

## The Role of Nitrous Oxide (N<sub>2</sub>O) in Modern Dentistry

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### Abstract:

Nitrous Oxide (N<sub>2</sub>O) plays a crucial role in modern dentistry, serving as a key analgesic and anxiolytic agent that significantly enhances patient comfort during dental procedures. It addresses the complex nature of dental pain and anxiety through minimal sedation, preserving patient consciousness, and leveraging its neuropsychological effects to offer substantial pain relief and reduce anxiety. The clinical applicability of N<sub>2</sub>O extends to enhancing pediatric patient cooperation, managing hypersensitive gag reflexes, and diminishing intraoral sensory perception, thereby broadening its clinical utility.

Historically, the introduction of N<sub>2</sub>O to dentistry in the 18th century has underscored its foundational role in pain management and patient comfort. The advent of technologies like the eAdvantage<sup>®</sup> System represents significant progress in N<sub>2</sub>O delivery, optimizing its administration to align with the patient's respiratory dynamics. This exemplifies the integration of technology to improve patient-specific care through precise and efficient analgesia delivery.

In summary, Nitrous Oxide (N<sub>2</sub>O) remains indispensable in dentistry, improving clinical outcomes and patient satisfaction through effective pain and anxiety management strategies. Its application, coupled with technological innovations, underscores an ongoing commitment to patient-focused, efficient, and environmentally conscious dental care practices.

### Introduction:

Pain, encompassing both acute and chronic types, stands as the predominant complaint within the dental field, significantly influencing patients' quality of life. The diverse nature and characteristics of dental pain are integral to clinical diagnostics. However, the objective assessment of pain presents notable challenges.

Dental practitioners frequently encounter complex cases of pain in the head and neck region, complicating the establishment of differential diagnoses. Such diagnoses span a range of conditions, from dental infections and inflammatory diseases to temporomandibular disorders, headache syndromes, trigeminal neuropathies, and idiopathic or centralized pain syndromes.

To address this challenge, the International Association for the Study of Pain (IASP) refined the definition of pain in 2020 to emphasize its nature as "an aversive sensory and emotional experience typically caused by, or resembling that caused by actual or potential tissue injury." This definition highlights the complexity of pain, recognizing it as an experience influenced by biological,

psychological, and social factors, thus extending its expression beyond mere verbal descriptions (Matsuda, et al., 2022).

Acute dental pain, affecting both the hard and soft tissues of the oral cavity, spans all age groups and occasionally necessitates emergency department visits for analgesia. The American Dental Association's guidelines for the selection of analgesics tailor pain management strategies to the anticipated degree of pain, categorizing it into four severity levels—mild, mild to moderate, moderate to severe, and severe—based on the type of dental intervention. This approach is crucial for developing effective, patient-specific pain management strategies, highlighting the importance of proactive and tailored pain management (Matsuda, et al., 2022).

N<sub>2</sub>O, with its remarkable analgesic and anxiolytic properties, plays a pivotal role in relieving dental pain and anxiety. By inducing a state of minimal sedation while maintaining the patient's consciousness, N<sub>2</sub>O enhances patient comfort and cooperation during dental procedures, offering a versatile and patient-friendly

option for alleviating the multifaceted experience of dental pain as defined by the IASP. Furthermore, the World Health Organization's (WHO) recognition in May 2021 of the urgent global need for enhanced oral health care highlights the interconnection between oral health and overall well-being. The Sustainable Development Goals (SDGs) contextualize the significant impact of oral health issues, such as pain, on an individual's quality of life and societal participation (Matsuda, et al., 2022), reinforcing the importance of effective pain management solutions like N<sub>2</sub>O in modern dental practices.

### **Clinical Implications of Nitrous Oxide Use in Dentistry**

The clinical implications of Nitrous Oxide (N<sub>2</sub>O) usage in dental care, especially regarding its neuropsychological effects, underscore its vital role in providing patients with a more comfortable and anxiety-free experience. N<sub>2</sub>O is renowned for its analgesic and anxiolytic properties, arising from its complex interaction with the central nervous system (CNS). These interactions are crucial for understanding how N<sub>2</sub>O effectively manages the neuropsychological effects of pain and anxiety, supporting its widespread application in dental care.

*Analgesic Properties:* The analgesic effects of N<sub>2</sub>O are primarily mediated through its action on the CNS, inducing the neuronal release of endogenous opioids such as enkephalins. These opioids bind to specific receptors involved in modulating pain perception. By activating these receptors, N<sub>2</sub>O alters the pain pathway, providing significant relief without needing more potent systemic analgesics. Furthermore, N<sub>2</sub>O's effect on the descending gamma-aminobutyric acid type A (GABA<sub>A</sub>) receptors and noradrenergic pathways further modulate nociceptive processing at the spinal level, enhancing its analgesic efficacy (AAPD, 2023). This multifaceted approach allows N<sub>2</sub>O to offer substantial pain relief during minor to moderately invasive dental procedures prevalent in clinical practices.

*Anxiolytic Effects:* The anxiolytic effects of N<sub>2</sub>O are critically crucial in pediatric dentistry, where patient anxiety can significantly impact the success of dental treatments. By interacting with the GABA<sub>A</sub> receptor, N<sub>2</sub>O induces a state of CNS depression, effectively reducing anxiety levels. This mechanism, which can be facilitated directly or indirectly through the benzodiazepine binding site (AAPD, 2023), helps in

creating a calming effect without the deep sedation associated with other agents. N<sub>2</sub>O's ability to reduce anxiety and create a more relaxed environment is crucial for ensuring cooperation and reducing excessive fear in patients of all ages during dental procedures.

*NMDA Receptor Antagonism:* N<sub>2</sub>O's antagonism of NMDA receptors adds to its multifunctional mechanism, contributing to its anesthetic, analgesic, and amnesic properties (AAPD, 2023). This antagonism is vital for a comprehensive approach to managing pain and anxiety, offering relief that extends beyond simple analgesia. The inhibition of NMDA receptors is particularly relevant in modulating the long-term synaptic changes associated with pain perception and memory (Kalmoe, 2020), thereby improving the overall experience during dental procedures.

*Pharmacokinetics and Safety Profile:* Characterized by rapid onset and recovery times (2-3 minutes), low tissue solubility, and no biotransformation, N<sub>2</sub>O's pharmacokinetic profile supports its efficacy and safety in dental care for all age groups. Its minimal alveolar concentration (MAC) value of 105% indicates that while it cannot achieve complete anesthesia alone, it excels in reducing pain and anxiety. The fact that N<sub>2</sub>O is transported as free gas and does not bind to hemoglobin ensures that its effects are quickly reversible, allowing for a quick return to baseline consciousness and physiological function post-procedure (AAPD, 2023). These pharmacokinetic attributes and stable cardiovascular functions (Tanaka, 2004) highlight N<sub>2</sub>O's safety, making it a preferred option for managing pain and anxiety in diverse dental settings.

### **The Role and Historical Significance of Nitrous Oxide in Dental Care**

Discovered in 1772 by Joseph Priestley and brought into the dental field by Horace Wells in 1844, N<sub>2</sub>O has solidified its position as an integral component of dental care. Wells' initial application underscored its anesthetic and analgesic properties, catalyzing its broad acceptance for dental pain management. Today, nitrous oxide stands as an essential tool in managing dental anxiety and fear, distinguished by its rapid onset, minimal side effects, and quick recovery time (Gillman M. A., 2019). Such characteristics affirm its status as a remarkably safe and efficient means of analgesia, catering not just to pediatric patients, who might display nervousness towards dental

interventions, but also to adults desiring a more agreeable dental treatment experience. The journey of N<sub>2</sub>O from a novel discovery to an indispensable element in dental pain management exemplifies its vital contribution to enhancing dental practices. The ongoing and historical influence of N<sub>2</sub>O in dental care underlines its significance in encouraging a caring and adequate dental care environment, positioning it as a critical aspect of clinics striving for comprehensive and patient-focused care.

### **Addressing Needle Phobia in Dentistry.**

Needle phobia constitutes a significant challenge in dentistry, creating obstacles that often extend into adulthood. This anxiety, frequently stemming from early childhood experiences, presents a considerable barrier in performing vital dental procedures, including routine care. According to Professor Samina Ali, as many as 10% of adults experience needle phobia, a condition deeply ingrained from childhood encounters (Sweetman, 2023). Such fears can lead to the avoidance of critical treatments. In addressing this issue, applying Nitrous Oxide (N<sub>2</sub>O) in dental procedures associated with pain is valuable, going beyond its role as an agent for immediate pain and anxiety relief. N<sub>2</sub>O plays a crucial role in reducing the development of needle phobia by offering a non-invasive, needle-free option for pain management. This approach improves the dental care experience for young individuals and shows the potential to decrease the prevalence of needle phobia among adults.

By diminishing the traumatic experiences associated with needles in dentistry from a young age, N<sub>2</sub>O becomes key in facilitating patients' long-term psychological health. Its success in preventing needle phobia underscores the importance of incorporating gentle and minimally invasive pain management strategies in dental practices. N<sub>2</sub>O's application transcends providing temporary relief, underlining the need for care methodologies that consider their long-term psychological impact (Sweetman, 2023).

### **Nitrous Oxide as an Alternative to General Anesthesia for Pediatric Dental Patients with Special Challenges.**

In pediatric dentistry, addressing anxiety and pain in children, especially those with special healthcare needs or intensified fear, constitutes a critical component of dental care. Nitrous Oxide (N<sub>2</sub>O) is an exceptionally efficacious means for providing conscious sedation as an

alternative to general anesthesia. Its application in pediatric dental treatments not only alleviates anxiety and discomfort but also significantly improves patient compliance, a crucial factor in treating pre-cooperative children or those with intellectual disabilities. This approach's effectiveness is supported by substantial research conducted at the Bambino Gesù Pediatric Hospital in Rome. An extensive study involving 688 pediatric patients, ranging from 4 to 17 years old, revealed an impressive success rate of 86.3% in utilizing N<sub>2</sub>O for conscious sedation. This outcome is particularly relevant for patients for whom general anesthesia poses increased risks or potential complications. The findings underscore N<sub>2</sub>O's capability to simplify dental procedures in children by promoting high cooperation levels, even in individuals with limited pain tolerance or intellectual challenges (Galeotti et al., 2016).

### **Managing Hypersensitive Gag Reflex in Dental Procedures with Nitrous Oxide**

The gag reflex, an involuntary defence mechanism that protects the pharynx and throat from foreign objects, can become a significant challenge during hypersensitive dental treatments. This heightened sensitivity can make therapeutic procedures distressing and, occasionally, difficult or impossible to perform, presenting notable challenges in dental care (Eachempati et al., 2019). Addressing a hypersensitive gag reflex, whether from somatogenic (physical) or psychogenic (psychological) origins, is crucial for the effectiveness of both treatment and diagnostic procedures. Nitrous Oxide (N<sub>2</sub>O) has been identified as an effective means of managing this reflex, significantly improving patient comfort and facilitating cooperation during dental procedures, thereby ensuring the successful completion of necessary dental work.

Clinical evidence supports using N<sub>2</sub>O in various concentrations to suppress the hypersensitive gag reflex. A pivotal study involving patients suffering from this reflex underwent tests such as placement of a digital X-ray sensor or simulated dental procedures has shed light on N<sub>2</sub>O's utility for this purpose. Research findings indicate variability in patient responses to N<sub>2</sub>O, with some showing adequate tolerance at lower concentrations of 30% N<sub>2</sub>O, while others required higher concentrations, up to 70%, to comfortably undergo dental procedures without the gag reflex interfering (De Veaux et al., 2016).

The study's methodology included an initial baseline assessment using room air, followed by a gradual increase in N<sub>2</sub>O concentration from 30% to 70% to identify the minimum effective concentration necessary for each patient to tolerate sensor placement without triggering the gag reflex. Notably, a mixture of 70% N<sub>2</sub>O and 30% oxygen proved effective for all patients, allowing them to comfortably endure the placement and retention of a digital X-ray sensor for a duration sufficient to capture a clear periapical radiograph. This finding highlights the adaptability of N<sub>2</sub>O in managing dental anxiety and procedural discomfort and its vital role in overcoming specific challenges, such as the hypersensitive gag reflex (De Veaux et al., 2016). Consequently, N<sub>2</sub>O facilitates a broader range of dental treatments and diagnostics, reinforcing its importance in modern dental practice.

### Enhancing Pediatric Dental Cooperation

In dentistry, securing patient cooperation, especially among young children who experience dental anxiety or have undergone traumatic dental experiences, is required. The American Academy of Pediatric Dentistry advocates using nitrous oxide (N<sub>2</sub>O) and oxygen (O<sub>2</sub>) sedation as an effective strategy to improve cooperation during dental treatments. A retrospective study involving 371 children aged between 4 and 10 years, identified for showing signs of dental anxiety or previous treatment refusal, highlights the efficacy of N<sub>2</sub>O/O<sub>2</sub> analgesia in increasing patient cooperation (Memè et al., 2022).

The protocol for this study began with the administration of 100% oxygen to the children, followed by a gradual increase in N<sub>2</sub>O concentration to a maximum of 35%. After the dental procedure, pure oxygen was supplied to patients for five minutes to facilitate a safe recovery. The findings revealed a substantial enhancement in the children's cooperation, as measured by the Venham score, compared to their initial cooperation levels (Memè et al., 2022).

A significant insight from the study was the noticeable improvement in cooperation among the younger cohort (ages 4–6 years), who initially demonstrated lower levels of cooperation but reached optimal cooperation levels under N<sub>2</sub>O/O<sub>2</sub> analgesia. Hence, N<sub>2</sub>O/O<sub>2</sub> analgesia is a reliable and effective method for boosting cooperation in pediatric dental patients. This approach alleviates anxiety and maintains open communication between the

dentist and the child, crucial for assisting the child in overcoming fear and comfortably receiving dental treatments. The study underscores the importance of implementing non-invasive, child-friendly analgesic techniques in pediatric dentistry, significantly reducing the need for general anesthesia, encouraging better dental health from childhood, and ensuring a more positive dental care experience for young patients (Memè et al., 2022).

### Nitrous Oxide's Impact on Intraoral Taste and Tactile Sensory Modulation in Dentistry

Nitrous Oxide (N<sub>2</sub>O) significantly influences intraoral sensory perception, notably affecting taste and tactile sensations during dental procedures. This sensory modulation is crucial for enhancing patient comfort and alleviating dental treatment-related apprehensions.

Studies reveal that N<sub>2</sub>O markedly raises the threshold for intraoral sensory inputs, including taste and tactile sensations. Research involving healthy volunteers, incorporating taste testing via electrogustometry and tactile function assessment using the Semmes-Weinstein monofilaments (SWM) test, demonstrated that N<sub>2</sub>O analgesia substantially increases the recognition thresholds for these sensations. Specifically, the study observed that inhalation of N<sub>2</sub>O significantly elevated the threshold for detecting taste and tactile stimuli compared to baseline conditions such as room air (RA), 100% O<sub>2</sub>, and during post-recovery phases.

This indicates that N<sub>2</sub>O's ability to modulate sensory input can effectively reduce the unpleasant sensations frequently associated with heightened patient anxiety and fear, thereby significantly diminishing discomfort and anxiety linked to dental treatments (Kuroiwa et al., 2021).

Reducing intraoral sensitivity presents a non-invasive approach to improve the dental experience. By reducing the intensity of taste and tactile sensations, N<sub>2</sub>O assists in minimizing the sensory overload that often results in patient discomfort and anxiety. This sensory perception adjustment facilitates a more manageable and less distressing dental care environment. Furthermore, N<sub>2</sub>O's controlled sedation effect maintains the patient's consciousness and ability to communicate intact and is vital for safety during dental procedures (Khinda et al., 2023). This capability ensures patients can express discomfort or anxiety, allowing dental professionals to

modify the treatment approach accordingly (Kuroiwa et al., 2021).

### **Nitrous Oxide in Dentistry: Achieving Success, Satisfaction, and Charting Future Directions**

Adopting Nitrous Oxide/Oxygen Inhaled Sedation (NOIS) in dental procedures, particularly in pediatric dentistry, has significantly enhanced patient comfort and the efficacy of dental procedures. A notable study from a Swiss university hospital has provided compelling evidence of Nitrous Oxide's effectiveness, reporting high satisfaction rates among patients and clinicians and impressive success in dental treatments utilizing NOIS (Perez et al., 2023).

#### Exceptional Success and Satisfaction with Nitrous Oxide

This study revealed an exceptional overall treatment success rate of 98.2%, highlighting Nitrous Oxide's capability to ensure the completion and success of planned dental treatments. Remarkably, 75% of patients and 91% of clinicians expressed overall satisfaction with using N<sub>2</sub>O in dental procedures. The direct correlation between the facilitated procedures' high success rate and the satisfaction levels among participants emphasizes N<sub>2</sub>O's efficiency and acceptability in clinical settings (Perez et al., 2023).

#### Future Directions and Positive Outlook

The findings from the Swiss university hospital study not only affirm the effectiveness and acceptance of Nitrous Oxide but also open avenues for further research to optimize its application. Exploring the combination of Nitrous Oxide with other sedation techniques or pharmacological agents and incorporating advanced gas mixing and delivery systems, like the eAdvantage<sup>®</sup> system, could revolutionize patient comfort and treatment outcomes.

### **Combining Nitrous Oxide and Scented Masks to Control Dental Fear in Children**

Dental fear and phobia in children, often arising from negative sensory experiences, present considerable obstacles in pediatric dentistry. Effectively managing these fears is the key to successful dental treatments. The recent introduction of scented masks has emerged as a new advancement, making dental care more pleasant for young patients. This creative approach

transforms the dental visit into a more positive experience.

#### Understanding Dental Fear and Phobia in Children:

Dental fear and phobia are considerable psychological barriers in pediatric dentistry, ranging from mild apprehension to severe, incapacitating phobia. These fears not only complicate the condition of dental treatments but also lead to outright care refusal or disruptive behaviors during dental visits. The core of dental phobia lies in an intense, persistent fear of dental stimuli and procedures, driving some children to avoid dental care entirely. This avoidance can severely impact their oral health, highlighting the necessity of prompt and effective interventions to manage these fears. Early recognition and management of dental fear and phobia are crucial for preventing long-term dental treatment avoidance and maintaining optimal oral health (Gao et al., 2023).

The Innovation of Scented Masks: A recent study exploring the effect of scented masks on improving mask acceptance among young dental patients (2–10 years) revealed that scented masks, infused with pleasant fragrances like strawberry or cherry, significantly enhanced behavioral scores, particularly among the youngest children (2–3 years). Introducing a positive olfactory stimulus seems to diminish distress behaviors, suggesting reduced discomfort and fear linked to mask application (Abukawa et al., 2023).

#### Enhancing Pediatric Dental Care with Scented Masks and N<sub>2</sub>O Sedation:

Integrating scented masks with Nitrous Oxide (N<sub>2</sub>O) analgesia introduces an innovative method to address dental fear and resistance, especially in young patients. Utilizing N<sub>2</sub>O nasal masks infused with child-friendly scents presents a novel solution to the ordinary apprehension associated with dental procedures and mask usage. This approach transforms a potentially daunting experience into a more welcoming and comfortable one, decreasing anxiety levels in children.

The combined impact of N<sub>2</sub>O's established analgesic effects with the comforting presence of familiar scents markedly improves children's acceptance of dental treatments. N<sub>2</sub>O, by inducing minimal sedation, helps alleviate immediate fear and anxiety, while the agreeable and familiar scents distract the young patients, further reducing their apprehensions. This comprehensive approach enhances the trust between

the child and the dental practitioner, significantly diminishing children's long-term dental fears and anxieties. Encouraging a positive initial experience contributes to a more favourable view of dental care, encouraging sustained oral health care.

### **Innovations in Nitrous Oxide Delivery: Precision and Patient-Centered Care in Modern Dentistry**

The growth in dentistry has significantly benefited from innovations designed to enhance precision in treatment and emphasize patient-centred care. This paradigm shift highlights the dedication to improving clinical outcomes and upgrading the patient experience through technological advancements. A prime example of such innovation, embodying the modern character of precision and patient focus, is the eAdvantage® System—a leading evolution in nitrous oxide delivery technologies.

The eAdvantage® System incorporates an Electronic Pressure Sensor with unparalleled sensitivity, capable of detecting inhalation efforts smaller than  $-1.0$  cmH<sub>2</sub>O. This sensor ensures the N<sub>2</sub>O/O<sub>2</sub> mixture's administration is precisely synchronized with the patient's respiratory physiology, mirroring each breath's natural dynamics. Inhalation, initiated by diaphragm contraction, generates a negative pressure in the thoracic cavity, facilitating gas intake. Leveraging this physiological mechanism, the eAdvantage® System's electronic sensor predicts and adapts, optimizing the mechanism of analgesia delivery.

This synchronization with the patient's respiratory efforts, combined with the system's low trigger threshold requiring minimal effort from the patient, achieves the lowest possible work of breathing (WOB) (Dargaville & Keszler, 2013), ensuring a smooth transition between active inhalation and passive exhalation phases, thus significantly improving patient comfort during treatment.

Furthermore, the eAdvantage® System's advanced trigger sensitivity marks a significant improvement in patient care by reducing the effort required to initiate gas flow compared to pneumatic demand valves, which typically have higher trigger sensitivities within the  $-2$  to  $-5$  cmH<sub>2</sub>O range and may increase patient exertion and work of breathing. Inspired by mechanical ventilation principles for patients with spontaneous breathing, which recommend the lowest possible trigger threshold

to minimize the work of breathing and avoid trigger delay that could lead to asynchrony (Dargaville & Keszler, 2013), the eAdvantage® System's refined trigger sensitivity ensures rapid, precise, and seamlessly coordinated gas delivery for patients of all ages, significantly enhancing comfort and the effectiveness of analgesia. Moreover, this sensor technology enables dynamic gas flow modulation, showcasing clinical innovation. It adjusts in real-time to changes in tidal volume (VT) and respiratory rate (RR), crucial during procedures that induce stress or pain— factors known to affect respiration by increasing its flow, frequency, and volume (Jafari et al., 2017).

By tailoring gas mixture delivery to these varying respiratory parameters, the system ensures analgesia is perfectly matched to the patient's immediate needs, removing the need for manual adjustments and the inaccuracies that dynamic respiratory patterns under stress might introduce. Additionally, it eliminates the need for ongoing monitoring of minute volume and gas reservoir levels required by traditional continuous flow systems, streamlining clinical workflow and enhancing patient care. Beyond its clinical advantages, the eAdvantage® System also addresses economic and environmental concerns within dental practices. Modulating gas delivery to match patient demand considerably reduces N<sub>2</sub>O wastage and decreases the environmental footprint, aligning with the sustainable and economically efficient practices that modern healthcare increasingly prioritizes.

In summary, the eAdvantage® System not only sets a new standard in analgesia delivery systems but also represents the broader objectives of modern dentistry in improving patient comfort and overall experience, alongside promoting environmental stewardship and operational excellence.

### **Conclusion:**

Nitrous Oxide (N<sub>2</sub>O) is a critical component in modern dentistry, effectively addressing dental pain and anxiety with its significant analgesic and anxiolytic capabilities. It extends its utility to various clinical challenges and notably improves dental care experiences. The introduction of the eAdvantage® System has marked a notable advancement in the field of N<sub>2</sub>O delivery systems, demonstrating the critical role of technology in



enhancing patient-specific care through precise and efficient analgesia delivery.

Applying N<sub>2</sub>O through innovative delivery systems like eAdvantage® ensures a more comfortable and minimally invasive dental experience, directly impacting the quality of care, patient satisfaction, and treatment outcomes. This blend of standard analgesic use with cutting-edge technology underscores N<sub>2</sub>O's integral role in dentistry, promising advancements in pain and anxiety management approaches. The commitment to ongoing research and innovation in N<sub>2</sub>O application promises a future where dental care is increasingly patient-focused, efficient, and environmentally conscious, reinforcing its indispensable value in dental practices.

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