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Volume 13

1984

BLACKWELL SCIENTIFIC PUBLICATIONS
Oxford London Edinburgh Boston Palo Alto Melbourne

SERUM IgG, IgA AND IgM IN ASTHMATIC CHILDREN

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Summary

Serum levels of immunoglobulins G, A and M were determined in forty-five asthmatic children and in the same number of controls. Mean IgG and IgA levels in the asthmatics were not significantly different from those in the controls. Conversely, mean IgM values in female controls and all the controls taken as a group, were significantly higher than those in their asthmatic counterparts. There was no relationship between severity of asthma and the mean levels of the various immunoglobulins. However, the mean IgG value in asthmatic children with positive skin sensitivity tests was significantly higher than the mean value in those who had negative reactions. It is concluded that the serum levels of these immunoglobulins are of limited value in either the diagnosis of asthma or in the grading of its severity.

Résumé

Les valeurs sériques des immunoglobulines G, A, et M ont été déterminées chez quarante-cinq enfants asthmatiques et dans un groupe contrôle de quarante-cinq autres. La différence des valeurs moyennes des IgG et IgA n'étaient pas significatives entre les deux groupes d'enfants. Par contre, les valeurs moyennes des IgM dans les contrôles de sexe féminin et de tous les contrôles en général étaient plus élevées que dans le groupe d'enfants asthmatiques. Il n'y avait pas de rapport entre la

gravité de l'asthme et les taux des différentes immunoglobulines. Toutefois, les valeurs moyennes des IgG chez les enfants asthmatiques avec des tests cutanés positifs étaient plus élevées que chez les asthmatiques ayant des réactions négatives différence significative. En conclusion cette étude révèle que les taux sériques de ces immunoglobulines ont une valeur limitée tant pour le diagnostic de l'asthme que pour déterminer sa sévérité.

Introduction

While there are many reports on the close relationship between bronchial asthma and immunoglobulin E (IgE) (Editorial, 1972; Havnen *et al.*, 1973; Aderole *et al.*, 1984) information on the role played by other classes of immunoglobulins is more scanty. Yet, it seems reasonable to suppose that asthma, being an immunological disease, may also have some relationship with other immunoglobulins. That this may be so was suggested by Bryant, Burns and Lazarus (1973) who reported a group of adult asthmatics whose allergic reactions were apparently due to short-term anaphylactic IgG antibodies and not IgE. Furthermore, the British Thoracic and Tuberculosis Association Research Committee (1975) has recently reported higher serum levels of IgG, IgA and IgD, but not IgM, in adult asthmatics than in controls. Similar studies in children have been few and include those by Lin *et al.* (1977) which revealed serum IgM levels greater than 2 standard deviations (s.d.) above age-matched normal values in 51% of 224 American asthmatic children. Conflicting results have,

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however, been reported by Collins-Williams *et al.* (1967) and Kaufman and Hobbs (1970). In the present study, we have determined the serum IgG, IgA and IgM levels in asthmatic children, compared them with corresponding levels in normal children (controls) and related the levels in asthmatics to the severity of the disease and the atopic status of the children as indicated by their reactions to allergens, on skin testing.

Materials and methods

Forty-five asthmatic children (twenty-six males and nineteen females) attending the Asthma Clinic, Department of Paediatrics, University College Hospital (UCH), Ibadan, formed the subjects of this study. The diagnostic criteria for asthma and the gradings of its severity have been described elsewhere (Aderere, 1979). They were selected from among those who had not had steroid therapy during the previous 6 months. Fourteen of the forty-five asthmatics had mild asthma, ten moderate, while the remaining twenty-one had severe asthma. The mean ages of the asthmatics were 7.7 and 8.5 years for males and females respectively. The controls consisted of apparently healthy children matched for age, sex and socio-economic classes with the asthmatic subjects. Their mean ages were 7.7 years for males and 8.4 years for females. They had no personal or family history of atopy. Informed consent was obtained from the parents of both the asthmatics and controls.

Venous blood was withdrawn from each subject or control. The serum was separated soon after collection and kept in a freezer at -20°C (with a drop of sodium azide) until required for analysis. Skin sensitivity tests, carried out only in the asthmatics, were performed by the prick method as previously described (Aderere & Oduwale, 1981).

Serum concentrations of IgG, IgA and IgM were estimated, using a modification of the single radial diffusion technique of Fahey and McKelvey (1965), as described by Salimonu (1976). The values obtained were logged and statistical tests were carried out on the log values. The Student's *t*-test was used to

determine the significance of the differences between means. The numbers of subjects and controls were too few to allow for meaningful analysis of results according to age groups.

Results

Serum IgG, IgA and IgM levels

IgG. As shown in Table 1, the mean IgG level in male asthmatics was 1114 mg/100 ml compared with 1093 mg/100 ml in the females; the overall mean in both sexes was 1105 mg/100 ml. Comparative values in controls were 1235, 1260 and 1245 mg/100 ml, respectively. The mean IgG values in the males were not significantly different from those in females (both asthmatics and controls). Similarly, there were no significant differences in the mean IgG levels in male or female asthmatics when compared with corresponding controls.

IgA. Although the mean IgA levels in female asthmatics (169 mg/100 ml) and female controls (190 mg/100 ml) were higher than corresponding levels in the males (159 mg/100 ml in asthmatics; 170 mg/100 ml in controls), these differences were not significant (Table 1). Similarly, the mean IgA level in either male or female asthmatics was not significantly different from the corresponding levels in the controls.

IgM. While the mean IgM value of 123 mg/100 ml in asthmatic males was similar to 128 mg/100 ml in male controls, the mean IgM of 175 mg/100 ml in female controls was significantly higher than 122 mg/100 ml in female asthmatics ($P < 0.01$). Similarly, the overall mean IgM in controls of both sexes was significantly higher than that in all the asthmatics ($P < 0.05$) (Table 1). Unlike IgG and IgA, the mean IgM in female controls was significantly higher than that in the male controls ($P < 0.02$).

Serum IgG, IgA and IgM in relation to severity of asthma

As shown in Table 2, there was no significant relationship between the severity of asthma and the levels of immunoglobulins G, A and M.

TABLE 1. Serum IgG, IgA and IgM levels in asthmatics and controls

	Asthmatics			Controls			p*
	No. of cases	Mean log values	s.d.	No. of cases	Mean log values	s.d.	
Males							
IgG	26	3.0469 (1114)	0.1329	26	3.0917 (1235)	0.1277	NS
IgA	26	2.1990 (159)	0.1648	26	2.2313 (170)	0.1766	NS
IgM	26	2.0898 (123)	0.1012	26	2.1061 (128)	0.1910	NS
Females							
IgG	19	3.0385 (1093)	0.1380	19	3.1002 (1260)	0.1593	NS
IgA	19	2.2261 (168)	0.1494	19	2.2788 (190)	0.2401	NS
IgM	19	2.0870 (122)	0.1535	19	2.2427 (175)	0.1839	<0.01
Both sexes							
IgG	45	3.0433 (1105)	0.1337	45	3.0953 (1245)	0.1404	NS
IgA	45	2.2106 (162)	0.1573	45	2.2515 (179)	0.2049	NS
IgM	45	2.0886 (123)	0.1246	45	2.1642 (146)	0.1981	<0.05

Figures in parentheses are geometric means (mg/100 ml).

*Paired t -test on log values.

NS = not significant.

TABLE 2. Serum IgG, IgA and IgM levels according to severity of asthma

	Severity of asthma	No. of cases	Mean log values	s.d.
IgG	Mild	14	3.0636 (1158)	0.1161
	Moderate	10	2.9663 (925)	0.1330
	Severe	21	3.0646 (1160)	0.1369
IgA	Mild	14	2.2226 (167)	0.1491
	Moderate	10	2.1911 (155)	0.1852
	Severe	21	2.2117 (163)	0.1559
IgM	Mild	14	2.0876 (122)	0.0980
	Moderate	10	2.1051 (127)	0.1920
	Severe	21	2.0820 (121)	0.1074

For IgG, IgA and IgM: mild *v.* moderate, P = not significant; mild *v.* severe, P = not significant; and moderate *v.* severe, P = not significant.

Figures in parentheses are geometric means (mg/100 mg).

Serum IgG, IgA and IgM in relation to atopy in the asthmatics

Twenty-three (51%) of the forty-five asthmatic children reacted positively to various allergens. While the mean IgA and IgM values were not significantly different between those who reacted to allergens and others who did not, the mean IgG level of 1221.0 mg/100 ml in the twenty-three asthmatic children (mean age, 9.1 years) with positive skin tests was significantly higher ($P < 0.05$) than the observed mean value (1002.1 mg/100 ml) in

the remaining twenty-two (mean age 7.5 years) with negative skin tests (Table 3).

Discussion

There were no significant differences between the mean levels of IgG and IgA in asthmatics and controls in the present study. By contrast, however, IgM mean levels were significantly higher in female controls and all controls taken as a group, than in their asthmatic counterparts. Our finding of higher mean IgM levels in female

TABLE 3. Serum IgG, IgA and IgM levels in relation to skin sensitivity reactions in asthmatics

	Skin reaction	No. of cases	Mean log values	s.d.	<i>p</i> *
IgG	Positive	23	3.0867 (1221)	0.1498	< 0.05
	Negative	22	3.0009 (1002)	0.1000	
IgA	Positive	23	2.2118 (163)	0.1656	> 0.5
	Negative	22	2.2111 (163)	0.1552	
IgM	Positive	23	2.0922 (124)	0.0911	> 0.5
	Negative	22	2.0842 (121)	0.1577	

*Paired χ^2 -test on log values.

Figures in parentheses are geometric means (mg/100 ml).

than in male controls confirms previous similar reports (Allansmith, McClellan & Butterworth, 1967; Buckley & Dorsey, 1970; Grundbacher, 1972; Salimonu, 1976). The reason for the IgM elevation in females may be connected with the observation that the X chromosome carries gene(s) affecting the blood concentration of IgM (Grundbacher, 1972). Furthermore, Salimonu *et al.* (1982) have reported higher antibody titres (and higher IgG levels) to malarial antigen in malarial infected females than in the infected males. It is therefore, also possible that humoral immune responses to some antigens may be better in females than in males, thus leading to higher immunoglobulin (G and M) levels in the former.

Various workers (Collins-Williams *et al.*, 1967; Kaufman & Hobbs, 1970; BTTA, 1975) have compared levels of immunoglobulins in normal and asthmatic children. Kaufman and Hobbs (1970) reported no difference in IgG levels in both groups. Similarly, Lin *et al.* (1977) have reported few significant differences in the serum levels of IgG between asthmatic and normal children. However, others (BTTA, 1975) have reported an increased mean IgG levels in asthmatics. Yet, another group of workers (Collins-Williams *et al.*, 1967) have reported lower than normal values for IgG in children with severe asthma. The above-reported differences are difficult to explain, but may be related to the selection of patients for such studies, the number of samples and the method of assay.

With respect to IgA, various workers (Collins-Williams *et al.*, 1967) have reported lower than normal values in asthmatics, although others (Kaufman & Hobbs, 1970; Lin *et al.*, 1977) were not able to document any such difference.

The significance of the higher mean IgM values in controls when compared with the asthmatics in the present study, is not clear and it is contrary to a recent report by Lin *et al.* (1977) of hyper-M-immunoglobulinemia in some American asthmatic children. It is, however, possible that the increased production of IgE which occurs in asthmatics (Havnen *et al.*, 1973; Aderere *et al.*, 1984) is at the expense of IgM synthesis, thereby resulting in depressed levels in the blood as observed in the present study.

The present study has shown no relationship between the levels of the various immunoglobulins and the severity of asthma. By contrast, and a bit surprising, was the significantly higher mean IgG value in atopic children than in those who were apparently non-atopic. This finding has led us to speculate that some of the positive skin-test reactions might have been mediated by the so-called short-term anaphylactic IgG antibodies as previously suggested by Parish (1970) and Bryant, Burns and Lazarus (1973). Another explanation for the difference may be related to a significantly higher mean age in the atopics than in the non-atopics. A previous report (Hsieh, 1978) has shown that serum IgG level rises steadily with age from its lowest value at 3 months up

till about 5 years when adult levels are reached. One might have expected that if atopy was to have any relationship with any of the three immunoglobulins involved in the present study, it would be with IgA, an immunoglobulin that protects from allergic disease by preventing the entry of foreign materials at the mucosal surfaces of the respiratory and gastrointestinal tracts. Taylor *et al.* (1973) have reported that in infants of atopic parents, low serum IgA at 3 months accompanied or predicted the development of atopy within the 1st year. The theory is that relative mucosal IgA deficiency leads to the abnormal entry of allergens and the subsequent development of atopy. If mucosal IgA levels mirror serum IgA, then one might expect atopic children to have significantly lower levels of IgA than non-atopics. That this was not so in the present series, could be due to the fact that mucosal IgA does not relate to serum IgA or that a relative deficiency which might have been present in some of the atopic children in infancy, was only transient and had been corrected with age as the IgA-producing system matures, as suggested by Soothill *et al.* (1976). Another explanation is that if there was indeed a deficiency of IgA, it was probably qualitative rather than quantitative.

The conclusion that may be drawn from the present study is that, as of now, IgG, IgA and IgM levels are not very helpful in either the diagnosis of bronchial asthma or the grading of its severity in children.

Acknowledgments

We wish to thank Dr E. N. Ekambi for the French translation of the summary. The study was supported by a University of Ibadan Research Grant to W.I.A.

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