

# Clinical Study of Diffusion Hypoxia After Nitrous Oxide Analgesia

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In order to estimate the incidence of diffusion hypoxia, arterial oxygen saturation was measured in 104 healthy adult dental patients who were administered nitrous oxide-oxygen analgesia and who did not receive postcessation oxygen. Pretreatment saturation levels as determined by pulse oximetry ranged from 93% to 100%. When the nitrous oxide-oxygen administration ceased, the saturation levels were from 95% to 100%. The mean saturation dropped about 2% over the next 4 min and then stabilized. No patient had a posttreatment oxygen saturation of less than 92%.

**I**t is standard clinical practice to deliver 100% oxygen for 3 to 5 min to dental outpatients to prevent diffusion hypoxia after the termination of nitrous oxide-oxygen analgesia.<sup>1</sup> Diffusion hypoxia occurs when excess nitrous oxide diffuses out of the blood and displaces the oxygen in the lungs, resulting in a drop in the oxygen saturation of arterial blood (SaO<sub>2</sub>).<sup>2</sup>

This phenomenon was first demonstrated by Fink<sup>3</sup> in the laboratory and subsequently observed in eight healthy gynecologic patients undergoing endotracheal anesthesia using 75% nitrous oxide (N<sub>2</sub>O) in oxygen (4 L/min) supplemented with intravenous thiopental. Fink reported an average 8% drop in SaO<sub>2</sub> when the patients were switched to room air. On the other hand, Selim, Markello, and Baker<sup>4</sup> showed only an average 2% drop in SaO<sub>2</sub> at 2 min post-N<sub>2</sub>O when 79% N<sub>2</sub>O was used but ventilation was maintained. It is likely the results of Fink represent respiration compromised by thiopental. Fanning and Col-

gan,<sup>5</sup> first in dogs and then in humans, demonstrated larger drops in oxygen tension during N<sub>2</sub>O washout after anesthesia with 75% N<sub>2</sub>O, again combined with other agents. Most reports,<sup>6,7</sup> however, have argued that even very high levels of N<sub>2</sub>O do not lead to clinically significant hypoxemia in healthy patients who maintain normal ventilation.

We feel the cases in medicine are not directly comparable to use of N<sub>2</sub>O in outpatient dental care because no supplementary drugs are usually given in the latter situation, the concentrations of N<sub>2</sub>O used are much lower, and the typical dental nitrous delivery system itself overestimates the true blood concentration. Thus, we hypothesized that significant diffusion hypoxia is unlikely in this setting. Nonetheless, we are unaware of any published clinical case reports from the dental office, so we conducted a clinical trial to estimate the incidence and consequences of the phenomenon.

## METHODS

The subjects in the study were 104 volunteer adult patients in the community general dental practice of the senior author (FQ). The mean age of the subjects was 36.4 years (SD = 11.2 years). Forty-two percent of the subjects were male. Ninety percent of the subjects were American Society of Anesthesiologists physical status classification 1, and the remainder were class 2. Of 104 subjects, 18 were smokers, with 1- to 30-year smoking histories. One patient was excluded because of significant respiratory disease. Subjects were screened for alcoholism but none was excluded based on a 20 drinks per week cutoff.

An Ohmeda 3700 pulse oximeter with a photoelectric probe placed on the finger was used to measure SaO<sub>2</sub>. The saturation levels were recorded continuously on a Biox 2100 chart recorder for the first 40 patients. The recordings were divided into 10-sec intervals, and the lowest readings for each interval were recorded to arrive

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at SaO<sub>2</sub> values for premedication, conclusion of treatment, and removal of the mask phases, and at 30-sec intervals for 5 min posttreatment. In the remaining patients, the lowest SaO<sub>2</sub> reading during 30-sec intervals by treatment phase was recorded manually from the LED readout on the pulse oximeter.

Subjects received N<sub>2</sub>O analgesia in conjunction with outpatient dental care. Nitrous oxide and oxygen were delivered using a single machine (Bird Nitrous Oxide Oxygen Blender) utilizing a semi-closed circuit. In this system, exhaled gas mixes with fresh gas (1.5 L/min) and is re-breathed. The circle included a carbon dioxide absorber, which was vented to the central vacuum. The subject was seated, the mask placed, and the N<sub>2</sub>O was then titrated to effect. At the conclusion of dental treatment, the N<sub>2</sub>O was discontinued and the mask removed. No supplementary oxygen was given. The subject remained in the dental operatory for the remaining 5 min and was instructed to sit quietly. At the conclusion of the study, patients were questioned regarding side effects of the medication.

## RESULTS

Nitrous oxide analgesia was administered at an average concentration of 35.6% (range 10–50%) for periods from 3 to 98 min. The average treatment lasted 21 min.

Pretreatment SaO<sub>2</sub> levels ranged from 93% to 100% (mean = 97%). At the conclusion of N<sub>2</sub>O delivery, SaO<sub>2</sub> values ranged from 95% to 100% (mean = 98%). The mean SaO<sub>2</sub> level dropped about 2% over the next 4 min and stabilized. No patient had a posttreatment SaO<sub>2</sub> below 92%.

When questioned at the conclusion of the appointment, 11 of 104 subjects reported side effects of the medication, including light-headedness (7), dizziness (2), decrease in respiration (1), and a sense of impending unconsciousness (1), all of which we interpret as typical effects of the drug.

Given that no patient experienced diffusion hypoxia, it is possible to develop a confidence interval for the probability of experiencing diffusion hypoxia after N<sub>2</sub>O analgesia. Such a confidence interval would run from a lower limit of zero to an upper limit that depends on the confidence level specified and the number of patients observed.\*

\* The upper limit,  $p_u$ , for a  $100(1 - \alpha)\%$  confidence interval can be defined as the largest probability of diffusion hypoxia in a single patient such that the cumulative probability of having zero occurrences in  $n$  patients is less than or equal to  $\alpha$ . For a 95% confidence interval, the upper limit can be found as the solution to the equation

$$(1 - p_u)^n = 0.05$$

so that  $p_u = 1 - (0.05)^{1/n}$

For the observed sequence of  $n = 104$  patients, the upper limit of the confidence interval equals 0.0284, so that a 95% confidence interval for the incidence of diffusion hypoxia runs from 0% to 2.84%.

As additional experience accumulates without an episode of hypoxia, the upper limit for the 95% confidence interval will approach (but never equal) zero at the following rate:

$n$ = number of N <sub>2</sub> O cases observed without a diffusion hypoxia episode	$p_u$ = upper 95% confidence limit for probability of diffusion hypoxia
104	0.0284 (2.84%)
200	0.0148 (1.48%)
500	0.0060 (0.60%)
750	0.0040 (0.40%)
1000	0.0030 (0.30%)

Thus, as more cases are observed without any episode of diffusion hypoxia, the corresponding upper limit can be taken as a conservative estimate of the occurrence of this event.

## DISCUSSION

The results of this study suggest that significant diffusion hypoxia appears not to be a clinically frequent event for normal, healthy adults treated without adjunctive drugs in a community practice delivering routine dental care. Thus, the inhalation of 100% oxygen for 3 to 5 min following cessation of N<sub>2</sub>O at the concentrations used in this study appears unnecessary. Instead, careful observation of patients during the first few minutes postoperatively is appropriate. As oxygen saturation stabilized in all patients within 4 min of the removal of the mask, any respiratory problems that occurred could then be managed conservatively. This is consistent with the recommendations of Fanning and Colgan<sup>5</sup> in that N<sub>2</sub>O is being used alone and such patients are not prone to respiratory irregularities associated with other anesthetic drugs. The empirical results are also consistent with our theoretical calculations. Extrapolating from data published by Sheffer, Steffenson, and Birch,<sup>8</sup> at 50% N<sub>2</sub>O and a 5 L/min volume for spontaneously breathing patients, there would be a 2% to 3% drop in alveolar oxygen tension during washout. This would leave an oxygen saturation well above the level at which clinical hypoxemia develops.

In the normal, healthy patient with a baseline SaO<sub>2</sub> of 95%, a drop of 10% in saturation would not produce clinically apparent hypoxemia. Thus, even the drop to 88% SaO<sub>2</sub> seen by Fink<sup>3</sup> following 75% N<sub>2</sub>O plus thiopen-

tal would not be expected to produce clinically meaningful hypoxemia in dental patients. Certainly, given the use of no more than 50% N<sub>2</sub>O in healthy, otherwise unmedicated patients, postcessation oxygen seems unnecessary.

The benefit associated with postcessation oxygen is minimal in the healthy patient. Our data support the theoretically low risk of not providing postcessation oxygen. Our statistical analysis also suggests that published reports of additional cases from other settings, following a similar protocol, are needed.

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