Physiological Effects, Psychomotor Analysis, Cognition, and Recovery Pattern in Children Undergoing Primary Molar Extractions under Nitrous Oxide Sedation Using Two Different Induction Techniques: A Split-mouth Randomized Controlled Clinical Trial

Vineet Khinda1, Dinesh Rao2, Surender PS Sodhi3, Gurlal S Brar4, Nikhil Marwah5

ABSTRACT
Nitrous oxide inhalation sedation (NOIS) has been in use as a tool for pharmacological behavior modification and relative analgesia (RA) for well over 170 years now since its discovery in 1844 by the American Dentist Horace Wells. Advantages include raising of the pain reaction threshold, alteration of both pain sensitivity and pain reaction, reduction of fatigue, and time awareness that helps to handle stress and lengthy appointments. In addition, the most important clinical consequences of Nitrous Oxide (N2O) pharmacokinetics are rapid induction and recovery, reversibility, titrability, and adjustability. The goal of the current investigation was to analyze the safety aspects of nitrous oxide sedation. It was carried out on 25 patients within the age group 7–10 years requiring extractions of two primary molars in each patient. Split-mouth design was followed, with the first extraction done under traditional slow induction while the second extraction was done following the rapid induction technique of NOIS. N2O was studied for its physiological effects, psychomotor analysis was done, cognition and recovery patterns were analyzed utilizing the two different induction techniques. Based on the results obtained, it was found that N2O is a very safe and useful drug that delivers a comfortable patient for dental treatment.

Keywords: Cognition, Conscious sedation, Induction, Nitrous oxide, Oxygen, Psychomotor analysis, Rapid analgesia, Recovery.

INTRODUCTION
Delivery of dental care without causing adverse psychological impact upon the child is a challenge that all pediatric dentists face. One of the primary responsibilities of the dentist is to eliminate the anxiety and fear of the patient. Dental fear and anxiety (DFA) is experienced by many patients, which results in a considerable amount of stress in dentists who are under an obligation to treat such patients.1-3 In patients with severe DFA, the non-pharmacological methods may not work. Pharmacological methodologies which include sedation and general anesthesia (GA) may be the only way forward with such patients.4
‘Sedation and analgesia’ is a continuum of states and it ranges from minimal sedation (anxiolysis) through general anesthesia. The states have been defined by the American Dental anesthesia.5

In GA the patient’s cooperation is not essential for its success. The patient is unconscious, amnesia is present and there is no response to pain, and it may be the only technique that will prove successful for certain patients, such as medically compromised children. The disadvantages that limit its use are the depression of the vital signs and the protective reflexes (can cause laryngospasm). Also, the patient is unconscious which may not be the ideal requirement in certain situations. For administrating general anesthesia, special equipment, advanced training, and an ‘anesthesia team’ are required. Due to greater risks involved in elective GA procedures, laboratory tests, chest X-rays, and ECG are

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Nitrous oxide can be administered by two different techniques:

- Conventional slow induction
- Rapid induction

Conventional slow induction begins with the administration of 100% O₂. In children, a flow rate of 4–5 L/min (6–7 L/min in adults) is utilized to settle the minute volume followed by raises in the N₂O concentration of 5–10% for every 1–3 minutes. Generally, between 15 and 20% N₂O, first cortical signs of sedation are observed, referred to as baseline sedation. Adequate sedation and analgesia obtained for carrying out the dental procedure are usually achieved by administering around 30%–40% N₂O. An incremental increase of N₂O by 10% for every 3 minutes till a desired level of consciousness is generally considered safe, thus preventing unintended over sedation. However, the amount of time taken, and gases consumed during induction are a liability and can contribute to occupational hazards.

During rapid induction, concentrations of ≥50% N₂O are administered directly as a STAT dose in an uncooperative child till he/she gains his/her composure. After the child settles down, N₂O concentrations are appropriately adjusted either upward or downward.

The goal of the current investigation was to analyze the safety aspects of nitrous oxide sedation. The results and their interpretation could be a valuable addition to the one already available in literature and help the clinicians gain a better understanding of NOIS.

**Materials and Methods**

**Materials**

**Armamentarium**

A continuous flow type conscious sedation unit (World Wide Sedation, Unicorn Dentmart, Ltd), a finger pulse oximeter (Oxee Check™, Romsons, SN-113026 301212, Model-MD300C26), (Fig. 1), Trieger Dot Test cards (Appendix III) and Single Number Cancellation Test Sheets (Appendix II).

**Inclusion Criteria**

- Patients between ages 7–9 years.
- Patients requiring extractions of primary molars.

**Fig. 1:** Continuous flow sedation unit and pulse oximeter
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Exclusion Criteria
- Patients with upper respiratory tract infections i.e., cough, common cold, sinus problems (acute and chronic), chronic mouth breathing, bronchitis, and tuberculosis.
- Patients with compulsive personalities.
- Patients having claustrophobia.
- Patients who are not willing to undergo nitrous sedation.

Materials and Methods
A total number of 25 patients within the age group 7–10 years requiring extractions of two primary molars each were selected for the study. Parents/guardians were supplied with an informed consent form [Appendix I] to read, ask, understand and sign. A thorough health history of the subjects was recorded. In the first appointment for extraction, the induction was done by the traditional method of slow induction. Calculation of the minute volume is the first step and was achieved in the following manner. The flow of O₂ was started at 5 liters per minute (LPM), the nasal hood was positioned over the nose of the patient (Fig. 2), and the patient was reminded to breathe through nose. The hoses of hood were wrapped around the headrest and secured in place by adjusting the slip ring. Patient was enquired of any discomfort if present while breathing and was made comfortable. In case the patient had difficulty in breathing, the minute volume was be increased by one liter a minute. Patient was allowed to breathe 100% O₂ for 2 minutes as part of the preoxygenation procedure after which the titration of nitrous oxide was started. The titration was carried out at a rate of 0.5 mL of N₂O every 20 seconds. A similar decrease of 0.5 LPM of O₂ was done. The titration continued till adequate sedation was achieved. The flow of gases was maintained for few minutes. At the adequate sedation level, local anesthesia was administered, and the extraction was carried out.

When the same patient reported back for the extraction of another primary molar, rapid induction was done with a preadjusted mixture of 50% oxygen and 50% nitrous oxide. In both the groups, the physiological parameter evaluations (pulse and respiratory rates, blood pressure and oxygen saturation) for the patients were recorded in three stages, as follows: 1. P1 (presedation): the patient’s baseline physiological parameters when the patient was seated in the chair; 2. P2 (induction): measured after placing the mask and achieving the optimal titration with which to sedate the patient; 3. P3 (end): 5 minutes following the discontinuation of N₂O (at the end of postsedation oxygenation).

Psychomotor skill evaluation (Trieger Dot Test) was performed in two stages, 1. M1 (presedation): at the moment the patient was seated in the chair and 2. M2 (end): immediately upon the end of postsedation oxygenation of 5 minutes. Cognitive pattern evaluation including that of attention and concentration was done with help of Letter Cancellation Test. This was also carried out in two stages, 1. R1 (presedation): at the moment the patient was seated in the chair and 2. R2 (end): immediately upon the end of postsedation oxygenation of 5 minutes. Clinical record was maintained. (Appendix IV).

Results and Discussion
The present study was conducted in the Department of Pedodontology and Preventive Dentistry, Dasmesh Institute of Research and Dental Sciences, Faridkot, India with the goal to assess and compare for the parameters for physiological effects, psychomotor skills, cognition, and recovery pattern post nitrous oxide sedation in 25 children aged between 7 and 9 years. The same patients were subjected to two different techniques of induction, slow induction, and rapid induction, during separate appointments.

Statistical Analysis
The results are displayed in frequencies, percentages and mean ± SD. The Paired t-test was used to compare change in continuous variables. The Pearson correlation coefficient was calculated. The p-value < 0.05 was considered significant. Analysis was carried out on IBM SPSS version 23.0. The studied sample consisted of 13 males (52%) and 12 females (48%) with a mean age of 7.96 years (±0.84) Figure 3.

Usually the blood pressure is not influenced by the N₂O concentrations commonly used in ambulatory setting. In the present study, a statistically significant difference was found between the systolic blood pressure (SBP) and diastolic blood pressure (DBP) from presedation to induction and end (p = 0.0001) in both the groups. In group A, presedation SBP

Fig. 2: Placement of nasal hood

Fig. 3: Distribution of patients according to age and gender
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Changes in heart rate cannot be directly accredited to N₂O. However, as with blood pressure, as the anxiety is reduced, the heart rate may also decrease. Also, as part of the preoxygenation procedure, the patient is made to breathe hundred percent oxygen at the start of the procedure. Inhalation of hundred percent oxygen is connected with a slight fall in both heart rate (3–4 beats/min) and cardiac output (10%–20%). There was significant (p = 0.0001) mean change in pulse rate (PR) from preoxygenation to induction and end in both the groups. In Group A, presedation PR was 98.12 ± 6.05 which became 93.84 ± 3.68 at induction and 93.44 ± 3.66 at the end. In Group B, presedation PR was 97.44 ± 5.71 which became 92.44 ± 3.67 at induction and 93.44 ± 3.66 at the end. Figure 4.

Bloch M found that the fall of blood pressure, reduction of the heart rate, and loss of muscle tone may be produced by N₂O when it is used in surplus of a 50% mixture with O₂. In case the blood pressure readings lie within 10 mm Hg (both systolic and diastolic) compared with preoperative readings, these are deemed to be within a range regarded as acceptable. Similarly, postoperative PR within 10 beats and respiration rate (RR) within 5 breaths are acceptable parameters for comparison.

There was significant (p = 0.0001) mean change in RR from preoxygenation to induction and end in both the groups. In Group A, the presedation RR was 18.96 ± 0.73 which became 18.00 ± 0.40 at induction and 18.12 ± 0.44 at the end. In Group B, the presedation RR was 18.60 ± 0.81 which became 17.68 ± 0.90 at induction and 17.68 ± 0.74 at the end. N₂O does not irritate the pulmonary epithelium. Variations in RR or depth are possibly a result of the reduction in anxiety due to sedation (slower, deeper) or as the excitement stage approaches (Guedel anesthesia stage 2) (rapid, shallow); direct action of N₂O on the respiratory system is not the reason.

In Group A, the presedation SpO₂ was 98.80 ± 0.45 which became 99.76 ± 0.43 at induction and 99.08 ± 0.27 at the end. In Group B, the presedation SpO₂ was 98.78 ± 0.45 which became 99.79 ± 0.43 at induction and 99.06 ± 0.27 at the end. In both the groups, there was significant (p < 0.01) mean change in SpO₂ from preoxygenation to induction and end. There was no significant (p > 0.05) difference in SpO₂ between Group A and Group B at both time periods.

Improved oxygen saturation can be attributed to the fact that in addition to N₂O, the patient is flooded with a very high concentration of O₂ throughout the procedure. This included 100% O₂ delivery at the start and termination of procedure. Even at its worst, when the patient is receiving N₂O as high as 70%, at 30%, the patient is still receiving O₂ which is approximately 1.5 times that of the one which is being breathed through the atmospheric air (20.9%) (Fig. 5).

Trieger Test is a useful measure in ascertaining recovery from sedation. It evaluates patient’s motor coordination, it being an objective measurement of the patient’s capability to execute fine motor movements. The patient is instructed to carefully

Fig. 4: Comparison of hemodynamic parameters from preoxygenation to induction and end
join all the dots on a figure. Based on the number of dots that are missed completely, the scoring of the test is decided. Time taken and general quality of the lines are also factored in. Five dots missed preoperatively while seven missed after sedation is not significant.25 There was no significant (p > 0.05) mean change in number of dots missed from presedation to end in both the groups. In group A, the presedation number of dots missed was 3.80 ± 1.29 which became 4.36 ± 1.70 at the end. In group B, the presedation number of dots missed was 3.68 ± 1.10 which became 4.12 ± 1.74 at the end. There was no significant (p > 0.05) mean change in number of dots missed from presedation to end. There was no significant (p > 0.05) different in number of dots missed between group A and group B at both the time periods.16–19 Positive results obtained for this test of psychomotor analysis during recovery from sedation indicates good recovery of the patients’ perceptual-motor ability and return to their own pre-anesthetic baseline (Fig. 6).

The presence and severity of visual scanning deficits is evaluated with the Single Letter/Number Cancellation Test (SLCT) (Fig. 7). Otherwise known as Visual Perceptual Motor Deficit, Visual Perceptual Disorder affects a child's ability to understand visual information. The score is calculated by subtracting the number of omissions (3’s that were not crossed out) from the possible perfect score of 124. Higher scores indicate better performance. Omissions of four or more have been found to be pathological.20–24 The group A presedation net score was 120.24 ± 2.55 which became 118.04 ± 5.10 at the end. The group B presedation net score was 119.96 ± 2.40 which became 117.24 ± 3.71 at the end. There was no significant (p > 0.05) different in net score between group A and group B at both the time periods. Also, there was no significant (p > 0.05) correlation of number of dots missed with net score at presedation and end.

The omissions were found to be within the acceptable limit of 4 dots in both groups. Also, there was absence of statistically significant difference in the net score between the two groups. These parameters indicate that good recovery took place in both the groups regarding the cognitive pattern, attention and concentration and absence of any visual scanning deficits. The discharge was uneventful as well. Only two of the patients missed 8 dots each and were provided with additional O2 for 5 minutes after which the test was repeated and was found satisfactory.

**Conclusion**

Based on the results obtained in this study, the following conclusions can be drawn:

There was a significant drop between the systolic and diastolic blood pressure, mean heart and respiratory rates from presedation to induction and end. The decreased blood pressure resulting from relaxation lowered anxiety provided by N₂O coupled with preoxygenation is of major benefit when providing dental treatment to hypertensive patients. Drop of heart and respiratory rates is attributable to the relaxation and decrease of anxiety that the N₂O produces and is not a direct result of the drug itself. The significant improvement in the mean change in SpO₂ from presedation to induction and end can be attributed to the fact that in addition to N₂O, the patient is flooded with very high concentration of O₂ throughout the procedure. Oxygen is a universal drug in majority of emergencies encountered in dental setting and good SpO₂ lessens the chances of the patient landing in an emergency during the course of the treatment. The patients had good recovery postsedation. The good of recovery was verified by the positive results of the tests for psychomotor skill evaluation and cognitive pattern evaluation. The discharge was uneventful. Based on the present study, it can be
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APPENDIX I

Informed Consent for N₂O-O₂ Sedation

I understand that my child’s treatment today will include the procedure of N₂O-O₂ administration.

I, ____________, have been informed of the purpose of the procedure and how it will benefit my child’s treatment. The procedure has been described to me and I understand how it will be accomplished. My child should feel more relaxed and less anxious.

I understand that certain risk(s) may be associated with this procedure, such as headache, dizziness, nausea, and vomiting. Some patients at high levels of N₂O can experience dreaming and hallucinations. I understand the risk(s) associated with this procedure and I further understand the risk(s) that may occur if the procedure is not completed.

I also realize that my child’s doctor must know if my child has taken any type of medication or drugs within the past seventy-two (72) hours because these may cause an adverse reaction when N₂O-O₂ is administered. I verify that I have told my child’s doctor about any such medication and drugs.

I have been informed of the alternatives to N₂O-O₂ sedation and their associated risks. I have also been informed that all the expenses of the dental procedures will be taken by the concerned doctor. All of my questions and concerns have been satisfactorily answered and addressed.

Therefore, I give my informed consent to the administration of N₂O-O₂ sedation to my child and agree to hold harmless, release, and indemnify agents, servants, students, and employees of the office/clinic of ____________ from any and all causes of action, claims, demands, or liability that may arise out of such treatment on behalf of myself, my heirs, my executors, administrators or assigns; or on behalf of my minor child or children or his/her (their) heirs, executors, administrators or assigns.

Signed: __________________________ Date: __________________________
Witness: __________________________ Date: __________________________
**APPENDIX II**

**Single Number Cancellation Test**

| Name: ___________________ | Date: _______________
| Session: ___________________ |
| Target Number: 3 |
| Instruction: Cancel the above number with a slash in the given text, at your maximum speed. |

**Maximum Possible Score: 124**

1 2 3 4 5 6 7 8 9 10 11 12
13 14 15 16 17 18 19 20 21 22 23 24
25 26 27 28 29 30 31 32 33 34 35 36
37 38 39 40 41 42 43 44 45 46 47 48
49 50 51 52 53 54 55 56 57 58 59 60

| Clinical Record |
|-----------------|
| Date: __________ | Patient: __________ | Age/Gender: __________ |
| ASA Classification: I II III IV |
| FRANKL Behavior Rating Scale: I II III IV |
| Medical Consultation Needed: Yes/No |
| Operative Procedure: __________ |
| Procedural Data: |
| BP: __________ __________ __________ |
| Pulse rate: __________ __________ __________ |
| Respiration rate: __________ __________ __________ |
| O₂ Saturation (%): __________ __________ __________ |
| N₂O Start Time: __________ | N₂O Finish Time: __________ |
| Length of Procedure: __________ |
| Titration % of N₂O: __________ | Postoperative O₂ __________ (In minutes) |
| Comments: __________ |