

Evaluation of skin prick test sensitivity for 37 allergen extracts in atopic patients with nasal polyposis

Ashour Z. A.^a, Hosam Rabee^b, El-Melegi H. A.^b, Mohamed Yousef Attia^a, Hesham Sanad^a

^aAllergy and Clinical Immunology Unit, Internal Medicine Department, ^bENT Department, Faculty of Medicine, Ain-Shams University, Cairo, Egypt

Correspondence to Z. A. Ashour, Assistant Professor of Internal Medicine, Department of Internal Medicine, Allergy and Clinical Immunology, Faculty of Medicine, Ain-Shams University, Cairo, Egypt
Tel: +20 122 388 2837;
e-mail: zashour@yahoo.com

Received 12 February 2014

Accepted 10 March 2014

The Egyptian Society of Internal Medicine
2014, 26:80–85

Background

Skin prick test (SPT) is a gold standard test for diagnosis of allergic [immunoglobulin E (IgE)] diseases. There is a subset of patients who have positive nasal provocation to allergens, despite having a negative SPT. The aim of our study was to evaluate SPT sensitivity in atopic patients with allergic nasal polyposis. We chose 56 patients (discussion with the patients regarding the benefits and hazards of the study was performed and informed consent was taken from them) with bilateral nasal polyposis (as diagnosed by full history taking, clinical examination, nasal endoscopic examination, and sinonasal computed tomography) who proved to be allergic (by full history taking, clinical examination, positive serum total IgE, serum-specific IgE, and tissue-specific IgE). SPT was performed using a panel of 37 allergen extracts.

Results

A total of 15 patients showed negative results to SPT representing 26.8%. In all, 41 patients showed positive results to SPT (73.2%); six patients (14.6%) showed positive result to only one allergen (monosensitized), whereas the remaining patients were polysensitized. The most common allergens found to be positive by SPT were: 'House Dust' with positive results in 19 patients representing 46.3% of patients with positive results to SPT (41 patients), followed by 'Pollens' with positive results in 18 patients (43.9%), 'House Dust Mite' with positive results in 17 patients (41.5%), and then 'Molds' with positive results in 14 patients (34.2%).

Conclusion

Negative SPT does not exclude allergy in atopic patients with nasal polyposis. Thus, before delivering a diagnosis of nonallergic rhinitis in patients with negative SPT to common allergen, further tests are needed. We recommend further studies to evaluate the prevalence, immunopathology, and management of local allergic rhinitis.

Keywords:

allergy, nasal polyposis, skin test

Egypt J Intern Med 26:80–85

© 2014 The Egyptian Society of Internal Medicine
1110-7782

Introduction

Skin prick testing (SPT) is an essential test procedure to confirm sensitization in immunoglobulin E (IgE)-mediated diseases such as asthma, rhinoconjunctivitis, eczema, and anaphylaxis [1]. Worldwide, allergic rhinitis affects between 10 and 30% of the population, and sensitization (IgE antibodies) to foreign proteins in the environment is present in up to 40% of the population [2].

SPT is simple, quick, and is regarded as a gold standard method for allergy diagnosis [3]. The results of this test correlate with those of nasal challenge and bronchial challenge, which can also be used as surrogate tests to test clinically relevant sensitization [1].

Alvares *et al.* [4] studied a subset of patients who had positive nasal provocation to allergens, despite having a negative SPT. They hypothesized that these patients have localized allergic rhinitis. They found that the prevalence varies greatly, ranging from 0 to 100% of skin test-negative individuals. This wide range in prevalence

is likely related to differences in methodology, including differences in allergen manufacturers, concentrations, and numbers of allergens tested and, perhaps most importantly, criteria for a positive nasal challenge [4].

Aim of the study

The aim of the study was to evaluate SPT sensitivity in atopic patients with nasal polyposis.

Patients and methods

- (1) This study was a cross-sectional descriptive study. It was conducted in both ENT departments and Allergy and Clinical Immunology unit of internal medicine department, Ain-Shams University from September 2009 to March 2012.
- (2) The study was approved by Research Ethical Committee of the Faculty of Medicine, Ain-Shams University.

Patients

A total of 56 patients with bilateral nasal polyposis (consents: discussion with the patients regarding the benefits and hazards of the study was performed and informed consent was taken from them) were enrolled in the study after informed consent about the research and the procedures was taken.

All patients were subjected to the following:

Full allergy history especially exposure to allergens and its association with clinical presentation and ENT history taking and clinical examination including SNOT-22 sinonasal outcome test-22 Questionnaire [5], nasal endoscopy, nonenhanced PNS-CT [6], and the diagnostic allergic workup, which included the following tests.

Skin prick test

The panel for skin testing was composed of histamine and saline, in addition to 37 different allergen extracts for both inhaled and ingested allergens. The panel of allergen extracts were prepared in allergen extract unit, Department Of Allergy And Immunology, Ain-Shams University Hospitals. They were prepared by aqueous vaccine method (weight/volume) [7] (Table 1).

A drop of solution of each test allergen was placed on the flexor surface of the forearm, and a midpoint was used to prick the skin. SPTs were read at 20 min. The reaction to a SPT was considered positive if the wheal area caused by allergen was greater than 3 mm in diameter.

Serum total IgE level

Enzyme-linked immunosorbent assay was used for the quantitative determination of IgE concentration in human serum (BioCheck IgE Enzyme Immunoassay; BioCheck Inc., Foster City, California, USA) [8].

The total IgE level in a normal, allergy-free adult is less than 100 IU/ml of serum. The minimum detectable concentration of IgE by this assay is estimated to be 5.0 IU/ml.

Serum-specific IgE

Enzyme-linked immunosorbent assay was used for the quantitative determination of circulating allergen-specific IgE in human serum 'RIDASCREEN Spezifisches IgE (A0249)' (R-Biopharm AG, Darmstadt, Germany) [8].

Interpretation of results was performed using multiallergen discs; results of at least 0.35 IU/ml was considered positive.

Table 1 Shows allergen extracts used in the study

Saline
Histamine
Aspirin
House dust
Mixed pollens
Mixed mites
Mixed grasses
Hay dust
Straw
Maize
Cotton dust
Mugwort
Mixed molds
<i>Rhizopus</i> spp.
<i>Aspergillus fumigates</i>
<i>Candida</i> spp.
Horse epithelium
Cat epithelium
Dog epithelium
Rabbit epithelium
Goat epithelium
Sheep wool
Camel epithelium
Mixed feathers
Pigeon
Cockroach
Tobacco
Milk
Eggs
Mixed fish
Solanecea
Banana
Strawberry
Wheat
Sesame
Cacao
Soya
Apricot
Latex

Tissue-specific IgE

Tissue homogenates were prepared from surgically removed nasal polyps in 38 patients and from tissue biopsies obtained during endoscopy in 18 patients. The tissues were homogenized with a mechanical homogenizer (B. Braun, Melsungen, Germany), centrifuged, and separated. Supernatants were assayed for specific IgE levels using enzyme immunoassay for the quantitative determination of allergen-specific IgE as performed in human serum.

Inclusion criteria

All patients included in the study had history and clinical examination suggestive of allergy, positive serum total IgE, positive serum-specific IgE, and positive tissue-specific IgE.

Exclusion criteria

- (1) Nonallergic polyyps (such as antrochoanal, cystic fibrosis, etc).
- (2) Patients with negative results for the three allergy tests (SPT, serum-specific IgE, and tissue-specific IgE).
- (3) Generalized skin allergy, severe dermatographism, and severe asthma.
- (4) Patients with immunological disorders (autoimmune diseases).

Results

The age of the patients varied from 14 to 64 years, with a mean age of 33.4 years. There were 22 male patients (39.3%) and 34 female patients (60.7%).

With respect to positive history of bronchial asthma, there were 20 patients with positive history of bronchial asthma, representing 35.7% of patients. With respect to positive family history to allergy, there were 31 patients with positive family history to allergy, representing 55.4% of patients.

The symptoms were evaluated using the SNOT-22 test for all patients. Total SNOT-22 for each patient and grand total SNOT-22 for all patients were calculated. On analysis of the 22 presenting symptoms of the SNOT-22 test, we found that the most common annoying presentation for all patients was 'nasal blockage and congestion' with the highest grand total score of 210, followed by 'embarrassment' with a grand total score of 184 and 'decreased sense of taste and smell' with a grand total score of 184. With respect to sneezing and postnasal discharge as allergy-related symptoms, the grand total scores were 124 and 128, respectively.

Skin prick testing

All patients underwent an SPT. A total of 41 patients showed positive results of SPT (73.2%); six patients showed positive result to only one allergen (14.6%), four patients showed positive result to two allergens (9.8%), 12 patients showed positive result to three allergens (29.3%), and 19 patients showed positive result to more than three allergens (46.3%). However, 15 patients showed negative results to SPT (26.8%). Table 2 shows the results of SPT.

Total IgE

With respect to total IgE, all patients had a positive total IgE (>100 IU/ml). The total IgE ranged from 106 to 273 IU/ml with mean of 164.6 ± 38 .

Table 2 Results of SPT

Allergen	Number positive results [n (%)]
Horse epithelium	2 (4.9)
Dog epithelium	2 (4.9)
Rabbit epithelium	2 (4.9)
Tobacco	2 (4.9)
Milk	2 (4.9)
Fish	2 (4.9)
Banana	2 (4.9)
Strawberry	2 (4.9)
Straw	1 (2.4)
Maize	1 (2.4)
Egg	1 (2.4)
Feather	1 (2.4)
Camel epithelium	1 (2.4)
Cockroach	1 (2.4)
Latex	1 (2.4)
House dust	19 (46.3)
Mixed pollens	18 (43.9)
House dust mite	17 (41.5)
Mixed molds	14 (34.2)
Hay dust	8 (19.5)
<i>Aspergillus fumigates</i>	8 (19.5)
<i>Rhizopus</i> spp.	8 (19.5)
Cat epithelium	6 (14.6)
Aspirin	5 (12.2)
Grass	5 (12.2)
<i>Candida albicans</i>	5 (12.2)
Sheep wool	5 (12.2)
Mugwort	4 (9.8)
Goat epithelium	3 (7.3)
Cotton dust	2 (4.9)

SPT, skin prick test.

Serum-specific IgE and tissue-specific IgE (nasal polyp)

Both serum-specific IgE and tissue-specific IgE were performed for all patients. Eight allergen showed positive results in both tests (>0.35 IU/ml).

In all, 56 patients (100%) showed positive results of serum-specific IgE and tissue (polyp)-specific IgE to the tested allergens. The most common allergens were the same in both tests: 'Pollens' with positive results in 30 patients representing 53.6%, followed by 'House Dust' with positive results in 28 patients representing 50%, 'House Dust Mite' with positive results in 23 patients representing 41.1%, and then 'Molds' with positive results in 22 patients representing 39.3%.

Discussion

In the common practice of respiratory allergy, the standard tool available is a careful history taking and physical examination followed by confirmation of etiological diagnosis by high IgE level to specific inhalant allergen that is associated with the occurrence and duration of symptoms [9].

SPT provides evidence for sensitization and can help to confirm the diagnosis of a suspected type I allergy. It is minimally invasive, inexpensive, results are immediately available, and reproducible when carried out by trained health professionals [1].

A recent study compared the results of nasal provocation test (NPT) and nasal IgE test in 55 children with rhinitis during the periods when *Alternaria* spores are present in the air. A concomitant positivity of NPT and nasal IgE test to *Alternaria* was observed in about 70% of patients, whereas positivity of SPT and NPT was observed in 27% of patients, the difference being highly significant ($P < 0.0001$). This suggests that sensitization to *Alternaria* is frequently expressed by exclusive production of specific IgE in the nasal mucosa [10].

Of note, it was recently reported that, in patients with positive IgE tests but with no clinical symptoms — that is, the patient with asymptomatic atopy, there are no local IgE in the nasal, and it seems conceivable that this should account for being asymptomatic. Patients with local but not systemic IgE — that is, with negative results to IgE tests — have clinical symptoms, whereas patients with systemic but not local IgE are asymptomatic [11].

Furthermore, the majority of allergen-specific IgE in the blood of allergic patients does not originate from blood-derived B cells or plasma cells. This result of Eckl-Dorna *et al.* [12] suggests local IgE production in tissues as a major source for allergen-specific IgE.

In this study, we depended on positive history taking, clinical examination, total IgE, serum-specific IgE, and tissue-specific IgE for diagnosis of allergic rhinitis instead of NPT, and we checked SPT sensitivity.

The sensitivity of a test is defined as the proportion of the patients who were reported as positive by the test [3]. We found that 41 patients showed positive results to SPT (73.2%) and 15 patients showed negative results to SPT (26.8%). Demoly *et al.* [13] considered SPT as highly sensitive test, 80–97%, to diagnose inhalant allergies. The positive predictive value to diagnose allergic rhinitis based only on the clinical history was 77% for persistent allergy and 82–85% for intermittent seasonal allergy [14]. This increased to 97–99% when SPT was utilized [14].

Sensitivity of SPT is lower for food allergens, ranging from 30 to 90% depending on the type of allergen and methods utilized — that is, pricking with extracts versus prick-to-prick techniques described earlier [15]. Double-blind placebo-controlled challenge studies in

children demonstrate that SPT possesses a positive predictive value of 76 and 89% for clinical reactions to cow's milk and hen's egg, respectively [16].

The clinical relevance of SPT results varies, depending on the allergen utilized and the population tested. For example, sensitization to house dust mite (HDM) occurs in some individuals in the absence of clinical relevance [17]. Furthermore, sensitization to aeroallergens, as measured by SPT, may precede symptomatic allergy. Prospective studies showed that 30–60% of such individuals become allergic depending on the type of allergen tested and the time to follow-up [1].

Sensitization rates vary depending on the geographic region as measured in population-based and in patient-based studies. Exposure rates and genetic differences can explain some of these variations [18]. With increased human mobility, differences in exposure to various flora or alterations in the allergenicity of pollen, possibly caused by pollution [19] and by changes in sensitization, occur over time [20]. Longitudinal studies investigating sensitization over time provide data on such trends [21].

Our study carried out over a period of 2.5 years [1] advised that studies on allergic sensitization should be conducted over an extended period of time, ideally a year, as (i) skin test reactivity increases during the pollen season [22] and (ii) allergic individuals tend to seek care when they have symptoms. This can skew detected prevalence of sensitization in such studies.

Patients with nasal polyposis who show positive result of SPT range from 24 to 75%. In a study conducted by Munoz Del Castillo *et al.* [23], which involved 190 patients with nasal polyposis and 190 normal individuals as a control group, they found that 63.2% of the patients with nasal polyposis had positive SPT for at least one allergen, and 36.8% had negative results, showing a significant difference compared with the control group.

In the present study, the most common allergens with positive results in SPT were 'House dust' with positive results in 19/41 patients (46.3%) and 'Pollens' with positive results in 18/41 patients (43.9%).

Some studies revealed extensive sensitization (80% of patients with nasal polyposis) especially to HDM, which is a much higher percentage than that observed in our study, which was 17/41 patients (41.5%).

Although there is little information about the prevalence of fungal allergies among patients with chronic rhinosinusitis, it is estimated to be 52%. In

2009, a study conducted shows that 22.4% of patients with nasal polyposis with allergy signs and symptoms had positive IgE to some fungal allergens [24].

In our study, the prevalence of fungal allergies among the SPT-positive patients was 46.3% (19/41). The most common fungal allergens that elicited a reaction in the SPT were a mixture of fungal allergens 'mixed molds' in 14/41 (34.2%), *Aspergillus fumigates* in 8/41 (19.5%), and *Rhizopus* spp. in 8/41 (19.5%).

In 2000, in a study conducted by Asero and Bottazi [25], they found that 40% of patients tested were positive to *Candida albicans*. Our results show that only 12.2% (5/41 patients) were positive to *C. albicans*.

El-Tarabishi *et al.* [26] studied 40 patients with allergic fungal sinusitis attending Ain Shams ENT and Allergy clinics and detected *C. albicans* in 10 patients with allergic fungal sinusitis (25%), *Aspergillus niger* in six patients (15%), and *Rhizopus* spp. in five patients (12.5%).

A study conducted by Collins *et al.* [27] supported the opinion that nasal polyps may have a more common relationship with food allergies than typical IgE-mediated inhalant allergies. They found that 43% of their patients with nasal polyposis had positive SPT and 70% had positive intradermal food test to an average of four foodstuffs.

On the basis of questionnaires, food allergy was reported by 22% [28] and 31% [29] of patients with nasal polyposis, which was significantly higher than in non-nasal polyposis controls.

Our results were different from this study, as there were only 17.1% (7/41) patients with positive SPT to six food allergens among 11 food allergens included in the test: milk 4.9% (2/41), fish 4.9% (2/41), banana 4.9% (2/41), strawberry 4.9% (2/41), egg 2.4% (1/41), and maize 2.4% (1/41). Only one patient had isolated SPT to food allergen 'Banana', whereas the other patients showed positive results to both food and inhalant allergens. Hence, our patients with nasal polyposis were much more sensitive to inhalant allergens than ingested allergens. This result is in agreement with the study conducted by Elshayeb *et al.* [30], which detected the prevalence of food allergy among 150 patients attending Ain Shams allergy clinic with allergic rhinitis. They estimated the prevalence of food allergy to be 26% in test population and found that the prevalence of sensitization to specific food allergens ranged from 2.6% for wheat to 33.3% for strawberry. They concluded that the prevalence of probable

IgE-mediated food reactions is indeed uncommon in adults with allergic rhinitis.

In this study, we found that 15 patients showed negative results to SPT (26.8%). This result is comparable with Rondon *et al.* [31] study. They defined local allergic rhinitis (LAR) on the basis of negative SPT and serum-specific IgE and positive NPT. It was diagnosed in 25.7% patients in a survey conducted on 428 patients with rhinitis. The HDM was the main sensitizing aeroallergen both in LAR and allergic rhinitis (60 and 54%, respectively) in their study [31].

Thus, before delivering a diagnosis of nonallergic rhinitis or asthma in patients with negative SPT to common allergen, further tests are needed [9].

Diagnosis of allergy has obvious consequences on patient management, including allergen avoidance, patient's education, and specific immunotherapy. We have to consider allergic rhinitis with negative SPT and LAR in management of patients with nasal polyposis to not miss diagnosis of allergy.

Further studies will be required to further define the immunopathology, prevalence, practical diagnostic tests, and management.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

References

- 1 Heinzerling L, Mari A, Bergmann K, Bresciani M, Burbach G, Darsow U, *et al.* The skin prick test — European standards. *Clin Transl Allergy* 2013; 3:3.
- 2 World Health Organization. White book on allergy — executive summary 2011.
- 3 Ashaari ZA, Suhaimi Y, Yusof RA, Rushdan I, Maraiana CHC. Comparison of serum specific IgE with skin prick test in the diagnosis of allergy in Malaysia. *Med J Malaysia* 2011; 66:33–65.
- 4 Alvares ML, Khan DA. Allergic rhinitis with negative skin tests. *Curr Allergy Asthma Rep* 2010; 11:107–1412.
- 5 Fokkens W, Lund VJ, Mullol J. Position paper on rhinosinusitis and nasal polyyps. EAACI Task Force. *Rhinology* 2007; 20:40.
- 6 Mygind N, Lund V. Nasal polyposis. Gleeson M, Browning GG, Burton MJ, Clarke R, Hibbert J, Jones NS, Lund VJ, Luxon LM, Watkinson JC eds. *Scott-Brown's otolaryngology, head and neck surgery*. 7th ed. London: Hodder Arnold; 2008. 121:1549–1559.
- 7 Malling HS, Djump R. Diagnosis and immunotherapy of mould allergy, VII IgE subclass response and relation to the clinical efficacy of immunotherapy with cladosporium. *Allergy* 1988; 34:60–70.
- 8 El-Shami AS, Aloba O. Liquid phase in vitro allergen IgE assay with situimmobilization. *Adv Biosci* 1989; 74:191–201.
- 9 Incorvaia C, Fuiano N, Canonica GW. Seeking allergy when it hides: which are the best fitting tests? *World Allergy Organ J* 2013; 6:11.
- 10 Fuiano N, Fusilli S, Incorvaia C. A role for measurement of nasal IgE antibodies in diagnosis of *Alternaria*-induced rhinitis in children. *Allergol Immunopathol (Madr)* 2012; 40:71–74.
- 11 Fuiano N, Fusilli S, Passalacqua G, Incorvaia C. Allergen-specific immunoglobulin E in the skin and nasal mucosa of symptomatic and

- asymptomatic children sensitized to aeroallergens. *J Investig Allergol Clin Immunol* 2010; 20:425–430.
- 12 Eckl-Dorna J, Pree I, Reisinger J, Marth K, Chen KW, Vrtala S, *et al.* The majority of allergen-specific IgE in the blood of allergic patients does not originate from blood-derived B cells or plasma cells. *Clin Exp Allergy* 2012; 42:1347–1355.
 - 13 Demoly P, Bousquet J, Romano A. In vivo methods for the study of allergy. In: Adkinson NJ, Yunginger J, Busse W, Bochner B, Holgate S, Simons Feds. *Middleton's allergy — principles and practice*. 6th ed. Philadelphia: Mosby; 2003. 430–439.
 - 14 Crobach MJ, Hermans J, Kaptein AA, Ridderikhoff J, Petri H, Mulder JD. The diagnosis of allergic rhinitis: how to combine the medical history with the results of radioallergosorbent tests and skin prick tests. *Scand J Prim Health Care* 1998; 16:30–36.
 - 15 Rance F, Juchet A, Bremont F, Dutau G. Correlations between skin prick tests using commercial extracts and fresh foods, specific IgE, and food challenges. *Allergy* 1997; 52:1031–1035.
 - 16 Verstege A, Mehl A, Rolinck-Werninghaus C, Staden U, Nocon M, Beyer K, Niggemann B. The predictive value of the skin prick test weal size for the outcome of oral food challenges. *Clin Exp Allergy* 2005; 35:1220–1226.
 - 17 Burbach GJ, Heinzerling LM, Edenharter G, Bachert C, Bindslev-Jensen C, Bonini S, *et al.* GA(2)LEN skin test study II: clinical relevance of inhalant allergen sensitizations in Europe. *Allergy* 2009; 64:1507–1515.
 - 18 Van den Oord RA, Sheikh A. Filaggrin gene defects and risk of developing allergic sensitisation and allergic disorders: systematic review and meta-analysis. *BMJ* 2009; 339:b2433.
 - 19 Bryce M, Drews O, Schenk MF, Menzel A, Estrella N, Weichenmeier I, *et al.* Impact of urbanization on the proteome of birch pollen and its chemotactic activity on human granulocytes. *Int Arch Allergy Immunol* 2010; 151:46–55.
 - 20 Burbach GJ, Heinzerling LM, Rohnelt C, Bergmann KC, Behrendt H, Zuberbier T. Ragweed sensitization in Europe — GA(2)LEN study suggests increasing prevalence. *Allergy* 2009; 64:664–665.
 - 21 Shaaban R, Zureik M, Soussan D, Neukirch C, Heinrich J, Sunyer J, *et al.* Rhinitis and onset of asthma: a longitudinal population-based study. *Lancet* 2008; 372:1049–1057.
 - 22 Oppenheimer JJ, Nelson HS. Seasonal variation in immediate skin test reactions. *Ann Allergy* 1993; 71:227–229.
 - 23 Munoz Del Castillo F, Jurado-Ramos A, Fernández-Conde BL, Soler R, Barasona MJ, Cantillo E, *et al.* Allergenic profile of nasal polyposis. *J Investig Allergol Clin Immunol* 2009; 19:110–116.
 - 24 Munoz Del Castillo F, Jurado-Ramos A, Soler R, Fernández-Conde BL, Barasona MJ, Cantillo E, *et al.* Fungal sensitization in nasal polyposis. *J Investig Allergol Clin Immunol* 2009; 19:6–12.
 - 25 Asero R, Bottazi G. Hypersensitivity to molds in patients with nasal polyposis: a clinical study. *J Allergy Clin Immunol* 2000; 105:186–188.
 - 26 El-Tarabishi MN, Sabri SM, Fawaz Samia A, Gouda Amr S, Ashour Zeinab A, Dessouky Osama Y, *et al.* Specific fungal immunotherapy in patients with allergic sinusitis. *Egypt J Otolaryngol Allied Sci* 2006; 7:65–79.
 - 27 Collins MM, Loughran S, Davidson P, Wilson JA. Nasal polyposis: prevalence of positive food and inhalant skin tests. *Otolaryngol Head Neck Surg* 2006; 135:680–683.
 - 28 Klossek JM, Neukirch F, Pribil C, Jankowski R, Serrano E, Chanal I, El-Hasnaoui A. Prevalence of nasal polyps in France: a cross-sectional, case-control study. *Allergy* 2005; 60:233–237.
 - 29 Rugina M, Serrano E, Klossek JM, Crampette L, Stoll D, Bebear JP. Epidemiological and clinical aspects of nasal polyposis in France; the ORLI group experience. *Rhinology* 2002; 40:75–79.
 - 30 Elshayeb MA, Ashour ZA, Shahin RY, Elgendy AM. Prevalence of food allergy among patients with allergic rhinitis. *N Egypt J Med* 2012; 30:18–24.
 - 31 Rondon C, Fernández J, López S, Campo P, Doña I, Torres MJ, *et al.* Nasal inflammatory mediators and specific IgE production after nasal challenge with grass pollen in local allergic rhinitis. *J Allergy Clin Immunol* 2009; 124:1005–1011.