Nitrous oxide and internal tamponade during vitrectomy

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Abstract
We analysed the nitrous oxide composition of the intraocular gas bubble following vitrectomy and fluid-air exchange in 12 patients. Samples were taken under standardised conditions at 20 minutes after completion of the fluid-air exchange. Analysis was conducted by a Medishield MS2 mass spectrometer. The percentage composition of nitrous oxide in the samples varied between 4 and 21% (mean 9%). This influx of nitrous oxide was associated with an increase in intraocular pressure. Pressure rises of greater than 20 mm Hg were not seen owing to venting of gas through the sclerostomies. An inverse relationship was noted between the extent of retinal detachment preoperatively and the amount of nitrous oxide entering the eye. A possible explanation for this relationship is proposed. The importance of nitrous oxide movement is stressed.

Historically the movement of nitrous oxide into air-containing spaces in the body was first recognised during the 1950s when treatment for pulmonary tuberculosis included artificial pneumothorax. Interest in this phenomenon relating to ophthalmic practice increased following the 1973 Edward Jackson memorial lecture given by Norton. From then several studies have reported experimental results in animals, stressing the importance of nitrous oxide movement and its effect on intraocular pressure (IOP).

Wolf et al demonstrated both a rise in IOP1 and an increase in volume2 in the presence of neat intravitreal sulphur hexafluoride (SF₆) in cats maintained on nitrous oxide anaesthesia. Smith et al3 working on rhesus monkeys demonstrated a similar rise in IOP when nitrous oxide was used to maintain anaesthesia in the presence of an intravitreal air bubble.

The inference from these studies has been that peroperative movement of nitrous oxide into a gas filled eye is potentially very important and has influenced vitreoretinal practice ever since. None of these studies, however, have quantified the nitrous oxide influx, and all have been performed on animals. We therefore decided to investigate this phenomenon further in a group of our patients.

Materials and methods
Following the approval of the Ethical Committee and informed consent from the individuals concerned 12 American Society of Anesthesiologists Class I patients undergoing vitrectomy were recruited into the study. The details of the patients and indications for surgery are shown in Table 1. None of the patients had an abnormal intraocular pressure preoperatively. A standard anaesthetic technique was used in all cases. Anaesthesia was induced by intravenous thiopentone and muscle relaxation with atracurium. Anaesthesia was maintained by 65% nitrous oxide in oxygen and 1 to 2% enfurane with supplements of alfentanil and droperidol as required. Respiration was controlled to maintain the end-tidal carbon dioxide concentration at 4%. Residual muscle relaxation was reversed with glycopyrrolate and neostigmine.

A standard 20 gauge, 3-port vitrectomy in combination with a fluid-air exchange was performed on 12 eyes of 12 patients. During the fluid-gas exchange the pressure in the eye was maintained at 25 mm Hg by means of a Greishuber air pump using filtered room air (Fig 1). Immediately on completion of the fluid-air exchange the instrument ports were sewn tightly and the infusion port connected to the manometer to allow repeated measurement of the IOP.

The eye was left undisturbed for 20 minutes, and IOP readings were taken every two minutes. At the end of the equilibration period a 1-0 ml sample of intravitreal gas was taken by means of a pars plana stab with a 25 gauge needle on a gas syringe. The IOP was immediately restored by means of the air pump. The sample was analysed by a Medishield MS2 mass spectrometer.

We had considered the factors known to influence gas transfer4 and endeavoured to keep as many as possible constant. Agitation was avoided by leaving the eye for 20 minutes without interference, while variations in blood flow and partial pressure were minimised by a standardised anaesthetic technique and stable haemodynamic parameters during the study period. The solubility coefficient is constant for a given gas. However, the diffusion coefficient may vary, as for example in aphakic eyes, in which the surface of the iris is available for gas transfer as well as the retinal surface. Similarly, aphakia will influence the surface area of the bubble as will high myopia. Diffusion distance

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Details of patients</th>
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<tr>
<td>Patient</td>
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RRD=rhegmatogenous retinal detachment. TRD=tractional retinal detachment.
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with the line of best fit. The correlation coefficient is 0.72, indicating that not all the variation is attributable to this factor. However, a $\chi^2$ test shows significance at the $p<0.02$ level.

No correlation between percentage of nitrous oxide, that is the extent of influx of the nitrous oxide, with the peak IOP during the study period was noted. This is presumably because of the uncontrolled and unquantified leakage from the sclerostomy sites which was apparent in all cases.

Discussion

The influx of nitrous oxide into an air-filled eye during anaesthesia occurs because of the high partition and diffusion coefficients (0.468 and 2.6 respectively) of nitrous oxide. Equivalent values for nitrogen are 0.0147 and 2.01 respectively, and for sulphur hexafluoride are 0.004 and 1.16. These high values for nitrous oxide ensure a net influx into the bubble even though other gases such as nitrogen and carbon dioxide are leaving the eye down their concentration gradients. What then is the clinical effect of this influx of nitrous oxide? Theoretically there are two situations to consider.

(1) Increment. If the nitrous oxide is added to the intraocular bubble, the IOP must rise, and according to the gas laws this can theoretically cause pressures in excess of 100 mm Hg.

$$PVT = \text{constant}$$

where $P$ is in mm Hg atmospheric, and $T$ is in degrees Kelvin. In our study we did record pressure rises of up to 40 mm Hg. However, above the level of 40 mm Hg the sclerostomies leaked, thereby preventing more serious pressure rises. These leaks occurred despite purposefully closing the sclerostomies tightly at the beginning of the period of study.

(2) Displacement. If the nitrous oxide simply displaces the other constituents it will result in a dilution effect; for example, 20% SF$_6$ (a commonly used non-expansile concentration) will be reduced to approximately 18%. This reduction will shorten the duration of action of the internal tamponade and may adversely affect the outcome of the surgery. Had the influx of nitrous oxide been relatively constant in all the cases

Results

INTRAOCULAR PRESSURE

A consistent pattern was observed in all the eyes studied. The IOP rose steadily over the first few minutes to a peak level which was 18–20 mm Hg above the baseline. Thereafter no further rises occurred, but gas bubbles were noted to be escaping from the sclerostomy sites. In the last few minutes of the study period the IOP was frequently observed to fall back towards the baseline level.

NITROUS OXIDE MOVEMENT

The percentage composition of nitrous oxide in the gas samples in each patient is shown in Table 2. The values ranged from 4 to 21% with a mean of 9%. The column on the right represents the number of quadrants of attached retina in each case. This was the only variable which showed a correlation with the percentage of nitrous oxide in the samples. We found no effect from any of the other parameters previously mentioned.

The correlation between the percentage composition of nitrous oxide and the number of quadrants of attached retina is shown in Fig 2

![Diagrammatic representation of apparatus.](image)

Figure 1 Diagrammatic representation of apparatus.
studied, it would have been possible to compensate for the dilutional effect by using a higher initial concentration. As our results show, however, there was a great deal of variation in influx between cases (from 4 to 21%). Hence any estimate of the final concentration in any one case is unlikely to be accurate.

We consider that peroperative rises in IOP secondary to nitrous oxide movement are not of significance in vitrectomy because of the venting effect of the sclerostomies. At the end of the anaesthetic, however, the nitrous oxide leaves the eye as quickly as it entered, and this will result in a precipitous drop in intraocular pressure which cannot be compensated for by increased aqueous production or movement of nitrogen or carbon dioxide into the gas bubble. The dramatic nature of this efflux was shown in an experiment by Lincoff et al. They found that nitrous oxide injected into the vitreous cavity of a cat was removed so rapidly when the animal was ventilated with air that the cornea became concave within 15 minutes.

The correlation coefficient of 0.72 in Fig 2 implies that there are other factors involved in the movement of nitrous oxide during anaesthesia. Their identification has not been possible owing to the small numbers in the present study; to identify them would require multivariate analysis and very large numbers of subjects. The inverse relationship between the extent of the detachment prior to the surgery and the percentage nitrous oxide in the samples suggests a definite trend. One possible explanation of this correlation is that gas transfer occurs more readily across retinal pigment epithelium which has maintained its normal anatomical and biochemical relationships. Mere physical reposition of the retina and pigment epithelium, as occurs during a fluid-air exchange, does not appear to result in immediate recovery of function. This might have been expected, since it is well known that a detached retina does not recover its normal transparency for several hours following successful reattachment.

The question whether the anaesthetist should be asked to turn off the nitrous oxide during vitrectomy remains contentious. Our results have led us to conclude that nitrous oxide should be turned off, for two reasons. The first is because the nitrous oxide displaces an unpredictable amount of the other gaseous constituents, and the second because of the problems associated with a period of hypotony postoperatively, namely, plasmoid aqueous production with a fibrinous iritis, and choroidal detachment or haemorrhage.