Narang JK. Nanomedicines for dental applications-scope and future perspective. Int J Pharm Investig. 2015;5(3):121-128. https://doi.org/10.4103/2230-973X.160843
44. Singh R, et al. Role of Nanomedicine and Nanotechnology in Dentistry-A Narrative Review. Dent Med Res. 2024;12(2):49-51. https://doi.org/10.4103/dmr.dmr_31_23
45. Vohra D, Agrwal D, Chaudhari D. The impact of nanotechnology on drug delivery: current trends and future perspectives. Int J Pharm Res Appl. 2024;9(6):1339-1344. https://doi.org/10.35629/4494-090613391344
46. Pandey A, et al. Nanoparticles in biomedical and clinical research: a current perspective and future implications. In: Nanomaterials for Biomedical and Bioengineering Applications. Springer; 2024. p. 415-457. https://doi.org/10.1007/978-981-97-0221-3_17
47. Arya A, Yashan N. The nanorevolution in medicine: advancing drug delivery systems with nanomaterials and nanodevices. J Nanomed. 2024. https://doi.org/10.31224/4266
48. Foulkes R, et al. The regulation of nanomaterials and nanomedicines for clinical application: current and future perspectives. Biomater Sci. 2020;8(17):4653-4664. https://doi.org/10.1039/D0BM00558D
49. Borodulina EA, Zhilinskaya KV, Vdoushkina ES. The potential of personalized nanomedicine: New horizons for diagnosis and treatment. Med Sestra. 2024;26(7):49-53. https://doi.org/10.29296/25879979-2024-07-07
50. Alzubaidi MA, et al. Interventions to Reduce Intra-Operative and Post-Operative Pain Associated with Routine Dental Procedures in Children: A Systematic Review and Meta-Analysis. Dent J (Basel). 2024;12(6):163. https://doi.org/10.3390/dj12060163
51. Gao F, Wu Y. Procedural sedation in pediatric dentistry: a narrative review. Front Med (Lausanne). 2023;10:1186823. https://doi.org/10.3389/fmed.2023.1186823
52. Petkova-Ninova V, et al. Phobia, fear, and anxiety of dental treatment in pediatric patients: Etiology and clinical implications. Probl Dent Med. 2025;51:1-8. https://doi.org/10.3897/pdm.51.e167362
53. Nathan J. Managing Challenging Child Behaviour in Pediatric Dentistry Using Pharmacologic Approaches: A Vanishing Art. J Clin Pediatr Dent. 2024.