Oxygen saturation and diffusion hypoxia in children following nitrous oxide sedation

Tamara Dunn-Russell, DMD   Steven M. Adair, DDS, MS   Deirdre R. Sams, DDS, MS
Carl M. Russell, DMD, MS, PhD   James T. Barenie, DDS, MS

Abstract

Oxygen saturation of arterial blood (SaO_2) was assessed in children after discontinuing N_2O/O_2 sedation for dental procedures. Two post-treatment methods were used: breathing 100% O_2 for 5 min after the procedure, and breathing room air for 5 min. Participants were 24 healthy children ages 41 to 113 months. Each child was treated twice and a crossover design was used. The mean length of procedures that were followed by O_2 was 28.8 (± 10.9 SD) min; for those followed by room air, 28.3 (± 12.4 SD) min. SaO_2 was monitored continuously by pulse oximetry and recorded at predetermined intervals before, during, and after N_2O/O_2 administration. When participants received post-treatment O_2, the mean SaO_2 at 1 min after N_2O cessation (99.91 ± 0.63 SD) and 5 min after cessation (99.94 ± 0.17 SD) was statistically significantly higher than the pretreatment value of 99.28 (± 0.63 SD). When participants received post-treatment room air, the mean SaO_2 1 min after N_2O cessation (99.44 ± 0.8) was also statistically significantly higher than the pretreatment mean (99.08 ± 0.96). After 2 min, however, the mean SaO_2 decreased and was statistically indistinguishable from the pretreatment level after 5 min (99.13 ± 0.9 SD). Fluctuations in SaO_2, though statistically significant, were less than 1%. Allowing children to breathe room air immediately after cessation of N_2O/O_2 inhalation did not reduce SaO_2 below clinically acceptable levels. This study further documents the safety of N_2O/O_2 sedation, and gives the clinician additional information concerning the safe and effective administration of inhalation sedation. (Pediatr Dent 15:88–92, 1993)

Introduction

Nitrous oxide (N_2O) has long been a valuable analgesic in both adult and pediatric dental practice. In pediatric practice, N_2O/O_2 is especially effective when caring for mildly to moderately anxious children. Numerous reports have confirmed its ease of administration, wide margin of safety, analgesic and anxiolytic effects, and rapid reversibility.[1-5]

The adverse side effects of N_2O/O_2 analgesia, which appear to be minor, include intra-administration dreams and postadministration headache, nausea, vomiting, and possibly diffusion hypoxia.[5, 6] Side effects were not common in work reported by Hogue et al.[5] Although Houck and Ripa[7] reported vomiting with N_2O use in 8% of children studied, they concluded that some of these children had a tendency to vomit regardless of exposure to N_2O. According to Langa,[8] the most undesirable side effect of N_2O/O_2 administration was nausea and vomiting, but the incidence of these conditions was less than 1%.

Diffusion hypoxia, frequently discussed as a possible untoward respiratory consequence of N_2O/O_2 use, reportedly accounts for most occurrences of headache, nausea, and lethargy after N_2O/O_2 sedation as employed in dentistry.[9] Hypoxia theoretically occurs when N_2O administration is discontinued and the absorbed N_2O diffuses out of the blood and into the alveolar spaces. Because N_2 is less soluble in blood than the N_2O that replaced it, the uptake of N_2 into the blood occurs more slowly than the excretion of N_2O. This dilutes alveolar oxygen and potentially lowers the oxygen saturation of arterial blood (SaO_2).[3]

The greatest excretion of N_2O occurs in the first 3 – 5 min following cessation of administration.[9] In standard clinical practice, 100% O_2 is administered during this period, ostensibly to prevent diffusion hypoxia.

Fink[10] first reported the principle of diffusion hypoxia in 1955 after an in-vitro experiment and a clinical study in which SaO_2 dropped an average of 8% in eight healthy gynecologic patients who received anesthesia and recovered in room air. Anesthesia included endotracheal intubation for administration of 75% N_2O in O_2 and intravenous administration of 2.5% thiopental. Fanning and Colgen[11] concurred with Fink after demonstrating a clinically significant drop in SaO_2 after administering 75 % N_2O and thiopental to both animals and humans. The level of N_2O used in these studies is considerably higher than that typically used in dentistry. Quarnstrom and coworkers[12] stated that the results of these studies could be explained by the compromising effects of thiopental, which is known to cause respiratory depression in some patients.

Numerous studies have questioned whether diffusion hypoxia is clinically significant. Frumin and Edelist,[13] who found that alveolar dilution caused by N_2O diffusion in healthy patients produced clinically insignificant changes in SaO_2, concluded that diffusion hypoxia did not occur clinically. In their study, 18 surgical patients were changed from breathing 79% N_2O to room air. Arterial blood was withdrawn periodically and blood gas determinations were made by radiometer electrode. Of the patients with-

out respiratory obstruction, only two demonstrated SaO_2 values < 90%, but persistent significant shunting was suspected in those cases. Other studies also have concluded that diffusion hypoxia is clinically insignificant when respiratory ventilation is adequate.[14-17]

In a study of 42 children who underwent minor outpatient surgery, the ratio of N_2O to O_2 was as high as 70%, but no clinically significant episodes of hypoxia were observed.[18] We are unaware of published studies assessing hypoxia attributed to N_2O administration in children undergoing routine dental care. When N_2O is used in outpatient dental care, drugs other than local anesthetics rarely are administered, and the ratio of N_2O to O_2 is lower than that used in general anesthesia. Quarnstrom and coworkers[12] noted that for these reasons, the use of N_2O in surgery is not directly comparable to its use in outpatient dental care. Their study of adult dental patients indicated that diffusion hypoxia is extremely rare; no cases occurred among 104 adults (95% confidence interval upper limit, 2.84%).

To assess the significance of hypoxia attributed to N_2O diffusion and elimination in pediatric dental patients, we compared two methods of discontinuing N_2O/O_2 administration: 1) breathing 100% O_2 for 5 min after the procedure and, 2) breathing room air for 5 min.

Methods and materials

Clinical procedures

We recruited 24 children ages 41 to 113 months (mean 67.2 ± 20 SD months) from the Medical College of Georgia Hospital and School of Dentistry Clinics. All children were healthy, ASA Class I patients who required at least two visits for completion of dental treatment and who were scheduled to receive N_2O/O_2 analgesia for mild to moderate anxiety. Procedures were expected to last less than 60 min. The parents were fully informed and gave written consent for their children to participate in the study, which met all requirements of the institution's Human Assurance Committee. Parents were instructed not to give the children anything by mouth for at least 2 hr prior to the procedure to reduce the risk of nausea and vomiting.

Dental treatment was rendered by five pediatric dental residents who were calibrated in administration of N_2O/O_2. N_2O was administered to a maximum concentration of 40% in O_2 using a Fraser MDM® N_2O/O_2 machine and scavenging nasal mask (Matrix Medical, Inc., Orchard Park, NY). The flow rate was individually adjusted to maintain proper reservoir bag inflation. The gas mixture was adjusted from 100% to a minimum of 60% O_2 in 10% increments; each step lasted at least 20 sec. At the end of the procedure, the patient recovered in room air or O_2 based on prior random assignment in a crossover design. Because of the narrow criteria for entry into the study (mild to moderate anxiety), behavior was not a factor in the randomization scheme. When O_2 was to be received, the reservoir bag was flushed and the flow immediately

changed to 100% O_2. When room air was to be received the flow of gases was discontinued, and the mask was removed. The reservoir bag was flushed with O_2 and the mask was retained close to the patient for emergency use.

Oxygenation of each patient was monitored throughout the procedure by using a Nellcor N-100® pulse oximeter (Nellcor, Inc., Hayward, CA) with the probe attached to the index finger. SaO_2 was recorded at 30-sec intervals five times before the nasal mask was placed. During the procedure, SaO_2 was recorded at 5-min intervals. At the end of the procedure, the SaO_2 was recorded for 5 min at 15-sec intervals. Recording was done by one of three individuals who did not know the post-treatment procedure being used. Parents were instructed to report any post-treatment symptoms that might indicate adverse effects of sedation.

Statistical analysis

We analyzed five, three, and 21 measurements from periods before, during, and after N_2O/O_2 administration, respectively. Only the first three measurements taken during sedation were used because for several patients the procedures required only 10 min. For each patient, the mean measurement was calculated for the first two periods (before and during) and for each 1-min subdivision of the third period (after), for a total of seven mean values.

Summary statistics by post-treatment method were generated. One-sample t-tests were employed to evaluate the differences in SaO_2 between each post-treatment measurement (minutes 1–5) and the pretreatment value within each method (N_2O or room air). The crossover design allowed the use of one-sample t-tests of the differences in the differences between pretreatment and post-treatment SaO_2 values across the two post-treatment methods. To detect experimental design problems, analysis of variance was used to test for differences by method in SaO_2 before and during treatment. Analysis of covariance was used to test for the effect of method on the response values recorded after treatment, while controlling for the values before treatment, the crossover design, and the length of the procedure.

Results

Procedures lasted from 10 to 60 min. The mean procedure length when O_2 was used postoperatively was 28.8 (± 10.9 SD) min and 28.3 (± 12.4 SD) min when room air was used. The difference by post-treatment method in mean length of procedure was not statistically significant. Fig 1 displays frequency distributions of the numbers of subjects by procedure length for each post-treatment method. A preliminary model (using analysis of covariance) evaluating the effect of procedure duration indicated no significant effect ($P > 0.25$). The N_2O delivery protocol employed in this study ensured that administration of N_2O was consistent for all procedures.

The mean and standard deviation of the SaO_2 was determined for each study segment by post-treatment

method (Fig 2). The mean difference between each post-treatment value and the pretreatment value is given in the Table for both post-treatment methods. When O_2 was used postoperatively, all differences between the pretreatment SaO_2 level and the given post-treatment levels were significantly different from zero (Table). When room air
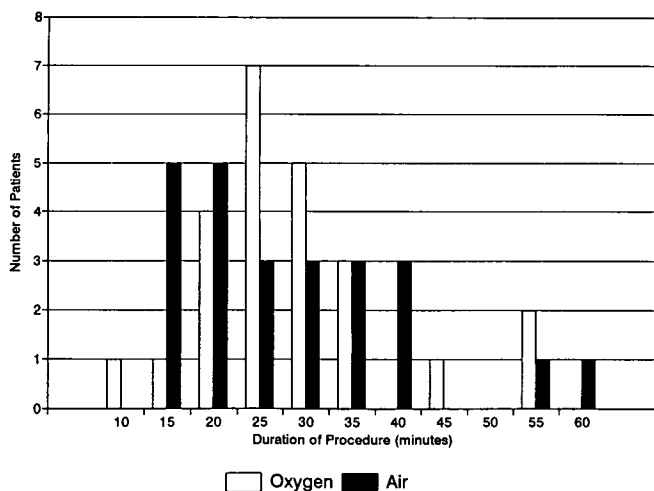

Fig 1. Distribution of numbers of children by duration of procedure for each post-treatment method.
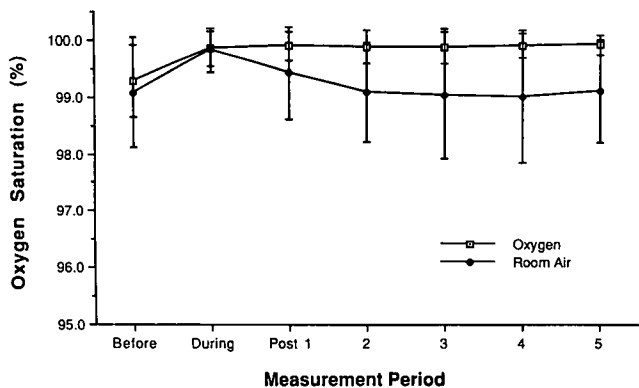

Fig 2. Mean oxygen saturation of patients before, during, and after breathing nitrous oxide/oxygen by post-treatment method. Error bars indicate standard deviation.

was used, the pre- and post-treatment SaO_2 levels were significantly different only for the first post-treatment minute; subsequent post-treatment levels returned to baseline. The actual post-treatment levels for the two methods were also compared. The first post-treatment values were not significantly different between the two methods; subsequent values were significantly higher for the O_2 post-treatment method. The post-treatment SaO_2 levels for the O_2 method were equivalent to levels observed during the dental procedure. The mean post-treatment SaO_2 values for the room air method did not drop below the mean pretreatment values. No parents reported adverse post-treatment signs or symptoms. All patients met the criteria outlined by the American Academy of Pediatric Dentistry for discharge following sedation.[20]

Analysis of variance detected no group effect on SaO_2 before and during treatment ($P > 0.22$; $P > 0.31$). The results of analysis of covariance were consistent with those of the paired t-test of the differences (Table), and offered no additional insight into the data. These analyses were performed to detect design and randomization problems in our study. None was found. Because duration of procedure was not a significant factor, only the t-tests are reported.

Discussion

SaO_2 did not drop below 95% for any measurement taken during any procedure. Our results suggest that hypoxia attributed to N_2O elimination and diffusion may not be clinically significant for healthy pediatric dental patients, whether they receive room air or oxygen postoperatively. None of the untoward clinical side effects of diffusion hypoxia and N_2O/O_2 sedation after dental procedures were reported when room air was breathed. The crossover design controlled for any differences in behavior between the post-treatment group assignments, because every patient received both post-treatment methods. Assuming that no child's behavior changed drastically, the effect of behavior and any other transient confounders were controlled by the experimental design. If, in fact, there was a learning effect, this also was controlled by the random assignment of patients to room air or O_2 as the first or second treatment session. A preliminary analysis

Table. Mean (SD) difference in oxygen saturation between pretreatment and five post-treatment periods

Minutes After Cessation of N_2O	Post-treatment Method							
	Oxygen		P value*	Room Air		P value*	Difference		P value*
1	0.63	(0.65)	0.0001	0.37	(0.77)	0.0284	0.26	(0.91)	0.1797
2	0.61	(0.70)	0.0003	0.03	(0.83)	0.8640	0.58	(0.95)	0.0064
3	0.61	(0.69)	0.0002	−0.02	(0.83)	0.8939	0.64	(1.02)	0.0058
4	0.64	(0.62)	0.0001	−0.04	(0.88)	0.8107	0.69	(1.00)	0.0026
5	0.65	(0.62)	0.0007	0.05	(0.72)	0.7370	0.60	(0.88)	0.0026

* P values from paired t-test.

detected no effect for session order. Crying was a rare event, and behavior did not affect the N_2O delivery protocol. The large standard deviations in the raw SaO_2 scores (Fig 2) indicate that no child was in danger of hypoxia.

When children breathed 100% O_2 postoperatively, post-treatment SaO_2 was higher than their preoperative level. When children breathed room air postoperatively, no difference in SaO_2 was noted between the pretreatment level and the second or later post-treatment measurement. Thus, the SaO_2, which reached a mean of nearly 100% during the procedures, rapidly returned to the pretreatment level when patients breathed room air.

The 5-min monitoring period after N_2O cessation was sufficient to include the excretion of 99% of the inspired N_2O.[9] In studies that have reported diffusion hypoxia, it occurred during the first 4 min in the majority of cases.[10, 11] It is possible, though unlikely, that SaO_2 could have continued to decline after 5 min of breathing room air. Reported drops in SaO_2 of 5 to 10%[10] lasting several minutes should be detectable by the Nellcor® pulse oximeter. Young et al.[21] reported pulse oximeter response times of 17 to 150 sec in detecting a sudden 10% decrease in SaO_2. The mean reaction time of the Nellcor oximeter with a finger probe to this change was less than the mean reaction time for the 11 oximeters tested. We are confident that measurements every 15 sec over the 5-min post-treatment period would have detected significant diffusion hypoxia.

The duration of treatment and concentration of N_2O were typical of pediatric dental procedures. The concentration of N_2O in O_2 used in dentistry is generally low compared with that used for general anesthesia, in which higher levels of N_2O are often combined with other drugs that may have synergistic or independent effects on the physiology of respiration. Diffusion hypoxia was not found to be a problem at the N_2O levels used in this study, which were consistent with pediatric dental practice and considered optimal for most patients.[9]

These findings are not meant to convince clinicians to discontinue the use of oxygen in the immediate post-treatment period. In fact, use of a scavenging system that removes expired gas before it enters the office environment is an indication for post-treatment O_2 administration by nasal mask. The importance of this study lies in its additional documentation of the safety of N_2O/O_2 sedation.

Conclusions

1. SaO_2 did not fall below 95% at any measurement.
2. During N_2O/O_2 administration, mean SaO_2 increased slightly but statistically significantly from baseline levels to nearly 100%.
3. Mean post-treatment SaO_2 was sustained at nearly 100% when participants breathed 100% O_2.
4. When participants breathed room air postopera-

tively, the mean SaO_2 at the second post-treatment minute and the mean pretreatment value did not differ, which indicates that no clinically detectable diffusion hypoxia occurred.
5. No untoward effects were reported by any participant regardless of the post-treatment method (O_2 or room air).

Dr. Dunn-Russell is in private practice in Atlanta, Ga. Dr. Adair is associate professor and chairman, Dr. Sams is assistant professor, and Dr. Barenie is professor, Department of Pediatric Dentistry, Medical College of Georgia, Augusta, Ga. Dr. Russell is statistician, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control, Augusta, Ga.

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