Rhinology, 34, 160-162, 1996

Comparison of SPT and NPT in the ascertainment of nasal mucosa as shock organ*

B. Testa, C. Mesolella, F. Testa, L.V. Gallo, D. Testa

Department of Otolaryngology, School of Medicine, Second University of Naples, Italy

SUMMARY

The Skin Prick Test (SPT) is the principal tool in allergic diagnosis, but in allergic rhinitis – an immunological disease which affects 12% of the total population – the Nasal Provocation Test (NPT) allows more reliable results to be obtained. In our study a positive response to NPT has been found in four subjects with a history of symptoms suggesting allergic rhinitis, who had a negative SPT. Subjects with a positive SPT for two or more inhalant antigens have a significantly reduced number of antigen responses to NPT. Moreover, in two cases, the antigen that induced a positive response to NPT was different from the antigen that induced positive SPT. So, NPT is a reliable way of diagnosing allergic rhinitis. A more specific and reliable ascertainment of the antigen responsible for allergic reaction avoids unnecessary and ineffective immunotherapeutical attempts based on false assumptions.

Key words: allergic rhinitis, nasal provocation test

INTRODUCTION

Allergic rhinitis is a frequent immunological disease which affects about 10-12% of the total population (Druce and Kaliner, 1988). A careful history, the Skin Prick Test (SPT) and RAST allow an easy diagnosis to be made in a good percentage of cases. But when the symptom complex is not fully expressed or when the SPT is negative, the diagnosis is more difficult. However, it is possible that the allergy might be localized exclusively to the nose and be demonstrated by the Nasal Provocation Test (NPT; Berg et al., 1971; Malmberg, 1979; Motta et al., 1995). Nonetheless, this observation has not been confirmed. Our study investigates whether:

(1) immunoreaction to antigens may be localized exclusively to the nose; i.e., can subjects with a negative SPT have a positive NPT?
(2) do subjects with a positive SPT to common inhalant allergens have a positive NPT for the same antigens?

Finally, a reflection is made on the factor that induces the high reactivity of the nasal mucosa to inhalant allergen.

MATERIAL AND METHODS

The study included 39 patients (age range: 11-39 years) having symptoms suggestive of allergic rhinitis (nasal obstruction, rhinorrhoea, and sneezing) for at least one year.

All patients were non-smokers and had not taken steroids for at least one month prior to the study. Other exclusion criteria for entry were: (1) recent history of upper respiratory tract infection; and (2) anatomical anomalies, such as deviated nasal septum, nasal polyps or turbinate swelling, that made it impossible to carry out rhinomanometry.

To reduce interference from pollen allergy, the study was carried out in the late autumn and winter of 1993-1994. On the preliminary visit, complete history taking and clinical examination were made for each patient.

Patency of the nasal airway was also evaluated by rhinoscopy and anterior rhinomanometry. SPT and nasal airway baseline resistance (NAR) measurements were made for each subject. Although RAST is intrinsically less sensitive than the bio-assay (Berg et al., 1971), RAST was performed on subjects with a negative SPT.

On subsequent visits, after challenge with 80 µl saline solution, the patients were challenged with inhalant antigens: *Parietaria,* grasses, *Dermatophagoides,* and *Olea.* Patients who underwent challenge with more than one allergen were tested on separate occasions, at least one week apart. The inhalant antigens were obtained from Bayer SpA, in a concentration of 400 AUR/ml. Concentrations of 30, 60, and 90 AUR were given. Doses were controlled by varying the concentration of the solution; the solutions were diluted in sterile saline. All challenge agents were delivered to the nasal cavity via a nasal spray in a volume of 80 µl. The dose of the allergens was not the same for all

* Received for publication June 9, 1995; accepted January 8, 1996

patients, since the response to nasal challenge varied according to individual differences in responsiveness. The dominant allergen was the one that induced positive responses at a lower concentration. Active anterior rhinomanometry was done 10 and 120 min after antigen challenge. All measurements were performed at a reference pressure of 150 Pa; duplicates were performed on each occasion.

NPT was considered positive when NAR increased by more than 100% of the control (saline) value and was accompanied with onset or increase of at least one of the other key symptoms (rhinorrhoea, sneezing, or nasal obstruction). The mean NAR measurement after allergen challenge was calculated and compared with the control value (Figure 1).

RESULTS

From 39 subjects with symptoms suggestive of allergic rhinitis, 27 patients have shown a positive response to SPT; 29 patients have shown a positive response to NPT (Table 1). In particular, responses to SPT show that nine subjects were sensitive to one allergen; 11 subjects were sensitive to two allergens; six subjects were sensitive to three allergens; one subject was sensitive to four allergens; and 12 subjects showed no response. Responses to NPT show that 26 subjects were sensitive to one allergen; three subjects were sensitive to two allergens, one being dominant; and 10 subjects showed no response.

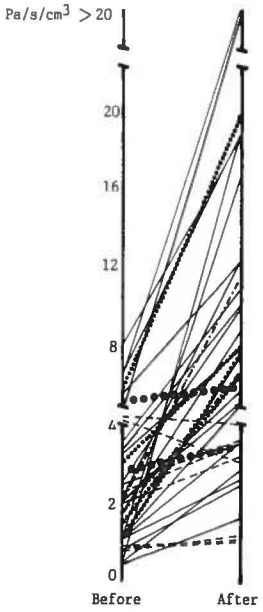

Figure 1. Effect of nasal challenge on nasal airway resistance (NAR) measured by anterior rhinomanometry before and after challenge (each line represents a different individual; continuous line: patient with positive SPT and NPT; broken line: patient with negative SPT and NPT; dotted line: patient with negative SPT and positive NPT; circles: patient with positive SPT and negative NPT; dash-and-dotted line: SPT and NPT positivity induced by different antigens).

Table 1. Relationship between SPT and NPT in 39 suspected allergic rhinitis patients. Nos. 32-39 have not responded to NPT and SPT and are not shown. Nasal provocation test (NPT) and skin prick test (SPT), nasal airway resistance (NAR), rhinorrhoea (R), sneezing (S), and obstruction (O) registered for one single allergen, when NAR value increased more than 100%, or symptoms appear after antigen nasal challenge.

patient No.	grasses		Parietaria		Dermatophagoides		Olea		nasal airway resistance (NAR)				symptomatology: rhinorrhoea (R) sneezing (S) obstruction (O)
	NPT	prick	NPT	prick	NPT	prick	NPT	prick	before	after	before	after	
1			#	++++		+++			3.3	10.3			S
2	#	+++	#	++++				++	3.3	9.7	4.5	27.8	RSO
3					#	++++		+	9.4	32.0			RO
4				+++	#			++	2.1	6.5			RS
5		++			#	+++			8.2	18.0			RO
6		+	#	+					5.5	12.8			SO
7		+++			#	+++		++	9.3	19.5			RO
8			#	+++		++++			3.0	7.3			R
9					#				1.5	6.3			RS
10							#		0.8	6.5			RO
11					#				3.1	9.3			RO
12			#	+++					1.6	6.5			RS
13			#			++			2.5	5.6			R
14			#	++++		+++			2.2	12.0			RSO
15			#	++++					1.1	7.5			RSO
16		++	#	+++					2.0	4.9			S
17						++++			0.8	1.2			
18			#	++++					1.5	8.5			SO
19		+++		+++		++++			1.0	1.3			
20		++					#	+++	1.1	3.5			R
21			#						3.0	7.8			RS
22			#	++++				++	0.5	3.5			S
23		+++		+++	#				1.8	11.0			SO
24		+++			#	++++		+	1.0	4.8			RS
25		+			#	+			2.4	9.4			RO
26	#	+++				+++		++	0.8	3.8			RS
27					#	+++			0.5	9.8			SO
28					#	++			1.0	2.6			S
29		++	#	+++	#	++++			5.8	19.5	6.0	13.1	RO
30					#	+++			1.0	7.7			SO
31	#	++	#	++++		+++		+	0.5	18.5	1.1	16.1	RSO

Comparison of the SPT and NPT data shows that 25 patients were SPT- and NPT-positive, but in two patients the inhalant allergen that induced a positive response to NPT was different from the antigen that induced a positive response to SPT.

Two subjects with a positive SPT had a negative NPT; four subjects with a negative SPT showed a positive response to NPT; eight subjects showed no response to SPT and NPT (Table 1).

Comparison of the mean NAR measurements before and after nasal challenge shows a highly significant increase in NAR ($T= -4.880$, $p<0.001$; Figure 1), together with onset or increase in the other three key symptoms (rhinorrhoea, sneezing and obstruction) in 29 out of 39 subjects (Table 1).

DISCUSSION

RAST is less sensitive than SPT, which is the principal tool in the allergic diagnosis (Brown et al., 1981), but in allergic rhinitis NPT rather than SPT affords a more certain diagnosis and greater response specificity. Knauer et al. (1983) stated that "when tests are carefully performed using the same allergen preparation, 10–25% of the patients with positive challenge test will have negative RAST."

In our study, nasal mucosa challenge with inhalant antigen in saline solution allowed the allergic nature of the nasal pathology to be ascertained in four patients (10.2%) with a negative SPT. Since in two cases the antigen that induced a positive NPT was different from that which induced a positive SPT response, the positivity of NPT could rise to 15.3% and this percentage might be increased further if the number of commercially available antigen extracts for NPT were greater.

The study has also shown that subjects with a positive SPT for more than one inhalant antigen are sensitive to NPT for only one or two antigens (with one of these being dominant). For this reason, there is no constant correlation between SPT and NPT. In fact, in our study we have observed 27 positivities to SPT and 29 positivities to NPT; and a decrease of polysensitivity for each patient: nine subjects were sensitive to SPT for one antigen and 18 subjects were sensitive for two or more antigens. In contrast, 26 subjects were sensitive to NPT for one antigen and three subjects for two antigens.

The highly specific nasal mucosa reactivity may be due to the condition of the nasal mucosa, which is the major route of entry for inhalant antigens and an area of chronic antigenic stimulation.

The local IgE production, the high tissue levels (Huggins et al., 1975; Tada et al., 1970) or the large number of basophilic cells (Okuda et al., 1984) may be responsible for the high nasal mucosa sensitivity. However, immunohistochemical studies with monoclonal antibodies in nasal mucosa specimens of allergic and non-allergic control subjects did not present evidence for high IgE tissue concentrations in either group; indeed, very low concentrations were found (Testa et al., 1992). Relative proportion and distribution of lymphoid and non-lymphoid cells is similar in both allergic and normal nasal mucosa (Cuccurullo et al., 1989; Hameleers et al., 1989; Linder et al., 1993). Dendritic cells, basophilic cells, T- and B-cells, cytokines, *et cetera*, all are determining factors in IgE synthesis and allergic reaction, but the factors that induce nasal mucosa as the shock organ, as well as specific nasal mucosa reactivity to one or more antigens, should perhaps be investigated elsewhere. The answer is likely to be found in the genetic code (Schoeder et al., 1995). However, the high nasal mucosa reactivity to the allergen challenge was shown by the greater positivity and specificity response observed in our patients.

In addition, two patients were observed with a positive SPT and a negative NPT for all the antigens tested, and this suggests that nasal disorders are not due to the SPT-tested allergen. These results show the usefulness of nasal antigen challenge in the diagnosis of allergic rhinitis. In the light of these results, it is clear that hyposensitization treatment, especially in patients with polysensitivity, should not be based merely upon a positive SPT or RAST, but also on NPT, in order to avoid unnecessary and ineffective immunotherapy. It is to be hoped that when a greater number of commercial allergen extracts is available, NPT may be employed as a routine test for the ascertainement of allergic rhinitis.

REFERENCES

1. Berg T, Bennich H, Johansson SGO (1971) In vitro diagnosis of atopic allergy. Int Arch Allergy 40: 770–778.
2. Brown HM, Su S, Thantre YN (1981) Prick testing for allergens standardized by using a precision needle. Clin Allergy 11: 95–98.
3. Cuccurullo L, Testa B, Mesolella C, Ferraraccio F (1989) Le système lymphatique diffus de la muqueuse nasale dans la rhinopathie allergique. Ann Oto-Laryng 106: 51–56
4. Druce HM, Kaliner MA (1988) Allergic rhinitis. JAMA 259: 260–263.
5. Hameleers DMH, Stoop AE, Van der Ven I, Biewenga J, Van der Baan S, Sminia T (1989) Intra-epithelial lymphocytes and non-lymphoid cells in the human nasal mucosa. Arch Allergy Appl Immunol 88: 317-322.
6. Huggins KG, Brostoff J (1975) Local production of specific IgE antibodies in allergic-rhinitis patients with negative skin tests. Lancet 2: 148–150.
7. Knauer KA, Adkinsons NF (1983) Clinical significance of IgE. In: E Middleton, CE Reed, EF Ellis (Eds.) Allergy. CV Mosby, St Louis, pp. 673–688.
8. Linder A, Karlsson-Parra A, Hirvelä C, Jonsson L, Köling A, Sjöberg O (1993) Immunocompetent cells in human nasal polyps and normal mucosa. Rhinology 31: 125–129.
9. Malmberg H (1979) Symptoms of chronic and allergic rhinitis and occurrence of nasal secretion granulocytes in university students, school children and infants. Allergy 34: 389–394.
10. Motta G, Salzano FA, Motta S (1995) Il trattamento della rinite vasomotoria allergica. Problema diagnostico ed immunoterapia locale. Acta ORL Italica Suppl 48.
11. Okuda M, Ohtsuka H, Kawabori S (1984) Characteristics and role of the surface basophilic cells in nasal allergy. In: JE Veldman et al. (Eds.) Immunology, Autoimmunity and Transplantation in Oto-rhinolaryngology. Kugler Publications, Amsterdam, pp. 267–272.
12. Schroeder SA, Gaughan DM, Swift M (1995) Protection against bronchial asthma by CFTR F508 mutation: A heterozygote advance in cystic fibrosis. Nature Medicine 1: 703–705.
13. Tada T, Ishizaka (1970) Distribution of E-forming cells in lymphoid tissue of the human and monkey. J Immunol 104: 377–387.
14. Testa B, Cuccurullo L, Mesolella C, Ferraraccio F (1992) Immunoglobulin E distribution in atopic nasal mucosa. Laryngoscope 102: 327-329.

Prof.dr. B. Testa
Via Bernini, 25
I-81100 Caserta
Italy