

Different role of secretory IgA in the pathogenesis of RAST-positive and RAST-negative atopic dermatitis

A. PLEBANI, V. MONAFO, M. CESPÀ, A. GIANNETTI and A. G. UGAZIO

Departments of Dermatology and Pediatrics, University of Pavia, Italy

(Received 21 July 1981; accepted for publication 10 September 1981)

Summary

Secretory-IgA (SIgA) concentrations were determined in whole saliva, unstimulated or stimulated by lemon juice, of thirty-eight children with atopic dermatitis, which comprised three adolescents, sixteen with IgE detected by RAST to one or more common allergen and twenty-two without specific IgE by RAST. There were thirty healthy controls matched for age and sex.

The mean amount of total IgE was significantly greater in the RAST-positive than in the RAST-negative group. The mean SIgA concentration in unstimulated saliva of the RAST-positive atopic dermatitis group was less than that of the RAST-negative atopic dermatitis group and control groups, though the mean concentrations of SIgA of stimulated saliva were not significantly different in the three groups. It is suggested that the pathogenesis of atopic dermatitis may differ in children with or without specific-IgE antibodies; in those who were RAST-positive deficient exclusion of allergen by the intestinal barrier contributed to the pathogenesis, but not in those who were RAST-negative.

Introduction

Derangement of secretory immunity, in particular of secretory IgA (SIgA), have been claimed to play a significant role in the pathogenesis of atopic disorders (Rajka, 1975).

Allergens triggering atopic dermatitis (AD) may enter the body through the gastro-intestinal or respiratory mucosa facilitated by a deficiency of SIgA. In order to test this hypothesis we examined the concentrations of salivary SIgA in children with AD and appropriately matched controls. The results indicate that SIgA levels are significantly lower in AD patients with circulating IgE against common allergens than in those without circulating IgE.

Methods

Subjects

Thirty-five children and three adolescents affected with AD, with or without circulating IgE directed against one or more allergens were included in the study; diagnosis was on clinical evidence only, and patients were included in the study before knowledge of laboratory data was obtained; patients with AD associated with other atopic disorders were not included.

Controls were age- and sex-matched healthy children with a negative personal and family history for atopy. Patients and controls were taking no drugs at the time of the study.

Assay of SIgA

Samples of lemon-juice-stimulated and unstimulated whole saliva were collected from patients and controls using a soft plastic tube connected to a disposable syringe as previously described (Burgio *et al.* 1980). Briefly, salivary SIgA was assayed by electroimmunodiffusion (EID) as previously described (Shuller, Levefre & Tompe, 1972) with slight modifications. The samples of saliva were applied to 1% agarose plates that were run at 10 V/cm for 5 hr. Then the plates were washed, dried and stained with Coomassie brilliant blue. A working standard serum was calibrated with reference to a preparation of purified dimeric IgA and used throughout the study. As reported with the Mancini technique (Mancini, Carbonara & Heremans, 1965) monomeric IgA alters the height of the peaks only if present in concentrations higher than 20%, a value usually not exceeded in normal secretions (Newcomb & De Wald, 1969). To control for significant contamination with serum proteins, and monomeric IgA, albumin concentration was measured in all samples of unstimulated saliva by EID. Albumin was present in low concentrations ($4.6 \text{ mg/dl} \pm 0.6 \text{ s.e.}$) except in rare samples containing more than 10 mg/dl which were excluded from the study.

Serum immunoglobulins, total and specific circulating-IgE

Samples of blood were collected from all patients and serum IgG, IgA and IgM were assessed by the Mancini technique (Mancini *et al.*, 1965), specific IgE by the RAST technique (Wide, Bennich & Johansson, 1967) and total IgE by the PRIST technique (Ceska & Lundkvist, 1972). Student's *t* test was used to establish the statistical significance of the differences between the mean values of SIgA and IgE.

Results

Of the thirty-eight patients with AD, sixteen had specific circulating-IgE as demonstrated by a positive RAST to one or more of the common allergens tested. Mean serum concentration of total IgE was significantly higher ($P < 0.05$) in the RAST-positive ($617 \text{ iu/ml} \pm 161 \text{ s.e.}$, $n = 13$) than in the RAST-negative group ($226 \text{ iu/ml} \pm 51.4 \text{ s.e.}$, $n = 17$). The mean ages of the former ($6.1 \text{ years} \pm 0.9 \text{ s.e.}$, $n = 13$) and latter groups ($6.7 \text{ years} \pm 1.1 \text{ s.e.}$, $n = 17$) were not significantly different ($P > 0.05$). Serum concentrations of IgA, IgG and IgM were in the age-normal range in all patients. The concentrations of SIgA in unstimulated, as well as stimulated saliva were not significantly different in patients with AD and in controls (Table 1). However, when the patients were split into RAST-positive and RAST-negative groups (Fig. 1), the mean concentration of SIgA in

Table 1. Concentrations of SIgA in stimulated and unstimulated whole saliva from subjects with AD and normal controls.

Subjects	<i>n</i>	Mean SIgA (mg/dl)	
		Unstimulated saliva	Stimulated saliva
Atopic dermatitis	38	9.5(±7.1)*	3.1(±2.4)
Healthy controls	30	10.3(±4.5)	2.9(±1.8)
<i>P</i>		NS	NS

* Standard deviations in brackets.

† *P* values determined using Student's *t* test.

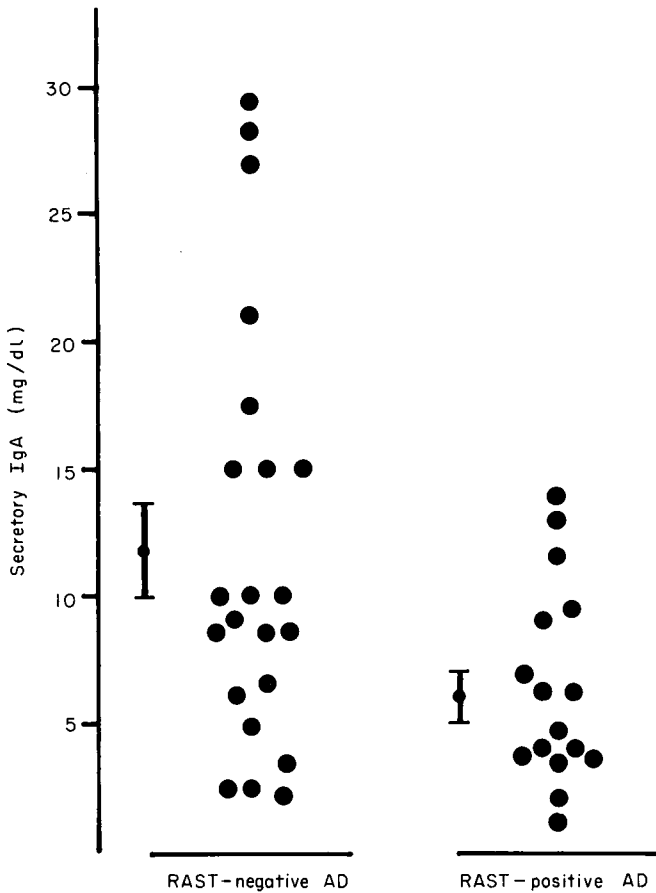


Fig. 1. Concentration of SIgA (mg/dl) in unstimulated whole saliva from RAST-negative and RAST-positive AD patients. The difference is highly significant ($P < 0.01$); the mean $\pm$ 1 s.e. is also reported for each of the two groups.

unstimulated saliva was significantly lower in the former ($P < 0.01$) than in the latter group; furthermore the concentration of SIgA was significantly less in the RAST-positive group than in healthy controls ($P < 0.005$), while no significant difference was found when comparing RAST-negative AD patients with controls ($P > 0.05$). No significant differences between groups were observed in the SIgA values of stimulated saliva.

Discussion

The results of the present investigation show that patients with AD without circulating IgE directed against common allergens have a normal concentration of SIgA in either unstimulated or stimulated saliva. On the contrary the unstimulated saliva of AD patients with circulating allergen-specific IgE contains a lower than normal concentration of SIgA. It has been claimed that allergens crossing the intestinal or respiratory mucosa play a crucial pathogenetic role in AD (Buckley, Wray & Belmaker, 1972; Taylor *et al.*, 1973; Kaufman & Hobbs, 1970). However, the observation that only about 50% of the patients with AD have demonstrable circulating IgE directed against common allergens (Rajka, 1975) has raised doubts about the atopic pathogenesis of AD. In fact the results of the present study suggest that AD might be a heterogeneous disease. The low concentrations of SIgA in unstimulated saliva in AD patients with specific IgE (RAST-positive AD) might be a part of the pathogenetic mechanism leading to atopy via deficient allergen exclusion by the mucosal barrier. On the other hand the normal level of SIgA in AD without specific circulating-IgE (RAST-negative) indicates that the underlying pathogenetic mechanism is different in this group of patients and is unrelated to allergen exclusion. The hypothesis that RAST-positive and RAST-negative AD may result from different pathogenetic mechanisms is further strengthened by the finding that serum concentration of IgE was significantly higher in RAST-positive than in RAST-negative AD.

It is difficult to rule out the possibility that the differences in SIgA levels are the result, rather than the cause of the presence or absence of specific IgE; however this hypothesis appears very unlikely. The normal levels of SIgA in stimulated saliva of all patients with AD might simply indicate that the deficiency in RAST-positive patients is not severe; in fact these patients—unlike subjects with selective IgA deficiency—are apparently able to cope successfully with most respiratory infections. On the whole the results of the present study raise the interesting possibility that AD includes at least two distinct clinical entities characterized by different pathogenetic mechanisms; RAST-positive AD is perhaps the result of reduced allergen exclusion at the mucosal level, while RAST-negative AD might result from a different, as yet unrecognized, pathogenetic mechanism.

Acknowledgments

We thank Mr. Attilio Ascione for his excellent technical assistance and Mrs. M.G. Corona for her expert secretarial assistance. This work was supported in part by Consiglio Nazionale Ricerche, Roma, Italy.

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