The African Journal of MEDICINE and Medical Sciences

Volume 11
1982

BLACKWELL SCIENTIFIC PUBLICATIONS
Oxford London Edinburgh Boston Melbourne

practised. This dust can in turn be inhaled and may also result in bronchoconstriction. It seems to us therefore, that the relationship between asthma and helminths needs to be further explored, especially in countries like Nigeria where ascariasis is endemic and bronchial asthma is not uncommon.

In 1979, Aderele observed that some Nigerian asthmatic children had positive skin reactions to the *Ascaris* antigen. Since then, further studies on a larger number of asthmatic children have been carried out. In these studies, we have sought to focus attention on *Ascaris* antigen by establishing the characteristics of asthmatic children reacting to it and relating the positive reactions to the severity of asthma, presence of *Ascaris* ova in the stool and the blood eosinophil levels. We have also attempted to determine any possible aetiological relationship between the worm and bronchial asthma.

Materials and methods

The subjects were 270 asthmatic children attending the Paediatric General and Chest Clinics at the University College Hospital (UCH), Ibadan. The diagnosis of asthma was based on the fulfilment of at least two of the following criteria: (1) a minimum of three distinct episodes of breathlessness associated with cough and wheezing; (2) auscultatory findings of wide-spread expiratory rhonchi either at the initial examination or during subsequent follow-up, where the chest signs responded to bronchodilator therapy; (3) a minimum of 20% increase in the respiratory peak flow rate as measured by Wright's peak flow meter, after the administration of a bronchodilator in those presenting in acute attacks; and (4) demonstration of bronchial lability by exercise-testing. The severity of the disease was graded as mild, moderate and severe as indicated in an earlier report (Aderele, 1979). Two hundred and twenty healthy children, aged between 2 and 13 years, from similar socio-economic background to the asthmatic cases and who were not currently receiving corticosteroids, antihistaminics or immunosuppressive drugs were included as controls. Informed consent was obtained from the parents or guardians of the controls.

Skin tests were carried out by the prick method, using a commercially prepared *Ascaris* antigen solution (Bencard). For comparison, skin reactions to five other antigens comprising *D. pteronyssinus*, feathers, house dust, flower and shrub pollen and cotton flock were determined in the asthmatics. The first 150 of the 220 controls were also tested with these five antigens. In each case, a control solution was also used to determine positive results. A reaction to an antigen which was 2 mm or greater in diameter than the control wheal, was regarded as positive (Pearson, 1973). Faecal and blood specimens for eosinophil counts were obtained from both asthmatics and controls, while sputum from some asthmatics only, were examined for ova and cysts of helminths within 48 hr of the skin tests. Two further faecal specimens were later obtained from 185 of the asthmatics and fifty-three of the controls, within 60 days of the initial specimen.

The chi-squared (χ^2) tests were used for statistical analysis.

Results

Age and sex distribution

The 270 cases were between 1 and 13 years with a peak at 5 years. There were 159 males and 111 females, a M:F ratio of 1.4:1.

Severity and duration of disease

One hundred and eleven (41%) had mild asthma, seventy-eight (29%) moderate and the remaining eighty-one (30%) had severe asthma. Asthma had lasted for 1–9 years in 216 (80%) of the 270 cases.

Skin reactions

As shown in Table 1, 73 (27%) of the 270 cases had positive reactions to *Ascaris* antigen, compared to eighteen (8%) of 220 controls. The difference was significant ($P<0.001$). Reactions varied, though not directly with age groups; the highest proportion of positive reactors were aged between 7 and 9 years (Table 2). With regards to the severity of

Afr. J. Med. med. Sci. (1982) 11, 161–166

ASCARIS AND BRONCHIAL ASTHMA IN CHILDREN

W. I. ADERELE AND O. ODUWOLE

Department of Paediatrics, University College Hospital, Ibadan, Nigeria

Summary

Skin tests with the *Ascaris* antigen were carried out in 270 children with bronchial asthma and 220 controls. Faecal and sputum specimens were also examined for helminths. Twenty-seven per cent of the asthmatic children had positive reactions to the *Ascaris* antigen compared with 8% of controls ($P<0.001$). The positive reactions were, however, not related to the sex of the patients, severity of asthma, the presence of *Ascaris* ova in the faeces or the blood eosinophil counts. Larvae of helminths were not found in sputum specimens examined. While the present study indicates a possible association between *Ascaris* and asthma in children, further studies, including provocation tests and controlled anthelminthic drug trials, are required to confirm, as well as elucidate this association. It is however, suggested that routine screening for helminthiasis be undertaken in asthmatic children in the tropics and deworming carried out in those with positive results.

Résumé

Des tests cutanés, utilisant l'antigène *Ascaris* ont été pratiqués sur 270 enfants souffrant d'asthme bronchique et sur 220 contrôles également. En même temps, la recherche d'helminthes a été faite sur les expectorations et les selles. Vingt-sept pour cent d'enfants asthmatiques ont montré des réactions positives à l'antigène ci-dessus cité contre 8% seulement dans le groupe contrôle ($P<0.001$). Les réactions positives étaient indépendantes du sexe des malades, de la gravité de l'asthme, de la présence d'oeufs d'*Ascaris* dans les selles ou du degré d'éosinophilie sanguine. Aucun prélèvement n'a montré des larves d'helminthes dans les expectorations. En plus, aucun cas n'a été étiqueté syndrome d'éosinophilie tropicale. Cette étude révèle une association possible entre les *Ascaris* et l'asthme chez les enfants. Toutefois, afin de confirmer et d'élucider cette association, d'autres études parmi lesquelles des tests de provocation et des essais thérapeutiques avec des antihelminthiques sont nécessaires. Néanmoins, en milieu tropical, nous recommandons une recherche d'helminthes de routine chez les enfants asthmatiques et un déparasitage dans le cas de résultats positifs.

Correspondence: Dr W. I. Aderele, Department of Paediatrics, University College Hospital, Ibadan, Nigeria.

0309–3913/82/1200–0161 $02.00

Introduction

The role of helminths in the aetiology of bronchial asthma is controversial. While some workers (Tullis, 1970) believe that helminths may cause asthma, others (Rees *et al.*, 1974) have found no evidence for any active role of these parasites. Yet, it is known that the larvae of certain worms, particularly the *Ascaris*, pass through the lungs. It is conceivable that during this passage, allergic reactions to them may occur and result in bronchoconstriction in susceptible individuals. Furthermore, the products of *Ascaris* and other helminths may form part of dust, particularly in places where defaecation on open grounds is

TABLE 5. Helminths isolated from the stools in 228 asthmatic cases and 166 controls

Helminth	No. of asthmatic cases	% of 228	No. of controls	% of 116
Ascaris	141	62	68	59
Trichuris	57	25	23	20
Hookworm	23	10	11	9
E. histolytica	14	6	3	3
Strongyloides	11	5	2	2
Giardia lamblia	11	5	5	4
Trichomonas	2	1	0	0

In comparison, the size of the reactions in control subjects was 2 mm in fifteen and 3 mm in the remaining three cases.

Family history of asthma

Twenty-seven (37%) of the seventy-three with positive skin tests to *Ascaris* antigen had positive family history of asthma compared with seventy (35%) of the 197 with negative reactions, a difference which was not statistically significant.

Faecal and sputum parasites

Ova and cysts of a number of helminths were isolated from the stool in 160 (70%) of 228 asthmatics compared with eighty (69%) of 116 controls, a difference which was not significant. *Ascaris* was isolated from 141 (62%) of the 228 asthmatic cases, a proportion similar to that in the controls.

Results of stool microscopy were available in sixty-three of the seventy-three who had positive reactions to *Ascaris*. Only thirty-six (57%) of the sixty-three had *Ascaris* ova in the stool. A further seven (11%) of the sixty-three had other helminths and the remaining twenty (32%) had normal stools. There was no correlation between the severity of asthma and the presence of *Ascaris* ova in the stool, both in those with positive skin reactions to *Ascaris* and in others with negative reactions ($P>0.5$). Sputum obtained from twenty-four of the older asthmatic children did not contain ova or cysts of helminths.

Blood eosinophils

The mean eosinophil count in 238 of the asthmatics was 1126.6/mm^3 compared with a significantly lower mean of 454.6/mm^3 in 191 controls ($P<0.001$). Similarly, the mean count of 1125.6/mm^3 in seventy-two asthmatics with positive skin tests to *Ascaris* was significantly higher than the mean in controls ($P<0.001$). However, that mean count in the seventy-two asthmatic children with positive skin tests to *Ascaris*, was similar to one of 1130.9/mm^3 in 166 asthmatics with negative skin reactions.

Discussion

The aim of the present study was to define the nature of the association, if any, between the *Ascaris* antigen and bronchial asthma in childhood. The study has shown a significantly higher proportion of asthmatic children than controls, reacting to the *Ascaris* antigen. Moreover, the degree of significance of this positive reaction was greater than that of the reaction to any of the other antigens tested. The reaction to the *Ascaris* was not related to the sex of the patients or to the severity of the disease; neither did it correlate with the presence of the parasite in the stool or the blood eosinophil levels.

There have, over the years, been speculations on the association between helminthiasis and pulmonary symptoms. Hookworm, *Ascaris* and strongyloides have, at various times, been incriminated in the causation of various pulmonary symptoms including bronchial asthma (Zuelzer & Apt, 1949; Beaver, 1969; Nwokolo & Imohiosen, 1973). A direct evidence of the possibility of *Ascaris* causing

TABLE 1. Skin reactions to *Ascaris* antigen in asthmatics and controls

Subjects	No. tested	No. positive	Positive (%)
Asthmatics	270	73	27.0
Controls	220	18	8.2

$\chi^2 = 28.5$ on 1 d.f.; $P<0.001$

TABLE 2. Age distribution in seventy-three asthmatics with positive reactions to *Ascaris*

Age group (years)	No. tested	No. positive	Total tested (%)
1– 3	64	9	14
4– 6	104	27	26
7– 9	63	27	43
10–13	39	10	26

disease, twenty-three (21%) of 111 mild cases had positive reactions compared with twenty-four (31%) of seventy-eight moderate cases and twenty-six (32%) of eighty-one severe ones. These differences were not statistically significant. For comparison, Table 3 shows that there were significant reactions to three of the other five antigens tested namely: *D. pteronyssinus*, feathers and house dust, while the reactions to the other two antigens were not significant.

Size of reactions to Ascaris *antigen*

The positive reactions to *Ascaris* antigen varied in size (Table 4). In fifty-six (77%) of the seventy-three, the sizes were between 2 and 4 mm larger than reactions to control solution.

TABLE 3. Skin reactions to other antigens in asthmatics and controls

Antigen	Asthmatic cases		Controls			
	No. tested	Positive (%)	No. tested	Positive (%)	χ^2	P
D. pteronyssinus	270	20	150	11	5.2	<0.025
House dust	270	14	150	5	7.59	<0.01
Feathers	270	12	150	3	8.71	<0.005
Flowers and shrubs	270	9	150	6	1.11	>0.2
Cotton flock	270	8	150	5	1.21	>0.2

TABLE 4. Size of positive reactions to *Ascaris*

Size (mm)*	No. of asthmatic cases	Total (%)	No. of control cases	Total (%)
2	33	45	15	83
3	18	25	3	17
4	5	7	0	0
5	6	8	0	0
6	5	7	0	0
7	3	4	0	0
9	3	4	0	0

*Reaction to antigen minus reaction to control solution.

References

Aderele, W.I. (1979) Bronchial asthma in Nigerian Children. *Arch. Dis. Child.* 54, 448–453.

Bazaral, M., Orgel, H.A. & Hamburger, R.N. (1973) The influence of serum IgE levels of selected recipients, including patients with allergy, helminthiasis and tuberculosis, on the apparent P-K titre of a reaginic serum. *Clin. Exptl. Immunol.* 6, 131–134.

Beaver, P.C. (1969) Tropical eosinophilia. In: *Textbook of Paediatrics.* (eds, W. E. Nelson, V. C. Vaughan and R. J. McKay) p. 739. W. B. Saunders Company, Philadelphia.

Bullock, J.D., Bodenbender, J.C., Deamer, W.C. & Frick, O.L. (1971) Skin window eosinophil response in house dust allergy. *J. Allergy Clin. Immunol.* 48, 153–160.

Godfrey, R.C. (1975) Asthma and IgE levels in rural and urban communities of Gambia. *Clin. Allergy*, 5, 201–207.

Jarrett, E.E.E. (1972) Potentiation or reaginic (IgE) antibody to ovalbumin in the rat following sequential trematode and nematode infections. *Immunol.* 22, 1099–1101.

Jarrett, E.E.E. & Kerr, J.W. (1973) Threadworms and IgE in allergic asthma. *Clin. Allergy*, 3, 203–207.

Jarrett, E.E.E. & Stewart, D.C. (1972) Potentiation of rat reaginic (IgE) antibody to helminth infection. Simultaneous potentiation of separate reagins. *Immunol.* 23, 749–755.

MacFarlane, J.T., Bachelor, M., Ridyard, J.B. & Ball, P.A.J. (1979) Asthma, IgE and environment in northern Nigeria. *Clin. Allergy*, 9, 333–337.

Nwokolo, C. & Imohiosen, E.A.E. (1973) Strongyloidiasis of respiratory tract presenting as asthma. *Brit. Med. J.* ii, 153–154.

Pearson, R.S.B. (1973) Asthma in Barbados. *Clin. Allergy*, 3, 289–297.

Rees, P.H., Gitoho, F., Mitchell, H.S. & Rees, C. (1974) Some aspects of the aetiology of asthma in Nairobi with special reference to parasites and the house dust mite. *E. Afr. Med. J.* 51, 729–733.

Salako, L.A. & Sofowora, E.O. (1970) Bronchial asthma associated with intestinal parasites. *N. Eng. J. Med.* 283, 265.

Sarsfield, J.K. (1974) Role of house dust mites in childhood asthma. *Arch. Dis. Child.* 49, 711–715.

Sprent, J.F.A. (1949) On the toxic and allergic manifestations produced by the tissues and fluids of *Ascaris*. I. Effect on different tissues. *J. Infect. Dis.* 84, 221–229.

Stanworth, D.R. (1971) The experimental inhibition of reagin mediated reactions. *Clin. Allergy*, 1, 25–35.

Tullis, D.C.H. (1970) Bronchial asthma associated with intestinal parasites. *N. Eng. Med. J.* 282, 370–372.

Wolstenbolme, R.J. (1979) Bronchial asthma in the southern Maldives. *Clin. Allergy*, 9, 325–332.

Zuelzer, W.W. & Apt, L. (1949) Disseminated visceral lesions associated with extreme eosinophilia: pathologic and clinical observations on a syndrome of young children. *Am. J. Dis. Child.* 78, 153–181.

Received 9 *April* 1981; *revision received* 17 *February* 1982; *accepted* 29 *March* 1982

asthma was reported in 1949 when Sprent documented the development of asthmatic symptoms in himself when he inhaled dried *Ascaris* tissues. Similarly, Tullis (1970), in a study of 201 asthmatic cases, suggested an aetiological relationship between asthma and helminths. In the rat, the levels of circulating IgE to a variety of non-helminthic antigens, including house dust, can be greatly elevated following experimental infection of the animal with certain nematodes and trematodes (Jarrett, 1972; Jarrett & Stewart, 1972). More recently, it has been suggested that hypersensitivity to threadworm allergen absorbed from the bowel, might have contributed to allergic symptoms in a group of adults and children with asthma (Jarrett & Kerr, 1973). By contrast however, other workers have either been sceptical about or have denied such association between intestinal parasites and asthma (Salako & Sofowora, 1970; Rees *et al.*, 1974). Indeed, Godfrey (1975) and Bazaral, Orgel and Hamburger (1973) have suggested that saturation of binding sites on bronchial mucosal mast cells by high levels of endogenous helminth-specific antibodies would tend to block their availability for binding by other allergens and thus protect against asthma; a theory first suggested by Stanworth (1971). However, the finding of high helminthiasis rates in both the asthmatic patients and controls in the present series, as well as reports by others (Wolstenholme, 1979; MacFarlane *et al.*, 1979) would invalidate this theory.

The present study has shown no consistent correlation between positive skin test to *Ascaris* and the presence of the parasite in the stool. Moreover, a recent uncontrolled trial of regular anthelminthic therapy in asthmatic children with faecal ascariasis and positive skin reaction to the *Ascaris* antigen did not yield a consistent response (unpubl. data). It is therefore, tempting to dismiss the significant reaction to the *Ascaris* antigen in the present study as being wholly fortuitous. However, it is to be noted that the significance of the reaction was greater than that of any of the other antigens compared, including *D. pteronyssinus*, which is generally accepted as being the most important causal factor in childhood asthma (Bullock *et al.*, 1971; Sarsfield, 1974). In the Nigerian environment, a majority of children, especially those in the low socio-economic class, harbour *Ascaris* and other helminths in health and disease. It is however, possible that a proportion of such children are sensitized to one or more of these helminths, in the same way that only a proportion of children who come in contact with *D. pteronyssinus* and other antigens, react to them. Therefore, not every child that harbours or comes in contact with *Ascaris* would necessarily react to it. However, since the association between *Ascaris* and asthma in the present series have, as yet, not been shown to be causal, further studies are required in this and similar areas where ascariasis and asthma are prevalent. Such studies would include immunological, bronchial provocation tests with the *Ascaris* antigen and controlled clinical trials of regular anthelminthic therapy.

Meanwhile, the controversy on the role of helminths in asthma remains unresolved. It seems to us that one of the main thrusts of the controversy is how 'bronchial asthma' is defined. Does a child who has recurrent breathlessness, cough and wheezing, without evidence of cardiac disease and with no demonstrable allergy other than *Ascaris* skin sensitivity, have asthma in the 'traditional' sense or does he, because he lives in the tropics, suffer from Loeffler's syndrome or tropical pulmonary eosinophilia? On the basis of the classical descriptions of the latter two conditions, it is most unlikely that the subjects in the present series suffered from either condition. In any case, it seems to us that what is of more practical importance is the realization that symptoms of asthma may possibly be due to helminths, the products of which may be inhaled from dust or ingested. Although no causal relationship between the two have so far, been proved, it is suggested, as did Nwokolo and Imohiosen (1973), that asthmatic patients from areas where strongyloidiasis and ascariasis are endemic, should have their stools, and where possible sputum examined for parasites, and the presence of any of such parasites be adequately treated as part of any anti-asthma regimen.

Acknowledgement

The study was supported by a University of Ibadan Senate Research grant to W.I.A.