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# *Effect of Nitrous Oxide on the Oxyhemoglobin Dissociation Curve and $P_{O_2}$ Measurements*

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**Blood from 20 ASA physical status I patients collected before and after induction of anesthesia was used *in vitro* to reexamine the effects of nitrous oxide on the oxyhemoglobin dissociation curve and the response of the oxygen electrode. The preinduction $P_{50}$ values with and without 70% $N_2O$ were 28.4 ± 0.1 mmHg and 26.8 ± 0.1 mmHg, respectively. The postinduction $P_{50}$ values with and without $N_2O$ were unchanged, namely 28.4 ± 0.1 mmHg and 26.8 ± 0.1 mmHg, respectively. Our data confirm the observation that $N_2O$ causes a small elevation of $P_{50}$ ($P < 0.001$) and that this effect is both rapidly inducible and reversible. Our results also indicate that $N_2O$ has no effect on polarographic $P_{O_2}$ measurements. (Key words: Anesthetics, gases: nitrous oxide. Blood, hemoglobin: oxyhemoglobin dissociation; oxygen saturation. Measurement techniques: electrode; oxygen. Oxygen: oxyhemoglobin dissociation ($P_{50}$); oxygen saturation; tension.)**

$N_2O$ IS THE MOST commonly used inhalational anesthetic today. Data on the effects of $N_2O$ on the oxyhemoglobin dissociation have been conflicting. In 1970, Smith *et al.*[1] studied the effects of $N_2O$ on $P_{50}$ and showed that there is a small increase in $P_{50}$ (shift to the right). In 1984, Fournier and Major[2] reported a 9 mmHg decrease in $P_{50}$ (shift to the left) when blood samples were treated with $N_2O$. Fournier and Major also indicated that in the presence of $N_2O$, $P_{O_2}$ values were falsely increased. If $N_2O$ truly interferes with $P_{O_2}$ measurements and decreases $P_{50}$ to 18 mmHg, as reported by Fournier and Major, it could have impact on critically ill patients in whom $N_2O$ is used as an anesthetic adjunct. In addition, this could complicate studies where oxygen consumption, $P_{O_2}$, and oxygen content of blood are measured in the presence of $N_2O$. Accordingly, we reexamined the effects of nitrous oxide on the oxyhemoglobin dissociation curve and on polarographic $P_{O_2}$ measurements.

## Methods

With the approval of the Committee for the Protection of Human Subjects, we included in our study 20 ASA physical status I patients who were to receive balanced anesthesia with iv fentanyl, 70% $N_2O$, and 30% $O_2$. Venous blood samples were drawn from each of these patients before anesthesia was induced and 1 h after anesthesia had been maintained with 70% $N_2O$ and 30% $O_2$. Each of the preinduction blood samples was equilibrated in an IL 237 Tonometer® with: 1) gas mixtures containing 3.5% $O_2$, 4% $O_2$, and 4.5% $O_2$, with 5.6% $CO_2$ and balance $N_2$; and 2) similar gas mixtures in addition to 70% nitrous oxide for 15 min at 37° C. The samples collected during anesthesia were equilibrated with the same gas mixtures but in reverse order, *i.e.*, those containing $N_2O$ first. These certified gas mixtures were supplied by MG Industries, scientific gases (Valley Forge, PA) and were tested by us using a mass spectrometer (SARA, Chemetron, Medical Division, St. Louis, MO). At the end of each equilibration, total hemoglobin (Hb), oxyhemoglobin saturations, and carboxyhemoglobin (COHb) were measured in a Radiometer OSM2 Hemoximeter® (determination of COHb levels were done in Radiometer, OSM2 Hemoximeter® by using Radiometer 904212 deoxygenation capillary kit), and blood gases were measured in a Corning® 168 *p*H/blood gas analyzer. The Radiometer OSM2 Hemoximeter® and *p*H, $P_{CO_2}$, and $P_{O_2}$ electrodes of Corning® 168 *p*H/blood gas analyzer were calibrated before and after each set of measurements. The measured $P_{O_2}$ data were corrected to *p*H 7.40 using the Severinghaus formula.[3] Because the carbon dioxide tension in the gas mixtures was uniformly 40 mmHg and the blood gas measurements were done at 37° C, no $P_{CO_2}$ or temperature corrections were needed. A three-point saturation curve was plotted in the linear portion of the oxyhemoglobin dissociation curve and $P_{50}$ was obtained for each sample.

Before we proceeded with a $P_{50}$ measurement of each blood sample, we equilibrated 2 ml of the blood with 100% $N_2O$ as well as with a gas mixture containing 50% $N_2O$ and balance $N_2$ for 15 min at 37° C. At the end of each equilibration, blood gases and $O_2$ saturation were measured.

Statistical analysis was done for all the measured $P_{50}$ data using students paired *t* test.

## Results

Results of this study are shown in tables 1 and 2. $P_{50}$ was 26.8 mmHg without $N_2O$ and 28.4 mmHg with $N_2O$

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TABLE 1. Preinduction Values of Effect of $N_2O$ on $P_{50}$

| Samples (n = 20) | Without $N_2O$ Mean | Without $N_2O$ SEM | With $N_2O$ Mean | With $N_2O$ SEM | P |
|---|---|---|---|---|---|
| 3.5% $O_2$ | | | | | |
| $P_{O_2}$ (mmHg) | 26.5 | 0.03 | 26.6 | 0.04 | >0.8 |
| $O_2$ sat % | 49.0 | 0.05 | 45.0 | 0.08 | <0.001 |
| 4.0% $O_2$ | | | | | |
| $P_{O_2}$ (mmHg) | 30.2 | 0.04 | 30.1 | 0.03 | >0.8 |
| $O_2$ sat % | 58.0 | 0.07 | 53.0 | 0.09 | <0.001 |
| 4.5% $O_2$ | | | | | |
| $P_{O_2}$ (mmHg) | 34.4 | 0.05 | 34.2 | 0.06 | >0.8 |
| $O_2$ sat % | 66.0 | 0.08 | 63.0 | 0.08 | <0.001 |
| $P_{50}$ (mmHg) | 26.8 | 0.09 | 28.4 | 0.09 | <0.001 |

($P < 0.001$). The effect of $N_2O$ on $P_{50}$ was rapidly induced (table 1), and this effect of $N_2O$ on $P_{50}$ was also rapidly reversible as $P_{50}$ returned promptly to 26.8 mmHg when blood samples were equilibrated with gas mixtures that contained no $N_2O$ (table 2). The measured $P_{O_2}$ values agreed with the $P_{O_2}$ present in the gas mixtures. No oxygen was detected in the blood samples equilibrated with known gas mixtures containing $N_2O$ but no $O_2$. This ruled out the possibility of erroneous $P_{O_2}$ values measured in our blood gas machine in the presence of $N_2O$.

All patients had an Hb between 12 and 15 g/dl and COHb of less than 1%.

TABLE 2. Postinduction Values of Effect of $N_2O$ on $P_{50}$

| Samples (n = 20) | With $N_2O$ Mean | With $N_2O$ SEM | Without $N_2O$ Mean | Without $N_2O$ SEM | P |
|---|---|---|---|---|---|
| 3.5% $O_2$ | | | | | |
| $P_{O_2}$ (mmHg) | 26.5 | 0.05 | 26.4 | 0.04 | >0.8 |
| $O_2$ sat % | 45.0 | 0.07 | 49.0 | 0.04 | <0.001 |
| 4.0% $O_2$ | | | | | |
| $P_{O_2}$ (mmHg) | 30.2 | 0.04 | 30.1 | 0.05 | >0.8 |
| $O_2$ sat % | 53.0 | 0.08 | 58.0 | 0.06 | <0.001 |
| 4.5% $O_2$ | | | | | |
| $P_{O_2}$ (mmHg) | 34.1 | 0.06 | 34.3 | 0.04 | >0.8 |
| $O_2$ sat % | 62.0 | 0.05 | 66.0 | 0.07 | <0.001 |
| $P_{50}$ (mmHg) | 28.4 | 0.09 | 26.8 | 0.08 | <0.001 |

## Discussion

Our $P_{50}$ values are in agreement with those published by Smith *et al.*[1] but disagree with those of Fournier and Major.[2] Although a statistically significant change in $P_{50}$ is seen during $N_2O$ anesthesia, it is not clinically significant. Possible mechanisms by which $N_2O$ can interfere with the measurement of $P_{O_2}$ include the presence of silver deposition on the polarographic platinum electrode.[4] Silver deposition on the cathode increases with age and use of the electrode.‡ Unlike halothane, $N_2O$ cannot be reduced on pure platinum or gold surfaces.[5] $N_2O$ also interferes with $P_{O_2}$ measurements in certain polarographic oxygen analyzers when the battery output is low or uneven or an incorrect battery is used.§

In conclusion, our data indicate that there is a small but statistically significant shift of $P_{50}$ to the right in the presence of $N_2O$, and the effect of $N_2O$ on $P_{50}$ is both rapidly inducible and reversible. There was no demonstrable interference by $N_2O$ with our polarographic measurements of $P_{O_2}$.

‡ Severinghaus JW, Bradley AF: Blood gas electrodes or what the instructions didn't say. San Francisco Medical Center, Internal Report, 1969. Copenhagan, Denmark: Radiometer A/S Booklet ST59, 1971.

§ Foregger-Air products, Pamphlet XIV: Oxygen analyzer operating and maintenance.

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