The effect of nitrous oxide on the measurement of single-breath transfer factor

C.L. Phillips, R. Simmul, A.I. Smith, N. Berend

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ABSTRACT: One hour after a bone marrow biopsy and inhalation of Entonox gas (50% nitrous oxide (N₂O) and 50% oxygen), a patient had a markedly reduced transfer factor of the lung for carbon monoxide (T_{L,CO}). Three hours after Entonox, the patient had a normal T_{L,CO}. Since carbon monoxide (CO) and N₂O have similar spectral wavelengths, it was proposed that residual N₂O in the lungs was interfering with the infra-red analysers used to detect CO concentrations. Experiments were performed to verify the "interference" effect and its duration.

Five healthy volunteers performed serial triplicate T_{L,CO} measurements over 3 h on two randomized days (Control vs N₂O). The first triplicate T_{L,CO} on each day served as a baseline measurement. Following the baseline measurement on the N₂O day, each subject inhaled Entonox for 10 min. To serve as a control for the infra-red effect, the identical protocol was repeated using a gas chromatography method for T_{L,CO} determination.

The infra-red method showed a marked reduction (>50%) in T_{L,CO} 30 min after N₂O inhalation. This reduction did not return to baseline levels for at least 2 h. In comparison, the gas chromatography method showed no significant reduction in T_{L,CO}.

In a group of healthy nonsmoking subjects, N₂O markedly affected the measurement of the transfer factor of the lungs for carbon monoxide using infra-red analysers. The time course over which the measurement was reduced was at least 2 h for a 10 min inhalation period. The effect was entirely due to a measurement error associated with infra-red technology.

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Dept of Respiratory Medicine, Royal North Shore Hospital, St Leonards, NSW, Australia

Correspondence: C.L. Phillips
Respiratory Investigation Unit
Level 6, Main Block
Royal North Shore Hospital
St Leonards
NSW 2065
Australia

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Patients diagnosed with lymphoma and leukaemia routinely undergo pulmonary function tests, including single-breath transfer factor of the lungs for carbon monoxide (T_{L,CO}), before and in the months following bone marrow transplant. This group of patients receive a diverse regimen of therapy, including chemotherapy and total body irradiation, both of which have been shown to have adverse effects on the lungs. The serial lung function tests enable assessment of any adverse effects of therapy or detection of complications of transplantation. Staff in the pulmonary function laboratory may be unaware of procedures performed immediately prior to testing.

A chance observation in a patient with lymphoma revealed a markedly reduced T_{L,CO} following a bone marrow biopsy 1 h previously. During this biopsy, Entonox gas (comprising 50% nitrous oxide (N₂O) and 50% oxygen) was administered for analgesia for approximately 10 min. A normal T_{L,CO} measurement was subsequently obtained 3 h after the Entonox inhalation. Since carbon monoxide (CO) and N₂O have similar spectral wavelengths [1], the hypothesis was proposed that residual N₂O was still diffusing out of the blood and soft tissue and was subsequently interfering with the infra-red analysers used to detect CO concentrations during the T_{L,CO}

test. The false detection of N₂O as CO would result in a markedly reduced T_{L,CO}. Upon introducing Entonox directly into the gas sample tube for the infra-red analysers, the measured output for CO was substantially increased. A further series of experiments were carried out to verify the "gas interference" effect, and to document the time course over which this effect occurs following a 10 min inhalation of nitrous oxide.

Materials and methods

Subjects

Five healthy (nonsmoking) volunteers (4 males and 1 female) with a mean age of 41 yrs (range 34–48 yrs) were recruited for this study.

Experimental protocols

Each subject performed serial T_{L,CO} measurements on each of two randomized treatment days (Control vs N₂O) at 30 min intervals for 3 h. T_{L,CO} measurements were

performed in triplicate at each time-point. The first time-point on each day served as a baseline measurement. Following the baseline measurement on the N_2O day, each subject inhaled Entonox for 10 min at tidal breathing rates (8–10 L·min⁻¹). $T_{L,CO}$ measurements were performed using the SensorMedics 2200 $T_{L,CO}$ cart (SensorMedics Corporation, Yorba Linda, CA, USA), which uses infra-red analysers for determination of CO concentration. Thus, each subject served as their own control.

In order to confirm the effects observed as being entirely due to a measurement error associated with infra-red technology, the identical protocol was repeated on three of the original five subjects using the Med Graphics $T_{L,CO}$ cart (Medica Graphics Corporation, St. Paul, MN, USA) which uses gas chromatography for determining the CO concentration.

Informed consent was obtained from all subjects, together with approval from the local Ethics Committee for the experimental protocols.

Analysis

Data for each method of $T_{L,CO}$ determination was analysed using paired t-tests. Total carboxyhaemoglobin (COHb) was determined in two of the three subjects before and immediately following the final $T_{L,CO}$ measurement on the control day, when the gas chromatography method for $T_{L,CO}$ determination was being used. These results were used to assess the cumulative effect of CO inhalation over the entire 3 h test period.

Results

Figure 1 shows the mean $T_{L,CO}$ using the infra-red method (n=5 subjects) and gas chromatography method

Fig. 1. — Time course of changes in transfer factor of the lung for carbon monoxide ($T_{L,CO}$) using the infra-red method (IR) (broken lines) versus the gas chromatography method (GC) (solid lines). Values are presented as mean±SE. —□—: IR control; —●—: IR N_2O ; —□—: GC control; —●—: GC N_2O . *: $p < 0.05$, compared to gas chromatography method

(n=3 subjects) for paired t-tests at each time-point (Control vs N_2O). There was a significant reduction in $T_{L,CO}$ measured with the infra-red method following a 10 min inhalation of N_2O , and this reduction persisted for at least 2 h. In contrast, there was no significant reduction in $T_{L,CO}$ following the N_2O inhalation when using the gas chromatography method.

The mean COHb (n=2 subjects) prior to performing any $T_{L,CO}$ tests on the gas chromatography control day was 1.1%. This increased to 12.1% following the final time-point when 21 single-breath $T_{L,CO}$ tests had been performed. The difference between the $T_{L,CO}$ corrected for COHb vs the uncorrected $T_{L,CO}$ at the first time-point was less than 0.5 mL·min⁻¹·mmHg⁻¹. In comparison, the mean difference at the last time point was 4.0 mL·min⁻¹·mmHg⁻¹. This demonstrates the likelihood that the reduction in $T_{L,CO}$ after the 3 h of measurements on both treatment days and in both methods of measurement was probably due to a raised level of COHb.

Discussion

The results clearly demonstrate that the presence of N_2O in expired gas can markedly reduce the transfer factor of the lungs for carbon monoxide, when determined using infra-red analysers. This reduction is entirely due to a measurement error and has no physiological basis. In a recent letter, GILBERT [2] reported a similar observation, although without experimental verification. These findings have important ramifications for the interpretation of lung function testing, and necessitate the careful recording of an appropriate history prior to the conduction of $T_{L,CO}$ tests when using infra-red analysers. Textbook descriptions [3] of rapid elimination of N_2O from the lungs may provide a false sense of security, even when there is awareness of previous administration of Entonox. If the separation of N_2O and CO is technically difficult to achieve when using infra-red analysers, then a period of at least 3 h should be allowed following N_2O inhalation before a measurement of transfer factor of the lungs for carbon monoxide is performed.

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References

1. Hewlett Packard 4721 OA Capnometer. Operating Guide. Section H. Principles of measurement. Part A. Infrared Measurement Technique. January, 1982.
2. Gilbert R. False-low carbon monoxide diffusing capacity measurement after general anaesthesia (Communications to the Editor). *Chest* 1996; 109: 592.
3. Goodman Gillman A. The Pharmacological Basis of Therapeutics. 8th edn. In: Goodman Gilman A, Rall TW, Nies AS, Taylor P eds. Oxford, Pergamon Press, 1990.