these patients is helpful for assessing the mechanism and severity of impairment of their gas exchange.

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Thorax 1994;**49**:725–727

Spontaneous improvement in a patient with the hepatopulmonary syndrome assessed by serial exercise tests

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Abstract

A 37 year old patient with chronic active hepatitis progressing to cirrhosis presented with increasing breathlessness and was found to be hypoxic with finger clubbing. A progressive exercise study with measurement of oxygen saturation (Sa_{O_2}) showed abnormally high ventilation and desaturation to 81% at 100 W. Serial studies over nearly two years showed, first, deterioration, then improvement with lower ventilation and higher saturation levels at all work loads. This could not be correlated with any change in treatment with azathioprine, prednisolone, or propranolol.

(*Thorax* 1994;**49**:725–727)

About one third of patients with hepatic cirrhosis are found to have arterial hypoxaemia without any of the usual cardiorespiratory causes. A few have obvious cyanosis with clubbing. The hypoxia is due either to right to left shunts through large arteriovenous connections within the lungs, or to peripheral vasodilatation of the fine branches of the pulmonary artery at both precapillary and capillary levels[1 2] leading to incomplete diffusion equilibration between alveolar and end capillary blood. The pathophysiology has recently been fully reviewed.[3]

Case report

The patient presented at the age of 27 with nose bleeds, jaundice, anaemia, and swelling of legs and abdomen. Chronic active hepatitis was diagnosed by liver biopsy and, over subsequent years, further biopsies showed progression to cirrhosis despite treatment with prednisolone and azathioprine which had been prescribed for about five years, in varying dosage, before the present study. The cause of the chronic active hepatitis was never established. An autoantibody screen, including antibodies to smooth muscle and mitochondria, was negative. Hepatitis B serology was negative, and hepatitis C serology was not available at that time. The concentration of plasma α_1-antitrypsin was not directly measured, but the level of α_1-globulin was increased.

Ten years after his first attendance he complained of breathlessness and was referred for respiratory assessment. He was clubbed but not cyanosed at rest. He said he was unusually short of breath on exertion, but there was no serious limit to his exercise tolerance and throughout the period of the study he worked full time as a welder on a British Rail track gang, and could play 36 holes of golf in a day without discomfort. During the period of study standard liver function tests were abnormal, and varied without any systematic trend with ranges as follows: bilirubin 55–90 μmol/l, albumin 30–32 g/l, alkaline phosphatase 191–344 IU/l, gamma-GT 93–134 IU/l, and alanine transaminase 28–87 IU/l. He continued to drink alcohol, but it was difficult to assess in what quantity.

Blood gas measurements were obtained sitting (Pa_{O_2} 9·2 kPa, Pa_{CO_2} 4·3 kPa) and lying (Pa_{O_2} 9·3 kPa, Pa_{CO_2} 3·8 kPa). Pure oxygen was given from a balloon reservoir with careful exclusion of leaks from the breathing circuit whereupon Pa_{O_2} rose to 60·6 kPa. A pulmonary perfusion scan with technetium-99 m labelled albumin microspheres, analysed according to the method of Chilvers *et al*,[4] showed that 42% of the tracer passed through the lungs. The chest radiograph was normal. Lung volumes, both static and dynamic, were normal, but transfer factor for carbon monoxide (T_{LCO}) and transfer coefficient (K_{CO}) were

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Received 20 July 1993
Returned to authors
25 August 1993
Revised version received
2 September 1993
Accepted for publication
14 September 1993

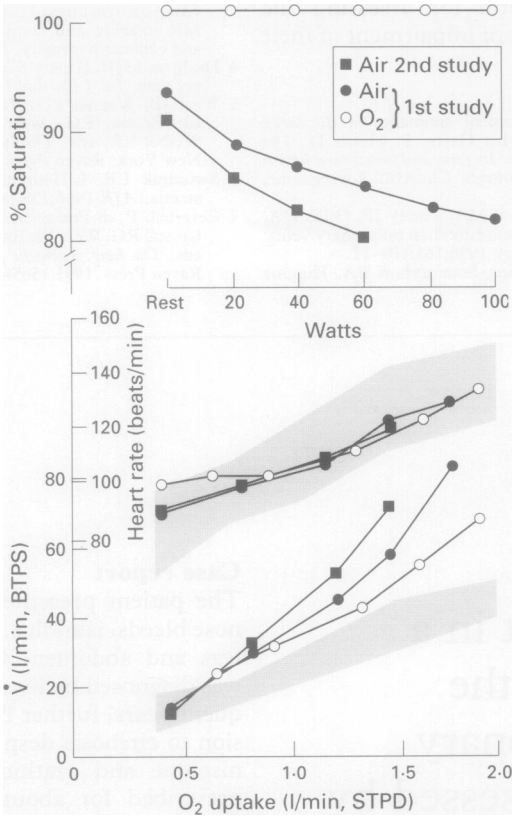

Figure 1 Heart rate, ventilation, and arterial oxygen saturation during the first incremental exercise test with air and oxygen breathing and, in a second test 35 weeks later, air breathing only. Shaded areas denote range of normal values.

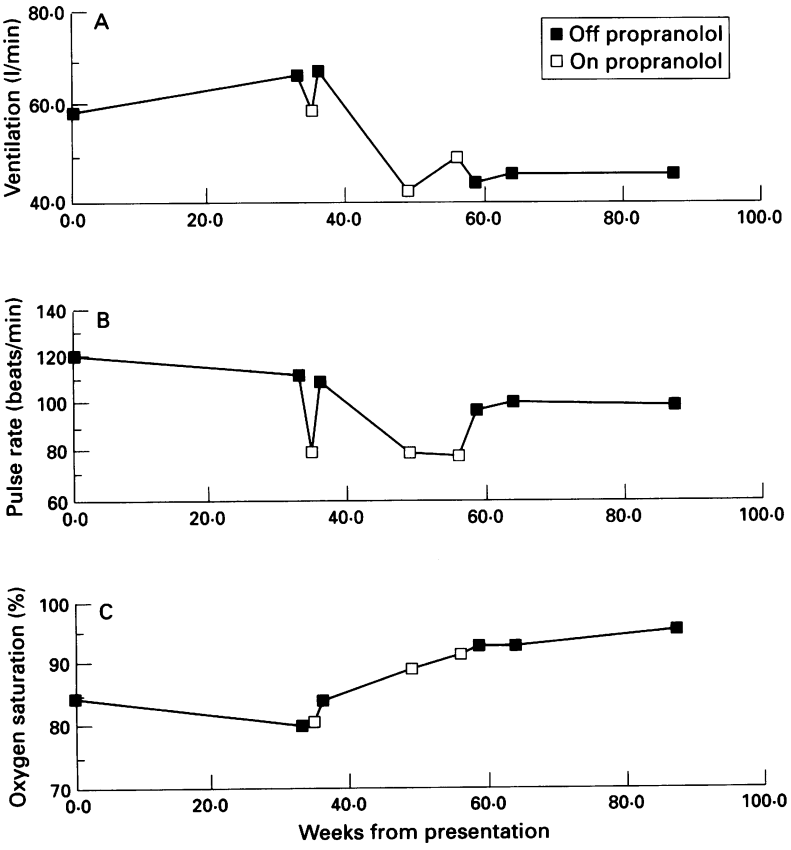

Figure 2 (A) Ventilation, (B) pulse rate, and (C) percentage arterial oxygen saturation at 60 W taken from a series of progressive exercise tests. Open symbols denote tests done when the patient was on propranolol, 40 mg three times daily. BTPS = body temperature and pressure, saturated with water vapour.

low (6·2 mmol/min/kPa and 0·85 mmol/min/kPa/l respectively), predicted normal values being 10·6 and 1·7.

A progressive exercise study was done with two minute increments measuring pulse rate, ventilation breath-by-breath, and Sao_2 by pulse oximetry (Biox). The study was ended by the supervisor when saturation fell to 80% at 100 W (fig 1), although the patient was comfortable and had not contemplated stopping. Pulse rates were normal, but ventilation approached double normal values at higher loads.

A second study performed 35 weeks later had to be ended when saturation fell to 80% at only 60 W. We anticipated that the patient would continue to deteriorate and might require liver transplantation, and decided to assess his problem by serial exercise studies. Results taken from these studies at the single work load of 60 W are shown in fig 2. Results at other work loads were concordant; 60 W was the highest work load which was completed on every attendance with saturation more than 80%.

At the same time propranolol 40 mg three times daily was prescribed both as a prophylactic against bleeding from varices,[5] and because it might improve oxygenation by slowing flow through dilated pulmonary vasculature. A third study (fig 2) after two weeks of treatment with propranolol showed the expected fall in pulse rate, some decrease in ventilation, but no change in saturation. A fourth study was done a week after stopping propranolol and the drug was then again prescribed between weeks 36 and 56. Pulse rate again slowed as expected but, to our surprise, ventilation fell at all exercise levels from 70 l/min to 45 l/min at 60 W, and saturation levels improved from 84% to 92% at 60 W.

We then stopped treatment with propranolol. Pulse rate rose, but to lower levels than originally, and the improvements in ventilation and saturation were maintained or enhanced over a period of six months. Finally, the patient could exercise to 100 W with Sao_2 falling only to 93%.

At this stage the perfusion scan was repeated, showing that the percentage of tracer passing through the lungs, previously 42%, was now less than 2%. Pao_2 was 10·3 kPa and $Paco_2$ 4·8 kPa at rest. TLCO and KCO were still low, however, and hardly changed (6·42 and 0·93 respectively); the patient was still clubbed.

Discussion

Our patient had the typical signs and investigative findings of the hepatopulmonary syndrome,[3] with the exception of platypnoea. It is likely that in such patients some powerful circulating pulmonary vasodilator interferes with hypoxic vasoconstriction and produces functional and, after a time, structural vasodilatation of the pulmonary microvasculature. Hypoxia is caused by anatomical shunting within the lung, through large arteriovenous connections to areas with high local flow relat-

ive to ventilation, and by impairment of diffusion of oxygen to the central rapid stream through grossly dilated microvessels. The relative importance of these three mechanisms appears to vary widely between patients, and the studies reported here do not allow us to distinguish between them in this case.

During the period of study treatment with prednisolone (20 mg every other day) and azathioprine (150 mg daily) was unchanged. We cannot correlate the improvement with beta-blockade since there was no response to the initial two weeks of treatment and subsequent improvement was maintained and enhanced over a period of six months with no propranolol (fig 2). It is possible that a period of beta-blockade might permanently switch off or diminish the secretion of some undefined vasodilator, but this is so speculative that we prefer the hypothesis that the improvement was unrelated to treatment. If so, one must treat with caution reports of improvement following drug treatment in individual patients.[6] The improvement in lung function was not matched by any correlated change in liver function. No biopsy was performed during the study period.

Although a fall in SaO_2 during exercise would be predicted in patients with low resistance pathways through the lungs, we know of no other systematic study of this point in patients with the hepatopulmonary syndrome. In particular, although it is well known that in the hepatopulmonary syndrome administration of pure oxygen will raise SaO_2 to 100% at rest, we think this is the first demonstration of the same effect in moderate exercise. Serial exercise studies with non-invasive measurement of SaO_2 proved to be an effective method of assessing this patient, and we recommend them providing they are supervised by appropriate staff and terminated if necessary at previously determined tolerance levels.

The authors thank Dr J D Maxwell for referring the patient for assessment.

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Thorax 1994;**49**:727–728

Late asthmatic response to inhaled glacial acetic acid

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Received 15 February 1993
Returned to authors 28 May 1993
Revised version received 5 August 1993
Accepted for publication 27 October 1993

Abstract

A patient with bronchial asthma who developed a late asthmatic response to inhalation challenge with glacial acetic acid is presented. This is believed to be the first description of a reaction to this allergen in an asthmatic patient.

(*Thorax* 1994;**49**:727–728)

Exposure to glacial acetic acid has so far been reported to induce either reactive airway disease, as described following accidental exposure,[1] or interstitial pneumonitis.[2] We report a patient with suspected asthma to glacial acetic acid who developed a late reaction to inhalation challenge with glacial acetic acid carried out in a special environmental chamber.

Case report

The patient was a 58 year old man who had developed asthma over the previous two years. He reported having asthma during childhood, but had been symptom-free from the age of 11 to 56 years. Over the previous two years, however, he had been exposed to glacial acetic acid in the canning factory where he worked. Glacial acetic acid was used in the pickling of cucumbers and the fumes were released into the surrounding air. Exposure to glacial acetic acid fumes occurred during the 10 minute process of heating the mixture when the patient stood in the vicinity unmasked. A few months after the initial exposure he began having asthmatic attacks which were relieved with salbutamol. Symptoms occurred initially only on working days, but soon became more frequent, occurring also over weekends and on holidays. As the symptoms worsened he was given daily treatment with high dose beclamethasone dipropionate (800 μg/day), supplemented with salbutamol as required.

Exposure to a small amount of glacial acetic acid was on a daily basis, and occasionally to increased amounts, with subsequent worsening of symptoms. Shortness of breath occurred a few hours after exposure to glacial acetic acid and continued also at home. Occasional exposure to cigarette smoke, cold air, or other irri-