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Chronic stable asthma and the normal arterial pressure of carbon dioxide in hypoxia

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Summary and conclusions

Arterial blood-gas tensions, pH, and peak expiratory flow rate were measured in 29 patients with chronic asthma in a stable state. The hypoxia in these patients was found to be comparable with the hypoxia seen in normal subjects at high altitude in its effects on arterial pressure of carbon dioxide (P_{aCO_2}).

These results suggest that in patients with asthma the P_{aCO_2} taken as normal should be related to the arterial oxygen tension. Any increase in the observed value compared with this predicted value indicates impaired respiratory control. This may well help in assessing the patients at greatest risk during an attack of asthma.

Introduction

Patients with asthma often have an arterial carbon dioxide tension (P_{aCO_2}) lower than the generally accepted normal value. The same patients, however, may be moderately or even severely hypoxic. We consider that a parallel should be drawn with normal subjects acclimatised to the hypoxia of altitude, in whom P_{aCO_2} is reduced linearly with hypoxia.¹ Patients with asthma may remain in a comparatively stable state with few symptoms and yet be hypoxic. If such patients respond to hypoxia in a similar fashion to normal subjects acclimatised to the hypoxia of high altitude they will also lower their P_{aCO_2} . In order to investigate this possibility we measured arterial oxygen tensions (P_{aO_2}) and P_{aCO_2} in patients with chronic stable asthma.

Patients and methods

Patients were prospectively selected for this study if they fulfilled five criteria. (1) They had a history of asthma since childhood; (2) peak expiratory flow rate or forced expiratory volume in one second increased by over 15% either spontaneously or after inhalation of 200 μ g isoprenaline sulphate; (3) skin-prick tests to two common allergens were positive and there was a history suggesting that symptoms increased on exposure to these allergens; (4) there was an excess of eosinophils in the sputum or blood, or both; and (5) no appreciable change in exercise tolerance, wheeze, or tightness of the chest had occurred in the preceding week.

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All patients had extrinsic asthma. We excluded those with clinical features suggesting chronic obstructive bronchitis. Most patients were studied at a routine follow-up asthma clinic; a few were studied on admission to hospital for investigation or treatment of chronic intractable asthma. Criteria for chronicity were based mainly on history and a normal arterial pH. In a few patients peak expiratory flow rate was known to have been stable over the preceding week.

Arterial blood samples were obtained by percutaneous puncture of the non-dominant radial artery. Arterial blood was analysed for pH, P_{aO_2} , and P_{aCO_2} with an IL 213 blood-gas analyser. Calibrations for pH were made using standard buffers (N B S Washington) and for P_{aCO_2} and P_{aO_2} using known gas mixtures previously analysed with the Haldane apparatus. Patients were excluded from the study if their arterial pH was outside the range 7.35–7.46, as this suggested that the asthma was not chronic. Peak expiratory flow rate was measured within a few minutes of arterial puncture.

Results

Twenty-nine patients with extrinsic asthma (21 men and eight women), whose ages ranged between 19 and 44 years, were included in the analysis. Peak expiratory flow rate varied between 100 and 490 l/min. The table shows arterial blood-gas tensions, arterial pH, and peak expiratory flow rate for each patient.

Arterial pressures of oxygen (P_{aO_2}) and carbon dioxide (P_{aCO_2}), pH values, and peak expiratory flow rate in patients with chronic stable asthma

Case No	Sex	pH	P_{aO_2} (kPa)	P_{aCO_2} (kPa)	Peak expiratory flow rate (l/min)
<i>Outpatients</i>					
1	M	7.43	10.5	3.7	140
2	M	7.44	8.5	3.9	110
3	F	7.42	8.0	3.6	120
4	M	7.38	8.5	3.6	140
5	M	7.14	14.0	5.1	360
6	M	7.42	10.9	4.7	400
7	M	7.41	13.7	5.1	230
8	M	7.43	11.6	4.8	240
9	M	7.40	10.1	4.4	480
10	M	7.42	10.5	4.8	160
11	M	7.41	9.9	5.1	120
12	F	7.41	13.6	5.3	420
13	M	7.44	10.1	5.2	
14	M	7.46	8.4	4.1	150
15	M	7.44	10.5	4.5	280
16	M	7.43	12.7	5.1	242
17	M	7.40	10.8	5.1	490
18	M	7.44	11.2	5.1	460
19	M	7.41	10.1	4.7	460
20	M	7.41	8.4	4.4	320
21	F	7.43	10.7	4.9	300
22	F	7.42	12.3	5.1	270
<i>Inpatients</i>					
23*	F	7.42	10.1	4.5	160
24*	F	7.45	8.3	4.4	
25	F	7.45	6.7	3.6	100
26	F	7.43	8.0	4.1	100
27	M	7.40	10.0	4.5	200
28	F	7.44	10.7	4.4	280
29	M	7.41	11.7	5.2	180
30	M	7.40	11.1	5.1	200

*Values recorded in same patient during two separate admissions. Mean arterial pH was 7.423 pH; mean peak expiratory flow rate 254 l/min. Conversion: SI to traditional units— P_{aO_2} and P_{aCO_2} : 1 kPa $\approx$ 7.5 mm Hg.

Figure 1 shows the relation between P_{aCO_2} and P_{aO_2} . The trend towards a lower P_{aCO_2} accompanying a low P_{aO_2} is highly significant ($p < 0.001$). The relation is: $P_{aCO_2} \text{ predicted} = 0.23 P_{aO_2} + 2.2 \text{ kPa}$ (or $P_{aCO_2} \text{ predicted} = 0.23 P_{aO_2} + 16.6 \text{ mm Hg}$). This is not significantly different from the relation given by Wolff¹ for normal subjects acclimatised to altitude hypoxia.

Discussion

Asthma is defined as reversible airflow obstruction. Despite considerable variation in the degree of obstruction, however, many patients maintain remarkably stable arterial blood-gas tensions. Often, despite improvement in peak expiratory flow rate after admission to hospital, the arterial blood-gas tensions fail to improve for several days.² Rebuck and Read² showed that

the mechanism leading to the fall in P_{aO_2} is only partially related to peak expiratory flow rate. Reduction in P_{aO_2} is associated with plugging of small airways, leading to a shunt effect.^{2–4} Persistence of small-airway dysfunction, with associated hypoxia but few symptoms, is well documented in asthma.⁵

We studied arterial blood-gas tensions in patients with chronic stable asthma to investigate whether there is a relation between P_{aO_2} and P_{aCO_2} similar to that found in normal subjects

FIG 1—Relation between P_{aCO_2} and P_{aO_2} in 29 patients with chronic stable asthma.

— = Least squares regression line. --- = Regression line extrapolated below 6.7 kPa (50 mm Hg). = Relation between P_{aCO_2} and P_{aO_2} calculated by Wolff¹ for normal subjects acclimatised to altitude hypoxia.

Conversion: SI to traditional units— P_{aCO_2} and P_{aO_2} : 1 kPa $\approx$ 7.5 mm Hg.

FIG 2—Relation of P_{aCO_2} and P_{aO_2} in patients with status asthmaticus (from Rees *et al.*²). The line is the least squares regression line in our patients with chronic stable asthma (see fig 1). All the patients of Rees *et al.* had P_{aCO_2} values above the line, reflecting hypoventilation in relation to the ventilation expected from the degree of hypoxia.

O = Patients with pH value 7.35–7.46. ■ = Patients with pH > 7.46 . ▲ = Patients with pH < 7.35 . ○ = Two patients at same point.

Conversion: SI to traditional units— P_{aCO_2} and P_{aO_2} : 1 kPa $\approx$ 7.5 mm Hg.

acclimatised to altitude hypoxia. An arterial pH within the range 7.35–7.46 was taken to indicate stability of the clinical condition, suggesting that the patient was neither acutely hypoventilating nor hyperventilating. The causes of the hypoxia in normal subjects at altitude and in patients with chronic stable asthma differ. In the normal subjects the arterial hypoxaemia is due to a low inspired oxygen concentration, whereas in our patients it resulted from a shunt effect. Despite the different mechanisms, the close similarity between the relations of P_{aCO_2} to P_{aO_2} in our patients and in normal subjects acclimatised to altitude hypoxia (fig 1) suggests that the ventilatory control system in patients

with chronic stable asthma responds appropriately to hypoxia. We suggest that in the presence of chronic hypoxia the value of PaCO_2 taken as "normal" should be that predicted by the relation of PaCO_2 to PaO_2 shown in figure 1—that is, a PaCO_2 of 5.3 kPa (40 mm Hg) would be normal if PaO_2 were 13.3 kPa (100 mm Hg) but abnormally high and indicating hypoventilation if PaO_2 were low. The "normal" PaCO_2 would be 3.7 kPa (28 mm Hg) at a PaO_2 of 6.7 kPa (50 mm Hg).

We considered that patients who are severely ill from asthma might not show the acclimatisation response to hypoxia because respiratory control is abnormal or because of severe mechanical impairment to ventilation. Rees *et al*³ reported arterial blood-gas values for patients with status asthmaticus. We examined the relation of PaCO_2 to PaO_2 by plotting the values obtained in their patients on the day of admission (fig 2). In all patients PaCO_2 was above the value predicted from our patients with chronic stable asthma. Many of the patients of Rees *et al* would already be regarded as severely ill on the basis of their arterial blood-gas and pH values. There remains a group with a PaCO_2 of about 5.3 kPa (40 mm Hg), however, in whom we suggest ventilatory control was impaired. These patients had therefore failed to adjust their ventilation normally, even though most of them had probably been severely ill and hypoxic for several days.⁶⁻⁸

In conclusion, we suggest that the relation between PaCO_2 and PaO_2 in patients with chronic stable asthma (PaCO_2 predicted = $0.23 \text{ PaO}_2 + 2.2 \text{ kPa}$ (or 16.6 mm Hg)) be adopted as a criterion for assessing adequacy of ventilatory control. Values of PaCO_2 above this predicted normal indicate impaired ventilatory control and may give early warning of impending decompensa-

tion in patients severely ill from asthma even when the arterial pH is normal.

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Changes in glycosylated haemoglobin after poor control in insulin-dependent diabetics

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Summary and conclusions

Glycosylated haemoglobin (HbA_{1c}) was measured in seven insulin-dependent diabetic patients before, during, and after a seven-day period of monitored poor control. There was considerable individual variation in the pattern and degree of change in HbA_{1c} concentration induced by poor control and the time when it occurred. Greater increases in HbA_{1c} were seen during the period of metabolic derangement than in the subsequent two months.

More information is required before HbA_{1c} estimations are widely used clinically to monitor control in individual diabetics.

Introduction

Concentrations of glycosylated haemoglobin (HbA_{1c}) are raised in diabetic patients and, since the glucose linkage is considered

to be relatively stable, are thought to reflect the mean blood glucose concentration during the preceding one to two months. Hence HbA_{1c} estimations are being used as a means of monitoring the degree of overall control of blood glucose achieved in individual diabetics. There are, however, many problems associated with measuring HbA_{1c} and neither the time relation between changes in blood glucose and HbA_{1c} concentrations nor the stability of HbA_{1c} nor its sensitivity in detecting poor control has been clearly defined.

We compared two common methods of estimating HbA_{1c} and examined the change in concentration of HbA_{1c} resulting from a period of poor control deliberately induced in longstanding, insulin-treated diabetic patients maintained under strictly monitored, metabolic conditions.

Patients and methods

One male and six female diabetic patients being treated with insulin were studied (table I). All were fully ambulant, none was obese, and none had retinopathy, neuropathy, or nephropathy. All gave informed consent to the investigation.

The study covered 13 weeks and was divided into three periods. In the initial three-week assessment period patients were at home following their usual diet and insulin regimen and undertaking normal activity. They were visited each week on the morning after completing a 24-hour urine collection for measuring urinary glucose excretion, and fasting blood was taken for estimating whole blood true glucose, serum lipid, and HbA_{1c} concentrations.

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