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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}

	Without N_2O		With N_2O		
Samples (n = 20)	Mean	SEM	Mean	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}

	With N_2O		Without N_2O		
Samples (n = 20)	Mean	SEM	Mean	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. Copenhagen, Denmark: Radiometer A/S Booklet ST59, 1971.

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

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