ARTERIAL OXYGEN TENSIONS MEASURED CONTINUOUSLY IN PATIENTS BREATHING 21% OXYGEN AND NITROUS OXIDE OR AIR

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Increases in $P_{A_0}$ and $P_{A_O}$ during the uptake of 79% nitrous oxide in 21% oxygen, and their decrease during the elimination of this mixture while breathing room air has been observed by many investigators (Rackow, Salanitre and Frumin, 1961; Heller, Watson and Imredy, 1967; Frumin and Edelist, 1969; Shah et al., 1971). However, except for the work of Heller, Watson and Imredy (1967), who used an intra-arterial oxygen electrode in dogs, to our knowledge there have been no studies of changes in arterial oxygen tensions measured continuously in man breathing 79% nitrous oxide in 21% oxygen or room air. In this study $P_{A_0}$ was continuously recorded in anaesthetized patients using an oxygen electrode of new design in order to assess the variations in $P_{A_0}$ when changing from nitrous oxide in oxygen to air and back again.

PATIENTS, MATERIALS AND METHODS

This study was approved by the ethics committee of The London Hospital. In order to measure $P_{A_0}$ accurately and continuously in the presence of nitrous oxide, an intra-vascular oxygen electrode (Kontron Medical) developed by Eberhard, Feilman and Mindt (1979) was used (fig. 1). Compared with random arterial blood-gas analyses using a blood-gas analyser (ABL2 Radiometer), the electrode demonstrated an accuracy resulting in a correlation coefficient of 0.99 (fig. 2). In addition to accuracy, the sensor had to meet the following requirements: sterility; small diameter; adequate response time; freedom from fibrin deposition; insensitivity to high nitrous oxide concentrations.

The first requirement was met by using gamma sterilization, the second was fulfilled by using an electrode 0.55 mm in diameter which permitted continuous concurrent pulsatile arterial pressure measurements and intermittent blood sampling when inserted through a 20-gauge intra-arterial cannula. The third requirement was met by a
surgical procedures. These patients were chosen because there would be no manipulation of the thorax or abdomen which could cause changes in the $P_{a_o_2}$. The age range was from 17 to 75 yr.

Following control measurement of $P_{a_o_2}$ while the subject was breathing room air, anaesthesia was induced with thiopentone. Muscle paralysis was produced with tubocurarine and tracheal intubation was performed. The lungs were ventilated using a Brompton Manley ventilator with enfurane and nitrous oxide in oxygen mixtures. Fentanyl was given i.v. Halothane was not used because of its adverse effect on the accuracy of oxygen electrodes. The end-tidal carbon dioxide concentration was measured continuously with an infra-red carbon dioxide analyser and the ventilator was adjusted such that $P_{e_c_o_2}$ was maintained between 4.65 and 5.32 kPa. Arterial pressure was monitored continuously. $F_{i_o_2}$ was monitored by a fuel cell which was calibrated on room air and 100% oxygen. After the sensor was inserted it was calibrated in vivo against multiple blood-gas samples obtained while the patient was on low or zero concentrations of nitrous oxide.

After being ventilated with nitrous oxide in oxygen ($F_{i_o_2} = 0.4$) for at least 30 min to ensure complete nitrogen washout, the patients' lungs were ventilated with 79% nitrous oxide and 21% oxygen and, after 20 min, the breathing mixture was changed to room air supplied via an air compressor. After 10 min on room air the inspired gas was again changed to the 79:21 mixture. In some patients this manoeuvre of changing from the mixture to air and back was repeated several times with at least 10 min between nitrous oxide in oxygen and air breathing to ensure adequate nitrogen washout. At the end of these observations the patients’ lungs were ventilated with 60% nitrous oxide in 40% oxygen until the end of the surgical procedure. Data are presented as mean (±SD). Statistical analysis was with Student's paired $t$ test.

**RESULTS**

The mean control value of $P_{a_o_2}$ obtained from all subjects while they were awake and breathing air was $11.0 ± 1.89$ kPa. The lowest $P_{a_o_2}$ was in a 75-yr-old man who had a control value of 9.0 kPa and who developed bronchospasm during anaesthesia. The highest control $P_{a_o_2}$ was in a 17-yr-old man who was hyperventilating involuntarily when the sample was drawn. His $P_{a_o_2}$ was 14.1 kPa and his $P_{a_c_o_2}$ 4.0 kPa.
TABLE I. $P_{aO_2}$ values (kPa): control, after ventilation of the patients' lungs with 79% nitrous oxide in 21% oxygen for 20 min; after ventilation with air for 10 min; after return to ventilation with the gas mixture

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Control (kPa)</th>
<th>$79% N_2O-21% O_2$ for 20 min (kPa)</th>
<th>After air for 10 min (kPa)</th>
<th>After return to $N_2O-O_2$ (kPa)</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>12.8</td>
<td>19.8</td>
<td>15.5</td>
<td>20.8</td>
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<td>2</td>
<td>9.3</td>
<td>11.8</td>
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<tr>
<td>6</td>
<td>9.0</td>
<td>10.2</td>
<td>8.5</td>
<td>11.0</td>
</tr>
<tr>
<td>7</td>
<td>14.1</td>
<td>15.4</td>
<td>13.4</td>
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<td>8</td>
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<td>11.4</td>
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</tr>
<tr>
<td>9</td>
<td>9.4</td>
<td>10.9</td>
<td>10.0</td>
<td>11.4</td>
</tr>
<tr>
<td>Mean</td>
<td>11.0</td>
<td>14.1</td>
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<tr>
<td>SD</td>
<td>1.89</td>
<td>2.95</td>
<td>2.27</td>
<td>2.77</td>
</tr>
</tbody>
</table>

**Fig. 3.** Recording of $P_{aO_2}$ using intra-arterial electrode while changing inspired gases from a mixture of 79% nitrous oxide-21% oxygen to air and back to the mixture. Artefacts from electrocautery included to demonstrate electrode stability.

The increase in $P_{aO_2}$ over the mean control values when patients were ventilated for 20 min with 79% nitrous oxide in 21% oxygen as the inspired gas was $2.74 \pm 1.88$ kPa ($P < 0.002$). The mean steady state value with this gas mixture was $14.1 \pm 2.95$ kPa. There was a significant decrease ($P < 0.001$) in $P_{aO_2}$ to a mean of $12.0 \pm 2.27$ kPa when the patients' lungs were ventilated for 10 min with air without changing any other conditions. The mean decrease amounted to $2.22 \pm 0.94$ kPa. In only the two patients discussed above did the $P_{aO_2}$ at this point decrease below control values. However, there was no significant difference ($P < 0.1$) between mean control values and the mean $P_{aO_2}$ at this point in the study.

When the patients were again ventilated with 79% nitrous oxide in 21% oxygen, the $P_{aO_2}$ increased significantly ($P < 0.001$) to a mean
value of 13.8±2.77 kPa. The mean increase amounted to 2.21±0.96 kPa. The values obtained from this study are shown in table I. A recording of the cycles of events which took place during a study is given in figure 3. The artefacts were caused by cautery and were included to demonstrate the rapid return of the electrode output to precautery values.

An "overshoot" of $P_{a,O_2}$ was seen in most patients upon resumption of ventilation with 79% nitrous oxide in 21% oxygen after ventilation with air. This is shown in the recording. However, there was no significant difference ($P < 0.22$) between the values obtained while ventilating with the mixture before and after ventilation with air. At no time were significant changes seen in arterial pressure, ECG, heart rate or end-tidal carbon dioxide concentration.

DISCUSSION

The oxygen electrode used in this study was polarized at 600 mV or less and the cathode material was silver. This was done to ensure relative insensitivity to the high concentrations of nitrous oxide used in this study. Figure 4 (Eberhard and Mindt, 1979) shows polarograms which demonstrate the sensitivity of most oxygen electrodes to nitrous oxide and this can cause errors up to 30% above true oxygen tension (Evans and Cameron, 1978). This problem has been studied extensively (Hahn et al., 1979, 1981).

It is noted here that, in so far as can be determined, none of the electrodes used to measure arterial oxygen tensions in previous studies of this kind, was corrected for the error caused by the presence of nitrous oxide in the inspired gas mixture.
The improved technology in oxygen sensors has made it possible to measure $P_{A_{O_2}}$ accurately and continuously in man during the uptake and elimination of nitrous oxide. The ease of its use permits un gloved but sterile insertion intravascularly through any 20-gauge cannula without disturbing the measurement of other items usually measured by intravascular means, thus enhancing its usefulness.

Farhi and Olszowka (1968) constructed a mathematical model using end-expired oxygen ($P_{A_{O_2}}$) as the unit of measurement to analyse the uptake and elimination of nitrous oxide as a soluble inert gas. Based on their calculations, it was predicted that the “average” alveolus would show a $P_{O_2}$ increase of 6.5 kPa when the inspired gas was changed from air to 78% nitrous oxide in 22% oxygen. They predicted also that, upon changing back to air, the $P_{O_2}$ would decrease initially by 2.66 kPa. They reasoned that the above increase in $P_{O_2}$, along with a 0.27-kPa increase in $P_{A_{CO_2}}$, would occur as a result of the “concentration” effect of nitrous oxide resulting from the rapid absorption of this gas from the alveolus. This would result in diminished alveolar volume with subsequent increases in the pressures of oxygen and carbon dioxide. They also reasoned that the initial decrease in $P_{O_2}$ during the elimination of nitrous oxide by breathing air would be less than the increase, because of the buffering effect of nitrogen entering the alveoli and countering the “dilution” effect of nitrous oxide as it diffused back into the alveoli. In addition, they felt that the haemoglobin would release more oxygen as it reached the steep part of the dissociation curve and that this oxygen would also diffuse back into the plasma to help counter the “dilution” effect.

Since the publication of the above data several workers have investigated changes in $P_{O_2}$ during the uptake and elimination of nitrous oxide by using various techniques. Frumin and Edelist (1969) found that, in patients breathing 79% nitrous oxide in 21% oxygen spontaneously, arterial oxygen tensions decreased minimally when the inspired gas was changed to air (a maximum decrease of 1.2 kPa in one patient out of nine after 3 min on air). Shah and colleagues (1971) used eight volunteers in a sitting position breathing 79% nitrous oxide in 21% oxygen and found that the mean increase in $P_{A_{O_2}}$ after 80 s was 4.0 kPa (less than the 6.5 kPa predicted by Farhi and Olszowka (1968)). They stated that the $P_{A_{O_2}}$ increased after nitrous oxide in oxygen, but gave no figures for the mean increase and concluded that the lesser increase in $P_{A_{O_2}}$ as compared with $P_{A_{O_2}}$ was the result of an increase in alveolar-arterial difference.

In a study using a mathematical lung model and three subjects, Scrimshire and Tomlin (1973) predicted the increase in $P_{A_{O_2}}$ after 16 breaths of 79% nitrous oxide in 21% oxygen would be 4.39 kPa if the lungs were inflated at a constant volume. They predicted that the decrease in $P_{A_{O_2}}$ upon changing to air would be 2.66 kPa initially and implied that the reason for the difference between the increase and decrease in $P_{A_{O_2}}$ was the rapid nitrogen wash-in upon changing to room air.

In reviewing our data which are based on arterial oxygen tensions, we found that the mean increase of 2.74±1.88 kPa with 79% nitrous oxide in 21% oxygen as the inspired gas was less than the predicted increase in $P_{A_{O_2}}$ suggested by both Farhi and Olszowka (1968) and Scrimshire and Tomlin (1973). This difference may be accounted for by the fact that these previous studies measured changes in alveolar oxygen tension using end-tidal oxygen, whereas, in this study, continuous arterial oxygen tensions were measured. We found that the mean decrease of 2.22±0.94 kPa in $P_{A_{O_2}}$ when the inspired gas was changed to air was close to that predicted by the above authors. The outstanding point of difference between their data and ours was that the increase in $P_{A_{O_2}}$ after breathing 79% nitrous oxide in 21% oxygen was much less than they predicted for the increase in $P_{A_{O_2}}$. We believe that the lesser increase in $P_{A_{O_2}}$ was a reflection of an increase in alveolar-arterial difference. Our findings are at variance with those of Scrimshire and Tomlin (1973), who predicted a decrease in alveolar-arterial difference when nitrous oxide in oxygen was the inspired gas. However, because our patients were anaesthetized and in a supine or prone position, an increase in shunt would be more likely than in “awake” volunteers or mathematical models. Alternatively, a reduction in functional residual capacity on changing from the awake to the anaesthetized state could account for these differences.

Although there was no significant difference between the $P_{A_{O_2}}$ values found while breathing 79% nitrous oxide in 21% oxygen before and after air breathing, in most patients there was a definite “overshoot” as high as 1.33 kPa upon
resumption of breathing nitrous oxide in oxygen. After 2–3 min in all patients the Pa\textsubscript{o\textsubscript{2}} decreased to the mean values listed. The probable explanation of this overshoot is the very rapid absorption of the soluble nitrous oxide during the first 2–3 min, with a consequent increase in Pa\textsubscript{o\textsubscript{2}} as the result of the rapid shrinkage of the alveoli. The return to the mean values of Pa\textsubscript{o\textsubscript{2}} after the initial increase can be explained on a steady state basis wherein the blood concentration of nitrous oxide reaches a value at which the net exchange of nitrous oxide across the alveoli is negligible and there is stabilization of alveolar volume. Another possible explanation of the overshoot could be that areas with low ventilation:perfusion ratios receive more soluble gas (for example nitrous oxide) when the mixture is changed from room air to nitrous oxide. The ventilation:perfusion ratio in these areas will become higher temporarily.

The fact that there was no significant difference in mean Pa\textsubscript{o\textsubscript{2}} between awake control values and while being ventilated with air during anaesthesia, would indicate that the patients were not hypoxic at any time.

The following conclusions can be drawn from this study:

(1) It is now feasible clinically to use an intravascular oxygen sensor when one is needed.

(2) "Diffusion hypoxia" does not exist if patients have an adequate cardiorespiratory system and there are no changes in respiratory volume when changing from nitrous oxide in oxygen to air (hypoxia being defined as Pa\textsubscript{o\textsubscript{2}} during air breathing which decreases significantly below baseline values.)

(3) Unless high oxygen tensions are needed, the use of high concentrations of nitrous oxide (up to 79%) results in more than adequate oxygenation in patients with normal cardiorespiratory systems.

This finding may be helpful in anaesthetizing patients when hyperoxia might be harmful. It might also be possible to use lower concentrations of supplementary anaesthetic agents. This does not negate the probable desirability of using higher oxygen concentrations at the end of anaesthesia or when the cardiorespiratory system is likely to be depressed.

REFERENCES


