

Effect of hypercapnea and hyperventilation on human intraocular pressure during general anaesthesia following acetazolamide administration

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SUMMARY The changes in intraocular pressure due to blood pH, PCO_2 , and PO_2 alterations induced by hyperventilation and hypercapnea in man undergoing routine general anaesthesia were studied. It was shown that hypercapnea produces elevation of intraocular pressure, while hyperventilation lowers it. Acetazolamide pretreatment did not alter these IOP responses to PCO_2 , PO_2 , and blood pH changes.

Several factors, especially drugs, influence the intraocular pressure during general anaesthesia. All these are evaluated during intraocular surgery or in the determination of intraocular pressure in children. Among them the effect of hypercapnea and hyperventilation has not been sufficiently elucidated yet. Changes in intraocular pressure due to blood pH alterations are well known, and the IOP-decreasing effect of diabetic acidosis and coma has been reported since the beginning of the century. Recently interest in the correlation between the blood pH and intraocular pressure has increased. Duncalf and Weitzner,¹ Beaugié and Samuel,² and Kieler *et al.*³ have shown either in dogs or in man the IOP-increasing effect of hypercapnea as well as the decreasing effect of hyperventilation. On the other hand Krupin *et al.*⁴ have proved that acidosis, induced by intravenous administration of HCL, lowers the intraocular pressure in rabbits, while alkalosis, due to intravenous administration of Na bicarbonate, increases it. These 'contradictory' observations support a hypothesis that probably different mechanisms are involved in the IOP responses to blood pH changes, depending on the causes of these pH changes.

In the present paper we study the effect of different blood pH, PCO_2 and PO_2 on human intraocular pressure induced by primary respiratory mechanisms (hyperventilation, hypercapnea) during general anaesthesia. And the effect of oral acetazolamide

pretreatment on these IOP responses is also investigated.

Patients and methods

Twenty-four patients, of both sexes, aged 28 to 54 years, scheduled for various routine operations (in the supine position) under general anaesthesia were used in this study. They were selected from others after a complete examination (either systemic or ophthalmological) in order to exclude any possibility that the achieved pH 'borderline' values could have any side effects on them. All patients were premedicated with atropine (0.6 mg) and meperidine (75 mg). Anaesthesia was induced with thiopentone sodium. An endotracheal tube was inserted after pancuronium (4 mg) given intravenously. As is well known, these drugs only slightly affect the intraocular pressure. Anaesthesia was maintained with $N_2O + O_2$ in 5:2 mixture under control of ventilation. Respiratory alkalosis was achieved by hyperventilation manually and respiratory acidosis by insufficient administration of oxygen and isolation of the soda-lime circuit. During the operation the pulse rate and blood pressure were continuously determined, and ECG was recorded as well. Arterial blood samples were collected from the radial artery and analysed for PCO_2 , PO_2 , and pH values by an automatic analyser (Radiometer, Copenhagen). The intraocular pressure was measured by means of the Perkins handheld tonometer, using fluorescein strips. Benoxinate ophthalmic solution 0.4% was used for corneal anaesthesia before induction of general anaesthesia.

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The patients were divided in 2 groups. 14 (group I) underwent our standard experimental protocol: IOP determination before induction to anaesthesia, immediately after that, half an hour later, when the patients were in 'maximal' alkalosis, and finally

half to 1 hour later, when the 'maximal' acidosis was achieved. Also, immediately after induction of anaesthesia as well as during alkalosis and acidosis the blood pH, PCO_2 , and PO_2 were determined. In 10 more patients (group II), we repeated the same procedures 1 hour after a single dose of acetazolamide (500 mg) given orally. Intraocular pressure was also determined just before acetazolamide administration.

All results are expressed as the arithmetic mean \pm the SD of the mean. Student's *t* test (paired) was used for the statistical evaluation of the results.

Results

As Fig. 1 shows there was a slight decrease of intraocular pressure after induction of anaesthesia compared to the premedication values, due to administration of barbiturates and pancuronium. Under general anaesthesia half an hour after induction the achievement of respiratory alkalosis (pH: 7.46, PCO_2 30 mmHg and PO_2 112 mmHg) produced a marked fall in the intraocular pressure (average of both eyes 4.5 mmHg), which is highly significant ($P < 0.01$). Finally, when respiratory acidosis was achieved (pH 7.27, PCO_2 49 mmHg and PO_2 95 mmHg), the intraocular pressure was elevated (average of both eyes 7 mmHg) significantly ($P < 0.001$).

In the second set of experiments the same procedures were repeated 1 hour after acetazolamide administration. The mean IOP value of 10 patients, in whom the intraocular pressure was measured before premedication and acetazolamide administration, was decreased significantly (average of both eyes 4.6 mmHg ($P < 0.001$) after induction to anaesthesia. This was mainly due to acetazolamide pretreatment as well as to barbiturates and pancuronium administration (Fig. 2). Respiratory alkalosis (pH 7.47, PCO_2 28.5 mmHg and PO_2 122 mmHg) achieved half an hour after induction of anaesthesia further decreased the intraocular pressure (average of both eyes 2.5 mmHg). After that, half an hour to 1 hour later, an increase of intraocular pressure occurred (average of both eyes 6.25 mmHg) when respiratory acidosis was attained (pH 7.26, PCO_2 53.5 and PO_2 96 mmHg). This elevation of intraocular pressure is statistically highly significant ($P < 0.001$). Thus the preadministration of acetazolamide did not alter the IOP responses to blood pH, PCO_2 , and PO_2 changes. The changes in intraocular pressure during either alkalosis or acidosis in both phases of experiments were observed in every case, and so every patient acted as his own control.

The effects of either alkalosis or acidosis on

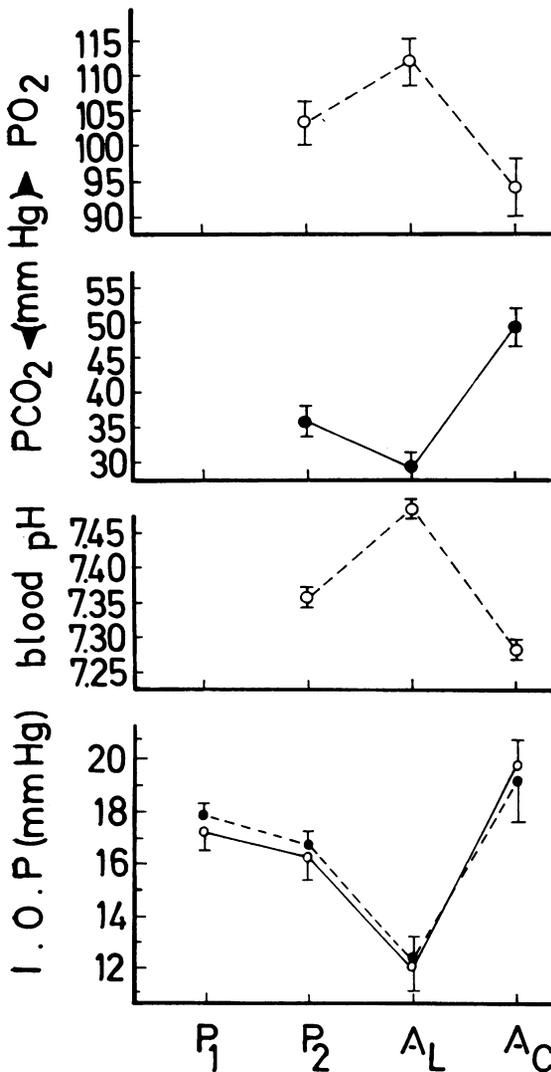


Fig. 1 Intraocular pressure changes due to blood pH, PCO_2 , and PO_2 alterations induced by primary respiratory mechanisms during general anaesthesia (number of observations = 14; vertical bars = SD of the mean). P_1 = before induction of anaesthesia and P_2 = immediately after that (baseline measurements). A_L = alkalosis, hyperventilation (roughly 1/2 hour after induction). A_C = acidosis, hypercapnea (approximately 1 hour after induction of anaesthesia and usually near recovery time).

intraocular pressure were not associated with changes in blood pressure and heart rate, which did not vary significantly to affect the intraocular pressure throughout the operation time.

Discussion

From these data we can conclude that PCO_2 alterations result in changes of intraocular pressure, which are not preventable by acetazolamide administration. Respiratory alkalosis decreases the intraocular pressure, while respiratory acidosis increases it. Our results are consistent with those of prior studies of intraocular pressure changes due to PCO_2 alterations in man and dogs.^{1,5} Partial disagreement with the results of Wistrand and Maren⁶ in rabbits is probably due to different experimental procedures. We also confirmed the opinion of Beaugié and Samuel² and Kielar *et al.*³ that the blood pH is neither a sensitive nor a determining factor in regard to IOP changes. So blood pH can fall with either rise or fall of intraocular pressure and vice versa (see baseline pH values on Fig. 1 and 2 and compare with IOP values on the same figures). Metabolic acidosis due to diabetic ketosis, severe muscular exercise, and acid or acetazolamide administration lowers intraocular pressure and also blood pH.^{4,7-10}

On the other hand respiratory acidosis, due to an increase of end-tidal CO_2 in a closed-circuit rebreathing system^{3,5} or to hypoventilation and isolation when using soda-lime circuit (as we did) lowers blood pH but increases the intraocular pressure. All these, as well as the fact that metabolic acid/base equilibrium disturbances are partially compensated by respiratory mechanisms and vice versa, could explain the apparent controversies about the results of the effects of these disturbances on intraocular pressure due to respiratory or metabolic causes.

The mechanism(s) of IOP elevation associated with PCO_2 increase is not clear yet. Increased venous pressure^{1,5} and/or increased uveal blood

flow¹¹ are the most likely explanations. Trying to prevent this IOP rise induced by increased PCO_2 , and in order to investigate whether or not an active secretion mechanism is also involved, we tested the effect of acetazolamide on IOP rise due

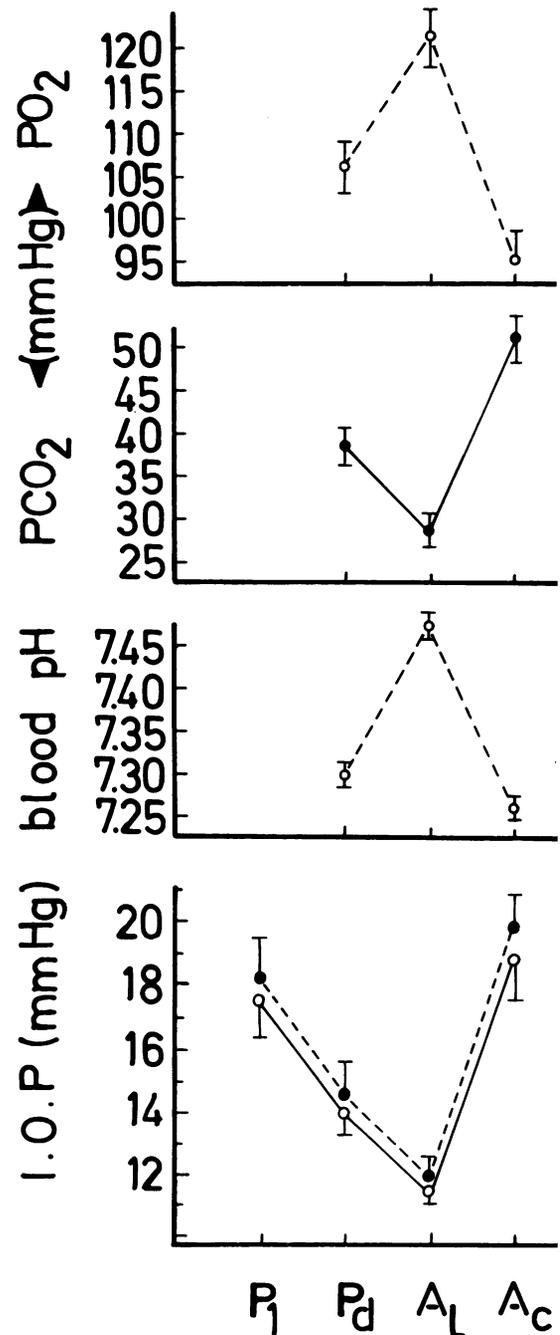


Fig. 2 Lack of effect of acetazolamide on IOP changes induced by hyperventilation and hypercapnea during general anaesthesia (number of observations = 10; vertical bars = SD of the mean). P₁ = IOP values before acetazolamide administration. P_a = IOP values 1 hour after acetazolamide administration orally and immediately after induction of anaesthesia. A_L = Hyperventilation, alkalosis (roughly 1 1/2 hour after induction). A_C = Hypercapnea, acidosis (approximately 1 hour after induction of anaesthesia and usually near recovery time).

to increased Pco_2 . The difficulties in explaining our results were due to the mechanism whereby acetazolamide reduces intraocular pressure, which is not entirely clear.

One theory is that part at least of the decrease in IOP which occurs after acetazolamide administration is explained by an induced systemic acidosis.^{7,8} Others^{12,13} seem to favour a vascular theory, suggesting that the mechanism of reduced aqueous formation may be due to vasoconstriction in afferent ciliary processes, decreasing ultrafiltration. Neither theory accounts for the inhibition of carbonic anhydrase. Inhibition of this enzyme, resulting in inhibition of bicarbonate formation, appears to be the basic explanation of the reduced secretion of aqueous humour.¹⁴

In our experiments according to the vasoconstrictive theory the pretreatment with acetazolamide should prevent the uveal vasodilation induced by increased Pco_2 , but no antagonism was observed. Moreover, the systemic acidosis induced by acetazolamide administration was uncompensated, because pulmonary hyperventilation was mechanically prevented (manual control of ventilation), and so the increased CO_2 was not removed. This should result in potentiation of the IOP-decreasing effect of acetazolamide and not its abolition. As a matter of fact the most suitable explanation is that the increased venous pressure, as well as the uveal vasodilation, induced by increased Pco_2 and not affected by acetazolamide (at least in the administered doses), were capable of reversing the IOP-decreasing effect of acetazolamide. Evidently more elaborate experiments in animals are required to clarify the role of acetazolamide in IOP changes induced by Pco_2 alterations.

We believe that our results have clinical value. This is in the determination of intraocular pressure in children, which always requires general anaesthesia. Probably the intraocular pressure which is measured without determination of Pco_2 is rather inaccurate whatever the anaesthetic agent used. Also, there is a problem in patients undergoing intraocular surgical procedures such as cataract extraction under local anaesthesia. These patients

are always hypoventilated because of the grossly limited breathing space due to the covering of their face. Sometimes the harmful and (inexplicable) elevation of intraocular pressure during the critical time of the operation is due to increased Pco_2 , and according to our results (and to our experience in 4 cases) the routine preoperative administration of acetazolamide does not prevent this result.

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