SOME EFFECTS OF MAINTAINING PULMONARY NITROGENATION DURING ANAESTHESIA

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SUMMARY

The effect of maintaining pulmonary nitrogenation on venous admixture during halothane anaesthesia and on postoperative hypoxaemia was studied in patients undergoing either abdominal surgery or the removal of varicose veins. In both groups venous admixture was greater when nitrogen replaced nitrous oxide in the anaesthetic gas mixture. In the varicose vein group hypoxaemia was more severe in those who received nitrogen but in the abdominal group there was little difference. It is suggested that changes in pulmonary perfusion may have influenced these results.

It has been known for many years that arterial desaturation may follow intrathoracic operations, but only comparatively recently has it been appreciated that it may also follow other types of surgery (Nunn and Payne, 1962). This reduction in arterial oxygenation occurs in the apparently uncomplicated case and it may last for several days (Knudsen, 1970).

It occurs in the postoperative period even when there is no detectable hypoventilation, airways obstruction or decrease in cardiac output. It has been suggested that the condition is due to the opening up of subpleural vessels which increase the anatomical shunt, but no clear basis for this has been demonstrated. There are left the possibilities that it is the result of either patchy alveolar collapse or increased ventilation/perfusion imbalance.

One factor implicated in the alveolar collapse theory is the nature of the carrier gas used during anaesthesia. It is suggested that if the airway to an alveolus becomes obstructed, oxygen will be absorbed by the continuing perfusion of the alveolus, but the nitrogen will remain to provide a "skeleton" holding the alveolus patent. Nitrous oxide is a more soluble gas and in the event of obstruction of an airway the alveolus will collapse because of absorption of its contents. The collapse may remain in the post-operative period, with the blood perfusing it remaining unoxygenated.

It was decided to investigate the effect of maintaining pulmonary nitrogenation during anaesthesia on postoperative arterial oxygenation.

METHODS

Two groups of 20 patients were studied: Group I comprised patients undergoing upper abdominal surgery and Group II comprised patients having varicose vein operations. The patients were unselected except that those with cardiorespiratory disease or who were over the age of 65 years were excluded. Informed, signed consent was obtained. The patients were randomly assigned to receive 50% nitrous oxide or 50% nitrogen as a carrier gas with oxygen.

Anaesthesia.

The patients were premedicated with morphine 10 mg and atropine 0.6 mg given i.m. approximately 1 hour before the operation, and anaesthesia was induced with thiopentone 150-350 mg i.v. Endotracheal intubation was performed with the aid of either pancuronium 6 mg (Group I) or suxamethonium 50 mg (Group II). Anaesthesia was maintained with halothane 0.5-2%. Group I patients were artificially ventilated by hand and Group II patients were allowed to breathe spontaneously. In both groups a non-rebreathing system was used so that samples of inspired and expired gas could be obtained. Postoperative pain was treated with morphine 10 mg i.m. given when required by the patient and all patients received routine chest physiotherapy.

When the patient was first seen, arterial blood was sampled for gas analysis and the haemoglobin concentration of peripheral venous blood was estimated.

Twenty to thirty minutes after induction of anaesthesia, when the patient was assumed to be in a steady state, a sample of inspired gas was drawn into
a glass syringe from the inspired gas reservoir bag and mixed expired gas was collected in a Douglas bag. Arterial blood was withdrawn at the same time.

Arterial blood was sampled also at 24 and 72 hours after operation in Group I, and at 6 and 24 hours in Group II. All arterial sampling, except during anaesthesia, was carried out with the patient sitting. Blood was drawn into glass syringes, the deadspace of which had been filled with heparin. These were sealed, placed in an ice/water mixture and taken without delay to the laboratory. The patient's temperature at the time of sampling was noted so that appropriate correction factors could be applied.

**Measurements and calculations.**

The appropriate radiometer micro-electrode units were used to measure pH, $P_{O_2}$ and $P_{CO_2}$. Calibration was with two standard buffer solutions for pH, two measured gas mixtures for carbon dioxide, and nitrogen and water equilibrated with air at 37°C for oxygen. Base excess was derived from pH and $P_{CO_2}$ using the Siggaard-Andersen alignment nomogram. Inspired $P_{O_2}$ ($P_{I_o}$) and the mixed expired oxygen and carbon dioxide pressure ($P_{E_{O2}}$ and $P_{E_{CO2}}$) were measured on the same apparatus, the span of the oxygen electrode being calibrated with air.

The following form of the shunt equation

$$\frac{Qs}{Qt} = \frac{(C_{c'O_2} - C_{aO_2})}{(C_{c'O_2} - C_{vO_2})}$$

was used to estimate the percentage venous admixture. The ideal alveolar $P_{O_2}$ ($P_{A_{O2}}$) was calculated:

$$P_{A_{O2}} = P_{I_{O2}} - P_{CO_2} \times \frac{([P_{I_{O2}} - P_{E_{O2}}]/P_{E_{CO2}})}{P_{E_{CO2}}}$$

End-pulmonary capillary and arterial oxygen contents ($C_{C'O_2}$ and $C_{aO_2}$) were calculated from the general expression

Oxygen content = \( \left( \frac{\text{% saturation}}{100} \right) \times (\text{haemoglobin concentration}) \times 1.39 + 0.003 P_{O_2} \)

with appropriate correction factors for patient's temperature, pH and base excess being made before estimating saturation from $P_{O_2}$ using a line nomogram (Kelman and Nunn, 1966). $C_{C'O_2}$ was assumed to equal $P_{A_{O2}}$.

Sampling of mixed venous blood was not considered justifiable and fixed values for the arterio-venous difference in oxygen content were assumed. As assumed differences of both 3.5 and 5.0 ml per 100 ml of blood have been used previously (Webb and Nunn, 1967), calculations were performed using both figures.

Statistical analyses were made using the Student $t$-test with Bessel correction.

**RESULTS**

The data concerning the patients and the blood-gas results of the two groups are shown in tables I and II. These tables show that the patients in the two subgroups in Group I were comparable but in Group II those who received nitrogen were slightly heavier than those who received nitrous oxide (mean weights 69 and 59 kg). This difference was statistically significant, though there was little difference in preoperative $P_{a_{O2}}$ (mean values 91 and 93 mm Hg).

The postoperative reductions in $P_{a_{O2}}$ are illustrated in figure 1. These changes were independent of changes in ventilation as is evident from the minimal changes in $P_{a_{CO2}}$ (tables I and II).

In group I the degree of postoperative hypoxaemia in patients who had nitrous oxide was virtually identical with that in the patients who had nitrogen. In the former the $P_{a_{O2}}$ decreased from 91 to 75 mm Hg 24 hours after operation and on the third postoperative day was still only 76 mm Hg. In the latter group the respective figures were 92, 77 and 79 mm Hg.

![Figure 1](https://academic.oup.com/bja/article-abstract/46/9/680/255682)

**FIG. 1.** $P_{a_{O2}}$ before and after operation in two groups of patients receiving either $N_2$ or $N_2O$ as a carrier gas.
TABLE I. Data of the patients in Group I. Gas tensions and partial pressures in mm Hg.

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Pre-op.</th>
<th>24 hr Post-op.</th>
<th>Intra-op.</th>
<th>6 hr Post-op.</th>
<th>24 hr Post-op.</th>
<th>Intra-op.</th>
<th>6 hr Post-op.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrogen</td>
<td>M</td>
<td>SD</td>
<td>Probability</td>
<td>SD</td>
<td>M</td>
<td>Probability</td>
<td>SD</td>
</tr>
<tr>
<td>Nitrous oxide</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*No calculation of PAo2, Qs/Qt, etc., because of technical problems with gas collection.*
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TABLE III. Per cent venous admixture in the two groups of patients. The carrier gases and assumed A-V oxygen differences are as indicated.

<table>
<thead>
<tr>
<th>GROUP</th>
<th>ASSUMED A-V OXYGEN DIFFERENCE (VOLS %)</th>
<th>CARRIER GAS</th>
<th>MEAN % VENOUS ADMIXTURE</th>
<th>SD</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>3-5</td>
<td>N₂</td>
<td>73</td>
<td>39</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N₂</td>
<td>83</td>
<td>40</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>II</td>
<td>3-5</td>
<td>N₂</td>
<td>79</td>
<td>50</td>
<td>&gt;0.03</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N₂</td>
<td>102</td>
<td>55</td>
<td>&gt;0.03</td>
</tr>
<tr>
<td></td>
<td>5-0</td>
<td>N₂</td>
<td>57</td>
<td>38</td>
<td>&lt;0.04</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N₂</td>
<td>74</td>
<td>41</td>
<td>&lt;0.03</td>
</tr>
</tbody>
</table>

In Group II, the varicose vein group, the changes were less severe and less prolonged. In the nitrous oxide subgroup, the mean Pao₂ decreased from 93 to 86 mm Hg a few hours after surgery and had virtually returned to normal after 24 hours. In those patients who had nitrogen, however, the decrease was greater (91 to 74 mm Hg) and at 24 hours after operation the mean Pao₂ of 80 mm Hg was still significantly less than in the nitrous oxide subgroup (P<0.025).

Table III shows the calculated figures for venous admixture during anaesthesia in both groups of patients. In both, venous admixture was greater in patients who received nitrogen than in those who had nitrous oxide but the difference was not statistically significant with either of the assumed figures for arteriovenous oxygen difference.

DISCUSSION

Many factors are known or are thought to influence the degree of postoperative hypoxaemia (Marshall and Wyche, 1972). These include the site of operation, the age of the patient, the presence of cardiorespiratory disease, obesity, postoperative complications and possibly the duration of operation and anaesthesia.

In order to allow for the above, only healthy patients having standard types of operation were studied. Upper abdominal operations are known to be associated with severe and prolonged hypoxaemia (Knudsen, 1970), whereas any change in the lower limb group was unlikely to be affected by such surgical factors as wound pain and interference with the action of muscles used in respiration. The difference in severity and duration of hypoxaemia between the two groups is shown clearly in figure 1. Figure 2 illustrates the known effect of age on arterial oxygenation. Not only does the older patient have a lower initial Pao₂ but his postoperative decrease is greater than that of the younger patient.

The degree of hypoxaemia in the varicose vein-nitrogen subgroup was quite severe (mean 80 mm Hg), almost approaching that of the abdominal groups (means 77 and 75 mm Hg) 24 hours after operation. The explanation for this is not immediately apparent, though the fact that this subgroup was heavier than the others may be contributory. However, it would seem that the maintenance of nitrogenation during anaesthesia does not prevent or reduce postoperative hypoxaemia.

This finding is in conflict with the work of others who have studied maintenance of pulmonary nitrogenation. Dery and his colleagues (1965) demonstrated that functional residual capacity was maintained in anaesthetized patients ventilated with a 50/50 nitrogen/oxygen mixture, but that it was reduced when the inspired gas was changed to pure oxygen. This they attributed to absorption of the more soluble oxygen leading to alveolar collapse. Browne and her colleagues (1970) examined radiographic evidence of atelectasis in post-thoracotomy patients who had been ventilated with nitrogen/oxygen mixtures and found a much lower incidence than in a group who received nitrous oxide and oxygen.
Both these studies concluded that maintenance of nitrogenation was of benefit to the patient.

Webb and Nunn (1967) have also studied maintenance of nitrogenation by comparing venous admixture during anaesthesia in patients receiving either nitrous oxide or nitrogen. As in the present study, the nitrogen group was found to have the greater degree of venous admixture. (The actual values found were greater than in the present study, presumably because they used only 30% oxygen in the inspired gas.) Webb and Nunn (1967) considered that their results could be explained in terms of differences in cardiac output between the two groups and that no advantage in arterial oxygenation was to be gained by replacing nitrous oxide with nitrogen during anaesthesia.

Possibly the improvements in alveolar patency suggested by Dery et al. (1965) and Browne et al. (1970) are outweighed by changes in pulmonary perfusion. One of the factors maintaining normal ventilation/perfusion ratios at the alveoli is the hypoxic pressor response. Animal studies have shown that this reflex is depressed by halothane and stimulated by nitrous oxide (Sykes et al., 1972). In the patients who received nitrogen more halothane may have been required (though this was not clinically apparent) and with no compensatory nitrous oxide effect the reflex may have been depressed. If this effect were to continue into the postoperative period it might also explain the greater hypoxaemia seen in the lower limb group who received nitrogen. However, two facts are against this. First, there was no difference in the degree of hypoxaemia in the upper abdominal groups and, second, the effect of anaesthetic drugs on the hypoxic pressor response in animal preparations ended when they were withdrawn (Sykes et al., 1972).

CONCLUSIONS

It would seem that maintenance of nitrogenation during anaesthesia does not improve oxygenation either during or after surgery.

ACKNOWLEDGEMENTS

We would like to thank Mr T. J. McNair and Mr J. W. W. Thomson for permission to study patients in their care; the staff of the Surgical Unit, Chalmers Hospital, Edinburgh, for their co-operation and assistance; and Mr A. McKinnon for advice on blood-gas analysis.

REFERENCES


