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

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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 (TL,CO). Three hours after Entonox, the patient had a normal TL,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 TL,CO measurements over 3 h on two randomized days (Control vs N2O). The first triplicate TL,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 TL,CO determination.

The infra-red method showed a marked reduction (>50%) in TL,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 TL,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.


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 TL,CO measurements on each of two randomized treatment days (Control vs N2O) at 30 min intervals for 3 h. TL,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 N2O 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 (n=3 subjects) for paired t-tests at each time-point (Control vs N\(_2\)O). There was a significant reduction in \(T_{L,CO}\) measured with the infra-red method following a 10 min inhalation of N\(_2\)O, and this reduction persisted for at least 2 h. In contrast, there was no significant reduction in \(T_{L,CO}\) following the N\(_2\)O 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\(_2\)O 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. The results described [3] of rapid elimination of N\(_2\)O 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\(_2\)O 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\(_2\)O inhalation before a measurement of transfer factor of the lungs for carbon monoxide is performed.

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References