Allergy Workup in Allergic Rhinitis at Jeddah, Saudi Arabia

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Citation

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Abstract

Background: Appropriate medical diagnosis and therapy of allergic rhinitis (AR) necessitate the identification of an IgE mediated sensitization to allergen.

Objective: To explore the spectrum of allergy investigations in patients with AR.

Settings: King Abdulaziz University Hospital (KAUH), Jeddah, Saudi Arabia.

Methods: This is a prospective cross-sectional study. 41 patients with symptoms and signs compatible with AR examined at ENT clinics were sequentially included. AR diagnosis was confirmed at Allergy clinic by a positive reaction to an in-vivo skin prick test (SPT) to common inhalant allergens (sensitization). AR cases then underwent different in-vitro tests: total peripheral eosinophil count (TPEC), total serum IgE, and specific IgE antibodies to common inhalant allergens by immuno-CAP system (Phadiatop).

Results: AR confirmed by positive SPT was detected in 30 cases (73%). Their ages ranged between 16 – 52 years old (mean 27 ±9SD), and females constituted 60%. The predominant allergens were house dust mites (HDMs): Dermatophagoides pteronyssinus 70 % and D. farinae 67%, Cat 33%, Cockroach 33%, Salsola pestifer 23%, and Aspergilus 20%. TPEC ranged 10-1200 cell/mm3 (mean= SD), and eosinophilia (?450 cells/mm3) was found in 23%. Total IgE ranged 8 – 2000 IU/ml (mean= SD), and was elevated (>190 IU/ml) in 47%. Phadiatop was positive in 83% of AR cases. A very significant correlation between SPT and Phadiatop (df=1, P<0.001) was found.

Conclusion: The prevalence of sensitization to inhalant allergens, particularly HDMs, by both in-vivo and in-vitro methods was common in AR cases at Jeddah. The presence of eosinophilia and/or high total IgE in the context of compatible clinical findings may help in the diagnosis of AR. This work advocates the importance of allergy workup for allergen sensitization in both AR diagnosis and the subsequent care of patients by promoting avoidance strategies.

INTRODUCTION

Allergic rhinitis (AR) is a common health problem for which many patients do not seek appropriate medical care (International 1994, Dywickz 1998, Fuad 2003). World wide, AR may affect 10-30% of the general population (Mygind 1996, Stracan 1997, Bousquet 2001). In a recent survey at Saudi Arabia, the prevalence of chronic rhinitis in children was found as high as 26%, and 62% of them were allergic based on positive skin prick test (SPT) (Sobki 2004). Although AR is not a life-threatening condition in most cases, it has a substantial impact on public health quality and the economy (Malone 1997, Weiss 2001, Sullivan 2001). Globally, these are on the rise today because of the increasing prevalence of allergic conditions and the higher cost of new medications (Tripathi 2001, Bousquet 2003, William 2004).

AR is a symptomatic disorder of the nose induced by an immunoglobulin (IgE)-mediated inflammation of the nasal membranes in response to allergen exposure (King 1998, Druce 2003). Allergen exposures result in the bridging of 2 adjacent IgE molecules, leading to the release of preformed mediators from mast cell granules. These mediators (ie, histamine, leukotrienes, kinins) cause early-phase symptoms such as sneezing, rhinorrhea, and congestion. Late-phase reactions begin hours later and are caused by newly formed inflammatory cells (ie, eosinophils), which prolong the

earlier reactions and lead to chronic inflammation.

The diagnosis of AR is based on the clinical history, physical examination, and allergy workup is used mainly to confirm the presence of IgE mediated hypersensitivity (atopy) (Dykewicz 1998, King 1998, Shaikh 2004). Allergy workup includes a group of in-vitro and in-vivo tests. An elevated peripheral eosinophil count (eosinophilia) has been documented in some patients with AR, but it is less sensitive than nasal eosinophilia (Naclrio 1994, Druce2003, Shaikh 2004). Total serum IgE has been detected in as many as 30-60% of patients with AR (Hendrson 1971, Shaikh 2004). Antigen-specific IgE antibodies are the most important in-vitro allergy tests in establishing the diagnosis of inhalant allergy (Lasley 2000, Hamilton 2003). The in-vivo allergy skin testing is generally considered to be the standard of allergy workup (Wood 1990, Hamilton 2003). The classic wheal-and-flare responses result from the interaction between the antigen and sensitized mast cells in the skin.

Appropriate medical diagnosis and care of patients with AR necessitate the identification of an IgE mediated sensitization to allergen. Once the clinically relevant allergen is identified measures to promote its avoidance can enhance the control of AR symptoms (Fireman 1997, Osguthorpe 1998, van 2000). Hence this prospective study has been conducted to explore the spectrum of allergy workup in patients clinically suspected to have AR at KAUH.

METHODS

CANDIDATES

Cases with history and physical examination compatible with AR were sequentially selected from patients visiting E.N.T (ear, nose and throat) out patient clinics at KAUH. Cases with other medical or allergic illnesses or are on any chronic medication were excluded. Verbal consent was obtained by explaining the study purpose to the candidates.

IN-VIVO ALLERGY TESTS

Routine non-invasive laboratory tests used at KAUH for the assessment of common allergic disorders have been selected for the evaluation of these rhinitis patients. The diagnosis of AR was confirmed at the Allergy clinic by conducting standard skin prick test (SPT), an in-vivo allergy test, with common inhalant allergens on patients forearm. Allergen extracts were obtained from Greer® laboratories at United States of America.

The allergen panel include: Trees pollen: Acacia, Atriplex canescens Cupressus arizonica, Eucalyptus globulus, Prosopis juliflora; Weeds pollen: Artemesia tridentata, Amaranthus hybridus, Ambrosia trifida, Chenopodium alba, Plantago lanceolata, Salsola pestifer; Grasses pollen: Cynodon dactylon, Phelum pratense; Molds: Alternaria alternata, Aspergillus mix, Candida albicans, Cladosporium herbarum, Fusarium moniliforme, Penicillium notatum, Rhizopus nigrcans; Cat hair; Mixed Feathers (Chiken, Duck, Goose); House dust mites (HDMs): Dermatophagoides pteronyssinus (Dp), Dermatophagoides farinae (Df); Cockroach mix (Periplaneta amer, Blateela germanica).

A positive SPT was any reaction showing > or = 3 millimiter wheal with erythema to one or more allergens than the negative control (the diluent). Candidates should be free of any antihistamines or other drugs that might inhibit the skin prick test for the appropriate duration in relation to the effect of each medication. A solution of 5% histamine was used as a positive control, and a weal size reaction of ?5 millimeter was considered adequate. Candidates with confirmed diagnosis of AR by positive SPT to one or more inhalant allergens were selected to undergo further in-vitro allergy tests.

IN-VITRO ALLERGY TESTS

On the AR cases with positive SPT, venous blood samples were drown for routine complete blood count (CBC) and other laboratory tests for allergy workup. The blood analysis for total peripheral eosinophil count (TPEC) was performed by the Celldyn-3500® hematology counter made by Abbot® Laboratories. In this study an elevated TPEC (eosinophilia) was considered it TPEC >450 cells / mm3 of blood (Best 1993, Lucey 2002). The original method for obtaining an IgE count, the radioallergosorbent test (RAST), has evolved from a radioimmunoassay to a test that involves enzymatic or fluorometric processes. Total serum IgE, and specific IgE antibodies to common inhalant allergens (UniCap Phadiatop) were measured by the radioimmunoflurecense Cap system made by Pharmacia® from Sweden available at the clinical immunology laboratory at KAUH. Normal range of total serum IgE is 10 – 190 IU/ml serum, and elevated total IgE at KAUH immunology laboratory is any level > 190 ku/l. The Phadiatop test is a multi-allergen in vitro test that contains a mixture of several allergens bound in the matrix to detect whether any of the most common specific IgE types are present in the serum (Errikson 1990). It reports either a positive or negative result for a statistically significant level of specific IgE but does not detect the presence of a particular specific IgE type. Additionally, in order to explore the correlation between SPT and in-vitro

specific IgE antibodies, Phadiatop test was performed also on the rhinitis cases with negative SPT.

DATA ANALYSIS

The data was entered into a personal computer. Frequency tables and correlation analyses by (Pearson's test and Chi-square test) were carried out by using a SPSS statistical program (Version 12).

RESULTS

Out of 46 cases with the clinical diagnosis of AR, only 41 were included. The diagnosis of AR was confirmed by positive SPT (sensitization) in 30 cases (73%). Their ages ranged between 14 – 48 years old (mean= SD). Female sex was in 18 cases which constituted 60% of the studied cases.

The predominant allergens with positive SPT were both HDMs: Dp 70 % and Df 66.7%, Cat 33.3%, Cockroach 33.3%, Salsola pestifer 23.3%, and Aspergillus 20%, see table-1 for the frequency of other allergens with their range of wheal size and its mean.

Figure 1

Table 1: The predominant inhalant allergens with positive reaction on SPT in patients with AR

Allergen	Number	Percent	Wheal size in mm	
			Range	Mean ±SD
D. pteronyssinus D. farinae	21 20	70.0 % 66.7 %	3 – 18 3 – 20	8 ±4 7 ±5
Cat hair	10	33.3 %	3 – 15	6 ±4
Cockroach mix	10	33.3 %	3 - 6	4 ±1
Salsola pestifer	7	23.3 %	3 – 10	6 ±2
Aspergillus mix	6	20.0 %	3 - 8	4 ±2
Prosopis juliflora	5	16.7 %	3 - 5	4 ±1
Plantago lanceolata	5	16.7 %	3 - 5	4 ±1
Artemsia tridentate	4	13.3 %	3 - 8	5 ±2
Cynodon dactylon	4	13.3 %	3 - 10	6 ±3
Mixed Feathers	3	10.0 %	3 - 4	4 ±1
Eucalyptus globules	3	10.0 %	3 - 7	5 ±2
Chenopodium album	3	10.0 %	3 - 4	3 ±1
Atriplex canescens	3	10.0 %	3 - 4	3 ±1
Alternaria alternate	3	10.0 %	4 - 8	7 ±2

The results of in-vitro laboratory tests in patients with AR were as follow: total peripheral eosinophil count ranged from 10 -1200 cell/mm3 (mean= SD) and elevated peripheral eosinophil count (Eosinophilia) was found in 7 cases (23%). Total IgE in serum ranged from 8 – 2000 IU/ml (mean= SD) and was elevated (>190 IU/ml) in 14 cases (47%). In-vitro specific IgE antibodies (Phadiatop) test was positive in 25 cases (83%). Table-2 summarizes the results of allergy tests workup in patients with AR confirmed by positive SPT.

Figure 2

Table 2: In-vitro Allergy tests results in patients with AR

Category	Number	Percent
Total Rhinitis patients	41	100%
Total AR patients	30	73%
Eosinophilia	7	23 %
Elevated Total IgE	14	47 %
Positive Phadiatop	26	83%

Using the Chi-square test, there was a very high significant correlation between in-vivo SPT and in-vitro Phadiatop results of all rhinitis cases (df=1, P<0.001), see table-3.

Figure 3

Table 3: Cross-tabulation of skin prick test and specific IgE antibodies to common inhalant allergens (Phadiatop)

Skin prick test	Phadiatop		Total
	Negative	Positive	
Negative	11	0	11
Positive	5	25*	30
Total	16	25	41

* df=1, P<0000.1

DISCUSSION

Many medical care providers make a presumptive diagnosis of AR based on the patient's clinical assessment, and empirically manage them with antihistamines, decongestants, or intranasal steroids (Fuad 2003, Shaikh 2004). This is a reasonable and effective approach in many patients. In patients with significantly discomforting or disabling symptoms that are not controlled with standard measures, specific allergy testing may be warranted. Specific allergy workup can help establish the correct diagnosis of AR and identify the offending allergens (King 1998, Bosquet 2001, Hamilton 2003).

In this study, SPT was positive in 73% of the cases that were clinically suspected to have AR, which is within the lower range of some international reports (Lane 2001, Abdulnoor 2002, Gendah 2004). In a study at the east of Saudi Arabia, SPT was positive in 62% of children with chronic rhinitis (Sobki 2004). These data showed higher rates of allergic disease, which could be attributed to environmental, social or genetic factors. The search for other diagnosis, other than AR, should be undertaken in patients with negative SPT, such as chronic non allergic rhinitis (vasomotor rhinitis or non allergic rhinitis with eosinophilia, and others).

Indoor allergens were the predominant sensitizing allergens detected on SPT of patients tested at KAUH, particularly house dust mites (HDMs). This is expected, because Jeddah as a coastal city on the Red sea at the Western region of Saudi Arabia, and its weather is characterized by high humidity especially in the summer, which makes it a favorable environment for the growth of HDMs (). Currently, majority of people are spending most of their time indoors, and there is a great concern on the role of indoor allergens (HDMs, cat, cockroach, and some molds) in relation to the etiology of atopic diseases (Platts 1997, Custovic 1998).

Eosinophilia was detected in as much as quarter of the confirmed cases of AR at KAUH, which is within the range of many international studies (Druce 2003, Naclerio 1994). Eosinophilia can also present in cases with nonallergic rhinitis with eosinophilia syndrome (NARES), asthma, other atopic diseases, parasitic infection, and others (Lucey 2002, Druce 2003, Shaikh 2004).

On the other hand, total serum IgE was elevated in as near as half of the confirmed cases of AR, which is on the upper range of international references (Hinduson, Tschopp 1998, Shaikh 2004). The difference in the type of the sensitizing allergens, their concentration levels, and the prolonged duration of exposure to allergens in closed indoors has been correlated with higher IgE levels. This advocates the need for the investigation of the types and concentrations of common indoor allergens at homes of patients with AR at Saudi Arabia. Elevated total serum IgE can also present in cases with asthma, atopic dermatitis, other atopic diseases, parasitic infection, allergic fungal sinusitis, hyper IgE syndrome, and others (King 1990, Shaikh 2004). Although, eosinophilia and total serum IgE are neither sensitive nor specific to AR, they can be helpful when combined with other findings in differentiating between allergic versus nonallergic rhinitis, and also in epidemiological studies (King 1988, Hamilton 2003).

In contrast to eosinophilia and total IgE, in-vitro antigen-specific IgE antibodies are very important in the diagnosis of inhalant allergy, and is more specific than SPT (Tschop 1998, Gendo 2004, Chinoy 2005). It is not affected by skin reactivity or medications, has no risk of systemic reaction and is better tolerated, because it is less traumatic. However, in-vitro testing is less sensitive than skin testing (Tschop 1998, Chinoy 2005). Also, the results are not available immediately and must be verified with skin testing before immunotherapy can be started.

This study revealed a very high correlation between in-vitro UniCap Phadiatop inhalant allergen mixture and in-vivo SPT results (Wood 1999, Li 2000, Lane 2001). The UniCAP Phadiatop test has been shown to be highly sensitive and specific in differentiating individuals who are sensitized to common inhalants from those who are not. In vitro multiallergen IgE test is recommended to all health care professionals as an aid in diagnostic, referral decisions, mass-screening programs for patients suspected of having an inhalant allergic diathesis (Williams 2001, Gendo 2004, Matricardi 1990).

As per AR impact on asthma (ARIA) management guidelines, once the identification of clinically relevant sensitizing allergen is established, applying strategies for its avoidance can leads to better symptoms control and should be an integral part of a management plan (Bousqet 2001, AAAI 2001). Allergen avoidance measures often are difficult to implement and costly, but after specific testing, they can be targeted to allergens to which the patient is known to be allergic. Additionally, specific allergy testing provides guidance about which allergens to include in allergen immunotherapy, which is a therapeutic option in AR especially when avoidance and medications no longer control the patient's symptoms (Veling 2001, Ross 2001, Wilson 20003).

In conclusion, the prevalence of allergic sensitization to common inhalant allergens using in-vivo SPT and in-vitro specific IgE antibodies methods was a common feature in patients with AR at Jeddah. Sensitization to HDMs dominated among other common inhalant allergens. The very high correlation between SPT and in-vitro specific IgE antibodies to common inhalant allergens advocates the importance of allergy workup for allergen sensitization by either methods (depending on availability) in the diagnosis and the subsequent care of AR patients. Promoting avoidance strategies after allergen identification in AR may leads to better symptoms control. This research represents a good model for the cooperation among ENT and Allergy subspecialties for ideal patient care. Further research is needed to explore the clinical sequel post allergic exploration and implementation of environmental control in AR patients.

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