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Specific IgE antibodies in nasal secretions: correlation with serum values and clinical tests

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The presence of specific IgE in external secretions and the possibility of quantifying it has aroused the interest of many research workers. Nevertheless, there is still disagreement with regard to how useful this practice is from a clinical point of view. We have compared the presence of Dermatophagoides pteronyssinus (Dp) *specific-IgE in the nasal secretion of 17 patients suffering from rhinitis with the results of prick tests and nasal and/or conjunctival challenge tests. As a preliminary step we have updated techniques and made a correlation between the parameters mentioned.*

The results for total IgE (n = 17) show a correlation coefficient (r = .39, NS) between serum values (251 ± 239) U/L and those obtained in nasal secretion (28 ± 36) U/L. (2) Serum and nasal-Dp-specific-IgE values (13 ± 15 and 5 ± 9, respectively: (r = .72, P = .0011) match in 14 of the 17 determinations. In two of them, the serum values of Dp-specific-IgE. but not the nasal ones, match the in vivo tests. In the others, it is the nasal secretion determination that matches the in vivo tests while the serum and nasal determinations match (82%). These results match in 86% of cases with prick tests and in 93% with nasal/conjunctival challenge tests. We found a good correlation between the local specific-Dp IgE and the reference tests (challenges) but local specific-Dp IgE does not exceed the serum determination. We conclude that the determination of specific IgE in nasal secretions, although it may be useful for the management of certain patients, does not provide any advantage in daily clinical practice.

INTRODUCTION

The diagnosis of allergic disease such as rhinitis implies the identification of allergens that produce or aggravate the symptoms. The allergy specialist has various tests at his disposal (designed to identify the antigens responsible), such as skin tests and tests for the levels of specific IgE in serum which demonstrate the presence of skin and blood reactions, respectively. Re-exposure tests are available to the allergy specialist to enable a determination of clinical sensitivity. These tests may have false negative results and challenge testing is not always possible on a routine basis.

Samter was the first to demonstrate the presence of specific IgE in nasal secretions using the Prausnitz-Küstner test in 1947.[1] His discovery was later confirmed using radio- and immunoenzyme techniques.

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When the inhaled allergen comes into contact with the nasal mucus, an IgE reaction takes place as a result of the stimulation of immune-competent cells. The finding of a high IgE/IgG relationship in nasal secretions compared with serum suggests local production of specific IgE.[2]

There is disagreement between researchers on the significance of specific IgE in nasal secretions: Hugging and Brostoff in 1975[3] and Miadonna in 1983[4] found specific IgE to *Dermatophagoides pteronyssinus* in the mucus of patients reacting positively to specific nasal challenge tests and negatively to skin tests and serum RAST. This suggests local production of reagins and they postulated that nasal fluid might produce a positive RAST where the serum RAST failed to show positive. Nevertheless, Marcucci demonstrated in 1987[5] that during exposure to allergen, local presence of IgE was observed in the majority of subjects (55% RAST negative). This coincides with results of Deuschl who stated that a positive RAST in nasal secretions does not indicate a diagnosis of allergic rhinitis.[6] These differences of opinion may be attributed to differences in selecting patients and to different techniques used in collecting nasal secretions.[7]

Immunohistochemical studies have demonstrated the existence of IgE-synthesizing plasma cells in nasal mucus, suggesting that 80% of the IgE found in nasal fluid may be produced locally.[8,9] There is therefore no agreement on the origin and significance of this immunoglobulin. The question of whether the nasal IgE response is at least partly independent of the serum response is still being studied. Neither is it clear what role its determination plays in clinical practice.

OBJECTIVES

In this study we have compared the measurement of specific IgE against *Dermatophagoides pteronyssinus* (*Dp*) in the nasal secretions of 17 patients affected by rhinitis, with the clinical symptoms produced under experimental conditions and with specific IgE present in skin and serum.

We evaluated correlations be-

tween nasal RAST, serum RAST, cutaneous tests (TC), nasal challenge tests (TPN), and conjunctival tests (TPC).

METHODOLOGY AND MATERIALS

Patients

Seventeen patients with perennial clinical rhinitis were selected (seven men and ten women) aged 7 to 19 years, mean age 11 years 2 months. The mean duration of the disease had been 2 years 7 months.

All patients' medical histories were studied including family histories of atopy (asthma, rhinitis, and atopic dermatitis), as were the characteristics of disease episodes and their duration together with the treatment administered and its effectiveness.

Cutaneous Tests

The prick technique was used on the upper surface of the forearm, using *Dp* extracts supplied by Pharmacia Iberica (Uppsala). Standard biologic units of the extracts were used and diluted in human albumin to various concentrations (100, 1,000, 10,000, and 100,000 BU). Controls with 1% histamine, physiologic saline, and 9% codeine phosphate were performed in all cases. The results were read after ten minutes and considered positive when a wheal was of equal or greater diameter to that produced by the histamine.

Nasal Challenge Test

This was performed using passive anterior rhinometry (Heyer Rhinometry). The same extracts used in the prick tests were aerosolized and used in the same concentrations. The interval between challenges was one day.

The test was considered positive when there was a pressure increase in excess of 200% with respect to baseline pressure, or when there was an intranasal temperature increase equal to or greater than 2 °C.

Conjunctival Challenge Test

This consisted of introducing a drop of *Dp* extract into the tear duct with 15-minute intervals between administrations. The test was performed in the absence of conjunctival symptoms, antihistamine treatment (seven days prior to the test), and ketotifen prophylaxis (15 days prior to the test). Topical cromolyn sodium treatment was also discontinued 48 hours beforehand. The same extracts and concentrations were employed as for prick and nasal challenge tests. The test was considered positive when burning, tearing, or conjunctival injection occurred. Only one allergen was tested each day.[10]

Nasal Secretions

These were stimulated using 1 mL of a 20% solution of sodium chloride. The hypertonic solution was withdrawn immediately from the nose. The nasal secretions were collected in a plastic tube five minutes after stimulation. Tween 20 (Merck) 50 μL/mL was added to each sample and homogenized in an agitator for 30 minutes. This was then stored at −20 °C.

Serum Samples

Blood was obtained by venipuncture in all subjects and the samples obtained were stored at −20 °C until analysis.

Determination of Total IgE

The IgE concentrations in both sera and nasal secretions were determined using the PRIST technique (Pharmacia Iberica). The results were expressed in U/mL.

Determination of Specific IgE

The determination of specific IgE in both sera and nasal secretions was performed by RAST (Pharmacia Iberica). Results were expressed in PRU/mL.

RESULTS

Concentrations of total IgE in sera and nasal secretions ranged between 7 to 980 U/mL and 0.5 to 120 U/mL, respectively (Table 1).

The coefficient of correlation between the total IgE in serum and nasal secretions was not statistically significant. Figure 1 shows the regression of total nasal IgE against serum IgE.

The concentrations of specific IgE in sera and nasal secretions where this was detectable, ranged from 0.5 to 50 PRU/mL and 0.5 to 30 PRU/mL, respectively (Table 1).

The estimated coefficient of correlation between the serum RAST and the nasal secretion RAST was statistically significant ($r = .72$; $P = .0011$) (Table 2, Fig 2). The determinations of *Dp*-specific IgE in sera and nasal secretions when it was detected matched in 82% of cases (53% both positive and 29% both negative). In all cases where the *Dp*-specific IgE was undetectable in serum it was also undetectable in nasal secretions. Three positive results were obtained in the serum RAST in patients found to be negative to the nasal RAST (Table 2).

Comparison of the skin test results with those for the serum RAST produced a match in 82% of the determinations (14 out of 17). Only 76% of the nasal determinations (13 out of 17) produced a match when compared with the skin test results (Table 3). The serum RAST results were positive in all cases where skin test results were positive (9 out of 17). Nevertheless, in 3 out of 17

Table 1. Levels of Total and Specific IgE in Sera and Nasal Secretions with Regression Coefficients

	N	Mean	SD, U/L	r	P
Total IgE					
Sera	17	251 U/mL	239		
Nasal secretions	17	28 U/ml	36	.39	NS
Specific IgE					
Sera	17	13 PRU/mL	15		
Nasal secretions	15	5 PRU/mL	9	.72	.011

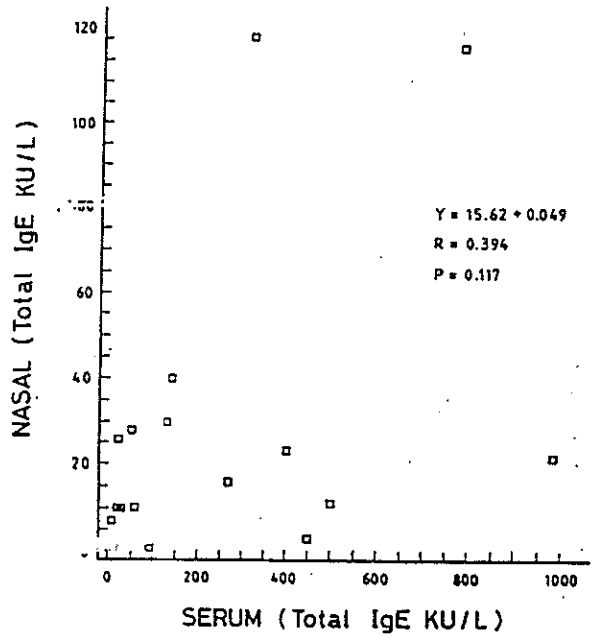

Figure 1. Regression of total nasal IgE on serum.

Table 2. Match Between the Serum RAST and the Nasal Secretion RAST

	RAST: Positive Serum		RAST: Negative Serum		P*
	n	%	n	%	
RAST-positive nasal	9/17	53%	0	0	.0047
RAST-negative nasal	3/17	18%	5/17	29%	.0047

* Fisher's exact test.

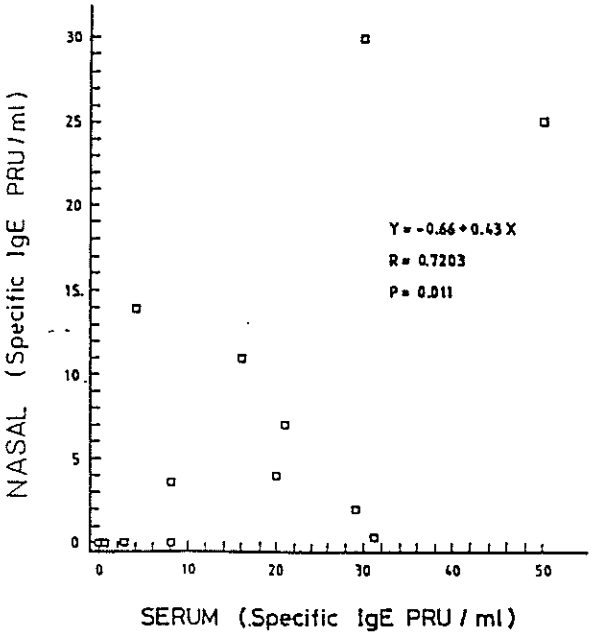

Figure 2. Regression of specific nasal IgE on serum.

cases (18%) the serum RAST was positive when the skin test result had been negative. The skin test positive results were linked to nasal RAST positive results in 7 of 17 cases (41%).

For the skin test negative patients six had negative nasal RAST and five were negative to serum RAST.

Comparison of the results of nasal RAST with the challenge tests produced an 82% match (14 out of 17 cases, Table 4). In all cases where challenges were positive (10 out of 17) the serum RAST was also positive. Nasal RAST was positive in eight cases of positive challenge (47%). The negative challenges were associated with six cases of negative nasal RAST (35%) and in five cases with negative serum RAST (29%).

DISCUSSION

The method used to collect nasal secretions, although simple and harmless to patients, is rather irritating and unpleasant.

Our findings, which agree with those of Bachert et al[11] and Partriarca et al,[12] are that nasal secretion RAST and the serum RAST show a significant correlation, suggesting a diffusion of IgE from the submucosal capillaries. The IgE transport mechanism is not fully understood, it does not appear to be explicable simply in terms of transudation. Although other work supports the hypothesis of local production of IgE antibodies,[8,12,13] we have found no evidence to support this hypothesis.

The determinations of total IgE and specific IgE in nasal secretion using PRIST and RAST techniques, respectively, demonstrated no greater reliability than determinations in serum. The matches found between specific IgE in nasal secretions and serum (82%), between specific nasal IgE and prick tests (76%), and between specific nasal IgE and challenge tests (82%) allow one to say that measuring specific IgE in nasal secretion may be useful in substituting for the serum

Table 3. Match Between Skin Tests and Serum/Nasal RAST

	Positive Skin Test		Negative Skin Test		p*
	N	%	N	%	
Serum					
RAST-positive	9/17	53%	3/17	18%	.009
RAST-negative	0	0	5/17	29%	.009
Nasal					
RAST-positive	7/17	41%	2/17	12%	.044
RAST-negative	2/17	12%	6/17	35%	.044

* Fisher's exact test.

Table 4. Match Between Challenge Tests (Nasal and Conjunctival) and Serum and Nasal RAST

	Positive Challenges		Negative Challenges		p*
	N	%	N	%	
Serum					
RAST-positive	10/17	59%	2/17	12%	.0033
RAST-negative	0	0	5/17	29%	.0033
Nasal					
RAST-positive	8/17	47%	1/17	6%	.013
RAST-negative	2/17	12%	6/17	35%	.013

* Fisher's exact test.

RAST in those cases where blood samples are difficult to obtain. Under normal circumstances there is no advantage to analyses of nasal secretions.

In those cases where there are mismatches between the serum RAST, cutaneous tests, and challenges, the determination of nasal RAST may be useful in producing a better diagnostic profile.

The measurement of specific IgE in nasal secretions after specific challenges may be of considerable interest in the study of patients where extrinsic rhinitis is suspected and skin tests are negative or where specific IgE is undetectable in serum. With regard to future studies, it would be desirable to standardize nasal secretions. Perhaps the levels of total IgE, proteins and other components of nasal secretions could prove useful here.

Determinations of total IgE and specific IgE in nasal secretions using PRIST and RAST techniques do not show any differences with respect to practicability or reliability compared with serum although the measurement of specific nasal secretion may be used to substitute for the serum RAST in cases where there are difficulties involved in obtaining a blood sample. In view of discrepancies between serum RAST, skin tests and provocation tests, the determination of the RAST in nasal fluid at baseline or after specific provocation may be very interesting. In daily practice the determination of specific IgE in nasal secretions does not offer advantages over serum determination.

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