**The Role of Nitrous Oxide Inhalation Sedation in Diverse Dental and Medical Settings**

Nitrous oxide, a colorless and nearly odorless gas with a faint, pleasant scent, functions as an effective agent for reducing pain and anxiety. It induces depression in the central nervous system and a sense of euphoria, while having minimal impact on the respiratory system. The utilization of nitrous oxide (N2O) for painless dental and surgical procedures was originally discovered by Horace Wells, an American dentist, on December 11, 1844, in Connecticut, who is now widely regarded as the pioneer of anesthesia. Over time, the practice of nitrous oxide inhalation sedation (NOIS) has evolved significantly. It has transformed into a crucial tool for modifying behavioral responses and providing rapid pain relief. Unlike its initial use as a stand-alone technique, which often led to complications, current standards emphasize the importance of mixing nitrous oxide with oxygen (O2) to achieve the desired level of control.

The modern approach prioritizes the sedative, calming, and euphoria-inducing effects of diluted nitrous oxide-oxygen (N2O-O2) combinations, rather than focusing solely on analgesia associated with high concentrations. Global guidelines underscore the reliability and value of titrated nitrous oxide in oxygen as a valuable method for dental sedation. It is particularly endorsed as a primary choice, especially for pediatric patient. The benefits of N2O encompass anxiety reduction, mild pain relief, and memory suppression. This gas often referred to as an anxiolytic agent,is recognized for its effective ability to induce a soothing state of relaxation. Additionally, it possesses the capacity to elevate a patient's tolerance for pain, thereby augmenting the effects of any locally applied anesthetic agent. It mitigates discomfort and ensures the patient's comfort during procedures.

Fig 1: Dental Nitrous Oxide Inhalation Sedation Unit

The medical device or techniques hence in use have clearly defined objective to achieve certain established goals. At the same time these goals can be attained only if there is an understanding of its application.

**Objectives:**

The use of Nitrous oxide –oxygen sedation in various medical and dental procedures serves several key objectives such as: There are various uses of Nitrous oxide –oxygen sedation for which clinician must have a thorugh understanding of indications and contraindications to minimize any difficultiy and complications for its use

The Nitrous oxide –oxygen inhalation sedation offers several benefits for pain management and anxiety reduction during medical and dental procedures but careful consideration of its advantages and disadvantages depending on its application and contextis essential

**Technique of Administration**

The process of administering N2O-O2sedation consistently commences and concludes with the patient receiving pure 100% oxygen. Subsequently, the patient is allowed to inhale slowly. Typically, a flow rate of 5–6 L/min is well-tolerated by most patients. Adjustments to the flow rate can be made based on observations of the reservoir bag. This bag should gently pulsate with each breath, maintaining a balanced inflation without being over or underinflated.

The procedure involves introducing 100% oxygen for a period of 1–2 minutes, followed by gradual adjustments in N2O concentration using 10% increments. During N2O-O2 sedation for pain relief and anxiety reduction, it's generally recommended to keep the N2O concentration below 50%. The level of N2O can be increased incrementally until the desired effects are achieved. It's crucial to remind the patient to breathe through their nose to ensure the gas takes effect. Regularly checking in with the patient about their feelings is essential to ensure the appropriate level of nitrous oxide is being administered, as therapeutic levels can vary from person to person. Maintaining an optimal balance is essential. If the administered nitrous level is too low, it won't provide effective anxiety relief. Conversely, excessive nitrous oxide can lead to unwanted side effects.

Note: Whenever possible, appropriate medical specialists should be consulted before administering analgesic/anxiolytic agents to patients with significant underlying medical conditions (e.g. severe obstructive pulmonary disease, congestive heart failure, sickle cell disease, acute otitis media, recent tympanic membrane graft, acute severe head injury).

Use of N2O-O2 in dental procedures involve a partial mask that covers the nose, leaving the mouth accessible. For surgical anesthesia, a full face mask encompassing both the nose and mouth is used. Alternatively, administration through an endotracheal (ET) tube is also an option. Regardless of the method chosen, ensuring the proper equipment, vigilant monitoring, and the integrity of storage units is crucial to prevent unintended gas leaks or excessive exposure. N2O sedation via a dental sedation unit is recommended for its safe and effectivepractice.The administration of N2O-O2 mixture performed using a mask that covers the patient's nose allows them to inhale the gas comfortably. This administration method allows for controlled and gradual sedation, leading to a relaxed state while maintaining the patient's ability to communicate and cooperate throughout the procedure.

**Multidisciplinary Application of N2o-O2 Sedation**

 Due to its anaesthetic and analgesic qualities, as well as its safety profile when delivered correctly, Nitrous Oxide-Oxygen has a number of applications across several medical and dental professions.It is widely used across various departments in order to help patients be calm and to manage pain or anxiety during treatments.

1. **Dentistry:**

N2O-O2 is commonly used in dental offices to help patients relax during various procedures, such as fillings, extractions, cleanings, and root canals. It eases anxiety and discomfort while allowing patients to remain conscious and responsive.While N2O significantly transformed pain management in dentistry, local anesthesia remains the foundational element of contemporary dental practice. N2O-O2 is frequently employed alongside local anesthesia, particularly for patients who experience discomfort with needles. Pain and fear serve as significant hindrances to seeking dental care, leading over 40% of the population to avoid dental visits due to these factors. N2O-O2 sedation presents an approach to surmounting these barriers.

Dentistry has maintained a substantial role in advocating for and implementing N2O-O2 sedation. This sedation method has been applied across various procedures and specialties within the fieldincluding periodontics, prosthodontics, orthodontics, dental hygiene, restorative dentistry, oral and maxillofacial surgery, endodontics, geriatrics, and notably in pediatric dentistry. Recent research attests to the efficacy of N2O-O2 sedation in effectively reducing an overly sensitive gag reflex, which can pose challenges during dental interventions.

N2O-O2 is commonly utilized in **minor oral surgical procedures** to provide a level of sedation and anxiety reduction for patients. Its effectiveness in inducing relaxation and reducing apprehension makes it a valuable tool in scenarios such as tooth extractions, dental implant placements, or gingival and periodontal surgeries which evokes feelings of apprehension and nervousness in patients. N2O-O2 analgesic and anxiolytic properties help to alleviate pain and reduce anxiety, making the experience more manageable for both the patient and the dental team.

The utilization of **N2O-O2in pediatric dentistry** offers a range of advantages, primarily aimed at alleviating children's anxiety and discomfort during dental procedures. In a study by Davis MJ et al,4 they estimated that about 88% of pediatric dentists incorporate N2O-O2 sedation method into their practices. Children often exhibit varying levels of apprehension and fear when visiting the dentist, which can make procedures challenging for both them and the dental professionals. N2O-O2provides a child-friendly solution by inducing a state of relaxation and euphoria. This can help children remain calm, cooperative, and less resistant to the dental treatment they require like endodontic therapy, extraction or minor oral surgical procedures where there are more chances of pain and the child is anxious and fearful. The administration of N2O-O2in pediatric dentistry is typically performed using a specialized mask that fits over the child's nose. The child inhales a carefully controlled mixture of N2O-O2, which allows them to feel at ease while staying conscious and able to communicate with the dentist. This is particularly important in pediatric cases where maintainingcommunication and cooperation is essential for a successful procedure. One of the significant benefits of using N2O-O2 in pediatric dentistry is its rapid onset and offset of action. This allows for real-time adjustments in sedation levels to match the child's response and comfort. Additionally, the effects of N2O-O2 wear off quickly once the gas is discontinued, enabling the child to recover swiftly after the procedure and resume normal activities. By providing a comfortable and anxiety-free experience, N2O-O2can have a lasting positive impact on a child's perception of dental visits. It helps build trust and confidence in dental care, contributing to better oral health practices as they grow older.

1. **Medical Procedures:**N2O-O2can be used in various medical settings to alleviate pain and anxiety

**A. Dermatology:**

In procedures like hair transplantation, use of N2O-O2is recognized to be effective in relievingpainwithout negatively impacting patient cooperation or causing adverse effects. A study conducted by Sadick and Militana et al5 revealed that a substantial majority of patients, ie, 94% expressed a preference for N2O-O2over 10mg diazepam (Valium) and the Dermajet technique of lidocaine administration. Given that this surgery involves multiple administrations of local anesthetic, the pain-relieving and sedative properties of N2O-O2contribute to improved patient tolerance. An advantage of N2O-O2in hair transplantation is its swift elimination compared to other substances like diazepam, which has a much lengthier duration of action without an easy reversal.

N2O-O2sedation can also be used procedures such as chemical peeling, skin cancer surgeries and liposuction. In liposuctionprocess, local anesthetics are often combined with intramuscular (IM), intravenous (IV), inhalation sedation, or general anesthesia. While many drugs can interact with the local anesthetics required for this procedure, it has been found that N2O-O2 does not have such interactions. Although dermatologists have limited experience with N2O-O2, they acknowledge its complementary effects when used alongside local anesthetics. Maloney et al6in their study stated that nearly all patients expressed a desire for N2O-O2in future visits.

**B. Podiatry:**

In 1966, Arancia L et al7had successfully completedan ambulatory foot surgery procedure using N2O-O2 sedation which marked the initial documentation in literature regarding the utilization of N2O-O2in this field.In another study conducted in 1972, Mosher and Sorkin et al8 presented observational evidence involving 21 patients who underwent various podiatric procedures while receiving N2O-O2titrated to appropriate levels. The study observed no significant adverse effects, with 19% of patients experiencing amnesia. All patients reported a sense of relaxation and well-being. Some of the procedures performed using N2O-O2included digital arthroplasty, nail matricectomy, subungual exostosectomy, bunionectomy, excision of digital mass, digital arthrodesis, excision of hallux ossicle, tailor's bunionectomy, and excision of plantar mass.In research conducted in 1982, Harris WC et al9encouraged combination ofN2O-O2with a 10mg dose of diazepam. They reported they that achieved positive outcomes in over 150 instances.

**C. Ophthalmology**:

In eye surgery, the prevalent anesthesia approach typically encompasses IV sedation along with retrobulbar block or solely utilizing topical anesthesia. N2O-O2can serve as an alternative to IM premedication or preparing patients for the subsequent administration of local anesthetics. McMahan et al10 achieved significant success employing N2O-O2therapy on 800 patients undergoing cataract surgery. Corboy JM et al at11 the Hawaiian Eye Surgicenter, incorporated the use of N2O-O2during implant surgery as a component of the process. They stated thatutilizing a mixture of 50% N2O and 50% O2 they found tranquilizing and memory-dulling effects and were able to swiftly recuperate the patients and timely discharge them.

**D. Psychiatry and Psychology:**

Patients displaying persistent anxiety and individuals dealing with depression when administeredN2O-O2, have experienced alleviation through N2O-O2therapy. In a study by Brill NW et al12, N2O was discovered to be more efficacious than thiopental when used alongside electroconvulsive therapy for managing depression. Nevertheless, the prevailing practice continues to involve methohexital or propofol along with succinylcholine as the primary choices.

The application of N2O-O2in treating schizophrenic patients has been approached cautiously due to the varying biological responses among individuals and the potential to trigger their psychotic symptoms. Gillman et al’s13 study stated that three out of four patients experienced a state of relaxation following N2O-O2usage. However, he also recorded issues with one of the patients.

Studies on sexual research has also explored the utilization of N2O-O2 therapy. A study conducted by Gillman and Lichtigfeldet al14demonstrated that females who previously experienced difficulties in achieving orgasm became capable of experiencing multiple orgasms through therapy involving N2O-O2. N2O-O2therapycan also be used in managing hyperactivity. deWet et al15 had explored the utilization of N2O as a potential treatment approach for managing hyperactivity. Their findings suggest a favorable response rate of 50%.

**E. Addiction Withdrawal:**

N2O has been explored as a potential therapeutic agent for aiding in the withdrawal from certain substances of addiction. The initial mention of this approach was made by Kripke and Hechtman et al16in 1972 where they employed it to treat pentazocine addiction. Pentazocine was administered in significant quantities to alleviate the persistent severe pain caused by a potassium hydroxide injury in a 14-year-old girl. Subsequently, the patient developed an addiction to the drug, and medical professionals employed N2O-O2to gradually withdraw her from it. This therapy offered the benefits of pain relief and ease of administration within her home environment.

Lichtigfeld and Gillman et al17conducted a study that demonstrated the effectiveness of N2O-O2for managing alcohol withdrawal in over 5000 cases in South Africa. Through a single 20-minute administration of N2O-O2analgesia upon a patient's admission to a treatment facility, initial withdrawal symptoms were relieved without inducing substantial sedation. This approach allowed for the immediate implementation of additional social detoxification therapies. Another study by Gillman and Lichtigfeldet al18reported that 90% of acute alcoholic withdrawal episodes were reversed within the initial 60 minutes after a single application of N2O-O2.

**F. Acute Myocardial Infarction**

Analgesic doses of N2O-O2have proven effective in alleviating acute pain during instances of myocardial infarction (MI). The pathophysiological process of an MI results in intense pain and often accompanies substantial anxiety. From 1962 to 196519, various studies in the former Soviet Republic demonstrated the success of N2O-O2in managing MI-related pain. The use of this approach was also documented in the United States during that time. Study by Thompson and Lown et al20 stated that around 74% of patients experienced some level of pain relief. Patients with milder pain tended to experience more significant relief compared to those with moderate to severe pain, where narcotics were often used in conjunction to enhance pain management. N2O-O2 has also demonstrated its advantages for individuals receiving treatment for coronary artery disease in an outpatient environment by enhancing oxygen delivery to the heart. O2 is crucial for supplying the myocardium, and N2O functions as an analgesic-sedative for the patients undergoing the procedure.

**3. Pediatric Care:**

N2O-O2sedation is particularly useful in pediatric settings to help children remain calm during medical or dental procedures that might otherwise cause anxiety or distress.Healthcare professionals face unique challenges when dealing with pediatric patients. Positive experiences in healthcare during childhood can significantly influence children's behavior during future visits, and these positive experiences tend to shape adult attitudes and behaviors as well. Negative childhood experiences can lead to adult patients' anxiety due to these memories. Even when there is a trustworthy, compassionate, and gentle relationship between healthcare workers and children, certain procedures can be painful. Regardless of how clinicians prepare children for pain psychologically, the memory that stands out is often the sensation of the needle prick.Amnestic and hypnosuggestive properties of N2O-O2 prove beneficial when working with pediatric patients. Children often have limited attention spans, necessitating extra care and time during procedures. The calming effect and distortion of time perception resulting from N2O-O2 sedation significantly aid healthcare providers. Children are generally more susceptible to hypnosis and suggestion compared to adults. Utilizing a calm, unhurried, and soothing tone of voice greatly enhances the effects of N2O-O2 sedation.

Over a span of nine years, Griffin et al21conducted research involving more than 3000 children and teenagers undergoing minor surgical procedures while under N2O-O2. These procedures encompassed tasks such as repairing lacerations or fractures, excising nevi, removing warts, incising abscesses, and extracting foreign objects like splinters, needles, nails, and fishhooks. An impressive 99% of the patients expressed their preference for N2O-O2sedation for future visits, showcasing the effectiveness and positive impact of this approach.In another study conducted byGamis et al22 at Children's Mercy Hospital in Kansas City, Missouriexplored the use of N2O-O2 for pediatric patients needing laceration repair in the emergency department. In this study, thirty-four children were enrolled and divided into two groups: one group received a mixture of 30% N2O and 70% O2, while the other group received 100% O2(control group). The results revealed a notable clinical difference in pain scores among children aged over 8 years. Although there wasn't a statistically significant distinction in the 2–7 age group, the utilization of N2O-O2was linked to reduced pain scores. Also, children diagnosed with cancer who require lumbar puncture and bone marrow aspiration have responded positively to a combination of N2O-O2 and midazolam used for pain relief during these procedures.

**4. Emergency Rooms:**

In emergency departments, N2O-O2 can be administered to reduce pain and anxiety in patients, especially for procedures likevenous cannulation, wound repair or setting fractures.In**prehospital emergency care in the ambulance,** N2O-O2works as apain-controlling analgesic drug that have rapid clinical action, no effect on level of awareness, no substantial side effects, and no masking of other conditions that might subsequently interfere with the diagnostic assessment at the hospital. A systematic review by Faddy and Garlick et al23on prehospital treatment of patients 50% O2 and 50% N2O concluded that N2O and O2 might be safely administered by lay responders due to the low prevalence of reported adverse outcomes.

The use ofN2O-O2 has shown success in managing orthopedic fracture care within hospital emergency departments.White et al24 stated that N2O could enhance prehospital pain management, particularly for patients with limb fractures. They recognized N2O as a feasible option. N2O-O2 can be employed in various patient care scenarios involving the skin, such as suturing and suture removal, incision of abscesses, removal of cysts, nevi, or warts, wound debridement, and dressing burns. For non-neurological head injuries, N2O-O2 may be a successful treatment, including procedures like abrasion debridement, drainage or removal of abscesses or cysts, extraction of foreign objects from ears, and tooth removal or replacement following trauma. Other procedures where N2O-O2 can be beneficial include drain removal or replacement, catheterization, biopsies, splinting, extrications, complex patient transfers, and various musculoskeletal injuries like strains, sprains, and dislocations.

**5. Obstetrics and Gynaecology:**

N2O-O2is sometimes used during labor for pain relief, providing a less invasive alternative to other pain management options.In 1880, a Russian medical practitioner, Marx GF et al25 introduced the application of N2O-O2 as a pain-relieving agent during childbirth. His experiments led him to the conclusion that it provided relief from labor pain without posing any harm to either the mother or the baby. Santos AC et al26, a Swedish in his literature also support the safety of N2O-O2anesthesia, with records indicating that nearly 300 women exposed to N2O showed no adverse reproductive effects.

In 1981, a hospital-based study in Wales by Arthur GJ et al27assessed the effectiveness of administering Entonox(50% N2O and 50% O2; BOCHealthcare, Manchester, UK), delivered through a nasal catheter, to women in labor. Both midwives and mothers agreed that Entonox effectively alleviated labor pain. While the nasal catheter administration method was comfortable and nonintrusive, it is not recommended due to concerns about environmental contamination.Another study conducted in Toronto in 1994 by Carstoniu et al28 indicated no significant statistical difference in outcomes between patients using N2O-O2 or compressed air. However, patients were able to differentiate between the two gases, and when given the choice, they preferred N2O-O2. O2 desaturation was not a significant factor, and the authors suggested that O2 levels actually improved between contractions. Fortescue and Wee et al29 proposed that factors such as distraction, relaxation, and perceived control might explain why previous researchers failed to achieve statistical significance between N2O-O2and air.Vallejo et al30reported that a 40% N2O concentration effectively reduced anxiety during cesarean section procedures, particularly at the time of injection and incisions.

In Gynaecologic laparoscopy procedure, conventionally carbon dioxide (CO2) has been employed as the insufflation gas butN2O could be incorporated as a component of a combined approach. The American Association of Gynaecologic Laparoscopists31 reported that more than 20,000 procedures involving the utilization of N2O-O2in some manner showed no occurrence of adverse incidents.

**6. Endoscopy:**

In gastrointestinal endoscopy procedures like colonoscopy, gastroscopy or bronchoscopy, NOIS can help patients tolerate discomfort more easily.Diehl et al32 in a study utilizing N2O-O2during gastrointestinal endoscopy procedurestated success in an outpatient setting with notably reduced expenses. Furthermore, patients typically responded positively to the procedure, and medical practitioners found the administration of N2O-O2unproblematic and patients' tolerance substantial. The study also explored the distinctions between using N2O-O2and intravenously infused barbiturates but found no statistically notable differences.

In a study by Forbes et al33, they concluded that the combination of 50% N2O and 50% O2 was suitable for a considerable number of patients undergoing colonoscopy. The report suggested that this mixture could potentially serve as a viable choice for certain patients, highlighting the benefit of quicker recovery. Theodorou et al34 supported this notion as they compared the use of total IV sedation with N2O-O2and sevoflurane inhalation sedation.In the United Kingdom where flexible sigmoidoscopy are typically conducted in an outpatient setting without anesthesia, a study by Harding et al35, employing a placebo-controlled approach, concluded that the use of N2O and O2 was advantageous in reducing patient discomfort during this procedure.

**7. Radiology:**

N2O-O2 sedation might be used for patients who are apprehensive about certain radiological procedures, enhancing their cooperation during imaging.In a study by Katzen BT et al35involving radiologic procedures, they found that 50 out of 53 patients reported improved experiences with N2O-O2 sedation. Some of the procedures suitable for N2O-O2sedation include aortoperipheral arteriography, percutaneous biopsy, visceral arteriography, percutaneous cholangiography, biliary catheter placement, biliary stone retrieval, bilateral ureter stent placement, hepatic artery catheter placement, liver abscess drainage, and bilateral temporomandibular joint arthroscopy. Patients under N2O-O2sedation tend to be more cooperative in remaining still during procedures compared to those under IV sedation.

The MRI process can pose challenges or even be inadvisable for individuals experiencing claustrophobia. This procedure involves being enclosed in a confined space and maintaining immobility for a prolonged duration. Often, patients necessitate sedation to manage their anxiety and guarantee the procedure's precision. N2O-O2sedation presents a feasible solution for this scenario. Nevertheless, there might be a need to investigate methods for enhancing the accessibility of delivery equipment within the limited confines of the MRI apparatus.

**8. Palliative Care:**

N2O-O2 can provide comfort to terminally ill patients by reducing pain and anxiety in their final stages of life.For patients battling cancer or facing terminal stages of illness, pain can become excruciating. In these instances, ensuring adequate pain management becomes a central concern for the patient's family and those close to them. Fosburg and Crone et al37 observed that certain patients opt to continue receiving intravenously infused narcotics alongside N2O-O2 treatment, while others prefer the use of N2O-O2 alone. Keating and Kundrat et al38documented an 81% success rate in alleviating pain through N2O-O2 treatments, with the positive effects lasting between 30 minutes and 2 hours. In numerous cases of terminal illness, N2O-O2 therapy contributed to improved mood, activity levels and appetite, fostering more open communication among patients.

**Summary:**

 Nitrous oxide inhalation sedation is a widely used and safe method for managing pain and anxiety in various dental and medical procedures. It is a valuable asset where patient comfort and cooperation are paramount. It offers several advantages, including rapid onset, adjustability, and minimal side effects, making it a valuable tool for improving patient comfort and compliance during various treatments.Patients often experience relief from pain and anxiety within minutes of inhaling the gas. This rapid onset is especially beneficial in time-sensitive procedures or when patients are in distress.

 The versatility of N2O-O2sedation is a noteworthy feature. Healthcare providers have the ability to fine-tune the level of sedation to suit each patient's specific needs. Whether a patient requires mild relaxation or deeper sedation, N2O-O2 can be adjusted accordingly. This adaptability ensures a tailored approach to patient care, promoting both safety and comfort.Another critical aspect of N2O-O2sedation is its safety profile. When administered by trained professionals who adhere to appropriate protocols, N2O-O2is considered a safe and reliable method of pain and anxiety management. The risk of overdose is low, and its effects dissipate rapidly after the gas supply is discontinued. Consequently, patients can often leave the healthcare facility shortly after the procedure, reducing the need for prolonged recovery periods. It is important to note here that N2O-O2sedation should be used with considerations. Healthcare providers must conduct thorough assessments to identify contraindications, ensuring that the technique is appropriate for each patient. Additionally, while side effects are typically mild and transient, they should be carefully monitored to maintain patient well-being.

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