HYPOXAEIA AFTER INHALATION OF 50% NITROUS OXIDE AND OXYGEN

C. J. WILKINS, P. N. REED AND A. R. AITKENHEAD

It is well known that hypoxaemia may occur when an inspired gas mixture containing 70-80% nitrous oxide is changed to air [1]. It is commonly thought that this does not occur after 50% nitrous oxide in oxygen. Unpublished observations from our department suggested that women given Entonox (50% nitrous oxide in oxygen) for pain relief during labour became hypoxaemic between uterine contractions. Hyperventilation during contractions is common and itself may promote hypoxaemia [2] because of reduced ventilatory drive caused by hypocapnia. This study was performed to determine if inhalation of Entonox may be followed by hypoxaemia in normal (non-pregnant) subjects and to assess the additional effect of hyperventilation.

METHODS AND RESULTS

The study was approved by the District Ethics Committee and 10 subjects (eight male) of mean age 28 yr (range 26-34 yr) gave informed consent to be studied. Each subject inhaled gas mixtures composed of 50% nitrous oxide in oxygen, 50% nitrogen in oxygen and 79% nitrogen in oxygen. The mixtures were made up from their constituent gases into Douglas bags with an accuracy of 1%, confirmed by mass spectrometry (Cen
tonic Medical MGA 2000). The mixtures were inhaled via a low resistance breathing system incorporating a tightly applied non-rebreathing mask. The mass spectrometer sampled from the mask for measurement of end-expired oxygen concentrations (\(Fe'_{O_2}\)) and a pulse oximeter (Nellcor N-100) was applied to the subject's first finger to measure changes in oxygen saturation (\(Sa_{O_2}\)). The outputs from these instruments were displayed on a chart recorder.

Baseline values of \(Fe'_{O_2}\) and \(Sa_{O_2}\) were taken as the lowest values obtained during an initial 10-min period, during which the subject breathed room air. Each gas mixture was inhaled for 2 min of hyperventilation and 10 min of resting ventilation. There was a 15-min measurement period (during which the subject breathed room air) and a 5-min rest period after each administration. The sequence was random.

No attempt was made to influence the subject's breathing pattern unless \(Sa_{O_2}\) decreased to < 80%, when the subject was instructed to take a deep breath.

Data were analysed by the Wilcoxon signed rank test.

SUMMARY

We have investigated, in volunteers, the effect of inhaling 50% nitrous oxide in oxygen on subsequent oxygenation. Subjects breathed either 50% nitrous oxide in oxygen or 50% nitrogen in oxygen during hyperventilation and normal ventilation. Arterial oxygen saturation and end-expired oxygen concentrations were lower after 50% nitrous oxide in oxygen than after the other mixture with both patterns of ventilation and were lowest after hyperventilation with 50% nitrous oxide in oxygen.
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### Table I. Minimum \( Sa_{O_2} \) and \( Fe'_{O_2} \) (mean (SD)) and duration of depression of \( Sa_{O_2} \) below baseline following each respiratory manoeuvre. *P < 0.05; **P < 0.01; ***P < 0.001 for comparisons of nitrous oxide in oxygen with the other mixtures (Wilcoxon signed rank test)

<table>
<thead>
<tr>
<th>Ventilatory pattern</th>
<th>Gas mixture</th>
<th>Minimum ( Sa_{O_2} ) (%)</th>
<th>Minimum ( Fe'_{O_2} ) (%)</th>
<th>Time less than baseline ( Sa_{O_2} ) (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyper-ventilation</td>
<td>79% ( N_2/O_2 )</td>
<td>90.1 (4.4)</td>
<td>12.5 (1.7)</td>
<td>285 (154)</td>
</tr>
<tr>
<td></td>
<td>50% ( N_2/O_2 )</td>
<td>93.0 (2.8)</td>
<td>12.8 (1.5)</td>
<td>254 (156)</td>
</tr>
<tr>
<td></td>
<td>50% ( N_2O/O_2 )</td>
<td>85.6 (7.6)*</td>
<td>10.4 (1.2)**</td>
<td>501 (176)**</td>
</tr>
<tr>
<td>Normal</td>
<td>79% ( N_2/O_2 )</td>
<td>97.2 (1.2)</td>
<td>13.8 (0.9)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>50% ( N_2/O_2 )</td>
<td>96.4 (1.3)</td>
<td>14.6 (0.6)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>50% ( N_2O/O_2 )</td>
<td>94.0 (2.0)**</td>
<td>12.2 (1.7)*</td>
<td>415 (141)**</td>
</tr>
</tbody>
</table>

Baseline \( Sa_{O_2} \) and \( Fe'_{O_2} \) were 96.8 (1.3)% and 15.7 (0.7)%, respectively (Table I). There were small but clinically unimportant decreases in \( Sa_{O_2} \) and \( Fe'_{O_2} \) after 50% nitrous oxide in oxygen with normal ventilation compared with the other mixtures. After hyperventilation, \( Sa_{O_2} \) and \( Fe'_{O_2} \) were depressed for all gas mixtures, but they were depressed most, in both magnitude and duration, following 50% nitrous oxide in oxygen.

**COMMENT**

It is established that a period of hypoxaemia may occur during air breathing after the administration of 70-80% nitrous oxide in oxygen [1], but it has not been reported after 50% nitrous oxide in oxygen. Indeed, it has been suggested that, during labour, maternal \( Pa_{O_2} \) is not worsened by administration of Entonox [3].

Hypoxaemia is known to occur after hyperventilation [4] because of reduced ventilatory drive caused by hypocapnia. Thus the reductions in \( Sa_{O_2} \) and \( Fe'_{O_2} \) seen in this study after hyperventilation were anticipated. However, there was a much greater reduction in \( Sa_{O_2} \) after hyperventilation with 50% nitrous oxide in oxygen than with the other mixtures. This suggests that the nitrous oxide had an effect additional to that of hyperventilation alone. The mechanism of this phenomenon is not clear, but it might result from: an effect of nitrous oxide on ventilatory drive; the ventilatory response to hypoxia; \( V/Q \) mismatch; or diffusion hypoxia.

**REFERENCES**