PAPERS AND ORIGINALS

Asthma deaths in Cardiff 1963-74: 90 deaths outside hospital

J B MACDONALD, A SEATON, D A WILLIAMS

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Summary

In a detailed study of factors associated with death from bronchial asthma outside hospital 90 patients were investigated. The fatal attack was typically short and was most likely to occur in patients with a long history. Deaths often occurred before effective medical help was obtainable, but occasionally the patient or the doctor underestimated the severity of the attack. Patients especially at risk were those recently discharged from hospital after a previous attack. These deaths might be prevented by better patient education, a self-admission service for selected asthmatics, and by doctors using objective measurements of severity of asthma for the control of treatment. The underuse of corticosteroids is an important factor associated with death.

Introduction

The death rate from asthma in Britain has shown a remarkable fluctuation, falling in the 1950s, rising in the 1960s by 45% overall, and falling again since then. These changes have been related to changes in treatment and especially to the introduction of corticosteroids and pressurised aerosol sympathomimetics, though opinion is divided as to how far the latter drugs have been responsible for contributing to death in these patients.¹⁻⁷ Although the death rate now seems to be declining, asthma remains an important cause of death at all ages. As acute episodes are potentially reversible, these deaths should be preventable if treated promptly and effectively. Since there is relatively little detailed information on the factors associated with death from asthma, we present an analysis of all deaths

known to have occurred from this disease in the Cardiff area since 1963. Here we consider the deaths that occurred before the patient reached hospital.

Methods

Cardiff and its surrounding towns had a population of around 300 000 during the period of the study. Since before 1960 every death in the area that has had "asthma" mentioned on the death certificate was notified to one of us, who then collected all available information about the patient by writing to the general practitioner, obtaining old hospital notes, and reviewing the necropsy reports. In all cases this was done shortly after the death occurred. Many of these patients had already attended the Cardiff asthma clinic and many of those dying outside hospital underwent necropsy, two facts that have increased the reliability of our data.

Criteria for inclusion in this analysis were death outside hospital and the presence of necropsy evidence of asthma or a convincing clinical history. In 66 of the 90 patients necropsy showed hyperinflated lungs that did not collapse on opening the thoracic cage and a bronchial tree extensively plugged with sticky mucus. Of the other 24 patients, 22 had attended the asthma clinic and had been shown to have reversible airways obstruction. Classical histories of asthma had been recorded in the remaining two patients. Patients whose asthma was possibly not the only cause of death or in whom the evidence for asthma was less convincing were eliminated.

Analysis of deaths

GENERAL FACTORS

Temporal variations—About 2% of the population of Cardiff—that is, about 6000 people—have asthma.^{8,9} Table I shows the number of deaths in Cardiff outside hospital in 1963-74. A similar rise in the mid-1960s to that which occurred nationally is apparent. Seasonal variations occurred only in those aged 5 to 34 years, who had almost three times as many deaths in spring and summer as in the rest of the year.

TABLE I—Asthma deaths outside hospital in Cardiff 1963-74

Year:	1963	64	65	66	67	68	69	70	71	72	73	74
No of deaths:												
In males ..	4	2	11	5	3	3	1	3	2	5	2	4
In females ..	2	2	8	8	5	2	4	2	1	3	1	7

Asthma Research Unit, Sully Hospital, Penarth, South Glamorgan CF6 2YA

J B MACDONALD, MB, MRCP, senior medical registrar (present address: City Hospital, Hucknall Road, Nottingham)

A SEATON, MD, MRCP, consultant physician

D A WILLIAMS, MD, FRCP, honorary consultant physician

Atopic status—At least one strongly positive prick-test reaction was present in 22 of the 47 patients tested, and 73% of these patients died between April and September. Over 40% of those in the younger age groups (5-34 or 5-19) who were tested were not atopic.

Sex ratio and age—Half of the 90 patients were male. The age of death ranged from 9 to 76 years with a mean of 45 years. There was no significant difference between the ages of males and females.

Time of death—The hour of death was known in 79 of the 90 patients and showed no significant trend.

SPECIFIC FACTORS

Severity of asthma—The age of onset of asthma was known in 75 patients; it ranged from 6 months to 70 years. One-third of patients had had their first attack by the age of 10 years and there was a second peak in the fourth decade. In 26 patients asthma started after the age of 40. There was a wide spectrum of length of history, from three months to 51 years (mean 16 years). Three patients died within six months of onset, though most were chronic asthmatics. The history of previous hospital admissions with severe attacks was known in 83 (92%) of the 90 patients. Thirty-three patients (40%) had never been admitted, while 23 (28%) had had three or more admissions. Twenty-eight patients (34%) had been admitted in the year before death and 10 of these had been admitted more than once. Five patients had been discharged less than one week and another nine within one month before death. Altogether 17 (21%) had been discharged less than two months before death. Of the 80 patients for whom adequate records were available 27 (34%) had never been referred to a clinic. Fifteen patients attended a clinic within a month of death but only eight of these had undergone adequate repeated tests of ventilatory function. Five had shown a deterioration at their last visit and the other three had been unchanged.

Drug treatment—Table II shows the patients' treatment at the time of death. Forty-two (47%) were on oral steroids and five on ACTH, though the doses tended to be lower than those known to be effective in severe asthma. Almost half the patients were not on steroids. Thirty patients were known to be taking bronchodilator inhalers and 33 oral bronchodilators. Of the 42 patients receiving prednisone four had an increase in dose in the month before death, while 10 had a reduction. Twenty-two remained on the same dose and information was not available in six.

TABLE II—Corticosteroid treatment before final episode in 90 patients

	No corticosteroids	Prednisone (mg/day)						Dose unknown	ACTH
		<5	7.5	10	15	20	>20		
No of patients	43	6	3	15	10	2	1	5	5

FINAL EPISODE

Table III shows the duration of the final episode in the 74 patients on whom information was available. The fatal exacerbation lasted less than 30 minutes in 17 (23%) patients, less than two hours in 25 (34%), and less than eight hours in 45 (61%).

TABLE III—Duration of final episode of asthma

Final episode: No of patients	<30 min	30 min -2h	-8h	-24h	-2d	-4d	-14d	>14d	Unknown
	17	8	20	13	5	4	5	2	16

In 20 cases the final illness came on too rapidly or was discovered by someone else too late to call a doctor. In a further 19 cases the patient and his relatives did not call the doctor, though time was available. The general practitioner was called and visited in 43 cases, but half these patients were dead (20) or dying (2) when he arrived. There was no evidence of delay in attending these patients. For the 21 patients still alive the doctors recommended hospital admission for only 12; two patients refused and 10 died in the ambulance or while waiting for it. There was no evidence that ambulance delay was a contributory

factor. In eight cases we did not know whether the general practitioner was called.

Details of treatment given to the 21 patients seen by a doctor before death were available for 12. Three were given parenteral aminophylline, three subcutaneous adrenaline, and three oral steroids (5 or 10 mg thrice daily). One was given tablets of unknown type and two had no change made in their existing regimen.

Discussion

In each of the last 12 years an average of seven of Cardiff's 6000 asthmatics have died of their disease without reaching hospital. Our aim in this investigation was to identify what improvements might prevent death.

Our most striking finding was the speed of onset of the fatal attack. A quarter of our patients died within 30 minutes of the onset of their attack, while only a third had attacks lasting over eight hours. Associated with this was our finding that three-quarters of the patients died before seeing a doctor. This could not be attributed to unreasonable delay on the doctor's part, as in half the attack proved fatal too quickly for a call to be made and in the other half the doctor arrived promptly but too late. When the doctor arrived to find the patient still alive, however, he was as likely as not to underestimate the severity of the attack and fail to advise admission to hospital. When admission was advised the patient occasionally refused.

The implications of these findings, which are similar to those of Frazer *et al.*¹⁰ are that patients must be educated to seek medical help early if an attack fails to respond to bronchodilators. Doctors must also be made aware of the danger signs—namely, failure to get relief from bronchodilators, distressed breathing, and tachycardia. Since fatal attacks may be so brief, the necessity for a hospital admission service independent of the general practitioner becomes clear. Such a service has recently been reported from Edinburgh.¹¹ This service gives immediate admission without the need for medical referral to all asthmatics previously in hospital with severe asthma. We have reassessed our patients to see how many lives could have been saved if a similar service had been available in Cardiff. Adequate information was available on 65 patients, of whom 33 could have admitted themselves because their attack was sufficiently long and help was available. Nineteen of these would have been eligible for the Edinburgh service, having previously been admitted with severe attacks.

Our investigation has proved a little disappointing in identifying patients most at risk of death from asthma. Most deaths, however, occurred in chronic asthmatics. Most of these patients had been admitted previously with severe asthma, a third of them in the year preceding death, and five patients actually died within a week of discharge. These deaths are the responsibility of the hospital, because symptomatic relief from asthmatic attacks occurs long before resolution of physiological and blood gas abnormalities.¹²

Other workers have emphasised the possible dangers of bronchodilators to such effect that many doctors now concentrate on blaming their patients for abusing these drugs without providing any effective alternative treatment. Since aerosols are ineffective in severe asthma because of poor penetration to their site of action,¹³ and since asthmatics die from plugging of bronchi with inflammatory exudate, the only effective treatment in such patients is corticosteroids. In our study, as in that of Frazer *et al.*¹⁰ only half of the patients were taking these drugs, and those that were were on relatively small doses.

As a result of our findings, we make the following suggestions for preventing death from asthma outside hospital.

(1) The patient should be aware that a distressing attack could be fatal and that he should seek medical help urgently if his aerosol bronchodilator fails to help him.

(2) The general practitioner should be aware of the rapidity of onset of many fatal attacks and of the danger signs of a distressed patient with a rapid pulse.

(3) Doctors interested in asthma should organise an Edinburgh-type admission service for selected patients from their clinics.

(4) Patients attending the asthma clinic should be encouraged to refer themselves back if their condition is deteriorating and should be prepared to put themselves on high-dose steroids at the same time.

(5) Every doctor looking after patients with asthma should be aware of the need for objective measurements (pulse rate and peak flow rate) in assessing the severity of the disease in his patients and should know how to institute emergency treatment. In severe cases the doctor should accompany the patient to hospital. Discharge from hospital of recovering patients should occur when objective measurements show a return to the patient's normal values. Steroid treatment should be continued at least until the patient is seen in the clinic.

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Immune response to HBsAg and the spectrum of liver lesions in HBsAg-positive patients with chronic renal disease

R M GALBRAITH, N EL SHEIKH, B PORTMANN, A L W F EDDLESTON,
ROGER WILLIAMS, V PARSONS, M BEWICK, C S OGG

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Summary

Evidence of chronic hepatitis was found on histological examination in nine out of 15 patients positive for hepatitis-B surface antigen (HBsAg) who had either chronic renal failure or a functioning renal transplant. Cirrhosis had already developed in three of the patients, who deteriorated rapidly and died. Liver biopsies from the remaining 12 patients showed the features of chronic aggressive hepatitis in two, chronic persistent hepatitis in four, and minor histological lesions in six. The persistence of HBsAg in patients with renal failure or in those receiving immunosuppressive drugs after a transplant must indicate some impairment of the normal immune response to hepatitis-B viral antigens. Nevertheless, cellular or humoral immunity to HBsAg was detected in all eight patients with chronic hepatitis tested compared with only one out of five with minimal liver lesions, which suggests that the severity of the liver damage may be directly related to the degree of immunocompetence.

Introduction

Infection with the hepatitis-B virus has been common in both haemodialysis and renal transplantation units.¹ Although some patients develop typical acute hepatitis, the course in most is more insidious. Biochemical abnormalities of liver function are less pronounced, hepatitis-B surface antigenaemia often persists, and progression to chronic liver disease may occur.² We report here a systematic investigation of liver dysfunction in a consecutive series of 15 such patients who had had hepatitis-B surface antigens (HBsAg) for six months or longer. Since immunosuppressive treatment may modify the underlying hepatic lesion, we compared the immune responses to HBsAg and the associated histological changes in patients receiving immunosuppressive treatment after successful renal transplantation with those responses demonstrable in patients maintained on haemodialysis or by dietary protein restriction alone.

Patients and methods

Of the 15 patients with chronic renal failure, two had been managed by protein restriction alone and seven were maintained on intermittent haemodialysis. The other six had functioning renal transplants and were receiving immunosuppressive treatment consisting of prednisolone and azathioprine. Tests for HBsAg including immunodiffusion, complement fixation, and radioimmunoassay³ gave positive results in every case. Four of the patients undergoing haemodialysis and all the transplant recipients had become HBsAg-positive during an outbreak of hepatitis-B infection in the renal unit at Guy's Hospital in 1969-1971⁴ and remained positive since. The remaining five patients were referred from other hospitals and had been HBsAg-positive for six to 18 months.

In addition to clinical examination and standard liver function tests (see table), a liver biopsy was carried out in each case for histological examination. Paraffin sections were also examined for HBsAg using both specific immunofluorescence and the orcein stain.⁵

Liver Unit, King's College Hospital and Medical School, Denmark Hill, London SE5

R M GALBRAITH, MB, MRCP, lecturer in medicine

N EL SHEIKH, MB, BS, visiting research fellow

B PORTMANN, MD, research fellow

A L W F EDDLESTON, DM, MRCP, senior lecturer and consultant physician

ROGER WILLIAMS, MD, FRCP, director of unit and consultant physician

V PARSONS, DM, FRCP, renal physician

Department of Nephrology, Guy's Hospital, London SE1

M BEWICK, FRCS, senior lecturer in surgery

C S OGG, MD, FRCP, consultant renal physician